

Emory University School of Medicine Alzheimer's Disease Research Center

ALLAN LEVEY, MD, PHD



A MESSAGE FROM THE DIRECTOR

This news- letter is exciting because it provides evidence of the col- laborations that are driving

memory research at Emory. There are collabora- tions between departments within Emory University and with external uni- versities and organizations which have resulted in exciting discoveries or new projects.

degeneration. A collaboration with Rush University found important differ- ences between people with mild cogni- tive impairment (MCI) and Alzheimer's. The Emory ADRC has joined a consor- tium of research centers to study the ge- netics of late onset Alzheimer's disease. Melanie Greenaway, PhD, who did a fellowship at Mayo Clinic in Rochester, Minnesota, reports on an interventional study for people with MCI. The Alz- heimer's Association, Georgia Chapter, collaborates with us on many programs including our Early Memory Loss Group and through their Multicultural Liaison to our Memory Clinic at Grady Health System.

ence center. The Emory ADRC will be part of this important initiative that will focus on promoting patient-centered care and distinctive health services that will require collaboration among many Emory divisions.

Of course the most important collabora- tors we have are the volunteers who par- ticipate in Emory ADRC clinical trials and research studies. These individuals donate a blood sample for genetic re- search, have annual paper and pencil testing, many test potential new medica- tions and many choose to donate their brain when they die. Without the par- ticipation of these dedicated volunteers, research to treat and eventually prevent Alzheimer's disease would not be possi- ble.

An Alzheimer's Disease Research Cen- ter (ADRC) pilot grant to David Lynn, PhD, Chair of the Department of Chem- istry resulted in a discovery about brain

We are excited that Dennis Choi, MD, PhD has joined Emory University to develop a comprehensive neurosci-

Neuroscientist Dennis Choi Named Executive Director of Emory Neuroscience Initiatives

Dennis W. Choi, MD, PhD, a neuroscientist renowned for his groundbreaking research on brain and spinal cord injury, has been recruited to lead two major neuro- science programs at Emory Uni- versity.

As Executive Director of Emory University's strategic neurosci- ences initiative, Dr. Choi will oversee the development of four key areas: neuroscience education, behavioral neuroscience and cog- nition, brain therapeutics, and molecular and translational imag- ing research. Each program builds on strengths across multiple units of the University and existing neuro- science programs, including our NIH-funded Alzheimer's Disease

Research Center, Emory's Center for Neurodegenerative Disease, a neuroimaging research center, neurosciences programs at Emory's Yerkes National Primate Research Center, the Fuqua Center for Late-life Depression, NIH- funded research programs in psy- chiatry and behavioral sciences and psychology, and research pro- grams funded through the collabora- tive Center for Behavioral Neuro- sciences.

Dr. Choi will also be the director of the new Comprehensive Neuro- science Center in Emory's Wood- ruff Health Sciences Center. This center will integrate clinical care, research, and education with a focus on patient centered care.

Late Onset Alzheimer's Disease (LOAD) Genetic Initiative

The Emory ADRC has joined a consortium of research centers focused on the discovery of genes important in the development of Alzheimer's disease. According to Richard Mayeux, MD, M.Sc. of Columbia Uni- versity, "many steps in the development of Alz- heimer's disease remain unknown, and the discovery of genes involved in the process will bring us critically important in- sights. Identifying the genes and then their function should be directly useful in the development of drugs to treat or possibly pre- vent the disease altogether."

More than 500 families affected by Alz- heimer's disease currently participate in the study. Emory will help increase the number of participating families to 1,000. This will accelerate the efforts to locate the genes in- volved in late-onset Alzheimer's, the most common form of the disease.

Allen Levey, MD, PhD, Emory ADRC's lead investigator, encourages families in which 2 or more siblings have Alzheimer's (AD) or severe memory loss to consider par- ticipating in this research effort. In order for a family to participate in this study, the two siblings with AD must be living and willing to participate. For additional information on participating in this research effort contact Ami Rosen, MS, CGC at 404-728-4956.

CONFUSION... A SAVVY CAREGIVER'S LESSON

KEN HEPBURN, PHD



Close your eyes and imagine. Imagine yourself on a snowy, icy road at dusk, keeping up with heavy traffic at 70 mph – using wipers that should have

been replaced last month. Now imagine the radio is stuck on a heavy metal station and the volume can't be adjusted. And your passenger is chattering away, asking you questions and telling you how to drive. And now, you see in your rear-view mirror that an 18-wheeler is bearing down on you, about to pass and splatter slush all over your windshield.

How are you feeling? And what would you like to do?

Most people who imagine this scene say they feel tension, panic and anxiety mixed with irritation – focused, in large part, at the passenger. Most say they want to shut the radio off, shut the passenger off (maybe even bark at the person), get off the road, and regain a sense of control and calm – and feel safe.

Confusion like this is a central caregiving issue in dementia and a constant threat for persons with dementia. The disease is taking away all the powers people use to keep their universe in line and to give themselves a sense of order. Things persons with brains that are not affected with a disease like Alzheimer's have the capacity to monitor when situations are getting out of hand. And they typically have a collection of strategies for bringing things back to an acceptable level.

But for persons with dementia, those safety systems are eroded by the disease. For them, increasingly, the universe is swirling around them, and they are vulnerable to the sense of terror you might have felt on that snowy, icy road. And the person with dementia is no longer able to steer off the highway and regain a sense of calm and order. All the person is likely able to do is feel the fright and perhaps strike out at whatever or whoever is near.

So what is a savvy caregiver to do about confusion?

Recognizing that confusion may be the underlying mechanism of agitated or disturbed behaviors is a good starting place. This perspective allows you to look at the whole scene to try to determine factors that might be prompting the confusion. It also allows you a care target: you want the person to feel calm and secure and that things are under control.

Look for possible sources of the confusion:

- Might there be a physical cause? Could the person be overly tired? Might the person be ill (check temperature) or in pain for one reason or another?
- Is whatever the person doing just too much? Dementia increasingly affects the person's ability to do things – even things he or she was good at. Tasks that exceed the person's capacity can overwhelm or frustrate a person.
- Is there too much going on in the environment? Are there too many stimuli for the person to handle? This capacity, too, changes and erodes as the disease progresses, so environments that might

have been pleasurable at one time (e.g., a shopping mall) may turn into places that overstimulate the person. Similarly, events that once were a joy (e.g., large family get-togethers) may now be too much.

- Are you doing something that might be adding to the confusion? Again, ways of interacting with the person gradually lose effectiveness over time and might become confusing.

So step back and look at the whole picture. You can provide a sense of security with your reassuring presence and perhaps with a distraction that you know usually engages the person. But, as you do these things, exercise control. Look for things in the scene you think might be disturbing the person and that you can change. And then change them – and see what happens. Try asking the person to help with smaller, less complicated tasks. Scale back on activities that you know were once pleasurable: instead of a large family gathering, scale back to smaller, perhaps individual visits; instead of excursions to the mall, keep on taking outings, but to quieter spots with fewer people. Look at the way you have been communicating with the person, and experiment with simpler ways. How you scale back will depend on how far the disease has progressed, but here are some suggestions: instead of "normal speech" (long sentences with lots of complications), use short, simple sentences; instead of speech alone, mix short directions with visual cues; replace words with touch.

Keep always in mind that dementia does not protect the person from other diseases and disorders. Having a relationship with a responsive primary care physician or nurse practitioner is important to the savvy caregiver. If you suspect that confusion has its roots in something physical, use that relationship. A call or visit sooner rather than later is a good rule.

Emory ADRC Fall 2007 Research Update:

Alzheimer's Disease Vaccines...A New Frontier in Alzheimer's Disease Research?

December 6, 2007 • 7:00-9:00pm

Nell Hodgson Woodruff School of Nursing, Room 101

**Donations to the Emory Alzheimer's Disease Research Center
December 1, 2006 through June 30, 2007**

Ms. Mary A. DeJesus
Mrs. Lori C. Levey
Mrs. Ruth Levey
Ms. Sarah C. Jackson
Mr. Michael J. Neiswander
Mr. J. David Penson
State Farm Companies Foundation

In Honor of Mr. Michael Jackson
Ms. Caroline M. Lowndes

In Honor of Ms. Sarah C. Jackson
Ms. Caroline M. Lowndes

In Memory of Mr. Daniel M. Bliwise
Ms. Charmion L. Haley

In Memory of Mr. John Crosswell, Sr.
Mrs. Pam McCranie Foster

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Contributions

If you would like to make a contribution to support the Alzheimer's Disease Research Center, please use the following contribution form.

Enclosed is my tax deductible gift of \$ _____

Please note that this contribution is: In Memory of In Honor of

Name: _____

Please send acknowledgement of this donation to:

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City: _____ State: _____ Zip: _____

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Please make checks payable to:

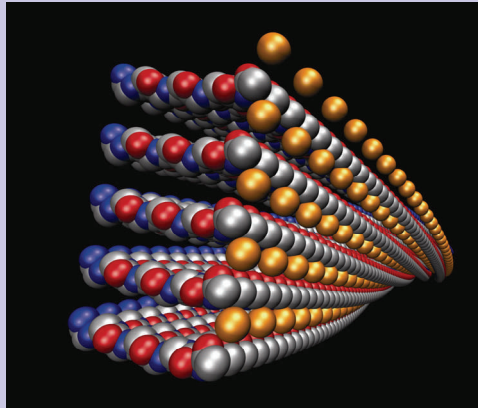
Emory Alzheimer's Disease Research Center
c/o Emory Univ. Health Sciences Development
1440 Clifton Road, Suite 112
Atlanta, Georgia 30322

THE COPPER STUDY

It has been known for many years that the senile plaques seen in the brains of Alzheimer's disease patients were comprised of a protein called Beta-amyloid. The mechanism by which Beta-amyloid contributes to brain cell death, however, has not been understood. Recently a multi-institutional team of researchers led by Emory University has discovered that in certain circumstances, copper can attach to structures composed of Beta-amyloid (called amyloid fibrils) in such a way that it leads to brain cell death.

"Not all amyloid fibrils are toxic," says David Lynn, Emory professor and chair of chemistry and principal investigator of the study. "Amyloid is made of proteins, and proteins normally fold into beautiful structures. However, for whatever reason, some misfold and the resulting misfolded structures are also beautiful, but sticky. They stick to themselves and then propagate to form fibrils." The researchers found that copper can bind

to amyloid in a very specific way that produces a toxic build up of the protein.



These misfolded amyloid fibrils are linked to the development of neurodegenerative diseases such as Alzheimer's, Parkinson's and Creutzfeldt-Jakob diseases. Those who suffer from Alzheimer's disease, for example, have an unusual amount of sticky amyloid fibrils in their brains. Over time, the fibrils build up inside the brain and interfere with the brain's structure and function.

In contrast, normally folded proteins are cleared from the brain shortly after they are produced.

While little is known about the precise mechanisms governing the formation of amyloid fibrils, the results of this study suggest that the exact way amyloid binds to copper ions affects the fibers' architecture and toxicity. This may impact surrounding neurons in such a way reminiscent of the degeneration observed in diseases such as Alzheimer's. However, says David Lynn, "Researchers are also finding situations in which amyloid is beneficial, such as in long term memory." Studies such as David Lynn's will help further our understanding of the balance between properly functioning and beneficial amyloid and the events that trigger its association with brain toxicity.

This study was reported in the August 14, 2007 Proceedings of the National Academy of Sciences and was funded through grants from the Department of Energy and the National Institute of Aging.

Clinical Trials & Research Studies: Fall 2007

Research Study	Eligibility	Contact Person
Emory ADRC Research Registry - Longitudinal study of changes in memory and other cognitive skills	<ul style="list-style-type: none"> • Aging people over 65 with no memory problems or • People of any age with Mild cognitive impairment or • Alzheimer's disease or • Other forms of dementia 	Megan Vucovich 404-728-6590 mmvucov@emory.edu
Lewy Body Disease	<ul style="list-style-type: none"> • Diagnosis of probable or possible Lewy Body Dementia • Stable on medications • Willing to spend 72 hours in a sleep research lab • Willing to undergo lumbar puncture 	Donald Bliwise, PhD 404-728-4751
Memory Rehabilitation Intervention in Amnesic Mild Cognitive Impairment	<ul style="list-style-type: none"> • Diagnosed with amnesic mild cognitive impairment • Study partner who can attend all cognitive rehabilitation sessions • Lives within 45-driving minutes of Wesley Woods Health Center at Emory University and/or will commit to come to all training sessions 	Noah Duncan 404-728-6544 nduncan@emory.edu
Neuroimaging study	<ul style="list-style-type: none"> • Diagnosis of Alzheimer's disease or • Normal cognition • Age 50 years and older • Right handed 	Heather Tovey 404-728-6589 htovey@emory.edu
Frontotemporal Dementia Caregiver Study	<ul style="list-style-type: none"> • A family member with frontotemporal dementia 	Susan Peterson-Hazan 404-728-6273 speter2@emory.edu

Do Mental Exercises and Taking Notes Help Memory Loss?

MELANIE C. GREENAWAY, PHD
NEUROPSYCHOLOGIST



Cognitive or lifestyle interventions for memory improvement in the elderly have been a hot topic in 2007. Memory interventions or rehabilitation can take two forms: 1) "memory building" techniques in which the goal is to regain/ maintain memory function through repetitive training paradigms or mental exercises or 2)

"memory compensation" techniques focused on using external aids to help overcome the effects of memory loss on daily life.

Mild Cognitive Impairment. A new strategy in memory rehabilitation at the Emory ADRC focuses on providing memory rehabilitation to individuals with memory loss earlier when they are classified as having Mild Cognitive Impairment (MCI) and not dementia. Amnesic Mild Cognitive Impairment (aMCI), the form of MCI in which memory loss is the primary concern, is the strongest identified risk factor for developing Alzheimer's disease (AD). When diagnosing aMCI doctors look for:

- memory complaints by the individual/family
- abnormal memory for age on testing

- otherwise normal thinking abilities
- normal ability to do daily tasks

A current research project at Emory is looking to determine the utility of a memory notebook system to compensate for memory loss in aMCI. Memory notebooks have been used for years to help individuals with traumatic brain injury with memory loss. We will follow 60 individuals with aMCI over the next two years to determine if this intervention can sustain or improve daily functioning, mood, and quality of life in both individuals with MCI and care partners.

MCI Research Information

Contact Noah Duncan at the Emory Alzheimer's Disease Research Center at 404-728-6544 for information on the MCI rehabilitation study.

Emory Researchers Moving Toward Early Identification and Treatment of Alzheimer's disease

JAMES LAH, MD, PHD



A collaboration between Emory ADRC Clinical Core leader, James J. Lah MD, PhD and Rush University has identified a promising new biomarker that has the potential to both identify Alzheimer's disease in very early stages of the disease as well as provide potential new targets for therapy.

Dr. Lah working with a team of researchers in the Emory ADRC and the Emory Center for Neurodegenerative Disease along with a team of researchers at Rush University have identified a strong link between the loss of a specific neuronal receptor called LR11 and the onset of mild cognitive impairment (MCI), a possible harbinger of Alzheimer's disease.

Utilizing data from participants in the Rush University's Religious Orders study, which includes more than 1,000 religious clergy who have agreed to undergo annual medical and psychological evaluations and brain donation after death, Dr. Lah and his team were able to measure protein levels in the brain cells and found the level of LR11 was affected in both Alzheimer's disease and MCI. In addition, changes in

LR11 directly correlated with cognitive ability among all individuals that were studied. This implies a direct link between LR11 and the stage of clinical disease. These findings suggest that the loss of LR11 occurs early in the disease process and therefore may be a biomarker that can predict Alzheimer's disease.

An explanation for the cause of the loss of LR11 has yet to be found. Researchers now understand that LR11 binds to both the apolipoprotein E (ApoE) protein that carries cholesterol and other fats throughout the bloodstream as well as the amyloid precursor protein that plays a role in the production and deposition of the toxic amyloid-beta peptide in the brain. Both ApoE and amyloid beta are strongly linked to degeneration of nerve cells in Alzheimer's disease.

This study would not have been possible without the Rush University's Religious Orders study. The clergy who participated in this study as well as the Emory ADRC brain donors are our collaborators and we are deeply grateful for their generosity.

This study was published in Annals of Neurology, Aug 24, 2007 and was funded by the National Institute of Health and the Luttrell Foundation.

Thank You Ms. Yokley & Good Luck! By: Angela Ashley, MD



The Grady Memory Assessment Clinic team would like to thank Ms. Adrian Yokley for her two years of extraordinary service to the patients of the Grady Health System and the Atlanta community at large. For the past two years Adrian served as the Alzheimer's Association's multi-cultural liaison to the Memory Clinic. While both patients and colleagues will miss her enthusiasm and commitment to the care and safety of our seniors, we also celebrate her professional development as she moves into her position as a clinical social worker at South Fulton Hospital. We will continue to enjoy the fruits of Adrian's labor, as we follow-up with our patients who are in better, safer living arrangements, have Safe Return bracelets in place, are receiving Caregiver Time Out respite services, and have a better understanding of their illness because of her diligent efforts to provide all accessible resources to patients and families in need. From all of those who were touched by her care, compassion and enthusiasm we say "Thanks Adrian and good luck! Your successor has some very big shoes to fill!"

CONTACT US**Emory Alzheimer's
Disease Research Center**

Wesley Wood Health Center
 1841 Clifton Road, NE
 Atlanta, GA 30329
 404-728-6950
<http://med.emory.edu/ADRC>

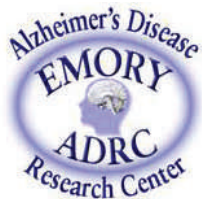
Memory Assessment Clinics

Wesley Woods Health Center 1841 Clifton Road, NE Atlanta, GA 30329 404-728-4936	Grady Memorial Hospital 80 Butler Street, SE Atlanta, GA 30335 404-616-4567
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To Register for a Class:

Please call Susan Peterson-Hazan at 404-728-6273, at least one week prior to the beginning of each class.

Event	Date	Location
Caregiver Challenges: Everything You Want to Know About the Middle Stage of Alzheimer's Disease (<i>Sponsored in part by a grant from the Wesley Woods Foundation</i>)	Friday ▪ 10:30 – 12:00 November 2, 9, 16, 23, 30 December 7, 14	Wesley Woods Health Center 1841 Clifton Road, NE Atlanta, GA 30329
Late Stage Alzheimer's Disease (<i>Sponsored in part by a grant from the Wesley Woods Foundation</i>)	Friday ▪ 10:30 – 12:00 January 4, 11, 18, 25	Wesley Woods Health Center 1841 Clifton Road, NE Atlanta, GA 30329
Early Memory Loss Group (<i>Co-sponsored by the Alzheimer's Association, Georgia Chapter</i>)	Friday ▪ 10:30 – 12:00 February 1, 8, 15, 22, 29 March 7, 14, 21	Wesley Woods Health Center 1841 Clifton Road, NE Atlanta, GA 30329
Caregiver Challenges: Everything You Want to Know About the Middle Stage of Alzheimer's Disease (<i>Sponsored in part by a grant from the Wesley Woods Foundation</i>)	Friday ▪ 10:30 – 12:00 April 11, 18, 25 May 2, 9, 16	Wesley Woods Health Center 1841 Clifton Road, NE Atlanta, GA 30329



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