December 11, 2015—(BRONX, NY)—Feeling stressed out increases the likelihood that elderly people will develop mild cognitive impairment—often a prelude to full-blown Alzheimer’s disease. In a new study, scientists at Albert Einstein College of Medicine and Montefiore Health System found that highly stressed participants were more than twice as likely to become impaired than those who were not. Because stress is treatable, the results suggest that detecting and treating stress in older people might help delay or even prevent the onset of Alzheimer’s. The findings were published online today in Alzheimer Disease & Associated Disorders.

Each year, approximately 470,000 Americans are diagnosed with Alzheimer’s disease. Many of them first experience mild cognitive impairment—a predementia condition that significantly increases the risk of developing Alzheimer’s in the following months or years. This study looked at the connection between chronic stress and “amnestic mild cognitive impairment” (aMCI), the most common type of MCI, which is primarily characterized by memory loss.
“Our study provides strong evidence that perceived stress increases the likelihood that an older person will develop aMCI,” said Richard Lipton, M.D., senior author of the study, vice chair of neurology at Einstein and Montefiore, and professor in the Saul R. Korey Department of Neurology and the Edwin S. Lowe Chair of Neurology at Einstein. “Fortunately, perceived stress is a modifiable risk factor for cognitive impairment, making it a potential target for treatment.”

“Perceived stress reflects the daily hassles we all experience, as well as the way we appraise and cope with these events,” said study first author, Mindy Katz, M.P.H., senior associate in the Saul R. Korey Department of Neurology at Einstein. “Perceived stress can be altered by mindfulness-based stress reduction, cognitive-behavioral therapies and stress-reducing drugs. These interventions may postpone or even prevent an individual’s cognitive decline.”

The researchers studied data collected from 507 people enrolled in the Einstein Aging Study (EAS), a community-based cohort of older adults. Since 1993, the EAS has systematically recruited adults 70 and over who live in Bronx County, NY. Participants undergo annual assessments that include clinical evaluations, a neuropsychological battery of tests, psychosocial measures, medical history, assessments of daily-living activities and reports (by participants and those close to them) of memory and other cognitive complaints.

Starting in 2005, the EAS began assessing stress using the Perceived Stress Scale (PSS). This widely used 14-item measure of psychological stress was designed to be sensitive to chronic stress (due to ongoing life circumstances, possible future events and other causes) perceived over the previous month. PSS scores range from 0 to 56, with higher scores indicating greater perceived stress.

The diagnosis of aMCI was based on standardized clinical criteria including the results of recall tests and reports of forgetfulness from the participants or from others. All 507 enrollees were free of aMCI or dementia at their initial PSS assessment and subsequently underwent at least one annual follow-up evaluation. They were followed for an average of 3.6 years.
Seventy-one of the 507 participants were diagnosed with aMCI during the study. The greater the participants’ stress level, the greater their risk for developing aMCI: for every 5 point increase in their PSS scores, their risk of developing aMCI increased by 30 percent. Similar results were obtained when participants were divided into five groups (quintiles) based on their PSS scores. Participants in the highest-stress quintile (high stress) were nearly 2.5 times more likely to develop aMCI than were people in the remaining four quintiles combined (low stress). When comparing the two groups, participants in the high-stress group were more likely to be female and have less education and higher levels of depression.

“*Our study provides strong evidence that perceived stress increases the likelihood that an older person will develop aMCI.*”

*Richard Lipton, M.D.*

To confirm that stress was independently increasing risk for aMCI in this study, the researchers assessed whether depression—which increases the risk for stress as well as for cognitive impairment and Alzheimer’s disease—might have influenced the results. They found that depression did not significantly affect the relationship observed between stress and the onset of aMCI. Similarly, stress’s impact on cognitive status was unaffected if participants possessed at least one e4 allele of the *APOE* gene, which increases their risk for developing late-onset Alzheimer’s.

The study is titled “*Influence of perceived stress on incident amnestic mild cognitive impairment: Results from the Einstein Aging Study.*”

In addition to Dr. Lipton and Ms. Katz, other Einstein-Montefiore authors were Carol Derby, Ph.D., Cuiling Wang, Ph.D., Ali Ezzati, M.D., Molly Zimmerman, Ph.D., and Jessica Zwerling, M.D., M.S. Martin Sliwinski, Ph.D., of Pennsylvania State University also contributed to the study. The research was funded by the National Institutes of Health, the National Center for Advancing Translational Sciences, the Leonard and Sylvia Marx Foundation and the Czap Foundation. The authors report no conflicts of interest.

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As Alzheimer’s prevention trials get underway, researchers are developing tools that can identify people at greatest risk for the disease and expedite their recruitment. Enter the newest resource—GeneMatch, announced this week by principal investigator Jessica Langbaum and colleagues at Banner Alzheimer’s Institute in Phoenix. The new program piggybacks on the Alzheimer’s Prevention Registry (APR), which has recruited more than 185,000 people who are interested in participating in AD research. Through GeneMatch, APR registrants will have the option of donating DNA for ApoE4 genotyping. Researchers will then be able to instantly identify participants who fit particular ApoE selection criteria, speeding enrollment into clinical trials.

“GeneMatch will dramatically shift how researchers conduct prevention studies,” said Pierre Tariot, director of the Banner Alzheimer’s Institute, at a press briefing announcing the program. Through GeneMatch, investigators will significantly cut the numbers of people they need to screen, saving significant time and money, he said.

“We need to engage the public in a major way and encourage them to participate in research to help move the field forward,” noted Stephen Salloway, Brown University, Providence, Rhode Island, adding, “GeneMatch could be a game-changer for AD research.” Salloway is an investigator in Banner’s upcoming Alzheimer’s Prevention Initiative APOE4 trial, which will test the ability of the Aβ vaccine CAD106 and the BACE inhibitor to prevent Alzheimer’s in people with two copies of the ApoE4 gene.

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GeneMatch grew out of the preparations for the API APOE4 trial. Led by Langbaum, Tariot, and Eric Reiman, also from Banner, that trial plans to screen about 80,000 people in order to find 1,300 eligible subjects who carry the requisite two copies of ApoE4, a genotype found in only 2 to 3 percent of the population. That leaves some 78,000 people, including non-carriers and ApoE4 heterozygotes, who still want to participate in research, but cannot join the trial for which they agreed to undergo genotyping in the first place. “We wanted to think about a mechanism to leverage this resource as a platform for other studies,” Langbaum told Alzforum. “GeneMatch creates a shared resource for the community.”

APR participants who are cognitively normal, live in the United States, and are between the ages of 55 and 75 can submit a cheek swab for ApoE genotyping. GeneMatch will not reveal that genotype to participants. However, volunteers may be referred to studies that reveal the information to them. They can then decide whether to learn their ApoE status. Genotyping will be carried out by Clinical Laboratory Improvement Amendments-certified labs, regulated by the Centers for Medicare & Medicaid Services. This will ensure the testing is held to accepted standards and the results are certified for the consumer. Some direct-to-consumer genetic tests are not CLIA-certified. GeneMatch is funded jointly by the National Institute on Aging, the Alzheimer’s Association, GHR Foundation, Banner Alzheimer’s Foundation, and FBRI. (FBRI is a subsidiary of FMR LLC, which also funds Alzforum.)

In developing GeneMatch, API scientists sought advice from experts in the ethical and legal implications of genetic disclosure, including Jason Karlawish, University of Pennsylvania, Philadelphia, and J. Scott Roberts, University of Michigan, Ann Arbor. They helped design the program so that communication with participants does not inadvertently reveal their ApoE4 genotype. For example, if a company or academic sponsor wants to test the effect of a given treatment in ApoE4 homozygous carriers, that sponsor invites people of all genotypes so that the simple receipt of an invitation does not give away genetic status.

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If a trial requires that patients learn their genetic status (most trials to date do not), investigators now have specific disclosure protocols designed to protect patients who may cope poorly with the revelation.

Langbaum did not specify which trials might use the database, but said that a number of scientists from outside API had expressed interest. Investigators will go through a rigorous application process because GeneMatch holds sensitive genetic information, said Langbaum. She and colleagues are still working out policies and procedures for access to the data.

Investigators in the United Kingdom, Germany, Spain, and France have expressed interest in expanding GeneMatch to their countries. Langbaum and colleagues are currently working out the requisite ethical and legal considerations.

GeneMatch joins several other initiatives that benefit from the interest of the general public to take part in research and clinical trials. Among these are the Brain Health Registry led by researchers at University California San Francisco, the Alzheimer’s Association’s Trial Match, the United Kingdom’s Join Dementia Research, and the Global Alzheimer’s Platform Trial-Ready Cohort. “There’s real momentum to build a global infrastructure to accelerate AD drug development,” said Salloway.

—Gwyneth Dickey Zakaib

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The Alzheimer’s Quilt Project Celebrates Its Six Year Anniversary

It was six years ago that the ADCS began looking for a better way to thank participants enrolled in ADCS clinical trials. After considering several options the ADCS decided to start a quilt program which began in January of 2010. Due to national publicity in an AARP publication and a national quilting magazine, as soon as quilters learned about the program to make and donate lap-sized quilts to be given to study participants, boxes began arriving in droves. Now six years later, the program is still going strong with quilts coming in and being shipped to research sites nearly every week. As of this writing the ADCS has received 3,760 quilts. The research site personnel tell the ADCS that the quilts have been the single most successful tool for keeping people engaged and enrolled in the studies.

So who are these good Samaritans who make and donate the quilts? There are over 450 quilters who make the quilts for the ADCS. They live throughout the U.S., in small towns and large cities alike. Some make their quilts as part of a quilting guild, others make them individually. Each has been affected by Alzheimer’s in some way be it a family member, a friend, or someone they know. The emotion and willingness to help runs deep.

**Ricky Polcer of Tyler, Texas** has been making quilts since her aunt taught her how at the age of eight years old. She has made between 800 and 1,000 quilts since 2001 when she got serious about quilt making upon her retirement from the civil service. Of that mind-boggling number she has made and donated 145 quilts to the ADCS Quilt Project. In the fall of 2010 she saw a small article about the project and felt compelled to make a quilt. Her father suffered from Alzheimer’s for over 10 years, the last eight months in a coma, and knew well what patients and their families endure. She says she makes quilts for the project because “it’s one way I can give back in his memory.” Ricky also makes smaller quilts for the Quilts for Kids chapter in Austin, Texas, an organization that provides quilts to children with life-threatening illnesses and children of abuse. Ricky’s says “I love knowing I’ve provided someone with warmth and love – the giving throughout the year is a good feeling.”
Quilts cont’d…………

Ricky’s other passion is fostering and adopting greyhounds. Since 2007 she has been involved with Greyhounds Unlimited of Dallas, Texas. She has fostered 10 with medical issues, and adopted eight. At this time she has two “greyts” as she likes to call them. When asked her favorite part of quilting she answered, “I treasure the quiet time with my greyhounds at my feet helping.” For Ricky, quilts and greyhounds go hand in hand.

Janet Burnett of Upland, California learned to sew in high school in Vancouver, British Colombia. She remembers her first sewing machine, a treadle, and how much she loved sewing on it. These days she uses a more advanced sewing machine, a Janome, but is the proud owner of her mother-in-law’s old Singer treadle machine, a treasure. Janet became captivated by quilt making when she moved to Redwood City, California where a neighbor introduced her to the art form. That was 40 years ago and she’s still going gangbusters. Like many others, Janet began making quilts for the ADCS Quilt Project when she saw a magazine article requesting quilts for study participants. A friend’s mother had passed away of Alzheimer’s; she wanted to do something special to honor the woman. Quilts seemed like a fitting way to do that. We are certainly grateful for Janet’s efforts. To date she has made us 169 quilts. We are not the only recipients of Janet’s talents. Her quilting guild makes and donates quilts to their local Sheriff’s department as well as quilts for foster children and a group called Santa Claus Inc that provides quilts to children at Christmas.

Like Ricky Polcer, Janet has a quilting assistant named Sami, a rescue cat (who refused to have her photo taken for this article). Sami will call to Janet to join her in the sewing room, Sami’s favorite place in the house. She can usually be found in one of the fabric bins, on Janet’s sewing table or sitting in the window critiquing Janet’s work.

The Glendale Quilt Guild located in Glendale, California has contributed 179 quilts since early 2012. Begun in 1980, the guild now sports 140 members. Their Loving Hands committee coordinates the making and donation of quilts to numerous worthy organizations besides the ADCS quilt project. Approximately 50 guild members regularly finish the quilts. The organizations that benefit from their efforts include LAC/USC Hospital, Glendale Adventist Hospitals, Veteran’s Residential Facility, Family Promise of East San Fernando Valley, Glendale YWCA Domestic Violence Shelter, Kaiser Hospice, MEND and Foster Care Project at All Saints’ Episcopal Church Pasadena.
Negative Beliefs About Aging Predict Alzheimer’s Disease

By Michael Greenwood, Yale University

Newly published research led by the Yale School of Public Health demonstrates that individuals who hold negative beliefs about aging are more likely to have brain changes associated with Alzheimer’s disease.

The study suggests that combating negative beliefs about aging, such as elderly people are decrepit, could potentially offer a way to reduce the rapidly rising rate of Alzheimer’s disease, a devastating neurodegenerative disorder that causes dementia in more than 5 million Americans.

The study led by Becca Levy, associate professor of public health and of psychology, is the first to link the brain changes related to Alzheimer’s disease to a cultural-based psychosocial risk factor. The findings were published online Dec. 7 in the journal Psychology and Aging.

“We believe it is the stress generated by the negative beliefs about aging that individuals sometimes internalize from society that can result in pathological brain changes,” said Levy. “Although the findings are concerning, it is encouraging to realize that these negative beliefs about aging can be mitigated and positive beliefs about aging can be reinforced, so that the adverse impact is not inevitable.”

Study authors examined healthy, dementia-free subjects from the Baltimore Longitudinal Study of Aging, the nation’s longest-running scientific study of aging. Based on MRIs, the researchers found that participants who held more negative beliefs about aging showed a greater decline in the volume of the hippocampus, a part of the brain crucial to memory. Reduced hippocampus volume is an indicator of Alzheimer’s disease.

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Then researchers used brain autopsies to examine two other indicators of Alzheimer's disease: amyloid plaques, which are protein clusters that build up between brain cells; and neurofibrillary tangles, which are twisted strands of protein that build up within brain cells. Participants holding more negative beliefs about aging had a significantly greater number of plaques and tangles. The age stereotypes were measured an average of 28 years before the plaques and tangles.

In both stages of the study, Levy and her colleagues adjusted for other known risk factors for Alzheimer's disease, including health and age.

Other authors include biostatistician Martin Slade of the Yale School of Medicine, neurologist Juan Troncoso of the Johns Hopkins School of Medicine, and a team of researchers from the Intramural Research Program of the National Institute on Aging (NIA), which included its scientific director Luigi Ferrucci, cognitive psychologist Alan Zonderman, and neuroscientist Susan Resnick. The study was made possible by grants from the NIA.
The following studies will be enrolling in 2016. For information on these studies in early 2016 please visit:

http://www.adcs.org/Studies/clinalResearchStudy.aspx