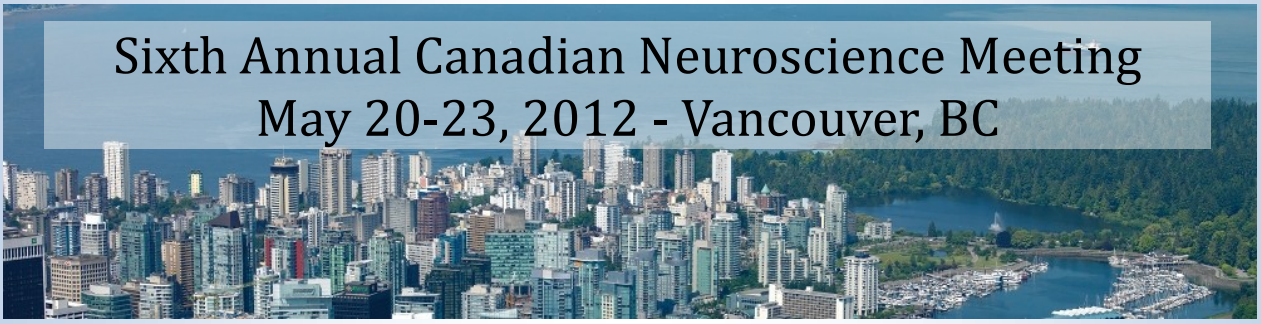


Meeting Highlights

The 2012 meeting of the Canadian Association for Neuroscience showcased current neuroscience research and demonstrated its relevance to all Canadians. Our Scientific Program Committee, led by Dr. Douglas Munoz with the help of co-chair Dr. Lynn Raymond, brought together an impressive list of top neuroscientists as speakers. All shared their insight, opinions and expertise on a wide range of neuroscience topics, including:

- ◊ Neurodegenerative diseases
- ◊ Neuronal development and repair
- ◊ Effect of socioeconomic status on mental health
- ◊ Autism
- ◊ The study of thought
- ◊ Neuroethics
- ◊ How to improve brain function
- ◊ Effects of aging on the brain

In addition to plenary speakers, many other neuroscience topics were the subject of parallel symposia and poster presentation. The full program is available at: http://www.can-acn.org/meeting2012/program.htm. Highlights of the plenary sessions are presented here.

What shapes the adolescent brain

The presidential lecture was given by Tomas Paus, from the University of Toronto. Dr. Paus uses population neuroscience, which brings together epidemiology, genetics and neuroscience, to ask what shapes adolescent brains, both from within (genes) and without (social and physical environment). He focuses on adolescence as it is a period when "biology" (sexual maturation) meets "sociology" (peer-peer interactions). Dr. Paus found testosterone has an effect on the maturation of white matter in typically developing male adolescents. He also discussed his work on drug experimentation and pointed out that one needs to take into account the social context of the peer-peer interactions to understand his findings suggesting that being born to mothers who smoked cigarettes during pregnancy might modify the brain and, in turn, increase drug experimentation

Research For All Canadians

Whether you are a daydreamer, the parent of a child whose brain development does not follow the norm, a person whose brain will age, or if you have a loved one who suffers from a neurodegenerative disease, like Huntington's disease, or are affected by a traumatic brain injury, the research presented at this year's meeting is relevant to you.

Drs. Doug Munoz and Tomas Paus

during adolescence. Dr. Paus concluded by reporting initial results obtained with fetal imaging and published data showing that a combination of adverse in utero environment with a particular genetic variation may explain a large amount of variance in the total area of the cerebral cortex.

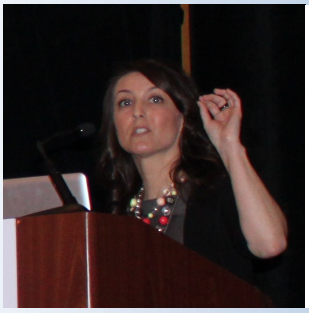
Two main reasons motivate Dr. Paus to ask what shapes the brain. First, it is likely that by uncovering sources of inter-individual variability in the (healthy) human brain, he will acquire knowledge about processes leading to a particular state of brain structure and function. Second, by gaining insights into these processes, he gets closer to predicting brain disorders. Over the long term, understanding the causes and associated processes that lead to impaired brain function, by comparison to the healthy state, will lay down the foundations for personalized and preventive medicine.

Fighting Neurodegenerative Diseases

Parkinson's and Huntington's are neurodegenerative diseases for which there are no cures. In both cases, neurons in the brain die prematurely, and only some of the symptoms of the disease can currently be treated. According to the Parkinson Society of Canada (www.parkinson.ca) more than 100,000 Canadians suffer from Parkinson's disease, while 1 in 10,000 Canadians are affected by Huntington's disease (www.huntingtonsociety.ca). The Monday morning plenary symposium featured four researchers presenting the latest findings about these devastating diseases.

The cause of Huntington's disease is a mutation in the huntingtin (HTT) gene, and it is inherited in a dominant fashion, meaning that if you inherit a diseased copy from one of your parents, you will develop the disease, usually as an adult.

Francesca Cicchetti, from Université Laval, studies an unorthodox method of treating Huntington's disease: brain tissue transplants. She, and others, want to determine if transplanting healthy brain tissue, devoid of mutations in HTT, could rescue the dying brain cells of Huntington's patients. In rodent and non-human primate models of the disease, such grafts were able to replace lost neurons and reduce symptoms. Unfortunately, in the limited human trials that were done, "very little, or even only marginal benefits of transplants were seen, and only in the first three years after transplant" says Dr. Cicchetti. She attributes this at least in part to the fact that transplanted cells simply degenerate in the toxic environment that is the Huntington's disease brain: glial cells, which support neurons , are not properly represented in graft tissue, blood does not flow well in grafts, and after a certain amount of time, the deleterious version of HTT is expressed in the previously healthy grafted cells. Knowing why transplanted neurons die will allow researchers such as Cicchetti to de-



Dr. Francesca Cicchetti

vise new ways of delivering healthy cells to diseased brains.

Edward A. Fon, from McGill University, recalls that until 1995, the causes of Parkinson's disease were thought to be uniquely environmental: toxins, pesticides, smoking, drug addiction were all viewed as probable causes of this disease. Today, in addition environmental causes, mutations in more that a dozen genes, like Park genes, Parkin and Pink1, have been identified that can cause Parkinson's disease, or are associated with an increased risk of developing Parkinson's for carriers. Mitochondria, which are the energy producing components of cells, play a key role in cell death associated with Parkinson's disease, as many genes involved in producing normal mitochondria are defective in Parkinson's patients. Parkin protein can be found in mitochondria derived vesicles, which are small membrane-bound structures cells use for transport. Dr. Fon has participated in a recent study showing that these types of vesicles are used to shuttle damaged portions of mitochondria to the lysosome, which breaks them down. This can be seen as "quality control" mechanism for mitochondria, a mechanism that would be defective in Parkinson's sufferers, resulting in the accumulation of toxic reactive oxygen species.

Genetics is truth

Matthew Farrer, from the University of British Columbia, is one of only 18 Canada Excellence Research Chairholders. Dr. Farrer stated that "genetics is truth", and that just as "eyes are windows into the soul, genetics are windows into neuroscience". Provocatively, he also stated that in contrast: "Neuroscience is a matter of opinion".

Dr. Farrer believes neuroprotection, which is the use of therapeutic agents to prevent the death of cells, is possible for Parkinson's disease. He sees genetics as a solid foundation he can use to identify targets for development of new drugs that will not only treat the symptoms of Parkinson's disease, but that will actually protect neurons and stop disease progression. Already, studies of families with high prevalence of disease have led to the identification of many mutations that cause Parkinson's disease, notably in many proteins involved in the trafficking of vesicles in cells. Dr. Farrer sees these as good targets for the development of therapeutic agents.


Dr. Matthew Farrer

Physiology is truth

James Surmeier, from Northwestern University, started his talk by stating "Physiology is truth", which sparked some smiling and applause in the room. He studies the interactions between two parts of the brain: the striatum, which he compares to a trusted advisor, and the cortex, which can be seen as the commander in chief. The striatum has to choose the right action in the right context, depending on the outcome of previous decisions. An increase in a neurotransmitter called dopamine is sensed as a positive outcome, while a decrease is recorded as a bad outcome. Using sophisticated physiological methods to generate activity (action poten-


Dr. James Surmeier

tials) in striatum-derived neurons, Dr. Surmeier was able to determine that the timing of events in neurons can lead to either activation of a "go" pathway that would inhibit "stop" signals, or the activation of the "stop" pathway, that would inhibit "go" signals.

Dr. Surmeier explains neurodegenerative disease based on this model: In Parkinson's disease, dopamine levels fall, which is interpreted as a negative outcome. The trusted advisor (striatum) always says "Don't move", and all events lead to activation of the "stop" pathway. In contrast, Huntington's disease causes a deficit in the "stop" pathway, which leads to over-activation of the "go" pathway. Patients therefore become hyperkinetic, i.e. they move too much, uncontrollably. This over-activation can become toxic to cells, a phenomenon called excitotoxicity, leading to cell death.

How to attract neurons

Alyson Fournier, from McGill University, studies neuronal guidance mechanisms. During growth, neurons respond to long range and short range cues, which include molecules that attract them (called chemoattractants) and molecules that repel them (chemorepellants). Neurons also grow based on direct contact interactions. Injured axons in the central nervous system, like those found in spinal cord injuries, mostly encounter repellants, which explains why these neurons don't just grow back. By looking at proteins found in the growth cone, which is the part of the neuron that regulates growth in response to its environment, Dr. Fournier found specific proteins, called 14-3-3 proteins, which mediate repellent responses. These, and other proteins identified by Dr. Fournier, could become targets for development of therapeutic agents.


Dr. Alyson Fournier

Edward S. Ruthazer, the CAN 2011 Young Investigator, from McGill University, studies how neurons reach their proper destination during development using the frog *Xenopus laevis*. The advantage of Xenopus is that it is transparent, which allows researchers to study the development of a single cell by injecting it with a dye. Using this approach, Dr. Ruthazer is able to see how the arbor (or branches) of a single neuron grow and retract day by day during development, and in response to specific stimuli. He has compared tadpoles placed in an environment in which both eyes see different things (asynchronous stimulus), with tadpoles reared in environments in which both eyes see almost the same thing (synchronous stimulus). The environment where stimulation is synchronous leads to stabilization of neuron connections, while asynchronous conditions increase the dynamic exploration of neurons, leading to a larger arborization. More visual stimulation also leads to the development of better visual acuity, or ability to distinguish smaller details, which can be measured either by behavioral responses or by directly measuring neuron response (electrophysiology).


Dr. Edward Ruthazer

Thomas Boyce is a behavioral pediatrician from the University of British Columbia who studies how the socio-economic status of children affects their health, and specifically their mental health. Depression, inattention, negative peer relations, poor academic competence and disease are all negatively correlated to the social position of children, even within the context of one kindergarten class. These results are also unfortunately replicated at the country level, higher levels of social inequality being associated with larger differences in neurodevelopment, while smaller differences are seen in more egalitarian countries, such as Sweden.


Dr. Thomas Boyce

Dr. Boyce also presented evidence of biological embedding of early social adversity: the amount of stress that a mother endures during the second trimester of pregnancy has a lasting effect that can be seen in 15 year old children. According to Dr. Boyce, we are currently in a historical moment for research, as we are uncovering the physical nexus of brain, genes and the environment, and their interplay. We have a "moral imperative to develop a more egalitarian society", he concludes .

Integration is the key

Daniel Geschwind, from the University of California at Los Angeles, sees an "amazing opportunity to develop therapeutics" in the current integration of genetics and neurobiology. He notes that the field is moving much faster than expected, and attributes this to integration of genetics, genomics, research on animal models and in vitro models, and studies of post-mortem human tissues. "We can't use only one element alone" insists Geschwind – all are needed to develop new therapeutic agents.

Dr. Geschwind has a specific interest in childhood degenerative diseases and autism. Autism is characterized by language/communication disorders, problems in social interactions and the presence of restrictive or repetitive behavior, and a diagnosis of autism requires that the onset occur before the age of three. But Geschwind notes that these behaviors are distributed along a normal curve, so defining a specific cutoff point for diagnosis of autism is hard. Genetically, autism spectrum disorders can be caused by many chromosome abnormalities or genetic syndromes, and most genes involved are not specific, as they are associated with other disorders also. Geschwind therefore suggests there exist multiple "autisms". The Autism Genetic Resource Exchange allows researchers to share genetic information and samples from more than 1300 families and has permitted the identification of risk alleles in humans. The genes affected can then be studied in animal models, in which therapeutic agents can be tested. The study of co-regulation of the identified genes has also allowed researchers to identify key genes that are central to important neuronal pathways that are disrupted in autism. Even though no one gene causes more than 1% of all cases of autism, integrative studies are beginning to untangle the network of links between autism genes, and, perhaps more importantly, to identify putative therapeutic targets.


Dr. Daniel Geschwind

Frédéric Charron, from Université de Montréal, is the 2012 CAN Young Investigator. He studies the signaling pathway of a gene called hedgehog (Hh) in development and disease. The Hh gene is conserved in evolution, and during embryonic development it is involved in cell differentiation, proliferation, but also in axon guidance. Dr. Charron has identified many genes involved in Hh signaling, including receptors (proteins on which Hh binds directly) and downstream elements. He has shown that Hh receptors can also be affected in certain cancers, and suggests one such receptor, called Boc, could be a therapeutic target for medulloblastoma patients. Studies of animals with mutated genes in the Hh pathway have also shown it is important for proper axon guidance for binocular vision.

Drs. Frédéric Charron and Brian MacVicar

Dr. Charron also shared some important advice with young investigators, which is to collaborate with others researchers as much as possible. His impressive publication list demonstrates how successful this strategy can be.

Do you daydream?

Kalina Christoff, from University of British Columbia, uses real-time functional MRI to investigate spontaneous thought in humans. "What do people think about when they think about thinking?" asks Christoff. The answer is usually goal directed, purposeful thinking, aimed at resolving some problem, or reasoning thought. Yet, says Christoff, 30% of our thoughts could be called mind wandering, spontaneous or even fanciful thought. And this may even be underreported, as society does not value this type of thought. By assigning repetitive tasks to subjects and interrupting them to ask subjects whether they were thinking about the task or not after a certain time period, Dr. Christoff investigates which brain regions are activated while mind wandering, using functional MRI. She noted that, in addition to what scientists have called the "default network", task-related brain regions are also activated during mind wandering. This broad activation is also seen during creative thinking. Furthermore, Dr. Christoff is now investigating whether subjects, and specifically meditators, which are highly trained in introspective observation, can modulate the activation of different brain regions if they can visualize their brain activity.

Dr. Kalina Christoff

Setting Research Priorities

Judy Illes is Canada Research Chair in Neuroethics at the University of British Columbia. Many ethical issues exist in brain research, and being proactive by attempting to consider these issues before they occur is a way to empower neuroscience and maximize the public good. Dr. Illes considers the voice of the stakeholder must be heard early, rather

An interested crowd takes part in Dr. Judy Illes' survey of neuroscientists, using clickers.

than late. As an example, she cites the potential issues of scanning "normal" brains: what if a previously unknown neurological problem is detected? How should the person be told? What follow-up should be done?

Dr. Illes is specifically interested in disorders of consciousness. She reminds us that nearly 1.4 million people in Canada live with the consequences of brain injury, there are 50 000 new cases every year, and an increasing number of patients survive previously fatal injuries. Many of them suffer disorders of consciousness, which can range from a deep coma to more moderate problems. Dr. Illes uses surveys and interviews to identify priorities for patient care, research, and more specifically, neuroimaging.

Dr. Illes took advantage of the packed conference room at the CAN meeting to conduct a survey of neuroscience researchers using "clickers", which allow participants in the room to register their answers to ethical questions and see the responses of their colleagues at the end of the survey. Difficult questions, such as questions about the desire to live and the balance between benefits and risks of research, can be evaluated using this method. By comparing the results she obtains from all stakeholders, patients, lawyers, ethicists, families, in addition to researchers, Dr. Illes will be able to provide validated priorities for research.

Giving Voice To Those Who Cannot Speak

John Connolly, from McMaster University, investigates how to detect consciousness in patients that cannot communicate. Event related potentials (ERPs), which are recordings of brain activity in response to various stimuli, can be used to evaluate whether a patient responds to language even in the absence of overt behavior. By looking at how brain activity changes in response to sen-

tences that make sense or not, Dr. Connolly can determine if a patient is conscious, in which case a rehabilitation program can be initiated.

Dr. Connolly also studies patients suffering from non-verbal autism, since ways of evaluating these individuals is lacking. People assume you are intellectually challenged if you cannot talk, but this is not always the case, he argues. Dr. Connolly's goal is to give voice to those who cannot speak.

Adrian Owen, from Western University, holds a Canada Excellence Research Chair. He brought all the morning's ideas together, by showing how to use directed thought to communicate with locked-in patients. The distinction between vegetative states, in which there is wakefulness without awareness, a locked-in state, in which patients are fully aware, but unable to communicate, and brain death, for which there is no chance of recovery is an important one, and one on which Canadian courts will be ruling on soon, so having clear evidence of consciousness is very important.

Dr. Owen suggests that proof of consciousness requires an act from the patient. As these patients cannot move, talk or otherwise physically act, he looks for "brain acts". Imagining a movement, such as playing tennis, activates regions of the brain in the pre-motor cortex, while imagining other actions, such as moving around in a house, activates other regions of the brain. Dr. Owen found that about 1 in every 5 "vegetative" patient can activate the proper brain regions when asked to imagine playing tennis or moving around in a house, thereby clearly demonstrating consciousness in the absence of movement. The brains of control individuals, when under sedation, do not perform these "brain acts", demonstrating specificity of the response. These acts have been used to communicate with patients, who can imagine playing tennis if they want to say yes, or moving around to say no.


Dr. Adrian Owen

Dr. Owen highlighted the importance of determining very carefully the questions you would ask such patients, because it is difficult to determine if patients are able to reason properly. Questions about the will to live are the most delicate and require the most ethical consideration, since without extensive discussion, it is difficult to know if patients understand the consequences of their answers. Read a recent profile of Owen, and more details about his experiments in a June issue of Nature.

Other plenary speakers at the meeting included Dr. David Lewis, Director of the Translational Neuroscience Program at the University of Pittsburgh, presenting his research about schizophrenia, and a public lecture by Drs. Max Cynader and Howard Feldman, from the University of British Columbia, who demonstrated how current neuroscience research provides new insights into how to boost brain power and how we understand the effects of aging on learning and memory.

Students and trainees have always been at the heart of Canadian Neuroscience Meetings. Complete poster abstracts are available, in addition to many pictures of the very lively poster ses-

sions. The top three BrainStar Awardees of 2011 also had a chance to present their award winning work at the 2012 CAN meeting. They are Vivek Swarup, Simon Girard, and Bahareh Ajami, who is the Marlene Reimer Brainstar of the year .

Drs. Bahareh Ajami and Anthony Phillips

Thank you to all participants for making this meeting a great success. The breath of the subjects discussed and the quality of the research presented at the 6th Annual Canadian Neuroscience Meeting demonstrates the importance and relevance of neuroscience research and communication to all Canadians.

Many thanks to our Sponsors and Exhibitors!

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Reminder

Next year's meeting will be held in Toronto, May 21-24, 2013!

- Hotel reservations already open! Sheraton Centre Toronto Hotel
- Call for Abstracts opens Fall 2012
- Registration will open in early 2013