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Sleep-Related Protein May be Target for Alzheimer Prevention

A protein that stimulates the brain to awaken from sleep may be a target for preventing Alzheimer’s disease (AD), a recent study suggests.

Scientists at Washington University have established links between sleep problems and AD. They have shown in people and in mice that sleep loss contributes to the growth of brain plaques characteristic of Alzheimer’s, and increases the risk of dementia.

The new research, in mice, demonstrates that eliminating a protein called orexin made mice sleep for longer periods of time and strongly slowed the production of brain plaques.

“This indicates we should be looking hard at orexin as a potential target for preventing Alzheimer’s disease,” said senior author David M. Holtzman, MD, head of the Department of Neurology. “Blocking orexin to increase sleep in patients with sleep abnormalities, or perhaps even to improve sleep efficiency in healthy people, may be a way to reduce the risk of Alzheimer’s. This is important to explore further.”

Brain plaques, which are mostly made of a protein called amyloid beta, accumulate in the brain before the onset of Alzheimer symptoms such as memory loss, personality changes and disorientation. These plaques continue to collect as the disease progresses. Scientists think that slowing or stopping this buildup could slow or stop the disease.

In the study, the researchers worked with mice genetically engineered to develop a buildup of amyloid in the brain, which is characteristic of AD. When the researchers bred these mice with mice lacking the gene for orexin, their offspring slept longer and developed only half as many Alzheimer plaques, compared with the mice that had the orexin protein.

Mice with no orexin typically slept an extra hour or more during the 12-hour period when mice with orexin became more active. When scientists reversed the experiment and artificially increased orexin levels throughout the brain, the mice stayed awake longer and developed more Alzheimer’s-like plaques.

But if the researchers changed orexin levels only in part of the brain – a change that did not affect the amount of time mice slept – plaque levels were unaffected.

“The fact that orexin can only affect plaques when it also affects sleep means we will have to think carefully about how to target it for Alzheimer prevention,” Holtzman said. “But the declines in plaque levels that we saw in the mice were very strong, so we’re still very interested in exploring its potential for reducing risk.”

Volunteers needed for Research Studies
Do you know of someone who might consider volunteering for a research project on cognitive aging?

The Memory & Aging Project of the Knight ADRC enrolls persons aged 65+, both those with mild memory problems and those who are cognitively healthy.

If you know of a potential volunteer, please ask that person to call the Knight ADRC at 314-286-2683. Thank you!
Congratulations to everyone who joined the Knight ADRC / Mallinkrodt Institute of Radiology (MIR) team for the Walk to End Alzheimer’s in August. The event, hosted by our close community partner the Alzheimer’s Association, is their largest fund and awareness raising event of the year. Alzheimer research at Washington University was represented in full force with a robust 124-member team which raised a combined $7,120. We had a wonderful morning and appreciate the time, effort, and enthusiasm of everyone involved.

Original Study Design Wins Mock Proposal Competition

Alaina Baker-Nigh, PhD, represented the Randall Bateman Lab at the Alzheimer’s Disease Fast Track workshop for postdoctoral researchers and graduate students, hosted by the BrightFocus Foundation in conjunction with the Society for Neuroscience meeting in Washington D.C. Dr. Baker-Nigh’s team won the mock grant proposal competition with an original study design “The Impact of Sleep Deprivation on AD Pathology Across the Spectrum of ApoE Genotypes.” The team had two days to prepare a project proposal appropriate for a 3-year, $500K award. The competition was judged by a panel of invited scientist speakers and foundation program officers, who found the proposal to be “legitimately fundable” and commented, “someone should do this project.” Shown right is a photo of the winning team, with Dr. Baker-Nigh 2nd from the left.

Transition Brings Change to Knight ADRC Genetics Core

After 22 years of service, Alison Goate, D.Phil departed Washington University in December. Dr. Goate was the Ludwig Professor of Genetics, Director of the Hope Center of Neurological Disorders, and Associate Director of the Knight ADRC, among other responsibilities.

Dr. Goate led the Knight ADRC genetics core since 1992 and was, as highlighted by Center Director John C. Morris, MD, “one of our most honored faculty in recognition of her internationally acclaimed contributions to the understanding of genetic factors underlying AD.”

Dr. Goate accepted a position in New York City at the Icahn School of Medicine at Mt. Sinai where she will set up a new center on Alzheimer disease and related disorders. Says Morris, “her departure will be felt deeply by us all.”

Dr. Goate will continue to be engaged in many collaborations at WU and remains as the Leader of DIAN’s Genetics Core. Moreover, her legacy will continue as her former mentee, Carlos Cruchaga, PhD, assumed leadership of the Knight ADRC Genetics Core.

Everyone at the Knight ADRC wishes the best for Drs. Goate and Cruchaga in their new positions.
Awards, Honors and Funding

The Knight ADRC, under the leadership of John C. Morris, MD, was awarded funding for the next 5 years of the Healthy Aging and Senile Dementia grant. The funding is provided by the National Institute on Aging and will cover years 31-35 of the project—a remarkable track record. Congratulations also to the faculty and staff of the Dominantly Inherited Alzheimer Network (DIAN) upon the successful funding of another 5 years of the DIAN study.

Andrew Aschenbrenner, doctoral student in the Cognitive Psychology Lab of Dr. Dave Balota, is the recipient of the 2014 Polotsky Award for accomplishments and contributions to the field of aging and dementia. Aschenbrenner was also an Alzheimer’s Association International Conference Student Poster Competition Finalist in Copenhagen in July.

David Balota, PhD received the 2014 Arthur Holly Compton Faculty Achievement Award. Dr. Balota is known for his work on the role of attentional control systems in memory, language, and age-related changes in cognition.

Matt Brier, Medical Scientist Training Program student in the Beau Ances Lab, won the 2015 Young Investigator Award at the Human Amyloid Imaging meeting in Miami.

David Carr, MD was awarded the Franz U. Steinberg Award for Teaching Excellence and was installed as the Alan A. and Edith L. Wolff Professor of Geriatric Medicine and Professor of Medicine and Neurology.

David Clifford, MD was honored with the Washington University School of Medicine Humanism in Medicine Award, as voted by current medical students. The award honors a faculty physician who exemplifies personal ethics, empathy, and service—essential qualities in the practice of patient-centered medicine.

Gregg Day, MD, MSc was selected to receive the 2015 Eugene M. Johnson, Jr. Weston Brain Institute Postdoctoral Fellowship.

Ida Goodwin Woolfolk, Chair of the Knight ADRC African American Advisory Board, was honored with the Community Leadership Award in January at the Saint Louis University Dr. Martin Luther King, Jr. Memorial Tribute.

Nupur Ghoshal, MD, PhD received a Biological Sciences Minority Investigator Travel Award from the Gerontological Society of America and presented “Alzheimer Disease: Through the Tau Looking Glass” at the November 5–9, 2014 meeting in Washington, DC. Ghoshal was also honored with the 2014 Outstanding Young Alumni Award by The Iowa State University.

David Holtzman, MD has been named a fellow of the American Association for the Advancement of Science (AAAS), the world’s largest general scientific society. The rank of fellow is the highest honor awarded by AAAS in recognition of distinguished efforts to advance science or its applications. Holtzman was awarded the Outstanding Scientific Achievement Award by the Sleep Research Society and elected to the National Alzheimer’s Coordinating Center Steering Committee for a 3-year term.

Phil Hsu, member of the Knight ADRC Imaging Core, was the 3rd place winner in the 2014 Society for Nuclear Medicine and Molecular Imaging Young Investigator Competition for his project “Longitudinal Amyloid Deposition is Associated with Changes in Cortical Thickness and White Matter Integrity in Cognitively Normal Adults.”

Jin-Moo Lee, MD, PhD received the Foundation for Barnes Jewish Hospital President’s Achievement Award.

Congratulations to Richard Perrin, MD, PhD and Erik Musiek, MD, PhD who have been elected to the National Alzheimer’s Coordinating Center Scientific Review Committee. They will replace, in part, outgoing committee member Nigel Cairns, PhD.

Suzanne Schindler, MD, PhD received a Washington University School of Medicine Building Interdisciplinary Research Careers in Women's Health Program grant. The grants support the career development of junior investigators who show exceptional promise for a career that will benefit the health of women.

Norman R. Seay, member and founding board chair of the African American Advisory Board, received the Rosa L. Parks Award for Meritorious Service to the Community during the 28th Annual Martin Luther King, Jr. Commemoration at Washington University.

B. Joy Snider, MD, PhD was elected Vice Chair of the Geriatric Neurology Section of the American Academy of Neurology.

Susan Stark, PhD was awarded a 3-year, $724,000 grant from the U.S. Department of Housing and Urban Development to study the effectiveness of home hazard removal to improve home fall protection for old adults.

A new report from Thomson Reuters’ Science Watch named David Holtzman, MD, John C. Morris, MD, and Marcus Raichle, MD among the most influential scientists in the field of neurology by analyzing citation data over the past 11 years to identify those who published work with the highest impact.

David Carr, MD (center) with John C. Morris, MD (left) and Lucy Morris, MD (right) at Carr’s installation as the Wolff Professor of Geriatric Medicine in August.
Accelerating Research with Charitable Contributions

Making a charitable contribution to Washington University School of Medicine to support the Knight ADRC in our research mission is an important decision – one that reflects your support of the fight against AD as well as your personal philanthropic and financial goals. Your generosity provides critically needed resources to continue our research and accelerate the pace at which we can develop promising new drugs and treatments that may aid in the prevention of Alzheimer dementia. If you would like to learn more about making a gift to support AD research, please contact Jennifer Phillips at 314-286-2882 for more information.

Inclement Weather at the Knight ADRC

Living in the midwest, St. Louis-area residents are used to the twists and turns our local weather can take. Winter snowstorms can be quickly followed by 65 degree days in a matter of weeks. No matter the weather, don’t hesitate to schedule your annual MAP assessment if it falls during the winter season. Knight ADRC faculty and staff are committed to the safety and comfort of our volunteers, and we work hard to ensure your visit is safe and smooth. The Knight ADRC offers close, convenient, and free parking right in front of our building. Or, our staff can work with you to schedule alternate transportation such as a cab when coming for your annual assessment. Washington University maintains a rigorous plowing and salting regimen to ensure parking lots are clear for pedestrians. If you have any questions or concerns, please call us anytime at 314-286-2683 and we will be happy to help!

New Team Members

Tiffany Earle – Memory and Aging Project Secretary
Jennifer Fisher Eastep, MA, CSP – Memory and Aging Project Psychometrician
Laura Swisher – DIAN-TU Research Coordinator

Fond Farewells

Davis Ryman, MD, PhD, Knight ADRC Fellow working in the DIAN Trials Unit, accepted an offer from AbbVie, a Chicago-based global biopharmaceutical company, to join their AD early clinical development team.
David Ruvolo, MA – Left his role as MAP Psychometrician to begin graduate study at Oxford University in England.

Neurology Funding Strong at WU

The Blue Ridge Institute for Medical Research recently released 2014 funding totals from the National Institutes of Health awarded to schools of Medicine and their Departments. Washington University School of Medicine ranks 4th in NIH awards. Three Knight ADRC investigators ranked in the top 25 of federally funded investigators in Neurology including John C. Morris, MD (#1), Randall Bateman, MD (#5), and David Holtzman, MD (#25).

Faculty and Staff Updates

Randall Bateman, MD – promoted to Charles F. and Joanne Knight Professor of Neurology.
Tammie Benzinger, MD, PhD – promoted to Associate Professor of Radiology.
David Carr, MD – stepped away from research assessments at the Memory and Aging Project, but will remain at the Knight ADRC as the African American Outreach Core Leader, and will continue to evaluate patients in the Memory Diagnostic Center and in his private geriatric practice.
John Cirrito, PhD - promoted to Associate Professor of Neurology.
David Holtzman, MD – appointed new Director of the Hope Center for Neurological Disorders in September, 2014. Dr. Holtzman played an integral role in creating the Hope Center in 2004 as a collaborative alliance between Hope Happens and Washington University, and he has been an active member of the Hope Center steering committee since its founding.
Doris Jones - recognized for 15 years of service to Washington University.
Renee Labarge - promoted to Clinical Research Study Assistant in the Memory and Aging Project.

Who is that masked man? Dr. John C. Morris was up bright and early during the January, 2014 snowfall to ensure the walkways were clear and secure for faculty, staff, and research volunteers.

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With the aging of the population, more people are likely to know someone who has been diagnosed with Alzheimer’s disease.

Alzheimer’s slowly causes changes in how people think, talk and take care of themselves. While forgetfulness and loss of memory often are the first and most obvious signs, people with Alzheimer’s also experience loss of meaningful roles and responsibilities, diminished activities and fading social relationships.

With support and encouragement from family and friends, people with Alzheimer’s can continue to live fulfilling lives.

It is important that family and others do not minimize or dismiss the significance of what is happening to the individual. Rather, allow the person to talk about what he or she is experiencing and feeling.

Let the person know that you care by really listening — without interruption, advice giving, criticism or correction. Learn to be patient as it may take a person with Alzheimer’s longer to think about and say what is on his or her mind. It’s OK to cue someone if a thought is lost or fill in missing words if he or she has difficulty speaking.

Also, pay attention to how you communicate.

Speak slowly and clearly. Use familiar words and short, simple sentences. Non-verbal gestures — nods, smiles and a gentle touch — can provide reassurance. Don’t worry that you don’t know what to say. Be understanding and accepting and talk to the person, not about the person.

Alzheimer’s touches all members of a family, including children.

Be open with children about their loved one’s memory loss. Explain symptoms in terms that are easy to understand, for example, she may forget your name; he may say things over and over.

Prepare them for changes they may see in their loved one’s personality or behavior that might cause worry, things like she may dress inappropriately; he may blame others when he loses his belongings.

Children can experience a range of emotions in response to such changes. Encourage them to talk about their feelings and to ask questions. Help them find ways they can help their loved one, such as visiting and doing activities together.

People with Alzheimer’s may find that doing things they enjoy will help take their minds off their memory problems for a while and lend purpose to their life.

When doing things together, choose familiar activities that are stimulating and make the most of their abilities. Build on previous interests, past memories, and cultural and religious traditions — a lifelong hobby or cooking favorite foods. Activities that involve family and friends provide a sense of togetherness and enhance quality of life for all.

While you cannot bring back lost memories, there are many ways you can support and nurture loved ones with Alzheimer’s.

Give them opportunities to feel useful, to be active and to have the companionship of others. Stay connected to them. Above all, treat them with respect and dignity.

Terri Hosto, MSW, LCSW is the senior social worker at the Knight ADRC and a research instructor of neurology at Washington University School of Medicine. The article first appeared in the January 15, 2015 issue of the St. Louis Post Dispatch.

Save the Date!
2015 State of the Knight Alzheimer’s Disease Research Center Lecture

Tuesday, June 23, 2015, 12:00 - 1:00 pm
Presented by John C. Morris, MD
Connor Auditorium in the Farrell Learning and Teaching Center. Everyone is welcome, and call Jennifer at 286-2882 for directions to the lecture.
HORIZONS is the newsletter of the Charles F. and Joanne Knight Alzheimer’s Disease Research Center (Knight ADRC) — a research program in the Department of Neurology, Washington University School of Medicine, funded by grants from the National Institute on Aging and private donations. The Knight ADRC supports and promotes interdisciplinary research on Alzheimer disease. The Memory & Aging Project (MAP) — the clinical research office of the Knight ADRC — provides expert clinical assessments of cognitive functioning in normal aging and dementia.

John C. Morris, MD, Director, ADRC; Director, MAP; Administration Core and Clinical Core Leader
Eugene M. Johnson, PhD, Associate Director, ADRC
David M. Holtzman, MD, Associate Director, ADRC
Virginia Buckles, PhD, Executive Director, ADRC

Krista Moulder, PhD, Associate Executive Director, ADRC
Andrea Denny, JD, MSSW, Outreach, Recruitment, and Education Core and Rural Outreach Core Leader
Jason Hassenstab, PhD, Psychometrics Leader
Nigel J. Cairns, PhD, FRCPath, Neuropathology Core Leader
Tammie Benzinga, MD, PhD, Imaging Core Leader
Chengjie Xiong, PhD, Data Management and Biostatistics Core Leader
David Carr, MD, African American Satellite Leader
Anne Fagan, PhD, Biomarker Core Leader
Carlos Cruchaga, PhD, Genetics Core Leader

Watch Your Mailbox! Invitations are coming soon for the Annual Memory & Aging Project Participants’ Breakfast Meeting on May 30, 2015.