Recent Breakthroughs in Alzheimer's Research

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AAIC 2018 HIghlights

AAIC 2018 Highlights: The Alzheimer's Association International Conference (AAIC), recently held in Chicago, IL in July 2018, is the world's largest gathering of researchers focused on Alzheimer's disease (AD) and other dementias, and the premier annual forum for presentation and discussion of the latest AD and dementia research. Here are some of the highlights from the 2018 AAIC.

Expansion in Results of Phase II Clinical Trial (Study 201) of BAN2401

As announced in previous findings, the trial resulted negative in its primary analysis. However, the secondary outcomes of the study, such as reduction of amyloid plaques and improvement of cognition and function, were more effective.

These results come from an 18-month, Phase II clinical trial of an investigational drug called BAN2401, an antibody that sets out to eliminate amyloid beta soluble fibers from the brain. An antibody is a Y-shaped protein used by the immune system in order to neutralize or eliminate disease-causing microorganisms such as bacteria and viruses. The trial included more than 850 people with mild cognitive impairment (MCI), a result of Alzheimer's disease or mild Alzheimer's dementia. Those involved in the study were randomly placed into one of five treatment groups, or a placebo.

In a secondary analysis, the researchers found noteworthy and significant results based on a combined measure of memory, function and cognition called the Alzheimer's Disease Composite Score. The results showed a slowing of disease progression after 18 months of patients receiving a 10mg/kg biweekly dose, compared to placebo.

In the highest dose at 18 months, cognitive decline as measured by the ADAS-Cog, a gold standard measure of cognition in Alzheimer's trials, was reduced 47 percent, a statistically significant finding. These new results are from secondary endpoints in this trial. These include 12- and 18-month analyses of: amount of amyloid in the brain, conversion from amyloid positive to negative, as well as change from the baseline in measures of memory, thinking and daily functioning, including ADCOMS, ADAS-cog, CDR-SB and MMSE.

According to the scientific community, it appears as though combination therapy may be on the horizon. Combination therapy may include anti-amyloid approaches as well as others that aim to address different aspects of the disease, and may also include manipulation of both the drug itself and lifestyle.

Alternatives in Treatment

Today, the need to treat and prevent Alzheimer's is at an all-time high, and continues to become more urgent each day, and may require the combination of alterations to drugs, lifestyle, and other non-drug options. The Alzheimer's Association — the leading non-profit funder of Alzheimer's research — sets an example of this change in procedure, as they are conducting the U.S. POINTER Study, the first large-scale study in the United States to evaluate the impact of lifestyle choices in older adults with increased risk for cognition decline.

Recruitment and Participation in Alzheimer's Disease Clinical Research

Due to the increase in both public and private investments towards Alzheimer's and dementia research, there is also an increase in the number of therapeutic targets. However, participation has fallen short of what is needed to be effective.

Representatives of the National Institutes on Aging (NIA) at the National Institutes of Health (NIH), with facilitation by the Alzheimer's Association, reported on progress of the National Strategy for Recruitment and Participation in Alzheimer's Disease Clinical Research, an effort to outline practical, proactive approaches to help study sites as well as researchers recruit and retain volunteers for Alzheimer's research studies. As the Alzheimer's disease and other forms of dementia epidemic continues to grow, new routes must be taken in order to find results, such as the new National Strategy which targets expanded research aimed at preventing and treating Alzheimer's disease. Diversity among participants is a focal point for this trial, expanding from local to international outreach. The national strategy notes that all recruitment and participation is local, and that it is a shared responsibility with shared results. Fighting Alzheimer's disease and related dementias requires effort from us all.

At the local level, two Alzheimer's research recruitment programs working in African-American communities reported successful efforts and methods at AAIC 2018, including registration in Alzheimer's Association TrialMatch. Requirements for these local-level facilities are: culturally competent recruitment of staff who are sensitive to the community background and educational materials that are appropriate to the cultural context.

Gut-Liver-Brain Axis in Alzheimer's Disease

In recent years, the impact of diet, particularly eating patterns, have been studied for their link to brain health and cognitive decline. Researchers have also seen inflammation and its markers — in the brain and other parts of the body — associated with Alzheimer's and other dementias. What is now being observed is the correlation between changes in gut bacteria with inflammatory and auto immune diseases, and thus showing impact towards brain health.

The researchers are currently trying to better understand the connection between altered liver and brain function in Alzheimer's, and possibly seek out new targets for treatment and prevention. While still in its early stages, this area of research is very exciting since it may give us a new window into why diet and nutrition are so important for brain health. For example, these findings may tell us more about how and why "good fats" are beneficial for the brain and keeping its health.
If bile acids prove to be effective and accurate markers of Alzheimer's disease, screening patients will become much more fluid, as a simple blood test could show results. A study showed that having low levels of plasmalogens, a class of lipids integral to cell membranes produced by the liver, could be associated with increased risk of developing the disease.

In a second study, gut microbiome-produced bile acids (those synthesized from cholesterol in the liver) were elevated in those with the disease as well as functional and physiological brain changes, including cognitive decline. Further, these bile acids were associated with increased amyloid and tau accumulation.

A third study found that that lipid metabolism (a major component of brain membranes) is disturbed in people with Alzheimer's. Obese and male subjects in the study had the strongest disturbance. Lipids are important for their ability to impact the accumulation of amyloid and tau, peptides that are related to Alzheimer's disease. Circulating lipids are synthesized in the liver and gut and are then supplied to the brain via blood flow.

A fourth study examined if Alzheimer's-related genes are related to cholesterol levels, bile acids and other compounds in blood. Low levels of cholesterol showed to be associated with health and repair of brain cell membranes.

Researchers hope that these findings will be validated and will thus be able to reveal causal pathways that could result in targets for therapies and prevention techniques.