

The Foundation Newsletter



THE SCOTTISH RITE
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OF CANADA

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SPECIAL EDITION

Welcome to a special edition of the Scottish Rite Charitable Foundation newsletter.

In previous years we have published only one edition per year. However, there are just too many exciting Foundation-sponsored research projects to squeeze into one edition. Thus, this issue.

The Scottish Rite Charitable Foundation sponsors basic research intended to discover the causes of, and cures for, intellectual impairment in children and adults. By its nature, basic research is time consuming, which is why the Foundation sponsors major projects for a number of years.

In last fall's edition we ran items describing five projects receiving Foundation funding for the first time. In this edition we bring you up-to-date on projects that have received funding in previous years.

What becomes clear when you read these items is the dedication of the researchers to their tasks, the importance of their work, and their gratitude to the Scottish Rite Charitable Foundation for our support. The Foundation thanks you for your support.

The brain reveals the unspeakable

Dr. John Connolly, at Dalhousie University, is having great success with a new technique to assess intellectual function in people who have sustained brain damage due to a stroke or head trauma.

The difficulty faced by doctors when someone has a stroke or brain injury is how to assess what intellectual function is left. The reason: brain damage impairs communication. Common consequences of

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Blue Envelope ... and more

Many ways to support the Foundation

Members of the Scottish Rite, by making donations to the Foundation, can provide valuable support for the work of the Foundation and at the same time benefit from the income tax incentives.

Here are a number of ways you can donate:

1. Cash donations - Donations by way of cheque, either through the Blue Envelope program, or directly to the Foundation at the Hamilton Office.

2. Gifts in Kind - During one's lifetime, or on death, property may be donated as an alternative to money. A gift of property is called a gift in kind. Examples include artwork, shares and real estate. A gift in kind is normally valued at its fair market value at the time of the gift and it is this value that establishes the amount of the charitable donation for tax purposes. The donation of property will constitute a disposal for tax purposes and therefore it is necessary to recognize any capital gain or income that would have applied had the property been sold for that price. Special rules apply to the taxation of gains on gifts in kind and only 25% of any gain will be taxed, a reduction of 50% from the normal treatment.

3. Gifts of Life Insurance - Permanent life insurance, such as whole life or universal life, may be donated by transferring ownership of the policy. The value of the gift will be the cash surrender value, plus any accumulated dividends and interest assigned, minus any policy loan outstanding. To the extent that the value exceeds the tax cost of the policy the excess will be regarded as income, as if the policy had been cashed. Future pre-

miums paid on a donated policy by the donor are considered an additional charitable donation.

4. Life Insurance Beneficiary Designation - The payment of a death benefit on any life insurance policies owned at the time of death, and on which a charity has been designated as the beneficiary, is considered a donation made before death. The amount of the death benefit may be claimed as a charitable donation.

5. Purchasing an Annuity - An annuity can be purchased, whereby a lump sum is contributed up front and the donor receives a fixed annual payment for the remainder of his or her life.

6. Charitable Remainder Trusts - Property that one might wish to donate, but from which the donor needs the income during his or her lifetime, can be accomplished by donating a "residual" interest in the property - that is the capital that will remain at death. Donating in this way has several attractions:

- * the Foundation gets a vested right to the property immediately
- * the donor gets an immediate tax credit based on the "residual value"
- * the donor continues to receive the income from (or use of) the property during his or her lifetime.

If you are considering any donation option other than cash you should discuss the donation with your financial/tax advisor or alternatively consult with the Foundation staff in Hamilton to ensure that you receive appropriate advice.

a stroke are aphasia, which is a loss of the ability to use and understand language, and apraxia, which is a loss of the ability to move in a coordinated, goal-directed fashion.

As a result, says Connolly, “Two-thirds of patients in the first few weeks after a stroke will have colossal problems in communication. This means the ability of a neuropsychologist to determine the functional consequence of a stroke - including what functions they have remaining - is really compromised, because the person cannot complete the tests. If you cannot speak or point to a correct answer, they can’t evaluate you.”

But with ERP, they can. Thanks to funding from the Scottish Rite Foundation, Connolly’s group has achieved exciting results. “We have developed a technique using Event-Related brain Potentials. These are not scans in the typical sense. They are measures of function based on the electroencephalogram. It lets us see oscillations in brain activity that can be linked to specific things such as memory, paying attention to something, recognizing a face of someone they know, or not recognizing a face of someone they don’t know.”

To illustrate the power of the technology, he uses test questions taken from neuropsychological tests. “I can say two sentences, ‘The piano is out of tune,’ and, ‘The pizza was too hot to sing.’ One makes sense, one doesn’t. But imagine someone who has aphasia after a stroke and is not able to respond and communicate. How can I evaluate their understanding of the test sentences?,” asks Connolly.

With ERP, they can actually see the machine register very different brain potentials, one linked with recognizing that a sentence makes sense, and the other indicating that the listener understands it was nonsense. If the readings show that both sentences seem like nonsense, that reveals more intellectual impairment.

“When you hear those two sentences, you show very different ERP for each of them. So if you had a problem communicating but still understood language, I could play those two sentences and the ERP would show that understanding was still there, even if communication was not possible. We could say, ‘he understands. He knows that pizza doesn’t sing.’”

Connolly’s group is now working with the National Research Council to develop a compact machine to make the technology more widely available in hospitals.

Brain chemicals battle Alzheimer’s

At McMaster University, funding from the Scottish Rite Foundation has Dr. Margaret Fahnestock hot on the trail of exciting new clues not only to the mechanism of Alzheimer’s Disease but also how to use the knowledge to develop a new therapy. The research involves putting neurotrophic factors under the microscope.

Neurotrophic factors are chemicals found in the brain that have profound effects on the way in which the nerve cells of the brain interact with one another - the complex processes that are the essence of human thought. There are two such factors of special interest: Brain-derived Neurotrophic Factor (BDNF) and Nerve

Growth Factor (NGF). Alzheimer's patients have low levels of BDNF, and that chemical deficit, its causes and effects, are what interests Fahnstock and her colleagues.

"BDNF supports the survival, proper functioning and interconnections of specific types of neurons in the brain. But it has many far-reaching and subtle effects throughout the brain. We're trying to understand what the deficits are, where they occur and what is happening."

In patients with Alzheimer's Disease, some of the neurons that show particular deficits extend to the hippocampus, an area of the brain associated with learning and memory. Fahnstock is looking closely at which neurons don't make enough BDNF, and how they interconnect with other neurons.

"NGF and BDNF are two members of a family with similar functions in the brain," she says. "Both are very important and many of their effects are similar, but some are very different." In particular, BDNF affects the quality of nerve cells in the hippocampus that allows them to form, maintain and change their interconnections, called synapses. "The whole pattern of how neurons fit together is how you learn and maintain memories. So it's very important for the brain to be able to continually make and break contacts between neurons," she says.

"One of the ramifications of not having enough BDNF is not being able to make and break these synapses as readily, and therefore not being able to store and access memories. And it's known that in Alzheimer's patients' brains, there is indeed a dramatic loss of synapses."

NGF has been studied a great deal in Alzheimer's work for many years. Researchers have observed that in a laboratory culture, neurons deprived of both neurotrophic factors - NGF and BDNF - will die. If you add NGF they will survive, Fahnstock says. "If you add BDNF they will also survive, but it takes a lot more BDNF to do this. That is why researchers have looked more at NGF in clinical trials. It looks like a more powerful survival factor."

Yet her work, supported by the Scottish Rite Foundation, has produced some surprising conclusions. "We are concentrating on BDNF because, even though it seems less powerful, it has all sorts of effects that NGF doesn't have." It seems to have a greater power to enhance plasticity - the ability to make and change interconnections - and to improve excitability - the ability of neurons to fire more rapidly. That, plus the fact that BDNF is more widespread in the brain, means that even if it is not as active, it may have more far-reaching effects in terms of Alzheimer's.

"It's promising, I can tell you for sure. I see good scientific reasons to use BDNF instead of NGF as a therapeutic agent, particularly because there is a deficit of it in the brains of Alzheimer's patients and there is no deficit of NGF."

Getting funding for her research is almost as tough a job as the research itself. "Alzheimer's disease is very hot in research circles and there is a great deal of competition, with the main focus on amyloid protein. But I don't think it's wise to put all your eggs in one basket. Clearly, the Scottish Rite Foundation agrees and I am extremely grateful for that."

Palm tree seed poses exotic puzzle

Dr. Christopher Shaw of the University of British Columbia is unraveling the beginnings of a great medical mystery: “We’re looking at a disease called ALSPDC, which stands for ALS-Parkinsonism Dementia Complex. It’s like Amyotrophic Lateral Sclerosis or ALS, also called Lou Gehrig’s Disease. But it’s much more than that. It occurs only on Guam and some of the surrounding islands, and it combines the features of ALS and a Parkinson’s-like form of Alzheimer’s. It’s very bizarre.”

The people of Guam have historically had this disease in such numbers that at one time 25 per cent of the adult population died from it. The incidence has since declined a great deal. The link between the disease and the lower incidence appears to be a reduction in the consumption of the seed of the cycad, a kind of palm tree.

Research has since focused attention on a toxin, one of many found in cycads. But this toxin, unlike the others, cannot be washed out with water during the preparation of the cycad seed as food. Shaw’s team has found that the flour made from washed cycad can be fed to experimental mice and they get the symptoms of ALSPDC, with all the main features of the human disease.

“We think that we have duplicated the disease in an animal model. And our view is that the various age-related neurological disorders - ALS, Alzheimer’s and Parkinson’s - share many features and are not so separate as many people think. They are certainly combined on Guam, and whether they share important factors elsewhere is very much the question. We think they do.”

He adds that the overlap among these diseases is greater in North America than people think, too. For example, people with ALS usually die before they develop dementia. But those that live long enough do develop a dementia very much like Alzheimer’s. Also, Parkinson’s is often associated with forms of dementia. And Alzheimer’s patients can display motor nerve problems that are Parkinson’s-like. Shaw’s toxin from Guam is an important clue in how these diseases are linked.

Therefore, Shaw and his team are studying in detail how the toxin they isolated does its damage. “What the Foundation is now supporting is our study of how this toxin impacts the nervous system.”

Using the cycad flour, they can now initiate the whole disease process in laboratory mice, examining them behaviorally and through dissection and tissue examination, to develop detailed information of how the degeneration takes place at every level.

But is the mouse disease a valid mirror of the human disease? There are many indicators that it is. For example, loss of olfactory function - the sense of smell - is common in the human disease, ALSPDC as well as ALS, Alzheimer’s and Parkinson’s taken separately.

“We found in our mice there was a complete destruction of the olfactory system. So the mice are showing the same thing as the human disease,” Shaw reports. “It’s one red flag among many. We’ve seen a series of these red flags, each an example of a human feature of the disease that we are also seeing in our mice. It suggests to us that we are on the right track.”

Scottish Rite funding makes it possible to take new, exciting steps, including “trying to use some therapeutic agents in mice to see if we can block disease progress. If that occurs it would be a great outcome,” says Shaw.

Using free radicals as a sponge

Dr. John Weil of the University of Saskatchewan is looking at a new and promising but still theoretical line of attack against Alzheimer's Disease.

He's looking at free radicals, which are highly reactive fragments of chemical compounds that arise in the body and cause other chemical reactions to take place - some of them beneficial and some of them detrimental.

"There is a deep suspicion that free radicals do a great deal of damage. There is a balance, as in so many things in nature, and they often do very important jobs they are meant to do but they can get out of hand."

Free radical have unpaired electrons, which is the thing that makes them so anxious to engage in chemical reactions - to link up those link-hungry electrons with other chemicals or other free radicals. "But these unpaired electrons not only mean the radicals are more reactive. It also makes them much more distinctive to see, if you've got the right tools."

They have such a tool, an Electron Spin Resonance machine, very rare in Canada, which can keep track of those free radicals.

"We're trying to make special free radicals which would react with other free radicals that should NOT be in or near the brain. We're trying to synthesize compounds that are hardly known. We're trying to make better and more pure types of free radicals that have two qualities. One, they have to be reasonably stable - it's no use making something that's gone in 10 minutes. And two, they must be water-soluble in order to be of eventual use in the human body. We have now prepared some that have these properties."

Such free radicals could eventually act as a chemical sponge, soaking up damaging free radicals that may have something to do with Alzheimer's. But that's years in the distance.

"The first stage is to make them, and to get them very pure. The next phase would

be toxicology studies in cell cultures - to see if they are toxic to cells. Next would come tests in animals to check for toxicity."

But the first step has been taken. "We have these radicals. They are stable and they are water-soluble. We can work with them." Their main focus, now, is to improve the purity of their compounds. "There has to be a very high degree of purity before we test for toxicity in cell culture to ensure the toxicity is not due to an impurity.

"We've wanted to do this for years," explains Weil. "Now we can finally bring it all together: a chemist who is interested in pharmacology; someone who can handle cell culture and work with very sophisticated machines involving some mathematical analysis; and the funding to push the whole project ahead. Without the Foundation's support we could not proceed."

Special events raise \$50,000 for Foundation

The members of the Scottish Rite Foundation thank all those Valleys who contributed a total of about \$50,000 at the annual meeting luncheon last Fall. The amount represents the income from special events held throughout the year such as golf tournaments, special fundraising dinners, proceeds from working at bingos, children's events such as Breakfast with Mr. & Mrs. Santa Claus, Steak Feasts and contributions from a specific year's class of candidates.

The Foundation also thanks Dr. Paul Fraser for his presentation on the search for a gene responsible for Alzheimer's Disease. His presentation was a confirmation of the Foundation's commitment to fund basic research.