Dr. Andres Lozano - 2014 Innovations in Neuropsychopharmacology Award Recipient

The 2014 Innovations in Neuropsychopharmacology Award will be presented to Dr. Andres Lozano at the 37th Annual Meeting of the Canadian College of Neuropsychopharmacology in Banff, Alberta. The Innovations Award, sponsored by Pfizer Canada Inc., is designed to recognize innovative research by Canadian scientists in research in the field of neuropsychopharmacology.

Andres Lozano is Professor and Chairman of Neurosurgery at the University of Toronto, and holds both the RR Tasker Chair in Functional Neurosurgery and a Tier 1 Canada Research Chair in Neuroscience.

Dr. Lozano’s research has focused on assessing the therapeutic potential of modulating the activity of dysfunctional brain circuits in patients with neurological and psychiatric disorders using deep brain stimulation (DBS). His initial work on Parkinson’s disease has helped bring DBS to over 100,000 patients throughout the world. More recently he and his team have made the leap of moving away from targeting motor circuits with DBS and are now focusing on targeting of mood and cognitive circuits to treat patients with psychiatric and cognitive disorders.

The Lozano group conducted the world’s first clinical trial of DBS for depression (Neuron 2005). They have obtained direct measures of cellular activity of neurons in the subgenual cingulate cortex and shown that neurons in this brain region process sad and disturbing emotions (Biological Psychiatry 2013). They have shown that there is baseline hyperactivity in Brodmann area 25 in patients with treatment-resistant depression—and that DBS corrects this metabolic abnormality (Neuron 2005). They have also identified metabolic hypoactivity in frontal cortical areas mediating motivation, drive and executive function in patients with treatment-resistant depression and that this abnormality can also be partially reversed with DBS (Neuron 2005).

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Dr. Lozano’s team is carrying out pioneering clinical trials in patients with treatment-resistant depression (Biological Psychiatry 2010, J Neurosurgery 2013). In addition, they have developed application of DBS in animal models of depression and have shown that DBS in the infralimbic cortex of rodents (the homologue of the human subgenual cingulate cortex) has antidepressant-like effects (Biological Psychiatry 2012). The human clinical results, supported by the data from animal models, have now been used to launch a Phase III clinical trial involving 18 centers in North America. To date 90 patients have been enrolled in this trial. With the promising initial results in depression, they have expanded this work to include other psychiatric disorders and have now performed DBS in patients with bipolar disease as well as anorexia. The anorexia work, the world’s first trial of DBS in this disorder, has recently been published in The Lancet (2013).

The Lozano group is influencing how we think of psychiatric disturbances, having been able to make the case that that psychiatric symptoms arise from dysfunctional neural networks and have suggested potential mechanisms through which DBS applied to these circuits may correct the physiologic abnormalities and perhaps lead to improved function (Neuron 2013). Working on the basis of this principle, they have now expanded their results and taken on the possibility of driving function in memory circuits in patients with Alzheimer’s disease and have conducted the world’s first clinical trial of DBS in this disorder (Annals of Neurology 2010). In this new series of novel and exciting experiments, they have shown that DBS in the fornix can drive activity in neural circuits and increase glucose utilization in the temporal and parietal lobe areas, which show decreased glucose utilization in Alzheimer’s disease. Dr. Lozano and his team have now received NIH and corporate funding to conduct a randomized Phase II, sham stimulation-controlled, double-blind trial of DBS of the fornix to treat Alzheimer’s disease. As of December 2013, 33 of 40 patients have been implanted and the trial enrolment should be completed in the spring of 2014.

To understand the mechanism of action of DBS, Dr. Lozano’s team has expanded these clinical results in Alzheimer’s patients to work in animal models, and have shown that the application of brain stimulation within memory circuits can drive neurogenesis (J Neurosurgery 2008, J Comparative Neurology 2011, Hippocampus 2011). This in turn results in improvements in spatial memory and conditional fear memory in these animals (J Neuroscience 2011).

Future work will focus on determining the mechanism of action of DBS within mood and cognitive circuits—an essential element for optimizing treatments and conducting clinical trials to determine...
whether therapeutic interventions within these circuits could be safe and beneficial to the multitude of patients with these disorders who continue to suffer despite the currently best available therapies.

Dr. Andres Lozano is undoubtedly a most deserving and worthy recipient for the 2014 CCNP Innovations in Neuropsychopharmacology Award. Congratulations to Dr. Lozano!
The 2014 Young Investigator Award will be presented to Dr. Alasdair Barr at the 37th Annual Meeting of the Canadian College of Neuropsychopharmacology in Banff, Alberta. The Young Investigator Award, sponsored by Pfizer Canada Inc., is designed to recognize outstanding contributions in the field of research in neuropsychopharmacology by a young basic or clinical investigator in Canada.

Dr. Alasdair Barr is an Associate Professor in the Department of Anesthesiology, Pharmacology & Therapeutics in the Faculty of Medicine at the University of British Columbia. He completed his doctoral research in the Neuroscience program at UBC, working with Dr. Anthony Phillips. He completed postdoctoral research at both UCSD and The Scripps Research Institute in molecular neurobiology before returning to a faculty position at UBC. He is the author of approximately one hundred peer-reviewed articles, and has published extensively in the area of schizophrenia, depression and substance abuse. He currently maintains an active research in both preclinical and clinical neuropsychopharmacology.

Dr. Alasdair Barr trained in neuropsychopharmacology through doctoral studies in Neuroscience at UBC under the supervision of Dr. Anthony Phillips. The central focus of his research was the utility of psychostimulant drug withdrawal as an animal model of anhedonia. Alasdair completed an impressive series of experiments on amphetamine withdrawal that remain to this day key to understanding the phenomenon, and help validate the relevance of the model to clinical depression in man (Barr et al., *Trends Pharmacol Sci* 2002; Barr et al., *Neurosci Biobehav Rev* 2005). While a student at UBC, Alasdair collaborated with the Honer laboratory and was the major contributor in planning and implementing a series of animal model studies of the role of the presynaptic SNARE proteins as molecular substrates for schizophrenia and antipsychotic drug therapy (Sawada et al., *Mol Psychiatry* 2002). A follow-up study with Dr. Barr as a key collaborator was the first translational report of the role of the SNARE-interacting proteins called complexin I and II as mediators of cognitive impairment in both rodent models and investigations in patients (Sawada et al., *Arch Gen Psychiatry* 2005).

Dr. Barr undertook postdoctoral work first at the University of California, San Diego with Dr. Mark Geyer. Alasdair acquired world-class training in animal models of schizophrenia, using translational behavioural techniques such as prepulse inhibition of the acoustic startle reflex (Barr et al., *Neuropsychopharmacol* 2004). A second post-doctoral fellowship was completed at The Scripps Research Institute with Dr. Tamas Bartfai. Alasdair performed important neuropharmacology research on the neuropeptide galanin as a potential antidepressant drug target (Bartfai et al., *Proc Natl Acad Sci USA* 2004; Lu et al., *Proc Natl Acad Sci USA* 2005). Alasdair also used sophisticated molecular biology techniques to characterize how antidepressant treatments modify gene expression in the rodent brain (Conti et al., *Mol Psychiatry* 2007).

After his return to UBC, Alasdair accepted a faculty position first in the Department of Psychiatry (grant tenure) in 2006. As a junior faculty member at UBC, part of Dr. Barr’s research involved continuation of work with the Honer laboratory on the role of presynaptic SNARE proteins in neuropsychiatric disorders. Studies included a report on the effects of antipsychotic drugs in the rodent brain (Barr et al., *Int J Neuropsychopharmacol* 2006), leading to follow-up studies in human postmortem brain tissue (Barakauskas et al., *Neuropsychopharmacol* 2009). Alasdair also contributed to examining the role of these presynaptic proteins as an integral component of neural reserve in aging, cognitive impairment, and dementing illnesses such as Alzheimer’s disease (Honer et al., *Transl Psychiatry* 2012; Boyle et al., *Ann Neurol* 2013). The Barr and Honer laboratories collaborate with the UBC Centre for Drug Research and Development, to screen libraries of over 100,000 compounds to identify those that can modify SNARE protein-protein interactions, and may provide novel therapeutic drug treatments for both schizophrenia and Alzheimer’s Disease.

In 2007, Dr. Barr was recruited into a full tenure-track position as Assistant Professor in the UBC Department of Anesthesiology, Pharmacology and Therapeutics. At this point, Alasdair made a conscious decision to expand his academic focus from purely preclinical research to establishing a program that was truly translational – bringing the insights from laboratory work on animal models into the clinic. As part of this focus, the Barr laboratory established de novo a productive line of preclinical research on the side effects of antipsychotic drugs (Boyda et al., *Trends Pharmacol Sci* 2010; Leung et al., *Pharmacol*
These side effects remain one of the key barriers to successful treatment in patients with psychosis, and are a tremendous burden for patients, and to the health care system. Alasdair has focused primarily on the metabolic side effects of the second generation antipsychotic drugs, as this issue represents one of the most common and serious concerns in patients treated with these agents. Using well-validated animal models, Alasdair and his team have been able to characterize drug-unique and dose-dependent effects of different antipsychotic drugs which accurately represent the clinical scenario (Boyd et al., *Prog Neuropsychopharmacol Biol Psychiatry* 2010; Boyd et al., *Neuropharmacology* 2012; Boyd et al., *Exp Clin Psychopharmacol* 2013; Boyd et al., *PLoS One* 2013). These models have been used to identify both non-pharmacological interventions such as exercise (Boyd et al., *Int J Neuropsychopharmacol* 2014) and pharmacological treatments (Boyd et al., *J Psychiatry Neurosci* 2012) that can improve metabolic health and decrease the side-effects of antipsychotic drugs. One of his most recent studies identified specific antidiabetic drug combinations for reversing the metabolic side-effects of the antipsychotic drug olanzapine (Boyd et al., *Prog Neuropsychopharmacol Biol Psychiatry* 2013). These combinations have never been tested in patients, and a translational clinical trial in patients at a tertiary mental health facility is now in preparation. The preclinical exercise-related studies also demonstrated that in rats, chronic treatment with olanzapine led to a reduction in the volume of the hippocampus, and this reduction was associated with increases in olanzapine-induced visceral fat and glucose intolerance (Barr et al., *Neurosci* 2013). Exercise ameliorated these effects of olanzapine in the rat model. Alasdair is now following up on this study in the clinical population at the BC Psychosis Program inpatient ward at UBC. He is leading an important MRI study that will be the first ever to examine the relationship between abdominal fat, metabolic syndrome and brain structure in patients treated with clozapine and other agents for relatively refractory forms of psychosis. Finally, Dr. Barr formed a productive collaboration with Dr. Ric Procyshyn to examine the prevalence and consequences of the poorly justified practice of treating patients with multiple antipsychotic drugs simultaneously. Here, as senior author in well-cited work in community-based adult patients (Procyshyn et al., *J Clin Psychiatry* 2010), and from child and adolescent inpatients (Procyshyn et al., *J Clin Psychopharmacol* 2014), Dr. Barr’s clinical studies were the impetus for examination in the rodent model of the consequences of antipsychotic polypharmacy for metabolism. This work demonstrated the adverse, additive effects of multiple antipsychotic drugs on glucose metabolism and insulin resistance (Boyd et al., *Exp Clin Psychopharmacol* 2013), further defines suitable animal models and research strategies to investigate the mechanisms of these side effects, and will guide development of novel strategies to ameliorate these debilitating actions in man.

Dr. Barr is now a tenured Associate Professor in the Department of Anesthesiology, Pharmacology and Therapeutics in the Faculty of Medicine. He currently has more than one hundred peer-reviewed manuscripts either published or under review. Dr. Barr’s h-index is 31, reflecting the impact of his publications on the field. His research has been funded by CIHR, NSERC and CFI, amongst others, and he was awarded both the CIHR New Investigator Award, and the Michael Smith Foundation for Health Research Scholar award. To summarize, Alasdair is one of the finest young talents in neuropsychopharmacology in Canada. His work establishes the relevance of animal models to specific aspects of the clinical features of neuropsychiatric illness, links preclinical studies of antipsychotic drug action and side effects to patients, and importantly uses his own clinical research findings in schizophrenia and psychosis directly as a source of inspiration for laboratory studies to broaden our understanding of some of the most severe mental illnesses.

Dr. Alasdair Barr is undoubtedly a most worthy recipient of the CCNP’s 2014 Young Investigator Award. Congratulations to Dr. Barr!
The 2014 Heinz Lehmann Award will be presented to Dr. Glenda MacQueen at the 37th Annual Meeting of the Canadian College of Neuropsychopharmacology in Banff, Alberta. This award, sponsored by Pfizer Canada Inc., is designed to recognize outstanding research achievements by Canadian scientists in the field of Neuropsychopharmacology.

Dr. MacQueen has been principal or co-investigator on projects funded by the Canadian Institute of Health Research, National Institutes of Health, Ontario Mental Health Foundation, the Stanley Medical Research Institute, NARSAD, the Scottish Rite Foundation, Ontario Brain Institute, and the National Centre of Excellence AllerGen Inc. She has studied various aspects of mood disorders across several levels of analysis. Early in her career she held a NARSAD award to study the effect of antidepressant treatment on behavior and molecular markers following early maternal separation. This work was conducted in conjunction with Dr. T. Young, with whom she worked closely for a number of years. Most of her research in the past decade has focused on studying the behavioral and neural markers of depression in humans. She has used novel and standard cognitive paradigms as well as neuroimaging methods to examine the changes that occur over the course of mood disorders. She has also participated in a number of clinical trials, examining the efficacy of novel medications and psychotherapy in the treatment of depression, and has published meta-analyses and systematic reviews related to treatment of mood disorders in high quality journals. She participated in a large Clinical Effectiveness Review examining treatment of depression following failure of first-line treatment. This review was requested by the American Academy of Family Physicians and funded by the Agency for Healthcare Research and Quality. She was the only psychiatrist on the team, which was led out of the Evidence Based Practice Centre at McMaster University.

Although Dr. MacQueen studies depression from a variety of perspectives, her work on understanding the relations between brain structure and function and depression has likely contributed the most to advancing understanding of the pathophysiology of depression. In a review published in Molecular Psychiatry, she and her colleague in this field, Dr. Thomas Frodl, describe how this work has shifted the understanding of depression from one that was primarily a ‘chemical imbalance’ to one that is understood to arise from and result in structural and functional alterations in key brain regions. These structural changes are now recognized to predict both short- and long-term response to treatment, and therefore are thought to reflect clinically important changes in brain structure associated with depression. In addition to studies in depression, Dr. MacQueen has also examined bipolar disorder from a similar perspective. She has examined the neural correlates of cognitive dysfunction in patients with bipolar disorder, novel strategies to treat this problem, and as with her work in major depression, has extended her work in bipolar disorder to meta-analytic examinations of the role of antidepressants and mood stabilizers in the treatment of bipolar depression. She was part of a large group on investigators associated with the International Society for Bipolar Disorder that recently published a consensus paper on the role of antidepressants in bipolar disorder in the American Journal of Psychiatry.

In addition to her own neurobiological studies of mood disorders, Dr. MacQueen has supported new investigators to expand the field of study in mood disorders. She was the PhD supervisor and later identified mentor for Dr. Valerie Taylor who received a New Investigator award from NARSAD to examine the somatic consequences of depression. Dr. Taylor is now an associate professor at the University of Toronto and the Chief of Psychiatry at Women’s College Hospital. She was the identified mentor for Dr. M. McKinnon who also received a highly competitive New Investigator Award from NARSAD to study autobiographical memory in depression. Dr. McKinnon is co-vice chair of research for the Department of Psychiatry at McMaster. Dr. Stefanie Hassel, a recent postdoctoral fellow joined the faculty of Aston University in the U.K. on July 1st, 2013 and Dr. Signe Bray, another postdoctoral fellow recently joined the faculty at the University of Calgary. Each of these researchers is now independently funded and contributing to various aspects of research in depression. In addition, Dr. MacQueen has been the primary supervisor for several other fellows (Drs. Marin, Campbell, Sokolowska, Yucel, Jaworska) and numerous graduate students. She provides both formal and informal mentorship to a number of faculty at the University of Calgary who are studying neurobiological aspects of both unipolar and bipolar depression. She is involved in current studies, for example, examining whether aerobic exercise is associated with measurable structural and functional changes in the hippocampus and whether
In addition to research and educational contributions relevant to advancing an understanding of mood disorders, Dr MacQueen has led clinical programs focused on translating the emerging knowledge of the neurobiology of mood disorders into clinical programs of relevance to patients with depression and related illnesses. Prior to moving to Calgary, Dr MacQueen was the Academic Head of the Mood Disorders Program affiliated with McMaster University for five years (2003-8). A major clinical initiative of the program was the development of the First Episode Mood Program. There are many established programs for first episode psychosis, but this was one of the first programs in Canada to develop a service dedicated to understanding the early brain changes that are associated with this stage of illness for people with mood disorders. Dr MacQueen also initiated the Somatic Health Service to focus addressing the metabolic dysregulation in mood disorders and a Cognitive Remediation Program that focused on studying and treating cognitive dysfunction in patients with mood disorders. Dr MacQueen is also a member of the board of the Canadian Network for Mood and Anxiety Treatment (CANMAT), and within CANMAT and the Canadian Psychiatric Association has contributed to many educational programs focused on translating current neurobiological findings and concepts into learning programs of relevance to clinicians. Through administrative and knowledge translation activities she has been committed to making research describing the neurobiological underpinnings of mood disorders and treatment relevant to patients and front line clinicians.

After moving to Calgary to assume the position of Head of the Department of Psychiatry, she became involved in several provincial and national initiatives focused on neurobiological and translational studies of depression. One of these, the Canadian Biomarker Integration Network for Depression (CANBIND) recently received $18 000 000 in funding from the Ontario Brain Institute. She is co-PI on the CANBIND submission, led by Dr Sidney Kennedy in Toronto, and she is also co-PI along with Dr Kennedy on a CIHR operating grant that was funded in March 2103 to study potential biomarkers in patients with depression.

Dr MacQueen has made sustained contributions to advancing our understanding of the neurobiology of mood disorders and the neural effects of treatments for these conditions. She has not only contributed to generating knowledge in this field, but through educational, service and knowledge translation activities, she has worked to make this knowledge relevant to clinicians and patients alike.

In summary, Dr. Glenda MacQueen has made significant contributions to the field of neuropsychopharmacology and is a very worthy co-recipient of the 2014 Heinz Lehmann Award. Congratulations to Dr. MacQueen!