Siblings Diagnosed with Early Onset Alzheimer’s Offer Hope for Research

By Niki Kapsambelis

Locked inside the brain of Kassie Rose is a biological map, as yet unread, that will reveal whether she is another branch on a family tree that has been stricken too soon with a disease that seems to defy statistics.

But so far, she’s not ready to find that out.

“I made a choice to live my life as normally as possible and leave it up to God,” says Rose, a young wife and mother of a toddler daughter. But, she adds, “I think about it every day anyway. I repeat things and wonder if I have it.”

“It” is early onset Alzheimer’s disease, a rare form of the illness that affected her father, Brian DeMoe, and four of his five siblings in their 30s and 40s as well as her paternal grandfather, who was diagnosed in 1989 and died at age 58.

Though no treatment is currently available that can cure the family, their participation in research at the Alzheimer Disease Research Center (ADRC) at the University of Pittsburgh is giving doctors reason to hope that future generations will be helped.

“This is a group of people who can lead the way,” says William E. Klunk, professor of psychiatry and neurology and codirector of the center.

Klunk met the family when he was contacted in 2005 by Karla Hornstein, the only one of the six siblings who does not carry the gene responsible for the disease. Hornstein had heard about the new brain imaging research studies in Pittsburgh and was interested to find out if her family could participate. Eventually, they were invited to come to Pittsburgh for annual tests that include three different brain scans. They also receive health, neurological, and psychological evaluations. These tests are usually completed over a two-day period worked around the schedules of the family’s lengthy flights to Pittsburgh.

Though time-consuming, the tests allow ADRC researchers to track the progression of the disease by looking at the amyloid plaques in the brain that are indicative of Alzheimer’s. The studies are possible thanks to an imaging agent, Pittsburgh Compound B (or PiB), that was developed at the University by Klunk and his colleague, Chester Mathis, professor of radiology and director of the UPMC PET (positron-emission tomography) Facility. PiB serves as one component in studies that seek to discover whether the amyloid plaques characteristic of Alzheimer’s can be...
The Alzheimer's Project
more about Alzheimer's Association. To learn ADRC participant and member of the discussion with ADRC investigators following the film, there was a panel scientific film, Mathis, PhD, and Chester research with Pittsburgh Compound B. Momentum in Science researchers and the effects this disabling made by the country’s leading Alzheimer’s discoveries ground-breaking made by the country’s leading researchers and the effects this disabling and fatal disease has on those affected and their families. ADRC researchers William Klunk, MD, PhD, and Chester Mathis, PhD, are featured in the scientific film, Momentum in Science, as a family that is involved in ADRC research with Pittsburgh Compound B. Following the film, there was a panel discussion with ADRC investigators Klunk; Mathis; Oscar Lopez, MD, and Judith Saxton, PhD, and two ADRC participants who are directly affected by the disease: Lori McIntyre, who was featured along with her family, in the film, and Alan Romatowski, an ADRC participant and member of the Alzheimer’s Association. To learn more about The Alzheimer’s Project or to view the series online, visit www.hbo.com/alzheimers.

ADRC Mission
The overall objective of the ADRC is to study the pathophysiology changes in the brain) of Alzheimer’s disease (AD) with the aim of improving the reliability of diagnosis of AD and developing effective treatment strategies. The ADRC is funded by the National Institute on Aging and, as part of its research program, provides a comprehensive neuropsychiatric evaluation, including medical, neurological, psychiatric, social, and cognitive assessments. A major focus of the ADRC is to conduct research in order to be followed by the center.

Autopsy Program Comforts Families, Furthers Research
The Alzheimer Disease Research Center (ADRC) offers a brain autopsy program to center participants as well as nonparticipants. A brain autopsy can either confirm or disprove a diagnosis of Alzheimer’s disease (AD) or other dementia. While this information is highly beneficial to researchers, it also can be valuable to a patient’s surviving family members. Many families find that getting such diagnostic confirmation provides closure or resolution to the caregiving experience. An autopsy report also may help to minimize concern and confusion during future discussions of the family medical history. In addition to studying the brains of individuals with a diagnosis of AD or another form of dementia, researchers are interested in learning more about changes that occur in the healthy brains of older adults. Studies like these are designed to identify exactly what changes are related to disease and which are related to aging.

Brain autopsies from people with and without dementia contribute greatly to medical research. For more information about the brain autopsy program, please call the ADRC at 412-692-2700.

Siblings Diagnosed with Early Onset Alzheimer’s Offer Hope for Research
“They are salt-of-the-earth kind of folk. They don’t allow themselves to spend that much time feeling sorry for themselves about it,” says Klunk. “You can’t interact with these families as a researcher without being changed by them.” McIntyre, who currently lives in Idaho, describes herself as forgetful. A former bookworm, she has difficulty reading now, consulting the dictionary more than she used to. But she remains practical. Already, she has picked out a nursing home where she would like to live, and she has preferences for funeral arrangements.

The only time she breaks down is when she recalls how she felt when one of her daughters was tested. She is free of the gene. The status of her two other daughters is unknown, as they have elected not to undergo the testing. “Are you scared?” her sister asks. Her answer is, typically, unselfish: “The only thing I’m scared of is that I’ll be a grandma and not know it.” Ultimately, what we want to do isn’t to treat someone with mild Alzheimer’s disease,” explains Klunk. “We want to treat you before it ever starts.” Families like the DeMoes give researchers an important head start on that goal.

ADRC, HBO, and the Alzheimer’s Association Host Reception and Preview of The Alzheimer’s Project
April 16, 2009, to preview the HBO documentary series The Alzheimer’s Project is a four-part documentary series, which examined the effects of the disease on patients and their families. “I consider this in some ways our salvation,” says Lori McIntyre, Hornstein’s sister, who has the disease and appeared in the film. “It gives us some meaning. Instead of feeling ‘poor us,’ it gives me hope that we could be part of a cure. I think I would be a mess if I wasn’t part of the research.”

Besides McIntyre, Hornstein’s four brothers—Brian DeMoe, Doug DeMoe, Dean DeMoe, and Jamie DeMoe—all have the disease. Hornstein advocates for them and keeps track of the research. “It’s what I can do,” she says. Of the five affected siblings, it is Rose’s father, Brian, whose disease is the most advanced. Unable to care for himself, he now lives in a nursing home in North Dakota, where the family is from originally.
The University of Pittsburgh Alzheimer Disease Research Center thanks the following individuals and companies for their generous donations received January 1–June 30, 2009.

In Memoriam

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Charles and Jean Stout

In Memory of Fay Fink
Edna Diamond

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Battelle
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Drs. Moskowitz, Fadden, Inglese, Zapadka, Kenney de Jesus, and Connelly,
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Visit Our Web Site

For up-to-date information about the Alzheimer Disease Research Center, the autopsy program, clinical trials, and community presentations, please visit www.adrc.pitt.edu.
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(Continued from page 5)

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Your contributions are greatly appreciated
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remember or honor a loved one by using
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send in your donation.

Pitt Medical Student Receives AAN Extended Neuroscience Award

The American Academy of Neurology (AAN) awarded to
2009 Extended Neuroscience Award to
Cyrus Raji, PhD, from the University of Pittsburgh.
Raji was honored for his research, which adds insight into the joint effects of aging and Alzheimer’s disease on the brain. Raji received the award at AAN’s 61st Annual Meeting in Seattle, Wash., held in April and May 2009. The Extended Neuroscience Award seeks to stimulate interest in the field of neurology as an exciting and challenging profession by offering highly competitive awards for the best essay. It is one of four Medical Student Essay Awards offered by AAN.

Raji’s paper, “Independent Effects of Age and Alzheimer’s on Gray Matter in a Community Cohort,” focuses on how certain regions of the brain are most strongly affected by both normal aging and Alzheimer’s disease. The essay will be published in the December 1, 2009 issue of Neurology.

“By identifying which regions of the brain are most affected by aging and Alzheimer’s disease, this research can help us understand why age is such a powerful risk factor for the disorder,” said Raji. “I am honored to be the recipient of this award and want to thank my research mentors for their skillful guidance during this project. I also would like to thank all of our research participants, because without them and the tireless support of their families, none of the work we do would be possible.”

Raji is a graduate student in the Medical Scientist Training Program in the molecular pathology program. He was mentored by ADRC Codirectors Oscar Lopez and William Klunk and ADRC Associate Director James Becker.

What Is Neuropsychological Testing?

By Beth Seitz, PhD

Neuropsychological testing is an evaluation of memory and thinking skills that usually is conducted with individuals for whom brain disease or injury is suspected or confirmed. A clinical neuropsychologist has expertise in how behavior and thinking skills are related to brain structures and systems.

What happens in a neuropsychological evaluation?

A neuropsychological evaluation consists of a patient sitting on one on a skilled clinical examiner for about one to two hours. The patient is asked to perform a number of different tasks that may include answering specific questions, learning lists of words, repeating a short story, copying simple drawings, or putting puzzle pieces together. These tasks were developed to measure a person’s current cognitive (thinking) abilities such as learning and memory, attention and concentration, language, visuospatial thinking and reasoning, and solving complex problems.

Most people find at least some of the tasks interesting and engaging, although many people also become anxious when being given a test. This is one of the most important things for patients is to try not to worry about failing—there is no such thing in neuropsychological testing—but simply to try their best and be reassured that the detailed information gathered will contribute to their care. It also is important to bring glasses or hearing aids, if they are used, to a neuropsychological evaluation.

How are neuropsychological test scores interpreted?

Test scores are compared to scores from other people who are similar to a patient in important ways, such as age and education. By using database scores from large groups of healthy people for comparison, the neuropsychologist can judge whether or not an individual’s scores are normal for his or her age and educational background. Patterns of

strength and weakness are identified in this way. If neuropsychological testing has been conducted in the past, then current scores are compared to previous scores to look for changes over time within a given individual.

How are neuropsychological test results used?

Test results can be used to help differentiate among illnesses, which is important because appropriate treatment depends upon an accurate diagnosis. Different illnesses result in different patterns of strengths and weaknesses in testing. Therefore, the results can be helpful in determining which areas of the brain might be involved and what illness might be operating. For instance, testing can help to differentiate among Alzheimer’s disease, stroke, and depression.

Here at the University of Pittsburgh Alzheimer Disease Research Center (ADRC), the entire clinical team uses neuropsychological test results along with the results of other tests, such as brain imaging, the medical and neurological exam, and blood tests, to come to the most informed diagnosis possible. Results are used to help with treatment recommendations (e.g., the kind and level of assistance likely needed) based on our best understanding of a patient’s level of functioning. Neuropsychological testing also is used in clinical trials to measure objectively how well a new treatment may prevent or slow the progression of Alzheimer’s disease. Finally, in addition to their use in clinical trials, neuropsychological test data are used in many ongoing ADRC research studies. An example of this is the Fif or Pittsburgh Compound B study, which uses PET brain imaging to determine how changes in amyloid plaque in specific areas of the brain relate to patients’ performances on memory tests and other neuropsychological tests and how this changes over time and across diagnoses.

Neuropsychological testing is a very important activity at the ADRC. We hope patients and their caregivers will feel comfortable asking us questions about the role of neuropsychological testing in diagnosis, treatment planning, and research studies at our center.


Topics at Noon Series

Thursdays, December 10, 2009

“Patient and Family Member Perspectives on Living with an MCI Diagnosis”
Jennifer Haggerty Lingler, PhD, MA, CRNP
Assistant Professor of Nursing
ADRC Education and Information Core Director
University of Pittsburgh

“Palliative Care in Alzheimer’s Disease: Selected Topics”
Robert Arnold, MD
Leo H. Crip Chair in Patient Care
Chief, Section of Palliative Care and Medical Ethics
University of Pittsburgh

Light refreshments will be served. Registration is not required. For more information, call 412-692-2700. CME and CMU credits are available.
Since 2005, Alzheimer Disease Research Center (ADRC) investigators have been evaluating the Computer Assessment of Mild Cognitive Impairment (CAMIC) in two underserved populations—rural elderly from Fayette, Greene, and Washington counties and urban elderly, predominantly African American from Allegheny County—in the Memory and Aging in Urban and Rural Communities (MAURC) Study. CAMIC is a user-friendly, easily administrable battery of cognitive tests that can be completed on a computer that is portable and uses a touch screen. The purpose of the MAURC Study, which was funded by the Commonwealth of Pennsylvania, was to test the effectiveness of a computer-like device in assessing memory problems. While the study visits with participants are now complete, data analysis is ongoing.

The study team partnered with the Southwestern Pennsylvania Area Agency on Aging, Inc., and the Alzheimer Outreach Center in the Hill District to present information on the study as well as on the signs and symptoms of memory loss to a number of older adults at senior centers, senior residences, and churches. Interested audience members were able to sign up to participate in the MAURC Study.

Participants in the study answered questions using the touch-screen computer and also completed some paper-and-pencil testing. Follow-up testing occurred up to two times, and participants could complete testing at a senior center, at a church, or in their homes. The recruitment goal for the study was approximately 600 participants in all—300 in the rural communities and 300 in the urban communities. The investigators were impressed that this goal for the study was so successfully met. The investigators and study staff wondered what factors were so effective in recruiting for this study, so they decided to hold some focus groups to investigate. They also were interested to know why some people who participated in the MAURC Study agreed to come to the ADRC for a full multidisciplinary memory evaluation and why some did not want to.

Running focus groups involves convening a small group of participants who are invited in-conclusion of a facilitator in order to gather information about participants’ knowledge, attitudes, and beliefs about a certain topic. The focus group participants are the experts regarding their own experiences, and their knowledge allows the investigators to hear directly from the experts.

The focus groups with participants of the MAURC Study were held in April and May 2009, and these data are now being analyzed. The investigators hope to learn valuable information about things that encourage study participation—things that make participating manageable and appealing to do—as well as the drawbacks to participating in research.

The investigators at both the MAURC Study and the ADRC hope that the focus groups will give them valuable insights into how to make research participation more feasible for more participants.

If you ask Leslie Dunn what the most rewarding part of her job is, she will tell you that it’s being involved with a research program that provides wonderful support to patients and families grappling with dementia.

“If we have a phenomenal clinical and research team that works well together and cares tremendously about our families. From a research standpoint, it is so inspiring to see the dedication of our scientists and to be involved with people who are doing cutting-edge science that will make a difference as we seek effective treatments and prevention of Alzheimer’s disease,” she says.

Dunn has worked at the Alzheimer Disease Research Center (ADRC) for 20 years. She is the administrator for several grants, studies, and programs and also is responsible for overseeing the day-to-day activities of the center. In addition, she is involved with budget, personnel, and regulatory issues; supervises the ADRC brain autopsy program; assists with fund development; and facilitates the writing of progress reports and grant applications. Dunn also helps to coordinate the biannual Pittsburgh-Barcelona Dementia Update in Spain with the ADRC’s Spanish colleagues.

Before joining the ADRC, Dunn worked with investigators in the University of Pittsburgh Department of Psychiatry on several psychiatric epidemiology research programs, including a study on the mental health effects of the Three Mile Island nuclear plant accident. Before moving to Pittsburgh, Dunn was the supervisor of a neuropsychology program at Tufts-New England Medical Center in Boston, Mass. Dunn earned a Bachelor of Arts degree in psychology at Smith College and an MS in psychiatric epidemiology from England Medical Center in Boston.

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Outside the ADRC, Dunn has been the board chair of the Alzheimer’s Association Greater Pennsylvania Chapter and is currently the National Assembly delegate for the chapter.

In her spare time, Dunn is an avid walker; practices Tai Chi; and loves to go to museums, gallery openings, and dance performances. She also enjoys traveling and shopping in Pittsburgh’s Strip District, a wholesale/retail market area in downtown Pittsburgh.
The University of Pittsburgh Alzheimer’s Disease Research Center (ADRC) is opening up to researchers and patients who study brain aging. We will be asking all of our cognitively normal participants to allow us to scan their brains as part of the regular ADRC evaluation. In addition to the typical pictures (or images) that participants are used to seeing, we will also use specialized sequences (the term used to describe the kind of image that will be taken) to measure the white matter—the bundles of tissue that connect various parts of the brain. In addition, we will measure the blood flow in the brain using a special technique that does not require any injections.

In many, if not all, clinical magnetic resonance imaging (MRI) centers, the scanners use a field strength—a measure of the magnetic field. The University of Pittsburgh is fortunate to have two MRI machines that operate at higher strength—three tesla units. This allows us to make brain images faster and with greater precision than we can with the older machines. Any ADRC participants who are entering the study today are now being scanned on the newer-generation machine.

These new brain images are important to the ADRC because they will allow us to examine the effects of normal, healthy aging on the structure and function of the brain. By learning this, we will then be in a better position to study how subtle changes in the brain may precede the development of Alzheimer’s disease or another dementia syndrome. We will do this using a variety of newly developed methods of analysis, which take advantage of our collaborations with neuroscientists, engineers, and computer scientists. And all of these data will be important for developing methods for detecting the earliest changes in the brain—prior to the onset of any changes in cognitive functions.

The scanning study will take approximately 2 hours—one hour of preparation and one hour of scanning. We will try to schedule the scan around the time of regular ADRC appointments, but, in some cases, we may have to move a visit to an earlier time. We plan to complete the scanning phase of the study by the end of March 2010. So, the clinicians will be speaking with control volunteers at their next visit, or control volunteers may get a telephone call from Mary Ann Oakley to discuss their participation.

The Alzheimer’s Disease Research Center (ADRC) is collaborating with the Andy Warhol Museum to plan a series of activities around an upcoming visit from contemporary Brazilian artist José Rufino. Rufino’s work deals with memory and the concept of interpersonal loss. In the fall of 2010, Rufino will do a one-month artist residency in conjunction with the Warhol Museum’s exhibition Flipping Pop: Roots and Practices of Brazilian Contemporary Art. Plans for the ADRC’s collaboration with the Warhol Museum include the development of workshops and special programs at the Warhol tailored for staff, families, patients, and caregivers as well as research on the intersections of art and health and related benefits to each field. Please stay tuned for information on opportunities to get involved with this initiative.

Flipping Pop: Roots and Practices of Brazilian Contemporary Art will present 10 artists’ work from the 1960s to the present and explore the confluences and divergences of Brazilian art practice and culture in the latter half of the 20th century with those of Andy Warhol and American culture. José Rufino’s artist residency is a key component of Flipping Pop, as it explores and recasts 1960s experimental art practices with an ethical and sociocultural intent.

Since 2006, the Andy Warhol Museum has been working with the University of Pittsburgh school of the health sciences and Center for Bioethics and Health Law on various initiatives exploring the intersections of art and science. Projects have included a small display incorporated into the exhibition Deadly Medicine: Creating the Master Race that critically explored parallel symbols of authority, such as the doctor’s white coat and the gallery’s white space, and the development of a pilot course for medical students that teaches critical thinking and observation skills through looking at art and gallery-based experiences in collaboration with the Carnegie Museum of Art.

Activities Planned around Upcoming Visit by Brazilian Artist José Rufino
Ask the Medical Professional

**Q: What can be done about sleeping difficulties in people with Alzheimer’s disease?**

**A:** The nature of sleep problems in Alzheimer’s disease (AD) is multifaceted. The prevalence of sleep disturbances increases with age. Other medical and psychiatric conditions such as AD can worsen these changes. Medications used to treat chronic illness and insomnia have side effects that can further disrupt sleep. As in many other aspects of AD, sleep can affect not only the person suffering from AD but the caregiver as well. Sleeping more than usual and waking early are relatively common. Nighttime awakenings often are less common but are more distressing to the caregiver.

One of the first steps in addressing this issue is to investigate factors that might keep people awake, such as pain, medications, fear and insecurity, noise, and excessive lighting. Secondly, practicing consistent good sleep hygiene is essential. Decreasing or eliminating caffeinated beverages near bedtime can be helpful. Purposeful, daily physical activity can promote more restful sleep. There are cases where medications may need to be considered in conjunction with behavioral techniques. It is important to consult with health care professionals to discuss these options.