By Michael Rafii, MD, PhD  
Director, Memory Disorders Clinic  
Associate Medical Core Director  
Alzheimer’s Disease Cooperative Study  
University of California, San Diego

As many of you have undoubtedly read or heard, results from multiple clinical trials were reported this past summer involving both Bapineuzimab and Solanezumab, two of the leading drug candidates under development for slowing down the progression of AD. Solanezumab and Bapineuzemab are both classified as immunotherapies. These drugs are monoclonal antibodies against beta amyloid, the protein that accumulates in the brain of patients with AD and is thought to be causative of the disease. The studies were all large, Phase 3, double-blind, placebo-controlled trials in patients with mild-to-moderate AD.

Although the trials were negative, a possible efficacy signal was discovered in prespecified secondary analyses of Solanezumab trials, offering a glimmer of hope. When data from the two Solanezumab trials were combined, the results suggested a significant slowing of cognitive decline in the overall study population. Furthermore, a statistically significant effect on cognition was noted in the mild AD patient subgroup, but not moderate AD subgroup, as compared to placebo. In its release of the trial results, Lilly emphasized that these are the first Phase III data with an anti-beta amyloid agent that appear to show a slowing of cognitive decline, and that the pooled data support the amyloid hypothesis.

The results indicate that drugs against beta-amyloid will need to be tested even earlier in the course of the disease, perhaps in the prodromal stage where symptoms are even milder. This concept of earlier treatment is akin to the need to start cholesterol medication years before a heart attack occurs in order to derive benefit from its use.

Despite the negative results for Bapineuzemab, Pfizer and Johnson & Johnson remain committed to its development as a potential therapy, and in fact, will continue with another trial of bapi that is being delivered as a subcutaneous injection, rather than intravenous treatment. This method of drug delivery may actually overcome some of the barriers faced by intravenous Bapineuzemab, in that the drug may linger in the system for longer by virtue of the subcutaneous route, and have longer access times to beta-amyloid in the brain.

The Alzheimer’s disease community now awaits the upcoming American Neurological Association (ANA) annual meeting and the Clinical Trials on Alzheimer’s disease (CTAD) conference in October, as the full analysis on the pooled and subgroup data are released.
Exposure to Light Could Help Alzheimer’s Patients Sleep Better

New research from RPI Looks at Circadian Light Exposure and Activity in AD Patients

By Rebekah Mullaney, M.S
Manager, Research Communications
Lighting Research Center
Rensselaer Polytechnic Institute

Individuals with Alzheimer’s disease and related dementias (ADRD) often sleep during the day and are awake at night. The situation can turn life-threatening if they leave their homes and wander around outside. This irregular sleep schedule and night wandering, and the consequent burden on their caretakers, is a primary reason individuals with ADRD are placed in more controlled environments such as nursing homes. A new study from the Lighting Research Center (LRC) at Rensselaer Polytechnic Institute lays the foundation for the importance of tailored light exposures as a viable treatment option for the reduction of sleep disturbances in older adults and those with ADRD.

Funded by a grant from the National Institute on Aging (NIA), the study is the first to collect circadian light exposures in individuals with ADRD. Results of the quantitative study show that individuals with ADRD experienced lower light levels, exhibited lower activity levels, and had greater disruption to their natural circadian rhythms than healthy older adults. The findings also show that people with ADRD experience lower levels of light exposure and greater levels of circadian disruption during the winter.

“We used light/dark and activity/rest patterns to assess circadian disruption and our results are consistent with previous studies. However, this is the first field study to examine the synchrony between the circadian light pattern and the activity response pattern to assess circadian disruption,” said Mariana Figueiro, associate professor at Rensselaer and director of the Light and Health Program at the LRC, who led the study. “Measurements revealed that those with ADRD experienced more circadian disruption than healthy older adults.”

Results of the study, titled “Field Measurements of Light Exposures and Circadian Disruption in Two Populations of Older Adults,” will appear in the Journal of Alzheimer’s Disease. Figueiro presented the research team’s findings at the Alzheimer’s Association International Conference in Vancouver on July 17.

Along with Figueiro, co-authors of the study are LRC Director and Professor Mark S. Rea, LRC Research Specialist Robert Hamner, along with Patricia Higgins and Thomas Hornick, clinicians at Case Western Reserve University and Louis Stokes Cleveland VA Medical Center in Cleveland, Ohio.

Growing evidence indicates that circadian disruption by irregular light/dark patterns is associated with reduced quality of life and increased risk of disease. Circadian rhythms are governed by the human body’s master clock in what is known as the suprachiasmatic nuclei (SCN), which has an intrinsic period slightly longer than 24 hours. On average, the SCN runs with a period of 24.2 hours. Light/dark patterns on the retina, the photosensitive part of the eye, synchronizes the SCN to the 24-hour solar day, regulating biological rhythms such as when we are active and when we sleep. Without exposure to a regular, daily pattern of light and dark, circadian rhythms can become irregular.

“Biology is driven by circadian rhythms at every level, and light is the main stimulus for synchronizing the circadian system to the solar day. By quantifying an individual’s light/dark exposure pattern, we can prescribe ‘light treatments’ promoting circadian entrainment, thereby improving health and well-being,” said Figueiro.
Exposure to Light Could Help Alzheimer’s Patients Sleep Better continued..

To collect data for the study, the research team used a Dimesimeter, a dime-sized device developed by the LRC, to record how much photopic and circadian light an individual is exposed to and whether they are active or resting. The data-logging device records these light and activity levels continuously over many days, and can be easily attached to shirt collars, lapels, hats, wristbands, or eyeglasses. The Dimesimeter enables researchers to examine light/dark and activity/rest patterns in those experiencing circadian sleep disorders, such as Alzheimer’s patients.

Data from the device can be downloaded to a computer and processed to calculate a cross-correlation of the activity/rest and light/dark exposure data, a measure of circadian entrainment/disruption.

“The Dimesimeter system allows researchers to accurately measure light/dark exposure and activity/rest patterns to quantify circadian disruption. In this way, we can collect ecological data on populations who suffer from circadian sleep disorders,” said Rea. “This new study using the Dimesimeter is a major step toward the goal of better understanding the impact of circadian disruption on human health.”

For the new NIA-funded study, the research team enlisted 16 healthy older adults and 21 adults with ADRD to wear a Dimesimeter on their wrists for one week. The research team in Cleveland collected data from those with ADRD and the research team in Troy collected the data from healthy older adults. From the resulting data, the researchers calculated two metrics for each subject: relative activity (RA) to measure activity, and phasor magnitude to measure both light exposure and activity. The analysis revealed that during winter, those with ADRD exhibited more circadian disruption than healthy adults as reflected by their significantly shorter phasor magnitudes and lower RA values. Those with ADRD studied in winter also had significantly shorter phasor magnitudes than those studied in summer. ADRD adults were less active during waking hours than healthy adults, and ADRD adults studied in winter were exposed to less light than healthy adults in winter and ADRD adults in summer. The research team is currently delivering a lighting intervention to those with ADRD and their caretakers and measuring its impact on their sleep efficiency and circadian disruption.

Looking forward, the Dimesimeter could one day allow physicians to predict the optimum timing of the light therapy necessary to resynchronize the circadian phase with the solar day. Such treatments could range from going outdoors for 15 minutes to sitting in front of a light box fitted with blue LEDs for a prescribed amount of time, according to Figueiro.

About the Lighting Research Center
The Lighting Research Center (LRC) is part of Rensselaer Polytechnic Institute of Troy, N.Y., and is the leading university-based research center devoted to lighting. The LRC offers the world’s premier graduate education in lighting, including one- and two-year master’s programs and a Ph.D. program. Since 1988 the LRC has built an international reputation as a reliable source for objective information about lighting technologies, applications, and products. The LRC also provides training programs for government agencies, utilities, contractors, lighting designers, and other lighting professionals.

For more information visit www.lrc.rpi.edu or contact:

Rebekah Mullaney
Phone: (518) 687-7118
E-mail: mullar2@rpi.edu
Another ADNI Milestone: First AD-related “Big Data” Project in US

Jeffree Itrich, MSW, MJ
ADNI Coordinating Center
University of California

In July, the Alzheimer's Disease Neuroimaging Initiative (ADNI) reached another big milestone in AD research when it became the first, pioneering "big data" project for Alzheimer's disease. A new partnership between the Alzheimer's Association and the Brin Wojcicki Foundation will enable scientists to obtain whole genome sequences on the largest cohort of individuals related to a single disease (the ADNI GO and ADNI 2 clinical trial cohorts) in the US.

Currently, 800 individuals from ADNI GO and ADNI 2 will be sequenced. The new ADNI whole genome sequencing work is expected to generate at least 165 terabytes of new genetic data. The project is a significant extension of ADNI.

Whole genome sequencing determines all six billion letters in an individual's DNA in one comprehensive analysis. Once the sequences are completed – which will take several months. The raw data will rapidly be made available to qualified scientists around the globe to mine for novel targets for risk assessment, new therapies, and additional insight into the causes of AD.

Sequencing the ADNI participants and making the genetic data immediately available to researchers around the world will significantly improve our understanding and approach to Alzheimer's disease. The ADNI team and the Alzheimer's Association are impressive in their ability to quickly make decisions that are truly in the best interest of people with Alzheimer's," said Anne Wojcicki from the Brin Wojcicki Foundation.

The ADNI leaders directing the project emphasize the potentially groundbreaking importance of the ability to match existing data from ADNI about Alzheimer's disease markers, indicators, and changes with newly-generated gene sequence data. The new data may enable scientists to better understand how our genes cause and are affected by bodily changes associated with Alzheimer's disease.

ADNI is unprecedented in that the research data - including brain scans, blood and cerebrospinal fluid samples, and cognitive profiles - are made freely available without delay to scientists around the globe, resulting in more than 500 scientific manuscripts so far.

"The current ADNI database already includes detailed, long-term assessments of neuropsychological measures, standardized structural and functional imaging, and precise biomarker measures from blood and spinal fluid. Adding whole genome sequences to this rich repository will allow investigators all over the world to discover new associations between these disease features and rare genetic variants, offering new clues to diagnosis and treatment," said ADNI Data and Publications Committee co-chair Robert C. Green, M.D., M.P.H., of Brigham and Women's Hospital and Harvard Medical School, who is leading coordination of sequencing efforts within ADNI.

Dr. Green is collaborating on the sequencing efforts with ADNI Informatics Core leader Arthur Toga, Ph.D., of UCLA and ADNI Genetics Core head Andrew J. Saykin, Psy.D., of Indiana University. The actual genome sequencing will be performed at Illumina, Inc.
HHS and the NIH Develop a New Resource Designed with the Caregiver in Mind

Easier access to information to support caregivers—HHS’ new website, www.alzheimers.gov, offers resources and support to those facing Alzheimer’s disease and their friends and family. The site is a gateway to reliable, comprehensive information from federal, state, and private organizations on a range of topics.

Visitors to the site will find plain language information and tools to identify local resources that can help with the challenges of daily living, emotional needs, and financial issues related to dementia. Video interviews with family caregivers explain why information is key to successful caregiving.

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In early August, the House Judiciary Committee reported HR 2800 – to reauthorize the Alzheimer’s Disease Patient Alert Program through FY2017. According to the Alzheimer’s Association, an estimated 5.2 million people have Alzheimer’s disease. The association reports that 6 out of 10 people with Alzheimer’s disease will wander from their homes or care facilities and as many as half of them will suffer serious injury or death if they are not found within 24 hours.

HR 2800 – legislation reported out of the House judiciary committee in August, would reauthorize the AD patient alert program and revise the program requirements to:

- Provide for competitive grants to nonprofit organizations to assist in locating missing patients with Alzheimer’s disease and related dementias;
- Expand the program to include locating other missing elderly individuals;
- Require the Attorney General to solicit grants for program applications in the Federal Register and on the Department of Justice (DOJ) website; and
- Change exclusive language to preferential language in awarding grants to national nonprofit organizations that have a direct link to patients with Alzheimer’s disease and related dementias and their families. Currently, grants may be awarded to only such organizations.

Specifically, H.R. 2800 would authorize the appropriation of $1 million annually over the 2013-2017 period for Department of Justice (DOJ) programs to locate missing persons with Alzheimer’s disease or similar conditions. Under the legislation, DOJ would provide grants to nonprofit organizations to run those programs. Assuming appropriation of the authorized amounts, the Congressional Budget Office estimates that implementing H.R. 2800 would cost about $4 million over the 2013-2017 period. Pay-as-you-go procedures do not apply to this legislation because it would not affect direct spending or revenues.

H.R. 2800 contains no intergovernmental or private-sector mandates as defined in the Unfunded Mandates Reform Act (UMRA) and would not affect the budgets of state, local, or tribal governments.

8/5/2011: Referred to the House Committee on the Judiciary

8/25/2011: Referred to the Subcommittee on Crime, Terrorism, and Homeland Security


8/1/2012: Committee Consideration and Mark-up Session Held.

8/1/2012: Ordered to be Reported in the Nature of a Substitute by Voice Vote
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.


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