Reviewing 2011 and Previewing 2012: Advances in Alzheimer’s Disease Research

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New diagnostic guidelines, new discoveries, and new directions highlighted AD research developments in 2011. The New Year offers an opportune time to look at the past – and the future – of AD clinical research endeavors.

The New Diagnostic Guidelines

2011 marked the publication of new diagnostic guidelines for AD formulated by committees sponsored by the National Institute on Aging and the Alzheimer’s Association. The NIA/AA also published guidelines for diagnosis of mild cognitive impairment (MCI) due to Alzheimer’s disease, and for preclinical AD. The guidelines will be important tools for clinicians to diagnose AD in its earliest stages, and represent the first revision in 25 years.

ApoE4

A very important paper by the Holtzman group at Washington University further established the relationship between ApoE4 genotype and decreased clearance of beta-amyloid from brain, both in humans and animal models. The idea that ApoE4 is less effective in removing beta-amyloid from the brain is not necessarily novel, per se, and had been previously shown. However, it had never been proven so convincingly and in such a complete manner in humans and animal models of AD. Together, the data suggest that ApoE variants contribute to a person’s risk for AD by affecting the clearance of beta-amyloid from the brain long before amyloid plaque deposition begins.

Later in 2011, the same group reported that, in mice, lowering the levels of ApoE4 results in fewer amyloid plaques. The results imply that ApoE-lowering treatments have a place among proposed AD therapies, including immunotherapy, gene therapy, as well as beta-, and gamma- secretase inhibitors.

Recent Posts from the ADCS blog…

- Reducing ApoE Lowers Beta-amyloid Levels in Brains of Mice
- Weight Change & Cognitive Function: Results from the Women’s Health Initiative

CTAD 2012 in Monte Carlo
October 29 - 31, 2012
5th Conference Clinical Trials in Alzheimer’s Disease (CTAD)

- Call for abstracts for symposia, oral and poster presentations will open on February, 15th, 2012.
- Again this year you will be able to submit online your abstract for symposia, oral communication or poster session.

CTAD Important Deadlines:

- May 15th, 2012: Deadline for submitting a symposium
- June 15th, 2012: Deadline for submitting an oral communication or poster presentation

http://www.ctad.fr/
**Amyloid Imaging**

An FDA advisory committee gave preliminary approval of the PET amyloid imaging ligand AV-45, citing work to be done to ensure consistency in reading PET scans. Full approval is expected sometime in the first half of 2012 following the FDA review and approval of a uniform training program for radiologists interpreting the scans.

The drug will be marketed to physicians for use as a diagnostic tool. The anticipated regulatory approval may capture the attention of the public – especially the “worried well” – as it will technically be possible to identify AD biomarkers very, very early in the disease process.

**Issues in Amyloid Imaging**

- Without available interventions, what does the patient do with the information?
- Amyloid is present in 100% of AD patients and is also found in approximately 30% of people without any AD cognitive symptoms.
- Do the people without cognitive symptoms, but with amyloid, somehow offset or compensate for the accumulation?

**ADNI, DIAN and the API**

Further progress in understanding the progression of the earliest stages of Mild Cognitive Impairment and AD with the Alzheimer’s Disease Neuroimaging Initiative (ADNI2), the Dominantly Inherited Alzheimers Network (DIAN) study and the Alzheimer’s Prevention Initiative (API) during 2012.

**Mild Cognitive Impairment**

Mild cognitive impairment involves the period of time that precedes full-on AD or dementia.

- The MCI phase of AD lasts about seven years before it begins to interfere with the activities of daily life.
- A person annually loses about 10% of their cognitive ability each year in the progression to AD.
- Approximately 10-20% of the population experience MCI after the age of 65.
- There are two subtypes of the condition with different trajectories.
  - Amnestic: In general, there are significant memory problems. Usually progresses to AD within 7-10 years. This is the most common type of AD.
  - Nonamnestic: In general, decisionmaking challenges, struggles with language and navigation and the execution of tasks. This type can be a forerunner of other kinds of dementia.
Clinical Trials

In terms of clinical trials, Gantenerumab, an antibody against beta-amyloid, was shown to clear plaques when given intravenously, according to results from a Phase 1 trial. The drug seems to be one of the most potent developed thus far in reducing plaques.

A Phase 2 gene therapy trial for Parkinson’s disease was deemed a success. A similar Phase II gene therapy trial for AD, called the Nerve Growth Factor Study, is currently ongoing and recruiting.

Multiple clinical trials, including the ADCS Phase III Resveratrol and Roche Phase II Gantenerumab trial are launching in 2012.

Sleep-Disordered Breathing

Results published in the Journal of the American Medical Association showed that women with sleep-disordered breathing (SDB)—pauses in breathing or reduced ventilation quality during sleep—are more significantly likely to develop cognitive impairment five years later. The biology behind this finding may include hypoxia, or decreased oxygen delivery to certain parts of the brain, including the hippocampus which is critical in memory function. In addition, sleep fragmentation, which can interfere with memory consolidation which occurs during certain stages of sleep, may also lead to cognitive problems. This study has really brought much needed attention to the evaluation of sleep as part of the work-up in individuals with Mild Cognitive Impairment.

Editors Note:

“Right Drug, Right Target, Right Time”

Last month, the publication of a commentary in the Science of Translational Medicine generated a significant amount of discussion within the AD research community. During the last year, several of the world’s preeminent clinical researchers have given significant consideration to the outcome of AD interventions over the last decade. The article suggests – like interventions for many cancers and for cardiovascular disease – that AD may be stage-dependent. Moreover, going forward, researchers are beginning to target selected therapies to specific stages of AD.

- 50% of memory circuit neurons are wiped out by the time a patient reaches the MCI phases of AD.
- It may be unlikely that any anti-amyloid therapy alone could rescue memory function at the dementia stage of the disease.

As clinical research moves to the preclinical stages of AD, the charge to find “the right drug, for the right target, at the right time” is under way. The ongoing development of biomarker research will play a crucial role in timing future interventions.

You can review the commentary at http://www.ncbi.nlm.nih.gov/pubmed/22133718?dopt=Abstract

Second NAPA Advisory Panel Meeting is January 17-18, 2012

January 17th and 18th, 2012
HHS 200 Independence Avenue SW, Room 800
Day One: 9:30 a.m. to 4 p.m.
Day Two: 9 a.m. to 2 p.m.

HHS will present an overview of the Draft National Plan to Address Alzheimer's Disease.

The Advisory Council will discuss and, as appropriate, vote upon recommendations to the Secretary of HHS on the Draft National Plan to Address Alzheimer’s Disease. The Advisory Council will also discuss how to engage stakeholders outside of the Federal Government in the writing and implementation of the National Plan. The Advisory Council will allow an open public session for any attendee to address issues or topics that should be addressed in the National Plan.
Public Comment/Meeting Attendance

HHS is asking that those wishing to attend the meeting in person e-mail Dr. Helen Lamont at Helen.Lamont@hhs.gov by COB Tuesday, January 10, 2012, so that their names may be put on a list of expected attendees and forwarded to the security officers at HHS. Any interested member of the public who is a non-U.S. citizen should include this information at the time of registration to ensure that the appropriate security procedure to gain entry to the building is carried out.

Public Input: Time is allocated on the agenda to hear public comments at the end of the meeting. In lieu of oral comments, comments may be sent to NAPA@hhs.gov.

Formal written comments may also be submitted for the record to: Helen Lamont, Ph.D
HHS Office of the Assistant Secretary for Planning and Evaluation
Room 424E, Humphrey Building
200 Independence Avenue, SW
Washington DC, 20201

ADCS Trials Enrolling...

Nerve Growth Factor Study (NGF)

The NGF is a Phase II clinical study of Ceregene’s CERE-110, a gene therapy product designed to deliver nerve growth factor (NGF) to the brain for the treatment of Alzheimer’s disease (AD) is currently underway. This study is a randomized, double-blind, placebo-controlled trial and employs gene therapy to deliver nerve growth factor (NGF) directly into the brain.

http://adcs.org/Studies/NGF.aspx

ADNI II Study

The goal of the Alzheimer’s Disease Neuroimaging Initiative Study is to learn how to stop the progression of mild cognitive impairment (MCI) and Alzheimer’s disease in future generations. Information from the study might, in the future, lead to new treatments

http://adcs.org/Studies/ImagineADNI2.aspx

This newsletter is intended to provide information to the public about developments in AD clinical research. It is compiled by the Alzheimer’s Disease Cooperative Study at the University of California, San Diego

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