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FACTORS LEADING TO INSTITUTIONALIZATION IN DEMENTIA

by Jeff Boyczuk

Nearly half of those Canadians who have been diagnosed with dementia currently live in institutions. Of the half who remain at home, most will also succumb to institutionalization during the remainder of their life. Delaying this unfortunate event would not only be beneficial to the patient, who would likely enjoy a better quality of life in familiar surroundings, but would also ease the economic burden on an

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COMBINING PSYCHOLOGY, BIOLOGY AND SOCIAL POLICY TO PROMOTE SUCCESSFUL AGING

An interview with Dr. Sonia Lupien, Director of Research on Aging and Alzheimer's Disease, Douglas Hospital

by Alison McTavish

For Dr. Sonia Lupien, aging research isn't just about memory deficits, it's about successful aging. As the Director of Research on Aging and Alzheimer's Disease at the Douglas Hospital and the Associate Director of the McGill Centre for Studies in Aging, Lupien makes a point of getting to know the people she studies. "I love working with older people," she explains. "I learn far more from sitting and talking to them than from just running scientific tests."

It was while taking an experimental psychology course at CEGEP that Lupien's career really began. She read a paper about Roger Sperry and Michael Gazzaniga's classic study of patients with split brains. In these patients, the link between the left and right brain hemispheres has been severed, leading to some unusual side effects.

"I was totally fascinated," recalls Lupien. "I took the paper to my CEGEP guidance counselor, told him to read it and tell me what I should study so I could have a career in the same field." Lupien followed his advice and went on to obtain



a Master's degree in neuropsychology from Université de Montréal.

At that time, however, Lupien also became more interested in the biological side of things. "I realized that there was more to the brain. There are neurotransmitters in there!" This led Lupien to move from psychology into neurobiology. She admits it was a lot of hard work for a neuropsychologist to begin work in a new field, but the work paid off when she received a PhD in neuroscience.

It was only then that she felt qualified to put her training in psychology and

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THE SYNERGISTIC EFFECT OF HIGH BLOOD PRESSURE AND APOLIPOPROTEIN E4 ON LATE-LIFE COGNITIVE FUNCTION

by Julie Comber

The apolipoprotein (apoE4) allele has been shown to be strongly associated with both familial (heritable) and sporadic Alzheimer's disease (AD). The apoE4 allele can effect the extent of neuronal cell loss, the rate of progression of AD, the buildup of amyloid plaques and total beta-amyloid production in the brain. ApoE4 is also considered to be a risk

factor for vascular disease. Recent studies show a subtle interplay between genetic risk factors for cardiovascular disease and protective agents that modulate the onset and progression of AD (Poirier, 2001).

Further, carriers for the apoE4 allele have been shown to exhibit poor reinnervation and compensatory plasticity in vulnerable brain

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FACTORS LEADING TO INSTITUTIONALIZATION IN DEMENTIA

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already overtaxed health care system. A recent Canadian study, led by Réjean Hébert of the Gerontology and Geriatrics Research Centre in Sherbrooke, Quebec, has outlined some of the factors that lead to institutionalization of elderly individuals with dementia.

The researchers followed 326 community-dwelling dementia patients and their informal (unpaid) caregivers over a five-year period and found at the end that 166 (50.9%) had been institutionalized. Not unexpectedly, the diagnosed severity of dementia proved to be the most important factor in determining whether the patient had remained at home during the study period. Type of dementia was also important, with those suffering from Alzheimer's, as opposed to vascular dementia, also being more at risk for institutionalization. More surprisingly though, geographic location of the patient also played a role, with those living in Quebec, B.C. and the Prairie Provinces being at greater risk for institutionalization. Hébert et al. believe this might be due to other regions of Canada, particularly Ontario and the Atlantic provinces, having comparatively higher levels of funding for home care services.

Several caregiver-related factors also turned out to be important. For instance, if the caregiver was over 60, or was not a spouse or child of the dementia sufferer, then there was an increased chance of institutionalization. If the informal caregiver bore "severe burden", which is associated with the degree of behavioral problems of the patient, and the depressive mood of the

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An interview with Dr. Sonia Lupien, Director of Research on Aging and Alzheimer's Disease, Douglas Hospital

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biology together to study the biological component of neuropsychological function. "Michael Meaney became my mentor, and I still work with him," says Lupien. Meaney has been studying the effect of stress on aging for a number of years (see Geronto-McGill's profile of Dr. Meaney in the January 2001 issue). "Michael does the animal part of the work and I try to see if the same applies to humans," she explains.

Right now Lupien is working on depression and stress in aging. She is involved with the Douglas Hospital Longitudinal Study of Normal and Pathological Aging, a study directed by Dr. Nair. The study has been following a group of patients for almost 15 years to determine what happens to their levels of the stress hormone cortisol as they age. It turns out that in some people cortisol levels increase with age and in others it decreases. The people with increased cortisol are also more likely to suffer from memory deficits.

Lupien is interested in why this happens. "Why does Mrs. X show a significant increase and Mr. Y doesn't?" she asks. "What is the difference between these two people?" Because cortisol is a stress hormone, Lupien thinks that patients whose cortisol is high may be more reactive to the stress of aging.

High levels of cortisol are also found in elderly people suffering from depression. "I've shown that if you are elderly and are exposed to high cortisol for a couple of years, you will begin to have problems with the hippocampus which is an area of the brain related to dementia." This finding led to a new study that Lupien is conducting at the moment.

The new study involves older adults who report feeling depressed and forgetful. The approach she's taken to this study reflects her educational background. "At first I was a pure neuropsychologist studying the impact of cortisol on memory," she explains. "Then I was more of a biologist looking at hippocampal volume, and now I've come back around to a more psychological point of view: Why are you more vulnerable? Is it because you are who you are? Are

optimists different from pessimists?"

Preliminary results from the study suggest that people with low self-esteem have higher levels of cortisol and lower hippocampal volumes. She is now trying to sort out what these new findings mean for the development of memory deficits and dementia. It is clear, however, that depression makes coping that much harder for the elderly.

"Certainly you can give a pill and cure depression in the elderly," she says. "But you can also cure depression by decreasing social isolation." The way Lupien sees it, it isn't just a question of doing clinical research on depression in the elderly, it's a question of changing social policy.

"I'm not a politician," she laughs, "but there is so much more we could be doing." She points out that mentorship programs would be a good way of not only reducing social isolation among the elderly, but of learning from them too. There is a wealth of experience in the aging population, skills that could be used by students, entrepreneurs and business leaders.

Lupien believes that we have to change our definition of aging as a society. She has noticed that if young people are asked their opinion about the elderly, the first thing they'll often say is that old people use a lot of health care. In truth, this is not really the case. She points out that only 30% of the aged are heavy users of health care. The rest don't use it more than younger people. In fact, another 30% are rarely seen in hospital because they are successful agers.

Until fairly recently, successful aging was not a popular field for research. When aging research began in the 1970s, it mainly centred on the deficits experienced by some people as they aged. Without meaning to, scientists contributed to the view of aging as a time of impairment and decline. "It's not necessarily true that you have to lose something as you age," says Lupien. "If you realize this, and also realize that you will soon be there yourself, then everything changes."

In fact, the field of aging studies did

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FACTORS LEADING TO INSTITUTIONALIZATION IN DEMENTIA

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caregiver herself, then the patient was also more likely to be institutionalized.

The study's authors note that such findings stress the need to develop intervention strategies focusing on the management of the behavior problems of the dementia patient, and the screening for and treatment of depression in caregivers, in attempting to delay or avoid institutionalization.

Hébert, R., Dubois, M., Wolfson, C., Chambers, L., & Cohen, C. (2001). Factors associated with long-term institutionalization of older people with dementia: Data from the Canadian study of health and aging. *Journal of Gerontology*, 56a, M693-M699.

An interview with Dr. Sonia Lupien, Director of Research on Aging and Alzheimer's Disease, Douglas Hospital

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begin to change after 1987 when a paper in the journal *Science* studied successful aging. The authors believed that it was the duty of scientists to devote as much research to successful aging as they did to aging deficits.

Lupien expects aging studies to change again as a result of the baby boom generation. She is sure that the baby boomers will not be the same as the generation who are over 65 today. "Aging is not static," she says. "It's a dynamic thing that changes according to the people going through the process. The baby boomers will be 65 in 2014 and you can be sure that they'll be on the government's case!"

So how does Lupien envision her own contribution to aging research? "I'd like to be able to say I contributed to giving the elderly back the respect they deserve. I would like to be able to tell my grandchildren that we used to think that older people were all the same. Today it's so obvious that older people are important. Now there are mentors in classrooms and the elderly have respect. For us, we had to work to prove that."

EVENTS

Strategic directions in research on aging

by Jeff Boyczuk

With the inception of the Canadian Institutes of Health Research (CIHR) in June of 2000 came thirteen "virtual" institutes, each of which focused on a specific domain of health research. Among these was the Institute of Aging (IA), which has as its scientific director Dr. Réjean Hébert. On February 12, 2002, Hébert came to the Douglas Hospital to present the newly formulated strategic plan of the IA to the McGill scientific community, and to take part in a roundtable discussion regarding the directions and future of funding for aging-related research in Canada.

The strategic plan of the IA was formulated between February and October of 2001 and has, at its core, five strategic orientations: 1) leadership 2) support of capacity-building initiatives and programs 3) support of research initiatives and programs 4) promotion 5) dissemination and application of research knowledge.

Guided by its overarching mission to advance knowledge in the field of aging, the IA aims to take a leadership role in setting directions for aging research in Canada. The IA has made an open call to all organizations and individuals associated with aging research to "share information and create opportunities for interaction". The Institute will also act as a meeting point for the diverse group of scientists in aging, with the hope of forming a consensus across disciplines regarding the proper directions for aging-related research in Canada.

The IA's capacity-building orientation focuses on the direct funding of Canadian researchers. While the IA lists as a major objective the support and recruitment of mid-career and senior scientists, the accent seems to be on young researchers. Hébert made special note of the "New Emerging Team" grants that provide funding over a five-year period to teams comprised of both established and junior scientists.

The IA has also pledged to aid in the "development and support of strategic aging research initiatives, programs, and projects". The wheels are already in motion with the Canadian Longitudinal Study on Aging (CLSA), which is in the formal planning stage. The CLSA will bring together a diverse group of researchers to compile data

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THE SYNERGISTIC EFFECT OF HIGH BLOOD PRESSURE AND APOLIPOPROTEIN E4 ON LATE-LIFE COGNITIVE FUNCTION

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areas. Indeed, the ability of a patient to recover from a traumatic head injury is highly dependent on the presence and copy number of the apoE4 allele. It was once thought that head injury was the most reliable environmental risk factor for AD until it was formally shown to only be the case for apoE4 carriers. ApoE facilitates the mobilization and redistribution of key lipid molecules in response to neurodegenerative changes and damage to the brain. Unlike all other mammals, humans express three distinct isoforms of apoE: apoE2, 3 and 4. The apoE2 and apoE3 alleles appear to be protective of the regenerative capacity of the brain, while the presence of one or two copies of apoE4 dramatically reduces this regenerative capacity. An injured or diseased brain can be viewed as a delicate balance between cell loss and compensatory remodeling of surviving neurons. Patients who carry the apoE4 allele have a reduced ability to remodel neuronal circuits in response to damage and cell death. As there is no other compensatory system to make up for this reduced ability, their loss of cognitive function is exacerbated (Poirier, 2001).

In this context, the recent report by Peila et al. (2001) can be viewed as another good example of poor compensation in apoE4 carriers. This large observational study found a synergistic association between high systolic blood pressure and the presence of apoE4 on late-life cognitive function. In these patients, years (even decades) of elevated systolic blood pressure caused brain injury. The negative effects of this brain injury on cognitive function were stronger in apoE4 carriers, but this adverse effect appeared to be reduced by antihypertensive medication. If confirmed, these findings could represent a breakthrough in the search for medication to prevent or treat late onset cognitive impairment.

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Peila, R., L.R. White, H. Petrovich, K. Masaki, G.W. Ross, R.J. Havlik and L.J. Launer Joint Effect of the APOE Gene and Midlife Systolic Blood Pressure on Late-Life Cognitive Impairment: The Honolulu-Asia Aging Study. *Stroke*. 2001;32:2882-2887

Strategic directions in research on aging

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on a wide array of physical, psychological, lifestyle, and socio-cultural factors from a cohort of elderly Canadians, in order to examine the role such factors play in the physical and cognitive changes observed in aging.

Promotion is always important, and the IA has also positioned itself to be the primary advocate for research on aging in Canada. Advocacy is directed not only towards government decision-makers, but also within the CIHR itself, where an objective of the IA is to increase its share of the overall health-research funding pie. A further, and related, objective of this strategy is to integrate aging research into the CIHR Peer Review System.

Finally, the IA will seek to facilitate communication of research findings both within the aging research community, as well as to outside groups, such as non-governmental organizations and charities. The hope is that this will promote the application of research knowledge in Canada through ongoing contacts with health care professionals, industry, health policy analysts, and decision-makers.

One of the most striking aspects of the IA's strategic plan is its emphasis on a multidisciplinary approach to aging research. In one sense, this is reflective of the broader CIHR mandate, which sets out four "pillar" areas of health-research: biomedical, clinical, health systems and services, and health of populations (including social, cultural and environmental influences). However, judging by the diverse backgrounds of the roundtable discussion panel and audience members attending the meeting (which included neurologists, endocrinologists, psychiatrists, epidemiologists, and social workers), an institute that encompasses research on aging is necessarily multidisciplinary.

During the roundtable portion of the meeting, the multidisciplinary approach, as outlined in the IA strategic plan, was largely supported by both the discussion panel members and the audience. However, some of the McGill researchers who were present did point out the difficulty in attempting too broad a degree of integration among disciplines. Panel member Howard Chertkow, a neurologist, supported the necessity for scientists to go "from molecule to patient" in their research, but also noted that there is an inherent conflict in adopting a cross-disciplinary regiment. Researchers

who broaden their training to include other disciplines must also necessarily devote less time to their primary research area. This may be an especially tough path for young researchers that are seeking to become established in their field, and who are often faced with tenure-track time pressures.

The issue of gerontology training at McGill also figured prominently during the discussion, and was raised earlier in the morning by Dr. Judes Poirier from the McGill Centre for Studies in Aging. Poirier pointed out that McGill has a woefully small offering of undergraduate aging-related courses. While this is certainly a target area for improvement, on the flip side, several of the researchers present noted that student interest in pursuing post-graduate research in aging-related areas seemed to be on the rise.

Years of cutbacks in federal funding have made scientists wary of new initiatives to fund health research. Although less than two years old, the creation of the CIHR and the Canadian Institute of Aging have thus far been a positive sign from the government for scientists who study the aging process. Nevertheless, as the crush of baby boomers in Canada nears retirement age in the next couple of decades, the question that remains on the minds of most is whether funding for research on aging will increase in proportion to the need.

The full text of the strategic plan of the Canadian Institute of Health can be found at: http://www.cihr.ca/institutes/iha/whatsnew/iha-strategic-plan_e.pdf

POLICY AND POLITICS

New publication standards for clinical trials sponsored by the pharmaceutical industry

by Alison McTavish

Three years ago Dr. Nancy Olivieri and the drug company Apotex had a disagreement over a clinical trial for a new drug. Dr. Olivieri believed that the drug produced unacceptable side effects, and she disclosed her findings. Apotex believed that Dr. Olivieri was wrong and challenged her disclosure. The battle that ensued continues today, and it helped spark the introduction of a tough new editorial policy at many of the world's leading medical journals.

Funding for university-based research has been cut drastically over the last decade. Increasingly medical researchers are receiving pharmaceutical industry support for their research, particularly for clinical trials of new drugs.

Typically, clinical trials are conducted in three phases. During Phases I and II, researchers determine how the drug is absorbed and metabolized, what is the acceptable dose and if it works without producing unacceptable side effects. In Phase III trials, large numbers of patients are given the drug and closely monitored. Clinical trials are particularly expensive to run, with costs estimated to run into a hundred million dollars for a single drug.

Currently about a third of all clinical trials published in medical journals are sponsored by the pharmaceutical industry. With so much money at stake it is perhaps not surprising that surveys of medical literature have shown that trials sponsored by drug companies are more likely to report results that are favourable to the drug being tested.

New editorial policy

Concerned about a number of cases like Olivieri versus Apotex, editors of the world's leading medical journals have hammered out a new editorial policy. They wanted to make sure that academic freedom came ahead of financial interest. According to the new policy, researchers who are sponsored by industry must have free and complete access to data and must have the right to analyze the data independently of the sponsor. In addition, the sponsor cannot have the right to withhold publication for any reason.

The policy has been agreed to by 12 of the world's best known medical journals including the *New England Journal of*

Medicine, *The Lancet*, the *Journal of the American Medical Association*, and the *Canadian Medical Association Journal*. It was publicly announced in a joint editorial that all the journals published in September of 2001.

In order to publish industry-sponsored papers in these journals, authors will now be required to provide details of exactly what part they and their sponsors had in the study. Some will even require that lead authors sign a statement indicating that they had full responsibility for the trial, had access to the data and controlled the decision to publish. Studies that have not been conducted in this manner will be neither reviewed nor published.

Pharmaceutical industry reaction

Reaction from the pharmaceutical industry has been supportive. Murray Elston, President of Canada's Research-Based Pharmaceutical Companies (Rx&D), a national association representing 60 pharmaceutical companies in Canada, called the guidelines "an additional step in ensuring our researchers continue to do their work in an independent environment." He also added that this standard should be applied to all researchers regardless of their affiliation.

In the United States, Dr. Bert Spiker, a Senior Vice-President at The Pharmaceutical Research and Manufacturers of America also issued a statement of support for the new regulations. "It is essential that academic researchers who participate in clinical trials have complete freedom to participate in and approve of all aspects of a trial," wrote Spiker, "including any publication that may result from such a trial." Meanwhile in Britain, the Association of the British Pharmaceutical Industry supported the new policy and pointed out that clinical research on behalf of the UK-based pharmaceutical industry is conducted to the highest ethical and scientific standards.

New rules proposed

Some researchers, however, feel that these new editorial standards alone are not enough to ensure a full and impartial analysis of clinical trial results. A recent paper in the *Canadian Medical Association Journal*

called for a new set of rules to govern relationships between universities and industry in Canada.

Under the new rules a standard nationwide contract would be developed to govern university-industry ties. This contract would give academics the freedom to publish and disclose potentially harmful side effects of new drugs without delay. In addition, all clinical trials would be registered and a certification system would be implemented to assess scientific integrity and the commitment to intellectual freedom.

The goal of these new standards is not to stifle research and development of new drugs, but rather to ensure that the results of trials are analyzed in an unbiased fashion. Not only will this help prevent future disagreements like Olivieri versus Apotex, but it will also help ensure that the public continues to have access to safe and effective new drugs.

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REGISTRY OF AGING-RELATED WEBSITES

by Julie Comber



SENIOR'S GUIDEBOOK TO SAFETY AND SECURITY

<http://www.rcmp-ccaps.com/seniors.htm>

Contains tips and advice about home security, safety on the street and in one's vehicle, con artists and typical con games, consumer fraud, crime prevention programs and community services.

PHONEBUSTERS

<http://www.phonebusters.com/> (Bilingual)

Canadian call centre for deceptive or fraudulent telemarketing, maintained by the Ontario Provincial Police (OPP) and the RCMP. PhoneBusters collects information on telemarketing complaints throughout Canada and passes this information on to the appropriate enforcement agency. The site includes tips for spotting scams and for reporting fraud. The site also has contact information for SeniorsBusters, a group of volunteers who provide telephone support and information to seniors who have become victims of telemarketing fraud.

THECAREGUIDE.COM

<http://www.thecareguide.com/?viewpage=&viewsection=home>

Provides information, currently only for Ontario, but soon for the rest of Canada as well, about seniors' housing and care services including retirement homes, nursing homes, home health care, adult lifestyle retirement communities, supportive housing and palliative hospice care. It also provides a listing of online resources and topics of interest to seniors. To access Member or Provider services, one has to sign up, which is free.

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MEETING ANNOUNCEMENT (IN FRENCH)

Le consentement à la recherche chez les personnes inaptes :
Peut-on concilier les enjeux éthiques, juridiques et scientifiques ?

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- des conférenciers chevronnés, spécialistes de l'éthique, du droit et de la recherche
- un débat sur la pertinence de modifier les règles législatives en matière de consentement substitué

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