Predicting Alzheimer’s 20 Years in Advance of Symptoms

IOA Affiliates Mark Sager (Prof., Geriatrics, UW-Madison) and Sterling Johnson (Assoc. Prof., Geriatrics, UW-Madison) presented two studies at the July International Conference on Alzheimer’s Disease in Hawaii. Both studies, involving the TOMM40 gene that was recently identified by Duke University Medical Center researchers, provide hope for early diagnosis of Alzheimer's.

Dr. Mark Sager studied 726 middle aged people from the Wisconsin Registry for Alzheimer’s Prevention who had a family history of Alzheimer’s. Of these, 129 had the low risk version of the TOMM40 gene and 229 had the high risk version. Results showed that healthy, middle aged people who had the high risk version of TOMM40 did significantly worse on tests of memory and learning than the group with the low risk gene. The problems exhibited by the high risk group were similar to changes seen in very early Alzheimer’s, allowing researchers to find evidence of the disease at least 20 years before any outward symptoms would be noticed.

In a second study, Prof. Sterling Johnson found that healthy, middle-aged adults with the high risk gene had a significantly reduced brain volume in a region of the brain known to be affected early in the course of Alzheimer’s disease. Brain imaging showed that the posterior cingulate area of the brain was significantly different among those who had the high risk version of the TOMM40 gene. This represents a possible neurosignal indicating risk for Alzheimer’s that can also be seen two decades in advance of showing outward symptoms.

Alzheimer’s is a disease that develops over the long term, and it is only after decades that the brain begins to fail. If people who are at risk can be identified in the disease’s early asymptomatic stages, then interventions can be developed to delay the onset of symptoms and slow the progression of the disease.

These findings will soon be published in the journal Alzheimer’s Disease and Dementia. For more details, see the link under “Highlighted Research” at the bottom of the IOA homepage (www.aging.wisc.edu) or go directly to: uwhealth.org/news/uw-researchers-discover-possible-way-to-predict-alzheimers-before-symptoms-develop/28017
Aging News
Fall/Winter 2010
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Aging News is the bi-annual newsletter of the UW-Madison Institute on Aging (IOA), where we are jointly focused on research addressing the problems and the potential of aging.

Subscriptions are free. Join our mailing list & view our back issues at: aging.wisc.edu/publications/newsletter.php

Aging News

Nonhuman Primate Aging Research

IOA affiliate Rozalyn Anderson (Asst. Prof., Dept. of Medicine, UW-Madison) was recently awarded an R01 grant from the National Institutes of Health/ National Institute on Aging. Dr. Anderson’s work focuses on nonhuman primate research involving the anti-aging regimen of caloric restriction (CR), which involves an approximately 30% reduction in calorie intake while avoiding malnutrition. Importantly, CR has been shown to prevent or delay the onset of numerous age-associated diseases including diabetes, cancer, and heart disease. Dr. Anderson’s R01 study, “Metabolic Regulators in Caloric Restriction,” probes the mechanisms by which CR can impact the complex process of aging, and will investigate the key molecules coordinating its anti-aging properties, thus gaining a unique perspective on the aging process that could lead to new targets for treatment.

Additionally, Dr. Anderson, along with Ricki Colman (Senior Scientist, UW Primate Center), were guest editors of a special issue devoted to aging research in the scientific journal Antioxidant and Redox Signaling (currently in press). The special issue points out that the opportunity to conduct mechanistic studies to gain insights into the underlying biology of aging is limited with human subjects, and underscores instead the potential for gaining these insights through nonhuman primate models. It also promotes studies that validate novel approaches and techniques with nonhuman primates prior to their adaptation for human health care.

End-of-Life Caregiving for Lung Cancer Patients

Lung cancer is the leading cause of death from cancer in the United States, with approximately 160,000 people, most over the age of 65, dying each year. The social stigma associated with the disease, which is reported by both smokers and non-smokers alike, along with the rapidly deteriorating course of the illness and the prevalence of uncontrolled symptoms, contribute to substantial isolation and distress for both patients and caregivers. IOA Affiliate Betty Kramer (Prof., Social Work, UW-Madison) recently co-authored two articles exploring the contributing factors that make end-of-life experiences especially challenging for families. Data for the research was drawn from an ancillary study of the Assessment of Cancer Caregiver Satisfaction (ACCESS) survey in the state of Wisconsin, which assessed the end-of-life caregiving experiences of approximately 150 spouses and adult children whose family members had died from lung cancer.

The first article examined the experience of family conflict at end-of-life. Thirty five percent of caregivers reported some type of conflict that included disagreements, resentments, and/or expressions of anger among family members. Not surprisingly, families

Robert D. Blank • Assoc. Prof., Endocrinology
Focus: The genetic basis for the biomechanical performance of bone and how it contributes to bone strength or fractures.

Barry T. Radler • Researcher, Institute on Aging
Focus: Using technology to enhance social science research methods and documentation.

Shinichi Someya
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welcome new IOA affiliates

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For more information on the work of IOA Affiliated Faculty and Researchers at the UW-Madison, see: www.aging.wisc.edu/research/affilindex.php
Complicated grief symptoms were higher among those who were caring for individuals who were afraid to die, unless hospice care was utilized

with a prior history of conflict experienced higher levels of conflict during the dying process. Other significant contributing factors included communication constraints (which are commonly reported by families of patients with lung cancer), and having a family member who asserted control in the decision making process without consulting other members.

The second article examined caregivers’ “complicated grief” responses following the death of a family member. Experienced by approximately 10-20% of bereaved family members, complicated grief involves persistent challenges that interfere with daily life, such as problems fulfilling social roles, difficulty trusting people, and feeling the future holds no prospect for fulfillment without the deceased. Analysis revealed several significant predictors of complicated grief. After controlling for contextual factors and time since death, complicated grief symptoms were higher among caregivers with less history of conflict but with more conflict at the end-of-life, as well as among those who had family members who had difficulty accepting the illness, and among those who were caring for individuals who were afraid of death. Interestingly, the patient’s fear of death did not lead to complicated grief when hospice was used, but did contribute to complicated grief for those who did not receive hospice care.

These results suggest several possible implications for end-of-life care for these families. Practitioners working with lung cancer patients should routinely obtain a history of family functioning to identify families at risk for conflict, consider psychotherapeutic interventions to enhance open communication throughout the continuum of the illness, assist family members who have difficulty accepting the illness, and support patients who are afraid of death. Developing interventions to better support families during critical junctures in decision making and in the aftermath of unresolved conflict across the continuum of cancer care are important goals for research and practice. Finally, lung cancer patients, who typically underutilize hospice care, may benefit from receiving timely hospice referrals.

Sources:


Inflation is when you pay fifteen dollars for the ten-dollar haircut you used to get for five dollars when you had hair.

—Sam Ewing
The aim of MIDUS is to study successful aging as a long-term journey involving multiple factors (psychological, social, biological). The study began in 1995 with over 7000 participants, aged 25-74. Follow-up interviews, including new biological and neurological assessments, began in 2004. Over 320 publications have utilized MIDUS data. Most are archived at: midus.wisc.edu/findings

Smoking in the US increased more than five-fold between 1920 and 1960, peaked around 1966, when roughly fifty percent of men and one third of women smoked regularly, and has declined steadily since 1975. This MIDUS study examined how trends in the social acceptance of smoking have interacted with genetic tendencies toward physical addictions to predict who will smoke. Results from the analysis of MIDUS twin data showed that on average, roughly one third (35%) of the reason people smoke regularly is due to genetic factors and the remaining two-thirds influence is due to whether their social environment encourages smoking. However, trends were also found in the level of genetic vs. environmental influence depending on the year one was born.

**Those who were born between 1925 & 1935** were in their late teens and young adulthood when smoking began to emerge from a disreputable activity to one accepted among the more conventional middle-class. This trend toward increased acceptance made it easier for those who were genetically inclined to begin smoking, and thus the genetic influence was better at predicting who would smoke for those who were born during this time.

**Those born between 1936 & 1942** came of age at a time when smoking was widely accepted. Cigarettes were cheap and available everywhere, and popular images showed famous people smoking. Social motivation to smoke overwhelmed the influence of genetic characteristics, and both social smokers not genetically predisposed and genetic smokers were more likely to smoke.

**Those born between 1942 & 1954** entered adulthood as the health risks of smoking were becoming clearer. In 1964, the Surgeon General began releasing warnings about the associations between smoking, lung cancer, heart disease, and low birth rate, as well as the dangers of second hand smoke. In 1965 the Surgeon General’s warning began appearing on cigarette packs. In 1971, smoking advertisements were banned from TV and radio. However, controversy over the dangers of smoking still left individuals free to make their own choices. During this time, genetic influences were stronger and better at predicting who would continue smoking, because those with less physical dependence on nicotine would be more likely to respond to social pressures and find it easiest to quit.

**Finally, those born after 1954 through the 1960s** were socialized at a time when laws began to be passed limiting smoking in public. Arizona was the first to do this in 1973. In 1975, Minnesota passed a law requiring non-smoking sections in restaurants. It was another 12 years before Aspen, Colorado became the first city to ban all smoking in restaurants. Smoking became stigmatized and expensive. When these institutionalized policies made smoking difficult for everyone, genetic influences held less sway, and both social and genetic smokers were less likely to smoke.
These results show the importance of bringing together sociological and genetic data, and not overlooking the influence of historical trends in social environment on enhancing or suppressing genetic tendencies.

**Source:**

**Sexuality Among Older Adults**

Sexuality is important to quality of life and has been associated with health benefits and longevity. This study analyzed the relation between self-rated health and several aspects of sexuality in middle aged and older adults. Two nationally representative samples were used, both the 1995-6 wave of MIDUS with 3032 respondents aged 25-74, and the National Social Life, Health and Aging Project (NSHAP) from 2005-6, with 3005 respondents aged 57-85.

**Sexual Activity:** By age 75, only 17% of women, compared with 39% of men, were sexually active. Among respondents with a sexual partner, these differences were much smaller, but men were still more likely to have a partner. From 70 to 80% of men across all age groups reported having a partner, compared with 68% of women aged 25-54 and fewer than 40% of women aged 75 and older. This reflects the longer life span of women and the higher proportion of older men with much younger partners. Also, men were more likely than women to be married and women were more likely to be widowed. Among those who were sexually active, the proportion engaging in sex once or more a week declined across age groups, but was similar among men and women.

**Attitudes about Sex:** Among those sexually active in middle age, about two thirds reported a good quality sex life. However, in later life, only 52% of women reported a good quality sex life vs. 71% of men. Men were also more likely to report being interested in sex than women and this interest was relatively stable across all age groups and did not vary by partner status. In contrast, women’s interest in sex dropped significantly in their mid-60s and was much lower among those without partners. Interest in sex among older men has also increased since 2000. Among men aged 57-64 in the two samples who were surveyed 10 years apart, significantly more men in the later group reported an interest in sex than men of the same age surveyed 10 years earlier. This may be in part a result of the availability of medicine to treat erectile dysfunction.

**Sexually Active Life Expectancy:** Overall, the study found that men live a significantly greater proportion of their adult life sexually active (due at least in part to more years of partnership than women). Results showed that at age 55, men can be expected to be sexually active for another 15 years, but women only for another 10.6 years. However, men lose more years of sexual activity as a result of poor health than women. This may be explained in part by the effects of common chronic illnesses (such as diabetes, high blood pressure, and prostate cancer) and their treatments on erectile dysfunction.

**Health and Sexuality:** Good self-reported health in middle age and later life was strongly associated with frequency of sexual activity (once or more a week), interest in sex, and feeling your sex life was of good quality. At the individual level, knowing that health is correlated with sex life may encourage seniors to maintain a healthy life style to prolong their years of sexual activity.

**Source:**

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**In the mid-1970s smoking began to be illegal in many public places**

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**DID YOU KNOW?**

72% of men over age 65 live with a spouse, vs. 42% of women

— Older Americans 2010: Key Indicators of Well-being at agingstats.gov

People in very good or excellent health were 1.5 to 1.8 times more likely to report an interest in sex

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This year we welcomed three new trainees to the IOA’s Biology of Aging Training Grant:

**Lisa Maurer**  
**Blood Clot Formation in Older Adults**
Lisa Maurer is a pre-doctoral trainee in Dr. Deane Mosher’s biomolecular chemistry lab. She is interested in thrombosis, or blood clot formation, which contributes to heart attacks and strokes, and is a major cause of mortality for older adults. She is studying how fibronectin contributes to clotting. Fibronectin is a protein that aids in the creation of clots by helping platelets clump together in the blood stream. Specifically, she is trying to understand how the platelet activator thromboxane A2 increases the ability of fibronectin to bind to platelets. Additionally, in order to get insights into the binding of fibronectin to the cell surface, she is looking at the interaction between fibronectin and a peptide from a fibronectin binding protein in bacteria, which may mimic the interaction between fibronectin and human cells. Her hope is to uncover new targets for drug development.

**Kim Farbota**  
**Age & Recovery from Brain Injury**
Kim Farbota is a pre-doctoral trainee in Dr. Sterling Johnson's lab in Geriatrics. She is interested in using neuroimaging techniques to study the effect of advancing age on recovery from traumatic brain injury (TBI). TBI is associated with mental problems, as well as motor control issues (difficulty coordinating voluntary movements, such as finger tapping) that are more severe in older adults. Kim’s first set of experiments at the UW has shown that human patients exhibit white matter recovery (white matter helps the brain carry signals efficiently between nerve cells) following brain injury in regions associated with coordinating movement of the limbs and hands. White matter recovery was associated with improved finger tapping speed, demonstrating that the changes in the brain during recovery were functionally relevant. Advancing age decreases the extent of recovery, both in the brain and on the motor task. Her future work will investigate the effect of age on other parameters of neuro-physiological recovery (such as cortical degeneration, which is predicted to be greater in older patients), as well as the effects on recovery when psychiatric disorders are present. Her innovative research will provide valuable information about the specific recovery processes of the aging brain, and inform future work developing treatments to maximize the recovery capacity of the injured brain in people of all ages.

**Auriel A. Willette**  
**Age-Related Brain Atrophy**
Auriel Willette recently received his Ph.D. in Biological Psychology with a minor in Neuroscience. One of his current projects examines caloric restriction in aging non-human primates with Dr. Sterling Johnson. He also examines human imaging data with Drs. Barbara Bendlin and Sterling Johnson in collaboration with Dr. Mark Sager at the Wisconsin Alzheimer’s Institute, in order to translate his animal work to people. He is interested in the biological underpinnings of atrophy in brain regions that are impacted in individuals at-risk for Alzheimer’s dementia. Despite advances in neuroimaging and genetics to better understand the functional and structural changes in these areas and their implied risk for dementia, there is little to no research investigating the individual and combined contributions of different physiological and behavioral systems on brain aging. Dr. Willette’s work combines structural and functional neuroimaging with proteomic, genetic, immunohistochemical, endocrine, and cognitive data by using sophisticated statistical modeling. Dr. Willette was one of the winners of this year’s New Investigator Awards (see opposite page) and has recently been first author of four articles regarding stress, aging, brain structure, and the effects of caloric restriction, as well as several forthcoming publications, including:

Willette, A. A., Bendlin, B. B., Kastman, E. K., Canu, E., McLaren, D. G., Kosmatka, K. J., et al. (in press). Homocysteine, neural atrophy, and the effect of caloric restriction, as well as the effects on recovery when psychiatric disorders are present. Her innovative research will provide valuable information about the specific recovery processes of the aging brain, and inform future work developing treatments to maximize the recovery capacity of the injured brain in people of all ages.

Age-related brain atrophy is associated with coordinating movement of the limbs and hands. White matter recovery was associated with improved finger tapping speed, demonstrating that the changes in the

The Biology of Aging and Age-Related Diseases Training Grant is administered by the IOA & has been funded by the National Institute on Aging since 1990. It supports 8 trainees who receive mentoring from UW-Madison researchers while learning to conduct aging research in their labs.

biologyofaging.wisc.edu

For more details, see: aging.wisc.edu/outreach

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If you missed our recent 22nd Annual Colloquium, you can still access some of the resources online at:
aging.wisc.edu/outreach/colloquium.php

VIEW VIDEOS & PDFs OF SPEAKER PRESENTATIONS
Halting the Aging Process  Craig S. Atwood, PhD
Asthma in an Aging Population  Sameer K. Mathur, MD, PhD
Reducing Barriers to Better Self Care: Changing Stereotypes  Susan M. Heidrich, PhD, RN
Keynote Speaker: Finding Happiness & Meaning: What the Research Tells Us  Richard M. Ryan, PhD

HEALTH & RESOURCE FAIR CONTACTS
Find descriptions & contact info for organizations offering local resources for positive aging.

AGING RESEARCH POSTERS
See the list of posters on recent aging research that were presented at the event. PDFs of some posters can be accessed in the “Highlighted Posters” section on our home page.

Auriel Willette
Poster entitled: Calorie Restriction in Old Rhesus Monkeys Confers Protection Against Adverse Physiological Processes in Critical Brain Regions Affected by Normal Aging

Mariana Pehar
Poster entitled: Increased Dosage of p44 Causes Memory Loss, Neurodegeneration, and Premature Death

2010 New Investigator Award Winners
Awards are given to UW–Madison students or advanced trainees to recognize outstanding achievement in aging studies. Winners receive a $300 award at the IOA Colloquium and their research is showcased in the event’s Poster Session. PDFs of their posters can be accessed on our website.

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Poster entitled: Calorie Restriction in Old Rhesus Monkeys Confers Protection Against Adverse Physiological Processes in Critical Brain Regions Affected by Normal Aging

Mariana Pehar
Poster entitled: Increased Dosage of p44 Causes Memory Loss, Neurodegeneration, and Premature Death

Donation Thanks
We are pleased that our event continues to grow & we hope to carry on our tradition of offering it free to the community. We give our thanks to the following people whose donation will help us toward this goal:

• Lauren Blough
• Betsy Haimson
• Frank Hansberry
• Carol McKy
• Jane Pizer
• Rochelle Stillman
• Ruth Tsotsis
• Lucy Wall
• Sharon Wheeler
• Beatrice Wright
• Sherri Zelazny

Donations can be made via our website any time during the year.

Join Us Next Year!
The 23rd annual Colloquium on Aging will be held at Monona Terrace in Madison, WI on
Tuesday, October 11, 2011

Registration for the colloquium will open in July. If you are not on our mailing list, join via our website, or

CONTACT:
aging
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(608) 262-1818

2010 had a record 550 attendees!
A community delegation created by United Way of Dane County has identified four key reasons why older adults end up in the hospital. The good news is that all four causes are potentially preventable. United Way brought together 38 local community leaders to form the **Delegation on Safe and Healthy Aging** in April of 2010. Its goal is to help focus the agency’s efforts to improve independence among older adults, a key part of the agency’s Agenda for Change.

Included on the team were UW Institute on Aging Affiliates **Steve Barczi** (Assoc. Prof., Geriatrics), **Barbara Bowers** (Prof., Nursing), and **Tracy Schroepfer** (Assoc. Prof., Social Work). The delegation recently released its **Impact Report** that outlines four primary reasons for hospital stays among Dane County seniors:

1. **Falls:** Wisconsin is the 2nd highest rated state for number of older adults who die from falls. Within Wisconsin, Dane County ranks third highest for hospitalization of seniors due to falls. Within Dane County, falls are the number one cause of hospitalization due to injuries.

2. **Adverse Drug Events (ADEs):** ADEs refer to unintended side effects from taking medications. Those taking a larger number of meds are at greater risk for ADEs. In Dane County, seniors take an average of 6.4 prescription meds and ADEs cause 11% of total hospitalizations. This percentage has been steadily increasing since 2003, when it was only 5%.

3. **Incontinence:** This refers to loss of bladder control. The Delegation was unable to capture local data, but national figures show that 29% of seniors aged 60-70 experience leakage when coughing, sneezing, or laughing and that incontinence is the 2nd leading cause of institutionalization.

4. **Reversible Dementia:** Dementia is a debilitating loss of mental functioning. It may be reversible or improved when exacerbated by drug side effects. No local data was available, but literature estimates up to 20% of dementia sufferers could experience partial reversal and up to 10% could have marked improvement in mental functioning.

By 2030, the 65+ age group is expected to increase 136% in Dane County. However, the above problems are not inevitable for this age group.

In early 2011, the Delegation will report on its recommendations to address and improve these issues in Dane County.

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**The aging process has you firmly in its grasp if you never get the urge to throw a snowball.** —Doug Larson