



SYMPOSIUM 2016
ABSTRACT BOOKLET

PLENARY LECTURER 1

Dr Bahador Bahrami

Institute of Cognitive Neuroscience, University College London, UK

Bahador Bahrami completed his PhD at University College London on attention and awareness and followed with a postdoc in social neuroscience in Aarhus, Denmark under the supervision of Chris Frith and Andreas Roepstorff. He is currently a group leader in the Crowd Cognition Lab at UCL. The Crowd Cognition Lab combines computational, behavioural and neurobiological investigations of human interactive decision making to answer the question- what makes collective decision making so fundamental to humans.

Dr Bahrami's lecture will focus on confidence reporting as a means of communication of uncertainty between human agents. The main idea is to understand the underlying cognitive basis of inter-individual variations in expression of confidence and how these variations can contribute to or impair collective decision making.

PLENARY LECTURE 2

Dr Terri Gilbert

Allen Institute for Brain Science, USA

Terri Gilbert joined the Allen Institute for Brain Science in 2010 and currently spearheads the user support program for the Allen Brain Atlas resources, designing and delivering live trainings and webinars to global audiences. Terri is a high-level science communicator with over 15 years of experience delivering technical presentations and training sessions to a variety of audiences, and has held positions in both academia and industry.

Terri has a Bachelor's degree in physics from the New Mexico Institute of Mining and Technology. She received her Ph.D. in biomedical sciences from the University of New Mexico, School of Medicine and has held postdoctoral fellowships at the University of New Mexico and the University of Washington.

Dr Gillbert will talk us through the development of the Allen Institute for Brain Science which was launched in 2003 to develop a comprehensive gene expression (in situ) map of the adult mouse brain, and rapidly expanded to include maps of the spinal cord, developing brain and the Institute's first forays into the human brain. In 2012, the Institute was re-funded for a new generation of open science projects aimed at more deeply understanding the human brain. This session will outline the online open-source data and tools available to scientists including our gene expression and connectivity maps, as well as our resources that describe cell characterization and function.

S01.1 THE ROLE OF EXCITATORY GABAERGIC SIGNALLING ON BENZODIAZEPINE-RESISTANT STATUS EPILEPTICUS

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Introduction: Status epilepticus (SE) describes a state of persistent seizures that are unrelenting, and is considered as a medical emergency. The first-line treatment includes using the benzodiazepines, which enhance endogenous GABAergic signalling. However, it has been reported that some patients are resistant to these agents. A possible explanation for this is the transient excitatory shift in GABAergic signaling that has been shown to follow periods of neuronal hyperexcitability. The aim of this project is to clinically characterise benzodiazepine-resistant SE in the South African paediatric population, and to explore the effect of benzodiazepines on GABAergic during prolonged seizure-like activity.

Methodology: Clinical data is being acquired from an on-going clinical trial run at the Red Cross Children's Hospital's emergency Unit. Experimental work includes local field potential recordings and both perforated and whole-cell patch-clamp recordings using both cultured organotypic and acute brain slices. In addition, we use a combination of both electrical stimulation and optogenetic manipulations to elicit GABAergic signalling.

Results: Our clinical suggests that that benzodiazepine-resistant SE in paediatric patient is a clinically relevant problem. Preliminary experimental results confirm that diazepam (DZP) enhanced inhibitory GABA signalling under normal conditions but is unable to terminate prolonged seizure-like activity using the 0 Mg²⁺ proconvulsant model. Furthermore, we demonstrate that there is a transient excitatory-shift in GABAergic signalling during seizure-like events is due to a reversible increase in intracellular chloride may be sufficient to maintain prolonged seizure-like activity.

Conclusions: These preliminary findings have confirmed that benzodiazepine-resistant SE is a relevant clinical problem in our context. Furthermore, we postulate that excitatory GABAergic signalling may be a driving-force perpetuating prolonged seizure-like activity.

S01.2 EFFECT OF HOUSING CONDITIONS ON RESPONSIVENESS TO IBOGAINE TREATMENT

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Introduction: Vulnerability to drugs depends on the intricate relationships between the user with the drug of choice, genetic predisposition, the psychotropic properties of the drug and importantly environmental factors such as housing conditions. Previous studies have highlighted that socially isolated animals develop a greater propensity for drugs and display aggressive tendencies. These mood instabilities related to aggression generate public health and safety-related concerns. Confrontational and aggressive behaviour can also perturb treatment as emotional disturbances vastly contributing to drug craving and relapse. Ibogaine, an indole plant alkaloid, has previously been shown to reduce locomotor activity, consumption and self-administration of cocaine. It has been speculated that ibogaine's mode of action could be attributed to it acting as a partial antagonist for NMDA receptors. The aim of this study was to evaluate the potential therapeutic anti-addictive and anti-aggressive effects of ibogaine on isolated and group housed mice pre-exposed to methamphetamine.

Methods: C57BL/6J mice were group housed or in isolation. The effect of ibogaine on locomotor activity, conditioned place preference and the resident-intruder test for aggressivity was assessed. NMDAR expression was also evaluated using polymerase chain reaction (PCR).

Results: Ibogaine blocked methamphetamine-induced place preference in group housed mice but not in isolated mice. However, ibogaine reduced aggressive behaviour in isolated mice without having a side effect on locomotor activity. These behavioural effects of ibogaine were associated with an increase in NMDA receptor expression in the hippocampus and the prefrontal cortex.

Conclusion: These results provide further support to the implication of NMDA receptors in addiction and aggression behaviour and highlight the critical role of housing conditions in responsiveness to ibogaine treatment. Further studies are necessary to explore the neural pathways underlying the interaction between environment and drug of abuse to predict individual responses to therapy.

S01.3 THE IMPACT OF SOCIAL ISOLATION ON THE ATTENTIONAL SYSTEM OF MALE AND FEMALE RATS IN A DEVELOPMENTAL ANIMAL MODEL OF SCHIZOPHRENIA DURING A 5-MINUTE ANALYSIS OF THE NOVEL OBJECT RECOGNITION TEST

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Introduction: In the human disorder of schizophrenia the attentional system becomes dysregulated such that responsiveness to novel stimuli is abnormal compared to non-affected individuals, those with a diagnosis of schizophrenia often exhibit neophobia. The socially isolated rat is a developmental animal model which is used to mimic the symptomatology of schizophrenia and investigate the mechanisms underlying cognitive disruptions of this nature. In this study neophobic responses were investigated using the novel object recognition test.

Methodology: After weaning at post-natal day 21 rats were separated into four groups; female socialised n=23, female isolated n=23, male socialised n=25 and male isolated n=23. Socialised animals were housed 4 per cage and isolated animals were housed alone, all animals were subjected to minimal handling. At p78-82 all animals underwent novel object recognition testing involving familiarisation to two identical objects, then one of the familiar objects was replaced with a novel object and each animal was recorded for 5 minutes exploring this environment.

Results: When the recordings were analysed using tracking software it was found that both isolated females and isolated males spent more time in the novel object-containing area than in the familiar object-containing area, $p=0.0045$ and $p=0.0055$ respectively. Socialised females, isolated females and socialised males all made more entries into the novel object-containing area than the familiar object-containing area, $p=0.0264$, $p=0.0155$ and $p=0.0450$ respectively. It was also found that females covered a greater total distance than males, $p<0.0001$.

Discussion: The effect of social isolation in the current study led to isolates spending greater time with the novel object, contrary to existing studies showing a neophobic response by isolates. In addition, sex differences were evident, where females showed greater activity, irrespective of rearing condition. To conclude, further study is required to determine what resulted in the contrary findings in our isolated animals.

S01.4 EARLY-ETHANOL EXPOSURE DIFFERENTIALLY ALTERS ENERGY-RELATED PROTEINS IN THE DEVELOPING RAT BRAIN: A PROTEOMICS STUDY

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Introduction: The maternal consumption of alcohol during pregnancy results in a spectrum of long-term neurobehavioural deficits. The mechanisms behind the persistent effects of early-alcohol exposure are largely unknown. Alcohol exposure may alter the developing neurons and glial cells by modifying the expression or functionality of structural-, energy-, signalling- and neurotrophine-related proteins. This study aimed to explore the long-term effects of early-ethanol exposure on proteins in the brain using a rat model.

Methodology: Male Sprague-Dawley rat pups were exposed to 12 % ethanol (4 g/kg/day i.p.) or volume controlled saline from postnatal day (P) 4 to P9 which is considered to be equivalent to the third trimester of human pregnancy. Rats were sacrificed in adolescence, at P31. The prefrontal cortex (PFC) and dorsal hippocampus (DH) were removed for proteomic analysis by iTRAQ labelling and quantification by liquid chromatography mass spectrometry. A fold change >2 identified differentially expressed proteins and a fold change >1.2 in the same direction indicated a supporting trend.

Results: Early-ethanol exposure down-regulated (>2 fold change) energy metabolism-related proteins such as ATP synthase (subunit g) and glycogen synthase kinase-3 β in the DH. This result was supported by a decrease (>1.2 fold change) in ATP synthase (subunits alpha, beta and gamma), ATP synthase F(0) complex subunit B1, cytochrome c oxidase (subunits 5B and 7C), the mitochondrial phosphate transporter, SLC25A3, acetyl-CoA acetyltransferase, acetyltransferase component of pyruvate dehydrogenase, aldehyde dehydrogenase, and 2-oxoglutarate dehydrogenase. This decreased capacity for ATP production was not observed in the PFC. Early-ethanol exposure up-regulated NADH dehydrogenase (ubiquinone, 1 alpha subcomplex 9) and dynactin, a cytoskeletal protein in the PFC.

Conclusion: The data suggest that early-alcohol exposure results in differential long-term alterations in energy-related proteins in the brain. This may provide insight into the mechanisms behind the neurobehavioural deficits observed in fetal alcohol spectrum disorders.

S01.5 THE INFLUENCE OF CHILDHOOD TRAUMA, MAJOR DEPRESSIVE DISORDER AND TELOMERE LENGTH ON HIV-ASSOCIATED NEUROCOGNITIVE DISORDERS

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Introduction: HIV/AIDS is a major source of morbidity in South Africa and affects approximately 10.5% of the population. Despite improvements in access to antiretroviral medication, the prevalence of HIV-associated neurocognitive disorders (HAND) continues to increase and produce substantial impairment in daily functioning. Interestingly, previous research suggests that stress-related psychiatric conditions and depression are positively correlated with HIV disease progression and the development of neurocognitive impairment. This is of particular relevance to the South African context where the high prevalence of both HIV and stress-related psychiatric conditions essentially produces a double burden of disease. We sought to examine whether telomere length attrition, a marker of biological aging independently associated with childhood trauma, major depressive disorder and HAND, may act as a biological correlate mediating the relationship between HAND and psychological stress.

Methods: HIV-positive and negative women (n=133 and n=150 respectively) were recruited and underwent a battery of neuropsychological tests to measure cognitive function, depression and childhood trauma. Quantitative polymerase chain reaction using primers specific to telomeric repeats and the reference gene human β -globin was performed on DNA extracted from peripheral blood mononuclear cells.

Results: Generalised linear modelling found no significant effects of HIV status, childhood trauma, depression or telomere length on cognitive function. However, HIV positive status was predictive of reduced telomere length.

Conclusion: Our results support previous findings of telomere length attrition in seropositive individuals. Further longitudinal studies are needed to determine if change in telomere length is associated with altered cognitive function and whether depression and childhood trauma may mediate this relationship.

S01.6 EXPLORING THE MICROBIOME IN POSTTRAUMATIC STRESS DISORDER (PTSD): A PILOT STUDY

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Introduction: The aetiology of complex psychiatric disorders, such as PTSD, is characterised by the interplay of genes and environment. However, it has become apparent that the number of bacterial cells harboured by humans outnumbers that of our own human cells. The study of the microbiome therefore provides a novel investigate avenue into the aetiology of complex disorders; the gut-brain axis is of particular interest in anxiety and stress-related disorders. The aim of the study was to investigate the gut microbiome in PTSD subjects and trauma-exposed (TE) controls, to identify microbial profiles unique to PTSD.

Methodology: Bacterial DNA was extracted from stool samples from 18 PTSD and 12 TE control subjects. 16S rRNA amplicons were generated in the V3 and V4 regions, and sequenced via Illumina HiSeq paired-end 100bp sequencing. Operational taxonomic units from the sequences were analysed using both alpha-diversity and beta-diversity metrics (unweighted, weighted UniFrac). Sequences were compared to the Greengenes Database for taxonomic classification.

Results: The overall gut microbiome of participants in this population was dominated by *Firmicutes* and *Bacteroidetes*. The two most dominant phyla were *Bacteroidetes* & *Firmicutes*; furthermore, a subset of PTSD subjects had high relative abundance of *Cyanobacteria* and low relative abundance of *Actinobacteria* and *Firmicutes* (both have probiotic properties). *Cyanobacteria* have been associated with neurodegeneration through production of neurotoxic β -N-methylamino-L-alanine (BMAA). Bacteria enriched in the microbiome of these PTSD patients possibly promote gut inflammation, facilitate bacterial translocation to the bloodstream with subsequent gut-brain axis dysregulation and neurodegeneration. Our preliminary results warrant further investigations in larger sample sizes.

Conclusion: This is the first study to report on the microbial composition associated with PTSD. Much larger sample sizes are required to validate and clarify these findings.

[S02: SANS members Postgraduate and Postdoctoral fellow presentations](#)

S02.1 INVESTIGATING DIFFERENTIAL EXPRESSION IN PTSD PATIENTS VERSUS CONTROLS: AN RNA-SEQ STUDY

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Introduction: Post-traumatic stress disorder (PTSD) is a debilitating neuropsychiatric disorder underpinned by complex, multi-factorial interactions. To date, most genetic studies have only focused on specific candidate genes involved in PTSD and therefore, lack a holistic view that can be gained by a whole-transcriptome RNA-Sequencing (RNA-Seq) approach. In this preliminary study we aim to utilise RNA-Seq in order to investigate molecular mechanisms and possible blood biosignatures in South African PTSD patients.

Methodology: In this case-control study design, mixed ancestry, female individuals diagnosed with PTSD (N = 19) were compared to trauma-exposed control (N = 29) individuals. RNA was extracted from whole blood and sent for RNA-Seq using the Illumina HiSeq 4000 platform at a sequencing depth of 50 million paired end reads. Bioinformatics analyses were then performed followed by downstream co-expression analysis to investigate co-regulated differentially expressed gene sets between groups.

Results: A total of 556 differentially expressed genes were identified of which 196 (22 upregulated and 174 downregulated) genes were determined to be biologically relevant based on an ontology driven prioritisation approach. Co-expression analysis revealed a network of 4 highly co-expressed upregulated genes and a large co-expression network consisting of 36 downregulated genes. The 4 co-expressed upregulated genes (RPL6, RPS6, RPS3A and EEF1B2) and 6 highly connected co-expressed downregulated genes (DHX9, BCLAF1, THRAP3, EIF4G1, HSPA4 and MCL1) were identified as potentially relevant links contributing to the pathology of PTSD.

Conclusion: This hypothesis-generating study provides supporting evidence of a blood transcriptomic response involved in PTSD. Additionally, the study identifies genes possibly involved in the molecular underpinnings of this debilitating disorder. Future studies are however warranted to support these findings and should include miRNA profiling in order to identify a more robust signature of potential blood based biomarkers.

S02.2 MENTALISING THE BODY: SPATIAL AND SOCIAL COGNITION IN ANOSOGNOSIA FOR HEMIPLEGIA

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Introduction: Following right-hemisphere damage, a specific disorder of motor awareness can occur called anosognosia for hemiplegia (AHP), i.e. the denial of motor deficits contralateral to a brain lesion. The study of AHP can offer unique insights into the neurocognitive basis of awareness. Typically, however, awareness is assessed as a first person judgement and the ability of patients to think about their bodies in more 'objective' (third person) terms is not directly assessed. This may be important as right-hemisphere, spatial abilities may underlie our ability to take third person perspectives. This possibility was assessed for the first time in the present study.

Methodology: We investigated third person perspective taking using both visuospatial and verbal tasks in right-hemisphere stroke patients with AHP (n = 15) and without AHP (n = 15), as well as neurologically healthy controls (n = 15). Using voxel-based lesion-symptom mapping approaches, we also investigated the brain lesions associated with third person perspective taking on the experimental tasks.

Results: In both tasks, AHP patients showed specific deficits in third person perspective taking abilities, with the severity of unawareness being related to greater impairments in such perspective taking. In voxel-based lesion mapping we also identified the lesion sites linked with such deficits, including some brain areas previously associated with inhibition, perspective taking and mentalising, such as the inferior and middle frontal gyrus, as well as the supramarginal and superior temporal gyrus.

Conclusion: These results suggest that neurocognitive deficits in perspective taking may contribute to AHP and provide novel insights regarding the relation between self-awareness and social cognition.

S02.3 VISUAL FOOD CUE-REACTIVITY DECREASES AND EXECUTIVE FUNCTION IMPROVES FOLLOWING A CLINICALLY RELEVANT WEIGHT LOSS: AN EEG STUDY

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Introduction: Here we test the thesis that a clinically meaningful weight loss associates with attenuations in visual food cue processing, improvements in executive function, and pronounced measures of parasympathetic nervous system activity.

Methodology: 20 successful dieters retaining a clinically meaningful weight loss ($\geq 5\%$ of initial body weight), and 25 controls matched for body mass index (BMI) but with no history of weight reduction participated in the study. Mental and physical health, dietary and physical activity surveys were completed. 2 Stroop tasks (one with food image inserts, the other with neutral image inserts) were completed with record of EEG, ECG and respiratory frequencies.

Results: Successful dieters showed 2 differences in EEG event-related potential (ERP) component presentation: right parietal (P₄) P300 peaked later upon visual food cue exposure, indicative of down-regulated food cue-reactivity during late processing ($p = 0.04$); and left cingulate (C₃) P200 peaked earlier upon Stroop conflict cue exposure, demonstrative of greater degrees of executive function during preconscious processing ($p = 0.03$). Food cue induced right parietal (P₄) P300 latency correlated negatively with BMI ($r = -0.4$, $p = 0.02$) and objectively assessed % fat mass ($r = -0.4$, $p = 0.01$). Last, food image-related P200 latency (C₃) correlated positively with ECG-sourced high frequency power ($r = 0.66$, $p < 0.01$), confirming that attenuations in food cue-reactivity coincide with up-regulated parasympathetic nervous system activity.

Conclusion: Successful dieters show ERP indices indicative of astute executive functioning during preconscious attention, followed by food association network inhibition during maintained attention. Moreover, abated food-specific ERP components correspond with lower overall body adiposity, and peripheral measures indicate that weight loss maintainers experience lower levels of laboratory induced stress when presented with palatable visual food cues. These results underscore the importance of cognitive remediation for the effective treatment of persons with obesity.

S02.4 ACTION PLANNING IN HEALTHY POPULATIONS: A MOTOR TASK PARADIGM TESTING FOR IMPULSIVITY

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Background: Research shows that impulsive individuals may be more sensitive to time constraints and are less able to time their actions than non-impulsive people. Motor timing aspects of temporal processing, regulating the generation of timed motor responses, has received little interest in the study of impulsivity. The main question explored was whether impulsivity trait reflects in the timing of self-initiated actions in non-clinical populations.

Methods: Thirty seven participants were divided into two groups according to the mean impulsivity score obtained in the Stop Signal Test (SSRT). Individuals were tested at two times (week1 and 8), demographics were obtained, and four motor timing tasks were conducted (motor reactivity; motor synchronisation; distractibility; and cognitive control).

Results: No significant test retest variability was found for any of the motor tasks. No significant group differences were found in motor reactivity measures between high and low impulsive individuals. Significant differences were found on synchronisation abilities and distractibility. The high impulsivity group had larger inter response intervals at fast tempi (300ms, $p < .01$) and was less able to synchronize movements at slow tempi (900ms, $p = .04$). High impulsivity participants were also more distractible ($p = .04$) than low impulsive individuals. Additionally the high impulsivity group was found with significantly lower cognitive control after an error was made compared to the low impulsivity group.

Conclusions: This research shows that non-pathological impulsivity affects the strategic coordination of temporal processing of voluntary motor behaviour. As the motor timing test battery revealed high test-retest stability, it is now being applied to a substance use disorder study. This study explores the prognostic value of motor timing with regard to treatment outcome and relapse.

SPECIAL LECTURE

FORMS OF PLASTICITY IN MOTOR CIRCUITS INDUCED BY HEMODIALYSIS: BOLD-FMRI STUDY

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Introduction: Recent studies demonstrated that hemodialysis in the context of chronic renal failure originates oxidative stress (OS) that is a known factor contributing to long-term complications of dialysis. Thus, multiple cellular defections are observed and might yield later various diseases such as cardiovascular disease and neurodegenerative diseases. Despite recent progress on the choice of hemodialysis membrane, hemodialysis sessions are still causing side effects on general health especially on brain function. This includes plasticity and functional control organization of the anatomical entities involved in the control of given function. The goal of this study is to demonstrate the basic neuroanatomical and neurophysiological changes induced by hemodialysis. Such impact on plasticity is studied in contexts of using two biocompatible hemodialysis membranes.

Methodology: 12 male volunteers following chronic hemodialysis (HD) for more than 6 months were recruited. Diabetic, smoking and patients with episodes of infection or treatment with iron or erythropoietin injection were excluded. BOLD-fMRI was performed before and after HD using motor paradigm immediately before and after HD sessions; the fMRI data was processed using SPM12 package.

Results: The earlier biological results of this study showed that hemodialysis increases the oxidative stress in these patients. [Malondialdehyde before hemodialysis = $3,550 \pm 0,580\mu\text{M}$ vs. Malondialdehyde after hemodialysis = $9,899 \pm 8,367\mu\text{M}$; $p=0,002$]. BOLD-fMRI revealed significant activation of the motor cortex, the BOLD signal in the activated site is inversely correlated with level of oxidative stress.

Conclusion: Hemodialysis raises the inflammatory state of the brain tissue reflecting increased oxidative stress, while it was expected to decrease considering the removal of free radicals responsible of oxidative stress by hemodialysis procedure. Hence, particular care must be paid to hemodialysis patients considering the long term impact on general health and brain tissues in particular.

EMOTION AND MOTOR ALTERATION IN CANNABIS ADDICTED HUMANS: BOLD-FMRI STUDY

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Introduction: Long term cannabis use has been expanding drastically over the last two decades and has become a major health issue worldwide. Recent studies demonstrate that brain complications in adults with cannabis use are associated with cognitive and emotional impairments, but little is known about the relationship between structural alterations and behavioral manifestations. Therefore studying the relationship between alterations of emotional system, in parallel with structural degenerative phenomena is very critical. Hence, the aim of this study is to demonstrate such alterations by making use of appropriate paradigms during BOLD-fMRI scans. Positive, negative and neutral emotions were examined, in relations with DTI and functional connectivity.

Methodology: 12 cannabis addicted patients volunteered for the study. Volunteers were fully healthy. However, any additional comorbidity was a strict criterion of exclusion, and a healthy general state was a must. All patients underwent BOLD-fMRI and anatomical MRI using both motor and emotional paradigm. The fMRI data was processed using SPM12 package. A sample of 12 age-matched controls was also included.

Results: The present results are based on preliminary analysis of behavioral and BOLD-fMRI data of 12 patients and 12 age-matched controls. Analysis of behavioral data showed an alteration of emotional abilities in cannabis addicted patients compared to controls. In addition, cannabis addicted patients appeared to display an altered motor state. Analysis of fMRI data revealed significant changes of activation within a large cortical network including motor cortex, prefrontal cortex and parietal cortex, and that emotional responses and BOLD signal were inversely correlated.

Conclusion: These preliminary findings demonstrate that the brain of cannabis addicted patients undergoes cognitive and emotional alterations that parallel silent structural degenerative phenomena. Although the causal mechanisms are still to be investigated, the fact that functional impairments can be detected in emotional, cognitive and motor domains calls for the development of preventive measures using neurobehavioral tools for this patient population, and even in at risk users.

RF01: Neurogenetics students IBRO Advanced school in neurogenetics

RF01.1 A PILOT STUDY TO EVALUATE A TARGETED RESEQUENCING APPROACH FOR IDENTIFICATION OF PATHOGENIC MUTATIONS IN SOUTH AFRICAN PARKINSON'S DISEASE PATIENTS

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Background: Parkinson's disease (PD) is a neurodegenerative disease that affects 1-2% of individuals over the age of 60 years. PD is one of the leading cause of disabilities globally. PD-causing mutations in genes such as *PARK2*, *PINK1*, *DJ-1*, *ATP13A2*, *SNCA*, *LRRK2*, *VPS35*, *EIF4G1* and *CHCHD2* have been identified and studied predominantly in European, American, North African Arab and Asian. Little is known about the genetics of PD in sub-Saharan Africa (SSA). Information from other populations might not represent SSA. Hence, further study is warranted. This study used a high-throughput next generation sequencing to screen for pathogenic mutations in candidates gene in South African PD patients.

Methods: Genomic DNA was extracted from seven blood samples and one saliva sample. The quality of the DNA was assessed using the Agilent Bioanalyzer 2100 and gel electrophoresis. The Ion AmpliSeq™ Neurological Research Panel (Thermo Fisher Scientific) comprising 751 genes was used and sequencing was done on an Ion-Torrent personal genome machine (PGM). Ion Reporter software 5.2 was used for data analysis.

Results: All samples produced sequencing reads of good quality. We found a high number of single nucleotide variations (SNVs) in all of the samples. In 11 PD genes, a total of 125 exonic SNVs were found. 67 SNVs in the black, 41 in the white and 17 in mixed ancestry patients. Of these SNVs, 111 were common SNPs, 14 were rare variants (MAF<0.01), while 6 variants were potentially pathogenic rare variants that are specific to black patients but their functional significance in PD needs to be elucidated.

Conclusion: This pilot study revealed that the Ion Ampliseq Neurological panel is a time and cost-effective method for the screening of sequence variants in DNA extracted from both blood and saliva samples. Black individuals appear to have more sequence variations in the 751 genes studied here.

RF01.2 THE ROLE OF THE IMMUNE SYSTEM IN BIPOLAR DISORDER TYPE 1

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Introduction: BD has a lifetime prevalence of 0.6 - 1% and is associated with significant health care costs, functional decline and high mortality rates. Heritability estimates of BD are high, suggesting a genetic component to the disorder. Molecular studies have revealed that the immune system may be involved in the aetiology of this disorder. The aims of this study were to identify variants in candidate genes related to the immune system and to establish whether these variants are associated with BDI in a South African cohort. The objectives were to i) select a list of BPD candidate genes, ii) genotype the candidate genes using SNaPshot™ mini-sequencing and iii) analyse the genotyping data with the appropriate statistical methods.

Methods: Candidate genes were selected based on significant findings from previous publications and an association with the immune system. A South African cohort consisting of 289 individuals (189 cases and 102 controls) of Caucasian and Mixed Ancestry was genotyped using SNaPshot™ mini-sequencing for the variants rs2239547, rs4332037 and rs16944 located in the genes *ITIH4*, *MAD1L1* and *IL-1B*, respectively. Genotyping was validated with direct cycle sequencing and logistic regression and M_{QLS} was used to statistically analyse the data.

Results: After Bonferroni correction for multiple testing only the *ITIH4* variant (rs2239547) remained significantly associated with BDI amongst individuals of Mixed Ancestry ($p=0.014$, $OR=4$).

Conclusion: The SNP rs2239547 may be associated with BDI. However, the nominal association identified in this study warrants replication in a larger cohort. Further investigation is necessary to determine the specific effects of these variants on gene expression of the respective genes.

RF01.3 WORKING MEMORY AND EYE MOVEMENT DEFICITS AMONG PATIENTS WITH SCHIZOPHRENIA: A COMPARISON WITH FIRST DEGREE RELATIVES AND HEALTHY CONTROL

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Introduction: Schizophrenia as a 'mega-phenotype' is commonly seen as too complex for effective biological study, hence the need for endophenotypes such as working memory and eye movement deficits. This study aimed to examine working memory and eye movement deficits among patients with schizophrenia, compared with their first degree relatives and healthy control.

Methodology: The study was conducted at the outpatient clinics of the Neuropsychiatric Hospital, Aro Abeokuta, Nigeria. Consenting patients [n=26] with diagnosis of schizophrenia were assessed using a socio-demographic questionnaire, the Working Memory Index (Digit Span and Letter Number Sequencing) of the Wechsler Adult Intelligence Scale, and the Eye Movement section of the Cambridge Neurological Inventory. The tests were also administered to one first degree relative of each patient [n=21], and to a group of healthy control [n=25].

Results: Significant difference was found between performance of schizophrenia subjects and healthy control on the digit span ($p<0.001$). Half (50%) of the schizophrenia patients had deficits in 'extent' of smooth pursuit eye movement (SPEM), compared with 9.5% of their first degree relatives and none of the healthy control ($p<0.001$). 61.5% of the patients had deficits in 'smoothness' of SPEM, compared with 19% of first degree relatives and 4% of healthy control ($p<0.001$). Gaze impersistence with repeated deviation was found among 42.3% of patients, and none of the first degree relatives and healthy control ($p<0.001$). No differences were found with respect to smoothness, blink suppression and lateral movement of saccadic eye movements.

Conclusion: The study showed that patients with schizophrenia performed poorer on digit span than healthy control, and supports other reports of SPEM being a possible endophenotype for schizophrenia. The greater occurrence of deficits in extent and smoothness of SPEM among first degree relatives of schizophrenia patients compared to healthy control suggests a possible familial or genetic predisposition.

RF01.4 DIFFERENTIAL EXPRESSION OF BDNF AND ITS PRECURSOR PRO-BDNF IN COCAINE-INDUCED DRUG SEEKING BEHAVIOUR IN C57BL/6 MICE

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Introduction: The brain-derived neurotrophic factor (BDNF) and its precursor pro-BDNF activate different neural pathways and are inversely implicated in neural plasticity. Chronic exposure to cocaine is associated with an upregulation of BDNF. However, the expression of BDNF and pro-BDNF in brain regions that control basic motivational drives such as the thalamus and the hypothalamus remains undetermined.

Methodology: Cocaine-induced drug-seeking behavior in C57BL/6 mice was demonstrated by establishing a conditioned place preference to a distinctive location paired with cocaine. Cocaine (10 mg/kg) and/or saline were administered intraperitoneally during 10 consecutive days. BDNF and pro-BDNF mRNA and protein expression levels in the thalamus and hypothalamus were evaluated with real time PCR and western-blot respectively.

Results: The obtained results confirmed the cocaine-induced drug seeking behavior and showed an increased BDNF mRNA level and pro-BDNF protein level in the thalamus but no significant effect was found in the hypothalamus.

Conclusion: This data suggests that chronic exposure to cocaine in mice may alter motivational drive through an apoptotic mechanism that might be initiated by the increased pro-BDNF level in the thalamus.

RF01.5 A PHARMACOGENETIC ASSOCIATION STUDY OF THE CYP2D6*17 POLYMORPHISM AND TARDIVE DYSKINESIA IN BLACK PSYCHOTIC PATIENTS ON TYPICAL ANTIPSYCHOTICS

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Introduction: Tardive dyskinesia (TD) is a debilitating, intractable, hyperkinetic movement disorder which contributes to an increase in psychiatric morbidity. Reduced function *CYP2D6* alleles have been associated with TD pathogenesis amongst Caucasians and Asians, with *CYP2D6*4* and **6* and *CYP2D6*10* being implicated in these races respectively. No similar study has been successfully conducted in black Africans. Our objective was to determine the relationship between TD and *CYP2D6*17* (the major reduced function *CYP2D6* allele in Africans).

Methodology: AIMS scoring and *CYP2D6* genotyping were carried out on psychiatric patients exposed to typical antipsychotic medications in an unmatched case control study. A case of TD was defined as a patient with an AIMS score ≥ 2 in two body areas OR ≥ 3 in one body area

Results: A total of 18 cases and 32 controls made up the study sample. The sample's mean age was 36.9 ± 12.0 years with median treatment duration of 7.0 years (range: 0.25 to 38 years). Multiple logistic regression revealed no significant association between TD and *CYP2D6*17* (OR=0.252; 95% CI: 0.038 to 1.647; $p=0.150$). However, use of chlorpromazine (OR=5.754; 95% CI: 1.024 to 32.328; $p=0.047$) and age at treatment initiation (OR=1.146; 95% CI: 1.021 to 1.287; $p=0.021$) were independent predictors of tardive dyskinesia.

Conclusion: These findings suggest that there is no association between *CYP2D6*17* and TD in African psychotic patients on typical antipsychotics. However, more studies with larger sample sizes are required to provide more definitive conclusions regarding the nature of the relationship between *CYP2D6*17* and TD.

RF01.6 POPULATION AGEING AND COGNITION IN A RURAL SOUTH AFRICAN POPULATION

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Introduction: In South Africa, we hypothesise that the health burden due to cognitive decline in ageing populations is increasing as life expectancy increases. Genetic variation influences healthy ageing and cognitive decline. Genomic association studies on ageing and cognition have primarily been performed in populations of European origin and are largely unexplored in Africans. African genetic diversity may help to find common and rare variations which may influence both the rate of decline and dementias including susceptibility to Alzheimer's disease. Evaluating the prevalence of cognitive decline is challenging due to variability in diagnostic criteria of cognition tests, geography of the sample population, cultural and lifestyle differences between rural and urban environments, language, literacy and level of education.

Methodology: This study is nested in the HAALSI¹ cohort in Agincourt, Mpumalanga. A comprehensive dataset is available on 3500 Shangaan South Africans aged between 40 and 90 years. This includes an IQCode for diagnosis of dementia and Alzheimer's disease, demographic and health related data, anthropometry and blood and urine biomarkers. In addition, data on physical activity, diet and education will be analysed for associations with cognitive phenotypes and genetic variation.

Results: Preliminary data show that education is a major influence on cognitive performance in this population; while a relationship with hypertension and diabetes is discernible. It is apparent that variables such as obesity, smoking and SES should be considered as moderators in genomic association tests. These results will form the basis of a larger study titled, 'Genetic and environmental factors associated with cognitive decline and the dementia spectrum in an ageing South African population.'

¹ Health and Aging Study in Africa cohort MRC/Wits Rural Public Health and Health Transitions Research Unit

Conclusion: We plan to examine several candidate genes and pathways as well as telomere length to better understand the mechanisms and pathways involved in age-related cognitive decline. Regions of interest include APOE, FOXO, proinflammatory pathway genes and genes linked to anaemia.

RF01.7 FINE-MAPPING OF ANTIPSYCHOTIC RESPONSE GWAS REVEALS NOVEL REGULATORY MECHANISMS

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Introduction: Schizophrenia treatment response is highly heritable, yet poorly understood. Recent studies show that noncoding variation displays regulatory effects on disease and the treatment thereof, however most studies relate function to the closest gene without investigating regulatory potential. This study aimed to investigate the potential functionality of previously implicated noncoding variants on schizophrenia treatment response.

Methodology: The variation within regions identified from previous GWAS examining antipsychotic treatment response was analysed using recently developed predictive tools to determine regulatory potential. Prioritised variants were assessed for association(s) with antipsychotic treatment outcomes in a South African first episode schizophrenia (FES) cohort (n = 103).

Results: Both *in silico* and subsequent association results implicated an important relationship between regulatory variants, expression of three genes (*MANBA*, *COL9A2*, and *NFKB1*), and schizophrenia treatment outcomes. Three of these rSNPs were significantly associated with poor post-treatment outcomes in the negative symptom domain (rs230493: $P = 1.88 \times 10^{-6}$; rs3774959: $P = 1.75 \times 10^{-5}$; rs230504: $P = 1.48 \times 10^{-4}$).

Conclusion: This study has thoroughly investigated previous antipsychotic GWAS findings to pinpoint variants that likely play a causal role in poor treatment outcomes. The regulatory variants identified in this study suggest novel roles for *MANBA* and *COL9A2* in antipsychotic response, and confirm the significance of immune regulation in schizophrenia.

RF02: Neuroimaging students IBRO Advanced school in Neuroimaging

RF02.1 METABOLIC ACTIVITY IN BRAIN TUMORS ASSESSMENT USING MAGNETIC RESONANCE SPECTROSCOPY

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Introduction: The aim of this study is to assess the usefulness of magnetic resonance spectroscopy (MRS) data in differentiation of brain tumors and nonneoplastic diseases mimicking brain tumor on regular MRI. Additionally we illustrated MRS usefulness to characterize cerebral glioma grading.

Methodology: This study included 51 patients aged from 6 months to 65 years with expansive brain process; the study lasted from February 2012 to September 2016. All data was acquired using a 1.5 Tesla MRI system (Sigma, General Electric; Milwaukee, United States). The examination protocol included T2 and T1-weighted images, FAIR, diffusion weighted images b-factor 1000 mT/m², and T1 images after contrast bolus injection. Multi voxel MR spectroscopy was performed using a spin-echo mode sequence (SE) with intermediate TE of 144 ms and short TE of 35 ms. The identified metabolites included N-acetylaspartate (NAA) at 2.0 ppm, creatine (Cr) at 3.0 ppm, choline (Cho) at 3.2 ppm, lipid at range between 0.7 and 1.3 ppm, lactate at 1.3 ppm and myoinisitol at 3.5 ppm. Calculated ratios included Cho/NAA and Cho/Cr.

Results: Identified brain expansive processes on MRI were organized in groups including: Secondary (Metastatic) Neoplasms (n= 3): that demonstrated elevated signals of lipid, lactate, and choline and reduced or

absent NAA signal. Primary central nervous system lymphoma (n=3): that showed increased choline and decreased NAA with reversed choline and creatinine ratio. Low grade glioma (n=12): that expressed low choline level and increased Cr peak, Cr and Cho peaks were almost at equal level (Cho/Cr ratio: 1.0) with absence of lactate and lipids. Glioblastoma (n= 19): exhibited an increased Cho peak, decreased creatine peak with Cho/Cr > 2, decreased NAA peak, Lac peak was the highest with double-peaked. Tumefactive demyelinating Lesions (n= 4): showed slight decrease of NAA peak, absence of lactate peak, and elevated of choline peak. Tuberculous abscesses (n= 4): demonstrated high lipid and lactate peaks with no peaks for amino acids. Leukodystrophie: included Canavan's disease (n= 1) with increased NAA resonance peak with NAA/Creat > 4.4. it included also others (n= 6): that showed an elevated Cho/Cr, decreased NAA/Cr and elevated Cho/NAA ratios were the dominant finding. Ischaemia (n= 3): that showed an increased Lac peak.

Conclusion: MRS provides information on biochemical processes in brain tissue which occur before possible visibility in structural images. Therefore MRS was elected a non-invasive method for diagnosis and grading of brain tumors. In addition, the analysis of metabolite peaks and their ratios in MR spectra provides useful additional information for identification of CNS lymphoma, demyelinating processes, ischemic and metabolic brain diseases.

RF02.2 YIELD OF REPEATED INTERMITTENT EEG FOR SEIZURE DETECTION IN CRITICALLY ILL ADULTS

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Introduction: Seizures are common in critically ill patients and its prevalence can exceed 30% in neuro-intensive care unit (ICU). Continuous EEG monitoring (cEEG) is the goal standard for seizure detection in critically ill patients. To determine the yield of intermittent EEG (iEEG) to detect critically ill adult patients with seizures and to identify the factors that affect this yield.

Methodology: We retrospectively analyzed cEEG data and medical records from 977 consecutive critically ill patients undergoing cEEG. We included those presenting at least one electrographic seizure during the first 24 hours of cEEG. Patients with hypoxo-ischemic encephalopathy were excluded. We reviewed for seizure six 30-minutes epochs on cEEG selected at H0, H3, H6, H12, H18 and H24.

Results: Seizures occurred in 10.75% (105/977) of patients. Level of consciousness was impaired in 79 (75%) of patients, with 42 (40%) in coma. Review of the H0 epoch on cEEG permitted to detect seizure in 61(58%) patients. These figures increased to 70 (67%), 75 (71%), 91(87%) and 97 (92%) patients for a sampling every 24, 12, 6 and 3 hours respectively (p=0.02). Frequency of seizures on cEEG was the only factor significantly affecting the probability of seizure detection. Sampling every 6 hours revealed seizures in all patients with more than six seizures per 24 hours.

Conclusions: iEEG repeated every 6 hours can accurately detect patients presenting seizures, especially when seizure frequency is greater than six per 24 hours. These findings have practical implications for electrographic seizure detection in critically ill patients in settings lacking cEEG.

RF02.3 COMPARATIVE BRAIN CT PERFUSION PARAMETERS IN HIV-SEROPOSITIVE ADULTS WITH AND WITHOUT NEUROCOGNITIVE IMPAIRMENT IN NIGERIA

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Background: Neurocognitive disorder (HAND) as a complication of Human Immunodeficiency Virus (HIV) infection affect more than two million people in Nigeria. Despite increasing access to treatment and use of highly active antiretroviral therapy (HAART), the prevalence of HAND continues to rise and has been associated with cerebrovascular disease (CVD) and brain perfusion abnormalities. The cerebral hemodynamics of HAND in a homogeneous black population is unknown. The aim of this study is to comparatively quantify global and regional cerebral blood flow parameters in neurocognitively impaired and unimpaired HIV-infected individuals in an observational cohort study in Nigeria.

Methods: Twenty-four, age and sex matched individuals from the Ibadan Cohort on NeuroAids (ICON) with and without neurocognitive impairment had Brain CTP. Imaging was performed with a 64-slice Toshiba CT scanner.

Regional CBV, CBF and MTT relative to the basal ganglia (BG) were evaluated in cerebral cortices as well as in white matter areas. Correlations of CBV, CBF, MTT values with immunologic and neurocognitive data will be analyzed.

Results: Preliminary findings of CBV, CBF, MTT ratios in the cerebral cortices of cognitively impaired Individuals compared to controls will be presented. Demonstration of HAND patients MTT, CBV, CBF and TTP ratio values in the all cortices and basal ganglia will show differential flow measurements. Cognitively unimpaired subject's ratios of cerebral and basal ganglia values will be compared with values of unimpaired individuals. The significant correlations of CBV, CBF, MTT values and CD4 T cell count or viral load will be shown.

Conclusions: Brain CT perfusion allows the assessment of African HAND patients at different stages cerebral dysfunction. Racial differences may influence cerebral perfusion parameters in HAND patients stimulating further research in genomic implications of differential cerebral perfusion in HIV.

RF02.4 THE EFFECT OF EARLY ABSTINENCE FROM METHAMPHETAMINE ON BRAIN METABOLITES USING ¹H-MAGNETIC RESONANCE SPECTROSCOPY (¹H-MRS)

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Introduction: Methamphetamine (MA) use, using proton magnetic resonance spectroscopy (¹H-MRS), has been shown to reduce neuronal integrity and viability, and reduced metabolism of cellular membranes. Previous ¹H-MRS studies on MA dependence have investigated short-term (3-9weeks) and long-term (20+weeks) effects of MA abstinence. This ¹H-MRS MA dependence study investigated the acute (<2weeks) to short-term (<6weeks) effects of MA abstinence.

Methods: Adult MA dependent (n = 31) and healthy-matched control participants (n = 22) underwent 2D-chemical shift imaging ¹H-MRS (TR2000ms, TE30ms), voxels included bilateral frontal white matter (FWM), anterior cingulate (ACC), and dorsolateral prefrontal cortices (DLPFC). Control participants were scanned only once. MA dependent participants underwent scanning twice: (1) when acutely abstinent from MA use, 1.5±0.6 weeks (n=31), and (2) after short-term MA abstinence of 5.1±0.8 weeks (n=22). Metabolite concentrations, relative to Creatine with Phosphocreatine (Cr+PCr), extracted were *n*-acetyl-aspartate (NAA), *n*-acetyl-aspartate with *n*-acetyl-aspartyl-glutamate (NAA+NAAG), glutamate (Glu), glutamate with glutamine (Glu+Gln), *myo*-inositol (Ins), and glycerophosphocholine with phosphocholine (GPC+PCh).

Results: *Acute abstinence from MA*, compared with controls, showed: decreased NAA and NAA+NAAG for left DLPFC; and decreased GPC+PCh for left FWM. *Short-term abstinence from MA*, compared to controls, resulted in: decreased NAA and NAA+NAAG for left DLPFC; decreased GPC+PCh for left FWM; and decreased NAA and increased Ins were found for right ACC. Several ¹H-MRS correlates were found with duration of MA use and age of initial MA use during acute and short-term abstinence. *Over time, from acute to short term MA abstinence*, differences included: decreased NAA and NAA+NAAG in right ACC and right FWM; and decreased Ins in left FWM were found.

Conclusion: Our findings support decreased neuronal integrity and viability with MA use. This is the first study to show the presentation of neuroinflammation from acute to short-term MA abstinence. These data may provide insight to management of MA dependent user recovery.

RF02.5 COGNITIVE OUTCOMES OF INFANTS POST-HIVE INFECTION: AN EVENT-RELATED POTENTIAL STUDY

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Introduction: Children exposed to the human immune-deficiency virus (HIV) are at increased risk for neuro-developmental impairments in cognitive, language, motor, and socio-behavioral skills. The outcome of these children in sub-Saharan Africa may be particularly poor due to lack of anti-retrovirals. Further, a lack of robust assessment techniques in rural Africa could result in poor assessment of outcome.

Methodology: A study of 50 HIV exposed children aged between 6 and 35 months born of HIV positive mothers was conducted to examine how their brain event-related potential components in response to novel stimuli compared with those of age-matched community controls.

Results: The results showed HIV infected children had longer P1 latencies compared to controls [main effect of Diagnosis, $F(1, 78) = 17.093, p < 0.001$] suggesting that children exposed to HIV processed novelty differently than unexposed children. There was a developmental trend of decreasing P1 amplitudes with age in the control group but this was not evident in the HIV exposed children. Further, an interaction of Diagnosis by Age showed that this effect was particularly pronounced in younger children. The P2 latency did not reveal any diagnosis related differences but there were larger P2 amplitudes associated with the frequent stimuli in children infected with HIV compared to community controls.

Conclusions: These results suggest that children exposed to HIV may have difficulties with novelty processing associated with cognitive slowness, possibly due to disruption in the functions of the superior temporal cortices. This may suggest poorer cognitive outcomes in the HIV exposed group.

RF02.6 BRAIN COMPUTER INTERFACES IN CONTROLLING PROSTHETIC / ORTHOTIC HANDS

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Brain computer interfaces (BCI) can restore some essential hand functionality in motor-impaired patients by processing electroencephalography (EEG) waveforms in order to control a prosthetic or orthotic hand. However, current implementations only allow limited functionality and degrees of freedom. This paper attempts to discriminate the EEG associated with the novel combination of wrist extension and flexion, finger extension and flexion and the tripod pinch in both left and right hands individually in a four-class BCI problem. Real and imagined movement data was recorded from healthy test subjects. Independent component analysis (ICA) was used as a spatial filter, while a time-frequency technique extracted features from the mu and beta EEG frequency range. Single-stage 4-class classifier architecture was compared to two-stage 4-class architecture. Artificial neural networks, support vector machines, Mahalanobis distance clustering, and a group classifier were compared. It was found that the two-stage group classifier produced the highest results. The average accuracies obtained for real and imagined movements were 68 % and 62 % respectively. These results validate the possibility of multiclass EEG discrimination for hand movements and suggest the existence of different underlying neural mechanisms that control wrist and finger movements. This is an important step towards allowing a BCI to control more degrees of freedom of a prosthetic or orthotic hand.

RF02.7 ACTIGRAPHY IN THE ASSESSMENT OF SLEEP PATTERNS IN SICKLE CELL DISEASE PATIENTS CAMEROON (SUB-SAHARAN AFRICA)

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Background: Sleep disorders have been reported to be more common Sickle Cell Disease (SCD) patients than controls in Western countries, but almost no data exist on the subject in Africa. This study sought to characterize sleep patterns in SCD patients using actigraphy, a validated and user-friendly sleep study tool.

Methodology: 13 SCD children and 13 age and sex-matched controls wore wrist actigraphs for a minimum of 72hrs and kept a sleep diary. Actigraphy data was analyzed with Action4® and MATLAB® software. Data on total sleep time, sleep onset latency (SOL), sleep cycle mesor, acrophase, amplitude, inter-daily stability (IDS), intra-daily variability (IDV) and F-ratio were collected, analyzed and reported.

Results: SCD patients took significantly shorter time to fall asleep than controls (mean SOL: 75 ± 15.35 versus 113.41 ± 11.79 minutes, $p=0.02$), and slept significantly shorter (mean SOL: 422.66 ± 33.24 versus 528.75 ± 24.10 minutes, $p=0.0084$). In addition, they also displayed a lower sleep ratio (0.593 ± 0.045 versus 0.424 ± 0.044 , $p=0.0071$), and less frequent night awakenings (14 ± 1.47 versus 20.42 ± 2.29 , $p=0.014$). But for the mesor (156.27 ± 4.34 and 142.55 ± 4.55 , respectively for SCD and controls, $p=0.02$), cosinor rhythmometry was not significantly different for both groups for the acrophase time, amplitude, the F-ratio and goodness of fit.

Conclusion: This is the first report in Cameroon showing that sleep and circadian rhythm disorders that are common in SCD patients, can be easily characterized using actigraphy. We propose the use of actigraphy in routine sleep evaluation in SCD patients after validation of the technique.

POSTER PRESENTATIONS

P1 BEHAVIOURAL AND EMOTIONAL COMORBIDITY OF ACUTE SEIZURES IN YOUNG KENYAN CHILDREN: A POPULATION-BASED STUDY

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Background: Acute seizures in young children in Africa may be associated with poor behavioural and emotional problems. It is unclear if behavioural and emotional comorbidities of acute seizures are related to the seizures, or shared genetic susceptibility and neurological damage.

Methods: We conducted a population-based study on 3,273 young children aged 1-6 years on the Kenyan coast to examine the relationship between acute seizures and behavioural and emotional problems, and to determine the factors associated with the comorbidity. Prevalence of behavioural and emotional problems was derived from the inverse link of a logit model. Generalised linear models were used to measure the independent association between acute seizures and behavioural and emotional problems, and to determine associated risk factors. Sobel-Goodman mediation tests were used to perform mediation analysis.

Results: The crude prevalence of total behavioural and emotional problems was 30% (95%CI, 20%-43%) for children with acute symptomatic seizures and 25% (95%CI, 15%-38%) for those with febrile seizures; being greater than for those without seizures (11% (95%CI, 11%-12%); Chi-squared $p \leq 0.001$). Behavioural and emotional scores were higher in acute seizures than in those without seizures (Cohens $d=0.44$ (95%CI, 0.30-0.59)). Acute seizures were associated with total behavioural and emotional problems (risk ratio (RR)=1.92 (95%CI, 1.34-2.77)) after accounting for sociodemographic and medical confounders. The proportion of total effects of acute seizures on behavioural and emotional problems mediated by epilepsy was small (15.3% (95%CI, 4.5-34.9%)). Among children with acute seizures, important risk factors for mental health comorbidity included family history of febrile seizures (RR=3.36 (95%CI, 1.34-8.41)) for total problems, repetitive acute seizures ($\beta=0.36$ (95%CI, 0.15-0.57)) for externalizing problems and focal acute seizures (RR=1.80 (95%CI, 1.05-3.08)) for internalising problems.

Conclusion: Acute seizures are associated with substantial behavioural and emotional problems, which should be assessed and addressed in children with these seizures in this rural area of Kenya.

P2 THE PATHWAY TO ELUCIDATING BIPOLAR DISORDER GENETICS

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Introduction: Bipolar disorder (BD) is both a clinically and genetically complex disease. It has a global prevalence of approximately 3%, 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. This study has used whole genome sequencing data and a bioinformatics approach to identify variants in BD members of a family in an attempt to 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 metabolic pathways, neuroprogression, and immune pathways 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 BD as an illness.

P3 CLINICAL PROFILE OF CHILDREN EPILEPSY WITH HEREDO-FAMILIAL FEATURES AND GENETIC TRANSMISSION HYPOTHESES IN CONGOLESE ENVIRONMENT

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Introduction: Epilepsy is a worldwide disorder that can affect people at any age. About 50 million people suffer worldwide, including 10 million in Africa. The causes are multifactorial, with genetic factors involved in 40% of the cases. In sub-Saharan Africa, 6-60% of the cases are linked to family history.

Methodology: We performed a cross – sectional study which focused on children aged 0 – 17 year suffering from epilepsy. Family trees were analyzed using the criteria of various genetic diseases transmission modes including autosomal dominant mode, autosomal recessive mode, transmission X-linked and NOVO mutation. The study was conducted from March 2014 to June 2015 in three hospitals of Kinshasa.

Results: Children under investigation had an average age of 63,5±50,5 months. We noted a male predominance in 61.2% against 38.8% for females, with sex ratio M/ F of 1.57, that in all children. In the group of 252 epileptic children, the sex ratio M / F was 1.6 while it was 1.3 in epileptic children with epilepsy and hérédofamilial history and 1.7 in those without a history record. The average onset age of the first seizure was 33,53±37,51 months. Generalized seizures were the most frequent. Heredofamilial cases were characterized by lower frequency of multiple daily seizures. The signs of epilepsy with family history were mostly recorded at the second degree. The autosomal recessive mode predominates. Cognitive disorders were the most common associated with epilepsy.

Conclusion: This study describes the main clinical features of childhood epilepsy with hereditary family background in the Kinshasa area. These features comprise lower frequency of multiple daily attacks, epileptic family history, especially in the second degree and the prevalence of autosomal recessive mode.

P4 EPIGENETIC ALTERATIONS ATTRIBUTABLE TO CHILDHOOD TRAUMA EXPOSURE AND ADULT OUTCOMES: A SYSTEMATIC REVIEW

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Introduction: Multiple, chronic and repeated trauma exposure in childhood is associated with adverse outcomes in adulthood such as re-victimisation and the onset and severity of various mood, anxiety, personality and substance disorders. Biological mechanisms have been proven to partake in the development of psychiatric disorders following trauma exposure and epigenetic modification is a plausible mechanism mediating environment and biological interaction. This study aimed to review the current literature on epigenetic modifications related to childhood trauma and adult mental health outcomes and to determine areas in need of further research.

Methodology: We reviewed the current literature up to September 2016 in five databases (PubMed, Web of Science, EBSCO host and SCOPUS) with several keywords related to epigenetic changes and childhood adversity. Animal studies, non-original research and studies based on mental health outcomes in participants younger than 18 years of age were excluded.

Results: Fifty-four articles were selected. Most of the studies investigating candidate genes found significant differences in methylation profiles between participants with and without childhood trauma. The candidate genes investigated included: brain-derived neurotrophic factor (*BDNF*), glucocorticoid receptor/Nuclear Receptor Subfamily 3, group C, Member 1 (*NR3C1*), FK506 binding protein (*FKBP5*), serotonin transporter / Solute Carrier Family 6 (*SLC6A4*), D2 dopamine receptor (*DRD2*), and oxytocin receptor (*OXTR*). Differences

between the epigenetic profiles of participants with and without childhood trauma were also identified in genome-wide studies.

Conclusion: Differentially methylated genes were predominately related to neurochemicals, brain and neuronal development, the immune system and the Hypothalamic-Pituitary-Adrenal axis (HPA-axis). Childhood trauma may increase risk for a number of different types of psychological disorders and further research is needed to determine the pathways associated with childhood trauma and differential adult mental health outcomes.

P5 ASSESSMENT OF ALCOHOL USE DISORDERS AMONG GENERAL MEDICAL OUT-PATIENTS

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Introduction: Most alcohol-related harm is attributable to hazardous/harmful drinking. However, primary care setting has been identified as key for the reduction of alcohol-related harm, with General practitioners playing a significant role. The study aimed at identifying pattern of, and factors that are associated with Alcohol Use Disorders (AUDs) among General out-patients (GOP).

Methodology: Two hundred and forty five (245) participants were selected through a random sampling from a GOP population aged 18 to 65 years over a three months period. A pre-tested, semi-structured questionnaire, incorporating socio-demographics and the diagnoses made by the attending Physician was administered. The participants also completed the AUDIT questionnaire and the PHQ 9. A score of 8 and above for men; and score 7 and above for female on AUDIT indicated alcohol use disorders. Data were analyzed with SPSS version 16.

Results: The prevalence of AUDs among the population of general out-patients was 9.7%. The AUDIT scores of the participants range from 0-29 with a mean of 1.3 (SD=4.08). AUDs were significantly associated with gender, level of education, occupational class and the presence of significant depressive symptoms ($p < 0.05$). There was no statistically significant association between AUDs and participant age, employment status, marital status, religion and medical diagnoses.

Conclusion: The prevalence of AUD among population studied was lower compared with similar study in similar setting. AUDs were predicted by gender, lower education level, occupational group and the presence of significant depressive symptoms mostly in the mild to moderate form. The fact that those with lower education engaged more in manual works such as driving, bricklaying, laborers and similar occupations may have encourage use of alcohol as an “enhancer”. Identifying the group at risk in clinical setting may go a long way in reducing the adverse effect of AUDs in our society.

P6 TRACE ELEMENTS AND FERRITIN STATUS OF INDIVIDUALS IN LOCAL METAL INDUSTRIES IN IBADAN, OYO STATE

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Introduction: The adverse health effects associated with exposure to toxic heavy metals in the environment is a matter of serious concern globally. Accumulating evidence also indicates that work place exposure leads to generation of free radicals which when accompanied by inadequate antioxidant leads to an increase in oxidative stress. These risks are particularly enhanced in developing countries where there is often little information on the safe handling or transportation of chemicals in industry and agriculture.

Methodology: This study was carried out therefore to determine the levels of free radicals generated and oxidative stress status of thirty-seven metal workers and thirty-six non-exposed control subjects (age and sex matched) resident in Ibadan. Ten (10) mls of venous blood was collected from each subject into heparinized bottle and this was used to determine Cadmium (Cd), lead (Pb), zinc (Zn) and Manganese (Mn). They were analyzed using Atomic Absorption Spectrophotometer (AAS).

Results: There were significant increases in Lead ($0.0159 \pm 0.0029 \mu\text{g/L}$) and Mn ($31.92 \pm 7.79 \mu\text{g/dL}$) in the exposed group and significant decrease in Ferritin ($96.38 \pm 8.22 \mu\text{g/L}$) in the exposed group.

Conclusion: This study indicates that metal workers are exposed to toxic metals/substances in the local metal industries which result in increased plasma levels of lead and manganese. The decrease in iron store is probably as a result of interference in iron metabolism by lead and manganese.

P7 ALTERATIONS ON DOPAMINERGIC INNERVATIONS AND VOLUNTARY MOVEMENTS AFTER LONG PERIOD OF THIRST IN A SEMI DESERT RODENT *MERIONES SHAWI*: BEHAVIOURAL AND IMMUNOHISTOCHEMICAL STUDIES

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Dehydration is a powerful stimulus causing disequilibrium in homeostasis of water and electrolytes resulting from depletion in total body water. Most studies have focused on domestic and laboratory animals; however, the study of desert animals allows improved understanding about water balance and resistance to dehydration and associated behavioral changes, including those related to voluntary movements. *Meriones shawi* (Shaw's Jird) is a desert rodent characterized by its resistance to long periods of thirst that can extend for several months. In the present study, *M. shawi* were subjected to water deprivation for 1 month. We used tyrosine hydroxylase immunohistochemistry (TH: the key enzyme of catecholamine biosynthesis) to evaluate the effects of prolonged dehydration on the dopaminergic system in both substantia nigra pars compacta and ventral tegmental area (SNpc and VTA), which are the main sources of dopamine input to several brain areas; the immunolabelling was performed also in both the medial forebrain bundle and the caudate putamen (striatum). In addition, the open-field test was used to evaluate the effect of dehydration on locomotor activity in *M. shawi*. The results showed an increase in TH immunolabelling in both SNpc and VTA following 1 month of dehydration compared to control levels. The same results were obtained with fibers in both MFB and striatum. This augmentation of TH immunoreactivity was accompanied by noticeable changes in locomotor activity behavior of *Meriones*, the recording test shows the hyperactivity of animals which is probably caused by dehydration. Overall, the results indicate that dehydration is able to increase dopaminergic neurotransmission, which might be involved in generating hyperactivity in this desert animal.

P8 CHARACTERIZING DRUG INTAKE IN SOCIALLY ENGAGED MICE

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Introduction: The majority of animal models used to investigate the underlying mechanisms of addiction were studied with the animals in isolation as opposed to the actual condition in humans where addictive behaviours are practiced in a social context. Aim was to develop a rodent model of drug addiction within a social context.

Methodology: C57BL/6 female mice were placed in IntelliCages for 5 weeks during which they had free access to drinking bottles containing either water, 12% ethanol or 300mg/L cocaine solution. Their drinking behaviour were subsequently recorded. Parameters assessed included drug preference, spontaneous learning, drug motivation and consumption rate. Continuous assessments occurred before and after 7 days of drug withdrawal.

Results: Our results showed peak consumption of cocaine during the 1st and 4th week of exposure as indicated by increased visits, nosepokes and licks in corners housing the cocaine-containing drinking bottles. Interestingly ethanol consumption was high when cocaine consumption was low suggesting a periodic switch of taste preference between the two drugs. After drug withdrawal, mice displayed a stronger persistence for cocaine seeking compared to their pre-withdrawal behaviour. Surprisingly, the mice failed to learn to visit correctly the cocaine corners when given the scheduled alternation tasks.

Discussion/Conclusion: The data suggests an interchange between cocaine and ethanol consumption. The results further showed cocaine seeking and intake behaviours being enhanced by abstinence. The inability of the mice to learn the alternation tasks may be attributed to drug-induced cognitive deficits. Our model therefore appears to mirror aspects of substance abuse in humans very well.

P9 AUTOMATED DETECTION OF INTRACRANIAL ANEURYSMS: REVIEW

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Abstract: Brain aneurysm or intracranial aneurysm is an abnormal dilatation of the cerebral arteries. It is like a weak bulging spot on the wall of an artery. Detecting unruptured aneurysm remains a challenging task. However, it is difficult and time-consuming for neuroradiologists to detect intracranial aneurysm due to the complexity of cerebral vascular anatomy. To solve this problem, computer-aided diagnosis (CAD) approach has become a major tool allowing to assist neuroradiologists to interpret unclear findings and aspects mimicking aneurysms.

In this paper, we review state of the art literature researches on CAD system allowing to detect intracranial aneurysm with an emphasis on highlighting the advantages and of various approaches used in the field. A particular focus on 3D imaging modalities will be provided. A discussion and conclusion on future possibilities of CAD methodologies for detecting intracranial aneurysm will be produced.

P10 NEURONAL LOSS AND DISTORTION IN RODENT HIND-LIMB SUSPENSION: SIMULATE MICROGRAVITY

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The need for human exploration of the space is becoming increasingly important and it is necessary to determine the influence of such extreme environment on the biological system. This work is targeted towards examining the effect of hind-limb suspension (simulated microgravity) on the histo-architectural properties of neurons present in the prefrontal cortical region of the brain. Twelve wistar rats divided into two groups, control (n=6) and hind-limb suspension group (n=6) were used for this experiment. The hind-limb suspension group underwent two weeks of 30° head-down tilting while the control rats were maintained in their normal cages. Following the experimental period, prefrontal cortex of the brains were excised and processed for routine Haematoxylin and Eosin, Cresyl Violet and Sudan Black B staining. Results showed that hind-limb suspension (HLS) group had signs of pyramidal neuronal deformity and aggregation with increased dendritic offshoot. They also demonstrate decreased cellular density and lipofuscin deposition. The neuronal deformity observed shows that extreme exposure to hind-limb suspension (simulated microgravity) might be detrimental and can compromise neuronal functionality. This study suggests that appropriate counter-measures should be provided for astronauts in space as prolonged simulated microgravity exposure might elicit adverse histo-architectural/functional effects on the cells of the prefrontal cortex.

P11 COMPARATIVE EFFECTS OF DIAZEPAM AND ETHANOLIC LEAF EXTRACT OF *DICHRSTACHYS GLOMERATA* ON MEMORY AND LEARNING IN PENTYLENETETRAZOL-INDUCED EPILEPTIC MICE

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Introduction: With the contribution of medicinal plants to the treatment of diseases, the effects on memory and learning in Pentylenetetrazol-induced epileptic mice of the ethanolic leaf extract of *Dichrostachys glomerata* were compared with those of Diazepam.

Methodology: Twenty-eight male Swiss white mice split into four groups were employed in this study. Group I (control) received 0.9% normal saline (i.p.), group II (untreated epileptic) were administered pentylenetetrazol (PTZ, 60mg/kg, i.p.) to induce epileptic seizure. Groups III and IV were treated with DZP (1mg/kg, i.p.) and DG (4.5mg/kg, i.p.) respectively, 30 minutes before inducing epilepsy. The anti-epileptic effects of both drugs were assessed by the frequency and duration of seizures after inducing epilepsy. Post-seizure effects on cognitive and visuo-spatial memory in the animals were assessed using the Novel object recognition task (NORT) and the Morris water maze (MWM) respectively.

Results: Seizure activities were completely abolished in the DZP-treated mice, while significantly lowered in the *D. glomerata*-treated group of mice compared to their untreated epileptic counterparts ($p < 0.001$). In the NORT test, the index of discrimination was lower in the PTZ group for both short-term and long-term memory compared to control ($p < 0.001$). However, the index of discrimination in the DZP and DG-treated epileptic mice were higher compared to the PTZ ($p < 0.01$) both during the short-term and long term memory tests ($p < 0.01$), but significantly higher in the DZP when compared to DG treated groups ($p < 0.05$). In the MWM, the quadrant duration and frequency of annulus reversal crossings were higher in the DZP and DG groups compared ($p < 0.05$) to PTZ group.

Discussion/Conclusion: Both diazepam and *Dichrostachys glomerata* had anti-epileptic properties, but DZP was more potent. Both DZP and DG reversed memory impairment induced by seizures.

P12 CORRELATION OF NEUROIMAGING FINDINGS AND TREATMENT RESPONSE IN PATIENTS WITH SEIZURE FROM ETHIOPIA

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Seizures in developing countries are often poorly investigated and consequently poorly managed. Socio-cultural misconceptions, financial difficulties, and lack of facilities are often blamed. Chronic non communicable diseases, such as epilepsy, are increasingly recognized as important health care problems in developing countries. Community-based epidemiological studies of neurological disorders were performed in different part of Ethiopia. The most prevalent neurological disorder identified was epilepsy. This study will study the correlation of structural intracranial abnormalities associated with seizures and treatment response, and the proportion of these structural lesions that may benefit from surgery. We will conduct a cross-sectional study of 100 seizure patients attending the follow-up clinics of the departments of neurology at Federal Police Hospital, in Addis Ababa, Ethiopia, from September 2016 to December 2016. We will collect information using a standardized questionnaire which assesses demographic information, clinical history and neurologic function. We will conduct an Epilepsy MRI Protocol for all subjects and the correlation with treatment response and candidacy for surgery.

P13 PLACE FOR NEUROIMAGING IN MADAGASCAR: CURRENT SITUATION AND PERSPECTIVE

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Introduction/Methodology: Neuroimaging is an axis in neurology and imaging. Madagascar has these two specialties, but no neuroradiologist. Our goal is talk about the role of neuroimaging in Madagascar now and later.

Results: Currently Madagascar has 14 scanners, including 9 in Antananarivo and 2 MRI which are also there. University Hospital at Befelatanana Antananarivo, where the reference Neurology unit has no imaging. For 1040 admissions (January 2015 - June 2016) requiring imaging, only 288 (27.69%) were receiving a scanner and 03 (0.28%) MRI. Madagascar has 03 neurologists for 25,117,291 inhabitants and radiologists making all exercisers. However, neuroimaging is essential to develop support in neurovascular because, for example, our study conducted in 2014 found 53.16% of vascular dementia and 100% of dysexecutive disorders, needed special care.

Discussion: Reorganizing his speciality, neurology is training specialists since 2011. Currently, it has 09 registrars focus. There is one that comes from Besancon to ultrasound training. Three other just left for neurological emergencies, movement disorders and peripheral neuropathy. I shall go far with neuroimaging, performing an internship of one semester in radiology unit and participating in this training by IBRO. In the implementation, we will move to another hospital access to imaging and partner with clinics like CNaPS structures (National Social Insurance Fund).

Conclusion: So, this training should allow the thrombolysis in Madagascar.

P14 *RAUWOLFIA VOMITORIA* INHIBITS OLFACTION AND MODIFIES OLFACTORY BULB CELLS

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Introduction: The rising cost of orthodox medication has endeared so many to the use of herbs for the management of neurological conditions. *Rauwolfia vomitoria* (RV) one of such herbs is a rainforest shrub whose parts are used locally in the management of psychiatry and other medical issues. Its usefulness though not in doubt is wrapped with adverse reports as its active constituents deplete brain monoamine and dopamine stores. This motivated this research on the effects of the root bark extract on olfaction and the olfactory bulb of adult Wistar rats.

Methodology: Eighteen adult Wistar rats (220 g average) were divided into three groups (n = 6); control (placebo), 200 mg/kg and 400 mg/kg RV root bark extract, respectively. The oral administration lasted for seven days and on day 8, test of olfaction was carried out and the animals immediately anaesthetized with ketamine hydrochloride (i.p.) and perfuse-fixed with 10% neutral buffered formalin. All the brains were processed for histology and immunoreactivity.

Results: Results showed loss of body weights and olfaction in the 200 mg/kg and 400 mg/kg RV groups. There was hypertrophy and atrophy of mitral cells respectively, in the 200 mg/kg and 400 mg/kg RV groups, while there was hyperplasia of cells in the internal granular and plexiform layers of both groups. There was decreased neuron specific enolase (NSE) and neurofilament (NF) expression in the 200 mg/kg RV group, while NF and glial fibrillary acidic protein (GFAP) expression was decreased in the 400 mg/kg RV group. However, NSE expression was enhanced in the 400 mg/kg group, while GFAP expression was enhanced in the 200 mg/kg RV group.

Conclusion: These results suggest that these doses of RV affect olfaction and appetite, and stimulate adverse cellular changes in the olfactory bulb.
