



# an Ounce of Prevention

ALZHEIMER'S PREVENTION THROUGH DELAY

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## PREVENTION HIGHLIGHT

### **Specific NSAID Linked to Reduced Alzheimer's Risk**

A new study suggests those who use a specific NSAID regularly for five years or more have a reduced risk of developing Alzheimer's disease (AD).

To examine the effect of longer-term use of specific NSAIDs, Dr. Steven Vlad and his colleague from Boston University School of Medicine analyzed a total of 246,199 cases (196,850 controls) of subjects over 55 years old and with incident AD from the US national Veterans Affairs (VA) Health Care system.

Compared with no NSAIDs use, the adjusted odds ratios for AD among NSAID users decreased from 0.98 for  $\leq 1$  year of use to 0.76 for  $> 5$  year of use. This decrease was clearest, from 1.03 to 0.56, for ibuprofen users, and the effect increased with the duration of its use. Other NSAIDs showed inconsistent results.

Vlad SC, et al. *Neurology*. 2008; 70(19):1672-1677.

## RESEARCH UPDATES

### **Men are More Likely to Have Mild Cognitive Impairment**

A new study finds that mild cognitive impairment (MCI) is more prevalent in older men than in older women. This study was presented at the 60th Annual Meeting of the American Academy of Neurology by Dr. Rosebud Robert from the Mayo Clinic in Rochester MN.

Dr. Robert and colleagues evaluated 2,050 men and women ages 70 to 89 (52% age 80-89; 51% male; 47% less than 12 years of education) from Olmsted County, MN.

The researcher found that overall 73.6% had normal cognitive function and 16.5% MCI. The prevalence of MCI increased with age. In women, MCI prevalence was 8% for age group 70-79 and 19% for age group 80-89 years old. In men, MCI prevalence was 12% and 40% for age groups 70-79 and 80-89, respectively. After adjusting for age and education, men were 67% more likely to have MCI than women.

Robert RO. et al. The 60th Annual Meeting of the ANA, April 2008.

## **Small Vessel Disease Responsible for 1/3 of Risk For Dementia**

A large autopsy study of 3400 men and women in the Seattle region have shown that a third of those who become demented before death had evidence of small vessel damage in their brains. This study was presented at the American Society for Biochemistry and Molecular Biology in April 2008.

In the autopsied brains of people who had cognitive decline or dementia, 45% of the risk for dementia was associated with pathologic changes of Alzheimer's, and 10% Lewy body disease. One third of the risk for dementia was associated with damage to the brain from small vessel disease. Lead author Dr. Montine and his colleagues believe that this small vessel damage is the cumulative effect of multiple small strokes caused by diabetes and hypertension.

Montine T. et al. ASBMB. April 2008.

## **Developing Biomarkers for Parkinson's Disease**

The development of biomarkers for the diagnosis and monitoring disease progression in Parkinson's disease (PD) is of great importance to reduce diagnostic errors based on clinical parameters.

A research group lead by Dr. Mikhail Bogdanov from Department of Neurology and Neuroscience, Weill Medical College of Cornell University, New York Presbyterian Hospital, New York, NY, utilized metabolomic profiling using high performance liquid chromatography coupled with electrochemical coulometric array detection (LCECA) to look for biomarkers in plasma useful for the diagnosis of PD.

Metabolic profiles from 25 controls and 66 PD patients were examined. Results have shown, in PD patients, increased level of 8-hydroxy-2-deoxyguanosine (8-OHdG), a marker of oxidative damage to DNA, as well as reduced levels of uric acid and increased levels of glutathione.

Bogdanov M, et al. Brain. 2008; 131(2):389-396.

## **APOE-e4 May Be Beneficial in Recovery from TBI**

Persons with apolipoprotein e4 (APOE-e4) allele, known genetic risk factor for Alzheimer's disease, are suggested to have a worse recovery outcome from traumatic brain injury (TBI).

However, a study, lead by Willemsse-van Son and colleagues from Department of Rehabilitation Medicine at Erasmus Medical Center in Rotterdam, the Netherlands, have shown better long-term, global functional outcomes in patients with APOE-e4 after TBI.

79 moderate and severe traumatic brain injury patients were assessed at 3, 6, 12, 18, 24 and 36 months post injury for global functional outcome, on activity limitations and participation restrictions, and on community integration using the Glasgow Outcome Scale (GOS), the Sickness Impact Profile-68 (SIP-68) and the Community Integration Questionnaire (CIQ). The GOS measure was significantly better in patients with APOE-e4 while the other measures did not differ.

Willemsse-van Son AH, et al. J Neurol Neurosurg Psychiatry. 2008; 79(4):426-30.

## **Brain Atrophy Rates Accelerate in Amnesic Mild Cognitive Impairment**

Researchers found that rates of brain atrophy accelerate as individuals progress from amnesic mild cognitive impairment (aMCI) to typical late onset Alzheimer's disease (AD). Rates of atrophy were greater in younger patients than older patients with aMCI who progressed to AD (aMCI-P), and than patients with aMCI who did not progress (aMCI-S).

Rates of brain shrinkage and ventricular expansion were measured across available serial MRI scans in 46 patients with aMCI-P, 46 normal control, and 23 with aMCI-S. In aMCI-P, the change in pre to post index rate (i.e. acceleration) of ventricular expansion was 1.7 cm<sup>3</sup>/year, and acceleration in brain shrinkage was 5.3 cm<sup>3</sup>/year. Brain volume decreased and ventricular volume increased in all three groups with age. Among all patients with aMCI, rates of atrophy were greater in patients with the apolipoprotein E e4 carrier.

This study was lead by Dr. Clifford R. Jack Jr. and colleagues from Mayo Clinic, Diagnostic Radiology, Rochester, MN.

Jack Jr. CR, et al. *Neurology*. 2008; 70(19):1740-1752.

## **Obesity Associated with Increased Risk for Stroke in Middle-Aged Women**

Dr. Amytis Towfighi and colleagues from the University of Southern California examined gender differences in stroke prevalence among individuals of midlife age (35 to 64 years) in the United States and determined factors predicting stroke using two surveys, the National Health and Nutrition Examination Survey III (NHANES III; 1988-1994) and NHANES IV (1999-2004).

They looked specifically at stroke prevalence, medical histories, and biomarkers among age 35-54 men and women who reported that their doctors had diagnosed stroke (NHANES III: n=5,122; NHANES IV: n=4,594).

Among middle-aged women, stroke prevalence increased from 0.6% in NHANES III to 1.8% in NHANES IV, while it changed little in men (0.9% in NHANES III and 1.0% in NHANES IV). The abdominal obesity defined as a waist circumference over 88 cm also increased 47% to 59% in middle-aged women during the two-survey period (29% to 47% increased in men). Mean BMI also increased from 27.1 to 28.8 for middle-aged women and 27.2 to 28.4 for middle-aged men.

Towfighi A, et al. *Neurology*. 2007: June 20 e-Publication.  
Towfighi A, et al. 2008 International Stroke Conference, New Orleans, LA.

## **Effect of Folic Acid and B Vitamins on Risk of Cardiovascular Events and Total Mortality Among Women with High Risk of Cardiovascular Disease**

Although observational data suggests greater benefits of B-vitamin supplements against cardiovascular disease (CVD) in women, published randomized trials are very limited. To test whether a combination of folic acid, vitamin B<sub>6</sub> and B<sub>12</sub> lower CVD among high-risk women with and without CVD, a randomized trial was conducted by Dr. Christine N. Albert and colleagues from Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA.

Within ongoing randomized trial of anti-oxidant vitamins, 5,442 women who were US health professionals over 42 years old with either a history of CVD or 3 or more coronary risk

factors, were enrolled in a randomized, double-blind, placebo-controlled trial to receive a combination pill of 2.5mg of folic acid, 50mg of vitamin B<sub>6</sub>, and 1 mg of vitamin B<sub>12</sub>, and followed up for 7.3 years.

Results show that a combination treatment did not reduce a combined end point of total cardiovascular events (e.g. myocardial infarction, stroke, coronary revascularization or CVD mortality) among high-risk women, although a significant homocysteine lowering effect was observed.

Albert CM, et al. JAMA. 2008; 299(17):2027-2036.

## **Exercise Lowers Risk for Mild Cognitive Impairment**

Dr. Yonos Geda and colleagues from the Mayo Clinic, Rochester, MN, reviewed physical exercise data from 128 individuals ages 70 to 89 with mild cognitive impairment (MCI) and 740 cognitively healthy elderly persons.

For this study, subjects were asked about the frequency and intensity of their exercise regimen during the preceding year, as well as during ages 50 through 65. They found that moderate physical exercise (e.g. brisk walking, hiking, aerobics, strength training, golfing without golf cart, swimming, tennis doubles, moderate use of exercise machines, yoga, martial arts or weight lifting) 2 to 5 times per week during ages 50 to 65 was associated with a significantly reduced risk of MCI.

Geda Y. et al. The 60th Annual Meeting of the ANA, April 2008.

## **ABOUT MILD COGNITIVE IMPAIRMENT**

Persons with MCI have impairments limited to one category of cognitive function (e.g. memory, judgment, reasoning, executive function), but this impairment does not interfere with his or her activities of daily living. Persons with dementia have impairment in two or more cognitive functions and such impairment interferes with the person's ability to function in their usual manner in their social, family, personal or professional life.

Mild Cognitive Impairment is also identified as the first clinical stage of Alzheimer's Disease. The subtype of MCI associated with Alzheimer's Disease is called amnesic MCI and affects an individual's memory. Approximately 80% of people with amnesic MCI develop Alzheimer's disease within 6 years. According to the Mayo Clinic, 15-20% of MCI patients convert to Alzheimer's disease each year. In comparison, the conversion rate for the general population is 1-2%. Since MCI is the first symptomatic stage of Alzheimer's Disease, accurately detecting MCI enables medical professionals to then take the steps necessary to determine if a patient has early stage Alzheimer's Disease.