

**DEPARTMENT OF PSYCHIATRY RESEARCH DAY 2013 (June 6)
ABSTRACTS**

ORAL PRESENTATIONS - TRANSLATIONAL AND CLINICAL RESEARCH

Paradoxical longitudinal cognitive improvement in APOE ϵ 4 First-Episode Schizophrenia

Presenter: Fidel Vila-Rodriguez, Clinician Investigator Program Fellow
Faculty Sponsor: William G. Honer

APOE ϵ 4 is a genetic risk factor for schizophrenia, and is the main genetic risk factor for late onset Alzheimer's disease. Cognitive impairment in a wide array of cognitive domains is one of the most robust findings in schizophrenia, and these are present even at first clinical presentation of the disorder. Little is known about what are the genetic determinants of these cognitive deficits. Methods: A community based sample of FES (n=98), and Controls (Ctrl; n=76), was recruited for this study. Demographic, clinical, APOE genotype, and a neuropsychological battery were administered. Neuropsychological tests were grouped following MATRICS profile. Mixed multivariate models were used to test between- and within-effects for cognitive executive function, working memory, and verbal memory domains. Results: Patients performed worse on all MATRICS neuropsychological domains. While patient's executive function improved at follow up in both FES APOE ϵ 4 and non-APOE ϵ 4 FES-carriers, working memory remained unchanged, and, unexpectedly, verbal memory improved only in FES APOE ϵ 4 carriers. Conclusion: FES patients showed worse cognitive performance than controls on, and FES APOE ϵ 4 carriers show an improvement in verbal memory. APOE ϵ 4 may have an antagonistic pleiotropic effect on verbal memory in FES.

Gray and White Matter Brain Abnormalities in First Episode Mania with Psychosis

Presenter: Kam Keramatian, PGY4 Psychiatry Resident
Faculty Sponsor: Lakshmi Yatham

Introduction: Advances in neuroimaging data processing have made it possible to investigate neuroanatomical abnormalities in patients with a variety of psychiatric conditions including those presenting with early psychosis. Recent Magnetic Resonance Imaging (MRI) studies have consistently demonstrated that patients with early psychosis have reductions in cortical grey matter volumes in brain regions such as anterior cingulate, insular cortex and cerebellum. It is, however, unclear whether these morphological changes represent a general feature of vulnerability to psychosis or they are specific to primary psychotic disorders such as schizophrenia. Methods: We analyzed MRI data from the Systematic Treatment Optimization Program for Early Mania (STOP-EM) to investigate structural brain abnormalities in patients with first-episode mania (FEM) with and without psychosis. Results: Unlike non-psychotic FEM group, patients with psychotic FEM had significant volume reduction in both grey matter and white matter compared to healthy controls. Moreover, when directly compared with the non-psychotic FEM group, patients with psychotic FEM showed localized grey matter loss in brain areas implicated in the onset of non-affective psychosis. Conclusion: While preliminary, our findings suggest that abnormalities in certain brain circuits might underlie expression of psychotic symptoms regardless of whether they are a part of schizophrenia or mood disorder.

Depressive and Anxiety Symptoms in Academic Physicians

Presenter: Trish Nolan, PGY3 Psychiatry Resident
Faculty Sponsor: Raymond W. Lam

Introduction: Physicians may be at high risk for mental health symptoms and related work disability and may be less likely to seek help due to concerns about confidentiality and other issues. Our objective was to survey depressive and anxiety symptoms in a sample of academic physicians. Methods: All full-

time UBC Faculty of Medicine employees were invited via email to complete an anonymous web-based mental health screening survey which included the PHQ-9 and GAD-7, standardized tools to screen for depression and anxiety, and the novel LEAPS scale to measure work impairment. Results: 292 self-identified physicians responded to the survey. 8.1% met PHQ-9 criteria for depression and 5.9% met GAD-7 criteria for anxiety. Subjective work impairment was present in 6.3% and was uncommon in those who were not depressed. On all scales, men's average scores and rates of impairment were higher than women's but most of these differences were not statistically significant. 8.1% clicked through to the available internet self-management site. Conclusion: Academic physicians reported similar rates of clinically significant depressive and anxiety symptoms as community samples, but with some suggestion of a reversed sex difference. Low rates of appropriate mental health care seeking behavior were observed. Relevance/implications: More work is required to identify and address barriers to physician mental health.

POSTERS - TRANSLATIONAL AND CLINICAL RESEARCH

Schizophrenia Patients show differences in Functional Networks involved in Associative Memory Encoding

Presenter: Alexander Leung, PGY2 Psychiatry Research Track Resident
Faculty Sponsor: Todd Woodward

Introduction: Associative memory is selectively impaired in schizophrenia (Armstrong et al., 2012). Methods: During MRI scanning, 30 patients and 30 controls completed 90 word association encoding tasks. There were 45 easy association tasks, and 45 difficult tasks. Following scanning, subjects were asked to cue-recall the associations. Constrained Principal Component Analysis was used to elucidate functional networks from fMRI-BOLD data. Differences between estimated BOLD responses within networks was analysed using ANOVAs. Results: Recall was better for easy associations relative to difficult associations ($p < .001$). Controls' recall performance was superior to patients' ($p < .001$). Four networks emerged: 1) activations in dorsolateral prefrontal cortex (DLPFC) and Broca's area; 2) activations in left-lateralized task-positive network regions; 3) deactivations in default mode network regions; 4) deactivations in bilateral insula. The DLPFC-based network was more actively recruited in encoding recalled vs not-recalled associations ($p < .05$), and difficult vs easy associations ($p < .001$). Patients showed decreased activity in the DLPFC-based network while encoding difficult associations ($p < .05$). Conclusions: Results are consistent with literature findings that DLPFC has an important role in associative memory encoding. Relevance/implications: The reduced ability of patients to recruit the DLPFC-based network when encoding difficult word associations presents a biological basis for associative memory impairments in schizophrenia patients.

Reduced efficiency in cognitive flexibility in schizophrenia

Presenter: KaWai Leong, PGY2 Psychiatry Research Track Resident
Faculty Sponsor: Todd S. Woodward

Introduction: Previous studies have revealed impairment in cognitive flexibility (e.g., task switching) in patients with schizophrenia. Resolution of competition between two tasks involves the ability to detect that task changes are required, and to initiate and to apply a change in task. Past neuroimaging studies using functional magnetic resonance imaging (fMRI) reported activation of the anterior cingulate (ACC) and/or adjacent supplementary motor areas (SMA) in resolution of task-set competition in healthy subjects. In this study, we used fMRI to examine the extent to which switch in task set is processed differently by patients with schizophrenia and healthy controls. Methods: Thirteen patients with schizophrenia and thirteen healthy subjects performed a switching version of the Stroop task. Results: Constrained principal component analysis for fMRI revealed two functional networks. The first included

activation in the dorsal attentional network (including ACC and SMA); the second included activation reductions in the default-mode network. Schizophrenia patients demonstrated increased activity relative to controls in the first, but not the second, functional network. Conclusion/implications: The current findings suggest that reduced efficiency of functional networks in schizophrenia is characteristic of the dorsal attentional network but not the default-mode network, and that this contributes to impairment in cognitive flexibility.

**Non-suicide, non-methadone prescription overdose deaths in the BC Interior, 2006 – 2011:
Implications for psychiatrists**

Presenter: Julius Elefante, PGY1 Psychiatry Resident

Faculty Sponsor: Trevor Corneil

Introduction: This retrospective case series explores associations contributing to inadvertent, non-methadone prescription opioid dose deaths in the BC Interior, where the death rate is 2.1 times the provincial rate ($p=0.0064$, CI: 1.2-3.6). Methods: Coroners' records were examined. An inductive approach without a-priori hypotheses was used. Data were analysed using geographical-spatial information system analysis, age adjustment, dependency modeling, anomaly detection, and cluster analysis. Results: There were 110 deaths reviewed (mean age 49 years; 50% female). Although only 30% were on high-dose opioids, 60% were on two or more opioids and 80% had adjuvant medications that were found in posthumous serum toxicology including: antidepressants (63%), benzodiazepines (42%), antipsychotics (26%), and anticonvulsants (22%). Associated factors were: chronic pain (82%), and comorbid psychiatric diagnosis (45%). Conclusion: Recent guidelines for the management of chronic, non-cancer pain recommend lower opioid doses and use of adjuvant medications. While high-dose opioids no longer appear to be a significant risk factor in our analysis, the use of adjuvant medications may carry its own inherent risk. Risk of death is higher in those with psychiatric comorbidity. Relevance and Implications: Mitigation efforts should include education of primary care physicians, psychiatrists, and pharmacists. A sentinel surveillance program may include these practitioners. Active monitoring and ongoing counselling of at-risk patients are recommended.