Both environmental and genetic factors contribute to the risk of Alzheimer’s disease

By Brenda L. Plassman, Ph.D. and Kathleen M. Hayden, Ph.D.

The search for environmental factors has intensified as it has become clear that the AD risk genes that have been discovered only account for a small part of disease risk in the population. Environmental factors include physical activity, diet, and head trauma to name just a few. But so far, inconsistent results have been found. Other factors deserve more attention; among these are pesticides which are known to have negative effects on the nervous system. Much of the available evidence about the effects of pesticides is based on people who were exposed to high levels of pesticides. We know very little about the long term effects of chronic low-level exposure to pesticides on AD risk. However, in some studies, exposure to pesticides has been shown to increase the risk of other neurodegenerative diseases such as Parkinson’s disease (PD) and Amyotrophic Lateral Sclerosis (ALS).

A few studies have begun to provide evidence suggesting that pesticide exposures increase the risk of AD. One study from our research group, the Cache County Memory Study, has provided the strongest evidence linking pesticide use to risk of AD. Dr. Hayden and colleagues conducted this longitudinal population-based study in a group of 3,084 elderly people living in Cache County, Utah, an agricultural community. Interviews with study participants at baseline documented pesticide exposures from their lifetime occupations. Cognitive function was monitored for up to 10 years after the study started. A total of 572 people (mostly men) were exposed to pesticides during their working life. The findings showed that occupation-related use of any pesticide was associated with a 42% greater risk of AD compared to those who did not report job-related pesticide exposure. In addition, the use of a specific group of pesticides called organophosphates was associated with a 53% greater risk of AD.

Most observational studies on pesticides and AD risk are related to occupational exposure such as farming. But these chemicals are widely used in our environment. For example, they are used in residential settings to control insects. Based on the most recent figures available, the United States used an estimated 1.1 billion pounds of pesticides in 2007. Thus, it is likely that even people who have not worked in pesticide-related jobs have been

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Eleven years after the Duke Center for the Study of Aging and Human Development was founded in 1955, the postdoctoral research training program began. I was a fellow in the first year, and have been affiliated with the Center ever since. Being new, the program was very flexible, allowing fellows to pursue their interests without first having to submit a formal proposal. I came to it with academic qualifications in clinical and social psychology, and an interest in industrial psychology.

The initial topic I planned to examine, the social structure of a nursing home, turned out to be infeasible, since the home seemed likely to close. Based on a positive experience with an older employee of a local mortgage company (in contrast to the behavior of his younger co-worker), I decided to look at why people continue to work after retirement when they have no financial need to do so. This issue, using both new data and data already available, and with funding from Social Security’s extramural grant program and the National Institute on Aging (NIA), engaged me and my colleagues for many years, resulting in multiple publications, including a book on retirement.

Midway during this era, the Aging Center obtained funding to examine alternatives to institutionalization. Because of a conversation on my interest in institutions nearly 10 years earlier, I was invited to participate. We enjoyed the luxury of a planning year, during which a thoroughly multidisciplinary group of Duke faculty came together, learned each other’s languages, and developed the OARS (Older Americans Resources and Services) program. This program included a multidimensional functional assessment and service use questionnaire, together with a means for classifying people to determine need, evaluate programs, and make policy decisions regarding service allocation. Importantly, we assessed the reliability and validity of the OARS questionnaire. Consequently, the GAO (General Accounting [now Accountability] Office), interested in determining the impact of government services, selected the OARS questionnaire for its longitudinal study of Cleveland elderly.

OARS continues to be used widely in the U.S. and abroad (with translations into multiple languages), to ascertain both population and individual clinical status, determine service needs, and assess program impact. Interest abroad
EDITORIAL*
Will there be a war between the generations?*

By Erdman Palmore, PhD

Some alarmists assert that the increasing numbers of elders caused by the “boomer generation” coming of age, combined with the escalating costs of medical care and social security, will result in a kind of “war between the generations” in which each generation attempts to increase their share of public and private resources at the expense of other generations. Already there have been protests about the amount of the federal budget going to “greedy geezers”, and about how younger people are not receiving their fair share of support. For example, the National Journal recently published an article titled, “The Case against Parasitic Baby Boomers.”

It is true that there is concern in both generations about the future viability of entitlements for seniors; but protests about the share going to the older generation have been relatively mild and limited. There have been no significant decreases in the shares of public and private resources going to the older generation. On the contrary, the resources going to the older generation have been increasing along with their increasing numbers.

This is due to a combination of factors. Younger people realize that without the current public support for the older generation through Medicare and Social Security, the older members of their family would be more dependent on their children for support. Support for Medicare and Social Security remains strong in all generations. Also most young people realize that they themselves will probably become members of the “older generation” and will need such support in the future.

Secondly, the older and younger generations tend to share the same basic values, including intergenerational cooperation and support. There is now little or no evidence for a “cultural conflict” between the boomer and the younger generation.

So let’s remember that despite the alarmists on the right and the left, a “war between the generations” appears to be very unlikely.

* Adapted from Palmore, Older Can Be Bolder, (Amazon, 2011). Opinions expressed are those of the editor and do not necessarily reflect Center policy.

Both environmental and genetic factors contribute to the risk of Alzheimer’s disease, continued

These studies provide preliminary evidence that pesticide exposure throughout life may increase risk of AD in later life. This research needs to be replicated and a number of additional key questions need to be answered. In most dementia studies, exposures occur years before dementia onset and information about exposure comes from personal recall of pesticides used -- often decades earlier. Thus, detailed information on the type and amount of pesticides used has been lacking. Pesticide ‘use’ does not always equal pesticide ‘exposure’. Even among professional pesticide applicators, exposure can vary widely based on application method and use of protective equipment. Many other people may not regularly use pesticides, but still may be exposed to them. Also, some people may use multiple chemicals with neurotoxic effects, so it is hard to know which toxin is the risk factor. The difficulty in accurately measuring pesticide exposure poses a significant obstacle for the study of chronic exposures over time. Finally, it is unknown whether low levels of long term exposure are as detrimental as a few events of high levels of exposure.

* Adapted from Palmore, Older Can Be Bolder, (Amazon, 2011). Opinions expressed are those of the editor and do not necessarily reflect Center policy.
Gerontologist Linda Burton Appointed Dean of Social Sciences

Linda M. Burton, PhD, Senior Fellow at the Center for the Study of Aging, has been appointed dean of the Social Sciences Division within Duke University.

“As a James B. Duke Professor, Linda Burton brings an impressive scholarly record using ethnographic and demographic methods, and in administering multiple grants on a large-scale research project. She exemplifies Duke’s commitment to interdisciplinarity through her integration of spatial, geographic, survey, and ethnographic methods,” said Laurie Patton, dean of Arts & Sciences.

“Through her research focus on America’s poorest urban, small town and rural families, she also exemplifies knowledge in service to society. Professor Burton is known for being relentlessly constructive in solving problems and in bringing different voices to the table.”

As divisional dean, Burton plans to increase and enhance faculty research opportunities; explore ways to deepen and improve mentoring for graduate students and faculty at all levels; create opportunities for leadership training and continue to enhance diversity in departments. She is currently mentoring one of the Center’s Post-Doctoral Fellows, Lea Ritchie.

Burton came to Duke in 2006 from Penn State University where she was a full professor and directed a research center on family diversity and context. She was named a James B. Duke Professor in 2007. She is presently the director of the undergraduate honors program in the Department of Sociology, and has served as the department’s director of undergraduate studies.

Burton also has more than a decade of administrative experience from leading two National Institute of Mental Health consortiums. These programs aimed to foster collaborative interdisciplinary research among scholars nationally and to cultivate junior scientists through a national post-doctoral training program. In addition, she has a lengthy history of leading large-scale federally and foundation funded studies and at one time directed a team of more than 215 ethnographers and analysts as part of the Three-City Study of poverty, family processes and child development.

Burton said she intends to conduct research during her term as dean and feels that the “scholar dean” role will give her valuable perspectives in continuing to recruit and retain stellar faculty and in cultivating faculty’s programs of research.

Describing herself as an ethnographer who wants to influence local, state and national policy, Burton specializes in large-scale, longitudinal studies of poverty and intergenerational family dynamics in both rural and urban environments. Her work has been nationally recognized most recently with the Inaugural Wiley Alexis Walker Award for Outstanding Research in Family Science, conferred by the National Council on Family Relations. Other notable awards include the National Institute of Mental Health’s Family Research Consortium IV Legacy Award and the Distinguished Contribution to Family Therapy Research presented by the American Family Therapy Academy.

Burton holds a Ph.D. and M.A. in sociology from the University of Southern California, and a B.A. in gerontology. She is a Fellow of the Gerontological Society of America and a member of the Sociological Research Association.

She currently serves on the editorial boards of the American Sociological Review, the Journal of Marriage and Family, and Sociology of Race and Ethnicity. She also has served on advisory boards and committees for the Institute of Medicine, the National Center for Marriage and Family Research, the Family Process Institute and the Council on Contemporary Families, among others.

Congratulations, Professor Burton! ■
Duke leads a national effort to develop a blood test for Alzheimer’s

Two research developments are now bringing us closer to this possibility. The first is the refinement of a new laboratory technology called Metabolomics which allows for the analyses of thousands of metabolic changes simultaneously. The second is research showing that memory loss in Alzheimer’s disease (AD) may be preceded by changes in multiple metabolic networks, both in the brain and periphery.

The Metabolomics Consortium for Alzheimer’s Disease, headed by faculty in the Department of Psychiatry at Duke Medicine and working with several other companies and universities, has now begun to examine blood samples from a large national study (ADNI) using Metabolomics to provide the first detailed metabolic map of Alzheimer’s disease and those at risk for it.

“Think about your annual checkup where we measure 20 things like glucose and cholesterol. In a few years we will measure 500 chemicals that will tell us much more about your health including 100s of lipid fractions. Imagine all the things that need to happen before brain destruction occurs. Metabolism supports these changes. If we can look and see these earlier changes, they may tell us a lot about the disease and ways to try to stop it,” said Rima Kaddurah-Daouk, lead investigator from Duke Psychiatry.

The team pioneered the use of metabolomics and lipidomics to report specific metabolic changes in the blood of Alzheimer’s patients. Investigating lipidomics they have identified changes in several classes of lipids suggesting defects in membrane structure and function in AD. They have built the first metabolic network for AD revealing that several of these metabolic changes are interrelated, some linked to tau or amyloid-beta42.

Murali Doraiswamy, a collaborator and Senior Fellow at the Aging Center, stated that “Metabolomics holds promise for not only developing new diagnostic or predictive tests but also for identifying new targets for drug discovery. Ultimately we want a simple, cheap, and scalable test if it is to be used widely in every country and every type of clinical setting.”

The researchers hope to report initial findings from this national initiative in 2015.

The research has been funded by NIH, Alzheimer’s Drug Discovery Foundation, and private entities.

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SERVICE AWARDS PRESENTED

The following staff and faculty were presented service awards on July 14th AT 2:00 PM, in honor of their many years of service to the Duke Center for the Study of Aging:

Gwendolen Buhr
Bruce Burchett
Michele Burgess
Mary Caudill

Cathleen Colon-Emeric
Katja Elbert-Avila
Kay Fox
Mitch Heflin

Karen Ray
Rick Sloane
Yi Zeng

CONGRATULATIONS TO YOU ALL!
Faculty and students presented results of their research in ten papers at the annual meeting of the American Geriatrics Society in Orlando, FL, on May 15-17.

T. Dalton was coauthor on a paper titled Are residents performing the core competencies in care of older hospitalized adults? Initial data from a multisite study.

CONCLUSIONS: Residents often are not performing all of the AGS recommended core competencies.


CONCLUSIONS: Collaborative preoperative care for older high-risk patients undergoing abdominal surgery was associated with shorter length of stay and lower rates of discharge to skilled nursing facilities when compared to a historical (and possibly healthier) cohort of older adults undergoing similar surgeries.

N. Hastings and W. Bryan were coauthors of a paper on EQUIPPED: Enhancing Quality of Prescribing Practices for Elderly Veterans Discharged from the VA Emergency Department.

CONCLUSIONS: Initial data show the EQUIPPED intervention led to a significant reduction of Emergency Department provider-prescribed potentially inappropriate medications in older Veterans at the first site, that was sustained over 9 months.

S. Hastings was a coauthor of Evaluating an Electronic Health Record Medication Ordering Clinical Decision Support Tool.

CONCLUSIONS: A number of process and interface needs and barriers to using the EQUIPPED CDS tool were identified. These can be readily addressed to optimize the alignment between the CDS delivery and user-in-
CONCLUSIONS: Cumulative deficits in cognitive and sensory processes are progressively associated with disability and low self-reported health.

C. Nassaralla, S. Khosla, H. White, M. Yanamadala presented a paper on Reducing Medication Use in a Skilled Nursing Facility — A Quality Improvement Project.

CONCLUSIONS: Systematic analysis of the medication lists has decreased the total number of medications, the number of drug-drug interactions, and the number of medications listed in the 2012 Beers Criteria.

K. Schmader was a coauthor of Epidemiology of Drug-Disease Interactions (DDIs) in Older Veteran Nursing Home Residents.

CONCLUSIONS: DDIs were common in older Veteran nursing home residents with dementia/cognitive impairment and/or a history of falls/hip fracture.


CONCLUSIONS: The quality of organizational supports and care team interactions in SNFs might contribute to the inconsistent quality of transitional care in SNFs, and thereby the high incidence of bounce backs to hospitals after patients are discharged from SNFs to home.
E trespass to shrinking down to a more normal height, while short people can do some things to reduce this shrinkage. It can be caused by several processes. Reduced calcium absorption can make the bone segments shrink, so extra calcium and Vitamin D in your diet may help prevent this. Obesity or poor nutrition can cause the cartilage between the bones to shrink. Loss of muscle in your back and poor posture may make you slump down, so exercises for the back and better posture may reduce this cause.

Extra tall people may look forward to shrinking down to a more normal height, while short people can do some things to reduce this shrinkage. It can be caused by several processes. Reduced calcium absorption can make the bone segments shrink, so extra calcium and Vitamin D in your diet may help prevent this. Obesity or poor nutrition can cause the cartilage between the bones to shrink. Loss of muscle in your back and poor posture may make you slump down, so exercises for the back and better posture may reduce this cause.

It’s better to have loved a short man than never to have loved a’tall.

* Adapted from Palmore, Older Can Be Bolder, (Amazon, 2012).

FEATURED RESEARCHER: Gerda Fillenbaum, PhD, continued

has resulted in unexpected outcomes. On one occasion (before the days of e-mail), a physician from Brazil, studying in the UK, requested OARS information. Since I was going to London, I took the materials with me to save him postage costs. We met, found much in common, he translated OARS into Portuguese, ran a survey, analyzed the data, and then developed the first course on aging in Brazil. I was invited to speak. While there I met a psychiatrist who determined the suitability of one of the OARS scales as a measure of depression in Brazil. After a lapse of 15-20 years contact was renewed. We have been writing papers together ever since, analyzing data from Brazil.

Involvement with OARS had additional consequences – participation in the 10-year Duke Established Program for Epidemiologic Studies of the Elderly, which led to determining the incidence and prevalence of dementia in older African Americans and Whites (no significant differences were found); working with the World Health Organization and the Pan American Health Organization to develop functional assessments of the elderly, used in major international surveys; and becoming the project director of the Consortium to Establish a Registry for Alzheimer’s Disease (CERAD), which started in 1985.

CERAD, funded by the NIA, was mandated to develop a uniform set of measures to assess Alzheimer’s disease, for use in all NIA-funded Alzheimer’s Disease Centers, a move which permitted aggregation of data. The most broadly used measures continue to be the clinical/neuropsychological battery, neuropathology assessment, and Behavior Rating Scale for Dementia, but others are also available. CERAD measures have been translated into many languages, and norms developed. In addition to individual clinical use, CERAD has been used in epidemiological surveys to ascertain the prevalence and incidence of dementia, and in pharmaceutical trials.

Finally, I am also a member of the Duke Pepper Older Americans Independence Center, responsible for arranging monthly research seminars, and engaged in studies of obesity and health service use.

When I first came to Duke, both administrators and faculty offered an open door. Everyone was willing to offer help and advice. I learned from this, and have ever since tried to do the same. My feeling is that information is not information if it is not shared. For me, the Aging Center has been a welcome home, where members try to take care of each other. My initial physical introduction to the Aging Center was accidental – no office space was available in the Department of Psychology. For me, that lack was serendipitous.
The healthcare landscape is changing to an environment that is heavily focused on improving patient care outcomes. There is a strong need to train health care providers in quality improvement to support their engagement in activities that will improve patient care outcomes. Each year geriatric fellows at Duke University are trained in a year-long course in quality improvement skills led by Mamata Yanamadala, MD, MS and Gwendolen Buhr, MD, MEd. As part of the training the fellows conduct quality improvement projects aimed at improving outcomes of the care provided to older adults in our health system. This year the geriatric fellows have conducted two projects. One project, led by Shiv Khosla, MD and Thomas Dalton, MD, focused on recognition of delirium in patients admitted to the medical and surgical intensive care units at Duke Hospital. The project was presented as a poster at American Geriatrics Society (AGS) national meeting in Orlando in May and the American Geriatrics Society national meeting in Baltimore in June. The other project, led by Claudia Nassaralla, MD and Dr. Khosla, aimed to reduce unnecessary medications in the patients residing in the skilled nursing facility at Croasdaile Village. This work was presented at the AGS Annual Meeting and the Patient Safety and Quality Conference at Duke University in March. At the latter meeting, the project was recognized as the top abstract in patient safety category and received the Karcher Award at the patient safety conference. Each of these projects is described in detail by the authors below.

Improving Delirium Recognition in the MICU and SICU at Duke Hospital. Drs. Khosla and Dalton.

As geriatric trainees, we are well aware of the hazards associated with delirium in the intensive care unit (ICU). We set out to improve knowledge, self-efficacy, and screening behaviors for delirium amongst medical and surgical ICU nurses using an educational intervention. 106 out of 136 nurses completed this 2-step intervention. The first was a series of online modules titled, “Duke GEC: Delirium, an inter-professional Responsibility.” The main objectives of these modules are for the participants to be able to differentiate between different types of delirium, recognize risk factors, and implement strategies to better prevent and manage delirium. Knowledge and self-efficacy scores were tracked and improved significantly. The second part was a case-based, interactive lecture delivered by geriatric fellows to groups of MICU and SICU nurses. Delirium screening rates were systematically monitored in the electronic health record throughout the course of our educational program. Screening rates increased from 0 to 50% in the MICU and 0 to 56% in the SICU over a 3-month period.


In March 2014, the quality improvement project to reduce medication use in a skilled nursing facility received the Karcher Award, the first prize in the patient safety category at the Duke 9th Annual Patient Safety & Quality Conference. Polypharmacy occurs in 40% of long term care residents in the US, increasing the risk of adverse drug reactions, resulting in morbidity and mortality. This project, conducted at a 110-bed skilled nursing facility, reviewed medication lists of 80 eligible residents. Geriatric fellows flagged medications listed in the Beers criteria. Nursing students at Watts School, collaborating in this project, used a drug-drug interaction software to determine the number and severity of drug-drug interactions. Medication changes deemed appropriate were made by the patient’s geriatrician, reducing the average number of medications per patient by 6.84%. The average number of drug-drug interactions to be modified was reduced by 23.1% and those to be avoided by 44.7%. The average number of Beers criteria medications was decreased by 24.4%. All reductions are statistically significant. The majority of the discontinued medications occurred in the categories of gastrointestinal (26%), central nervous system (20%), supplement (18%) and analgesic (17%). Decreasing the medication burden generated a savings of $3,953 per month.
COMING EVENTS

October 16-18: Annual Education in Palliative and End-of-Life Care (EPEC) trainer conference. Chicago, IL. Contact info@epec.net or 312-503-3732.


