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## FOLIC ACID: BRAIN FOOD FOR ALL AGES

by Elaine Waddington Lamont

By now, most of us have probably heard that folic acid is good for developing brains and many young women that are trying to start a family have started taking folic acid supplements. A new study by Jane Durga, Martin van Boxtel, Evert Schouten, Frans Kok, Jelle Jolles, Martijn Katan, and Petra Verhoef suggests that folic acid may be good for older brains too. As part of a large study looking at the effect of folic acid supplements on heart health and cognitive function, over 800 older subjects received either a low dose of folic acid or a placebo daily for three years. Those who received folic acid showed significant improvement in global cognitive function, compared to subjects who received the placebo. More specifically, subjects in the

(Continued on page 5)

## FRESH PERSPECTIVES FROM A NEW RECRUIT

An Interview with Maria Natasha Rajah, Ph.D., Douglas Hospital Research Centre and Department of Psychiatry, McGill University

by Tania Elaine Schramek

The Douglas Hospital Research Centre recently welcomed another dynamic and highly creative scientist to its group. Maria Natasha Rajah, Ph.D., hailing from Berkeley University in California, joined the research team of the Geriatric Division of the Hospital and became an Assistant Professor in the Department of Psychiatry of McGill University.



(Continued on page 2)

## POLICY AND POLITICS

### JAPAN'S AGING POPULATION: LESSONS FROM A DEMOGRAPHIC SHIFT

by Daniel Auld

In many affluent countries, birth rates are declining and elder populations are growing. Japan is the most extreme example of this and the issues they are grappling with may serve lessons to other countries on how – or how not - to effectively deal with this world-wide phenomenon.

When one considers population and population density, Japan stands out as a highly populated country packed into a relatively small archipelago. But appearances can be deceptive, and in the case of Japan, they are. Except for a small peak in the early 1970s, Japan's birth rate

has been falling since the post-World War II baby boom that occurred in the late 1940s. The result of this was that in 1995, for the first time, the Japanese work force began to decline and has not stopped since. This problem will only become more pronounced, as a declining birth rate continues today. What's more, Japan is aging more rapidly than any other country in the world.

Thus, Japan has more and more people in the over 65 category, and fewer in the 15-64 working age group. For instance, seniors currently comprise

(Continued on page 3)

### IN THIS ISSUE

Folic acid: brain food for all ages.....	1
Interview with Maria Natasha Rajah .....	1
Japan's aging population: Lessons to draw.....	1
Proteins and late-onset Alzheimer's .....	4
The truth about cats and dogs.....	5
Taking back the mind from Alzheimer's.....	6

## **An Interview with Maria Natasha Rajah, Ph.D., Douglas Hospital Research Centre and Department of Psychiatry, McGill University**

*(Continued from page 1)*

Dr. Rajah completed her graduate training at the University of Toronto's esteemed Rotman Research Institute. Even at the Master's level, Dr. Rajah was publishing in highly-respected scientific journals and working with some of the leading authorities in the fields of memory processing and aging. She was initially interested in how a form of memory processing known as episodic memory takes place in young adults. Dr. Rajah explains that when we retrieve information in our memory we are often recalling specific episodes that have both temporal and spatial elements to them.

Throughout her studies she came to learn that in aging, the ability to recall when in time we have encountered an event or where it took place can decrease. "We can remember seeing someone but not where or when we saw them", she explains. Dr. Rajah became highly curious about how and why this occurs in aging and shifted the focus of her research as a result.

At the time, most studies looking at episodic memory processing in aging found that older adults were performing in a way that was disproportionately poor relative to their younger counterparts. In addition, the studies were using tasks designed to engage the activity of the hippocampus, a very important memory structure. Dr. Rajah and others suspected however that there was perhaps more to these noted deficits in episodic memory retrieval than just an age-related decline in the functioning of the hippocampus, which at the time was THE structure to examine.

Enter the prefrontal cortex. Dr. Rajah explains that impairments observed were likely not the result of a primary memory deficit but rather related to a change in the ability of the prefrontal cortex to organize information. She recounts the famous case of Phineas Gage who in 1848 survived an explosion that resulted in a 3 foot-long

tamping iron rocketing through the front of his skull causing severe brain damage. "His personality, social functioning, and thought processing were forever changed and his case was the first to teach us that the front parts of the brain were extremely important in our ability to organize and integrate information."

Her current studies examine precisely this, how prefrontal cortex (PFC) function changes with age. Dr. Rajah stated that her interest with this part of the brain stems from a longstanding fascination with the fact that our PFC is what distinguishes us from other species. "Ours is larger, more developed, intricately intertwined with other brain areas, is responsible for our ability to build civilizations and thrive within complex social structures." She continues "Understanding the exact functioning of the PFC represents a considerable challenge, it is elusive and that is why I am so motivated to meet the challenge head on."

The PFC is composed of many small areas that appear to be interconnected. Dr. Rajah uses functional magnetic brain imaging (fMRI) to examine how the activity of these different brain areas within the PFC changes in aging. This neuroimaging technique allows for the visualization of brain activity while a participant performs specific cognitive tasks. In fMRI studies the experimental groups differ in either their performance on the task or the anatomical structures activated by the task.

Many studies have found that young and older adults do not use the same brain areas for a given task. This difference between groups is also noted when cognitive performance is compared with older adults faring worst. In addition, other studies show that even when cognitive performance is the same between young and older individuals, activation patterns in

the brain are still different. Thus, the conclusion reached in the scientific community is that in the PFC there are age-related changes in its functioning.

Dr. Rajah recently conducted a meta-analysis (a study that combines the results of several studies looking at the same research question) in an attempt to verify if this was indeed true. Her results showed that overall, older individuals tend to use the same brain areas for episodic memory and working memory (short-term memory) as do younger adults but that a clear pattern of region-specific changes does emerge with age. Specifically, they found in older adults that the ventral part of the PFC in both hemispheres may show a decrease in function with age as does the dorsal part of the PFC in the right hemisphere. To compensate for this loss related to age, the left dorsal portion of the PFC may change its activity.

Dr. Rajah's findings have come to challenge the view that the PFC functions in a homogeneous manner. In other words, the whole PFC does not necessarily change with age but specific areas likely do.

Dr. Rajah is involved in several other studies. One is looking at genes, both structural and functional changes in the PFC and how all these impact on cognitive performance in aging. She would like to understand how it is that two people can be demographically identical, yet perform wildly differently on tests of memory and cognition.

Another research avenue Dr. Rajah is exploring is what brain networks are involved in specific types of cognitive processing, like episodic memory and working memory. She is well-versed in complex statistical analyses that will allow

*(Continued on page 4)*

## JAPAN'S AGING POPULATION: LESSONS FROM A DEMOGRAPHIC SHIFT

*(Continued from page 1)*

about 20% of Japan's population, and projections for 2055 have that number standing at a whopping 40%. Compare this to about 66% of the population being of working age at present, with just over 50% predicted for 2055.

One of the upshots of this aging trend is that the most affluent group of people in Japanese history – these are the people that built Japan into an economic powerhouse – are retiring and creating an aging and leisure economy. Amazingly, it has been estimated that people over 50 hold 80% of personal assets in Japan. Diverse industries, from travel to developers (of retirement communities), to health food producers, to adult education are benefiting from an influx of this spending power. Other 'retiring' Japanese might not simply sit down and relax and may elect to use their accumulated wealth in ways other than leisure. After spending their lives in a very work-conscious society, many may elect to open their own businesses, injecting their capital back into the economy in diverse areas.

Nevertheless, the picture for the Japanese economy as a whole is not as rosy. This ratio of seniors to young people presents many challenges. Notably, at what point will the shrinking working population not be able to support the social programs for the nation? Indeed, the most affluent generation is retiring and will cease contributing to the plan and begin to take their pensions. This problem will be confounded by the failing health of many individuals as they age. Other problems include reduced school classroom numbers, the closing of rural schools and the disappearance of small towns, as there are simply not enough young people to sustain them.

To help maintain the Japanese economy, the retirement age is being increased to 65, which will keep highly valuable workers in the workforce longer. Moreover, the age of eligibility for the national pension plan is likewise being increased. The government has also cut the benefits provided by the nation-wide pension plan in order to accommodate the increasing pressure. However, unless the young population begins to grow, these kinds of solutions can only be considered temporary or 'band-aid.'

In the hopes of a more long-term solution, the Japanese government has implemented proactive measures to increase their birth rate. These include tax incentives, medical benefits and maternity benefits. At this point, however, this has not reversed the decreasing birth rate. Countries like Canada attempt to maintain population growth despite low birth rates with open immigration policies (about two thirds of Canada's population growth is from immigration). But immigration is a hard sell in Japan. For hundred of years, Japan has been a rather isolated island without the same history of immigration as many Western countries.

The problems that face Japan right now and in the not too distant future should serve as a warning for other countries. Hopefully, the solutions implemented by Japan will maintain the high standard of living that both their young and senior populations have been used to in the past. Japan's successes and failures in this endeavor should serve as guides for other nations grappling with similar, if less acute, problems.

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**An Interview with Maria  
Natasha Rajah, Ph.D.,  
Douglas Hospital Research  
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*(Continued from page 2)*

her to do exactly this. Brain activation in fMRI may be found in the same brain region for 10 different types of tasks with distinct demands. One way to look at it is that while we use our quadriceps muscles to kick a ball and to walk, the quads will work in concert with different muscles in the leg for each of the tasks. The same might be said for the brain. Dr. Rajah wants to identify these neural networks for PFC functioning.

She is also heavily involved in the clinical aspects of her work. Dr. Rajah works in collaboration with physicians at the Geriatric Psychiatry Division of the Douglas Hospital. Currently she is looking at how to identify individuals at risk for falls and preventing such occurrences. She will also be involved in studies examining multi-sensory stimulation to reduce depression and agitation in older demented patients and at the effects of bright light therapy on individuals with Alzheimer's disease.

All told, Dr. Rajah is a busy young woman whose research will provide valuable insight into what neurobiological and cognitive changes differentiate healthy aging from diseases of aging. This of course will help in the development of behavioural and biomedical interventions to treat memory reductions in healthy elderly, which could possibly delay the progression of these deficits and, in the long-term, hopefully reduce the burden of dementia.

## **NEW CLUES FOR AN AGING BRAIN: PROTEINS AND LATE-ONSET ALZHEIMER'S DISEASE**

*by Daniel Auld*

Alzheimer's Disease (AD) is a devastating neurodegenerative disease that results in dementia, most often in older individuals. Relatively rarely, younger – usually defined as under 60 years – individuals also get AD. These cases are always associated with genetic mutations, and identifying the offending genes has provided much information about how the disease works. For instance, many of the mutations cause altered processing of a protein called the amyloid precursor protein (APP), leading to increased production of a toxic by-product protein called beta-amyloid 1-42 (also called A $\beta$ 1-42). However, genes or specific causes underlying the much more common late-onset AD have been more elusive. Recently, a team from the University of Toronto believes that they have identified a clue to the cause of at least some forms of late-onset AD. They found that changes in a protein called the neuronal sorting receptor, or SORL1, may be related to the cause of late-onset AD. In an interesting connection with early-onset AD, these changes in SORL1 modify processing of the APP protein. Thus, even if the root

causes of late and early-onset AD are different, there appears to be a link between their pathologies. This makes sense considering that the brain pathology that is evident in both cases is rather similar. The difference may be that the genetic mutations in early-onset AD likely result in a more extreme problem in APP processing, leading to the development of AD faster than the SORL1 changes, which lead to AD later in life. This would be analogous to pushing a cart down a hill: if you push it hard it will descend faster than if you push it gently, but in both cases the cart will get to the bottom of the hill.

**Source:**

*E. Rogaeva et al. (2007) The neuronal sortilin-related receptor SORL1 is genetically associated with Alzheimer disease. Nature Genetics 39(2):168-177*

## THE TRUTH ABOUT CATS AND DOGS

by Tania Elaine Schramek

Pet therapy can be found in most major hospitals and patient testimonials certainly suggest that these programs are successful. Cats and dogs are the top-used animals in these types of therapies. But when at home, which animal is associated with the best health outcomes in older adults? Cats or dogs?

New studies suggest that this one goes to the dogs. While individuals who have pets tend to be healthier overall with noticeable benefits on mood, dog ownership triumphs in terms of cardiovascular health. Older dog owners have lower cholesterol levels and lower blood pressure. In addition, they tend to suffer fewer minor ailments and serious medical problems. Deborah Wells, Ph.D., from Queen's University, Belfast, reviewed several studies and found that dogs also help in recovery after heart attacks and some have the ability to detect the onset of an epileptic seizure and can thus provide one with early warning.

When asked how she thought dog ownership leads to improved health outcomes she states that “it is possible that dogs can directly promote our well-being by buffering us from stress, one of the major risk factors associated with ill health.” Moreover, “the ownership of a dog can also lead to increases in physical activity and facilitate the development of social contacts, which may enhance both physiological and psychological human health in a more indirect manner.”

Those early morning trips to the dog park indeed engender social contact, and for older adults this can be a welcome addition to their lives. June McNicholas, Ph.D., a health psychologist who specializes in health benefits of pet ownership, further offered that “for older people, an animal can fulfill the 'need to be needed', perhaps after children have left home. In some cases, the social support offered by an animal is greater than the support that another human could offer.”

All in all, the title of ‘Man’s best friend’ is indeed befitting of the dog. (But for all you cat lovers out there, enjoy your companions anyway!)

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## FOLIC ACID: BRAIN FOOD FOR ALL AGES

(Continued from page 1)

folic acid group showed greater improvement on memory tests and were faster at processing information. In fact, subjects in the folic acid group performed a delayed memory task as well as subjects 7 years younger. Yet another reason to eat your leafy green vegetables.

### Source:

Durga, J., van Boxtel, M. P. J., Schouten, E. G., Kok, F. J., Jolles, J. Katan, M. B., & Verhoef, P. (2007). *Effect of 3-year folic acid supplementation on cognitive function in older adults in the FACIT trial: a randomised, double blind, controlled trial. Lancet, 369, 208–16.*

**SCIENCE HERE AND NOW****TAKING BACK THE MIND FROM ALZHEIMER'S DISEASE: DR. JUDES POIRIER**

by Elaine Waddington Lamont

Reading a list of Dr. Judes Poirier's credentials, it is impossible not to be impressed. He is a researcher at the Douglas Mental Health University Institute, Director of the McGill Centre for Studies in Aging, Professor of Neurology and Psychiatry at McGill University, and a Senior Scientist of the Canadian Institute for Aging. He is an editor for the journal *The Neurobiology of Lipids*. He has received numerous research grants from the Canadian Institutes of Health Research, the Alzheimer's Society of

Canada, and the Fonds de la recherche en santé du Québec. He has been awarded the Galien Prize, Canada's top award for biopharmaceutical research (1997), the Jonas Salk Award, named in honor of the inventor of the polio vaccine (1999), and was nominated to the rank of Knight of the Order of Québec (2004), to name just a few of his many distinctions. What is more impressive still is his research on the genetic basis of Alzheimer's disease (AD).

Dr. Poirier did his undergraduate work in biochemistry at the University of Montreal, and Ph.D. at the Clinical Research Institute of Montréal on the neurobiology of Parkinson's disease. He then did a postdoctoral fellowship at the Alzheimer's Disease Research Consortium of Southern California, at the Andrus Gerontology Centre, in Los Angeles. It was while working in Los Angeles that Dr. Poirier discovered the importance of apolipoprotein E (apoE) as a major genetic risk factor for Alzheimer's disease.

ApoE is a protein that transports cholesterol from the blood into the brain, where it is used to make cell membranes and new synapses for neurons. The gene encoding apoE type 4 (apoE4) has been linked with both familial and sporadic AD. Familial AD, as the name suggests, tends to run in families and begins at a younger age than sporadic AD, which is later onset (over age 65) and more common, representing 85-90% of all cases worldwide.

In 1989, Dr. Poirier joined McGill University and the Douglas Mental Health University Institute to develop a research program in neurodegenerative diseases. Since then, he has worked furiously to extend the work he began during his postdoc trying to understand the link between apoE4, cholesterol and AD. Brain cholesterol levels are reduced in the cortex and hippocampus of AD patients, but elevated in the blood. These findings support clinical work suggesting that individuals with elevated plasma cholesterol are at an increased risk for AD. The link between cholesterol and AD is that high levels of cholesterol are related to high levels of  $\beta$ -amyloid, the main

component of amyloid plaques that form in the brains of AD patients. In addition, the reduced cholesterol in the brain means that there is less raw material to repair and regrow neurons after damage or disease. Therefore, drugs which reduce cholesterol may also be protective against AD, and there are some clinical trials that are showing promising results with anti-cholesterol drugs. Since apoE acts to transport cholesterol into the brain, where it is lacking in AD patients, drugs which increase apoE are also proving to be beneficial in the treatment of AD.

Dr. Poirier has not limited himself to research, but has also sought to develop diagnostic tools and treatments for AD based on his discoveries. He is a co-founder of two biotech corporations based in Montreal called Nova Molecular Inc. (1996-2000), which was acquired by Nuvelo Inc. in 2003, and more recently Spectral Neuroscience Inc. By developing drug therapies designed for specific genetic profiles, it may be possible to delay the onset of AD even in people who are at high risk. This is truly welcome news for anyone affected by this devastating disease.

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