Impulsivity and compulsivity have been considered opposite poles of a continuous spectrum, but their relationship appears to be more complex. Disorders characterized by impulsivity often have features of compulsivity and vice versa. The overlap of the constructs of compulsivity and impulsivity, as well as their differences, suggest different pharmacological targets may be warranted. This presentation will discuss novel pharmacological interventions for compulsive and impulsive behaviors.

Many of the pharmacological options that reduce impulsive or compulsive behaviors in certain disorders may be useful for these cognitive domains seen in other disorders. For the purposes of this talk, I will focus on several classes of pharmacological agents and discuss to what extent they may be effective in reducing impulsivity and compulsivity. Of course, there are multiple forms of impulsivity and compulsivity, and different forms of each can co-occur within the same person. In some cases, there are data regarding which type of impulsivity or compulsivity the pharmacological agent is targeting. In those cases, this talk will discuss the subtype in more detail. Additionally, the presentation will discuss the implications of basic neuroscience for developing novel neuropsychopharmacological interventions, and the relevant clinical evidence-base.

References
Grant JE, Chamberlain SR. Impulsive action and impulsive choice across substance and behavioral addictions: cause or consequence? Addict Behav. 2014 Nov;39(11):1532-9
Pallanti S, Hollander E. Pharmacological, experimental therapeutic, and transcranial magnetic stimulation treatments for compulsivity and impulsivity. CNS Spectr. 2014 Feb;19(1):50-61

S5: New Advances in Precision Psychiatry
Chair: Gwyneth Zai, Canada
Co-Chair: Kazutaka Shimoda, Japan

Speaker 2: Tao Li, China
Title: Genetics of Response to Antipsychotic Medication in Chinese Patients
Abstract
Patients with Schizophrenia respond differently to antipsychotic drug treatment. The underlying mechanism for these individuals’ differences remains unknown. However, there is growing evidence indicating that genetic background contributes substantially to efficacy of antipsychotic drug. In order to test the genetic mechanism of treatment response of antipsychotic drugs, we performed exome sequencing in a group of patients with very good response and matched patients without response. And reduction rates of PANSS and sub-scales were used to evaluate treatment responses. We found that a number of genes (ZNF804A, PIWIL4, TG and KALRN) involved in treatment response of antipsychotic drug. Pathway analysis showed that pathways involved in glutamate, including the pathways involved in CNS and abnormal neurotransmitter level, and the N-methyl-D-aspartate (NMDA) and-α-Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) mediated synaptic pathways, were detected to implicate in treatment response of antipsychotic drugs. Especially, the treatment response for negative symptoms was more significantly associated with these two pathways.

Speaker 3: Gwyneth Zai, Canada
Title: Pharmacogenetics of Antidepressant Treatment Response in Obsessive-Compulsive Disorder
Abstract
Gwyneth Zai, Carolina Cappi, Vanessa Gonçalves, Roseli Shavitt, Euripides Constantino Miguel, Margaret A. Richter, James L. Kennedy.
1Neurogenetics Section, Centre for Addiction and Mental Health, Toronto, Canada 2Department of Psychiatry and Institute of Medical Science, University of Toronto, Toronto, Canada 3Behavioural and Clinical Neuroscience Institute and Department of Psychiatry, University of Cambridge, Cambridge, UK 4Frederick W. Thompson Anxiety Disorders Centre, Department of Psychiatry, Sunnybrook Health Sciences Centre, Toronto, Canada 5Department of Psychiatry, University of São Paulo School of Medicine, São Paulo, Brazil

Background: Precision medicine utilizing genetic testing has recently received much attention given that the variability of response and tolerability to psychotropic medications are partly due to an individual’s genetic variations. This has led to increasing research to investigate the role of specific genetic factors on psychotropic medication response and utility of testing in the clinical realm (Zai et al., 2014, Pharmacogenomics, 15, 1147–1157). Antidepressant medications are the first-line pharmacological treatment for mood, anxiety, and obsessive-compulsive and related disorders. However, 20–50% of patients show poor or minimal response to these medications.
Purpose: We aimed to investigate the genetics of antidepressant response in patients with obsessive-compulsive disorder (OCD) in two ethnic groups.

Hypothesis: We postulated that different genetic variations across known OCD candidate genes may predict antidepressant response in OCD patients with different ethnic background.

Method: We examined two independent and ethnically different OCD samples. The Canadian sample comprises of 222 Caucasian OCD subjects and we investigated 32 single nucleotide polymorphisms (SNPs) across 14 OCD candidate genes and their regulatory regions with antidepressant response data using a custom-made 32-SNP QuantStudio Flex Real-Time PCR System Chip. Individuals were grouped into those who improved following an adequate trial of antidepressant as compared with those who reported "minimal" improvement, "no change", or "worsening" using the Clinical Global Impression – Improvement scale. Pearson χ² test was performed to detect differences in the number of responders versus non-responders across genotype groups. The Brazilian sample consists of 192 Brazilian OCD individuals and 45 SNPs across 18 OCD candidate genes were genotyped. Of the 192 Brazilian OCD participants, 74 completed an adequate antidepressant trial and change of the Yale-Brown Obsessive-Compulsive Scale severity scores pre- and post-treatment were compared between genotype distributions of each examined SNP.

Results: For the Canadian sample, interesting associations (P<0.05) were detected for the serotonin genes, HTR2A and HTR1B in antidepressant response. For the Brazilian sample, significant associations were detected for a gabaergic system gene, GABRA3, and antidepressant response (P<0.05).

Conclusions: These variants may be clinically useful in predicting treatment resistance versus response in patients with OCD, thereby, reducing their duration of suffering via trial-and-error method of prescribing and improving clinical outcome.

Speaker 4: James Kennedy, Canada
Title: The IMPACT Study - “Psychiatry Pharmacogenomics Testing in Clinical Practice”

Abstract
In genomics the amount of information available is increasing rapidly. At the same time our knowledge of inter-individual differences in terms of response and side effects to medications is at an early stage. For example, an important dilemma facing psychiatrists when they need to select an antipsychotic medication for their patient is the forced choice between risk for weight gain and diabetes with the newer generation drugs versus the risk of tardive dyskinesia and other motor side effects with first generation antipsychotics. We have developed a model of seven genes (melanocortin-4 receptor, serotonin 2C, neuropeptide Y, others) that predicts 67% of the variance in risk for this weight gain (Tiwari et al, 2015). In terms of antidepressant treatment there are now several replicated studies showing a significant benefit of gene guided medication selection over treatment as usual (Altar et al, 2015). Genes tested include CYP450, 5HT2A, and 5HTTLPR. In addition to significant clinical improvement and reduction of side effects there is also a documented reduction in health care costs when genetic guidance is used in antidepressant treatment. Regarding the concern that physicians will not be able to efficiently translate complex genetic information into clinical decision-making, we have surveyed over 200 psychiatrists and family practitioners in our Toronto-based pharmacogenetics study (www.IM-PACT.ca; n=4,900 patients tested) and found that the overwhelming majority of physicians found our user-friendly genetic report to be readily understandable, and over 90% believe that pharmacogenetics testing will become standard of care in the future. We are now working on relevant epigenetic changes in the cortisol system genes, and in the serotonin transporter gene, that may affect medication response and side effects.

14.45 – 16.30

S6: Predicting therapeutic response in depression
Chair: Siegfried Kasper, Austria
Co-Chair: Yu Xin, China

Speaker 1: Siegfried Kasper, Austria
Title: Clinical and genetic findings in treatment response

Abstract
The Group for the Study of Resistant Depression (GSRD), a collaborative project between eight centers in Belgium, France, Greece, Italy, Israel and Austria developed a staging model that distinguishes between "non-responders" (patients who fail to respond to one form of treatment, administered for six to eight weeks), a condition which is now termed “insufficient response” by the European Medicines Agency (EMA), “treatment resistant depression” (TRD, patients that fail to respond to two or more adequate antidepressant trials of different classes of antidepressants), and “chronic resistant depression” (CRD, patients being treated with several antidepressants for more than twelve months). The clinical findings of the GSRD provide a set of eleven variables associated with treatment response, among them comorbid anxiety disorders as well as melancholic features (Souery et al., 2007, Journal of Clinical Psychiatry 68: 1062–1070). Although there is a plethora of hints in textbooks that switching the mechanism of action should be obtained when a patient does not respond to one medication, the results of the GSRD challenge this notion by describing that staying on the same antidepressant mechanism of action for a longer time is more beneficial than switching (Souery et al., 2011; World Journal of Biological Psychiatry 12: 364375). The clinical and genetic findings of the GSRD European multicenter project have been summarized by Schoesser et al. (European Neuropsychopharmacology; 2012; 22: 259–266) and recently expanded by Kautzky et al (European Neuropsychopharmacology; 2015; 25: 441–453) including machine learning techniques to handle the large amount of data obtained in this ongoing research protocol.

Speaker 2: Heon-Jeong Lee, Republic of Korea
Title: A hypothesis of circadian rhythm on the treatment response in depression

Speaker 3: Shigeto Yamawaki, Japan
Title: Impact of neuroimaging on treatment response in depression

Abstract
Major depressive disorder (MDD) is a heterogeneous condition in which a wide range of etiologies, risk factors and symptom profiles may be associated with a threshold diagnosis. Response rates in drug treatment are variable and often less than 50% due to a trial-and-error prescription of antidepressants. Despite significant