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Research Explores the Connection between Normal Pressure Hydrocephalus and Alzheimer's Disease

PHILADELPHIA (May 4, 2010) — Normal Pressure Hydrocephalus (NPH) is a neurological condition that typically affects adults ages 55 and older. This condition was first described in the 1960s as a triad of gait disturbance, dementia, and bladder incontinence. The ventricles of the brain appear enlarged although the cerebrospinal fluid (CSF) pressure remains normal. Once properly diagnosed, the progression of NPH can be delayed through the surgical implantation of a shunt, a device that channels CSF away from the brain to another part of the body where it can be absorbed.

An estimated 5.3 million Americans have Alzheimer's disease (AD), 5.1 million of which are 65 and older, and 200,000 of which are under 65 with early-onset AD. About 60 to 80 percent of all cases of dementia are attributed to AD. The proliferation of beta-amyloid plaque is considered a key factor in the development of AD. Beta-amyloid protein accumulates in the brains of patients with AD, activating immune cells that try unsuccessfully to remove it. That triggers the release of poisons that eventually kill nerve cells, leaving behind a trail of plaques and tangles - the remains of nerve cells and fibers, clogged up with beta-amyloid.

Research done at the University of Virginia Health Science Center in Charlottesville, Va., analyzed the clinical connection of NPH to AD. The results of this study, Elucidating the Etiology of Normal Pressure Hydrocephalus (NPH) and the Spectrum of Surgically Treatable Dementias, will be presented by Sebastian F. Koga, MD, 11:20-11:34 am, Tuesday, May 4, 2010, during the 78th Annual Meeting of the American Association of Neurological Surgeons in Philadelphia. Co-authors are David T. Bourne, MD, David E. Bruns, MD, and John A. Jane Sr., MD, PhD.

It is estimated that as many as 250,000 people in the U.S. who are experiencing symptoms of AD and dementia, may actually have related conditions such as NPH, and could benefit from CSF diversion surgery. "Because the symptoms are similar to AD, some patients with NPH are never properly diagnosed or treated, while others who are treated for NPH may suffer concomitantly from AD," stated Dr. Koga. New advances in neurodegenerative proteomics have led to the discovery of biomarkers in CSF that can be used to diagnose various forms of early dementia and perhaps to predict which patients will benefit from shunt implantation.

"Although there are certain differences in the clinical presentation of NPH and AD, our research suggests that these two forms of dementia are part of a wider spectrum of tau-protein abnormalities in the brain. This new perspective could change diagnostic criteria and redefine the surgical treatment options available to patients suffering from dementia," remarked Dr. Koga.

In an effort to mirror recent research advances in AD, this study evaluated CSF biomarkers and correlated these to cortical histopathology samples and neuropsychological outcomes. An ongoing prospective longitudinal study is being conducted at the University of Virginia to include NPH patients treated at this institution, with comprehensive testing performed before and after shunting. In the first 50 consecutive patients, CSF profiling was performed for biomarkers beta-amyloid, T-tau, P-tau, APOÎµ4 genotyping, and cortical biopsy evaluations for neuritic plaques and tau tangles. These results were analyzed in relationship to clinical progress and neuropsychological testing. The following results were noted:

- Failure to improve after shunting was closely correlated to large numbers of neuritic plaques on biopsy and increased beta-amyloid in CSF.
- The high number of plaques and tangles in frontal lobe biopsies would indicate an advanced form of AD in a significant number of patients.
- Analysis of T-tau, P-tau and beta-amyloid shows that NPH progression mirrors the changes seen in patients with AD.

"Up to 35 percent of NPH patients suffer clinical declines similar to AD patients. The likelihood and pace of this decline can be predicted using currently available CSF biomarkers, which should help reduce the number of shunt re-operations in the future. Improved screening methods are required to refine diagnosis and predict the benefits of CSF diversion. This study further elucidated that NPH is a surgically treatable form of dementia in many cases, and must be considered in the spectrum of tau-proteinopathies. Further in-depth studies are indicated," concluded Dr. Koga.

Dr. Koga and his senior colleagues at the University of Virginia are working to establish a Neurodegenerative Proteomics Laboratory and a specialized NHP Clinic to optimize and expand the treatment options for patients suffering from tau-protein dementias.

Founded in 1931 as the Harvey Cushing Society, the American Association of Neurological Surgeons (AANS) is a scientific and educational association with more than 7,600 members worldwide. The AANS is dedicated to advancing the specialty of neurological surgery in order to provide the highest quality of neurosurgical care to the public. All active members of the AANS are certified by the American Board of Neurological Surgery, the Royal College of Physicians and Surgeons (Neurosurgery) of Canada or the Mexican Council of Neurological Surgery, AC. Neurological surgery is the medical specialty concerned with the prevention, diagnosis, treatment and rehabilitation of disorders that affect the entire nervous system, including the spinal column, spinal cord, brain and peripheral nerves.

Disclosure: the author reports no conflicts of interest.

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Media Representatives: If you would like to cover the meeting or interview a neurosurgeon — either on-site or via telephone — please contact the AANS Communications Department at (847) 378-0517 or call the Annual Meeting Press Room beginning Monday, May 3 at (215) 418-2409.