ABSTRACTS

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Executive board

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Prof Lukoye Atwoli, Moi University School of Medicine, Kenya

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ORAL PRESENTATIONS: INVITED FACULTY

LECTURE 1

Neuroscience Based Nomenclature (NbN) – Can neuroscience change an outdated psychotropic classification?

Joseph Zohar
Sheba Medical Center Hospital, Tel Aviv, Israel

Current psychopharmacological nomenclature remains wedded to earlier period of scientific understanding, failing to reflect contemporary developments and knowledge, does not help clinicians to select the best medication for a given patient, and tending to confuse patients as they are being given a drug with a different name compared to their identified diagnosis (e.g. "Antipsychotic" for depression). Four major colleges of Neuropsychopharmacology (ECNP, ACNP, Asian CNP, and CINP together with IUPHAR) proposed a new pharmacologically-driven nomenclature focusing on Pharmacological Domain and Mode of Action. It includes also 4 dimensions of additional information: 1—Approved Indications; 2—Efficacy and side effects; 3 — Practical note; and 4— Neurobiology. Several surveys in four different continents were conducted in order to examine satisfaction with the current psychopharmalogical nomenclature, as well as test the NbN. A significant proportion of the participants in the surveys were in favor of the proposed nomenclature. It seems that clinicians found the available nomenclature system dissatisfactory and many times confusing for them and the patients. The proposed nomenclature seeks to up-end current usage by placing Pharmacology and Mode of Action (rather than indication) as the primary driven force.

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Zohar J, Nutt DJ, Kupfer DJ, Moller HJ, Yamawaki S, Spedding M, Stahl SM. 2014. A proposal for an updated neuropsychopharmacological nomenclature. Eur Neuropsychopharmacol. Jul;24(7):1005-14. doi: 10.1016/j.euroneuro.2013.08.004. Epub 2013 Sep 18.

Zohar J., Stahl S., Moller HJ., Blier P., Kupfer D., Yamawaki S., Uchida H., Spedding M., Goodwin GM., Nutt D., A review of the current nomenclature for psychotropic agents and an introduction to the Neuroscience-based Nomenclature, European Neuropsychopharmacology, Volume 25, Issue 12, December 2015, Pages 2318–2325.

LECTURE 2

Neuroimaging and psychotherapy

The neural bases of psychotherapy for anxiety and related disorders

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Brain imaging studies over two decades have delineated the neural circuitry of anxiety and related disorders, particularly regions involved in fear processing and in obsessive-compulsive symptoms. The neural circuitry of fear processing involves the amygdala, anterior cingulate, and insular cortex, while cortico-striatal-thalamic circuitry plays a key role in obsessive-compulsive disorder. More recently, neuroimaging studies have examined how psychotherapy for anxiety and related disorders impacts on these neural circuits. A summary of the findings of functional magnetic resonance imaging studies examining the neural bases of cognitive-behavioral therapy (CBT) in patients with anxiety and related disorders will be provided. It is concluded that, although each of these related disorders is mediated by somewhat different neural circuitry, CBT may act in a similar way to increase prefrontal control of subcortical structures. These findings are consistent with an emphasis in cognitive-affective neuroscience on the potential therapeutic value of enhancing emotional regulation in various psychiatric conditions.

LECTURE 3

Psychoneuroimmunology

Neuroinflammation and mood disorders: cause or co-incidence?

Brian E. Leonard
National University of Ireland, Galway Ireland

Inflammation is an important protective mechanism against invading microorganisms and oncogenes. It is also a component of the stress response. However, whereas inflammation may start as a time and site specific defence mechanism aimed at protecting the body against pathogens, it is also an important mechanism for removing damaged cellular debris by activating the peripheral (macrophages and monocytes) and central (microglia) scavenger cells. Should the inflammatory process be prolonged as a result of a chronic infection, autoimmune reaction or chronic stress for example, then maladaptive changes may occur. These changes are associated with a sustained increase in pro-inflammatory cytokines and chemokines and can contribute to both physical (for example, heart disease, diabetes and cancer) and major psychiatric disorders such as major depression and schizophrenia. Thus chronic low grade inflammation is a characteristic feature of many major psychiatric disorders and now forms the theoretical basis of psychoneuroimmunology. The conceptual importance of psychoneuroimmunology lies in emphasising the holistic link between malfunctioning immune, endocrine and neurotransmitter systems and psychopathology and raises questions regarding the potential importance of a novel class of psychotropic drugs which modulate the immune and endocrine axes. The macrophage hypothesis of depression seeks to explain how the impact of chronic low grade inflammation in the brain and periphery can initiate immune, endocrine and neurotransmitter changes which precipitate the major symptoms of depression. These changes involve an activation of the hypothalamic-pituitary-adrenal (HPA) axis leading to hypercortisolaemia, a reduction in the release of thyroid

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stimulating hormone and sex hormones. Chronic hypercortisolaemis is associated with the desensitisation of the glucocorticoid receptors and of the insulin receptors which contribute to disturbed brain glucose metabolism and type 2 diabetes. In addition, the proinflammatory cytokines not only contribute to increased neuronal apoptosis but also activate the neurotoxic arm of the tryptophan-kynurenine pathway which further enhances the neurodegenerative changes which often occurs in chronic major depression. While effective antidepressant treatment may attenuate some of these changes there is only limited evidence that their efficacy is a consequence of their anti-inflammatory effects.This opens the possibility that drugs specifically targeting neuroinflammation may offer a therapeutic advantage.

LECTURE 4

Major Depressive Disorder

Insights into the treatment and origins of generalized anxiety disorder

David Castle[1,2]
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[2]University of Cape Town, South Africa

A broad range of pharmacological and psychological approaches have been found efficacious in the acute treatment of patients with generalized anxiety disorder (GAD), but many treatment-seeking patients will not respond to current interventions. Others will respond, but then stop pharmacological treatment early because of untoward effects such as sexual dysfunction, drowsiness and weight gain. The findings of small randomized placebo-controlled studies suggest that augmentation of antidepressants with pregabalin or some antipsychotic drugs (olanzapine, quetiapine, risperidone) may be beneficial, but the evidence for quetiapine augmentation is inconsistent, and uncertain for ziprasidone augmentation. Guidance from the British Association for Psychopharmacology summarizes further options when patients with GAD have not responded to, or proved intolerant of, first-line treatments (Baldwin et al., 2014). Pregabalin is efficacious in most patient sub-groups and may be an option when antidepressant treatment has been associated with sexual dysfunction (Baldwin et al., 2015). There is a persistent role for benzodiazepines in patients with chronic, severe, distressing and impairing symptoms which have not responded to a sequence of other treatments (Baldwin et al., 2013). Investigations of challenge of healthy volunteers with inhalation of air 'enriched' with 7.5% carbon dioxide (CO2) suggest this technique provides a robust experimental medicine model of generalized anxiety, mirroring the subjective, autonomic and cognitive features of GAD. Prior administration of duloxetine, memantine, instruction in mindfulness techniques, and use of transcranial direct current stimulation can all mitigate at least some of the effects of CO2 challenge: and suggest this model may be useful in the evaluation of potential innovative pharmacotherapies or psychotherapies at the proof-of-concept stage.

References:

Baldwin DS, Aitchison K, Bateson A, et al. Benzodiazepines: risks and benefits. A reconsideration. Journal of Psychopharmacology 2013; 11: 967-971.

Baldwin DS, Anderson IM, Nutt DJ, et al. Evidence-based pharmacological treatment of anxiety disorders, post-traumatic stress disorder and obsessive-compulsive disorder: a revision of the 2005 guidelines from the British Association for Psychopharmacology. Journal of Psychopharmacology 2014; 28: 403-439.

Baldwin DS, den Boer J, Lyndon G, et al. Efficacy and safety of pregabalin in generalised anxiety disorder: A critical review of the literature. Journal of Psychopharmacology 2015; 29: 1047-1060.

LECTURE 5

Bipolar Mood Disorder

An overview of depression treatment guidelines

Gerhard Grobler[1,2]
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[2]Immediate Past President, South African Society of Psychiatrists (SASOP)

The use of guidelines in the treatment of complex conditions remains controversial. Guidelines aim to distill the best available knowledge into a useful format to guide clinical decision making and to standardize care to optimize quality of care. Clinical decision making however deals with unique individuals with unique conditions. This presentation will be an overview of the current treatment guidelines for major depressive disorder and how clinical decisions could be at variance with those.

LECTURE 6

Insomnia

Insomnia- A night to remember

Kerry-Ann Louw
University of Cape Town, South Africa

Insomnia is a prevalent complaint and for many patients a chronic disorder 1. The Diagnostic and Statistical Manual of Mental Disorders, 5th edition no longer distinguishes between primary and secondary insomnia. The diagnosis is made independent of the cause and regardless of the presence of medical and psychiatric conditions. This highlights the importance of insomnia as an independent disorder that requires clinical attention and acknowledges the complex, often bidirectional, interaction between insomnia and coexisting medical and mental disorders 2. Insomnia is associated with negative long-term health consequences including increased morbidity, respiratory and cardiovascular disease, anxiety, depression, pain and cognitive complaints 3. Insomnia also worsens patient outcomes including poorer level of functioning and quality of life, lower productivity in the workplace and greater health costs 4. Diverse treatments are available for insomnia: over-the-counter preparations, complementary

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and alternative medicines, sleep hygiene education, psychological, behavioural and pharmacological interventions 5. This talk aims to cover the following topics:

1. An approach to the diagnosis of insomnia, including taking an adequate sleep history
2. A brief overview of psychological/behavioural interventions
3. Evidence based pharmacological interventions
4. The efficacy and comparative effectiveness of combined treatments

References:

1. Morin CM, Benca R. Chronic insomnia. Lancet. Elsevier; 2012 Mar 24;379(9821):1129–41.
2. Khurshid KA. A review of changes in DSM-5 sleep-wake disorders. Psychiatric Times. 2015.
3. Kyle SD, Morgan K, Espie CA. Insomnia and health-related quality of life. Sleep Medicine Reviews. Elsevier; 2010 Feb 1;14(1):69–82.
4. Krystal AD, Sorscher AJ. Recognizing and managing insomnia in primary care and specialty settings. J Clin Psychiatry. 2016 Apr;77(4):e471–1.
5. Brasure M, MacDonald R, Fuchs E, Olson CM, Carlyle M, Diem S, et al. Management of Insomnia Disorder. Agency for Healthcare Research and Quality (US); 2015 Dec 1.

LECTURE 7

Post-traumatic Stress Disorder

Posttraumatic stress Disorder: Updates on diagnosis and treatment

Lukoye Atwoli
Moi University, School of Medicine, Kenya

Trauma exposure is common globally and even more so in Africa. For instance in South Africa, around three in every four people have been exposed to a traumatic event in their lifetime. While there are many possible outcomes of trauma exposure, posttraumatic stress disorder (PTSD) is a common outcome that causes significant social and occupational dysfunction among survivors. The diagnostic criteria for PTSD has recently undergone changes related to traumatic event definition as well as the organisation of symptomatology. There have also been significant advances in the psychopharmacological treatments available for PTSD, and research on newer agents continues. This presentation will review changes in the diagnostic criteria from DSM IV TR to the DSM-5, as well as the psychopharmacological treatments available for PTSD, and conclude with a reflection on future directions.

LECTURE 8

Obsessive Compulsive Disorder

Pharmacotherapy of obsessive-compulsive disorder

Dan Stein
Department of Psychiatry and Mental Health, University of Cape Town, South Africa

Obsessive-compulsive and related disorders are now classified as separate chapters in DSM-5 and the forthcoming ICD-11. This reflects in part evidence that they share some psychobiological features, as well as aspects of evaluation and management. This paper reviews evidence for the pharmacotherapy of obsessive-compulsive disorder (OCD), as well as some of the obsessive-compulsive and related disorders. Serotonin reuptake inhibitors (SRIs) remain the first-line approach to the pharmacotherapy of OCD, with some evidence that longer duration and higher doses are needed. The best studied approach to pharmacotherapy augmentation in OCD is addition of low dose dopamine blockers to the SRI, although there is also evidence that cognitive-behavioural psychotherapy is a particularly useful addition to medication. SSRIs also appear efficacious in body dysmorphic disorder and perhaps skin-picking disorder, but there is less consistent evidence for efficacy in hoarding disorder and trichotillomania. A range of other agents have been studied in treatment-refractory OCD, as well as in other obsessive-compulsive and related disorders, and will be considered.

LECTURE 9

Alzheimer's Disease and Geriatric Psychiatry Principles

Depression, dementia and poly-pharmacy of late-life

John Joska
University of Cape Town, South Africa

The proportion of the elderly >60 years will more than double by 2050. Reported severe memory impairment increases from 2.2% at age 60 to around 12% of 80-year olds. The greatest increases in dementia prevalence will be in Asia and Africa. This presentation will address three topics briefly (1) Depression in late life is commonly co-morbid with dementia. What is best-evidence for anti-depressant treatment? (2) Should prescribers combine memantine with cholinesterase inhibition in mild to moderate dementia? (3) The risks of poly-pharmacy following multi-morbid disease- the problem of “toxic scripts.

LECTURE 10

Substance Use Disorders

An approach to the pharmacological management of substance use disorders

Mike West
Department of Psychiatry and Mental Health, University of Cape Town, South Africa

The global burden of disease attributed to the use of alcohol, tobacco and illicit substances is significant, with substance use disorders associated with increased mortality and disability. It is estimated that there are up to 1.5 billion tobacco smokers worldwide, 2 billion alcohol users and 250 million users of illicit substances. Substance use affects the physical and mental health of individual substance users as well as the greater social community, thus representing a significant cost-driver in healthcare spending. Despite this, the treatment gap in provision of mental healthcare is widest in these populations. The co-

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morbid diagnosis of a severe mental illness and a substance use disorders usually predicts poorer outcomes, and continued substance use has a deleterious effect on the individual's recovery. There are now several effective psychopharmacological interventions available for the treatment of alcohol, tobacco and opioid use disorders, which have been shown to enhance various addiction-related outcomes – unfortunately, many of these treatments are not globally available or are prohibitively expensive, especially in developing economies such as South Africa. This presentation will follow an algorithm, and aims to provide the audience with a practical approach to screening, assessment and diagnosis of substance use disorders as according to the Diagnostic and Statistical Manual (DSM) of Mental Disorders (5th edition), highlighting the similarities and differences between this edition and the previous DSM-IV, and paying attention to the various possible confounders or co-morbidities that may complicate the presenting diagnosis. Specific evidence-based approaches to the pharmacological management of alcohol (naltrexone, acamprosate, disulfiram), tobacco (nicotine replacement, antidepressants, varenicline) and opioid use disorders (methadone, buprenorphine, diacetylmorphine) will be discussed, as well as their potential applications in a "harm reduction" based model of treatment. An analysis of the system-level, provider-level and patient-level barriers (and possible solutions) to the implementation of pharmacotherapy in low-to-middle-income-countries (LMIC) will provide the audience with insights into the various challenges faced by clinicians in these settings.

LECTURE 11

ADHD

Solly Rataemane
Sefako Makgatho Health Sciences University, South Africa

Attention deficit/hyperactivity disorder (ADHD) is characterized by symptoms of inattention and/or hyperactivity/impulsivity. The disorder is increasingly understood to be highly prevalent (up to 5% or more of children and 2% of adults) {Polanczyk, 2014} and associated with significant morbidity and functional impairment {Association, 2013}. Furthermore, the neurobiological basis and appropriate management of the disorder are becoming increasingly better understood {Sharma, A., et.al 2014}. Nevertheless, ADHD and its pharmacological management has frequently been the subject of negative media attention {Efron, 2015}.It has been claimed that in some schools, there is over-diagnosis of the disorder and that medication is simply used to control behaviour in healthy children. Concerns have been raised about the potential for abuse of methylphenidate and claims have been made about serious adverse events.

While over-diagnosis in some settings may occur, a far more likely occurrence is under-diagnosis. Given the high prevalence of ADHD, the number of scripts written for methylphenidate in South Africa presumably reflects under-treatment. And given the serious consequences of untreated ADHD such as increase in subsequent antisocial personality traits and substance abuse {Shaw, M, et.al 2012}, such under-treatment is in fact an important concern. Co-morbidities such as conduct disorders, substance abuse, poor educational performance and underlying physical disorders need serious attention.

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5. Shaw, M., et al. (2012). "A systematic review and analysis of long-term outcomes in attention deficit hyperactivity disorder: effects of treatment and non-treatment." BMC Med 10: 99

LECTURE 12

From Bench to Bedside: Current Translational Neuroscience

Brian Dean
Molecular Psychiatry Laboratory, the Florey Institute for Neuroscience and Mental Health, Parkville, Victoria 3052, Australia

The diagnoses of psychiatric disorders is still dependent upon careful clinical observations and the detection of specific symptom clusters1. This contrasts to many other areas of medicine where diagnoses is based on results from biologically based measures which are often made by testing levels of blood components. Whilst some advances have been made in identifying potential biomarkers for psychiatric disorders2, there is still no widely used test that can assist with the diagnoses of psychiatric disorders. The CRC for Mental Health was form in Melbourne to manage a program of research to develop clinically useful tools for use in diagnosing or helping treatment decision making in subjects with disorders of the human CNS. Within psychiatry the CRC has had two major focusses for biomarker discovery. The first was to develop a mechanism to identify a sub-set of people with schizophrenia that are defined by a marked decrease in cortical muscarinic receptors3 when they are alive and, subsequently, to determine if they have specific symptom profiles or preferentially respond to certain drug treatments. The second was to validate the finding that changes in the levels of a panel of cortical genes can be used to separate people with schizophrenia from controls and to determine whether levels of expression of this panel of genes can effectively diagnose schizophrenia

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using RNA from white blood cells. This presentation will review potential advances in the field of biomarker discovery in psychiatric illness and then focus on findings by the CRC for Mental Health.

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1. American Psychiatric Association. Diagnostic and Statistical Manual of Mood Disorders Fifth Edition, vol. 5. American Psychiatric Association: Arlington, 2013.
2. Scarr E, Millan MJ, Bahn S, Bertolino A, Turck CW, Kapur S et al. Biomarkers for Psychiatry: The Journey from Fantasy to Fact, a Report of the 2013 CINP Think Tank. Int J Neuropsychopharmacol 2015; 18(10): pyv042.
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LECTURE 13

Generalised Anxiety Disorder

Insights into the treatment and origins of generalized anxiety disorder

David Baldwin[1,2]

[1]Professor of Psychiatry, Faculty of Medicine, University of Southampton, UK

[2]Honorary Professor of Psychiatry, University of Cape Town, South Africa

A broad range of pharmacological and psychological approaches have been found efficacious in the acute treatment of patients with generalized anxiety disorder (GAD), but many treatment-seeking patients will not respond to current interventions. Others will respond, but then stop pharmacological treatment early because of untoward effects such as sexual dysfunction, drowsiness and weight gain. The findings of small randomized placebo-controlled studies suggest that augmentation of antidepressants with pregabalin or some antipsychotic drugs (olanzapine, quetiapine, risperidone) may be beneficial, but the evidence for quetiapine augmentation is inconsistent, and uncertain for ziprasidone augmentation.

Guidance from the British Association for Psychopharmacology summarizes further options when patients with GAD have not responded to, or proved intolerant of, first-line treatments (Baldwin et al., 2014). Pregabalin is efficacious in most patient sub-groups and may be an option when antidepressant treatment has been associated with sexual dysfunction (Baldwin et al., 2015). There is a persistent role for benzodiazepines in patients with chronic, severe, distressing and impairing symptoms which have not responded to a sequence of other treatments (Baldwin et al., 2013).

Investigations of challenge of healthy volunteers with inhalation of air 'enriched' with 7.5% carbon dioxide (CO2) suggest this technique provides a robust experimental medicine model of generalized anxiety, mirroring the subjective, autonomic and cognitive features of GAD. Prior administration of duloxetine, memantine, instruction in mindfulness techniques, and use of transcranial direct current stimulation can all mitigate at least some of the effects of CO2 challenge: and suggest this model may be useful in the evaluation of potential innovative pharmacotherapies or psychotherapies at the proof-of-concept stage.

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Baldwin DS, den Boer J, Lyndon G, et al. Efficacy and safety of pregabalin in generalised anxiety disorder: A critical review of the literature. Journal of Psychopharmacology 2015; 29: 1047-1060.

LECTURE 14

Schizophrenia

Bonga Chiliza

Stellenbosch University, South Africa

No abstract received

LECTURE 15

Drug-drug interactions

Drug interactions: summary of core knowledge for the psychiatrist

Eric DeCloedt

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Polypharmacy occurs frequently in patients treated for multiple comorbidities. Polypharmacy increases the probability of drug-drug interactions. Up to 20% of hospital psychiatric admissions have been reported to be due to unintended adverse effects attributed to drug-drug interactions. Drug-drug interactions occur commonly when a drug influences the metabolism of another by either increasing elimination with sub-terapeutic concentrations or decreasing elimination leading to toxicity. Pharmacodynamic drug interactions occur when multiple drugs with shared toxicity are combined. A commonly missed psychopharmacotherapy interaction is the potentiation of lithium toxicity when combined with diuretics or non-steriodal anti-inflammatory drugs. Although concommitant pharmacotherapy may not always be avoidable, prescribers should always aim to select drugs with minimal interactions using a reliable reference source. When polypharmacy with potential interactions are unavoidable, always ensure that the therapeutic benefit outweights the potential toxicity risk. Continue to monitor the therapeutic response and signs of toxicity and discontinue culprit drugs as needed with reconsideration of treatment options.

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LECTURE 16

Cross-cultural aspects of psychopharmacology

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Is the biology of people suffering from mental disorders universal? If that were the case it would enable psychiatrists across the world to prescribe psychotropics uniformly with a predictable and uniform response irrespective of individual cultural or ethnic differences. Psychiatrists across the world however have observed differences in individuals and groups when it comes to response to psychotropics. This is because the practice of psychiatry takes place in the background of many multicultural and multiethnic societies. Different factors can contribute to these variations in individual and group responses to psychotropics, including compliance, individual or personality factors, differences in lifestyle, social support and stress. Furthermore, assessment, diagnosis and interventions applied by psychiatrists may be influenced not only by the patient's ethnicity and cultural beliefs but also by similar bias in the treating psychiatrist. All these factors may contribute to differences that exist between individuals when it comes to response to psychopharmacological interventions. Other aspects which can compound these differences are genetic, biological, environmental, and psychosocial factors. Genetic polymorphisms in the cytochrome P-450 (CYP) enzymes involved in metabolizing most psychotropic medications is one example that has yielded some useful insights into explaining some of the differences observed in clinical practice. Variances in patient response to psychotropics and rates of metabolism of psychotropic medication have thus been explained on the basis of such polymorphism and individual or ethnic differences in genetic make-up. The influence and interaction of these factors in clinical practice will be discussed with a special focus on the South African setting.

LECTURE 17

Deep Brain Stimulation

Deep Brain Stimulation in obsessive compulsive disorder: a decade of experience

Damiaan Denys
Department of Psychiatry, Academic Medical Center (AMC), University of Amsterdam, and the Institute for Neuroscience, an institute of the Royal Netherlands Academy of Arts and Sciences, Amsterdam, The Netherlands.

OCD is considered one of the most disabling psychiatric disorders, causing serious impairment in patients' daily functioning and affecting professional, social, and personal lives. Thanks to a wide range of available pharmacologic treatments and cognitive behavioural therapy (CBT), most patients can be treated to a satisfactory level. However, 10% of patients experience inadequate response and remain severely ill. In the last decades, neuromodulating techniques have emerged as promising alternatives for the treatment of OCD. Different from the rather aspecific pharmacologic modulation of drug therapy, neuromodulation techniques enable modulation of distinct neuronal circuits by targeting specific brain structures. OCD may be particularly suitable for these interventions because of its strong link to discrete neuro-anatomic networks. Neuroimaging studies have consistently related OCD to aberrant activity within the orbitofronto-striato-thalamo-cortical (CSTC) network. A major advantage of neuromodulation is its potential of adjustable and reversible brain network manipulation. This lecture reviews studies on DBS for OCD.

LECTURE 18

Prescribing in pregnancy

Prescribing psychiatric medication in pregnancy – a review

Bavanisha Vythilingum
University of Cape Town, South Africa

Psychotropic medication has become some of the most commonly prescribed medication. With as many as 10-15% of women worldwide being diagnosed with depression during pregnancy, use of antidepressants during this vulnerable period has increased, which raises concerns for both healthcare providers and patients in terms of safety to the developing fetus. Furthermore, women with bipolar mood disorders and psychotic disorders are at high risk of relapse during pregnancy and risk of medication to the fetus needs to be balanced against the often devastating consequences of a relapse. Studies of exposure to antidepressants in pregnancy have produced conflicting results, with some studies showing an associated with miscarriage, premature delivery, cardiac defects-and, more recently, autism spectrum disorders. Other studies have not replicated these findings. Furthermore, even in the studies finding the greatest risk, the increase in absolute risk is small. Antipsychotics have not been associate with any clear teratogenic risk but concerns have been rasied, especially with the typical agents around neonatal exytapyramidal side effects. Mood stabilisers in contrast have all been associated with significant teratogenic effects. However, the most recent data suggests a lower risk for teratogenicity due to lithium than was previously thought, and encouragingly, little to no teratogenicity with lamotrigine. Meanwhile, antenatal mental illness itself is associated with adverse perinatal outcomes, and so far there is no clear data on whether the observed adverse fetal effects are related to the mother's medication use or her underlying maternal illness. It therefore is important that in every pregnant woman being treated for mental illness, the risks of treatment is carefully weighed against the risk of untreated depression for both herself and her child. These decisions should be made on cases by case

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basis, taking into account both patient's concerns and the unique circumstances of each particular patient and her unborn child.

LECTURE 19

Ethical issues to consider in psychiatric genomic research in Africa

Jantina de Vries
University of Cape Town, South Africa

Genomics research raises a host of ethical issues. Specific issues of concern in the African research context relate amongst others to comprehension in informed consent; the ethical acceptability of broad consent models; accommodating participant vulnerability caused by generally high levels of poverty, low health literacy and poor access to healthcare; and how to ensure fairness in international collaboration. Psychiatric research too has historically been seen as a discipline presenting important ethical and political challenges. When contemplated in the context of genomics it is likely that such research will present ethical challenges that need to be considered in research practice. One key concern relates to the fact that individuals with severe mental illness tend to be more readily stigmatized and discriminated against. A critical question then is how genetic attribution may contribute to or alleviate stigma associated with mental illness. Where severe mental illness means that decisional capacity is affected, individuals may struggle to fully engage in the consent process, raising questions not just about appropriate ways of seeking consent but also about possibilities to discuss complex concepts such as data and sample sharing, secondary use, and potential feedback of individual genetic research findings. Such challenges apparently place greater onus on alternative means of soliciting participant and community feedback epitomised in the field of community engagement. But there are questions about exactly how one can effectively engage communities of people with severe mental illness in African genomics research. In this talk, I will explore some of these issues and describe how they may impact on psychiatric genomic research practices.

Young Scientists Competition: Abstract presentations - Oral

Serotonin challenge normalizes deficits in executive functioning in patients with obsessive-compulsive disorder

Lian Taljaard,[1] Martin Kid[1], Dan J. Stein[2], Christine Lochner[1]
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Background: Obsessive-compulsive disorder (OCD) implicates dysfunction of frontostriatal circuitry and of the serotonin system. Neurocognitive data on impairments in executive functioning are inconsistent however. Although selective serotonin re-uptake inhibitors (SSRI's) are recommended as first-line pharmacological treatment for OCD, and have been shown to improve cognition in children and adolescents with OCD, the potential of serotonin challenge for altering specific executive functions in adult patients is not clear.
Methods: A randomized double-blind crossover study design was utilised to assess the effects of a single dose escitalopram (20mg) and placebo on specific executive functions (working memory and response control) in 24 OCD patients (60.7% female) and 28 matched healthy controls (54.2% female). Performance on 2 tasks of the CANTAB battery (i.e. the One-touch Stockings of Cambridge (OTS) and Stop-Signal Task (SST), respectively), were assessed 3-4 hours after oral administration of the pharmacological challenge / placebo, using a mixed model analysis of covariance (ANCOVA).
Results: On placebo, OCD patients performed significantly better than controls on both tasks (add p-values here). There were significant group/challenge interaction effects on both tasks; OCD patients performed significantly better after escitalopram challenge compared to placebo on both the OTS ($F(1, 47)=6.0040$, $p=.018$), and the SST ($F(1, 46)=5.0321$, $p=.029$). There was an order effect in the OCD group, with patients performing significantly better when the order was placebo-first on the OTS ($F(1, 47)=11.768$, $p=.001$), and a strong tendency for the same effect was observed on the SST ($F(1, 46)=3.6952$, $p=.06$).
Conclusion: Escitalopram challenge improved performance on tasks of working memory and response inhibition significantly in a group of OCD patients but not in controls. This provides additional support for the role SSRI's may play in the normalization of deficits of the frontostriatal circuitry typical of OCD.

Evidence for cognitive flexibility and symptom heterogeneity in the deer mouse model of obsessive-compulsive disorder

De Wet Wolmarans[1], Brian H Harvey[1], Dan J Stein[1]
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Introduction: Obsessive-compulsive disorder (OCD) presents with debilitating intrusive thoughts and seemingly purposeless motor patterns that interferes with the normal occupational and social routines of patients. The condition is phenotypically heterogenic and is typically diagnosed within one of the following symptom dimensions: 1) harm prevention and assurance seeking, 2) symmetry obsessions and ordering, 3) contamination concerns and washing, 4) repugnant obsessions associated with themes of violence, sex or religion, and 5) hoarding obsessions and collecting compulsions. Although many pre-clinical models of OCD have been described, research is mostly limited to one-dimensional approaches exemplifying singular characteristics of the condition. The deer mouse has been progressively characterized and validated as an animal model of OC-like behaviour.

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Pattern running and vertical jumping resembles the compulsive-like repetition of motor patterns observed in OCD as 1) it is apparently purposeless and time consuming, 2) it occurs with varying intensity throughout a normal nocturnal cycle, 3) it demonstrates sensitivity to chronic high-dose escitalopram treatment and 4) is associated with altered striatal serotonergic functioning. The current presentation will investigate the presence of heterogenic OCD-like behaviours in these animals, characterized by altered cognitive processing and sensitivity to changing social environments.

Methods and Results: 190 deer mice of both sexes were investigated with respect to group social interaction, marble burying activity and nest building. We found that deer mice interact differently within stereotypical cohorts, compared to their between-cohort interactions. Furthermore, high marble burying and large nest building (LNB) was identified that resemble unique orthogonal OC phenotypes. Moreover, both altered social interactivity and LNB were found to be sensitive to chronic high dose escitalopram treatment (graphical representations and statistics provided in the presentation).

Conclusion: These findings demonstrate cognitive flexibility and symptom heterogeneity in the deer mouse model of OCD, suggesting that understanding the thought-processes underlying rodent behaviour may indeed be possible through a suitably developed animal model. The deer mouse may therefore represent a holistic and robust animal model that will provide a pre-clinical framework to study the complex bio-behavioural and neuropsychological constructs of OCD.

Black seed oil ameliorated scopolamine-induced memory dysfunction, improves psychomotor behaviors and cortico hippocampal cyto-architectonic in male Wistar rats

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Objectives: This study was conducted to evaluate the potential efficacy of black seed oil (BSO) in scopolamine induced rat model of cognitive impairment, motor activity, anxiety-like behaviour, and cortical architectonic in Wistar rats.

Materials and Methods: Twenty eight Wistar rats weighing between 170 and 190 g were used in this study, randomly divided into four groups of seven animals each. Saline (1 ml/kg), scopolamine (1 mg/kg) and BSO were administered to the rats orally for 14 days. Morris water maze test (MWM) and Y maze test were used to assess memory indices while psychomotor activities were assessed in the elevated plus maze (EPM) and open field test (OFT). Haematoxylin and Eosin (H&E) and Cresyl Fast Violet (CFV) stained sections were used for cortical cyto-architectonic examinations in the rats.

Results: Scopolamine delayed latency in the MWM and reduced percentage alternation in the Y maze. Post-treatment with BSO mitigated scopolamine-induced amnesia, by significantly reducing latency period and increasing percentage alternation ($P \leq 0.05$). BSO also significantly increased frequent line crossing, rearing frequency and total alternation, which are measures of motor activities. It increased open arm explorations, head dip frequency and decreased freezing period and closed arm entry ($P \leq 0.05$), which are measures of anxiety-like behaviours and did not affect the cortico-hippocampal cyto-architectonic when compared with the control.

Conclusions: These results thus suggest the potential efficacy of BSO in reducing cognitive dysfunction, anxiety-related symptomology and probably psychomotor impairments.

Repetitive stress is associated with global DNA hypomethylation in the hippocampus

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Introduction: Exposure to repetitive stress has a negative influence on cognitive-affective functioning, with growing evidence that these effects may be mediated by a dysregulated hypothalamic-pituitary-adrenal (HPA) axis, abnormal neurotrophic factor levels and its subsequent impact on hippocampal function. However, there are few data about the effect of repetitive stressors on epigenetic changes in hippocampus. In the present study we examine how repetitive restrain stress (RRS) affects cognitive-affective functioning, HPA axis regulation, brain-derived neurotrophic factor (BDNF) levels, and global hippocampal DNA methylation.

Methods: RRS was induced in rats by restraining the animals for 6 hours per day for 28 days. The novel object recognition test (NORT) was used to assess cognitive functioning and the open field test (OFT) was performed to assess anxiety-like behaviour. Hippocampal BDNF levels, glucocorticoid (GR) and mineralocorticoid (MR) receptor mRNA were assessed using real-time PCR, while ELISAs were used to determine plasma corticosterone levels and the global methylation status of the hippocampus.

Results: Bonferroni post hoc analysis showed a significant difference in the exploration time between the control and the stressed animals during the 3 trials of the novel object recognition test ($p<0.01$), with stressed animals spending significantly less time with the novel object than controls. In the OFT animals that were stressed spent significantly less time in the center of the open field in comparison to control animals ($p<0.01$). Mann-Whitney U-testing indicated that exposure to repetitive stress led to a significant increase in plasma corticosterone concentration ($p<0.01$) and a significant reduction in hippocampal GR mRNA and MR mRNA levels ($p<0.05$). Real-time PCR further showed that hippocampal mRNA

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expression of BDNF was also significantly lower in stressed animals compared to controls ($p<0.05$). The data also showed that there was a significant decrease in global DNA methylation in the hippocampus of the stressed group of animals when compared to the control group ($p<0.05$) and a significantly positive correlation was found between the decreased exploratory behaviour exhibited during NORT and the status of hippocampal DNA methylation ($r(9) = 0.509$, $p = 0.0205$), suggesting that the effect of stress on NORT may be linked to alterations in DNA methylation.
Conclusion: The data here are consistent with previous work emphasizing the role of the HPA axis and neurotrophic factors in mediating cognitive-affective changes after exposure to repetitive stressors. Our findings further extend the literature by indicating that epigenetic alterations in the hippocampal genome may also play an important role in the development of certain behavioural abnormalities.

The impact of prenatal MA exposure on neurometabolites and neurocognitive development in children

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Background: Methamphetamine (MA) use among pregnant women is increasing and holds significant risks for the developing child. 1H-MRS studies on prenatal MA exposure of children younger than 5 and older than 9 years old, suggest aberrant neuronal development and abnormal metabolism. This study aimed to investigate neurometabolite changes and association with general cognitive ability over time in prenatally MA exposed children, aged 6 to 8 years old, during the first two years of formal schooling.
Methods: Prenatally MA exposed children and healthy-matched control children were recruited, underwent single-voxel 1H-MRS (TR 2000ms, TE 30ms) of the anterior cingulate cortex (ACC) and a neurocognitive assessment battery at two time points: i) at the age of six years old (MA exposed, n=14; controls, n=14) and ii) at the age of eight years old (MA exposed, n=13; controls, n=11). The change in neurometabolites and neurocognitive assessment results over time were also investigated (MA exposed, n=9; controls, n=7). Absolute metabolite concentrations reported are n-acetyl-aspartate (NAA), and n-acetyl-aspartate + n-acetyl-aspartyl-glutamate (NAA+NAAG), glycerophosphocholine (GPC), glycerophosphocholine + phosphocholine (GPC+PCh), myo-inositol (Ins), creatine (Cr), phosphocreatine (PCr), creatine + phosphocreatine (Cr+PCr), glutamate (Glu), glutamate + glutamine (Glu+Gln), .
Results: The MA exposed group performed significantly poorer on neurocognitive tasks at both time points, when compared to the control group. Over time, the MA exposed group scored higher than the control group in tasks measuring short-term and verbal memory. No metabolite differences were observed at either time point, however, over time increased NAA and decreased GPC and GPC+PCh were observed in the prenatally exposed group, when compared to the control group.
Discussion: Increased NAA, associated with increased neuronal integrity and viability, and decreased GPC and GPC+PCh, important in the synthesis and degradation of cellular membranes, together with increased scores on neurocognitive tests, indicate potential recovery in short-term and verbal memory of prenatally MA exposed children with time.
Conclusion: Neuronal maturation of the brain, indicative of positive reorganisation of the neural network within the ACC of MA exposed children, was observed. This is the first 1H-MRS study to report these positive changes and provides direction for future research.

Exploring stress re-stress as a mechanism to exacerbate depressive-like symptoms and induce antidepressant treatment resistance in Flinders Sensitive Line (FSL) rats

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Background: Treatment resistance hampers the effective management of depression. It is characterized by more severe depressive symptoms and also does not respond to a standard treatment with traditional antidepressants. The general lack of validated animal models of treatment resistant depression (TRD) limits preclinical research of the disorder and contributes to the current shortcomings in understanding this debilitating condition. The gene-X-environment hypothesis of depression is a relevant and popular concept, while the increased prevalence of TRD in posttraumatic stress disorder (PTSD) patients provides an interesting caveat for modelling the disorder. Thus, exposing animals with a depressive phenotype to severe stress may produce animals with enhanced depressive-like behaviours, accompanied by resistance to antidepressant treatment. In developing a preclinical model of treatment resistant depression (TRD), we combined Flinders sensitive line (FSL) rats, a genetic animal model of depression, with a stress re-stress PTSD-inducing paradigm and tested its subsequent behavioural response to treatment with a traditional antidepressant, imipramine.
Methods: Male FSL rats (n = 12 animals per group for behavioural assessments and n = 8 for neurochemical analysis; age 40 ± 1 days) were exposed to a time dependent sensitisation (TDS) (FSL+TDS) stress protocol and compared to stress-naive FSL controls (FSL-TDS). Seven days after TDS (21 days after start of TDS-protocol), depressive-like (immobility) and coping (swimming and climbing) behaviours were measured in the forced swim

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test (FST) and hippocampal and cortical noradrenaline and 5-hydroxyindoleacetic acid levels (5HIAA) levels were analysed. Response to sub-chronic imipramine treatment (IMI; 10mg.kg-1 s.c. x 7 days) was subsequently studied.

Results: FSL rats demonstrated bio-behavioural characteristics of depression. TDS-exposure in FSL rats (FSL+TDS) correlated negatively with weight gain, reduced swimming behaviour ($p < 0.01$) and increased immobility ($p < 0.001$) vs. FSL-TDS. IMI significantly reversed depressive-like (immobility) behaviour ($p<0.0001$) and enhanced active coping behaviour (swimming and climbing; $p < 0.005$ and $p < 0.0001$, respectively) in FSL-TDS rats. The latter was significantly attenuated in FSL+TDS ($p < 0.0001$). IMI reversed reduced 5HIAA ($p < 0.005$) levels in FSL-TDS while exposure to TDS negated (n/s) this effect. TDS sustained lowered NA levels with IMI significantly reversing this in the hippocampus.

Conclusion: Combining FSL rats with a PTSD paradigm produces exaggerated depressive-like and attenuated coping behaviour in the FST, coupled with alterations in NA and 5HIAA levels. Furthermore, the antidepressant effects of imipramine are attenuated in FSL animals after exposure to TDS. These data provide preliminary support for combination of a PTSD paradigm with an animal model of depression to produce an animal model of TRD.

An investigation into the antipsychotic and pro-cognitive properties of α2C-adrenoceptor antagonism in social isolation reared rats

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Introduction: Although typical antipsychotics, like haloperidol (HAL), are effective in managing the positive symptoms of schizophrenia, negative and cognitive deficits are often refractory. Clozapine (CLZ), however, is effective in refractory schizophrenia and improves associated cognitive deficits, an action that has, amongst others, been linked to its action at the α2C-adrenoceptor (AR). Early studies have suggested that selective α2C-AR-antagonism has anti-psychotic-like and pro-cognitive properties. However, these actions have not been demonstrated in a neurodevelopmental animal model of schizophrenia.

Methods: We investigated the ability of the selective α2C-AR antagonist, ORM-10921, to modulate deficits in cognition and sensorimotor-gating in a neurodevelopmental model of schizophrenia, the social isolation reared (SIR) rat, comparing its effects to that of CLZ and HAL. Following weaning on post-natal day (PND) 21, rats were either reared socially (SOC) (4 per cage) or in isolation (1 per cage). Novel object recognition (NOR) on PND 76 and prepulse inhibition (PPI) of startle on PND 77, as well as striatal levels of brain-derived neurotrophic factor (BDNF) on PND 78, were assessed. Moreover, the ability of ORM-10921 to augment the action of HAL was investigated. SIR rats received either ORM-10921 (0.01mg/kg s.c.), CLZ (5mg/kg s.c.), HAL (0.2 mg/kg s.c.), HAL+ORM-10921 (0.2 mg/kg + 0.01mg/kg s.c.) or vehicle once daily for 14 days. Statistical analysis was undertaken, as required: Two-way ANOVA, Tukey; Kruskal-Wallis, Dunn, rmANOVA, student's t-tests.

Results: SIR induced a deficit in discrimination index in the NOR compared to SOC rats ($p=0.002$) as well as significantly attenuated PPI ($p<0.0001$) and reduced striatal BDNF levels ($p=0.002$) vs. SOC animals. CLOZ ($p=0.02$) and ORM ($p=0.0004$) significantly improved SIR-induced recognition deficits in the NOR, as did HAL+ORM ($p=0.02$) but not HAL ($p=0.14$) alone. CLZ ($p=0.04$), ORM ($p=0.0003$) and ORM+HAL ($p=0.01$), but not HAL, increased %PPI in SIR rats. ORM ($p=0.002$) and HAL+ORM ($p=0.04$), not CLOZ ($p=0.12$), increased %PPI vs. HAL in SIR animals. HAL+ORM increased striatal BDNF levels in SIR rats vs. SIR controls ($p=0.03$) and vs. SIR + ORM ($p=0.03$). CLOZ tended to increase striatal BDNF levels in SIR animals ($p=0.06$).

Conclusions: In conclusion, selective α2C-AR-antagonism improves deficits in cognition and sensorimotor-gating in a neurodevelopmental animal model of schizophrenia, and bolsters the effects of a typical antipsychotic agent thereon, suggesting an important therapeutic role for α2C-AR antagonism in schizophrenia and warranting further study.

Investigation of the interaction between neurons and T cells in central nervous system tuberculosis

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Background: Tuberculosis (TB) remains one of the most life threatening communicable diseases in the world, claiming millions of lives annually. TB is caused by Mycobacterium tuberculosis (Mtb) and may affect any organ in the body including the central nervous system. CNS-TB is a disease due to secondary infection of the meninges as a result of the haematogenous spread of TB into the CNS. The tubercle bacilli dissemination to the CNS affects mostly children and immune suppressed adults and most deaths occur as a result of missed diagnosis and delayed treatment. Our research group previously reported that primary cells of the central nervous system, neurons are infected by Mtb during invitro and invivo infection in rodents. Neurons express certain surface proteins that suggest both antigen dependent and independent interaction with CNS infiltrated T cells occur during inflammation. The aim is to elucidate mechanisms associated with neuron- pathogen interaction and further define the influence of neurons on specific immunity under conditions of neuron T cell interaction.

Methods: Confluent primary neuron cultures from hippocampi of C57BL/6 embryos (E17) were infected with Mtb strain H37RV and BCG at 30:1 MOI for 24 hours. They

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were co-cultured with T cells from naive C57BL/6 mice sorted by CD3. Co-culture was established at a ratio of 1:1. The cells were collected after 48 hours of co-culture and stained with fluorescent labelled monoclonal antibodies for flow cytometry analysis.

Results: Our preliminary results shows that infection induces release of pro-inflammatory cytokines such as IL-1β and TNF. There is also activation of CD4+ and CD8+ T cells in infected co-cultures with a strong skew towards the Th1 phenotype and to a lesser extent Th2.

Conclusion: Neurons release inflammatory molecules in response to tissue damage and infection, and these molecules may activate intracellular signalling cascades that eventually lead to immune cell activation and proliferation. Elucidating these inflammatory bio-markers will results in knowledge for the development of robust immunochemical diagnostics with sufficient sensitivity and specificity for CNS-TB and the identification of novel immunomodulatory targets that could potentially be exploited for new therapeutic approaches.

Abstract presentations - Poster

Characterizing drug intake in group-housed mice

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The majority of studies using animal models to investigate the neuropathological mechanisms underlying addiction are designed in such a way that experiments are performed on individual subjects isolated from their cage mates. This poses a serious shortcoming in these models as humans, in general, practice their addictive behaviours in a social context. In our study we have utilized the Intellicage system in order to improve on existing methodology. This system allows mice to be group housed, provides the animals with free access to drugs, and their behaviours were automatically recorded. C57BL/6 female mice (N=32) were placed in two cages for 5 weeks during which they had access to drinking bottles in opposite corners containing either alcohol (12% ethanol) or cocaine (300mg/L). After the 5 week period, the animals were subjected to 7 days of drug withdrawal after which their drug seeking and intake were re-assessed. The following parameters were recorded to provide insights into their behaviour: corner visits, nose pokes (mice have to poke a door with their nose for it to open to gain access to a drinking bottle), and bottle licks. Our results showed a higher motivation and consumption of cocaine during the 1st and 4th week of exposure as indicated by increased visits with nosepokes (NP) to corners housing the cocaine-containing drinking bottles, as well as increased number of licks from these bottles. There were no significant differences in ethanol and cocaine consumption during weeks 2 and 3. Interestingly ethanol consumption was higher than cocaine consumption in the 5th week suggesting a possible periodic switch of taste preference between the two drugs during this time. After drug withdrawal, mice displayed a stronger persistence for cocaine seeking (more corner visits, NP and licks) compared to their pre-withdrawal behaviour. Collectively, the data suggest that alternation of drug seeking and consumption may occur when subjects have free access to drugs. The observations further indicate that drug withdrawal may enhance drug seeking behaviour and that during this period neurochemical changes may occur that underpin the development of addictive behaviour.

Anxiolytic (Benzodiazepine-Like) Properties of Mimosa pudica in Mice

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Mimosa pudica Linn. is a plant widely used in traditional African medicine to treat anxiety. The aim of the present study was to assess the anxiolytic and myorelaxant properties of M. pudica. Two months old mice, Mus musculus Swiss were acutely treated by different doses of M. pudica (3, 10 and 30 mg/kg) and anxiety related responses evaluated by analyzing stress-induced hyperthermia (SIH), elevated plus maze (EPM), open field and hole board parameters. The horizontal wire and rota-rod tests were also used to highlight possible myorelaxant properties of M. pudica. The decrease of SIH was observed with M. pudica (30 mg/kg) treatment. In the EPM, significant increase of open arms entries and percentage of time spent in the open arms with M. pudica (10 mg/kg) was observed. Neither diazepam (3 mg/kg) nor M. pudica (3 and 10 mg/kg) produced changes of motor activity. However the change of motor activity was observed with M. pudica (30 mg/kg). In the hole-board test, M. pudica (3 and 10 mg/kg) significantly increased the number and duration of the head-dips respectively. The anxiolytic properties of M. pudica as assessed using the EPM test were abolished by flumazenil (3 mg/kg), by bicuculline (5 mg/kg), and FG 7142 (10 mg/kg). In the Horizontal wire test, both M. pudica (3 and 10 mg/kg) and distilled water allowed animals to grasp within 30 s. M. pudica (3 and 10 mg/kg) did not impair the duration of the time spent on the rota-rod. However at the dose of 30 mg/kg, up to 60 min, the M. pudica significantly reduced the time that animals remained on the rota-rod. This study indicates that M. pudica contains an effective psychotropic agent that acts via the benzodiazepine site of the GABAA receptor complex as an anxiolytic at low doses and as a muscle relaxant at higher doses.

Switching from First – to Second Generation Antipsychotics: Findings in an Eastern Cape Psychiatric Hospital

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Background: Second generation antipsychotics (SGAs) are commonly prescribed despite the fact that large naturalistic studies have failed to show superior efficacy and tolerability when compared to first generation antipsychotics (FGAs). In addition to this, the availability of SGAs in South Africa is limited due to higher acquisition costs. Therefore judicious use of FGAs, which are affordable and more widely available, should be considered.
Objectives: This study aims to determine: (1) how frequently patients are switched from an FGA to an SGA in an acute psychiatric hospital in the Eastern Cape, (2) reasons for switching and (3) compare the profiles of the Switch group vs the Non-switch group.
Method: The study is a cross-sectional survey conducted as a retrospective chart review at a psychiatric hospital in the Eastern Cape over a study period of 2 months. The demographics, diagnostic data, antipsychotic drug used and whether a switch from an FGA to an SGA took place was recorded using a data collection document. The sample included 169 study participants.
Results: Of the 169 participants, 125 (74%) were initiated on an FGA and 44 (26%) on an SGA on admission. Of the 125 patients who were initiated on an FGA, 43 (34%) were switched to an SGA during the course of the admission. Therefore 87 (51%) participants were discharged on an SGA. The main reasons for switch was the emergence of extrapyramidal side effects (EPSE; 63%) followed by lack of efficacy (19%). The only statistically significant difference between the Switch and Non-switch groups was that the Switch group was on average younger than the non-switch group.
Conclusions: SGAs, with the exception of clozapine, have not been proven to be superior to FGAs. Although FGAs are more prone to cause EPSE, SGAs carry significant risks of their own. FGAs are also more freely available and cost effective in South-Africa. Despite these facts the prescribing of- and switching to SGAs remain prevalent in our setting with a switch rate of 34% and more than half of our patients being discharged on SGAs.

Prescribing practices and treatment response in obsessive-compulsive disorder: Results from a South African cohort

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Background: Most treatment guidelines recommend selective serotonin reuptake inhibitors (SSRIs) as first line pharmacotherapy for obsessive-compulsive disorder (OCD). It is important to ascertain whether local prescribing practices are in accordance with SA treatment guidelines for OCD, as well as patients' response to pharmacological treatment. Local data on existing prescribing practices in OCD can inform more specifically targeted education and training in the management of OCD.
Methods: Data on pharmacotherapy and response were collected. Adult patients with a primary diagnosis of OCD, at different stages of treatment, were interviewed. We aimed to determine which medications were used, duration of treatment, dosages, and correlates of treatment response. Descriptive statistics was used to quantify pharmacotherapy patterns for OCD in SA.
Results: 490 adult patients (53% female), with a mean age of 34.93 years (SD: 12.09) were included. The mean YBOCS score was 20.47 (SD 7.24), indicating moderate to severe illness severity overall. Most patients were taking a psychotropic drug (n=377 [76.9%]), with SSRIs the most common (299 out of 377 [79.3%]). Most were on an SSRI without neuroleptic augmentation (258 out of 299 [86.3%]), while a minority (41 of the 299 patients [13.7%] on SSRIs) augmented their treatment with a neuroleptic drug. Dosages (e.g. 10 – 80 mg fluoxetine) and duration of pharmacotherapy varied substantially, with a mean duration of 105 weeks. 57.4% of patients irrespective of their medication regimen reported good treatment response, whereas 60% of those on clomipramine/SSRIs and 66.7% of those on SSRIs with neuroleptic augmentation reported good treatment response. Comorbid major depressive disorder and increased OCD severity was significantly associated with poorer treatment response ($p<0.001$ for both). Additionally, increased treatment duration was also significantly associated with an improved treatment response ($p<0.001$).
Discussion: Findings suggest that most OCD patients in SA are taking at least one SSRI. Although the types of psychotropics taken were consistent with international and local treatment guidelines, dosages used and duration of treatment were not optimal. Treatment duration, comorbid major depressive disorder and increased OCD severity significantly affects pharmacological treatment response. This calls for more work locally to improve life for patients and families facing OCD.

Catatonia: Findings at a Psychiatric Hospital in the Eastern Cape

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Background: Catatonia is a psychomotor dysregulation syndrome seen in several illnesses. Uncertainties exist regarding its prevalence and causes. Studies from different countries provide differing estimates of occurrence, and it is unclear whether this is due to differing rates or under-diagnosis, particularly in developing countries. While data from developed countries show a strong association with mood disorders,

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data from India shows catatonia to be strongly associated with schizophrenia. South African data regarding catatonia is limited.

Objectives: Electroconvulsive therapy (ECT) is used as first-line management for catatonia at this psychiatric hospital. The study objective is to document the number of participants who received ECT for catatonia and identify the underlying diagnoses.

Method: A retrospective descriptive chart review of participants who received ECT for catatonia from 1 January 2012 to 31 December 2014 was conducted. Using the hospital ECT database, participants were identified. Demographics, psychiatric and medical diagnoses, signs indicative of catatonia, and other relevant data were abstracted from these files.

Results: Forty-two participants were identified in total.The median age was determined to be 23.5 years with an Inter-Quartile Range of 21.0 to 27.0. The majority were male (n=31;73.81%). More than half of the sample comprised of black participants (n=23;54.76%). Schizophrenia was the most common diagnosis (n=19;45.24%) followed by psychosis secondary to a general medical condition (n=8;19.05%). Other psychotic disorders included schizoaffective disorder (n=3;7.14%), substance induced psychosis (n=3;7.14%) and psychosis not otherwise specified (n=1;2.38%). Of the 8 participants with psychosis secondary to a general medical condition, HIV was most common (n=6;14.29%). Mood disorders diagnosed included bipolar 1 disorder (n=6;14.29%) and depression (n=1;2.38%). Clinical signs of catatonia included: mutism or negativism (n=38;90.47%), immobility, catalepsy or stupor (n=36;85.71%), peculiar movements (n=20;47.61%), echophenomena (n=15;38.10%) and excessive motor activity (n=4;9.52%). Substance use preceding admission was noted in 20 participants (47.62%). Cannabis use was most common (n=18;42.86%) followed by methamphetamine (n=9;21.43%).

Conclusion: The study supports the idea that catatonia may have different causes in different populations. Further investigation of local prevalence rates and causes is needed.

Prevalence and correlates of non-prescribed stimulant and related drug use in a sample of South African undergraduate medical students

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Background: The non-medical use of prescription psychostimulants or cognitive-enhancing substances in healthy college students is a growing concern. This use appears to be particularly high in medical students. To our knowledge, no literature is however available on the non-medical use of stimulants among South African medical students.

Objectives: To determine the prevalence and correlates of non-medical stimulant use as well as subjective opinion on peer numbers using stimulants and university attitude towards stimulant use among a sample of South African undergraduate medical students.

Methods: A descriptive observational study was conducted by means of a self-report questionnaire. Second and fourth year medical students (n=252) completed the questionnaire.

Results: Of the sample, 44 (18%) reported a lifetime use of stimulants for non-medical purposes and 33 (85%) of this group reported use within the past year. A total of 6 (2%) students reported a diagnosis of ADHD. In the group without a diagnosis of ADHD, there was an association between non- non- medical stimulant use use was associated with and year of study (p=0.03), with the majority of users of stimulants being in their second year of study. Another positive correlation was between non-medical stimulant use and other illicit substance use (p=0.01). Most of the students in this group (31, 32%) reported using stimulants to improve concentration.

Conclusion: Non-medical use of stimulants to improve concentration and academic performance is prevalent under the South African medical students sampled in this study. Further research at other institutions and in non-medical students would be helpful to assess the scope of this phenomenon.

Effects of escitalopram challenge on white matter integrity in obsessive-compulsive disorder and healthy controls

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Background: Involvement of the serotonergic system in OCD is well-known, with OCD responding to selective serotonin reuptake inhibitors (SSRIs). Chronic use of SSRIs changes brain connectivity in OCD, and a single dose of an SSRI dramatically alters functional connectivity throughout the brain in healthy subjects. The question is raised whether acute administration of an SSRI can also significantly alter white matter integrity in the brain of patients with OCD.

Methods: OCD patients (n=20) and matched healthy controls (n=24) received a single dose of escitalopram 20mg on one day, and a single dose of placebo on another day, in randomized order, under double-blind conditions. Diffusion tensor imaging (DTI) was used to compare white matter integrity of the whole brain between the groups. The impact of the SSRI challenge on white matter in these two study groups were subsequently investigated, controlling for age.

Results: There were no significant interaction effects (diagnostic group x pharmacological challenge) or effects in the OCD group separately. In controls, the escitalopram challenge had a significant impact on white matter diffusivity of the left post thalamic radiation (PTR-L) (F=7.84; p=0.01), the superior corona radiata bilaterally (SCR: F=7.99; p=0.01) and the sagittal stratum bilaterally

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(SS: F=6.64; p=0.02). In these tracts, FA was significantly higher and RD significantly lower after the pharmacological challenge compared to placebo.
Discussion: Acute administration of an SSRI did not significantly alter white matter integrity in the brain of OCD patients. It did however improve white matter integrity in tracts that connect regions that may be affected in OCD, in controls. DTI-derived parameters are differently affected in OCD and healthy controls, respectively, in structures within the fronto-striato-thalamo-cortical loop after chronic SSRI treatment. Alteration of white matter integrity may occur in OCD with longer treatment duration or at a different dosage with plasticity potentially playing a role.

Pupillometry as a novel emotional processing measure

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Background: Optimal parental care relies on the ability to respond appropriately to a child's affective state. The current study examined pupil diameter as a potential physiological index of mothers' affective response to infant facial expressions.
Methodology: A sub-study of mothers participating in an ongoing longitudinal study examining the mental health of in mother-infant dyads in the Cape Town metropolitan area, South Africa were included. 123 participants included in the current analyses were characterized as having no mental health disorder as assessed by a psychiatrist through clinical assessment and the Mini International Neuropsychiatric interview (MINI). An eye-tracking assessment was conducted at the infant age of 6 weeks. Pupillary time-series were measured in response to an array of photographic infant faces falling into four emotive categories based on valence (positive vs. negative) and arousal (mild vs. strong). Pupillary responses were acquired during explicit affect labelling and passive viewing conditions.
Results: An ample pupil constriction, that is, a decrease in pupil diameter during 300-1200 ms after stimulus onset was found in response to all face stimuli. Contrary to the hypothesis of increased pupil size in response to stimulus arousals, strong stimulus arousal was related to a decreased pupil size (i.e, increased constriction) within this early time window (strong <mild; conditions [$\Delta\text{Ø}$ > 0.02 mm, $t(84) = 3.20$, $p < .01$]. Whilst the hypothesized emotion-related increase in pupil diameter during constriction was not found for stimulus arousal, such an effect was found for stimulus valence (negative > positive; $\Delta\text{Ø}$ > 0.07 mm, $t(84) = 9.44$, $p < .001$]. That is decreased pupil constriction (i.e increased pupil diameter), was found for faces with negative vs positive emotional valence.
Conclusion: The results showed that pupil dilation was highly sensitive to the valence of facial expressions, being larger for negative vs. positive facial expressions especially in the passive condition. The results show the feasibility of using pupil diameter as a marker of mother's affective responses to ecologically valid infant stimuli.

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