POSTER PRESENTATIONS

1. Can we find natural clusters of Tuberous Sclerosis Complex Associated Neuropsychiatric Disorders? A Pilot feasibility study

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Background: Tuberous Sclerosis Complex (TSC) is an autosomal dominant disorder with multi-system involvement. The lifetime prevalence rates of TSC-associated neuropsychiatric disorders *(*TAND) are in the region of 90% and presents in an apparently unique pattern. This 'uniqueness' poses significant challenges for psycho-education and intervention planning. To date, no studies have investigated whether there may be natural clusters of TAND. The aims of this pilot study were a) to investigate the practicability of identifying natural TAND clusters, and (b) to identify appropriate multivariate data analysis techniques for larger-scale studies. **Methods:** TAND Checklist data were collected from 56 individuals with a clinical diagnosis of TSC (n= 20 from South Africa; n = 36 from Australia). Exploratory cluster analysis was performed using R, the open-source statistical platform. Methods examined included hierarchical clustering (WARD) and factor analysis. **Results:** Eight distinct clusters were identified- two 'impact/impairment' clusters, and six 'behavioural' clusters. The behavioural clusters included an 'ASD-like' cluster, a 'mood/anxiety' cluster, a 'scholastic' cluster, a 'behavioural dysregulation' cluster, a 'hyperactive/impulsive' cluster, and a 'neuropsychological' cluster. Intellectual ability and impact clusters showed strong correlation, and the behavioural clusters showed distinct patterns of co-occurrence across intellectual ability groups. **Conclusion:** These results suggest that natural TAND clusters may be identifiable using Ward hierarchical cluster analysis and factor analysis. Larger-scale studies are required to confirm and expand these findings and clusters need to be validated for face-validity.

2. Responses to novelty in male and female socially isolated rats as a developmental animal model of schizophrenia

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Background: The socially isolated rat model is a developmental model of schizophrenia. Although a dysregulated attentional system and abnormal response to novelty are features of schizophrenia, only a few studies have investigated response to novelty in socially isolated rats, and these are mostly in males. In the present study we aimed to investigate the novelty response in socially isolated male and female rats with novel-object recognition (NOR) testing. **Methodology:** Sprague Dawley rats (25 per group; male-socialised, male-isolated, female socialised, female-isolated) were housed 4 per cage (socialised) or alone (isolated) from postnatal day (p) 21. From p78-82 rats underwent NOR testing involving: open field exploration, habituation to two identical objects, and finally one familiar-object was replaced by a novel-object. These trials were analysed with tracking software to measure distance travelled (cm) and time spent (s) in object-containing quadrants of the arena. **Results:** When presented with the novel-object both isolated males and isolated females spent more time in the novel-object quadrant than the familiar-object quadrant, while socialised counterparts spent equal amounts of time in these quadrants. In addition, isolated males and females animals covered less distance than socialised animals, although in both groups of animals, males covered less distance than females. **Discussion:** The results of the study reinforce the usefulness of the socially isolated rat model as a model of schizophrenia, as an abnormal response to novelty corresponds to characteristic abnormalities in this condition. The findings also support the inclusion of both sexes in future experiments to further characterise the behaviour of the socially isolated rat.

3. The prevalence of and factors associated with antipsychotic polypharmacy in patients with serious mental illness: Findings from a cross-sectional study in a high-middle income country

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Objective: The aim of our study was to examine the prevalence of and factors associated with antipsychotic polypharmacy (APP) among patients with serious mental illness in the current South African health care context. **Methods**: We collected data on patient, illness and treatment characteristics of patients discharged on one or more antipsychotic agents from January to June 2014. We analysed the associations of APP with demographic and clinical variables using hierarchical multivariable logistic regression. Prescription patterns were examined. **Results**: The prevalence of APP in our study population of 577 patients was 28.4%. Demographic and clinical characteristics significantly associated with APP included age>29, male sex, diagnosis of schizophrenia, co-morbid intellectual disability, co-morbid substance use, greater number of hospital admissions and high-dose prescribing. First-generation antipsychotics and long acting injectable preparations were prominent in APP combinations. Co-prescription of anticholinergic agents and sodium valproate demonstrated significant association with APP. **Conclusion**: APP appears commonly in our population despite lack of evidence for the practice and possible risk of harm. Our findings suggest a complex interplay among patient, illness and treatment factors relevant to the practice in our setting that could be targeted for intervention.

4. Effect of nicotine use on prospective memory performance and associated intrinsic functional brain connectivity in binge drinkers

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Introduction: We tested the hypothesis that time-based prospective memory (TPBM), a cognitive domain that plays a crucial part in many aspects of everyday functioning, including medication adherence, will be impaired in binge drinkers compared to healthy controls. Group differences in the intrinsic functional connectivity of the right anterior prefrontal cortex, a key region involved in TPBM performance, were also assessed. **Methods:** Sixty participants were recruited from a community clinic in a peri-urban township in Cape Town (66.6% female, mean (SD) age: 38.3 (8.26) years), of whom 38 were classifed as binge drinkers. Current users of cigarettes or snuff were identified from urine samples. Bivariate tests were used to identify differences as a function of drinking and nicotine use status from the TBPM tasks in the Memory for Intentions Test (MIST), as well as whole-brain estimates of intrinsic functional connectivity with the right anterior prefrontal cortex (aPFC), obtained from 10 minutes of resting-state fMRI data. **Results:** No difference in TBPM performance was detected as a function of drinking status ($t = 0.570$, $p > 0.05$), though average task scores were lower in binge drinking nicotine users (1.94) than non-users (3.25; $t = 2.32$, $p = 0.026$). Connectivity between the aPFC and the left inferior parietal cortex in 24 binge drinkers was inversely associated with TBPM performance in nicotine users only ($N = 12$). **Discussion:** We present evidence that nicotine use but not binge drinking is associated with deficits in prospective memory function. Greater connectivity between the anterior PFC and a region within the frontoparietal executive control network in nicotine users with poorer TBPM may reflect a compensatory mechanism in binge drinkers.

5. The impact of abstinence from methamphetamine on brain metabolites

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Background: Methamphetamine (MA) use has become a global health concern. ^{1}H-MRS studies on MA use have reported decreased neuronal integrity and viability as well as decreased synthesis and degradation of cellular membranes. No previous studies investigated the change in metabolites from acute (<2 weeks) to short-term (<6 weeks) abstinence using ^{1}H-MRS. This study aimed to evaluate the relationship between MA use and neurometabolites to further understand the impact of MA and MA abstinence on cortical brain metabolites. **Methods:** Adults with past MA dependence (n=31) and healthy controls (n=22) were recruited. Two-dimensional ^{1}H-MRS imaging (TR2000ms, TE30ms) slice was collected and included voxels from bilateral anterior-cingulate (ACC), frontal-white-matter (FWM), and dorsolateral-prefrontal-cortices (DLPFC) was performed. Control participants were scanned once. The MA group was scanned twice, i) acute MAA (1.5±0.6 weeks, n=31) and ii) short-term MAA (5.1±0.8 weeks, n=22). The change in ^{1}H-MRS metabolites over time (n=19) was also investigated. Standard ^{1}H-MRS metabolites are reported relative to Cr+PCr. **Results:** Decreased NAA and NAA+NAAG were found in cortical tissues in the left DLPFC, FWM and right ACC, as well as decreased GPC+PCh in the left FWM. Further, in short-term abstinence there was evidence of neuroinflammation - decreased NAA and NAA+NAAG and increased Ins, within the right ACC. **Conclusion:** The study reports damage to neuronal integrity in acute abstinence, persisting into short-term abstinence – and is accompanied by neuroinflammation. This is the first ^{1}H-MRS study to report the development of neuroinflammation with MA abstinence, and provides insight for the development of early intervention strategies. *This abstract was presented at the Society for Neuroscience Conference from 12-16 November 2016 in San Diego, California, USA.

6. The Pathway to Elucidating Bipolar Disorder Genetics

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Introduction: Bipolar disorder (BD) is both a clinically and genetically complex disease. It is has a global prevalence of approximately 1%, and has serious effects on the lives of those who must live with it. BD is also known as manic-depressive disorder, as it is a fluctuation of mood episodes that cycle between mania and depression. These mood fluctuations may have a serious impact on an individual's ability to function, and yet there is no consensus with regards to the genetic origins of the disease. Genome-wide association studies (GWAS) have begun to establish associations of risk variants with small effect sizes at play in BD, and research is turning to the biological pathways that may be involved. The aim of this study is to use whole -genome sequencing data and a bioinformatics approach to identify genetic variants for BD in an affected family, and identify potential pathways that may have a role in this debilitating disorder. **Methodology:** Whole genome sequences of 4 BD-affected family members were used for pathway analysis, as a means of observing what biological processes may underlie the disorder. Several platforms, KOBAS 2.0, DAVID, and WebGestalt, were used. Candidate variants will be selected following pathogenicity prediction, and comparisons to previously-associated genes from GWAS studies. **Results:** Pathway analysis has indicated the influence of pathways in cancer (HSA05200), regulation of the actin cytoskeleton (HSA04810), and focal adhesion (HSA04510) in the BD-affected family members. **Conclusion:** Thus far, BD has remained an enigmatic disorder due to its complexity, but the advent of bioinformatics technology allows for research on a system-scale, rather than a sole focus on one gene at a time. The pathways discovered in this study have been implicated previously in this disorder, and give some insight into the nature of key cellular processes as components of BD pathology.

7. Differentiating psychotic disorders with EEG delta and alpha band frequency and the effects of brief high frequency repetitive transcranial magnetic stimulation

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Background: It is essential that the optimal medications are prescribed as soon as the initial psychotic episode has subsided as this provides the best prognosis to the individual that presents with a psychotic illness. We investigated whether a simple EEG system would aid delineation of different clinical psychosis phenotypes, and whether high frequency brief repetitive transcranial stimulation (brTMS) was able to affect change in EEG frequency activity. **Method:** In the present study we applied a simple (6-lead montage: F_3,F_4,C_3,C_4,P_3,P_4) EEG to psychotic disorders: schizophrenia (SZ=28), bipolar I disorder hx of psychosis (BPD=28), and methamphetamine-induced psychosis (MPD=24), as per DSM-IV SCID, and control group (CON=29). We report the data from a 3 min resting eyes closed condition, before and after brTMS (1000pulses@ 20Hz, 2000pulses@RMT) over the left and right dorsolateral prefrontal cortex. **Results:** SZ and MPD showed increased delta activity, decreased alpha, and increased delta/alpha ratios compared to controls for all electrodes. MPD showed increased delta activity for parietal electrodes, decreased alpha and increased delta/alpha ratio for right hemisphere electrodes compared to BPD. brTMS showed several tendencies to increase delta activity, decrease alpha, and increase delta/alpha ratios in SZ for left central and parietal electrodes. **Discussion:** These data support the use of EEG frequency analysis in the delineation of psychotic disorders. brTMS did not show benefit to EEG frequency activity, in fact it exaggerated the differences, specifically over the left central and parietal cortices. However, our finding contradicts the notion of reduced plasticity in SZ, as we saw depression in networks with stimulation where we expected to find the contrary. *This abstract was presented at the Society for Neuroscience Conference from 12-16 November 2016 in San Diego, California, USA.