Abstracts submitted to Anxiety Disorder Symposium March, 2008

SPEAKERS

PSYCHIATRIC E-LEARNING

Allgulander, C.
Dept of Clinical Neuroscience, Karolinska Institute, Stockholm

Teaching clinical psychiatry by textbooks is often supplemented by live patient demonstrations as well as electives in clinical settings. Now, learning can be facilitated by web-based educational courses that visually demonstrate all variations of psychopathology. Mental health professionals can impersonate typical cases of the major psychiatric disorders including substance use disorders. Web-based case videos can be used to enhance communicative skills by providing good and bad interview samples. They can be used to train clinical researchers in the use of rating scales to enhance interrater reliability, and also to demonstrate typical drug adverse reactions for research or clinical purposes. The technique of semi structured diagnostic interviewing (such as the MINI) can be demonstrated. Developing web-based learning is an investment in inexpensive and modifiable interactive multimedia. Web-based learning meets with modern criteria for interactive learning.

Examples from a web-course on involuntary psychiatric care and a MINI interview will be demonstrated

THE TREATMENT OF GENERALIZED ANXIETY DISORDER

Baldwin, D.
Clinical Neuroscience Division, University of Southampton

Generalized anxiety disorder (GAD) is a common and debilitating medical condition, associated with significant social and occupational impairment, and traditionally thought to run a chronic course, waxing and waning in severity. A range of pharmacological treatments for patients with GAD are available, including the tricyclic antidepressant imipramine, certain selective serotonin reuptake inhibitors (SSRI), the serotonin-noradrenaline reuptake inhibitors (SNRI) venlafaxine and duloxetine, some benzodiazepines, buspirone, and the novel anticonvulsant and anxiolytic drug, pregabalin. The conventional neuroleptic trifluoperazine and the second generation antipsychotic quetiapine have been found efficacious in acute treatment, and the second generation antipsychotic drugs risperidone and olanzapine have been found helpful in placebo-controlled augmentation studies in patients responding only poorly to initial treatment (Baldwin et al., 2005). Some psychological treatments, particularly cognitive-behaviour therapy, have also been found helpful, but at present it is uncertain whether combining pharmacological with psychological interventions is more beneficial, than is either treatment modality, when given alone. When treating patients with GAD, important considerations underlying treatment decisions include the overall efficacy of treatment, the time before an apparent onset of action, the relief of both psychological and physical symptoms of anxiety, the ability to achieve symptomatic remission and to minimise symptom-related disability, efficacy in sustaining response over the long-term, and the cost-effectiveness of treatment. In addition, the nature of treatment-emergent adverse events, the safety of treatment in physically ill patients (as GAD is often comorbid with general medical conditions) and the risks of developing tolerance or experiencing troublesome discontinuation symptoms will all affect treatment decisions. Little is known about the prediction of response to treatment, and there is a dearth of studies in patients who do not respond to first-line treatments. This presentation will summarise current evidence base for the treatment of patients with GAD, highlighting those areas where there is still room for improvement in optimising clinical outcomes.

UPDATE ON ANXIETY SCALES

Bandelow, B.
Dept of Psychiatry and Psychotherapy, University of Göttingen

Although there is an abundance of ratings scales for anxiety disorders, only a small number of standard scales is used routinely in clinical trials, e.g. the Hamilton Anxiety Scale (HAMA). This has the advantage that results are comparable among the studies. The choice of these standard rating scales, however, is partly determined by historical reasons rather than by the psychometric properties of the scales. A modern rating scale should be compatible with DSM or ICD classifications, should have good psychometric properties, should be sensitive enough to differentiate active drugs from placebo and should be easy to use. For panic disorder, there was a tendency to take reduction of panic attacks as outcome measure, but there is an increasing trend to use comprehensive panic scales, such as the Panic and Agoraphobia Scale (P&A). There different ways to define treatment success, e.g. the mean change of scale scores from baseline, the number of patients showing response or remission, or the ''number needed to treat'' (NNT). Al these methods have their advantages and disadvantages. For instance, ''response'' is commonly defined as a ≥ 50 % reduction on these standard scales. The definition of ''remission'' on standard scale scores varies from study to study and is also very subjective. An analysis of all available studies of the anxiety disorders showed that these definitions need to be revised. There is a trend to focus not only on symptom reduction, but also to measure improvements in overall quality of life (QoL). However, current treatments have a stronger effect on symptom reduction, whereas improvement

of quality of life scales do not improve to the same extend. As current studies are only powered for detecting active drug-placebo differences on a symptom scale, introducing of QoL measures would increase sample sizes.

COMORBID ANXIETY DISORDER IN SCHIZOPHRENIA SPECTRUM DISORDERS

Castle, D.J.
Dept of Psychiatry, University of Melbourne

There is a clear link between schizophrenia spectrum disorders (SSDs) and anxiety disorders though its nature remains unclear. This has important implications for psychiatric nosology, aetiology and treatment. This talk will review the literature on the comorbidity of anxiety symptoms/disorders and SSDs in terms of their prevalence rates in clinical and non-clinical populations, the temporal relationship of anxiety comorbidity to SSDs, and the effect of comorbidity on outcome. Treatment implications will also be covered, with particular emphasis on OCD and social anxiety disorder.

NEW DIRECTIONS IN THE TREATMENT OF CHILD ANXIETY DISORDER

Cooper, P.
Winnicot Research Unit, University of Reading

Recent meta-analyses of treatment for child anxiety strongly support the use of Cognitive Behaviour Therapy (CBT): with specialist and intensive CBT treatment around 60% of anxious children are diagnosis free. Two important questions are raised by this finding. First, can the form of CBT be modified to improve the rate of recovery; and, second, might a proportion of patients benefit from a less specialist less intensive form of the treatment? Studies of predictors of treatment outcome suggest that two related factors are of critical importance: anxiety disorder in the mother and disturbances in the mother-child relationship. We are currently examining both these possibilities. Two lines of treatment research will be described. In the first, a controlled trial is being run in which anxious children with anxious mothers are receiving standard individual CBT together with either CBT for the mother's anxiety or strategies designed to reduce maternal over-protectiveness and over-intrusiveness. In the second, a controlled trial is being run in which anxious children of non-anxious mothers receive guided CBT self-help.

SELF-HELP AND INTERNET INTERVENTIONS FOR ANXIETY DISORDERS: POSSIBILITIES AND CHALLENGES

Cuijpers, P.
Dept of Clinical Psychology, Vrije Universiteit Amsterdam

Anxiety disorders are highly prevalent and are associated with a marked impairment in quality of life and a huge economic cost to society. Unfortunately, a considerable number of people who struggle with anxiety do not seek or receive adequate treatment. Self-help interventions have been proposed to constitute a relatively cheap, effective, efficient and low-threshold intervention for anxiety disorders. In this presentation, a critical discussion will be given of the advantages and disadvantages of self-help interventions and the evidence for their effectiveness, with a specific focus on computer- and internet-based interventions. It will be shown that guided self-help can play a major role in mental health care for patients with anxiety disorders. However, several research questions need to be answered before broad-scale dissemination is possible. The Internet will continue to play a prominent role in the further development of this field of research and clinical practice

PHARMACOTHERAPY OF OBSESSIVE COMPULSIVE DISORDER

Denys, D.
Dept of Psychiatry, University of Amsterdam

Over the past 30 years, a large number of controlled studies have established the efficacy of pharmacological treatment for OCD. Thanks to pharmacotherapy, as many as 90% of OCD patients eventually will have a clinically meaningful response. This presentation reviews new developments of pharmacotherapy in OCD. During the past five years, developments of pharmacotherapy of OCD primarily involved the extension of evidence of efficacy of serotonin reuptake inhibitors (SRIs), the use of atypical antipsychotics in addition to SRIs for treatment refractory patients, new studies examining the combination of pharmacotherapy with behavior therapy, and a number of studies assessing predictors of response. In 2005, frontline pharmacological treatment of OCD still consists of drugs with potent serotonin reuptake inhibition properties such as clomipramine, fluvoxamine, paroxetine, sertraline, fluoxetine and citalopram. In case of non-response, treatment options consist of adding another drug, increasing the dose, switching drugs, or changing the mode of delivery. The combination of pharmacotherapy with behavioral therapy is still regarded as the optimal treatment for OCD. Addition of behavior therapy may be beneficial for responders as well as non-responders to drug treatment. Though prediction of effective pharmacotherapy is extremely valuable for OCD, there is currently little consistency regarding clinical and demographic predictors.

SEARCHING FOR ENDOPHENOTYPES FOR OBSESSIVE-COMPULSIVE DISORDERS

Fineberg, N.A.
School of Psychology, University of Hertfordshire

Epidemiological evidence has indicated that OCD may be one of the most prevalent and disabling of the psychiatric disorders. OCD patients have been found to demonstrate abnormalities in a broad series of measures and paradigms used in neuropsychiatric (eg neurological soft signs, olfactory identification, evoked potentials, prepulse inhibition, intracortical inhibition) and neuropsychological (e.g. executive function, visual memory function) research. Studies have consistently revealed an association with particular neurocircuitry (cortico-striatal-thalamic-cortical) and specific neurotransmitter systems (eg serotonin, dopamine). Recent advances include molecular imaging studies of specific receptors in OCD, the demonstration that certain gene variants can play a causal role, and proof-of-principle studies that deep brain stimulation can rapidly reverse symptoms. Obsessive-

compulsive disorders provide researchers with an opportunity to develop an integrated cognitive-affective neuroscience approach to psychiatric disorder. Factor analysis, brain-imaging and genetic linkage studies have identified dimensions within OCD that may share distinct neurobiological profiles. A consideration of the 'obsessive-compulsive disorders', rather than just OCD, further expands this potential. OCD has been linked with a group of purportedly nosologically -related 'spectrum' disorders considered to share neurobiological underpinnings with OCD. Examples include trichotillomania, Tourette's syndrome, body-dysmorphic disorder. These disorders are characterised by failures to inhibit mental and physical acts. The boundaries and underpinnings of the 'OCD-Spectrum' remain to be elucidated. It has been suggested that neuroscience-based measures (eg. neurocognitive profiles, structural/functional brain images) show potential in the search for 'psychiatric endophenotypes'. The endophenotype - model establishes continuity between pathologically afflicted subjects and non-affected family-members and expands diagnostic boundaries and categories to include a greater variety of phenotypes, representing ''upstream'' consequences of different genes. Exploring neuroimaging and neurocognitive endophenotypes for OCD and OCD-Spectrum disorders may help define the closeness of the relationships, and indicate new treatment strategies. In this lecture current findings from ongoing research in this field will be presented.

ATTENTION DEFICIT HYPERACTIVITY DISORDER AND ANXIETY DISORDERS IN CHILDHOOD

Mancini, C.
McMaster University Medical Centre, Ontario

Attention Deficit Hyperactivity Disorder (ADHD) is a life-long, chronic disorder, which has its onset in childhood and is associated with significant functional impairment. Epidemiological studies have estimated the prevalence of co-occurring anxiety and ADHD to be 22% in children. In clinic samples, between 25 – 45% of children with ADHD meet criteria for at least one anxiety disorder. There is significant symptom overlap between anxiety disorders and ADHD, making differentiation between these disorders difficult at times. This presentation will discuss the relationship between childhood anxiety disorders and ADHD, focusing on epidemiology, clinical presentation and the impact of comorbidity on treatment response.

THE IMMUNE SYSTEM AND OBSESSIVE-COMPULSIVE DISORDER

Marazziti, D.
Dept of Psychiatry, Neurobiology and Biotechnology, University of Pisa

The observation that at least 25% of OCD patients fail to respond to SRIs treatment (Thomsen, 2000) has driven the research focus towards other mechanisms not related to serotonin (5-HT9, such as those involving the immune system, but available data, albeit intriguing, are meagre. In particular, a childhood-onset OCD has been linked to an autoimmune cross-reaction driven by a -haemolytic streptococcal infection involving the neurons of the basal ganglia, and similar to that occurring in Sydenham's chorea .According to this model, antibodies against the streptococcus would cross-react with basal ganglia neurons, disrupt basal ganglia-thalamus-cortical circuit and generate OC symptoms: the different conditions originating from the reactions to streptococcal infections have been grouped under the name of ''paediatric autoimmune neuropsychiatric disorders associated with streptococcal infections'' (PANDAS). The role of immunological dysfunctions in this OCD subtype has been supported by the presence of high levels of B-cells reacting with a marker of rheumatic fever, the so-called monoclonal antibody D8/17 which has been found even in adult patients; nevertheless, the role of D8/17 positivity is still controversial. Following these observations, some children with severe streptococcal infection and concomitant exacerbations of OCD or tic disorders were shown to respond to plasma exchange and intravenous immunoglobulins, while the effectiveness of penicillin prophylaxis is unclear. Taken together, the available data on the immunological hypotheses of OCD should be considered preliminary, as underlined in a recent study where interleukin (IL) and TNF-alpha concentrations were found to be elevated at baseline in Tourette's syndrome and/or early onset OCD, as compared with healthy conditions. More interestingly, both these markers increased during symptom exacerbation, while suggesting that the worsening of the disorder might be associated with an inflammatory process spread to the central nervous system through local and systemic cytokines. Moreover, the persistence of high level of NK cells before and after treatments was observed in OCD patients, at variance with depressed patients who showed their normalization after the symptom improvement. Recently, we examined the effect of 12 months of treatment with different SRIs on lymphocytes subsets in 18, out of a total of 20 patients, evaluated at baseline and showing a significant increase of CD8+ and decrease of CD4+ lymphocytes, as compared with a similar group of healthy controls. The results showed that SRIs provoked a normalization of altered lymphocytes subsets in responder OCD patients and suggest that these drugs have potentially immuno-modulating properties.

FUTURE DRUG TREATMENT OF ANXIETY

Nutt, D.
Psychopharmacology Unit, University of Bristol

The future of anxiety treatments may take several or even multiple forms. Current approaches include

- refining current medications e.g. the SSRIs to improve efficacy and reduce adverse effects [e.g. sleep and sexual dysfunction], or new drugs that target their sites of action in the brain – e.g. drugs to reduce excess noradrenaline function such as prazosin
- understanding better the role of calcium channel blockers in anxiety so that new variants of pregabalin and related compounds can be developed and tested
- developing agents to reduce stress-related consequences in the brain – these include CRH [corticotrophin releasing hormone] antagonists and glucocorticoid receptor antagonists as well as antagonists of related hormones e.g. vasopressin
- developing agents to assist in psychotherapy – e.g. pro-learning agents such as D-cycloserine as well as

empathy-promoting drugs such as MDMA.
I will discuss the rationale for each of these approaches and give examples of pilot studies where they exist as well as discussing new translational approaches to testing promising compounds in volunteer models to select the best candidates for clinical trials

SUBSTANCE USE DISORDERS AND ANXIETY

Schuckit, M.
Dept of Psychiatry, University of California

There is significant comorbidity between anxiety symptoms, drinking, the consumption of illicit substances, as well as between substance abuse and dependence on the one hand and independent major anxiety disorders on the other. This lecture emphasizes the need to distinguish between use, temporary problems, and substance use disorders, and to tease out differences between anxiety symptoms and major anxiety disorders. The two classes of drugs most likely to be associated with anxiety symptoms include intoxication with stimulants (e.g., amphetamines, cocaine, prescription weight-reducing products, etc.), and withdrawal from depressants (including alcohol and sedative hypnotics). While anxiety syndromes (resembling social phobia, panic disorder, agoraphobia, etc.) are common as temporary manifestations of intoxication or withdrawal from these substances, there is also evidence of a small but significant enhanced risk for alcohol and drug use disorders in individuals with preexisting panic disorder, post-traumatic stress disorder, and possibly some additional DSM-IV anxiety conditions. The lecture will offer data regarding the prevalence of various types of comorbidities between substances and anxiety conditions, speculate on potential reasons for these relationships, and offer suggestions about how to best tease out temporary substance-related symptoms from independent major anxiety disorders.

ANXIETY DISORDERS: NEURONAL CIRCUITRY, MOLECULAR UNDERPINNINGS, AND PSYCHOSOCIAL TRAJECTORIES

Stein, D.J.
Department of Psychiatry, University of Cape Town

There are important clinical reasons for focusing on the anxiety disorders - they are the most prevalent of the psychiatric disorders, and amongst the most disabling. Generalized anxiety disorder, obsessive-compulsive disorder, panic disorder, posttraumatic stress disorder, and social anxiety disorder are increasingly viewed as independent disorders that chronic and costly, as well as underdiagnosed and undertreated, but that can be managed effectively and cost-efficiently. Much of the excitement about recent work on anxiety disorders derives, however, from our increasing ability to move from bench to bedside, translating laboratory findings into clinical approaches. This talk will emphasize how translational research is increasingly allowing us to address and to integrate multiple levels of data on anxiety disorders, including work on neuronal circuitry, molecular underpinnings, and psychosocial trajectories. The anxiety disorders provide an important "tool-with-which-to-think" about recent advances in modern psychiatry, as well as about the limitations of our current knowledge base. Where relevant, data from the South African context, which has a number of remarkable and unique features, will be used to exemplify the arguments put forward.

POST PARTUM ANXIETY/DEPRESSION AND THE EFFECTS ON CHILD DEVELOPMENT

Stein, A.
Dept of Child & Adolescent Psychiatry, University of Oxford

There is considerable evidence that maternal postnatal psychiatric disorder has an adverse influence on infant development. In attempting to examine the pathways of intergenerational transmission, most research has concentrated on genetic factors or on maternal behaviours during mother-child interaction. However, researchers have largely ignored the role of maternal cognition underlying behaviour, especially the thought and attentional processes involved in psychiatric disorders. In this I paper argue that a particular form of maternal cognition, namely 'preoccupation', is a key and under-recognised mechanism in the transmission of psychiatric disturbance. This is because preoccupation has the potential to interfere with specific aspects of mental functioning, especially attention and responsivity to the environment. This can impair the mother's parenting capacities and adversely affects mother-child interaction and child development. There is now emerging evidence that similar processes are present in fathers. I will present some examples from our longitudinal research as to how these mechanisms might operate as well as some preliminary data from a validation study of preoccupation in mothers with postnatal anxiety and/or depression.

ADULT ATTENTION DEFICIT HYPERACTIVITY DISORDER AND ANXIETY DISORDERS

Van Ameringen, M.
McMaster University Medical Centre, Ontario

Adult Attention Deficit Hyperactivity Disorder (ADHD) is a life-long, chronic disorder, which has its onset in childhood and is associated with significant functional impairment. Although childhood ADHD often resolves, upwards of 36% - 55% of childhood cases maintain symptoms into adulthood. The rate of lifetime DSM-IV adult ADHD in the community is 8.1%. This disorder appears to be highly comorbid, with mood disorders, anxiety disorders and substance use disorders. This presentation will specifically examine the relationship of ADHD to anxiety disorders (rates of comorbidity, impact on treatment response and outcome). We will also present new pilot data on adult ADHD in an anxiety disorders population.

TRANSCRANIAL MAGNETIC STIMULATION AND ANXIETY DISORDERS: FUNDAMENTAL OR CLINICAL APPLICABILITY

Van Honk, J.
Dept of Experimental Psychology, Utrecht University

Human anxiety is regulated by a complex compound of interacting brain circuits. Repetitive transcranial magnetic stimulation (TMS) may be capable of providing more insights into the workings of these affective circuits by modulating

brain activity in controlled designs and addressing effects on the brain and behaviour. TMS may even have potential for treatment in the disorders of fear and anxiety but likely only in selective patient groups. It has been established by animal research that changes in serotonin and dopamine turnover in subcortical structures contribute to the effects of rTMS which has promising implications. During the symposium I will review fundamental and clinical research that used TMS to investigate human anxiety and the disorders of anxiety. Also, I will discuss the possibility of using TMS not only as a way to locally change brain activity but also to measure brain connectivity, thus directly addressing brain communication. Finally, I will suggest a framework that can be applied for fundamental TMS research in anxiety and the disorders of anxiety.

UPDATE OF THE TREATMENT OF SOCIAL ANXIETY DISORDER

Westenberg, H.
Dept of Psychiatry, University Medical Centre Utrecht

Social Anxiety Disorder (SAD) is a common and chronic condition, afflicting a large proportion of the general population. SAD is often associated with significant psychiatric comorbidity and disability in the social and professional lives of patients. SAD presents as two subtypes: the severe and debilitating generalized form, and the non-generalized form, which is usually only present in performing situations. Psychiatric comorbidity, including mood and other anxiety disorders, are common in the generalized form of SAD. Epidemiological studies put the life-time prevalence as high as 13%. Despite this high prevalence and the disability it may cause, SAD remains an under-recognised, and thus under-treated condition. There are many barriers that prevent an individual with SAD from seeking help. SAD bears some relationship with shyness and most sufferers share the popular view that what they experience is merely shyness and not a serious and treatable medical condition. This explains the low rate of presentation to and recognition by health care providers. Now that effective treatments are available for SAD, it is important to increase the level of recognition by health care providers to overcome the barriers to seeking help by the patients. In recent years, a number of randomized controlled clinical trials have shown the efficacy of selective serotonin reuptake inhibitors (SSRIs) in the treatment of SAD. SSRIs are emerging as first-line treatment for SAD, based on their proven safety, tolerability and efficacy. Recent meta-analyses have shown that only SSRIs are superior to placebo; other classes of drugs have yielded inconsistent results or data are too scanty to draw firm conclusions. The classical MAOIs have demonstrated efficacy but the need for dietary restrictions has limited its use and conflicting results have been reported for selective and reversible MAOIs. Although benzodiazepines have the advantage that they work quickly, the number of controlled studies is limited. Recent studies also have shown efficacy for gapapentine, pregabalin and atypical antipsychotics. Managing SAD patients remains a challenging prospect, mainly because it is chronic disorder that is frequently comorbid with other psychiatric conditions. To successful treat a patient with SAD it is imperative to fully understand the benefits and limitations of drugs commonly used to treat SAD. Tolerability, safety and efficacy for comorbid conditions are therefore important issues when selecting the treatment. Managing treatment resistant patients is also an important aspect; the efficacy of adjuvant and combination therapy will be also be discussed in this presentation

EARLY/PREVENTATIVE INTERVENTION IN PTSD

Zohar, J.
Division of Psychiatry, Chaim Sheba Medical Center, Ramat Gan

PTSD is a pathological response to trauma. Only 10 – 20% of individuals who are exposed to traumatic events will develop a pathological fixation, namely PTSD. Although its prevalence in the general population will range from 3 – 6%, most patients are not being diagnosed, mainly as co-morbidity governing the clinical presentation. The cornerstones of PTSD include exposure to traumatic events, re-experiencing of the traumatic event, avoidance and increased arousal, which leads to a substantial decline in functioning. PTSD is unique among anxiety disorders, as the point of onset is clear. By definition, PTSD starts after a specific event, namely, after being exposed to an event where one has the subjective feeling that he could have died. As there is a point of onset, and often the symptoms are fully expressed right from the beginning, theoretically there is a 'window of opportunity' to intervene. It may be that the timing of the intervention is as important as the intervention itself. Moreover, the initial response to the trauma (composed of flashbacks, irritability, sleep disturbances, horror, intense fear upon re- exposure, avoidance) is universal and considered normal in the first days. Only when this 'normal response to the abnormal situation' continues for at least a month, the diagnosis of PTSD is given. Since the vast majority of individuals (80%) will eventually recover, one way to conceptualize PTSD is as a 'failure to recover'.

This type of conceptualization bears some therapeutic insight; most importantly, that in the first days (and weeks) after the traumatic exposure, the focus of treatment would be on how not to interfere with the recovery process. The challenge is to find out if and what type of early intervention during the 'window of opportunity' – the time from exposure until PTSD develops – is effective for those at high risk of developing PTSD.

POSTER PRESENTATION ABSTRACTS

A NONINFERIORITY COMPARISON OF DULOXETINE AND VENLAFAXINE XR FOR THE TREATMENT OF ADULT PATIENTS WITH GENERALIZED ANXIETY DISORDER

Allgulander, C.[1], Nutt, D.[2]; Erickson, J.[3]*; Spann, M.[3]; Dekte, M.J.3,4,5; Walker, D.[3]; Ball, S.G.3,4; Russell, J.M.[3]
*[1]Karolinska Institutet, Stockholm; [2]University of Bristol, Bristol; [3]Lilly Research Laboratories, Indianapolis; [4]Indiana University School of Medicine, Indianapolis; [5]Harvard Medical School, Boston; *Current affiliation Orexigen Therapeutics, San Diego.*

Purpose: The present study is a noninferiority comparison of the efficacy of duloxetine and venlafaxine extended-release (XR) for the treatment of adults with generalized anxiety disorder (GAD). **Methods:** Data were pooled, as planned a

priori for adequate statistical powering, from 2 nearly identical 10-week, multicenter, randomized, double-blind studies that each compared duloxetine 60–120 mg once daily and venlafaxine XR 75–225 mg once daily treatment with placebo. Patients were male or female adult outpatients (≥18 years) with DSM IV-TR-defined GAD. The primary efficacy measure was the Hamilton Anxiety Rating Scale (HAMA) total score. Based on an expert consensus panel's recommendations, the noninferiority comparison involved 6 statistical and clinical criteria and the use of a per protocol population, defined as patients who had ≥4 weeks of treatment, HAMA ratings after ≥4 weeks, compliance with study drug, and no protocol violations. **Results:** In the pooled sample, patients were randomly assigned to receive duloxetine (N=320), venlafaxine (N=333), or placebo (N=331). The per-protocol patients treated with duloxetine (N=239) or venlafaxine XR (N=262) were significantly more improved (mean HAMA reductions -15.4 and -15.2, respectively) compared with placebo (-11.6, P≤ .001, both comparisons). The intent-to-treat sample response rates were 56%, 58%, and 40% respectively. Adverse event-related discontinuation was significantly higher for duloxetine (13.4%, P≤.001) and venlafaxine XR (11.4%, P≤.01) groups compared with placebo (5.4%). **Conclusions:** Duloxetine 60–120 mg/day met all statistical and clinical criteria for noninferiority and exhibited a similar tolerability profile compared with venlafaxine XR 75–225 mg/day for the treatment of adults with GAD.

HOW ARE SYMPTOM SEVERITY AND FUNCTIONAL RECOVERY/RELAPSE RELATED?

Baldwin, D.S.[1], Bandelow, B.[2], Dolberg, O.T.[3]; Andersen, H.F.[3], Stein, D.J.[4]

[1]Clinical Neuroscience Division, University of Southampton; [2]Dept of Psychiatry and Psychotherapy, University of Göttingen; [3]H. Lundbeck A/S, Copenhagen; [4]Dept of Psychiatry, University of Cape Town and Mt. Sinai School of Medicine, New York

Background: Anxiety disorders are associated with significant disability. There is growing interest in the question of whether pharmacotherapy that effectively reduces symptoms also restores function. Recovery could potentially be defined as a lack of disability, with associated reduction in symptom severity. Conversely, relapse could potentially be defined in terms of either increased disability or increased symptoms. **Methods:** We analyzed a database of randomized controlled trials of escitalopram in generalized anxiety disorder and social anxiety disorder, focusing on the relationship between disorder-specific severity scales, and the Sheehan Disability Scale (SDS). In short-term studies, cut-points on symptom scales were derived for recovered function. In relapse prevention studies, the effects of defining relapse in terms of increased disability scores were examined. **Results:** In generalized anxiety disorder and social anxiety disorder, there was a close correlation between primary symptom severity scales and the SDS, both in the short-term and during relapse prevention. Thus, a lack of disability is associated with relatively low symptom severity scores, and rates of relapse – defined in terms of increased disability - are significantly lower on medication than on placebo. **Conclusion:** These data indicate that improvement in primary symptom scales in anxiety disorders is accompanied by improvement in functioning, and vice versa. Recovery and relapse can therefore be defined either in terms of symptom severity or in terms of functioning. Longer-term treatment of anxiety disorders is needed to ensure recovery.

HOW LONG SHOULD AN INITIAL TREATMENT PERIOD BE IN ANXIETY DISORDERS AND IN MAJOR DEPRESSIVE DISORDER?

Baldwin, D.S.[1], Stein, D.J.[2], Dolberg, O.T.[3], Bandelow, B.[4]

[1]Clinical Neuroscience Division, University of Southampton; [2]MRC Unit on Anxiety Disorders, University of Cape Town; [3]H. Lundbeck A/S, Copenhagen; [4]Dept of Psychiatry and Psychotherapy, University of Göttingen

Objective: To extend knowledge of the time course of symptom improvement of patients with major depression (MDD), panic disorder (PD), social anxiety disorder (SAD) and generalised anxiety disorder (GAD) participating in randomised placebo-controlled trials (RCTs); and to infer the optimal duration of initial escitalopram treatment in clinical practice, after which subsequent intervention might be reasonable. **Method:** Post-hoc analysis was made of the pooled clinical trial database for escitalopram in MDD (14 studies), GAD (4 studies), SAD (2 studies) and PD (1 study). 'Onset' of action was defined as 20% or more decrease from baseline score in the disorder-specific psychopathological rating scale: 'response' was defined as a 50% or more decrease from the baseline score. **Results:** For patients with MDD, there was a 43% probability of achieving response at Week 8 if no onset was apparent at Week 2, whereas for those patients demonstrating an onset of treatment effect at Week 2, this probability was nearly 80%. Similar patterns were observed in the randomised controlled trials in GAD, SAD, and PD. If no treatment effect had occurred by Week 2, the chance of patients with MDD, GAD, or SAD responding after Week 4 was 20% or less. In patients with PD and no onset of response by Week 6, findings from the small number of patients suggest that continuing existing treatment had little clinical utility. **Conclusion:** The pattern of response seen in these RCTs may suggest that for patients with MDD, GAD and SAD seen in wider clinical practice, a period of at least 4 weeks is worthwhile before a change in the therapeutic approach is considered.

RESULTS FROM A PHASE III STUDY OF ONCE-DAILY EXTENDED RELEASE QUETIAPINE FUMARATE (QUETIAPINE XR) MONOTHERAPY IN PATIENTS WITH GENERALISED ANXIETY DISORDER

Bandelow, B.[1], Bobes, J.[2], Ahokas, A.[3], Eggens, I.[4], Liu, S.[5], Brecher, M.[5]

[1]Dept of Psychiatry and Psychotherapy, University of Goettingen; [2]Department of Psychiatry, University of Oviedo, Asturias; [3]Mehilainen Clinic, Helsinki; [4]AstraZeneca R&D Södertälje; [5]AstraZeneca Pharmaceuticals, Wilmington

Background: To evaluate efficacy and tolerability of once-daily quetiapine XR (extended release) in patients with generalised anxiety disorder (GAD). **Methods:** 10 week (8-week active treatment, randomised phase; 2-week

post-treatment drug-discontinuation/tapering phase), multicentre, double blind, randomised, parallel group, placebo- and active comparator study (D1448C00011). Patients were randomised to quetiapine XR 50mg/day, 150mg/day, paroxetine 20mg/day or placebo. Primary efficacy outcome was change from baseline to Week 8 in HAM A total score. Other key outcomes included: change in HAM A total score from baseline to Day 4, HAM-A response (≥50% decrease from baseline) and remission (HAM A total score ≤7) at Week 8. Adverse events (AEs) were recorded throughout the study. **Results:** 873 patients were randomised: 221 quetiapine XR 50mg/day; 218 quetiapine XR 150mg/day; 217 paroxetine; 217 placebo. Mean HAM-A total score (overall baseline mean, 26.98) was significantly reduced at Week 8 by quetiapine XR 50 mg/day (-13.95, p<0.05), quetiapine XR 150 mg/day (-15.96, p<0.001) and paroxetine (-14.45, p<0.01) versus placebo (-12.30). Statistically significant separation from placebo (-2.90) in HAM A total score was observed at Day 4 for quetiapine XR 50mg/day (-4.43, p<0.001) and 150 mg/day (-3.86, p<0.05) but not paroxetine (-2.69, p=0.6). At Week 8, response rates were significantly higher for quetiapine XR 50mg/day (62.6%, p<0.05), 150mg/day (70.8%, p<0.001) and paroxetine (65.9%, p<0.001) versus placebo (52.1%). Remission rates were significantly higher for quetiapine XR 150mg/day (42.6%, p<0.01) and paroxetine (38.8%, p<0.05) versus placebo (27.2%). During Weeks 1-8 the most common AEs (>10%) were: dry mouth (15.9, 25.7, 9.8, 6.0%), somnolence (21.8, 25.2, 11.2, 4.6%), fatigue (15.0, 16.5, 9.3, 3.7%), dizziness (11.8, 15.6, 13.5, 6.0%), headache (16.4, 12.4, 17.2, 18.0%) and nausea (7.7, 6.4, 20.5, 7.4%) with quetiapine XR 50mg/day, 150mg/day, paroxetine and placebo, respectively. **Conclusions:** Once-daily quetiapine XR at 50mg/day and 150mg/day is effective and well tolerated in GAD, with onset of response as early as Day 4. Paroxetine was also well tolerated and effective compared with placebo, although onset of response was not observed by Day 4.

HIGH DOSE ESCITALOPRAM FOR REDUCING DISABILITY IN OBSESSIVE-COMPULSIVE DISORDER

Barak, Y.[1], Baruch, Y.[1], Rabinowitz, I.[2]

[1]Abarbanel Mental Health Center, Bat-Yam; [2]YOTAM treatment center. *Affiliated with the Sackler Faculty of Medicine, Tel-Aviv University*

Background: Although obsessive-compulsive disorder (OCD) has been found to be the 10th leading cause of disability of all medical conditions little is known about psychosocial functioning and disability in OCD, particularly with regard to their relationship with symptom severity. Psychosocial function assessed prospectively when studying the course of OCD demonstrates significantly impairment compared with published community norms. In addition, it has been shown that aspects of work, social life and family life that are markedly affected in individuals with OCD are associated with OCD severity and co-morbid depression severity. Although treated patients improve in adjustment levels, there is some evidence of persistent impairment, particularly in social and work functioning. In small scale studies analyses revealed that Sheehan Disability Scale (SDS)-work score at baseline was a predictor of response to SSRI treatment and that higher level of disability at the beginning of treatment are associated with a poorer response to SSRI. **Aim:** To analyze effects of high-dose escitalopram treatment on measures of depression and disability in patients suffering from OCD not responding to standard dose. **Method:** Subjects were recruited from patients treated at the YOTAM treatment centre, a large clinic specializing in mood disorders, anxiety, and OCD. The Abarbanel Mental Health Center's IRB approved the study protocol and written informed consent was obtained from patients eligible and willing to participate after they received a complete description of the study. After 4 weeks of treatment with escitalopram 20 mg/daily, patients defined as non-responders [Yale-Brown Obsessive Compulsive Scale (Y-BOCS) total score reduction ≤25%] continued treatment at higher escitalopram doses. Patients were assessed at baseline, weeks 1, 4, 6, 8, 11, 14, and 18 using the Y-BOCS Symptom Checklist, the MADRS, CGI and the Sheehan Disability Scale (SDS). The SDS is a three-item instrument for assessing functional impairment quantifies disruption by symptoms of work/school performance, social life and family life/home responsibilities. This scale is a sensitive tool for identifying primary care patients with mental health-related functional impairment. **Results:** Sixty-seven patients were enrolled in the present study. There were 33 women and 34 men, mean age of 34.8 years (SD=13.3, range=18-78). The mean Y-BOCS score at baseline was 29.6 (SD=3.9) reflecting a group of patients with severe OCD symptoms. The mean baseline MADRS score for the group was 28.3 (SD=4.9) indicating a relatively high rate of concurrent depressive symptomatology. The baseline CGI-Severity (CGI-S) and SDS scores demonstrate high levels of clinical severity and functional disability for these patients at enrollment. The mean baseline CGI-S score was 5.8 (SD=0.6) and the mean SDS score was 22.6 (SD=3.5). There was a significant improvement by week 6 compared to week 4 of treatment (20 mg/daily) for both the primary outcome measures, (Y-BOCS, MADRS, CGI-S), as well as the secondary outcome measures (CGI-I, SDS) by week 6 of treatment. This improvement was maintained throughout the rest of the study. All 3 items of the SDS improved significantly. However, residual mild to moderate disability was still reported by the majority of patients. **Conclusion:** Treating OCD patients with high-dose escitalopram can produce significantly positive effects on functional disability. It is possible that longer exposure to medication is needed to achieve complete remission.

ANXIETY IN SCHIZOPHRENIA

Blanc, O.

Attaché de Recherche Clinique,CHU de Clermont Ferrand

Evaluation of anxiety in schizophrenia is important from a clinical, psychopathologic and therapeutic point of view, but reliable, standardized, and widely accepted specific tools are scarce and of difficult use. Therefore, we built-up a specific scale (EAS) to specifically evaluate anxiety in schizophrenic patients. This is a hetero-evaluated scale, since the capacity of perception and expression can be modified in schizophrenia, and the observer can take into account objective manifestations. Twenty-nine items were selected by combining items of the Hamilton Anxiety Scale, (HAM-A), the Tyrer's brief scale for anxiety (BSA), Bobon's AMDP-AT anxiety scale and the Comprehensive Psychiatric Rating Scale (CPRS). A Likert-formatted questionnaire was independently revised by each

investigator. The Delphi method was therefore used to further evaluate the pertinence, reliability and limitations of the questionnaire by an expert committee. A study designed to evaluate the psychometric properties of the EAS scale in 200 schizophrenic patients was already set up. Analysis of unidimensionality, internal consistence and item responses will allow an estimate of the precision and reliability of the EAS scale. Independent evaluation of each patient by 2 investigators will allow estimating inter-rater reliability. External validity will be estimated by analyzing correlations between the EAS scale and other reference scales: HAM-A, the Visual Analog Anxiety Scale and the anxiety/depression factors of the Positive and Negative Syndrome Scale of Schizophrenia (PANSS). The use of the EAS scale can facilitate diagnosis, follow up and treatment of anxiety in schizophrenia.

PSYCHOMETRIC PROPERTIES OF THE MULTIDIMENSIONAL SCALE OF PERCEIVED SOCIAL SUPPORT IN YOUTH

Bruwer, B, Emsley, R, Kidd, M., Lochner, C., Seedat, S.
University of Stellenbosch

Introduction: There is increasing awareness of the contribution of perceived social support (PSS) to emotional and physical well-being. Numerous scales measuring PSS have been developed, including the Multidimensional Scale of Perceived Social Support (MSPSS). The psychometric properties of the MSPSS have been demonstrated in diverse samples although its reproducibility in South African youth has not yet been investigated. **Methods:** This study aimed to investigate the psychometric properties of the MSPSS in South African youth using confirmatory factor analysis. The relationship of PSS to depressive and anxiety symptoms, as well as the effects of gender and ethnicity, were investigated. Participants completed a battery of self-report measures, including the MSPSS, Beck Depression Inventory (BDI), and the Child PTSD checklist on a single occasion. Confirmatory factor analysis (CFA) was performed to validate the a priori factor structure of the MSPSS. In addition, Cronbach's alpha coefficients and intercorrelations (for clinical variables) were calculated. A missing value analysis was performed to assess the influence of missing data on our findings. **Results:** Data are reported for 502 youth (11.3 to 23.5 years). The three-factor structure of the MSPSS (significant other, family, and friends) fitted the data well. The MSPSS showed good internal consistency. PSS was also positively correlated with resilience, and negatively correlated with depression, exposure to community violence and other potentially life-threatening traumas. Females and youth of white or mixed race reported significantly higher levels of PSS than males and black youth, respectively. **Conclusions:** The MSPSS is a psychometrically sound instrument that can be applied to South African youth.

SUMATRIPTAN VS PLACEBO – A SINGLE BLIND CROSS-OVER STUDY OF DIFFERENCES IN SPECT BRAIN PERFUSION IN OBSESSIVE-COMPULSIVE DISORDER

Carey, P.D.[1], Warwick, J.[1 2], Lochner, C.[1], Stein, D.J.[1 3]
[1]MRC Research Unit on Anxiety Disorders, University of Stellenbosch; [2]Department of Nuclear Medicine, University of Stellenbosch; [3]Department of Psychiatry, University of Cape Town, Cape Town

Background: Treatment data, genetic findings, and some previous challenge data suggest a potential role for the serotonin 1B autoreceptor in mediating symptoms in obsessive-compulsive disorder (OCD). A previous study of sumatriptan, a 1B agonist and SPECT, found a heterogeneous clinical response with frontal brain regional perfusion attenuated with exacerbation of symptoms in OCD. Here we extended this study to include more participants and used whole-brain voxel-wise SPM analysis. **Methods:** Sumatriptan or matching placebo was administered in a double-blind, cross-over, counterbalanced design on separate days to 25 consenting participants with primary diagnosis of OCD. Participants were free of psychotropics, other primary psychiatric co-morbidity including depression, and consented to participation. Single photon emission computed tomography (SPECT) imaging followed a standardized rest period and injection with Tc-99m HMPAO. Repeated measures of OC and general anxiety symptoms were performed by trained clinicians to assess change in response to the drug challenge. **Results:** Behavioural responses of OC and anxiety symptoms did not differ significantly between placebo and sumatriptan. This masked the considerably heterogeneous response for OC symptoms. The majority (n=14) participants had an improvement in symptoms of anxiety, with mixed change more then half of the participants for OC symptoms and the remainder were unchanged. Improvement in OC symptoms was associated with attenuated regional perfusion in the right mid-cingulate, and left superior medial frontal cortex. Increased perfusion in the mid-occipital region in response to sumatriptan challenge was an unexpected finding. Improved anxiety symptoms correlated inversely with perfusion in the left fusiform gyrus, right precuneus, and left lingual gyrus. **Conclusions:** Drug challenge of the 5HT1D/B autoreceptor complex in OCD in the present study produced mixed responses in obsessive-compulsive symptoms and anxiety in OCD. In general, brain regional perfusion responses to sumatriptan challenge were seen in brain regions implicated in the functional neurocircuitry of OCD. In addition, whole brain voxel-wise analysis has enabled us to detect and speculate on the involvement of regions outside of this circuit. Our data also suggest that the change in frontal regional perfusion may be specific to OC symptoms following sumatriptan challenge.

QUETIAPINE AUGMENTATION OF SRIS IN TREATMENT REFRACTORY OBSESSIVE-COMPULSIVE DISORDER: IS RESPONSE TO TREATMENT PREDICTABLE?

Carey, P.D.[1], Kidd, M.[2], Stein, D.J.[1 3], Denys, D.[4]
[1]MRC Research Unit on Anxiety Disorders, University of Stellenbosch; [2]Centre for Statistical Consultation, University of Stellenbosch; [3]Department of Psychiatry, University of Cape Town; [4]Department of Psychiatry, Academic Psychiatric Centre, Amsterdam

Background: Response rates to first-line treatments in OCD remain unsatisfactory. Recent meta-analyses have demonstrated significant benefit for quetiapine addition to SRIs over placebo in treatment refractory obsessive-

compulsive disorder (OCD). Numerous studies have investigated a range of clinical and demographic variables that may predict response to first-line SRI treatment, but fewer data are available about predictors of response to SRI augmentation. We aimed to delineate predictors of response to quetiapine augmentation in refractory OCD. **Methods:** Data for 80 subjects was combined from two previously published placebo-controlled, augmentation studies using quetiapine that followed inadequate response to a minimum of 12 weeks SRI treatment. We combined data derived from the YBOCS checklist with a variety of putative clinical and demographic variables previously shown to predict treatment outcome in OCD. We then assessed the power to predict treatment outcome using best-subset logistic regression of all variables followed by logistic regression of the best-subset variables with YBOCS change as the dependent variable. **Results:** In univariate analyses, a lower number of previous SRI treatment trials was associated with YBOCS response. Our model, in which fewer previous failed SRI treatments, higher baseline obsession score, and having ordering and arranging compulsions, predicted better treatment outcome (YBOCS change), explained some 45% of the variance in treatment response. Using YBOCS endpoint scores as an alternate dependent variable, we found a lower number of previous SRI trials, higher baseline compulsion scores, counting/ordering and arranging compulsions together predicted 50% of the variance in treatment outcome. **Conclusions:** Despite the small sample, the data here suggest a number of predictors of response to quetiapine augmentation. These include fewer previously failed SRI trials and generally higher overall baseline scores for obsessions and compulsions as well as ordering and arranging as well as counting compulsions. Together these data suggest that other as yet unidentified factors may also contribute to predicting treatment outcome to augmentation with antipsychotics in treatment refractory OCD.

ESCITALOPRAM IN OBSESSIVE-COMPULSIVE DISORDER (OCD): RESPONSE OF SYMPTOM DIMENSIONS TO PHARMACOTHERAPY

Carey, P.[1], Stein, D.J.[2], Lochner, C.[1], Seedat ,S.[2], Fineberg, N.[3], Andersen, E.W.[4]

[1]MRC Research Unit on Anxiety Disorders, University of Stellenbosch; [2]Department of Psychiatry, University of Cape Town; [3]School of Psychology, University of Hertfordhshire; [4]H. Lundbeck A/S, Copenhagen

Background: There is a substantial body of evidence that OCD symptoms can be grouped into a series of discrete dimensions, and some evidence that not all OCD symptom dimensions respond equally well to pharmacological or psychotherapeutic intervention. The response of OCD symptom dimensions to 12 weeks of treatment with escitalopram or placebo was investigated. **Method:** Data from a randomized, double-blind placebo-controlled study of escitalopram in 466 adults with OCD were analyzed. Exploratory factor analysis of individual items of the Y-BOCS checklist was performed and subscale scores based on the extracted factors were determined. Analyses of covariance were undertaken to determine whether inclusion of each subscale score in these models impacted on the efficacy of escitalopram versus placebo. **Results:** Exploratory factor analysis of the individual YBOCS items yielded 5 factors (contamination/cleaning, harm/checking, hoarding/symmetry, religious/sexual, and somatic/hypochondriacal). Analyses of covariance including all the subscales demonstrated that escitalopram was more effective than placebo. There was a significant interaction for the hoarding/symmetry factor, which was associated with a poor treatment response ($p<0.001$). **Conclusion:** Escitalopram shows good efficacy across the range of OCD symptom dimensions. Nevertheless, hoarding/symmetry was associated with a poorer treatment response. Hoarding/symmetry may be particularly characteristic of an early-onset group of OCD patients, with the involvement of neurotransmitters other than serotonin. Further work is needed to delineate fully the subtypes of OCD, and their correlates with underlying psychobiology and treatment responsivity.

NEURAL RESPONSE UNDERLYING EMOTIONS PERCEPTION IN ANXIETY DISORDERS: PRELIMINARY RESULTS NESDA FMRI STUDY.

Demenescu, L.R.[1], Renken, R.[1], van Tol, M.J.[2], van der Wee, N.J.A.[2], Veltman, D.J.[3], Nielen, M.M.A.[3], den Boer, J.A.[4], Aleman, A.[1]

[1]BCN-Neuroimaging Center, University of Groningen; [2]Department of Psychiatry, Leiden University Medical Center; [3]Department of Psychiatry, VrijeUniversity Medical Center, Amsterdam; [4]University Hospital Groningen

In the past years, fMRI studies on anxiety disorder shared an increasing interest in the community. Increased amygdala and insula activation in response to threatening stimuli has been reported in anxiety disorders (Starube et al., 2005, Lira Yoon et al. 2007). Pillay et al. (2006) reported hypoactivation in amygdala and cingulated cortex in response to fearful faces in panic disorder (PD) patients, compared with controls. We hypothesized abnormal amygdala and insula activation in response to interpersonal threat stimuli, in patients with panic disorder, and patients with social phobia. To test these hypotheses, we conducted an event-related fMRI study of 33 individuals diagnosed with PD, 28 patients with social phobia (SP) and 64 healthy controls (HC). Brain activation was measured during presentation of positive, negative, neutral facial expressions and scrambled faces, in a gender discrimination task. For PD compared with HC, preliminary results showed increased visual cortex activation, in response to negative facial expressions and prefrontal cortex activation, in response to happy and neutral faces. SP patients compared with HC showed increased right hippocampus activation in response to neutral faces and increased left frontal middle gyrus and inferior temporal activation in response to happy faces. Further, comparing the two groups of anxiety disorder, SP versus PD, we found increased hippocampus activation in response to fearful and sad facial expressions. Moreover, increased prefrontal cortex activation was found in PD compared with SP. These results suggest: 1) that a specific neural network is responsible for emotional perception for each of the two different anxiety disorders considered; 2) that these patterns of neuronal activation are different from the activation pattern seen in HC. Increased hippocampus activation may be specific for SP. No evidence for differential

activation in amygdala and insula, to emotional faces was found in PD compared with HC or compared with SP.

EARLY LIFE STRESS MAY PREDISPOSE INDIVIDUALS TO SUBSTANCE ABUSE

Faure, F.[1], Stein, D.[2], Daniels, W.[1]

[1]Department of Biomedical Sciences, University of Stellenbosch; [2]Department of Psychiatry, University of Cape Town

Recent epidemiological data from the Medical Research Council's South African Community Epidemiology Network on Drug Use (SACENDU) show that methamphetamine ('tik-tik') abuse has grown to alarming proportions in South Africa and in particular the Western Cape. Since many clinical studies show that substance abuse often co-morbids with stress-related disorders, the present study investigated whether early life stress could be a precipitating factor in the development of drug preference behaviour. Maternal separation is a useful model to study the effects of early life stress in animals, while a classical conditioning strategy was adopted to investigate the development of drug-induced place preference. All drugs of abuse exert their addictive effects by altering mainly the dopaminergic transmission in the brain. Apomorphine (a dopamine receptor agonist) – induced locomotor activity was used to evaluate the function of the dopaminergic system. Preliminary data indicated that maternal separation results in a prolonged methamphetamine-induced preference behaviour; and reduced locomotor activity upon apomorphine administration to methamphetamine-treated animals. These results show that repetitive use of methamphetamine may cause a down-regulation of dopaminergic receptors which may be worsened by maternal separation. The study therefore suggests that early life stress may disturb the normal functioning of the central dopaminergic system that may predispose individuals to substance abuse.

THE RELATIONSHIP BETWEEN BEHAVIOURAL INHIBITION, ANXIETY DISORDERS, DEPRESSION, AND CD4 COUNTS IN HIV POSITIVE ADULTS: A CROSS-SECTIONAL CONTROLLED STUDY

Fincham, D.1, Smit, J.2, Carey, P.1, Stein, D.J.[1], Seedat, S.[1]

[1]MRC Unit on Anxiety and Stress Disorders, University of Stellenbosch; [2]Birmingham Children's Hospital

This study examined the relationships between behavioural inhibition, shyness, anxiety disorders, and stage of HIV illness among treatment-seeking HIV infected adults. Results indicated that while behavioural inhibition was significantly positively correlated with agoraphobia, social phobia, generalized anxiety disorder (GAD), and posttraumatic stress disorder (PTSD), shyness was not correlated with any anxiety disorder. In addition, neither behavioural inhibition nor shyness was significantly correlated with stage of HIV illness. The only anxiety disorder significantly associated with stage of HIV illness was panic disorder with agoraphobia. There were no significant gender effects for behavioural inhibition, shyness, stage of HIV illness, or an anxiety disorder diagnosis. The DSM-based Generalised Anxiety Severity Scale (DGSS).

THE DSM-IV-BASED GENERALISED ANXIETY DISORDER SEVERITY SCALE (DGSS): PRELIMINARY VALIDATION USING DATA FROM A TRIAL OF AGOMELATINE VERSUS PLACEBO

Stein, D.J.[1,2], Fincham, D.[2], Seedat, S.[2], Ahokas, A.[3], Fabiano, A.[4]

[1]Dept of Psychiatry, University of Cape Town; [2]Dept of Psychiatry, University of Stellenbosch; [3]Lääkärikeskus Mehiläinen, Helsinki; [4]Institut de Rechereches Servier (IRIS), Paris

Background: The Hamilton Anxiety Rating Scale (HAMA-A) is the most commonly used symptom severity measure in trials of generalized anxiety disorder (GAD). However, the nosology of this disorder has changed over time, with the DSM-IV-TR diagnostic criteria currently being the most widely used. It would seem appropriate to develop a DSM-IV-TR based GAD symptom severity scale (DGSS). **Method:** The DGSS, comprising 8 DSM-IV GAD symptoms assessed in terms of frequency and intensity was used in a trial of agomelatine and placebo for the treatment of GAD. Internal reliability, concurrent validity, and responsiveness to change of the DGSS were assessed. Thereafter, an exploratory factor analysis was performed to derive the factor structure of the DGSS. **Results:** The DGSS demonstrated acceptable internal reliability, correlated significantly with the HAM-A and CGI-S, and demonstrated a clear change in response to active medication. Furthermore, a two-factor structure of the DGSS was successfully derived. **Conclusion:** The DGSS is potentially a useful scale for the assessment of GAD in clinical trials of this disorder.

EXPLORATORY AND CONFIRMATORY FACTOR ANALYSIS OF THE MULTIDIMENSIONAL ANXIETY SCALE FOR CHILDREN (MASC) AMONG ADOLESCENTS IN THE CAPE TOWN METROPOLE OF SOUTH AFRICA

Fincham, D.[3], Schickerling, J.[1], Temane, M.[1], Nel, D.[2], De Roover, W.[3], Seedat, S.[3]

[1]Department of Psychiatry, University of Potchefstroom; [2]Department of Statistics, University of Stellenbosch; [3]Department of Psychiatry, University of Stellenbosch

Background: There are no published data on the factor structure of the Multidimensional Anxiety Scale for Children (MASC) among adolescents in the Cape Town metropole of South Africa. **Objectives:** (i) To establish the exploratory factor structure of the MASC using a principal components exploratory factor analysis (EFA), (ii) to confirm the derived factor structure using confirmatory factor analysis (CFA), and (iii) to examine gender, age, and race effects among adolescents in the Western Cape of South Africa. **Method:** A convenience sample of 1051 adolescents was selected from nine different schools in the Cape Town metropole of South Africa. **Results:** An EFA yielded a four factor structure congruent to the factor structure established previously in other samples. Furthermore, the CFA showed that the four factor structure fit the data well. Black participants reported significantly higher levels of Harm Avoidance than other racial groups, and Black and Coloured (Mixed race) participants reported significantly higher levels of Anxious Coping than White and Asian participants. Black and Coloured participants reported significantly higher levels of Separation/Panic than

White participants, and Black participants reported higher levels than Asian and Coloured participants. Finally, there were no significant age effects but females scored significantly higher overall and on all MASC subscales. **Conclusion:** The MASC appears to be a useful tool for assessing and distinguishing anxiety symptoms among adolescents in the Cape Town metropole of South Africa.

RECOGNITION OF ANXIETY IN SUBSTANCE USE AND PSYCHOSIS

Gilbert, M., Wyman, K., Castle, D., Chamberlain, J.
Dept of Psychiatry, University of Melbourne

Background: The dual diagnosis of substance use and psychosis is common and a number of treatment programs target this comorbidity. The term dual diagnosis may be misleading as research suggests that people with substance use and psychosis often experience a further diagnosis such as anxiety. **Aims:** This study examines the prevalence of anxiety in a sample of people with dual diagnosis; the relationship between anxiety and other psychopathology; and, the rate that anxiety was identified by client's case managers. **Method:** Data was collected from 87 outpatients identified by their case manager as having psychosis and substance use. Participants were administered the Mini International Neuropsychiatric Interview (MINI), Montgomery and Asberg Depression Rating Scale, Brief Psychiatric Rating Scale, Severity of Dependence Scale, World Health Organisation Quality of Life Scale and Locus of Control of Behaviour Scale. Their case managers completed the Health of the Nation Outcome Scales (HONOS). **Results:** 56% of participants had one or more anxiety disorders. Those with anxiety disorders compared to those without had greater psychiatric symptomatology and a poorer quality of life. Similarly the number of anxiety disorders was associated with psychopathology and quality of life; with more anxiety disorders being associated with worse outcomes in these domains. Case managers did not identify anxiety in 38% of clients who had an anxiety disorder according to the MINI. **Conclusion:** Anxiety in people with psychosis and substance use is an important area for further research and clinical attention.

IDENTIFICATION AND VALIDATION OF NOVEL SUSCEPTIBILITY GENES FOR ANXIETY DISORDERS

Hemmings, S.M.J.[1], Stein, D.J.[2 3], Uys, J.[4], Faure, J.[4], Moolman-Smook, H.[1]
[1]Division of Molecular Biology and Human Genetics, University of Stellenbosch; [2]MRC Unit for Anxiety and Stress Related Disorders, University of Stellenbosch; [3]Department of Psychiatry, University of Cape Town; [4]Department of Physiological Sciences, University of Stellenbosch

Anxiety disorders are the most common of all the psychiatric disorders, with a lifetime prevalence rate of 25%. These disorders are multifactorial, complex disorders with a significant portion of the aetiology due to genetic contributions. Most efforts at genetic mapping in anxiety disorders have focussed on candidate gene strategies, in which candidates are selected based on the limited existing knowledge regarding the pathophysiology of the disorders. The result is that the ''usual suspects'' are chosen as candidates in these studies, which frequently tend to be replicative rather than exploratory in approach. The present study aimed to identify and validate novel candidate genes that may play a role in the development of anxiety disorders. The effects of early-life trauma on global gene expression were investigated in the striata, frontal cortices and hippocampi of twelve male Sprague-Dawley rats, using PCR-based suppression subtractive hybridisation (PCR-SSH) methodology. Genes that were found to be up- or down-regulated included those that could be categorised as encoding proteins involved in cell signalling and differentiation, neurotransmitter uptake and/or release, as well as scaffolding proteins. Interestingly, overall, the most abundant category of proteins was found to be mitochondrial, especially in the striatum, where more than half of the differentially expressed genes were found to code for mitochondrial proteins. Genes identified by PCR-SSH as being up- or down-regulated during TDS-stress were validated using real-time RT-PCR. This study forms part of a larger study identifying novel susceptibility genes in anxiety disorders, and may help shed light on regulatory mechanisms underlying anxiety disorders.

FUNCTIONAL IMPAIRMENTS OF SOUTH AFRICAN CHILDREN AND ADOLESCENTS WITH OBSESSIVE-COMPULSIVE DISORDER

Hoppe, L.J., Bowles, S., Thomas, K.G.F.
ACSENT Laboratory and University of Cape Town

Background: The nature and extent of functional impairments in South African children with Obsessive-Compulsive Disorder (OCD) are not yet known. However, American and Scandinavian children with OCD are functionally impaired in multiple (and different) domains. In the only two studies conducted thus far on childhood OCD-related functional impairment, Piacentini et al. (2003) found that American children are more significantly impaired in the home and school domains compared to the social domain; Valderhaug and Ivarsson (2005), in contrast, found that Scandinavian children's impairments are mainly in the home domain. **Methods:** Participants were 8 South African children with OCD (mean age = 13 years; SD = 3.33) and their parents. The Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (KSADS-PL), the Children's Global Assessment Scale (CGAS), the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS) and the Child Obsessive-Compulsive Impact Scale-Revised (COIS-R) were used to assess children's past and current psychopathology, OCD symptom severity and OCD-related functional impairment. **Results:** Parents reported that school was the most significantly impaired domain; children, in contrast, reported significant functional impairments in both school and social domains. Overall, children rated more problems as being significant than did parents. Furthermore, parents and children differed regarding their ratings of the most significant individual functional problems. For instance, parents rated concentrating on school work as their child's most significant functional problem, whereas children rated going shopping or trying on clothes as one of the most significant functional problems. **Conclusion:**

These pilot study findings differ from those of previous studies in this domain, and thus provide the rationale for future research examining the effect of culture on childhood OCD-related functional impairment. This future research will have its most important implications in terms of alerting clinicians to the importance of considering culture when diagnosing and treating childhood OCD.

DOUBLE BLIND STUDY IN PATIENTS WITH OBSESSIVE COMPULSIVE DISORDER AND CO MORBID ADDICTIONS TREATED WITH NEUROMODULATION IN INFERIOR THALAMIC PEDUNCLE

Nicolini, H.[1,4,5], Jimenez, F.[2], Velasco, F.[2], Salin-Pascual, R.[1,3], Velasco, M.[2], Velasco, A.L.[2], Castro, G.[2], Lanzagorta, N.[1]

[1]Carracci Medical Group, Mexico City; [2]Functional Neurosurgery, Stereotactic and Radiosurgery Unit, Mexico's General Hospital; [3]Psychiatry and Medical Psychology Department, National Autonomous University of Mexico; [4]Genomic Sciences Postgraduate School, Mexico City Autonomous University; [5]Mexican Association for OCD, Mexico City

Background: Neuromodulation of limbic targets is a surgical treatment that promises success in the treatment of obsessive-compulsive disorder (OCD). The inferior thalamic peduncle (ITP) is a bundle of fibers connecting the orbito-frontal cortex with the non-specific thalamic system, in a small area behind the fornix and anterior to the polar reticular thalamic nucleus. Electrical stimulation elicits characteristic frontal cortical responses that confirm correct localization of this structure. We have successfully used this technique in the treatment of resistant depression. **Methods:** A double-blind protocol of neuromodulation was performed in three patients with OCD refractory to conventional treatments with co morbid cocaine, alcohol and tobacco dependence. Patients were invited to participate after signed informed consent (IRB reviewed) and having additional support from a medical committee. Bilateral stereo tactic implantation of cuadripolar electrodes was made in order to produce neuromodulation of bilateral ITP. Patients had bilateral eight-contact electrodes stereo tactically implanted for stimulation of areas in and around the ITP. Electrode's position was corroborated by unilateral electrical stimulation searching for recruiting responses and regional direct current shifts in the EEG. Patients underwent a double-blind period during one month, (with stimulation ''ON'' or ''OFF''). Afterwards, all patients had a neurostimulation ''ON'' period during the next 12 months. Assessments were obtained every three months during the one-year follow up stimulation. Diagnosis and disease severity were evaluated through the study with several scales. Statistical analysis was performed using Friedman and Wilcoxon tests, with the SPSS package. **Results:** Obsessive and compulsive symptoms decreased on average 50% by means of the YBOCS, and GAF improved from 20 to 70%. A neuropsychological battery did not show changes and side effects before and after stimulation excites. Drug and alcohol dependence measurements did not improve at all. **Conclusions:** Neuromodulation of bilateral ITP seems to improve OCD symptoms, but addiction behavior was not improved at all. These results may be against a growing body of literature that proposes common neurobiological pathways between addiction and OCD.

ONLINE INFORMATION PORTAL FOR EVIDENCE-BASED RESEARCH ON ANXIETY AND TRAUMA-RELATED DISORDERS

Ipser, J., Stein, D

Dept of Psychiatry, University of Cape Town

Background: The Internet has fast become one of the major sources of health-related information. Previous reviews of information on the Internet for the treatment of a variety of conditions have generally found the quality of the information to be poor. The availability of low quality information can have particularly profound consequences with regards to anxiety disorders, as this class of disorders are highly prevalent, and can result in severe impairment and high personal and socio-economic costs. It was for this reason that we decided to develop a website providing access to evidence-based information on the aetiology, phenomenology and treatment of anxiety disorders. **Objectives:** To construct of "proof of concent" pilot website containing up-to-date information on, and serving as a resource for, the evidence-based characterisation and treatment of anxiety disorders (with emphasis on trauma). This website forms part of the Cross-University Brain and Behaviour Initiative (CUBBI - http://www.psychiatry.uct.ac.za/cubbi/). The target audience for this information portal includes clinicians, patients with anxiety disorders, their family members, as well as service providers of evidence-based information on treatment interventions (eg. Cochrane Collaboration) and the general public. **Methods:** The site was developed using the Smarty PHP template engine (http://www.smarty.net/). The R statistical package (http://www.c-ran.org) forms the computational backend of the system, and is used for dynamic processing of data from randomised controlled trials of treatment interventions for anxiety disorders. Trial data is stored in a MySQL database. All software used in the development of this site is open-source. **Results:** The site currently consists of 3 sections. A section on the diagnosis and assessment of anxiety disorders contains (a) a plain language summary for each anxiety disorder, (b) their DSM-IV diagnostic criteria, and (c) a table of measurement scales used for screening and outcome assessment. The table of measurement scales contains the average validity and reliability statistics for each of these scales, as extracted from the peer-reviewed literature. A section on treatment consists of (a) treatment algorithms for each of the anxiety disorders (b) Cochrane reviews conducted on behalf of the MRC Anxiety and Stress Disorders Research Unit on the pharmacotherapy and psychotherapy of anxiety disorders, (c) cumulative meta-analyses plot charting the evolution of evidence for the efficacy of treatments for post-traumatic stress disorder and social anxiety disorder over time and, (d) a list of meta-analyses of anxiety disorders treatments published in peer-reviewed journals and including Cochrane reviews, with links to their MEDLINE entries. Finally, a section on online resources contains a table of anxiety disorder websites, with accompanying quality and importance ratings from the DISCERN quality rating scale and Google's PageRank system, respectively. Separate links to high quality sites from this table (such as that of the American Association of Anxiety Disorders) are also provided in this section. Finally, this section contains a table containing details of online search engines for the retrieval of published, unpublished and ongoing clinical trials, to assist those who wish to conduct their own

investigations. **Conclusion:** Every effort has been made to ensure that information presented on this website is based on research subscribing to the principles of evidence-based medicine. Planned future additions to the website include sections on the neuropsychology, imaging and genetics of anxiety disorders, with an initial emphasis on PTSD.

TO DETERMINE THE EFFECTIVENESS OF EXPOSURE RESPONSE PREVENTION (ERP), THOUGHT STOPPING (TS) AND COGNITIVE RESTRUCTURING (CR) TECHNIQUES FOR PATIENTS WITH OBSESSIVE DISORDERS.

Khodarahimi, S.
Eghlid Islamic Azad University

20 self-referred cases within a randomized controlled trial investigated in present study. Patients allocated to each of ERP, ST, CR and Control groups and their obsessions during pre-treatment, post-treatment and three and six months follow-up intervals measured by Yale¬Brown Obsessive-Compulsive Scale (Y¬BOCS). The therapeutic groups were different on post-treatment and 2 follow-up measures with control group. In addition, there is any significant difference among therapeutic groups on post-treatment and 2 follow-up assessment which shows therapy beneficiate for obsession elimination for all interventions modes. Within subjects' model analysis indicate therapeutic groups improved significantly while control group continued unchanged. Finally, ERP, ST and CR techniques efficacy for corruption and elimination of obsessional thoughts supported in present investigation.

DULOXETINE 60 TO 120 MG ONCE DAILY TREATMENT FOR THE PREVENTION OF RELAPSE IN ADULTS WITH GENERALIZED ANXIETY DISORDER

Korb, F.[1], Davidson, J. R. T. [2], Wittchen, H.[3], Llorca, P. MD4, Erickson, J.[5]*, Detke, M. J.[5,6,7]; Ball, S. G.[5,7]; Russell, J. M.[5]
*[1]Eli Lilly and Company, South Africa; [2]Duke University Medical School, Durham; [3]Technische Universitaet Dresden, Dresden; [4]C.H.U. Clermont-Ferrand, France; [5]Lilly Research Laboratories, Indianapolis; [6]McLean Hospital/ Harvard Medical School, Boston; [7]Indiana University School of Medicine, Indianapolis; * Current affiliation Orexigen Thereapeutics, San Diego*

Objective: To examine treatment with duloxetine 60–120 mg once daily for maintenance and relapse prevention in adults with generalized anxiety disorder (GAD). **Methods:** 887 patients [mean age=43.3 yrs; 61% female] with DSM-IV TR-defined GAD diagnosis entered open-label treatment with duloxetine 60–120 mg for 26 weeks. Treatment response was defined as ≥50% Hamilton Anxiety Rating Scale (HAMA) total score improvement to a score of ≤11 and clinician improvement rating of "much" or "very much improved" for the last 2 visits of open-label treatment. Patients who completed open-label treatment and met this definition were randomly assigned to receive duloxetine (N=216) or placebo (N=213) for the 26-week double-blind continuation phase. The primary outcome measure was percent of patients who relapsed, defined as either a ≥2 point increase from double-blind randomization in Clinical Global Impressions-Severity rating to a score ≥4 or discontinuation due to lack of efficacy. Role functioning and quality of life were assessed using the Sheehan Disability Scale and Quality of Life Enjoyment and Satisfaction Questionnaire (Short-Form), respectively. **Results:** During the double-blind continuation phase, 41.8% of placebo-treated patients relapsed compared with 13.7% of duloxetine-treated patients (P≤ .001). On secondary efficacy and functioning measures, placebo-treated patients significantly worsened compared with duloxetine-treated patients (P≤ .001, each comparisons). Discontinuation due to adverse events was 13.6% during open-label phase, and 1.9% in the double-blind continuation phase for duloxetine-treated patients. **Conclusions:** Duloxetine treatment was associated with significantly lower relapse rates than placebo, greater maintenance of quality of life and daily functioning, and was generally well tolerated.

THE ROLE OF TRAUMA HISTORY IN PREDICTING ANXIETY DISORDERS: A CROSS-NATIONAL STUDY

Lochner, C.[1], Seedat, S.[1], Allgulander, C.[2], Stein, D.[1], Gerdner, A.[3]
[1]MRC Research Unit on Anxiety and Stress Disorders, University of Stellenbosch [2]Dept of Clinical Neuroscience, Karolinska Institute, Stockholm [3]Mid Sweden University

Background: Increased rates of childhood trauma have been found in patients with anxiety disorders, including social anxiety disorder (SAD) and panic disorder (PD). This study, a collaborative effort between research groups from South Africa (SA) and Sweden entailed investigation and comparison of the predictive role of childhood trauma history in the development of SAD and PD. **Methods:** Given the historical context of SA, it was firstly expected that their rates and severity of childhood trauma would be much higher than that of the Swedish sample. Secondly, it was also expected that a broad range of traumatic experiences in childhood may have a predictive role in the manifestation of SAD and PD in later life in samples from both sites, respectively. Logistic regression analyses were done, with principal diagnoses (SAD or PD) considered as the dependent variables, and sex, age, and the subscale totals of the short form 28-item Childhood Trauma Questionnaire (CTQ) as the independent variables. CTQ data from a convenience sample of controls from SA were subsequently added for comparisons within the SA sample. **Findings:** Our findings confirmed the hypothesis that SA patients with anxiety disorders report much higher rates and more severe childhood trauma compared to their Swedish counterparts. Compared to controls from SA, SA patients also had significantly higher rates of childhood trauma, indicating a possible causative role for trauma in the manifestation of anxiety disorders in later life. However, regression did not confirm specific predictive role for childhood trauma in the development of these conditions. SA males had a much higher chance of developing SAD than females. In Sweden, higher rates of EA were found to be linked with a higher chance of developing SAD compared to PD. **Conclusions:** Although our findings suggest a role for trauma in these conditions, the exact mechanism remains unknown. Other possibly interacting etiological factors need consideration. The relative paucity of literature on the impact and interaction of such factors (including childhood trauma as well as demographic and other clinical factors such as sex, historical context (country)

and genetic influences) on psychiatric morbidity in later life warrants further investigation.

MATERNAL SEPARATION OF RAT PUPS INCREASES THE RISK OF DEVELOPING DEPRESSIVE-LIKE BEHAVIOR AFTER SUBSEQUENT CHRONIC STRESS BY ALTERING CORTICOSTERONE AND NEUROTROPHIN LEVELS IN THE HIPPOCAMPUS.

Marais, L.[1], van Rensburg, S.J.[2], van Zyl, J.M.[3], Stein, D.J.[4], Daniels, W.M.U.[1]

[1]Department of Biomedical Sciences, Stellenbosch University; [2]Department of Pathology (National Health Laboratory Services), Tygerberg Hospital and Stellenbosch University; [3]Department of Medicine, Stellenbosch University; [4]Department of Psychiatry, University of Cape Town

Children that are abused have an increased risk for developing psychiatric disorders later in life, because of the negative effects of stress on the developing brain. We used a maternal separation model in rats to see how neurotrophins, stress hormones, behavior and the antioxidant potential of serum are affected. Rat pups were separated from their mothers for 3 hours/day on days 2-14. Maternal separation causes changes in levels of NGF and NT-3 in the dorsal and ventral hippocampus, increased basal corticosterone levels and decreased ACTH levels after acute restraint stress. The antioxidant potential of the rat serum was significantly lower in the maternal separation group. Depressive-like behaviour, measured during a forced swim test, was seen in maternally separated rats after additional chronic stress during adulthood. Maternal separation caused downregulation of neurotrophins in the ventral hippocampus, possibly as an effect of high corticosterone levels, but compensatory mechanisms against cell death may be involved as neurotrophin levels increased in the dorsal hippocampus. Decreased antioxidant potential of serum could have been an effect of downregulated neurotrophin levels.

COMPARISON OF VISUAL WITH AUDITORY EEG BIOFEEDBACK (NEUROTHERAPY; NT) IN THE TREATMENT OF GENERALIZED ANXIETY DISORDER (GAD)

Moore, N.C.

Dept of Psychiatry, East Tennessee State University

Background: Most studies use eyes-closed auditory EEG biofeedback (neurotherapy; NT) for GAD. It is not known how well these benefits transfer into everyday life, where anxiety is experienced in the eyes-open condition. It is important to know whether eyes-open feedback is more effective in the NT of GAD. **Methods:** Visual was compared with auditory feedback in 10 participants (4 patients; 6 controls). They had 15 one-hour sessions of alpha-enhancement EEG biofeedback. Treatment A was eyes-open visual feedback, B was eyes-closed auditory feedback, and treatment C was eyes-open auditory + visual feedback. Practice effects were matched by using 6 orders of treatment: ABC, ACB, BAC, BCA, CAB and CBA. The Hamilton Anxiety Scale was done at baseline, and at the end of each of the three types of feedback. **Results:** Treatment A increased alpha by 2.34 + 7.01 mV (mean + SD), B by 6.79 + 9.35 mV and C reduced alpha by 1.18 + 8.62 mV. **Conclusion:** Eyes-closed auditory feedback is significantly more effective than eyes-open auditory + visual feedback in increasing alpha (p = 0.03 one-tail; 0.07 two-tail), and in reducing anxiety (p = 0.02 one-tail; 0.05 two-tail).

HYPOBARIC HYPOXIA INDUCED ANXIETY: MOLECULAR MECHANISMS INVOLED THEREWITH

Prasad, D., Hota, S., Barhwal, K., Solanki, P., Baitharu, I., Jain, V., Ilavazhagan, G.

Hypobaric hypoxia associated with ascent to high altitude has been known to adversely effect brain and cognitive functions. Though there have been several reports on memory impairment and alterations in hippocampal and cortical functions in hypobaric hypoxia, its effect on the anxiety levels and on the amygdala has been less studied. The present study aimed at exploring the effect of hypobaric hypoxia on anxiety levels in animal models. Behavioral studies were carried out to assess the anxiety levels in male Sprague Dawley rats exposed to hypobaric hypoxia. Both plasma and brain corticosterone levels were estimated. The expression of glutamate receptors and transporters in the CA1 region of the hippocampus that are reported to play a key role in contextual anxiety, were investigated during the present study. Serotonin levels and expression of serotonergic and glucocorticoid receptors that are critical for the anxiety response were also studied in different brain regions. The anxiolytic efficacy of herbal nootropic compounds in ameliorating hypobaric hypoxia induced anxiety response was also evaluated. The present study revealed the occurrence of anxiety in hypobaric hypoxia and the possible molecular mechanisms involved therewith. In addition the herbal formulation was found to effectively ameliorate hypoxic stress induced anxiety thus opening new vistas for therapeutics.

OUTCOMES SOF SINGLE VERSUS MULTIPLE TRAUMA IN SOUTH AFRICAN YOUTH

Suliman, S., Fincham, D., Kilian, S., Seedat, S.

MRC Research Unit on Anxiety and Stress Disorders, University of Stellenbosch

Background: Exposure to traumatic events has been linked to emotional distress, such as depression, anxiety and particularly the development of post-traumatic symptoms. Recent research suggests that exposure to multiple traumatic stressors is more prevalent than previously thought and a number of studies have shown that multiple exposure to traumatic events is associated with higher levels of psychiatric symptoms. **Objectives:** The current study intends to explore the severity of traumatic reactions in South African adolescents exposed to single and multiple traumatic stressors. **Methods:** 1140 Grade 10 students (mean age: 15.9 ± 1.22 years) from 9 Cape Town schools took part in the survey. Participation was voluntary and all Grade 10 students present on the day of the survey completed the anonymous self-report questionnaires. **Results:** On the Trauma Checklist 82, 7% of the sample reported being exposed to one or more traumatic events. The Childhood Trauma Questionnaire indicated that 88.9% of the sample was exposed to childhood trauma. 22.1% of the respondents reported having experienced PTSD symptoms that meet criteria for PTSD, with adolescents who were

exposed to two or more traumas experiencing more PTSD symptoms than those who were exposed to single traumatic events or no traumatic events at all. 19.7% reported meeting criteria for moderate depression on the Beck Depression Inventory, with adolescents who were exposed to two or more traumas experiencing more symptoms of depression than those who were exposed to single traumatic events or no traumatic events at all. **Conclusion:** adolescents in our sample were more likely to have experienced multiple, rather than single, traumatic events and those who were exposed to more than one traumatic event were more likely to experience symptoms of PTSD and depression than those who experience one or no traumatic event.

THE EFFECT OF PLAY THERAPY IN REDUCING THE ANXIETY OF INPATIENT LEUKEMIC CHILDREN: AN OPEN CLINICAL TRIAL

Shirazi, E.[1], Nersi, M [2], Bazmi, N. [2], Nohesara, S.[1]

[1]Iran University of Medical Sciences, Mental Health Research Centre, Iran; [2]Islamic Azad University, Iran

Background: Hospital admission can cause negative feelings in children. This study was performed to evaluate the effect of play therapy in reducing the anxiety of inpatient leukemic children. **Methods:** In an open clinical trial and with convenience sampling, the effect of play therapy was evaluated in 30, leukemic 9-12 year old children, admitted for 4-10 days in Tehran Children Medical Center for further medical and diagnostic evaluations, in first half of 2004. The play therapy was performed in 3 sessions, each of 1 hour duration, and using 3 play methods: The nervousness play, the doctor-patient play, and the drawing a coloured person play. The Spielberger State Anxiety Scale (SSAS) and the Draw a Coloured Person Test (DCPT) were used to measure the anxiety level as pre- and post-tests. **Results:** There were a significant difference between the pre- and post-tests' scores in SSAS (t=6.46, Pv<0.000) and DCPT. **Conclusion:** Play therapy may be an effective method in reducing the anxiety of inpatient leukemic children. Further studies are warranted.

EARLY ANXIETY AND DEPRESSION AFTER CORONARY ARTERY BYPASS GRAFT SURGERY: ARE THEY RELATED TO POMP-TIME?

Shirazi, E.[1], Shahrivar, Z.[2], Ghadiri, M.[1], Poornamdari, M.[1]

[1]Iran University of Medical Sciences, Mental Health Research Centre, Iran; [2]Tehran University of Medical Sciences, Iran

Background: Anxiety and depression are common psychiatric complications after Coronary Artery Bypass Graft (CABG) in patient undergoing this surgery. During CABG patients are connected to pomp to provide their blood circulation. Pomps although much improved in their standard, are not as efficient as the heart itself. Possible deficiencies in brain's blood circulations may be a precipitating factor for early anxiety and depression that patients experience after CABG. This study was performed to assess the relation of these side effects with the duration of time in which the patients are connected to the pomp (pomp-time). **Methods:** In an observational study and with convenience sampling, the anxiety and depression of 100 patients (72 males, 28 females) who were undergone CABG were measured by Symptom Checklist-90-Revised (SCL-90-R) 10 days after their surgery in 4 hospitals in Tehran during the second half of 1999.Patient with repeated heart surgery, serious medical complications after surgery, other chronic medical disorders, and previous major psychiatric disorders were excluded from the study. **Results:** There were significant differences in the mean scores of anxiety (t=-3.68, Pv<0.001), depression (t=-3.56, Pv<0.001), and Global Severity Index (GSI) (t=-4.45, Pv<0.001) of SCL-90-R between patients with short (<35 minutes) and Long (50 minutes<) pomp-times. The duration of anaesthesia, sex, age, and ejection fraction of patients did not show any relation with anxiety, depression, and GSI after CABG. **Conclusion:** Advancing the technology of pomps to improve their function and advancing surgical methods and the surgeon's skills to decreasing the pomp-times may be helpful in preventing early anxiety and depression after CABG.

DOES MENTAL PRACTICE WORK IN MENTALLY RETARDED STUDENTS?

Prof. Morteza Taheri[1], Abbas Sadeghi[2], sajjad Hosseini[3]

[1]Tehran university; [2]Imam khomeini University; [3]Abhar Azad university

The purpose of the study was to compare the effects of different combination of mental and physical exercise in the acquisition and retention of a motor skill in mentally retarded male students. Subjects were 40 guidance students who novitiate in the criterion skill (Basketball penalty shoot). They were selected randomly and were assigned into 5 groups (4 as experimental and 1 as control) with the same homogeny according to their pretest scores, IQ and based on their ability in mental imagery. The groups were as follow; 1: Physical, 2: Internal imagery, 3: External imagery, 4: Physical + Internal imagery, 5: Internal imagery + physical, 6: Physical + external imagery, 7: External imagery + physical and 8:control.They were taught how to perform the criterion skill. They exercised for 8 weeks; 3 sessions per week with 30 trails exercise in each session. All of the experimental methods caused significant improvement in the performance and learning of the motor skill in subjects, and significant differences were found among the different groups.

A FIVE-PHASE EXISTENTIAL TREATMENT MODEL FOR ANXIETY DISORDERS

Venter, H.

Department of Psychology, National University, San Diego

Despite its long and rich history, existential psychotherapy has remained largely on the fringes of mainstream practice and under-utilized in the treatment of anxiety disorders. A lack of clear definition and cohesiveness, being too esoteric, abstract, and vague, difficult to evaluate quantitatively with little practical application are cited as some reasons for its under-utilization. There has been a call for a more succinct, well-defined, and structured approach to existential psychotherapy to make it more practical and usable. It is the aim of this paper to describe a tangible and practical five-phase therapy model based on the core set of existential theory. It translates existential theory into a counseling process that is more readily accessible to practitioners and

one that provide a measurable impact on counseling outcomes. The five phases are: Impact; Meaning; Process; Action; Continuity (IMPAC). The model was utilized in the treatment of a Caucasian female with suffering from an anxiety disorder. The efficacy was evaluated by a single-case (N=1) Experimental Design with a baseline followed by a post-treatment assessment. The results showed a significant decrease in symptoms based on a comparison of the baseline data and the post-treatment assessment. This case of a patient suffering from anxiety showed that existential counseling is not only meant for well-adjusted individuals. The newly developed model effectively translated existential theory into a practical counseling process with a quantifiable outcome. It provided a measurable impact of the counseling outcome and allows for future experimental research. The IMPAC model makes existential therapy more readily accessible to practitioners and shows promise for use in patients with anxiety disorders.

ANXIETY DISORDERS REDUCTION PROGRAM AND QUALITY OF LIFE IN BREAST CANCER PATIENTS SUSHKO

Vyacheslav, V.[1], Sushko, V.[1 2]

[1]Odessa State Medical University, Odessa, Ukraine; [2]Odessa Regional Cancer Hospital, Odessa, Ukraine

Background: Women with breast cancer suffer from considerable stress related to the diagnosis, surgery, and medical treatment. Anxiety disorders are common problem and have a significant impact on the quality of life among breast cancer patients. **Aims:** The purpose of the present study was to investigate the effect of anxiety disorders reduction program for reducing anxiety disorders and improving quality of life in breast cancer patients after mastectomy. **Methods:** The study group included 87 breast cancer patients with anxiety disorders, aged 45-65, (stage I-II), after mastectomy, in Odessa Regional Oncology Hospital. The assessments were conducted before the intervention, after the intervention, and one year after the intervention and included psychiatric diagnostic interview and several self-reported measures regarding psychological distress (Symptom Distress Scale), anxiety (Profile of Mood States, Spielberger's State-Trait Anxiety Inventory), and quality of life (Quality of Life Test). The patients' of the study group participated in a four-week anxiety disorders reduction program that included coloring therapy and melatonin in a doze of 0,006 g/day, for 30 minutes before sleep. Two-hour, daily coloring therapy was used for management of the inner dialogue. The patients of control group have received traditional treatment for anxiety disorders. **Results:** Results of study include reduction in anxiety (decreased in anxiety-related indices ($p < 0.001$)) and improved coping skills after anxiety disorders reduction program. The effect of anxiety disorders reduction program was manifested by improved quality of life ($p < 0.01$), better appearance habitus and adaptation ($p < 0.01$). The anxiety disorders reduction program reduced reports of thought intrusion, interviewer ratings of anxiety, and emotional distress across one year significantly more than was seen with the control condition. **Conclusion:** The anxiety disorders reduction program is feasible, is a promising strategy for reducing anxiety disorders in breast cancer patients.

ASSOCIATION BETWEEN UTERINE ARTERY PULSATILITY INDEX AND ANTENATAL MATERNAL PSYCHOLOGICAL STRESS

Vythilingum, B.[1,2], Geerts, L.[3], Roos, A.[2], Faure, S.[2], Stein D.J.[1,2]

[1]Dept of Psychiatry, University of Cape Town; [2]MRC Research Unit on Anxiety and Stress Disorders, University of Stellenbosch; [3]Dept of Obstetrics and Gynaecology, University of Stellenbosch

Background: Antenatal maternal stress has been associated with poor obstetric outcomes, such as preterm labor, interuterine growth restriction and small for gestational age babies. [Hedegaard et al 1993, Lou et al 1994]. Altered fetoplacental blood flow has been postulated as a possible mechanism for these finding. However, studies of uterine blood flow show contradictory results. (Sjorstrom et al 1997,Texeira et al 1999, Kent et al 2002). **Objective:** To investigate whether maternal stress during pregnancy is associated with changes in uterine artery pulsatility index (PI). **Methods:** Uterine artery blood flow was assessed using colour Doppler ultrasound and maternal stress was measured using the K10 in 46 women at 13 weeks, 21 weeks and 32 weeks of gestation. A score on the K10 of > 20 indicates severe psychological distress, with a > 95% chance of having an Axis I psychiatric disorder. **Results:** Scores of >20 on the K10 were associated with significantly higher pulsatility index at 32 weeks ($p=0.011$) but not at 13 or 21 weeks. **Conclusion:** The results of this study show a relationship between maternal stress and uterine artery flow during the third but not the first or second trimester. This is in keeping with previous work and suggests that effects of stress on uterine artery flow are modulated by gestational age. Further studies are needed to examine this relationship and assess the effects of confounders such as smoking and alcohol use.