Memory Care Monthly

Supporting Healthcare Professionals in Caring for the Aging May / June 2009

KNOW THE 10 SIGNS: EARLY DETECTION MATTERS

Recent studies provide more evidence for the importance of early detection. Early detection not only allows the maximum benefit of currently available treatments, but also gives patients an opportunity to participate in the planning of their future care and personal matters.

In the effort to encourage early detection of Alzheimer's disease (AD) in the community, the National Alzheimer's Association has recently launched an educational campaign called "Know the 10 Signs: Early Detection Matters," along with an updated version of their 10 warning signs of Alzheimer's. The new "10 signs" include more descriptive symptoms of AD ranging from memory changes affecting daily life, to decreased or poor judgment, and to changes in mood and personality. They are also compared with typical state for these functions among the healthy.

For more information, please visit:
http://alz.org/alzheimers_disease_know_the_10_signs.asp

Also available at their site is a memory questionnaire for doctors visits, a 10 warning signs check list, and principals for a dignified diagnosis.

WHAT'S NEW?

MEET US AT ICAD 2009

This year, the Alzheimer's Association 2009 International Conference on Alzheimer's Disease (ICAD) will be held from July 11-16 in Vienna, Austria. Medical Care Corporation will be orally presenting its most recent research on the optimal scaling for memory assessment, which is incorporated in the MCI Screen Memory Performance Index available to all of our clients.

For more information, please visit ICAD 2009 site at http://www.alz.org/icad.

FOR MORE TIMELY NEWS, VISIT OUR BLOG: "BRAIN TODAY"

Myriad news reports about brain health are published every day. The news covers many related topics such as memory loss, Alzheimer's disease, drugs and treatments, risk factors, diagnostic tests, and published discoveries across the field. Some of the news is objectively reported, some is over-sensationalized, and some is intentionally misleading. This blog is devoted to interpreting the daily news and distilling its true value.

http://braintoday.blogspot.com

FEATURED ARTICLE

ACTIVIN A – ESSENTIAL FOR NEUROGENESIS FOLLOWING NEURODEGENERATION

Acute injury to the central nervous system, such as by stroke, is followed by enhanced neural progenitor cell proliferation and neurogenesis, and it has been speculated that this neurogenesis may contribute to recovery. However, emerging evidence suggests that such neurogenesis may be impaired in neurodegenerative disorders such as Parkinson's disease and Alzheimer's disease, but it is unclear why. Given the potential importance for the understanding of brain function, disease mechanisms, and pharmacotherapy, it is critical to investigate and understand the molecular mechanisms that regulate neurogenesis.

Activin A, a member of the transforming growth factor (TGF)-β superfamily, is expressed by neurons following excitotoxicity which contribute to nerve cell death in neurodegenerative diseases. A research group from the Garvan Institute of Medical Research, Sydney, Australia, showed for the first time that activin A, possibly working in conjunction with other TGF-β superfamily molecules, is essential for neurogenesis to proceed following neurodegeneration.

Using mouse models, they found that intraventricular infusion of activin A increased the number of newborn neurons in the dentate gyrus, CA3, and CA1 layers of the normal adult hippocampus and also, following lipopolysaccharide administration, had a potent inhibitory effect on gliosis in vivo and on microglial proliferation in vivo and in vitro. Consistent with the role of activin A in regulating central nervous system inflammation and neurogenesis, intraventricular infusion of follistatin, and activin A antagonist, profoundly impaired neurogenesis and increased the number of microglia and reactive astrocytes following onset of kainic acid-induced neurodegeneration. These results show that inhibiting endogenous activin A is permissive for a potent underlying inflammatory response to neurodegeneration.

Researchers also found that the anti-inflammatory actions of activin A account for its neurogenic effects following neurodegeneration because co-administration of nonsteroidal anti-inflammatory drugs reversed follistatin's inhibitory effects on neurogenesis in vivo.

This study provides implications for understanding and treating acute and chronic neurodegenerative diseases.

Abdipranoto-Cowley A et al. Stem Cells. 2009; 27:1330-46.
Full Text Available for Open Access at:
http://www3.interscience.wiley.com/journal/121607285/grouphome/home.html.

RESEARCH UPDATES

CSF BIOMARKER SIGNATURE IN ADNI SUBJECTS

A research group lead by Dr. Leslie Shaw from the University of Pennsylvania School of Medicine examined a cerebrospinal fluid (CSF) biomarker signature for mild Alzheimer's disease (AD) in Alzheimer's Disease Neuroimaging Initiative (ADNI) subjects.

Amyloid-β 1-42 peptide (Aβ1-42), total tau (t-tau), and tau phosphorylated at the threonine 181 were measured in (1) CSF samples obtained during baseline evaluation of 100 mild AD, 196 mild cognitive impairment (MCI), and 114 elderly cognitively normal (NC) subjects in ADNI; and (2) independent 56 autopsy-confirmed AD cases and 52 age-matched elderly NCs using a multiplex immunoassay.

They found that CSF Aβ1-42 was the most sensitive biomarker for AD in the autopsy group – receiver operating characteristic area under the curve of 0.913 and sensitivity for AD detection of 96.4%. In the ADNI group, a logistic regression model for Aβ1-42, t-tau, and APOE4 allele count provided the best assessment delineation of mild AD. An AD-like baseline CSF profile for Aβ1-42 was detected in 33 of 37 ADNI MCI subjects who converted to probable AD during the first year of the study.

Shaw LM et al. Ann Neurol. 2009; 65(4):403-13.

EXAMINATION OF "GOLD STANDARD" DIAGNOSIS OF MAJOR DEPRESSION IN AGED-CARE SETTINGS

Individual clinical interviews are usually viewed as the gold standard when diagnosing major depressive disorder (MDD) and when examining the validity of self-rated questionnaires. However, this approach may not be appropriate with older people due to their tendency to under report their depressive symptoms.

Dr. Tanya Davison from Deakin University, Melbourne, Australia, and her colleagues examined the effect of including informant interview on prevalence estimates of MDD in 168 residents (mean age: 84.68 years) with normal cognitive function in low-level aged-care facilities.

They found that the estimated point prevalence of MDD rose from 16% to 22% by including informant clinical interview in the diagnostic procedure. Overall, 27% of depressed residents failed to disclose symptoms in the clinical interview.

This study supports the use of an informant interview as an adjunct when diagnosing MDD among cognitively healthy aged-care residents.

Davison TE et al. AJGP. 2009; 17(5):359-67.

USE OF STROKE SECONDARY PREVENTION SERVICES IN STROKE BELT STATES

Stroke Belt states – 11 states consisting of Alabama, Arkansas, Georgia, Indiana, Kentucky, Louisiana, Mississippi, North Carolina, South Carolina, Tennessee, and Virginia - have been recognized by public health authorities for having an unusually high incidence of stroke and other forms of cardiovascular disease. Due to such high stroke outcomes, Dr. Joseph Ross and his colleagues from Mount Sinai School of Medicine examined whether there are disparities in the use of stroke secondary prevention services in these states.

Using the nationally representative 2005 Behavior Risk Factor Surveillance System, they examined self-reported use of 11 stroke secondary prevention services queried in the survey. They used multivariable logistic regression to examine the association between service use and age, gender, race, and Stroke Belt state residence, controlling for other socio-demographic and health care access characteristics.

Among 11,862 adults with a history of stroke, 16% were 80 or older, 54% were women, 13%

were non-Hispanic black, and 23% lived within a Stroke Belt state. Overall service use varied: 31% reported post-stroke outpatient rehabilitation, 57% regular exercise, 66% smoking cessation counseling, and 91% current use of antihypertensive medications. Age 80 or older was not associated with lower use of any of the 11 services. Women were less likely to report post-stroke outpatient rehabilitation and regular exercise when compared with men, yet there were no gender-based differences in use of the 9 other services. Blacks were less likely to report pneumococcal vaccination when compared with whites, but most likely to report post-stroke outpatient rehabilitation. There were no race-based differences in use of the 9 other services. Stroke Belt state residence was not associated with lower use of any of the 11 services.

Contrary to their hypothesis, researchers found no consistent age, gender, racial or Stroke Belt state residence disparities in care.

Ross JS et al. Stroke. 2009: 40:1811-19.

AWARENESS OF FUNCTIONAL DIFFICULTIES IN PERSONS WITH MILD COGNITIVE IMPAIRMENT

To determine whether patients with mild cognitive impairment (MCI) are fully aware of and able to provide reliable estimates of their functional status, self-reporting of functional ability in five cognitive domains (driving, financial abilities, medication management, grocery shopping, and telephone use) were compared to their performance on laboratory-based measures of these functions in 57 persons with amnestic MCI (aMCI) and 68 normal controls (NC).

The discrepancy between self-report and objective performance was significantly higher in patients with MCI than in NC only in financial abilities. Patients with MCI overestimated their abilities on this functional domain. Patients with MCI also overestimated their driving abilities, but this was not statistically significant.

This study suggests that awareness of functional difficulties is not uniform, and it varies across functional domains. It also suggests that self-report of functional abilities may be, as a whole, as accurate as in cognitively healthy older adults although supplementing self-reported information with objective functional assessment might improve detection of older adults who have begun to experience more functional restriction than is normal for their age.

Okonkwo OC et al. JAGS. 2009: 57(6);978-84.

MEMANTINE CAUSES REVERSIBLE NEUROLOGICAL IMPAIRMENT IN MS

A research group lead by Dr. Pablo Villoslada from the Department of Neurology, Hospital Clinic, Barcelona, Spain, examined the used of memantine for cognitive impairment (CI) in patients with multiple sclerosis (MS).

The trial was designed as a 1-year, randomized, double-blind crossover study comparing memantine 30 mg/day against a placebo in 60 patients with MS with CI.

Although 19 patients were included, the trial was halted after 9 patients reported a worsening of their neurologic symptoms that deteriorated their quality of life. 7 of 9 patients in the memantine group had blurred vision, fatigue, severe headache, increased muscle weakness, walking difficulties, or unstable gait. Only 2 cases in the placebo group reported neurologic symptoms and they were related with changes in their disease-modifying treatment. These adverse events occurred on reaching the maximum dose, and after stopping medication, these symptoms

reverted to their baseline disability within a few days.

Villoslada P et al. Neurology. 2009: 72(19);1630-33.

ASSOCIATION OF PRIOR STROKE WITH COGNITIVE FUNCTION AND COGNITIVE IMPAIRMENT

Researchers from the Mayo Clinic investigated associations between stroke history, APOE genotype, and subtypes of mild cognitive impairment (MCI).

Randomly selected 2050 residents of Olmsted County, Minnesota, aged 70 to 89 without documented dementia were evaluated through an informant interview, a neurological evaluation, and neuropsychological testing. Neuropsychological testing included 9 tests to assess memory, attention, executive function, visuospacial cognition, and language. Subjects were diagnosed by consensus as cognitively normal or as having MCI or dementia. A stroke history was confirmed in their medical record.

Of 2050, 1640 were cognitively normal, and 329 with MCI: 241 with amnestic MCI and 88 with nonamnestic MCI. A history of stroke was associated with a higher odds ratios of nonamnestic MCI than amnestic MCI. A stroke history was also associated with impaired function in each cognitive domain except memory. The association was strongest for attention and executive function. APOE e4 genotype was associated only with amnestic MCI and with impaired memory function.

Knopman DS. Arch Neurol. 2009: 66(5);614-19.

GLUCOCEREBROSIDASE MUTATIONS AND DEMENTIA WITH LEWY BODIES

It is known that mutations in the glucocerebrosidase (GBA) gene are associated with Lewy body (LB) disorders. Dr. Lorraince N. Clark and her colleagues from the Taub Institute for Research on Alzheimer's Disease and the Aging Brain at Columbia University, New York, conducted a study to determine the relationship of GBA mutations and the APOE4 genotype to LBD and Alzheimer's disease (AD) pathological findings.

Brain tissue samples of patients with primary neuropathological diagnoses of LB with or without AD changes (n=95), randomly selected patients with AD without significant LB pathological findings (n=60), and controls with neither LB nor AD pathological findings (n=32) were included in the study. GBA mutation status, APOE4 genotype, LB pathological findings, and AD pathological findings were measured.

GBA mutations were found in 18% (34/187) of all subjects, including 28% (27/95) of those with primary LB pathological findings compared with 10 (6/60) of those with AD pathological findings and 3% (1/32) of those without AD or LB pathological findings. GBA mutation status was significantly associated with the presence of cortical LBs, and GBA mutation carriers were significantly less likely to meet AD pathological diagnostic criteria.

This result indicates that GBA mutations may be associated with pathologically "purer" LB disorders, characterized by more extensive cortical LB, and less severe AD pathological findings, which may be a useful marker for LB disorders.

Clark LN et al. Arch Neurol. 2009: 66(5);578-83.

DONEPEZIL TREATMENT OF PATIENTS WITH MCI – A 48 WEEK RANDOMINZED, PLACEBO-CONTROLLED TRIAL

In this multi-center, randomized, placebo-controlled trial, subjects with MCI entered a 3-week placebo run-in period followed by 48 weeks of double-blind donepezil (5 mg/day for 6 weeks, then 10 mg/day for 42 weeks) or placebo treatment. Primary efficacy measurements included changes from baseline in the modified ADAS-Cog and CDR-SB after 48 weeks of treatment. Secondary measurements evaluated cognition, behavior and function.

Of 2037 patient screened, 821 were randomized into either treatment group (n=409) or placebo (n=412) and 60.8% completed the study (treatment group: 226; placebo: 273). These subjects, aged 45-90, expressed memory decline, and it was confirmed by their informant and neuropsychologic testings. Also they did not have a diagnosis of probable or possible vascular dementia or another types of dementia, a nerulogic or psychistric disorder, a treatment with ChEI or memantine for >1 months or within 3 months of screeing, and some other conditions associated dementia risk factors.

The dual primary efficacy endpoint was not reached in this trial. However, there was a small but significant decrease in the modified ADAS-Cog scores in favor of donepezil at study endpoint. Little change from baseline in the CDR-SB and secondary measurements was observed for both groups. Patient Global Assessment scores favored donepezil at all time points except week 12. The Perceived Deficits Questionnaire scores favored donepezil at week 24. The Clinical Global Impression of Change-MCI scores favored donepezil only at week 6.

The results suggest that donepezil yields small but significant improvement on the primary measure of cognition, but there was no effect on the primary measure of global function. Most other measures of global impairment, cognition, and function were not improved, possibly due to an insensitivity of these measures in MCI.

Doody RS et al. Neurology. 2009; 72(18):1555-61.

LATE-LIFE STATIN USE DOES NOT PREVENT DEMENTIA

In 2001, the first Cochrane review was published about statin use for the prevention of Alzheimer's disease (AD) finding that there was insufficient evidence to recommend it. To expand its scope to include all forms of dementia, Dr. Bernadette McGuinness and her colleagues from Queen's University Belfast, Belfast, UK, reviewed two large, randomized controlled trials (HPS 2002 and PROSPER 2002) that included 26,340 individuals aged 40-82 years across trials.

The PROSPER 2002 included 5,804 patients aged 70-82 years who were randomized to receive a 40 mg/day of pravastatin or a placebo. All participants had risk factors for or a history of vascular diseases. During a mean follow up of 3.2-year period, cognitive function of both groups declined at the same rate. There was no significant difference between 2 groups in performance on letter digit codes, picture word learning test, Stroop and Mini Mental State Examination. There was no evidence that statins were detrimental to cognition.

The HPS 2002 study conducted in 2002 included 20,536 patients with 5806 at least 70 years old at study entry. The mean follow up period was 5-years. Participants were randomized to 40 mg/day of simvastatin or placebo. Researchers found no difference in incidence of dementia (31 cases in the simvastatin group, 31 cases in the placebo group) nor in performance on the modified Telephone Interview for Cognitive Status at final follow-up (23.7% simvastatin group cognitively impaired vs 24.2% in placebo group). There was no difference in cognition between

groups either in relation to age at study entry or previous history of cerebrovascular disease.

This review suggests that statins given in late life to individuals at risk of vascular disease have no effect in preventing AD or dementia.

McGuinness B et al. Cochrane Database of Systematic Reviews 2009: Issue 2.

EFFECTS OF THE MENOPAUSE TRANSITION AND HORMONE USE ON COGNITIVE PERFORMANCE IN MIDLIFE WOMEN

Dr. Gail A. Greendale and her colleagues from UCLA examined cognitive performance during the menopause transition in 2,362 women from the Study of Women's Health Across the Nation for 4 years.

Results showed that, consistent with perceived memory difficulties reported by women in transition, perimenopause was associated with a decline in cognitive performance, characterized by women not being able to learn as well as they had during premenopause. Improvement rebounded to premenopausal levels in postmenopause, suggesting that menopause transition-related decline might be time-limited. Hormone initiation before the final menstrual period had a beneficial effect while initiation after the final menstrual period had a detrimental effect on cognitive performance.

Greendale GA et al. Neurology. 2009; 72(21):1850-7.

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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