Resveratrol News

Summer 2013

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Resveratrol for Alzheimer's Disease

Newsletter for Participants and friends of the Resveratrol for Alzheimer's Disease Clinical Trial

Dear Participants and Friends of the RES Study,

As you may know the Resveratrol Study recently completed enrolling participants for this novel approach to treating Alzheimer's. As I wrote last time, this study enrolled at a very rapid pace, faster than we anticipated. The participant recruitment period was planned for 12 months, but in fact it took only nine months. Don't get us wrong, we are not displeased with this outcome, to the contrary. One of the biggest reasons for the overall slow rate of Alzheimer's disease research has been the speed of enrollment in Alzheimer's studies. The longer it takes to enroll participants in a study the longer it takes to conduct the study and analyze the results. Conversely, when a study, like Resveratrol, enrolls quickly, the rest of the process also moves along much quicker. We have you to thank for enrolling in this study and helping us to accelerate the process.

In this issue we feature several articles that we hope you will find of interest. In our cover story, by Dr. Michael Rafii at the University of California San Diego, he explains a breakthrough in how scientists can look deep into the brain's circuitry. The techniques, called CLARITY, makes organs, in particular the brain, transparent and it allows scientists to see inside the brain. Scientists can see parts as small as a cell and can even differentiate between different types of cells. This technique will allow scientists to view brains in people while they are still alive and scientists will not have to wait until a postmortem autopsy to view brain diseases. This holds great promise for Alzheimer's research.

Other articles in this issue look at a new study that links air pollution to Alzheimer's disease, secrets of superager brains, how family history of Alzheimer's can predict brain atrophy in the part of the brain responsible for memory, and another about an Alzheimer's genetic risk gene that was discovered by screening patients DNA and using a scan to visualize their brain connections. These are important discoveries that ultimately will help enormously in the quest to find a solution for Alzheimer's, which I know for all of you, cannot come soon enough.

Finally, let me state once again how grateful we are to all of you for participating in the Resveratrol study. I hope you feel a great sense of satisfaction knowing that you are making a monumental contribution in the effort to eradicate this disease.

I look forward to reporting updates on the RES study later in 2013.

Sincerely,

Raymond Scott Turner

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Principal Investigator
Resveratrol for Alzheimer's disease

Seeing the Brain with CLARITY

By Michael Rafii, MD, PhD
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Associate Medical Core Director
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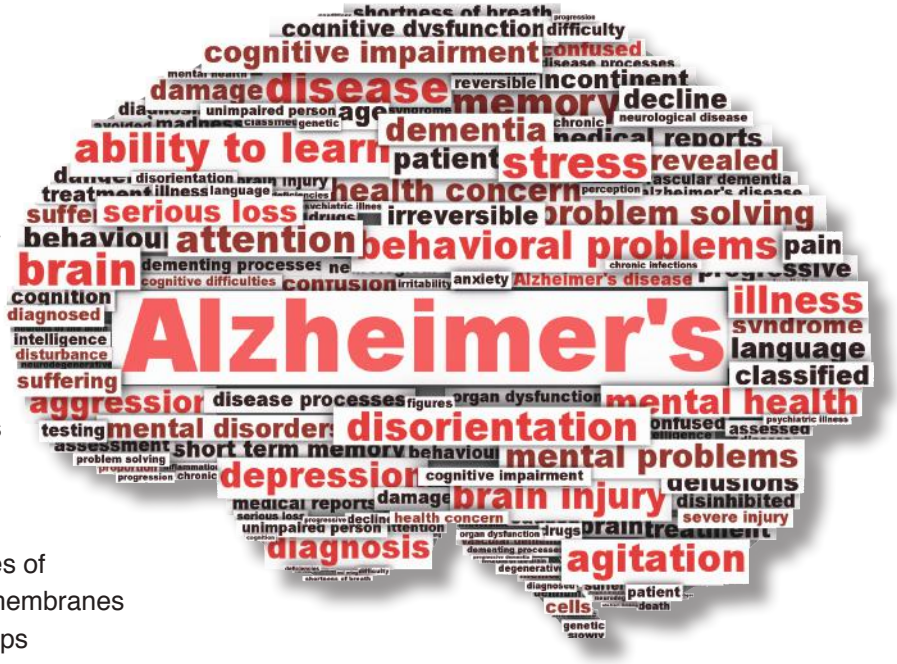


A team of engineers has developed a way to turn organs from mammals, such as lab mice or human bodies donated to science, transparent. Once transparent, scientists can add chemicals to the organs that attach to and highlight specific features, such as different cell types. The result is an intact organ that scientists can see inside and study.

The techniques, called CLARITY, involve a series of chemical treatments that replace the fatty lipid membranes surrounding cells with a chemical mesh that keeps microscopic details intact without scattering light like lipid does. Neurotransmitters and other important molecules remain in place and can be visualized with a rainbow palette of fluorescent dyes.

> **Until now, neuroscientists typically had to cut a brain into ultra-thin slices to visualize such features. But that destroys one of the things they're most interested in studying: the cable-like axons that carry signals from one part of the brain to another.**

Until now, neuroscientists typically had to cut a brain into ultra-thin slices to visualize such features. But that destroys one of the things they're most interested in studying: the cable-like axons that carry signals from one part of the brain to another. The new method makes it possible to visualize these long-range connections as well as the fine-scale anatomy and molecular make-up of neurons, the scientists reported recently in the journal Nature. This is probably one of the most important advances for understanding the structure of the brain in decades.

Although they developed the method in mouse brains, the team shows that it works on human post-mortem brain tissue too. In the Nature paper, they describe abnormal neural connections in an autistic boy whose brain had been stored in formalin for more than six years.

With this breakthrough, researchers plan to compare circuitry in banked tissue from people with other neurological diseases, including Alzheimer's disease, and from controls whose brains were healthy. Such studies in living people are impossible, because most neuron-tracing methods require genetic engineering or injection of dye in living animals. Scientists might also revisit the many specimens in repositories that have been difficult to analyze because human brains are so large.

Chung et al, Structural and molecular interrogation of intact biological systems, Nature 2013.

New Study Links Air Pollution to Alzheimer's Disease

High levels of exposure to air pollution may increase the risk of Alzheimer's disease, according to a new study completed with a grant from the Cure Alzheimer's Fund.

The study, led by Cure Alzheimer's Research Consortium member Sam Gandy, M.D., Ph.D., of the Icahn School of Medicine at Mount Sinai, examined how elements in air pollution such as nickel nanoparticles affect the levels of certain peptides in the brain that are found to be at heightened levels in patients suffering from Alzheimer's disease.

"We don't yet completely understand why the peptides accumulate, but we do know the genes responding to the peptides play an important role in developing Alzheimer's," said Gandy.

To test the correlation, mice were examined 24 hours after being exposed to air pollution where they showed a 72-129 percent increase in levels of the peptides.

"We were startled when three hours of air pollution exposure for the mice showed such a rapid and dramatic elevation," said Gandy.

> "We wanted to see if we could better explain why so many people were showing signs of Alzheimer's at such a young age"

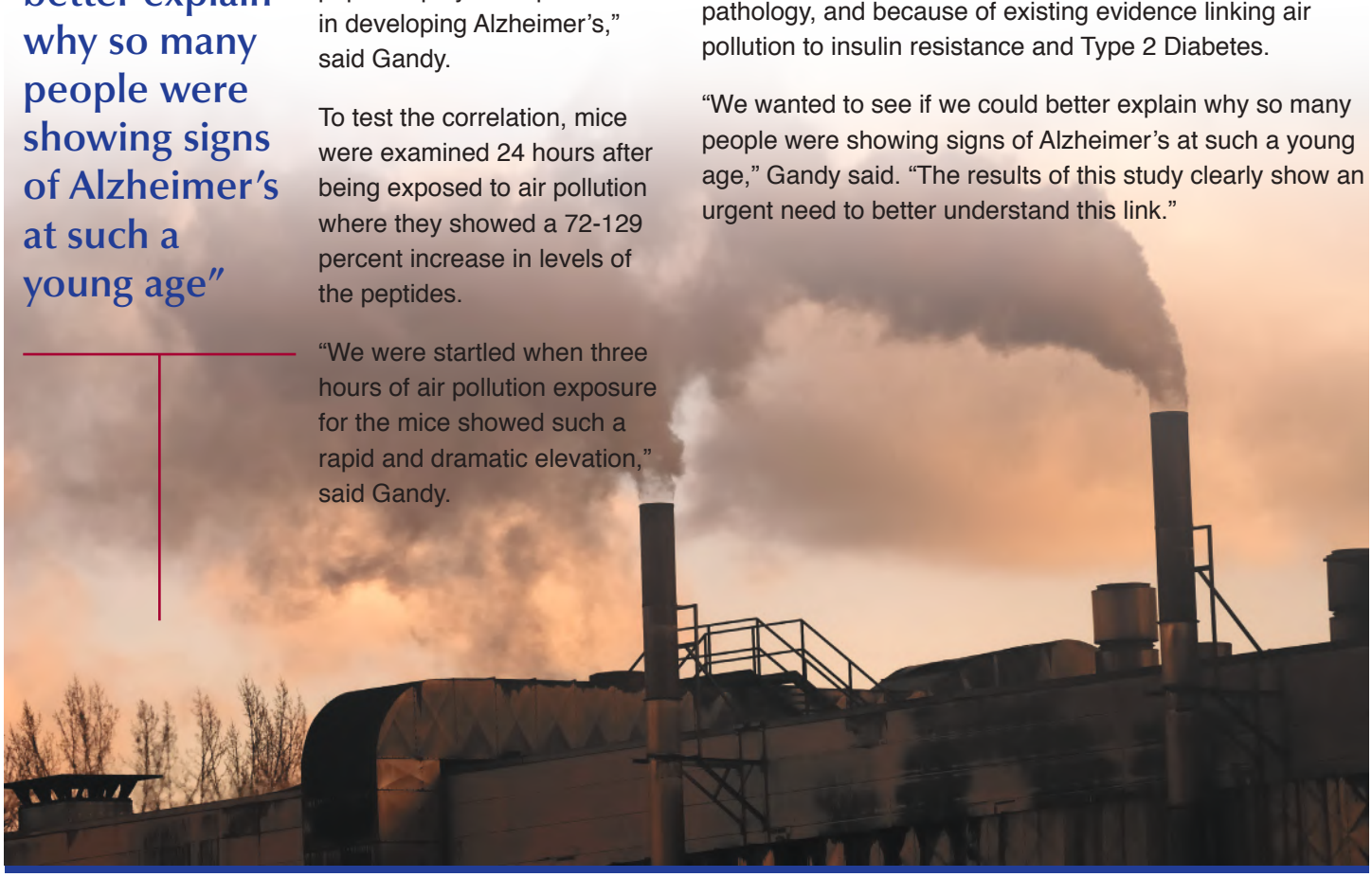
While the study links air pollution to Alzheimer's, Gandy emphasized that more research is needed to better understand the role of genetics saying, "There is probably some interaction between genetic susceptibility to air pollution that mitigates the response to the exposure."

Additionally, the study emphasized the need to better understand air pollution's effects on humans in a natural setting.

"We suspect that humans will have an even more dramatic reaction to air pollution than mice because the human molecule is far stickier, making it highly prone to clumping and accumulation," said Gandy. This could mean an even stronger link between air pollution and Alzheimer's than is reflected in the study's findings.

Interest in linking air pollution exposure to Alzheimer's disease started when studies showed young people living in highly polluted cities to have Alzheimer disease pathology, and because of existing evidence linking air pollution to insulin resistance and Type 2 Diabetes.

"We wanted to see if we could better explain why so many people were showing signs of Alzheimer's at such a young age," Gandy said. "The results of this study clearly show an urgent need to better understand this link."



Secrets of SuperAger Brains

Elderly SuperAgers have brains that look and act decades younger than their age

Researchers have found super aged brains had fewer fiber-like tangles than the brains of those who had aged normally. Tangles are found in moderate numbers in the brains of the elderly and increase substantially in the brains of Alzheimer's disease patients.

Researchers have long chronicled what goes wrong in the brains of older people with dementia. But Northwestern University researcher Emily Rogalski wondered what goes right in the brains of the elderly who still have terrific memories. And, do those people – called cognitive SuperAgers – even exist?

Rogalski's new study has for the first time identified a group of elderly people age 80 and older whose memories are as sharp as people 20 to 30 years younger than them. On 3-D MRI scans, the SuperAger participants' brains appear as young – and one brain region was even bigger – than the brains of the middle-aged participants.

She was astounded by their outer layer of the brain, important for memory, attention and other thinking abilities. Theirs was thicker than the cortex of the normal group of elderly (whose showed significant thinning) and closely resembled the cortex size of participants ages 50 to 65, considered the middle-aged group of the study.

"These findings are remarkable given the fact that grey matter or brain cell loss is a common part of normal aging," said Rogalski, the principal investigator of the study and an assistant research professor at the Cognitive Neurology and Alzheimer's Disease Center at Northwestern University Feinberg School of Medicine.

Rogalski is senior author of the paper published in the *Journal of the International Neuropsychological Society*.

By identifying older people who seem to be uniquely protected from the deterioration of memory and atrophy of brain cells that accompanies aging, Rogalski hopes to unlock the secrets of their youthful brains. Those discoveries may be applied to protect others from dementia.

"By looking at a healthy older brain, we can start to deduce how SuperAgers are able to maintain their good memory," Rogalski said. "Many scientists study what's wrong with the brain, but maybe we can ultimately help Alzheimer's patients by figuring out what goes right in the brain of SuperAgers. What we learn from these healthy brains may inform our strategies for improving quality of life for the elderly and for combating Alzheimer's disease."

By measuring the thickness of the cortex – the outer layer of the brain where neurons (brain cells) reside – Rogalski has a sense of how many brain cells are left.

"The thickness of the outer cortex of the brain provides an indirect measure of the health of the brain," she said. "A thicker cortex, suggests a greater number of neurons."

In another region deep in the brain, the anterior cingulate of SuperAger participants' was actually thicker than in the 50 to 65 year olds.

"This region is important for attention. Attention supports memory. Perhaps the SuperAgers have really keen attention and that supports their exceptional memories," Rogalski said.

Ten percent of the people who "thought they had outstanding memories" met the criteria for the study. To be defined as a SuperAger, participants needed to score at or above the norm of the 50 to 65 year olds on memory screenings.

For the study, Rogalski viewed the MRI scans of 12 Chicago-area Superager participants' brains and screened their memory and other cognitive abilities. The study included 10 normally aging elderly participants who were an average age of 83.1 and 14 middle-aged participants who were an average age of 57.9. There were no significant differences in education among the groups.

Northwestern co-authors on the study include Marsel Mesulam, M.D., Sandra Weintraub and Theresa Harrison, formerly with Northwestern and now a graduate student at UCLA.

This project was supported by a grant from The Davee Foundation and grants AG13854, P30 299 AG010129 and K01 AG030514 from the National Institute on Aging of the National Institutes of Health.

Family History of Alzheimer's Predicts Brain Atrophy in Healthy Adults

In order to more accurately predict who might go on to develop clinical symptoms related to Alzheimer's disease (AD), researchers at the University of Wisconsin, Madison needed to first understand the brain changes that happen prior to the appearance of clinical symptoms.

Several studies have now shown that having a parent who suffered from Alzheimer's disease (i.e., having a parental family history of Alzheimer's disease) is a major risk factor for developing the disease. To better understand those early brain changes that might indicate that someone might be at risk for developing clinical symptoms of AD in the future, the researchers focused on middle-aged adults who were both cognitively healthy and have a parental family history of the disease. In this study, the UW team analyzed brain scans from 108 cognitively-healthy, middle-aged adults enrolled in the Wisconsin Registry for Alzheimer's Prevention collected at two time points four years apart. The Wisconsin Registry for Alzheimer's Prevention was started in 2001 as a longitudinal registry of adults with and without parental family history of Alzheimer's disease.

"Several studies have now shown that having a parent who suffered from Alzheimer's disease is a major risk factor for developing the disease."

To verify that a participant's parent had Alzheimer's disease, the parent's medical records (including results of autopsy exams, when available) were reviewed by a team of physicians, psychologists, nurses and other health professionals. Similarly, absence of a parental family history of Alzheimer's disease was verified by conducting a detailed medical history survey and phone interview with the participant. The goal of the process was to determine that the participant's father survived to at least age 70 and the mother to age 75 without being diagnosed with dementia or showing any signs of thinking problems. All participants in the Wisconsin Registry for Alzheimer's Prevention were required to be completely free from cognitive problems and be between the ages of 40 and 65 at the time they enrolled in the study.

On average, the 108 adults studied were 54 years of age at the time of their first scan. Sixty of them had a parental family history of Alzheimer's disease whereas the other 48 did not. Researchers found that those persons with a parental family history of Alzheimer's disease had considerable shrinkage of the hippocampus (an important brain structure that helps us remember information and is also known to be affected by AD) over the four years they studied them, compared with the persons who did not have a parental family history of AD. They also looked at whether apolipoprotein E4 (APOE4), the strongest genetic risk factor for AD, had a similar effect on brain shrinkage, but did not find any evidence that it did. In addition, they found that those with a parental family history of AD were no different from those without a parental family history of AD on tests that assessed thinking abilities. Taken together, their findings suggest that having a parent with AD might put one at increased risk of experiencing brain changes related to the disease at a much younger age than initially thought, and long before any problems with thinking is picked up by standard cognitive tests.

Okonkwo OC, Xu G, Dowling NM, Bendlin BB, LaRue A, Hermann BP, Koscik R, Jonaitis E, Rowley HA, Carlsson CM, Asthana S, Sager MA, Johnson SC. Family history of Alzheimer disease predicts hippocampal atrophy in healthy middle-aged adults. Neurology. 2012; 78:1769-1776.

Brain Teasers

Commonyms

1. Hair ★ A Brain ★ An Ocean
2. A Bride & Groom ★ A Boat & Trailer ★ A Horse & Buggy
3. A Scale ★ A Tire ★ A Checkbook
4. An Aquarium ★ An Army ★ A Car
5. A Sports Page ★ A Movie ★ A Broadway Musical

Commonyms answers: 1. They have waves, 2. They are hitched, 3. They are balanced, 4. They have tanks, 5. They have scores

Mad Gabs (Hint: Sound out the sentence)

1. Able Owe Knees Hand Which
2. Ace Date Tough Gay Hoss
3. Ace Heal Ink Van
4. Ace Heck Hunch Ants
5. Ace Height Force or Rise

Mad Gabs answers: 1. A Bologna Sandwich, 2. A State of Chaos, 3. A Ceiling Fan, 4. A Second Chance, 5. A Sight for Sore Eyes