SPRING/SUMMER 2014

We humans have lost the wisdom of genuinely resting and relaxing. We don't allow our bodies to heal, and we don't allow our minds and hearts to heal.

— Thich Nhat Hanh

aging news

NEWSLETTER OF THE INSTITUTE ON AGING (IOA) | UNIVERSITY OF WISCONSIN-MADISON

IN THIS ISSUE:

institute on aging

2245 Medical Sciences Center
1300 University Avenue
Madison, WI 53706
608.262.1818
www.aging.wisc.edu

Reducing Reactions to Minor Stressors Can Benefit Future Health

Researchers often focus on how major life stressors, such as loss of a job or spouse, can affect our mental health. Few studies have questioned whether the minor hassles of daily living can also wear us out. A recent MIDUS study was the first to focus on whether daily stress can affect our mental health ten years later.

Participants reported whether they experienced minor stressors, such as traffic jams, work overloads, or arguments over household chores, during eight consecutive days at Time 1. They also reported daily negative affect through responses to questions such as how often they felt sad, restless, nervous, worthless, or hopeless. Levels of negative affect were compared on days with stressors vs. days without, to assess the extent to which participants reacted emotionally to stressors, known as affective reactivity. Levels of reactivity were compared to participants' mental health ten years later, at Time 2.

Results showed that those with higher affective reactivity at Time 1, who felt worse in response to daily stressors, experienced more emotional distress at Time 2, measured by levels of negative affect over the prior month. Reacting more negatively to stressors at Time 1 was also associated with increased reports of experiencing or receiving treatment for anxiety, depression, or another emotional disorder ten years later.

If your teeth are clenched and your fists are clenched, your lifespan is probably clenched.

— Terry Guillemets

A parallel MIDUS study showed that being more troubled by daily stressors was also associated with having more chronic physical health conditions (such as heart disease or diabetes) ten years later. Taken together, these results suggest that Nietzsche's adage, "That which does not kill us makes us stronger," may not be true. It is not only major life tragedies that appear to affect our health, but also the wear and tear of daily life. Results suggest that if we overreact to relatively minor daily hassles, it may negatively effect our health and well-being ten years later.

Sources: *Charles, S. T., Piazza, J. R., Mogle, J., Sliwinski, M. J., & Almeida, D. M. (2013). The wear and tear of daily stressors on mental health. Psychological Science, 24(5), 733-741. doi:10.1177/0956797612462222* and *Piazza, J., Charles, S., Sliwinski, M., Mogle, J., & Almeida, D. (2013). Affective reactivity to daily stressors and long-term risk of reporting a chronic physical health condition. Annals of Behavioral Medicine, 45(1), 110-120.*

Can a Questionnaire Predict Vitamin D Levels?

IOA Affiliate **Karen Hansen** (Assoc. Prof., Dept. of Medicine- Rheumatology, UW-Madison) coauthored a recent study that evaluated the effectiveness of a questionnaire to identify people with vitamin D insufficiency. Low vitamin D levels are common in Americans, especially among postmenopausal women, and can contribute to osteoporosis, low bone mineral density, and bone fractures. Blood tests for vitamin D, however, are expensive and routine screening is not recommended for all individuals.

The authors developed the *Vitamin D & Sun Questionnaire* and administered it to 609 post-menopausal women, 113 of whom were vitamin D-insufficient based on blood test results. Six variables from the questionnaire (listed in the table below) significantly predicted low blood levels of vitamin D. Unexpectedly, *not* using sunscreen predicted low vitamin D, even though sunscreen blocks the sunlight that promotes our skin's production of vitamin D. The authors suggested that those who use sunscreen are outside more often, so still may get more sun exposure.

Exposure to sunlight is our primary source of vitamin D.

A score of ≤ 2.25 on the questions below was 89% accurate in predicting low levels of vitamin D among postmenopausal women.

Vitamin D & Sun Questionnaire		Score
1. Body Mass Index (kg/m2)	BMI ≤ 28.0	1
	BMI > 28.0	0
2. Ethnic background	Black	0
	Other	1
3. Have you received a sun tan in the last 12 months?	Yes	1
	No	0
4. In the last 3 months, how often were you in the sunlight while lightly dressed?	Regularly	2
	Occasionally	1
	Never	0
5. How often do you apply sunscreen when going outside?	Always	1
	More often than not	.75
	Sometimes	.50
	Infrequently	.25
	Never	0
6. Do you take a vitamin D supplement?	Yes > 400 IU per day	1
	Yes ≤ 400 IU	0
	No	0

Having dark skin also predicted low vitamin D, because it too blocks sunlight. Questions not predicting vitamin D level included consumption of milk, fish, and cod liver oil (all rich in vitamin D).

A score of 2.25 or less on the six questions provided an 89% sensitivity for vitamin D insufficiency, suggesting that blood tests would be most cost-effective for postmenopausal women with a score in this range. The authors recommend additional studies in other populations, to create a reliable tool to aid clinicians in decisions about when to order costly vitamin D blood tests for their patients.

Source: *Nabak, A. C., Johnson, R. E., Keuler, N. S., & Hansen, K. E. (2014). Can a questionnaire predict vitamin D status in postmenopausal women? Public Health Nutrition, 17(04), 739-746. doi:10.1017/S1368980013001973*

26th Annual Colloquium on Aging

Keynote

The Day-to-Day Management of Chronic Illness: How Family Members Help and (Sometimes) Hinder

Karen D. Rook, PhD

Professor, Psychology and Social Behavior, University of California- Irvine

Managing a chronic illness often requires people to initiate and maintain changes in their health behaviors for extended periods of time, and adherence can be difficult. Not surprisingly, family members frequently seek to participate in patients' day-to-day illness management, but such involvement can have mixed effects. Some forms of family involvement may benefit patients' adherence and, in turn, their health outcomes. Other forms of family involvement may be ineffective or may succeed, but with unwanted side effects. This talk will discuss, and offer practical suggestions from, recent studies about helpful and unhelpful aspects of family members' involvement in patients' chronic illness management.

Aging Parents as Caregivers to Adult Children with Serious Mental Illness: Patterns of Vulnerability and Resiliency

Jan Steven Greenberg, PhD

Professor & Director, School of Social Work, UW-Madison

With the aging of the population and the shift to community care for persons with disabilities, an increasing number of parents face their retirement years with the responsibility of caring for an adult child with a major mental illness. While for some parents, this major life challenge takes a toll on their health, others find their lives transformed in positive ways. This presentation will focus on what is known about why caring for a son or daughter with a mental illness has a wear and tear effect on some aging families and for others, it leads to patterns of resiliency.

The March of Longevity: the Role of Genes, Behavior, Environment, and the Microbiome

Alberto Palloni, PhD

Samuel H. Preston Professor of Population Studies
Department of Sociology, UW-Madison

Life expectancy has increased steadily over the last one hundred years in most high income countries and is considered one of the most important achievements of *Homo sapiens*. We know quite well the factors that explain this change, but know less about whether or not it will be sustained or for how long. The road ahead is bumpy with potentially serious threats, including hard limits to continued increases in survival; the negative momentum of generations who experience smoking, obesity, and metabolic disorders; and the threat of climate change. This talk will review past achievements in survival, assess future risks, and discuss the possibilities opened by advances in our knowledge of the human genome & microbiome.

The Caloric Restriction Paradigm: Implications for Healthy Human Aging

Rozalyn Anderson, PhD

Assistant Professor, Department of Medicine, SMPH, UW-Madison
Health Science Officer, GRECC, Middleton Memorial Veterans Hospital

Aging itself is the most significant risk factor for a range of the most prevalent diseases including many cancers, cardiovascular disease, diabetes, and neurodegenerative disorders. Accordingly, interventions are sorely needed to help delay or prevent diseases/disorders associated with the aging process and thereby increase the period of time that aging individuals are in good health. Caloric restriction (CR) is widely agreed to be the most potent environmental intervention that delays the onset of aging and extends life span. A better understanding of CR will permit the development of novel treatments and preventive measures for age-associated conditions.

Health & Resource Fair

Resources to Improve Quality of Life:

Social & Educational Programs
Support for Independent Living
Volunteer Opportunities
Legal & Legislative Advocacy
Retirement Communities
Osteoporosis Screening
Blood Pressure Testing
Alzheimer's Treatment
Swallowing Disorders
Fitness & Nutrition

Poster Session

Meet with UW-Madison faculty, students, and trainees presenting recent aging research.

New Investigator Awards

Awarded to new UW-Madison researchers in recognition of outstanding aging research.

Details

Sponsored by the Institute on Aging. CEUs will be offered. Registration should open the first Monday in August (8/4/14) when the registration brochure is mailed out. If you are not on the mailing list, sign up via our website, or contact:
(608) 262-1818
aging@ssc.wisc.edu

Space is limited & fills up fast. When registration opens, we announce it first on our website:

aging.wisc.edu

SAVE the DATE: Tuesday, Sept. 30, 2014
Registration opens in August

FREE & OPEN to the PUBLIC
Held at Monona Terrace in Madison, WI

affiliate news

For more information on the work of IOA Affiliated Faculty and Researchers at UW-Madison, see: *www.aging.wisc.edu/research/affilindex.php*

Aging News
Spring/Summer 2014

IOA Director
Carol D. Ryff, PhD
Professor of Psychology

IOA Associate Director
Neil Binkley, MD
Professor of Medicine-Geriatrics

Aging News
Editing & Layout
Theresa Berrie
berrie@wisc.edu

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The biggest seller is cookbooks and the second is diet books- how not to eat what you've just learned how to cook.

— Andy Rooney

Studies Differ on Whether Dieting Promotes Longevity

Two long-term studies to determine whether restricting caloric intake can help humans avoid aging-related diseases and live longer have come to different conclusions. Several IOA Affiliates have been involved in a study that began in 1989 at the Wisconsin National Primate Research Center. They reported in 2009 that the rhesus monkeys in their research who did not have a restricted diet had a 2.9 increased chance of disease, and were three times more likely to die, than those eating a restricted diet with 30% less calories. In contrast, results from a similar study at the National Institute of Aging (NIA), published in 2012, showed no improvement in survival rates for their caloric restriction (CR) monkeys, whose rate of improved health did not reach statistical significance.

Wisconsin researchers suggest that the reason no difference was found between the non-dieting control & CR monkeys in the NIA study is because the control monkeys were also essentially on a calorie restricted diet. Whereas the Wisconsin control monkeys were allowed to eat as much as they wanted of a processed diet that was 29% sugar (mimicking American eating habits), the NIA control monkeys were fed fixed portions of a comparatively healthy diet of natural, whole foods that contained only 4% sugar. The NIA control monkeys were underweight compared to national standards, and one of them reached the maximum age for rhesus monkeys in captivity (40 years). This may mean that even the small caloric restriction in the NIA control animals' diet had its own advantages, suggesting that a caloric reduction of as little as 10% could retard aging.

Although some people join the Caloric Restriction Society, most others could not likely tolerate reducing their calories by 30%. IOA Affiliate **Rozalyn Anderson** (Asst. Prof., Dept. of Medicine-Geriatrics, UW-Madison) points out: "We are not studying [CR] so people can go out and do it….It's a research tool, not a lifestyle recommendation." They are trying to understand why aging is associated with an increased risk of disease. By discovering how CR delays aging, new treatments may be uncovered. Already outside drug companies are working to develop medicines that mimic CR.

Both studies cost millions of dollars and have taken decades to perform. At first glance the different results may seem disappointing, however, comparisons between the studies may be more informative than results from either study alone. It is clear that diet and diet composition play a role in aging and disease, the challenge now is to figure out how this occurs. Scientists from both groups are working together to analyze their combined data, taking into consideration the differences in their study design. Join us at the IOA Colloquium this Fall to learn more (see p. 3).

Sources: *Colman, R. J., Beasley, T. M., Kemnitz, J. W., Johnson, S. C., Weindruch, R., & Anderson, R. M. (2014). Caloric restriction reduces age-related and all-cause mortality in rhesus monkeys. Nature Communications, 5, Article 3557. doi:10.1038/ncomms4557* and *Mattison, J. A., Roth, G. S., Beasley, T. M., Tilmont, E. M., Handy, A. M., Herbert, R. L., . . . de Cabo, R. (2012). Impact of caloric restriction on health & survival in rhesus monkeys from the NIA study. Nature, 489(7415), 318-321. doi:10.1038/nature11432*

welcome new affiliates

Barbara B. Bendlin • **Assistant Professor**
Dept. of Medicine- Geriatrics & Adult Development
Focus: Identifying early brain changes in Alzheimer's Disease.

Dudley W. Lamming • **Assistant Professor**
Dept. of Medicine- Endocrinology, Diabetes, and Metabolism
Focus: Targeting the role of mTOR in the aging process in order to prevent aging-related diseases such as diabetes and Alzheimer's.

The P44 Gene Affects the Mental Decline Associated with Aging

Recent research has shown that the p53 gene, which is best known for its role in suppressing tumors, has four different forms, one of which is the shortened, naturally occurring p44 form that is believed to play a role in aging and Alzheimer's disease (AD). Mice engineered to have more p44 ($p44^{+/+}$) show accelerated aging, abnormal phosphorylation of the tau protein (a protein that maintains the shape of the brain's nerve cells), synaptic defects that affect communication between nerve cells in the brain, and premature mental decline. It is currently unclear how increased levels of p44 in the mouse brain leads to these defects. A recent article coauthored by IOA Affiliate **Luigi Puglielli** (Assoc. Prof., Dept. of Medicine-Geriatrics, UW-Madison) sought to clarify the molecular mechanisms responsible for the abnormal phosphorylation of tau in $p44^{+/+}$ mice in order to reveal its possible role in aging and Alzheimer's disease.

Phosphorylation involves the addition or removal of phosphates from proteins, which is key to regulating cellular metabolism. The authors demonstrated that the phosphorylation of the tau protein happens before its associated synaptic deficits. They then focused on specific tau kinases (enzymes Dyrk1A, GSK3β, and Cdk5) that can phosphorylate tau in live mouse brains. After eliminating other possibilities (IGF-IR and p75NTR signaling), they investigated whether p44 could act directly to activate tau kinases and result in more phosphorylation, either alone or by interacting with full-length p53. A series of tests (that included ChIP, DNA:protein pull down, and luciferase assays) resulted in the conclusion that the activation of the Dyrk1A, GSK3β, CDK5P35 and CDK5P39 enzymes observed in $p44^{+/+}$ mice is directly dependent on the activity of p44 and/or a combination of the p44 and p53 genes.

Researchers further showed that p44 increases significantly as a result of normal aging in mice and is accompanied by a parallel increase in the kinases that phosphorylate tau. As aging is the most important risk factor for Alzheimer's, p44 would need to increase with age in order for it to trigger the tau phosphorylation that is associated with AD. When tau is hyperphosphorylated, it tends to clump into the neurofibrillary tangles that are seen in AD.

During aging, a large segment of the human population will experience some degree of cognitive decline. Postmortem studies have shown that brain aging in humans is also accompanied by progressive accumulation of hyperphosphorylated tau. The severity of tau alterations seems to increase inexorably through the aging process and is also observed in people affected by Alzheimer's. The above findings indicate that p44 might be involved, at least in part, with the abnormal phosphorylation of tau and the increased propensity to the cognitive decline that characterizes human aging. The possible association with AD remains to be more fully explored.

Source: *Pehar, M., Ko, M. H., Li, M., Scrable, H., & Puglielli, L. (2014). P44, the 'longevity-assurance' isoform of p53, regulates tau phosphorylation and is activated in an age-dependent fashion. Aging Cell. Advance online publication. doi:10.1111/acel.12192*

When I was 40, my doctor advised me that a man in his 40s shouldn't play tennis. I heeded his advice carefully and could hardly wait until I reached 50 to start again.

— Hugo L. Black

IOA affiliate grants & honors

Affiliate **Luigi Puglielli** (Assoc. Prof., Dept. of Medicine- Geriatrics) has been invited to serve as a member of the **Cellular Mechanisms in Aging and Development Study Section** at the **Center for Scientific Review**. Members are selected on the basis of achievement in their scientific discipline and are responsible for reviewing grants submitted to the National Institutes of Health. Prof. Puglielli will serve on the study section from July 2014 to June 2018.

Affiliate **Ozioma Okonkwo** (Asst. Prof., Dept. of Medicine-Geriatrics) has received a **New Investigator Research Grant to Promote Diversity** from the **Alzheimer's Association**. His research group will be piloting an intervention to understand whether aerobic exercise can help delay cognitive and brain changes in middle-aged adults with a parental history of Alzheimer's disease.

Affiliate **Dawn Belt Davis** (Asst. Prof., Dept. of Medicine- Endocrinology) recently presented her research on diabetes risk and aging at meetings of the **American Federation for Medical Research** in Washington DC and Chicago, where she was awarded the **Junior Physician Award**. This award is given to honor only one or two young investigators nationally, who have held a faculty appointment for five or fewer years, and whose research projects complement an overall program of research, teaching, and clinical medicine.

new findings from MIDUS

MIDUS
Midlife in the United States

MIDUS studies aging as a long-term journey involving multiple factors (psychological, social, biological). It began in 1995 with over 7000 participants, aged 25-74, and continues with follow-up studies at 10 year intervals. Over 550 publications have utilized MIDUS data. They are archived at: midus.wisc.edu/findings

Gratitude bestows reverence, allowing us to encounter everyday epiphanies, those transcendent moments of awe that change forever how we experience life and the world.

— John Milton

Do Daily Spiritual Experiences Promote Helping Others?

Studies have shown a link between being religious and helping others. Researchers, however, disagree on the reason for this association. Sociologists focus on external behavioral aspects, believing that social networks in religious communities tend to encourage helping behaviors, whereas psychologists focus on internal aspects, such as that religious beliefs promote a sense of duty to help others. Some argue that external religiosity is more important, because certain findings show that internal factors do not predict helping when behavioral factors are taken into account. A recent MIDUS study used a new measure of spirituality to shed light on this debate. The Daily Spiritual Experiences Scale (DSES) assesses an aspect of spirituality not measured by earlier religious scales. Even if people don't consider themselves conventionally religious, or don't believe in God, the DSES allows them to report having experiences of transcendence, or spiritual connections to people or nature.

Links between the DSES and the prosocial helping behaviors of 1490 MIDUS respondents were analyzed. The DSES asks how often a person experiences, on a daily basis, feelings of deep inner peace or appreciation, of being deeply moved by the beauty of life, a strong connection to all of life, or a profound sense of caring for others. Prosocial behaviors included formal helping, such as volunteering or donating money to charitable organizations, and informal helping directed toward individuals, such as providing labor, financial assistance, or emotional support to close family members, moderately close others (friends and more distant relatives), and distant others (neighbors, people at church, or strangers on the street).

Results showed that daily spiritual experiences were significantly associated with helping behaviors and suggested two reasons for the link. Measures of sympathy ("I am moved when I hear of another person's hardship") did not explain the connection, but measures of mindfulness ("being more sensitive to the feelings of others") did. This may mean that daily spiritual experiences promote helping not through the development of sympathy for another's suffering, but by increasing the likelihood that we will *notice* their suffering.

Daily spiritual experiences can also affect helping behaviors by promoting a sense of moral extensivity. People whose spiritual experiences promote a feeling of connection to all life may feel morally obligated to all of humankind, instead of to just family and friends, and thus have a more extensive definition of their moral community. This is supported by the fact that the DSES better predicted help to distant others (such as strangers) than to friends or family.

These results underscore the importance of psychological factors in explaining why religion and spirituality are linked to helping others. The inclusion of other religious variables did not affect the relationship between the DSES and helping, with the exception of meditation, prayer, and mindfulness, which are similar to the DSES in that they are measures of internal religiosity. The private nature of daily spiritual experiences supports the view that internal religious life plays a significant role in our motivation to help others, separate from the external behavioral motivations that might come from being part of a religious community.

Source: *Einolf, C. J. (2013). Daily spiritual experiences and prosocial behavior. Social Indicators Research, 110(1), 71-87. doi:10.1007/s11205-011-9917-3*

Compensating for Everyday Memory Problems

It is not known whether memory declines, assessed by cognitive tests, are associated with greater memory problems in everyday life. It may be that poor performance on memory tests does not inevitably lead to daily memory problems due to use of adaptive behaviors that help with age-related losses, such as selective optimization with compensation (SOC) strategies. SOC strategies involve restricting activities to those that are most important. This selection can be elective, such as choosing to concentrate on work instead of hobbies, or loss-based, such as cutting back on hours at work and spending more time with family after an illness. Optimization strategies in SOC refer to employing extra effort to better achieve the goal selected. SOC compensation strategies involve using alternative means to achieve a goal you can no longer accomplish, such as seeking help with household chores if mobility is limited, or using an automated system to help remember medications.

Likewise, believing one has control over the possible outcomes in life is associated with better performance on memory tests, but has not been studied in association with daily memory problems. Those with a low sense of control may be more inclined to perceive aging-related memory changes as inevitable, and make no attempt to address them, whereas those with a higher sense of control may be more likely to use SOC strategies to help their memory performance.

A recent study addressed these issues with data from 103 participants of the Boston Longitudinal Study, a subset of MIDUS. Participants' working memory decline was measured using memory tests (repeating a span of digits forward & backward, and counting backwards by subtracting sevens) given in 1995 and ten years later (at Time 2). Time 2 also included a 12-week diary study that measured eleven kinds of everyday memory problems, such as how many days each week participants had started to do or say something and then forgotten what it was, or how many times they had forgotten why they went into a room. Fluctuations in weekly perceived control were measured via diary entries about how much a person felt in control of their life that week. Overall perceived control was measured at Time 2 with questions such as "I can do just about anything I really set my mind to," vs. "What happens in my life is often beyond my control." SOC strategies were measured through questions such as, "I always focus on the one most important goal at a given time" (elective selection), "When I can't do something important the way I did before, I look for a new goal" (loss-based selection), "If something matters to me, I devote myself fully and completely to it" (optimization), and "When things don't go as well as they used to, I keep trying other ways until I can achieve the same result" or "...I ask others for advice or help" (compensation).

Results showed that greater declines on memory test scores over the ten year period were associated with significantly more daily memory problems at Time 2. Overall perceived control, but not its weekly fluctuations, also predicted having a greater daily memory problems. However, during weeks of low perceived control, participants with greater working memory declines reported fewer daily memory problems if they used more SOC strategies. These results indicate that interventions that improve perceived control and encourage the use of selective optimization with compensation strategies may benefit those with memory problems.

Source: *Hahn, E. A., & Lachman, M. E. (2014). Everyday experiences of memory problems and control: The adaptive role of selective optimization with compensation in the context of memory decline. Aging, Neuropsychology, and Cognition. Advance online publication. doi:10.1080/13825585.2014.888391*

I have a memory like an elephant. I remember every elephant I've ever met.

— Herb Caen

Employment Affects Our Health & Happiness

A new MIDUS newsletter focuses on research about working Americans. The quality of our jobs & how work demands interact with family responsibilities have been shown to influence many aspects of our lives, including our health and happiness, although income seems to be only loosely tied to our overall satisfaction with life. Read the newsletter for more details at:

www.midus.wisc.edu/newsletter

institute on aging
University of Wisconsin–Madison
Room 2245 Medical Sciences Center
1300 University Ave.
Madison, WI 53706-1532

www.aging.wisc.edu
aging@ssc.wisc.edu
(608) 262-1818

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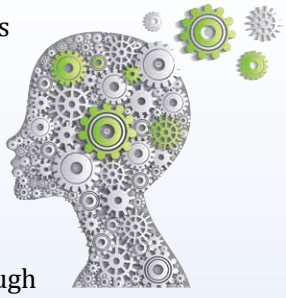
Age is like the newest version of a software-
it has a bunch of great new features,
but you lost all the cool features
the original version had.

— Carrie Latet

Does Diabetes Increase Risk for Alzheimer's Disease?

Type 2 diabetes, the risk for which increases with age, is characterized by insulin resistance and elevated glucose (sugar) levels. Insulin resistance affects the cell's ability to respond to insulin, the hormone that regulates the blood glucose that supplies our cells with energy. Insulin resistance has also been linked to risk of Alzheimer's disease (AD). Autopsies have shown that it is associated with an increase of the amyloid plaques that accumulate in the brains of people with AD. Several IOA Affiliates from the UW-Madison Wisconsin Alzheimer's Disease Research Center (**Profs. Sterling Johnson, Mark Sager, Sanjay Asthana, Barbara Bendlin**) were among the first to study the association between insulin resistance and amyloid plaques in living humans.

Study participants were from the Wisconsin Registry for Alzheimer's Prevention (WRAP), many of whom have a family history of AD. Fasting blood tests measured insulin resistance (via HOMA-IR) and blood glucose levels in 186 cognitively normal, late middle-age adults. Participants also underwent Pittsburg Compound B (PiB) Positron Emissions Tomography to scan for amyloid deposits in three regions of the brain that are affected by AD (the frontal, parietal, and temporal regions).



Results showed that in participants with normal blood glucose levels, higher insulin resistance corresponded to higher PiB uptake in frontal and temporal brain regions, reflecting increased amyloid deposits. This was not true for those with elevated glucose, although this result may reflect the relatively few research participants who had high glucose levels.

This study is the first human investigation to show that insulin resistance may contribute to the amyloid deposits believed to play a major role in AD. Although there is wide variation in the amount of amyloid plaques present in brains of aged adults, the elevated deposits found among these cognitively normal subjects, who are at risk for AD and just beginning to show an amyloid burden, indicate that interventions to reduce insulin resistance may be important to study as a route to reducing amyloid deposits, thereby helping to prevent Alzheimer's.

Source: *Willette, A. A., Johnson, S. C., Birdsill, A., Sager, M. A., Christian, B., Baker, L., . . . Bendlin, B. B. (in press). Insulin resistance predicts brain amyloid deposition in late middle-aged adults. Alzheimer's and Dementia.*