

9th International Conference on Alzheimer's Disease and Related Disorders

17-22 July, 2004; Philadelphia, USA

Dramatic developments in imaging techniques and therapeutic interventions were reported at the recent 9th International Conference on Alzheimer's Disease and Related Disorders.

In the first study to show a positive treatment effect on progression from cognitive impairment (MCI) to AD, the acetyl cholinesterase inhibitor donepezil slowed progression by about six months compared to placebo. The study randomised 769 people with mild cognitive impairment to vitamin E (up to 2000IU/day), donepezil (5mg per day for six weeks, increasing to 10mg) or placebo. They were followed up for three years and evaluated every six months. Reporting the results, Ronald Petersen, Mayo Clinic, Rochester, Minnesota, USA, said, "Progression to AD was slower with donepezil during the first 18 months of the study, but was then similar to placebo." Vitamin E had no effect.

Progression from MCI to AD was significantly slower with donepezil at 6 months ($p < 0.001$), 1 year ($p < 0.009$) and 18 months ($p < 0.035$). The average delay in disease progression was about six months in people who progressed to AD. This risk reduction was lost at three years, when progression to AD was similar in all three treatment groups. "It appears there is protection against progression to AD for the first 18 months of treatment," Dr Petersen noted, adding, "Perhaps we can intervene at an earlier stage of disease than previously thought – pre-AD."

An open label extension study of patients with MCI treated with flexible dosing of galantamine up to 24mg/day showed similar results, with a reduction in conversion to dementia during the first few months of treatment but no significant difference at two years. However, Michael Gold, Johnson & Johnson Pharmaceutical Research and Development, Titusville, USA, said there was reduction of about 20% in new conversions in favour of galantamine. He added that there was also a significant reduction in whole brain atrophy in favour of galantamine (0.619 for placebo vs 0.413 for galantamine).

The benefits of continuing donepezil treatment in patients showing unclear benefit after 12 weeks was demonstrated in results from the AWARE (Aricept Washout and Rechallenge) study showing behavioural benefits compared to those discontinuing therapy. The study randomised 193/619 patients who showed unclear benefit with 12 weeks' donepezil (10mg/day) to continue with the drug or switch to placebo. Results showed significant improvement in behaviour after a further 12 weeks' treatment with donepezil ($p < 0.05$) – with particular improvement in depression and dysphoria.

Reporting the results, Peter Johannsen, Righospitalet, Copenhagen, Denmark, said, "Behavioural symptoms should be considered when evaluating the treatment response in patients with mild to moderate AD."

Patients with AD living in residential care treated with donepezil on a long-term basis showed greater functional and cognitive benefits than those who stopped treatment, according to a retrospective analysis. The study – one of the first to study long-term treatment with donepezil – included 420 patients with AD who had been treated with donepezil for at least 60 days, with half (210) continuing donepezil therapy and half stopping treatment. Results showed that continued donepezil treatment resulted in significant improvements in behaviour frequency ($p < 0.05$), behaviour alterability ($p < 0.05$) and quality of life ($p < 0.05$), compared to baseline assessment. Patients discontinuing treatment showed significant declines in cognitive status ($p < 0.001$) and functional mobility ($p < 0.0001$).

A cost-effectiveness analysis showed that discontinuing donepezil was associated with an increase in average daily care costs, with a saving of \$6.90 per patient per day for patients remaining on treatment. David Smith, Texas A&M University, Texas, USA, reported, "Behaviour and quality of life improved; care costs of those who continued treatment were lower than for those who stopped."

Alzhemed (NC758) – an anti-A-beta amyloid agent – proved safe and well tolerated in a study of 58 patients with mild to moderate AD. Paul Aisen, Georgetown University Medical Center, Washington, USA, reported that the drug was detected in the cerebrospinal fluid (CSF), suggesting that it crossed into the brain. Results showed that levels of beta-amyloid protein circulating in the CSF fell after three months' treatment with the highest dose of NC758. "This indicated less amyloid accumulation in the brain," he proposed. He reported that there were no serious side effects associated with the drug.

A multicentre, randomised trial of A-beta immunotherapy AN1792 in 300 patients was stopped early after meningencephalitis occurred in 6% of immunised subjects (18/300). Although stopped early, after most patients had been given only two of six planned injections, 19.7% (59) developed an antibody response. No differences were found in cognitive measures including MMSE but Sid Gilman, University of Michigan, Ann Arbor, USA, reported that there was a difference in a composite score of several memory tests favouring antibody responders.

Results also showed that CSF-tau was reduced in antibody responders. Whole brain volume was decreased and ventricular volume increased. Autopsy samples suggested evidence of plaque clearance in all cases. Dr Gilman considered these were promising – although very early – therapeutic results.

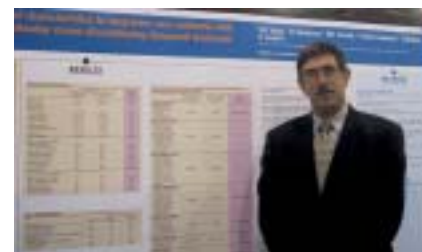
Imaging Studies Reveal AD Progression

Several studies were reported with the amyloid imaging PET tracer, Pittsburgh Compound-B (PIB), a novel amyloid-specific tracer. High specific activity PIB PET scanning data from a preliminary study of five people with MCI showed that the subjects fell into two distinct groups – one showed similar levels of amyloid deposition to normal, age-matched controls, while the second group showed evidence of amyloid deposition that was indistinguishable from patients with AD. PIB distribution closely resembled the known post-mortem distribution of amyloid in AD.

William Klunk, University of Pittsburgh, Pittsburgh, USA, said, "PIB-PET imaging may provide a quantitative assessment of amyloid deposition in living brain." He added, "Amyloid imaging with PET may be useful for predicting which people with MCI will progress to Alzheimer's in the near future. It might also help to determine the effectiveness of anti-amyloid therapies."

Dr Klunk noted that six centres throughout the world were now using Pittsburgh Compound-B in more than 100 different studies. He suggested that it could potentially be used in diagnosis (before symptoms), investigating pathophysiology and developing anti-amyloid therapies – with effects on PIB being used as a surrogate endpoint of efficacy. A very preliminary study from one patient treated with the anti-amyloid agent AN-1792 showed a remarkable decrease in PIB, he reported.

Another PET technique, using [F-18]FDDNP, which



binds to amyloid plaques and tangles of abnormal tau protein, showed that global [F-18]FDDNP binding was significantly higher for 13 patients with AD compared to that in 10 controls (1.17+0.03 vs 1.04+0.03; $p < 0.0001$). Global binding in 5 patients with MCI was also higher than in controls (1.10+0.05; $p = 0.005$). Different brain regions showed the expected pattern of AD pathology distribution.

Gary Small, University of California, Los Angeles commented, "These findings demonstrate the ability of [F-18]FDDNP binding to differentiate various degrees of cognitive decline in older populations." He added, "We believe this is the first time tau accumulation has been visualised in living patients. This technique may help us better differentiate between AD and other forms of dementia."

Prevention Studies

The importance of lifestyle factors in AD was illustrated in several studies showing that body weight, blood pressure, cholesterol level, lung function, leisure activity and dietary intake of vegetables were all linked to the risk of developing the disease.

A 10-year study from the Karolinska Institute, Stockholm, showed that individuals who were obese in middle age were

twice as likely to develop dementia later as those of normal body weight. For those who also had raised cholesterol and blood pressure, the risk of dementia was six times higher.

Another study suggested that leisure pursuits involving mental, social or physical activity all seemed to offer some protection against dementia. The greatest benefit came from complex pursuits combining two or three types of activity.

Findings from the long-running Nurses' Health Study demonstrated that high intake of leafy, green (such as spinach), or cruciferous (eg broccoli), vegetables was associated with less decline on cognitive tests than lower intake. "The difference amounted to being about one to two years younger in terms of cognitive ageing," reported Jae Hee Kang, Harvard Medical School, Boston.

"Although Alzheimer's is a complex disease with complex causes, studies at the conference bolstered evidence that we may be able to influence at least some factors in the mix," concluded William Thies, Vice-President of Medical and Scientific Affairs with the Alzheimer's Association.

Susan Mayor PhD,
Freelance Medical Journalist, London.

Epilepsy Specialist Nurse (ESNA) Conference

13-14th September 2004;
Sheffield, UK.

This is the third year the ESNA conference has been held in Sheffield. Organisers Chris Morley and Debbie Coker aimed to make the 2-day conference the best yet, adapting it based on members' comments about previous years. Speakers at the conference all work in the field of Epilepsy and presented current work or services in development. A group of excellent speakers covered a wide range of subjects, and this was well received by members (nurses working with adults, young people or children with Epilepsy, or nurses with an interest in Epilepsy). ESNA also held its Annual General Meeting. Below is a brief summary of the conference presentations.

Professor Trimble from the National Hospital for Neurology & Neurosurgery explained about innovative approaches to target seizure activity, including Transcranial Magnetic Stimulation, Vagal Nerve Stimulation, and Biofeedback.

Heather Sullivan, Epilepsy Nurse Specialist in Learning Disability, presented Dr Steven Brown's and the Epilepsy Nurses' findings of a telemedicine appointment for people with a learning disability in Cornwall. This initiative has been funded by Action on Neurology. It has helped to reduce waiting times to see the Consultant, reduced costs for travel expenditure and recorded some patients' seizures.

Dr Selway, Consultant Neurosurgeon at Kings College Hospital, London, discussed the different effects of brain stimulation to treat seizure symptoms. For example, subthalamic stimulation can help patients with partial seizures and caudate stimulation may affect mesial temporal lobe epilepsy and status epilepticus.

Julia Ackril, Senior Dietician for the Neurology Team at Birmingham Children's Hospital, spoke about the Ketogenic diet and the theory of how it can suppress seizures. She also highlighted common problems associated with the diet and presented a successful case study. Discussion followed on the diet's long term effects, risk of relapse, use with PEG feeds and the age at which patients could commence the diet.

Dr Turnpenny, Clinical Geneticist, Exeter, delivered a presentation on the risk for women with epilepsy taking anti epileptic drugs in pregnancy. Two teams from Exeter and Aberdeen have been helping to identify and follow up children with problems associated with anti convulsant

syndrome (ACS). He concluded that Nurses may be in a unique position to identify families affected by ACS.

Dr Marcus Reuber, Consultant Neurologist at the Royal Hallamshire Hospital, Sheffield, described seizure classification from 1052 BC to the present day. He explained the reasons the ILAE classification 1981/89 is changing. The new ILAE classification is recommended by the forthcoming NICE guidelines.

Mel Goodwin (ESNA chairman) and Jeff Bolton, Senior Product Manager, Pfizer Ltd announced a Nursing Award Practice for Achievements in the Care of Epilepsy. The details will be published in ACNR this year and the awards will be presented in 2005. There will be 3 categories with a total of 5 awards and prize money of £500 per winner. Epilepsy Action has been sponsored by Pfizer to send questionnaires to Epilepsy Nurse Specialists to identify their role. Watch out for your questionnaire arriving by post.

Jill Atkins, Lecturer at Buckingham University, discussed the results of her study on Epilepsy in later life. Her results conclude that it was most likely that the GP diagnosed that the patient had epilepsy - all the elderly people had hidden their diagnosis from their family, and the subject of their epilepsy was the main focus of the study. Also, the patients who had Epilepsy Nurses felt that they provided a lot of support. The patients wish they were seen in their own home. Jill aims to publish her study this year.

From my experience of talking to members, this was a very good conference. For those members who couldn't make it, I hope this brief update gives you some insight into the proceedings - and we hope to see you next year.

Finally the Malcolm Taylor award was won by Heather Gregory. Heather received her prize from Mrs Taylor, who spoke about her late husband's dedication to improving services for people with epilepsy.

Sally Collins,
Epilepsy Nurse Specialist, Rotherham General Hospital.



Mrs Anne Taylor, left
(wife of Dr Malcolm P Taylor),
presenting the Malcolm Taylor
Award to Heather Gregory.



See www.acnr.co.uk/conferences.htm for an additional report on the BSRM/Dutch Rehabilitation meeting.

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