

Memory Care Monthly

Supporting Healthcare Professionals in Caring for the Aging

November / December 2008

KEEP MEMORY ALIVE FOR THE COMING YEAR 2009

As the year comes to an end, we would like to remind you about the importance of memory assessment for your families, friends and patients.

There are many conditions that impair memory function. These conditions, including Alzheimer's disease, can be managed effectively with early detection and appropriate treatment.

Conditions and Diseases that Causes Short-Term Memory Loss

- Anxiety
- ADHD
- Depression
- Thyroid gland disease
- Diabetes
- Metabolic Encephalopathy
- Vitamin B-12 deficiency
- Infections- meningitis and encephalitis
- Medications (both prescription and OTC)
- Alzheimer's disease
- Parkinson's disease
- Frontal lobe dementia
- Head injury
- Cerebro-vascular disease
- Normal pressure hydrocephalus
- Seizure disorders / Epilepsy

Another important benefit of memory assessment is to accurately identify normal aging. Undue stress and anxiety over perceived memory impairment is harmful to one's health but can be easily relieved with an accurate verification of normal memory function.

While the MCI Screen is highly effective in detecting memory loss associated with Alzheimer's disease, it accurately identifies memory loss due to normal aging and to a wide range of medical conditions. An objective memory assessment with an instrument such as the MCI Screen is a practical step in delivering optimal care for all patients, especially those who are aging and those with evidence or concern about memory loss.

FEATURED ARTICLE

GINKGO BILOBA FOR PREVENTION OF DEMENTIA

While ginkgo biloba has been used for its potential effects on memory and cognition, comprehensive clinical trials to determine its effect on dementia have not been done. Dr. Steven T. DeKosky from University of Pittsburgh and the Virginia School of Medicine, and his colleagues conducted a randomized, double-blind, placebo-controlled clinical trial to determine the effectiveness of ginkgo biloba in reducing the incidence of all-causes of dementia and

Alzheimer's disease (AD) in elderly individuals with normal cognitive and those with mild cognitive impairment (MCI).

3069 community volunteers aged 75 years or older with normal cognition (n=2587) or MCI (n=482) were followed at 5 academic centers in the USA between 2000 and 2008 with a median follow-up at 6.1 years. These volunteers were randomly assigned for twice-daily 120 mg extract of ginkgo biloba (n=1545) or for placebo (n=1524), and were assessed every 6 months for incidence of dementia using a neuropsychological battery covering memory, construction, language, attention/psychomotor speed, executive and premorbid intellectual functions.

During the study period, 523 individuals developed dementia (placebo=246; ginkgo biloba=277) with 92% of the dementia cases classified as possible or probable AD, or AD with evidence of vascular dementia. The overall dementia rate was 3.3 per 100 person-years in ginkgo biloba group and 2.9 in placebo group. The hazard ratio for ginkgo biloba compared with placebo for all-cause of dementia was 1.12 and for AD was 1.16. Also ginkgo biloba did not have any effect on the rate of progression from MCI to dementia.

The study of ginkgo biloba at 120 mg twice a day did not show any benefit for either the overall incidence rate of dementia or AD incidence in elderly individuals with normal cognition or those with MCI.

DeKosky ST, et al. JAMA. 2008; 300(19): 2253-62.

RESEARCH UPDATES

LONG-TERM COURSE AND EFFECTIVENESS OF COMBINATION THERAPY IN ALZHEIMER'S DISEASE

A retrospective analysis was conducted to compare the real-world clinical effectiveness and long-term clinical course in patients with Alzheimer's disease (AD) treated with a combination (COMBO) therapy of cholinesterase-inhibitor (CI) plus memantine (MEM), CI alone, or no treatment (NO-RX) with either. This study was led by Dr. Alireza Atri from Harvard University Medical School.

Researchers reviewed data on 382 patients with probable AD who were evaluated and treated at the Massachusetts General Hospital Memory Disorders Unit from 1990 and 2005. All patients were followed at 6-month intervals (mean follow up: 30 months (4.1 visits)), and were assessed with the Blessed Dementia Scale (BDS) for cognition and with the Weintraub Activities of Daily Living Scale (ADL). 144 patients received standard care without CI or COMBO (NO-RX), 122 received CI, and 116 received COMBO.

The results show that the COMBO group had significantly lower mean annualized rate of decline in BDS and ADL scores compared with the CI and NO-RX group. Furthermore, for the COMBO group, Cohen's effect sizes increased with treatment duration.

Atri A et al. ADAD 2008; 22(3):209-21.

CENTRAL OBESITY AND INCREASED RISK FOR DEMENTIA

It is known that the abdominal distribution of fat, referred to as central obesity, is an independent and more potent risk factor for type 2 diabetes, insulin resistance, coronary heart disease, stroke and mortality than of total body obesity. Also, a recent population-based study has shown that obesity contributes to cognitive impairment, and also, as measure by BM in middle age, it increases the risk of dementia, Alzheimer's disease (AD), and neurodegenerative changes. However, whether central obesity contributes to increased risk for dementia is not known.

Dr. Rachel Whitmer from the Kaiser Permanente Division of Research and her colleagues conducted a longitudinal analysis of 6,583 members of Kaiser Permanente of Northern California who had their sagittal abdominal diameter (SAD) measured in 1964 and 1973. Diagnoses of dementia were extracted from medical records an average of 36 years later, January 1, 1994 to June 16, 2006. Data were adjusted for age, gender, race, education, marital status, diabetes, hypertension, hyperlipidemia, stroke, heart disease and medical utilization.

A total of 1,049 (15.9%) were diagnosed with dementia. Compared with those in the lowest quintile of SAD, those in the highest had nearly a 3-fold increased risk of dementia, and this was only mildly attenuated after adding BMI to the model. Those with high SAD (>25cm) and normal BMI (18.5-24.9) had an increased risk compared to those with low SAD (<25cm) and normal BMI. Those both obese (BMI>30) and with high SAD had the highest risk of dementia.

Whitmer RA et al. *Neurology* 2008; 71(14):1057-64.

ASSESSMENT OF BETA-AMYLOID IN A FRONTAL LOBE BY BIOPSY SPECIMEN AND BY [¹¹C]PIB PET

Dr. Ville Leinone and his colleagues from Kuopio University Hospital in Finland compared carbon 11-labeled Pittsburgh Compound B ([¹¹C]PiB) PET findings with and without beta-amyloid aggregates in frontal cortical biopsy specimens.

Ten patients who had undergone intraventricular pressure monitoring with a frontal cortical biopsy for suspected normal-pressure hydrocephalus were evaluated for cognitive impairment using neuropsychological battery. Also immunohistochemical evaluation for A-beta aggregates and hyperphosphorylated tau in the frontal cortical biopsy specimen and [¹¹C]PiB PET were conducted.

In PET imaging, patients with A-beta aggregates in the frontal cortical biopsy specimen had higher [¹¹C]PiB uptake in the frontal, parietal, and lateral temporal cortices and in the striatum as compared with the patients without frontal A-beta deposits. This result supports the use of [¹¹C]PiB PET to assess A-beta deposition in the brain.

Leinonen V et al. *Arch. Neurol.* 2008; 65(10):1304-9.

VITAMIN B12 STATUS AND RATE OF BRAIN VOLUME LOSS

To investigate the relationship between markers of vitamin B12 status and brain volume loss, Dr. Anna Vogiatzoglou and her colleagues from the Dept. of Physiology, University of Oxford conducted a prospective study of 107 community-dwelling volunteers aged 61 to 87 years without cognitive impairment at enrollment. Volunteers were evaluated yearly over the period of 5-years with clinical examination, MRI, and neuropsychological testing. Blood was collected at baseline for measurement of plasma vitamin B12, transcobalamin (TC), holotranscobalamin (holoTC), methylmalonic acid (MMA), total homocysteine (tHcy), and serum folate.

The results showed that the decreases in brain volume were greater among those with lower vitamin B12 and holoTC levels and higher plasma tHcy and MMA levels at baseline. Linear regression analysis showed that associations with vitamin B12 and holoTC remained significant after adjusting for demographics and other measures including initial brain volume, cognitive test scores and ApoE status. Using the upper (for the vitamin) and lower tertile (for the metabolites) as reference in logistic regression analysis and adjusting for the above covariates, vitamin B12 in the bottom tertile (<308 pmol/L) was associated with increased rate of brain volume loss. The same association was observed for low levels of holoTC (<54 pmol/L) and for low TC saturation.

Vogiatzoglou A et al. *Neurology* 2008; 71(11):826-32.

EDUCATION AND OCCUPATION AS PROXIES FOR BRAIN FUNCTIONAL RESERVE

Previous studies have shown that higher education is associated with more severe brain pathology in patients with Alzheimer's disease (AD), indicating that these individuals have a functional reserve provided by education, which masks the clinical expression of a higher degree of neurodegeneration. However, whether a similar reserve mechanisms exists in patients with amnesic mild cognitive impairment (aMCI) is not known.

Dr. Valentia Garibotto and her colleagues from Vita Salute San Raffaele University, Milan, Italy, have studied the impact of education (measured by the number of completed years of formal education) and occupation (occupational attainment rated according to the general NEST-DD project protocol) on brain glucose metabolism (rCMRglc) measured with FDG-PET in patient with probable AD (pAD; n=242), aMCI (n=72), and healthy control (NL; n=144).

The analysis showed a significant association between higher education/occupation and lower rCMRglc in posterior temporoparietal cortex and precuneus in pAD and aMCI converters (n=21), and no correlation in aMCI non-converters and NLs. This suggests that pAD and aMCI converters with higher education/occupation had a more severe rCMRglc reduction than those with lower education/occupation when submitted to FDG-PET for diagnostic evaluation. It also suggests that education and occupation plays a role even in the pre-dementia phase of AD.

Garibotto V et al. *Neurology* 2008; 71(17):1342-49.

DEPRESSIVE SYMPTOMS ASSOCIATED WITH AN INCREASED RISK OF CARDIOVASCULAR EVENTS

Depressive symptoms have long been recognized as a predictor for adverse cardiovascular outcomes in patients with coronary heart disease. However, the mechanisms responsible for this association are not known. To determine why depressive symptoms are associated with an increased risk of cardiovascular events, Dr. Mary Whooley and her colleagues from UC San Francisco and VA Medical Center San Francisco conducted a prospective cohort study (The Heart and Soul Study) of 1017 outpatients with stable coronary heart disease and followed up for a mean (SD) of 4.8 (1.4) years.

Depressive symptoms at baseline were assessed using the Patient Health Questionnaire (PHQ), and proportional hazard models were used to evaluate the extent to which the association of depressive symptoms with subsequent cardiovascular events (stroke, heart failure, myocardial infarction, transient ischemic attack, or death) was explained by baseline disease severity and potential biological or behavioral mediators.

During 4876 person-years of follow-up, 341 cardiovascular events occurred. The age-adjusted rate of cardiovascular events was 10.0% among the depressive symptoms (PHQ \geq 10) group (n=199) and 6.7% among the non-depressive symptoms group (n=818). After adjusting for comorbid conditions and disease severity, depressive symptoms were associated with a 31% higher rate of cardiovascular events. In summary, the association between depressive symptoms and adverse cardiovascular events was largely explained by behavioral factors, particularly physical inactivity.

Whooley MA et al. JAMA 2008; 300(20):2379-88.

HIGH-DOSE VITAMIN B SUPPLEMENTATION AND COGNITIVE DECLINE IN ALZHEIMER'S DISEASE

To determine the effect of vitamin B supplementation in the treatment of Alzheimer's disease (AD), a multi-center, randomized, double-blind controlled clinical trial was conducted in 409 individuals with mild to moderate AD (MMSE scores 14-26) and normal folic acid, vitamin B12, and homocysteine levels. This study was lead by Dr. Paul Aisen from Dept. of Neuroscience, UC San Diego.

Participants were randomly assigned to high-dose supplement (5 mg/d of folate, 25 mg/d of vitamin B6, 1mg/d of vitamin B12) treatment group (n=202) or placebo group (n=138) for 18 months. Cognitive changes were measured by ADAS-Cog.

The result showed no beneficial effect on the primary cognitive measure although the vitamin supplement regimen was effective in reducing homocysteine levels. A higher quantity of adverse effect involving depression was observed in the treatment group.

Aisen PS et al, JAMA 2008; 300(15):1774-83.

Free Patient Brochure

Make sure your patients know that you now offer memory assessment services. We can send you complimentary copies of our educational patient brochure, "About Memory Loss", in English and Spanish. To request copies, please email us at: customerservice@mccare.com and include the address to where you would like the brochures mailed.



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