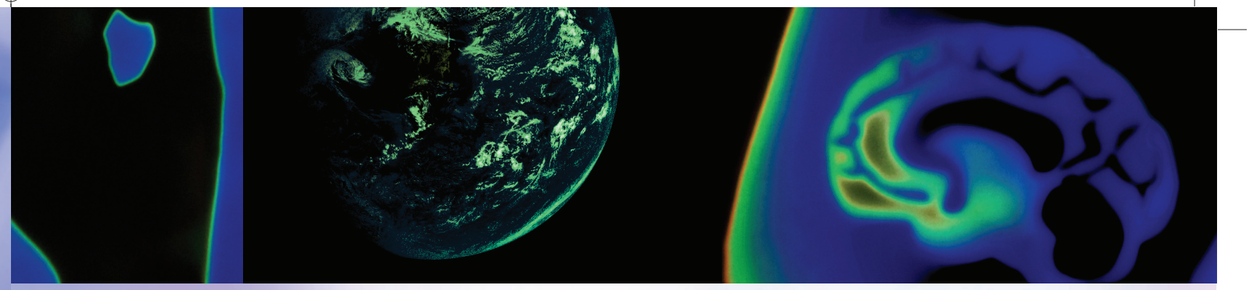

International Journal of

Psychiatry in Clinical Practice

EDITOR Siegfried Kasper

ASSOCIATE EDITORS Naomi Fineberg and Eric Hollander

13th international Forum on Mood and Anxiety Disorders
Monaco, 20–22 November 2013

ISSN 1365-1501

www.informahealthcare.com/jpc

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healthcare

Volume 17 Supplement 2 2013

International Journal of

Psychiatry in Clinical Practice

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13th International Forum on Mood and Anxiety Disorders
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Abstract book

Editors:
Siegfried Kasper
Stuart Montgomery

www.ifmad.org

Int J Psychiatry Clin Pract 2013; 17(Suppl 2): 1–38. © 2013 Informa Healthcare
ISSN 1365-1501 print/ISSN 1471-1788 online. DOI: 10.3109/13651501.2013.851555

International Journal of
Psychiatry in
Clinical Practice
informahealthcare.com/ijpcp

SO 01. Lithium Medicine or Myth

SO 0101. Lithium in the acute treatment of bipolar disorder

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In recent years the evidence base on lithium for bipolar disorder has substantially increased due to results from a number of industry generated approval trials, in which a lithium arm has been included to test the sensitivity of the study assay.[1] Accordingly, lithium has a major position in various recent evidence based treatment guidelines on bipolar disorder.

This presentation will in detail discuss the position of lithium in the recent updates of treatment guidelines on mania and on bipolar depression from the World Federation of Societies for Biological Psychiatry (WFSBP).[2,3] In these guidelines, the scientific evidence was categorized into six levels of evidence (A-F), where A is highest. Since these guidelines were intended for clinical use, each drug was additionally assigned a recommendation grade (1–5) which besides the evidence for efficacy reflected tolerability and practicability.

Despite the highest level of evidence for the acute anti-manic efficacy of lithium, the recommendation grade was 2, based on the mandatory requirement of monitoring the serum lithium concentration due to the risk of toxicity. Additionally, this requirement may lead to a relative delay in the onset of full action of lithium, limiting its role in the highly agitated patients. For bipolar depression lithium was given a low recommendation grad e of 5 due to conflicting evidence. However, in these guidelines also treatments assigned such low recommendation grade were considered first line treatments due to the few available options.

Taken together, lithium still has a substantial role to play in the acute treatment of bipolar disorder, in particular in mania, and not only in combination with other drugs but also occasionally in mono-therapy. A main advantage of using lithium acutely is its high level of evidence for subsequent prophylactic efficacy.

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SO 0102. Bipolar maintenance treatment

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Starting with Kraepelin, several long-term observational studies have demonstrated that the duration of the symptom-free interval is inversely linked to the number of episodes.[1] Likewise, aspects of cognitive impairment are associated with increasing episode frequency[2] leading to lasting psychosocial and work impairment. Finally, bipolar disorder is associated with an excess mortality including an increased risk of suicide.[3] Thus, prevention of new episodes is one of the ultimate goals in treating bipolar disorder. Long-term treatment in bipolar patients is traditionally divided into continuation and maintenance (or prophylactic) treatment, which are, in turn, associated with the starting points "remission" and "recovery", respectively. The fast majority of long term treatment regimens develop out of an acute treatment plan which has lead to symptomatic remission. Thus, and with the exception of lithium, the majority of evidence has been derived more recently from prolongation studies of acute responders to antimanic or antidepressive treatment in an enriched design. Aspects as enrichment and the ability to distinguish between relapse and recurrence need to be considered when giving recommendations for long-term treatment. Taking these aspects into account, the 2012 WFSBP guideline[4] backs up the still exceptional position of lithium, but also supports the evidence - based use of aripiprazol, carbamazepine, lamotrigine, olanzapine, quetiapine, and risperidone as monotherapies, together with some rigorously tested combination treatments.

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SO 0103. Lithium: Still the gold standard for augmenting antidepressants

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Antidepressant non-response remains an important issue in clinical practice. How best to deal with those patients who fail to respond or achieve remission is a continued source of controversy. While several approaches are in routine use for augmenting antidepressants, there are few studies available which directly compare these strategies. Undoubtedly, the use of lithium to enhance antidepressant response is the most extensively studied approach. There are now over 30 open-label studies and 10 placebo controlled studies supporting the efficacy of lithium. All commonly used antidepressants have at some stage been effectively combined with lithium. Currently available data support the view that more severely ill patients are likely to respond to lithium. In one random allocations study patients received either a tricyclic antidepressant together with lithium or a three week course of electroconvulsive therapy (ECT). The response rate in both treatment groups was similar but those given lithium responded more rapidly than those given ECT. Furthermore, where patients respond to both lithium and an antidepressant it is clear that for successful remission the combination needs to be sustained.

How does lithium produce a therapeutic response? It is a substance with a very broad spectrum of action and despite the fact that it has been in widespread therapeutic use in psychiatry for almost half a century the precise mechanism of action is not known. It does have the capacity to block key enzymes such as adenyl cyclase and GSB3β. Inhibition of the latter enzyme is associated with neurotrophic activity. A single nucleotide polymorphism within the promoter region of the GSB3β gene is associated with a good response to lithium augmentation.

Lithium remains the gold standard for antidepressant augmentation and the data for such an approach vastly outweighs that for any other strategy.

SO 02. The Hurtful Brain

SO 0201. The comorbidity of pain, anxiety and depression

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Pain, anxiety and depressive symptoms are commonly experienced symptoms which may – if severe, persistent and impairing – reach the criteria for a disease or disorder according to DSM-5 or ICD-10 (e.g. major depression, anxiety disorder, pain disorder). The reciprocal relationships between symptoms of pain, anxiety, and depression are well known and have been extensively examined on a dimensional level over the past decades. Only more recently, research also began to examine more closely the comorbidity between pain, anxiety and depression on a diagnostic level. For example, the National German Health Survey revealed that about every fourth adult with a pain disorder experienced a clinically relevant depressive disorder; every third met criteria for an anxiety diagnosis. The comorbidity of pain, anxiety disorders and/or depressive disorders is associated with tremendous negative consequences. For example, depressed patients with pain syndromes have a worse health related quality of life and higher rates of work days lost compared to patients without depression. At the same time, however, their help seeking behaviour due to emotional problems is reduced or delayed. Further, the prognosis for depressive patients is worse if they have co-occurring pain. Comorbid anxiety and depressive disorders are associated with an increased chronicity of pain syndromes. Thus, the comorbidity of pain, anxiety and depression is associated with considerable individual and societal burden and enormous direct and indirect costs.

SO 0202. Explaining the co-occurrence of pain, anxiety and depression

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Anxiety disorders and major depression frequently co-occur with various medical conditions including chronic pain. Comorbid chronic pain in these psychiatric conditions leads to worse outcomes and thus recognition in an early stage is important. The high degree of comorbidity between pain, anxiety and depression suggests that these conditions may share multiple neurobiological underpinnings.

Several hypotheses have been put forward to explain this relationship. 1) The pain matrix which is the brain network activated by pain-stimuli shows extensive overlap with neural networks implicated in anxiety and depression. 2) Dysregulation of stress/inflammatory pathways as witnessed by increased concentrations of pro-inflammatory cytokines promotes changes in brain circuitry that modulate mood, pain and anxiety levels. In depression and anxiety, as well as in pain increases have been observed in IL2, IL6 and TNF-α 3). A series of neuroimaging studies found that perception of pain can be influenced by inducing variations in mood and anxiety. In our own fMRI study we found that in healthy volunteers which are stratified on the basis of the level of their anticipatory anxiety, differences can be found in the response to pain stimuli. Interestingly healthy subjects with a high degree of anticipatory anxiety showed increased activation in the insula, prefrontal cortex and hippocampus, which also belong to the pain matrix. Available evidence converges to suggest that this bidirectional relationship could be explained by dysfunctions in overlapping neural networks and illustrate that there is a strong shared neuroanatomy between pain, anxiety and depression.

SO 0203. Psychotropics as treatments for pain

Michael Bach
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For the pharmacological management of pain conditions, not only the classical non-opioid and opioid analgesics are well established, but also a number of so-called "adjuvant analgesics". Among these, psychotropics play an increasing role during the last decades. Predominantly, antidepressants have shown efficacy for various pain syndromes, such as headache, fibromyalgia, neuropathic pain and others. The rationale for their use is supported by several lines of evidence. First, antidepressants are well-established treatments for mood and anxiety disorders that are common comorbid conditions in patients with chronic pain syndromes. Common pathways may involve signal transmission between amygdala, anterior cingulated cortex, and prefrontal cortex, as well as their modulation by antidepressants. Second, the chronification of pain is currently conceptualized through increased excitation and decreased inhibition of ascending pain pathways. Serotonin and norepinephrine are key transmitters in descending pain inhibitory pathways in the brain and spinal cord. Increasing the availability of these monoamines by antidepressants may promote pain relief. In addition, some of the antidepressants may play a role as NMDA antagonists and ion-channel blocking agents that may also mediate antinociceptive effects. The most effective antidepressants in chronic pain treatment are dual acting compounds, such as SNRI and tricyclics. However, properly conducted dose finding studies are still warranted for most of these compounds. In contrast, the role of antipsychotics as adjuvant analgesics still remains unclear with regard to their potential efficacy as well as their mechanism of action. Finally, tetrazepam and other benzodiazepines have been widely used for pain treatment due to their muscle relaxing component. However, several side effects limit their clinical use.

SO 03. Recovery – The New Treatment Goal in Depression? – A Debate

Moderator: Alan G. Wade, CPS Research, University of Strathclyde, Glasgow, UK
Debaters: Koen Demyttenaere, University Hospital Gathuisberg, Leuven, Belgium - Thomas E. Schlaepfer, Department of Psychiatry and Psychotherapy, University Hospital Bonn, Germany

Evaluation of treatment of depression is usually measured in terms of symptom reduction, often defined as response, remission and recovery (1). Response is typically defined as at least 50% improvement using a depression rating scale. Remission is usually defined as a score of 7 or less on the HAM-D (17 item version), or 10 or less on the MADRS. Remission can, therefore, be accompanied by residual symptoms that may be bothersome and even be associated with worse prognosis (2). Recovery is essentially a state of absence of depressive symptoms, but different definitions of recovery have been proposed (3). From a patient perspective, recovery may be exiting a depressive episode feeling in emotional control and participating in and enjoying relationships with family and friends (4).

Taking both patient's perspectives and traditional symptom assessment into consideration, this debate will address the following questions related to the optimal treatment goal for major depression:

- Is recovery a better treatment goal than remission?
- How should recovery be defined?
- What assessment tools should be used for evaluating whether the treatment goal has been achieved?
- What would be the best approach to changing treatment for patients not achieving the treatment goal upon antidepressant therapy?

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SO 04. Cognition as a Treatment Target in Mood Disorders

SO 0401. Cognition as a treatment target in obsessive compulsive disorders

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Obsessive-compulsive disorder (OCD) is a disabling illness characterised by obsessions (distressing, intrusive thoughts) and compulsions (repetitive, unwanted, stereotyped behaviours). Patients with OCD are significantly impaired in a broad range of cognitive tasks. However, the extent to which these deficits impact on everyday function, or influence treatment-response, remains unclear. The Cognitive Assessment Instrument of Obsessions and Compulsions (CAIOC-13) is a new scale that attempts to quantify the functional impact of cognitive impairment in OCD. A better understanding of the neuropsychological basis for these changes may guide treatment–allocation and drive forward development of more effective and perhaps faster acting therapeutics.

Accumulating evidence implicates underlying dysregulation of fronto-striatal neurocircuitry and monoamine systems. These abnormalities represent targets for existing

and novel treatment interventions. Failures in cognitive and motor inhibition have been demonstrated in OCD patients and unaffected family members and may represent trait markers for the disease. Structural brain imaging in OCD families has demonstrated changes in grey matter volume that correlated with the magnitude of the impulse-control deficit. Additionally, functional MRI probes of orbitofrontal integrity have identified under-activation in these neural systems during reversal learning. Functional disconnection of the orbitofrontal cortex was also found in individuals with OCD and stimulant dependence during rest. These data implicate a failure of top-down cortical inhibition, releasing striatally-mediated compulsive activity. Thus, compulsive symptoms could emerge from imbalance of activity within frontal cortex or striatum, or both.

Different circuits within the striatum may mediate goal-directed and habit-learning, with OCD biased towards habit. Enhanced avoidance-habits in OCD, which readily become compulsive, may have the capacity to create irrational fears that may in turn encourage repetition of the habitual behaviour. Thus, habit formation is another mechanism by which the chronic, self-perpetuating symptoms of OCD might develop. Striatal glutamatergic neurotransmission is thought to modulate goal-directed and habit-learning. Preliminary data suggesting a therapeutic role for ketamine, memantine and lamotrigine, support modulators of the glutamate system as novel therapeutic agents.

SO 0402. The treatment of cognitive deficits in major depressive disorder

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Background. The presence of cognitive deficits in patients with current major depressive episodes is recognised both in the listed diagnostic criteria and by objective tests of cognitive function.[1] There is also evidence for cognitive dysfunction even in the remitted and euthymic state.[2] Cognitive dysfunction is a potential target for psychological and pharmacological treatment, though little is known about the effects of antidepressant drugs on cognitive dysfunction.

Method. We conducted a systematic review of the literature, retrieving meta-analyses of cognitive deficits in depressed patients and studies of the effects of antidepressants on cognition, during major depressive episodes or in the euthymic state. The search was restricted to papers that were in the English language over the last ten years.

Findings. We identified rather few papers that met these criteria. Published studies employed differing tests for each aspect of cognitive function, making it difficult to form comparisons between studies. The findings from meta-analyses indicate that episodic memory, executive function, and processing speed are all correlated with the severity of depressive symptoms. A range of antidepressants, including fluoxetine, duloxetine, reboxetine and Lu AA21004 (vortioxetine) improved some aspects of cognition during the short-term treatment of some depressed patients. For duloxetine and reboxetine, these improvements in cognition were beyond the effect attributable to improved mood alone. Little is known about the time course of cognitive improvements or about the potential relevance of these to everyday functioning.

Implications. It is important to achieve a broad consensus on the preferred measures for assessing cognition. Similarly it would help to establish whether the measured improvements in cognitive function that are seen during short-term treatment persist over time, and to examine these improvements in performance on cognitive tasks translate into beneficial effects in the everyday function.

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SO 0403. Cognitive deficits in bipolar disorder

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Neurocognition has been the focus of extensive research in schizophrenia and, more recently, in bipolar disorder and in depression. Neuropsychological testing may represent a tool able to identify potential neuroimaging markers and endophenotypes and to better understand the underlying neurophysiology. However, only lately the highly consistent findings from research began to be applied to clinical practice, and many clinicians are not yet much aware of how neurocognitive deficits affect their patients' daily life, and, importantly, what can be done to prevent or at least mitigate cognitive impairment. Recent evidence suggests that neurocognitive status may be the most powerful predictor of functional outcome in BD, even more so than clinical features. Cognitive deficits may be related to neurodevelopmental issues, but in bipolar disorder the most accepted model is the "neuroprogression" one, in which recurring episodes and concurrent allostatic load contribute to neuropsychological difficulties and disability. Comorbidities and medication may also contribute to cognitive deficits. Research efforts are now focusing on drugs to ameliorate cognition and psychological interventions, such as functional remediation[1], that may have a positive impact on cognitive and functional outcome.

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SO 05. Cognitive Dysfunction in Major Depressive Disorder – Patient Perceptions and Objective Measures

Cognitive symptoms are common during depressive episodes. In addition, depressive patients in remission often suffer from these symptoms to a level that impairs everyday living. Standard scale-based definitions of response and remission do not fully overlap with patients' perceptions of successful treatment outcomes and the incidence and severity of cognitive symptoms are higher in patients who do not consider themselves to be in remission. This implies a discrepancy between the patients' and the medical community's perception of the importance of assessing and treating cognitive dysfunction of depression. This symposium aims at reviewing these discrepancies, describing the patients who suffer from cognitive dysfunction of depression and the impact of these symptoms on the patients' well-being and suggesting tools for assessment of cognitive dysfunction in depressed patients.

SO 0501. Do patients and physicians have the same perceptions of cognitive symptoms in depression?

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The presence of cognitive deficits in patients with depression is an acknowledged component of the disorder. These specific deficits represent a generalised impairment, which is commonly thought to improve as overall mood lifts. However, the significance of cognitive deficits in patients with depression appears to be under-appreciated: these deficits significantly affect patient function and recovery, are common in otherwise remitted patients and represent an area of unmet need. Increased awareness at all levels of health care will help understanding of the pervasiveness of cognitive dysfunction in patients with depression. Once identified, health-care practitioners have the option of seeking to improve cognition with pharmacological and other interventions. These ambitions would be substantially facilitated by the identification of at-risk cognitive domains and recommendations for appropriate screening measures. In this presentation, we will review the affected cognitive domains, the impact of cognitive impairment on recovery, approaches to appropriate cognitive screening and potential pharmacological strategies to improve cognitive function.

SO 0502. Cognitive dysfunction in depressed patients: prevalence, risks and consequences

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Depression is a commonplace and debilitating life-threatening disorder. By 2030, the World Health Organization projects that depression will become the leading cause of disability. In 2007, lost earnings due to depression amounted to £5.8 billion (approximately $8.7 billion) in England alone, while lower work productivity accounted for a further loss estimated at £1.7–2.8 billion (approximately $2.5–4.2 billion).

Depression is a cognitive disorder, as highlighted by the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition criteria for a major depressive episode. For instance, an individual with depression may have a "diminished ability to think or concentrate or indecisiveness", which are key elements associated with cognitive dysfunction. Depression is recognised as being associated with problems in 'cold' and 'hot' cognition. Early detection of depression is important in order for treatment to be administered early and effectively. This would help patients to achieve good quality of life, well-being and functionality in their daily lives, both at work and at home. Objective measurement of the problems of cognitive dysfunction is necessary in order to achieve this.

SO 0503. Assessment of cognitive dysfunction in depression

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Depressive disorders affect more than 300 million people globally and are projected to become the leading cause of disability worldwide. Studies of cognition in individuals who meet the clinical criteria for major depression indicate that episodic memory, attention and executive function are the most commonly and severely impaired cognitive domains in acute depression. Other domains notably impaired include processing speed, verbal fluency, scanning/visuo-motor, non-verbal learning and mental flexibility.

At first, such symptoms were thought to be entirely attributable to low mood but there is increasing evidence showing that cognitive dysfunction persists even in individuals whose core depressive symptoms have resolved. Moreover, psychotic depression, recurrent depression, depression in the medically ill and vascular geriatric depression may present with prominent cognitive deficits. In the elderly, the differentiation of geriatric depression with cognitive dysfunction from early dementia may present a clinical challenge.

The major consequences of cognitive dysfunction are functional disability and chronicity. Indeed, it has been suggested that executive dysfunction may be a greater predictor of relapse than memory deficits, although this needs further confirmation. Several techniques (eg, structural magnetic resonance imaging [MRI], functional MRI, positron emission tomography and event-related potential) are now available to map and investigate the neural circuit changes underlying cognitive dysfunction in patients with major depression, and research is underway to transfer these tools into routine clinical use. There is also emerging evidence that major depression impairs 'social cognition', which represents the cognitive processes our brain uses to interact with others.

From a clinical perspective, it should be noted that most depression rating scales do not fully capture cognitive symptoms or deficits and hence the magnitude of this problem may be under-appreciated in routine practice. Several neuropsychological tests and self-rated scales are available to screen for cognitive dysfunction and work-related disability, which help to enhance the optimum assessment and management of patients with major depression.

SO 06. Depression, Cognitive and Negative. Symptoms in Schizophrenia: Underlying Neurobiology and Novel Leads for Pharmacological Treatment

SO 0601. Do depressive cognitive and negative symptoms impact on outcome in schizophrenia?

Hans-Jürgen Moeller
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Cognitive, depressive and negative symptoms have great importance in patients with schizophrenic psychoses. They are highly prevalent during the course of illness at different timepoints like first admission to hospital, readmissions , follow up assessments. They are somewhat connected to different degrees at different time points, but principally they are independent dimensions, which can be assessed using validated rating scales. There timecourse is different: while depressive symptoms have a pattern of being mostly transient, cognitive symptoms as well as negative symptoms have e tendency to be persistent on a similar level or even declining. All these symptoms domains contribute to the rich clinical picture of schizophrenic psychoses and define different treatment interventions. They also have implications for acute and long term prognosis, in case of cognitive and negative symptoms indicating a poor prognosis in the sense of symptomatic outcome and social functioning. All three dimension should be in the focus of individualized treatment. As to drug treatment there are several unmet needs, especially concerning cognitive and negative symptoms, and the evidence base altogether is weak, even for the treatment of depressive symptoms in the context of schizophrenic psychoses.

SO 0602. Low doses of atypical antipsychotic drugs added to selective serotonin inhibitors produce a ketamine-like facilitation of prefrontal glutamatergic neurotransmission

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Background: About 50% of MDD patients respond inadequately to SSRIs and adjunct treatment with low doses of atypical antipsychotic drugs (APDs) may potently augment the antidepressant effect with a fast onset of action, although the mechanisms involved are poorly understood. Preclinical data propose that enhanced catecholamine output and facilitated NMDA-receptor mediated transmission in the medial prefrontal cortex (mPFC) may partly explain this effect. Recent data suggest however that the rapid and potent antidepressant effects of ketamine and scopolamine are critically dependent on AMPA receptor-mediated transmission in the mPFC.

Methods: We used *in vitro* intracellular single electrode voltage clamp recordings to study the effects of low nanomolar concentrations of olanzapine or asenapine, alone or in combination with fluoxetine and escitalopram, respectively, on both NMDA and AMPA induced currents in pyramidal neurons in the mPFC in rats. Moreover, the effect of a single antidepressant dose of ketamine was analysed on these glutamatergic receptors, 24h after its systemic administration. Statistical evaluation was made by Students t-test and one-way ANOVA followed by Newman-Keuls test.

Results: Our results show that add-on low dose APD to an SSRI, e.g. low nanomolar concentrations of olanzapine to fluoxetine or asenapine to escitalopram, may facilitate both AMPA- and NMDA induced responses in pyramidal cells of the mPFC, an effect not attainable by each drug alone, which could be blocked by a selective D1 receptor antagonist. Moreover, analogous effects on both AMPA-and NMDA responses in the mPFC were produced by a systemic antidepressant dose of ketamine 24h after its administration.

Conclusions: Since essentially analogous effects on AMPA-and NMDA responses were produced by a systemic antidepressant dose of ketamine, the effects on cortical glutamatergic transmission, in particular AMPA induced responses in the mPFC, may potentially explain the clinically well established rapid antidepressant augmentation obtained by adding low doses of APDs to SSRIs in treatment-resistant MDD.

SO 0603. Antidepressant drugs in schizophrenia and antipsychotic drugs in depression: basis and clinical perspective

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The use of antidepressants in schizophrenia has a long tradition and the administration increased since the introduction

of modern antidepressants represented by the selective serotonin reuptake inhibitors (SSRIs). In the beginning it was thought that these antidepressants could provoke positive symptoms in schizophrenia. However, it was soon evident that the addition of antidepressant medication to antipsychotics is of therapeutic value without this side effect. Interestingly, a group of atypical antipsychotics (AAPs) has a built-in antidepressant mechanism as demonstrated by the 5HT-2 blockade of these compounds and additionally the strong norepinephrine uptake inhibition represented by quetiapine as well as zotapine. A differential evaluation of schizophrenic and schizo-affective patients revealed that AAPs demonstrated a better outcome in schizo-affective patients (depressive subtypes) than schizophrenic patients without affective symptomatology. The use of antipsychotic drugs in depression has also a very long tradition already before the introduction of AAPs as typical neuroleptics were used for either sleep inducing properties or for a sedative component. A drug surveillance program of participating hospitals in Germany, Switzerland and Austria revealed a significant increase in the number of AAPs from the years 2000 to 2007 onwards from 13% to 28%. During the same time period the percentage of inpatient receiving typical neuroleptics demonstrated a significant decrease from 30% to 24%. AAPs are used in clinical practice for either augmentation strategies or associated symptoms like sleep disturbance or agitation. The clinical practice of using antidepressant drugs in schizophrenia and antipsychotic drugs in schizophrenia is insofar of importance since it emphasizes the fact that although controlled studies were either not apparent or scarce, health regulatory authorities did not provide treatment indications, this therapy principle was already used among clinicians to a large extent. For the addition of antipsychotic drugs in depression, there is now the indication in Europe for quetiapine only (not the other AAPs), however, the use of antidepressant drugs in schizophrenia has not as yet been granted by an indication of health regulatory authorities.

SO 07. Adherence with Treatment

SO 0701. Compliance counselling in bipolar disorder

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Bipolar disorder is a complex, chronic disorder leading to impaired patient functioning and a high social burden. Non-adherence is common in the management of bipolar disorder. The chronicity combined with the cyclical nature of bipolar disorder and the lack of illness awareness found in some bipolar patients often encourages pharmacological treatment nonadherence.

Other different factors have been found to influence treatment non adherence such as the amount of time being asymptomatic, psychiatric illness, living alone/no family support, complex medication regimen and low tolerability of medication. Patient-related factors for non-compliance in bipolar disorder include denial of illness (belief being recovered, hypomania, denial), impairment (lack of control over life, low education, low social support), medication-related issues (lapsed prescription, side effects) and co-morbidity (personality disorder, substance abuse). Illness-related factors include hyperthymia, manic type/symptom severity, cognitive dysfunction, and misdiagnosis (missed euphoria, mood-incongruent psychotic features). Euthymic bipolar patients with poor adherence are cognitively more impaired than healthy subjects. On one hand, impairment of memory or executive function may then lead the patient to not take the medication. On the other hand, as a part of a vicious cycle, nonadherence may lead to more relapses and hospitalizations and may have indirect negative consequences on cognitive function.

Finally, physician-related factors relate to knowledge about bipolar disorder and its treatments. Clinicians should look for, understand, monitor and optimally treat non-compliant patients. Long-term remission in bipolar disorder is hampered by barriers, interacting at various levels. A multidisciplinary approach is needed in which information, psycho-educational support, cognitive remediation programs and well-tolerated, effective, long-acting medication may help to overcome barriers and improve long-term outcomes.

SO 0702. Treatment of cognitive deficits in MDD

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There has been a renewal of interest in cognitive deficits of depressed patients. As Austin et al. (2001)[1] already stated this interest promoted a growing awareness that, like schizophrenia and neurological disorders, mood disorders may also be associated with a distinct pattern of cognitive impairment. Since then, a considerable number of papers on this issue have been published, also two major meta-analyses[2,3] showing that before all executive functions show deficits and that some of these deficits are not closely linked to the depressive symptomatology, i. e. are stable over time.

However, there has been up to now no clear effort to specifically treat cognitive symptoms in depressed patients, beside a few studies with sertraline, reboxetine and duloxetine. However, recently some studies with vortioxetine, a compound acting as a serotonin-transporter blocker and multi-serotonin-receptor agonist/antagonist have been published. Especially the trial of Katona et al. (2012)[4] could demonstrate in elderly depressed patients a superiority of this compound not only compared to placebo, but also compared to duloxetine.

In the presentation, the current knowledge of treating cognitive deficits in depressed patients will be discussed, also taking possible mechanisms of action into consideration.

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SO 703. Are any drug formulations inherently better of Adherence?

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It is well established that a maintenance treatment improves the prognosis of major psychoses and that the lack of compliance after the acute phase may complicate the prognosis. It is estimated that about 72.1% patients affected by a major psychosis discontinue a new treatment during 12-month follow-up period and no significant differences are reported for schizophrenia and bipolar disorder.[1] On the basis of these considerations, extended release formulations and long-acting formulations have improved treatment adherence. Extended release formulations result particularly indicated for partially compliant patients requiring a once a day administration. Traditionally long-acting formulation of an antipsychotics were reserved to severe and poor-compliant patients. More recently, the introduction of long-acting atypical antipsychotics (risperidone, paliperidone and olanzapine) has opened the possibility to use these formulations as first choice in early phases of illness (schizophrenia and bipolar disorder) regardless from compliance problems.[2] The benefits of long-acting atypical antipsychotics compared to oral formulations can be summarized as follows: a greater stabilization of plasma concentrations[3] continuity of drug treatment, reduction of the negative effects of a long duration of untreated illness (e.g. brain changes and immunological abnormalities) and good tolerability usually comparable than oral formulations.[4] In contrast, the cons consist in the availability of few molecules (risperidone, paliperidone and olanzapine) and greater problems in encountered management of acute side effects in comparison to oral formulations. Moreover, in the case of bipolar disorder, it is not yet clear whether the atypical antipsychotics have the same efficacy as mood stabilizers in terms of relapse prevention.[5] With few exceptions, to date there are no studies comparing the efficacy of atypical antipsychotics with lithium in terms of long-term stabilization in bipolar patients. In summary, the use of extended release and overall long acting formulations do not seem to improve just compliance, but also in compliant patients they can assure a better long-term outcome reducing relapses and neurodegeneration.[6]

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SO 08. The revised Diagnostic criteria of Mental Disorders (DSM-5): Bipolar disorder is bipolar again – revisiting the classics

Moderator: Michael Davidson, Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel
Discussants: Alan Swann, Baylor College of Medicine, Department of Psychiatry and Behavioral Sciences, Houston, USA - Eduard Vieta, Bipolar Disorder Program, Hospital Clinic, University of Barcelona, Barcelona, Spain

The launch of the new fifth revised edition of the Diagnostic Statistical Manual of Mental disorders, DSM-5, in May 2013 has received a lot of attention from both within as well as from outside the psychiatric community. In bipolar disorder, rather than taking a categorical approach to the disease, clinicians are now prompted to account for any presence of symptoms of the opposite pole.

Overall, this approach has been embraced by psychiatrists worldwide as being more in line with epidemiological and clinical evidence. A more thorough subtyping of bipolar patients is clinically relevant as it is well-known that these "mixed bipolar states" are more difficult to treat, have less favourable prognosis, and constitute a comparatively heavier burden for patients and carers. Historically, the co-existence of both manic and depressive symptoms has been a hallmark of bipolar disorder described by Kraepelin already in the beginning of the 20th century.

The DSM-5, just like its predecessors, has been met by criticism questioning the validity of the phenomenologically based diagnostic approach. But is this type of criticism really warranted? And most importantly, does it really apply to DSM-5 more than to previous versions of the DSM-Manual?

In this symposium, the validity and utility of the new DSM-5 criteria for diagnosing bipolar disorder will be discussed.

During the second part of the symposium the state of the art treatment of mixed mania and the spectrum of bipolar mania with depressive features, as recently redefined in the new DSM-5, will be reviewed. New data on the treatment of Bipolar mania with depressive features will be presented.

Finally the panel will discuss implications for clinical management, and how to improve recognition of depressive symptoms during manic episodes.

SO 09. Treatment Resistant Depression

SO 0901. Is resistant depression a signal for bipolar disorder?

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The response to antidepressant treatment is still unsatisfactory: about 40–50% of depressed patients do not respond to first antidepressant and about 60% do not reach remission at all leading to the status of resistant depression. Several clinical factors have been reported in association with antidepressant response, age, duration of illness, personality disorders, cognitive status, comorbidities are the strongest clinical factors associated with resistance but underlying bipolarity is an often undected issue.

In order to face this difficult situation, a number of strategies have been suggested, such as careful diagnosis, switching to another drug, combining two antidepressants and augmenting antidepressant treatment with other compounds. However there is a dearth of indication from guidelines about which is the best strategy and how to handle treatments.

The presentation will contribute to a better understanding of this challenge offering the latest updates in resistant depression treatment.

SO 0902. Favoured treatments for treatment resistant depression

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Treatment resistant depression includes both non responders to an adequate treatment with a single antidepressant and non responders to 2 or more treatment periods with different antidepressants. The first step to reduce the number of non responders is to use as first line treatment an antidepressant that is supported by firm evidence of superior efficacy and good safety, for example escitalopram. There is very little evidence to guide the choice of the second step treatment of non responders to a single antidepressant. The clearest finding comes from a large randomised study which shows that following non response to SSRIs or SNRI vortioxetine is significantly more effective than agomelatine. Less robust data are derived from a retrospective analysis of patients who had previously been treated but were none-the-less admitted to a series of randomised controlled comparator studies. Escitalopram was more effective than the SNRIs venlafaxine and duloxetine in second treatment.

Quetiapine as an add on treatment was significantly more effective than antidepressants alone or lithium in both non responders and two treatment failure TRD. The evidence that venlafaxine itself is effective in TRD is not as firmly based. Other candidate add on treatments include aripiprazole, mirtazapine, modafenil, folic acid and aspirin but further studies are needed.

SO 0903. New findings in resistant depression – focus on anxiety comorbidity

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In the 'real world', it is not always easy to disentangle depression from anxiety and vice versa. Moreover, long-life comorbidity of some of the anxiety disorders (Panic Disorder, Social Anxiety, etc.) with depression is high.

The governing school of thought regarding this sizeable group of patients is the hierarchical or primary-secondary approach. The underlying hypothesis being that the depressive component is secondary to the suffering induced by the anxiety disorder. According to this line of reasoning, only successful treatment of the primary cause will eventually lead to a subsequent resolution of the depression. Another treatment strategy of mixed anxiety and depression is the symptomatic approach, i.e. treating equally (and appropriately) the different symptoms. Unfortunately, the way most studies in anxiety and depression were conducted does not give us good footing as they used to exclude depression in anxiety studies and vice versa.

One of the most consistent finding of the Group for study of Resistant Depression (GSRD) is that comorbid anxiety disorder is the most powerful factor associated with treatment resistant depression (TRD).[1] Comorbid anxiety was found in nearly 40% of the resistant patients and only in 20% of the non-resistant patients. Having a comorbid anxiety disorder increased by 2.6 fold the risk of resistance to antidepressants treatment.

Following the above mentioned hierarchal approach the treatment should be aiming at the primer pathology (anxiety) and not the secondary phonotypical phenomenon (depression). Alternative conceptualization might be that the comorbidity of anxiety and depression present a different endophenotype of depression which require different approach. Those questions and the relevant therapeutic armamenterion will be presented.

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SO 10. Treatment of major depressive disorder (MDD)

SO 1001. The effect of comorbid anxiety on outcomes in major depressive disorder (MDD)

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Patients with major depressive disorder (MDD) will often present with co-morbid symptoms of anxiety. Up to 60% of MDD patients have a comorbid anxiety disorder, and up to 80% of GAD patients develop depression over their lifetime. Patients with comorbid depression and anxiety are at greater risk of suicide than those without comorbid anxiety and have ncreased incidences of alcohol and drug abuse. They typically suffer from a higher degree of impairment that pervades all aspects of life, including social and family interactions, workplace productivity and self-perception.

This situation presents the clinician with a number of additional complexities, both in terms of understanding and treating these patients. Comorbid syndromes should be treated with antidepressants that are effective in both conditions. Some medications were shown be effective in MDD, panic disorder, generalized anxiety disorder, social anxiety disorder, and obsessive compulsive disorder as well as in comorbid cases, according to a number of randomized controlled studies.[1] Also, evidence for psychological treatments for comorbid patients will be reviewed.

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SO 1002. Does being elderly alter response in MDD?

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A meta-analysis of 17 RCTs in the elderly found a benefit for antidepressants over placebo with NNTs ranging from 4 to 8 for different classes of drugs.[1] However, Walsh and Sysko[2] found that, in the elderly (>60years) subgroup of participants in 6 studies from a larger meta-analysis,[3] the antidepressant-placebo difference was significantly smaller (NNT 7–8) than in studies with younger adults (NNT 5). More recent meta-analyses have been in keeping with this. Nelson et al[4] identified 10 trials of newer antidepressants and found considerable heterogeneity between them, but an overall NNT of only about 10. Kok Nolen and Heeren[5] reviewed a broader range of trials (including both older and newer antidepressants and with relatively generous entry criteria) also found a modest overall superiority for active antidepressants against placebo. Tedeschini et al[6] found that although antidepressants were superior to placebo in the over 55s, the statistical significance of the difference was no longer apparent in the subset of studies with an age 65 entry criterion. They emphasised marked heterogeneity across studies and the relatively small number of 65 + studies available for inclusion. The also commented that physical comorbidity, executive dysfunction, chronicity of the depressive episode, and under-treatment might all have influenced treatment outcome adversely in the 65 + studies. However, since the publication of these meta-analyses two further positive placebo-controlled trials of antidepressants in people aged 65 and over have been published (Katona et al 2012; Heun et al 2013).[7,8] The clinical and research implications of these diverse findings will be discussed.

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SO 1003. Cognitive behaviour therapy (CBT) in treatment resistant depression

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If a trial were designed in which a pill, X, was added to ongoing drug treatment in depressed, nonresponding patients,

clear-cut improvement would be expected in those given X, rather than standard care, even if X were placebo.[1]

If X were replaced by a psychotherapy, Y, the outcome would be equally easy to predict. Undoubtedly, larger symptom reduction would be obtained in those receiving this extra dose of attention, whatever its nature. This talk-induced improvement could be due to the non-specific support provided, or to the fact that patients meeting regularly with a kind therapist may find it impolite to deny any improvement. Also, being regularly reminded of the nature of their condition may increase the patients' adherence to their medication. To claim that Y, in addition to such non-specific factors, exerts a specific effect, one would have to demonstrate superiority versus some other treatment.

The fact that psychotherapy studies are difficult to blind does not preclude the inclusion of a credible control.

If a paper were submitted to Lancet in which a drug had been evaluated as described above, it would have been mercilessly rejected, the reviewers harshly pointing out that a comparison with standard care permits no conclusion whatsoever regarding true Manuscript efficacy. But for studies of CBT, the journal applies very different standards, as illustrated by the contribution by Wiles and co-workers.[2–5]

This discrepancy is intriguing. Why is a design precluding conclusions less of a problem for CBT trials than for drug trials?

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SO 11. Hot Topics

SO 1101. Behavioral addictions in adult ADHD

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Different studies have found strong association between ADHD and addiction, including substance abuse, alcoholism, nicotine dependence and behavioral addiction.

There appears to be a common link between behavioral addiction as disordered gambling, and impulsivity, a common trait of ADHD. Retrospective study found that both alcoholics and pathological gamblers reported higher levels of ADHD behavior in childhood. Other studies found a high correlation between ADHD, pathological gambling and other impulse control disorders, including compulsive buying and compulsive sexual behavior. These results suggest that substance use, behavioral addiction, and ADHD are closely intertwined.

They also lend support to previous research in the neurological basis of impulse control deficits. Studies have hypothesized that both ADHD and problem gambling may be due to neurological deficits in the areas of the brain that control impulsiveness and executive functioning. ADHD has been associated with dysfunction in the frontostriatal region of the brain, as well as decreased brain volume, especially in the prefrontal cortex. Pathological gambling studies have found deficits indicating frontal lobe circuitry dysfunction and support the idea of executive function impairment.

Long-term outcomes studies highlight that drug use/addictive behavior, antisocial behavior, services use, and occupation that appeared to be least responsive to treatment, but showed, in fact a benefit of treatment.

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SO 1102. Biomarkers and prediction of response in major depressive disorder (MDD) – an update

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Despite over 50 years of pharmaceutical development of antidepressant drugs only about half of the patients with major depressive disorder (MDD) respond to the first antidepressant treatment trial, an even smaller proportion achieves remission. Therefore, the development of easy to obtain biomarkers to predict the likelihood of response in individual patients remains an important task. During the last years there have been a number of interesting studies on tests for the detection of current MDD and for the prediction of response to different treatments.

Research in potential biomarkers from body fluids has been successful in determining a range of analytes (i.e. growth factors, inflammatory cytokines, endocrine and metabolic

markers) that can differentiate MDD subjects from healthy controls and also prospectively distinguish responders from non-responders. Likewise, some genetic polymorphisms and epigenetic biomarkers could prove to be clinically valuable. However, to date, this discrimination is only possible on a group level, and no single test for MDD or response to antidepressant treatment has been published with sufficiently high test performance on an individual level.

Quantitative EEG markers for measuring treatment response, such as frontal theta cordance or the ATR (antidepressant treatment response) are a most interesting development.[1] Some of these neurophysiological parameters are measured before treatment, some during the early stages of treatment. It is hypothesized that these markers reflect dysfunctions in the rostral anterior cingulate (rACC) and in the prefrontal cortex. It is not surprising that other neuroimaging methods, such as functional magnetic resonance imaging (fMRI), single-photon emission computed tomography (SPECT) and positron emission tomography (PET) have also been successful in detecting increased pre-treatment rACC activity or changes in the serotonergic system to predict treatment response in MDD.

Currently, there exists no approved method for the prediction of response in MDD. Based on the present evidence, future studies should aim to combine multiple biomarkers in prediction scores to make a prognosis of treatment success in individual patients.

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SO 1103. Neuropeptide Y and CRH in Major Depressive Disorder (MDD)

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Etiology and pathophysiology of MDD are only partially elucidated and the major drugs used clinically are based on the monoaminergic mechanisms of action. Since about 25–40% of patients are only partial or non-responders, there is a major unmet need to better understand the biological underpinnings of the disease and develop novel treatments. While dysregulation of the monoamines is probably a sufficient cause of affective disorders, it is likely not a necessary factor. Ample evidence indicates that neuropeptides as well as the glutamatergic system play major roles. Thus, derangement of the HPA axis is a significant player in stress. This presentation focuses on neuropeptide Y (NPY), a peptide evolutionary exceedingly well preserved. In contrast to other neuropeptides, NPY is found in high concentrations in most brain regions, particularly those of relevance to emotionality and vegetative functions.[1,2] Decreased both mRNA and protein NPY are found in selected brain regions of genetic, e.g. the Flinders Sensitive Line rat,[3] and environmental, such as early life maternal deprivation and chronic stress, rodent models,[4] as well as in a model of alcoholism.[5] Moreover, NPY is reduced in a rat model of PTSD).[6] Conversely, all antidepressant treatments that rescue altered behavior in rodents and reduce symptoms in humans elevate NPY expression.[1,2,7] Clinical human data have demonstrated reduced CSF NPY in depression and in brains from suicide victims.[8] Conversely, all antidepressant treatments that rescue altered behavior in rodents and reduce symptoms in humans elevate NPY expression.[1,2,7,9] Lastly, NPY administered directly into rodent brain has potent anxiolytic and antidepressant effects. In summary, available data demonstrate that NPY system is altered in affective disorders and that increase in NPY effects in selected brain regions could be developed into novel treatment strategies for these disorders.

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P 01. Presentation of body dysmorphic disorder in dermatology

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Background: Body Dysmorphic Disorder (BDD), also known as dysmorphophobia and dermatological non-disease, is characterized by a* preoccupation with an imagined or slight defect in one's physical appearance.

Methods: This review focuses on the epidemiology, psychiatric comorbidities and treatment interventions for BDD in dermatology patients. We conducted a pubmed literature review of articles published between 1996 and 2011 using the key words: body dysmorphic disorder, dysmorphophobia, psychodermatology.

Results: BDD occurs in 0.7%–1.1% of community samples and 13% of psychiatric inpatients. About 21.7% of BDD subjects had one, 28.6% had two, and 41.4% had three or more axis-I psychiatric comorbidity.

Over 60 % of BDD patients had a lifetime anxiety disorder, 38 % had social phobia which tends to predate the onset of BDD. The psychiatric literature has debated BDD relationship to OCD based on high comorbidity and similarities between both conditions. Nearly all studies reported a high level of co-morbidity with depression and social phobia occurring in $>$ 70% of BDD patients.

BDD individuals present frequently to dermatologists (about 9%–14% of dermatologic patients have BDD). They are usually not formally diagnosed until 10–15 years after the onset. BDD co-occurs with pathological skin picking in 26–44.9% of cases. Skin picking was considered OCD spectrum disorder in 52% of cases. There are reported cases of BDD- by –proxy.

Delusional and non-delusional subjects had a similar probability of remitting from BDD over 1 year of prospective follow-up. Cognitive behavioral therapy (CBT) has the best established treatment results. SSRIs were effective in both delusional and non-delusional BDD variants.

Conclusion: BDD is a relatively common psychiatric disorder which is associated with high psychiatric comorbidity. BDD individuals frequently present to dermatologists often with pathological skin picking. CBT is the best treatment option and SSRIs may be used.

P 02. A population pharmacokinetic (PK)-pharmacodynamic (PD) meta-analysis of vortioxetine in patients with major depressive Disorder (MDD)

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Background/Aims: Vortioxetine (Lu AA21004) is an investigational antidepressant in clinical development for the treatment of MDD. *In vitro* studies indicate that vortioxetine is a 5-HT_3, 5-HT_7, and 5-HT_{1D} receptor antagonist, 5-HT_{1B} receptor partial agonist, 5-HT_{1A} receptor agonist and inhibitor of the serotonin (5-HT) transporter (SERT). Our aim was to develop a population PK and PK/PD model in patients with MDD.

Methods: Pharmacokinetic data from 10 MDD and 2 GAD studies (3160 patients) were included with efficacy data (MADRS) from short-term MDD studies (2537 patients). Doses of vortioxetine were 1, 2.5, 5, 10, 15 and 20 mg daily. One- and two-compartment PK models were evaluated as base structural PK model. The relationship between the average vortioxetine plasma concentration at steady-state (C_{av}) and change in MADRS total score from baseline (ΔMADRS) was investigated. The impact of covariates on the PK and PD parameters was assessed. In addition, the relationship between C_{av} or dose and the risk of nausea was investigated through logistic regression.

Results: A two-compartment model with first-order absorption and linear elimination best characterized the pharmacokinetics. Mean estimates for oral clearance (CL/F) and volume of distribution for the central compartment (V2/F) were 42L/hr and 2920L, respectively. Creatinine clearance, height, and region (EU, US or RoW) had statistically significant effects on CL/F, but clinically irrelevant effects on exposure ($\leq \pm$ 26% change in AUC or C_{max}). An E_{max} model best described the relationship between the ΔMADRS and C_{av}. Estimates of EC_{50} (concentration at half maximum effect) and E_{max} (maximum difference from placebo) were 24.9 ng/mL and 7.0, respectively. Age, region, BMI and weight had statistically significant effects on E_{max} and/or EC_{50}. Both C_{av} and dose had a statistically significant impact on the risk of nausea.

Conclusions: The exposure-response relationship was well characterized by the PK/PD model developed.

P 03. A course of the illness and clinical characteristics of mixed states in bipolar mania

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Background: The aim of the present study was to elucidate the course of the illness throughout a 12-month follow-up and clinical characteristics of mixed states in bipolar mania.

Methods: The subjects ($n = 171$) were inpatients diagnosed with bipolar I disorder, manic, between 2003 and 2010 and were classified into three groups: "pure mania" ($n = 67$), "probable mixed mania" ($n = 79$), and "definite mixed mania" ($n = 25$). Diagnoses were in accordance with the Cincinnati criteria, which include the DSM-IV-TR characteristics for a major depressive episode, except for

agitation and insomnia. The charts of subjects were retrospectively reviewed for demographic and clinical characteristics prior to the index episode, clinical data regarding the index episode, and course of the illness over a 12-month follow-up period.

Results: During the course of the illness over a 12-month, the inter-episode remission rate was significantly different among the three groups and was lower in the definite mixed mania group than in the probable mixed mania group. There were no significant differences in clinical data regarding the index episode such as the duration of index episode, change of medications, and the total number of medications. Suicidality was significantly different among the groups, with higher rates in the definite mixed mania group compared with the pure mania group and the probable mixed mania group. Subjects with definite mixed mania were more likely to be young at admission, to be female, to have familial affective loading, and to have a history of suicidality compared with the pure mania group in the final regression model evaluating the three groups.

Conclusion: The results of the present study suggest that mixed states in bipolar mania had different clinical characteristics and a more severe illness course, including a lower inter-episode remission rate, than did a non-mixed mania.

P 04. Is it useful to use the Korean version of the mood disorder questionnaire for assessing bipolar spectrum disorder among Korean college students?

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Backgound: The purpose of this study was to assess the usefulness of the Korean version of the Mood Disorder Questionnaire (K-MDQ) as a screening tool for the identification of bipolar spectrum disorder (BSD) among Korean college students.

Methods: A sample of 1,020 college students was stratified to reflect geographical differences among the students. The K-MDQ and an epidemiological survey were administered between November 2006 and February 2007. To validate the K-MDQ as a screening tool for BSD, the Korean version of the Bipolar Spectrum Diagnostic Scale (K-BSDS) and the Structured Clinical Interview for DSM-IV (SCID) were also administered.

Results: The rates satisfying MDQ criterion 1, and all three MDQ criteria, were 55.5% and 2.3%, respectively. According to the K-BSDS, 59.9% of the sample met the criteria for BSD using a threshold of 10, while no statistical differences were observed among subgroups. When we examined the diagnostic agreement between K-MDQ and K-BSDS, 79.5% of students who met MDQ criterion 1 were also positive on the BSDS. Sixteen (21.6%) of the 74 students who participated in the SCID interview were diagnosed with BSD.

Conclusion: Although the K-MDQ is a useful tool to assess BSD among inpatients and outpatients, it does not appear useful as a screening tool to detect BSD among college students.

P 05. Korean medication algorithm for depressive disorder: comparisons with other treatment guidelines

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Background: The Korean Medication Algorithm Project for Major Depressive Disorder (KMAP-MD) was developed in 2002 and then revised in 2006. In 2012 it was secondly revised to reflect current changes in pharmacotherapy for depressive disorder; Korean Medication Algorithm Project for Depressive Disorder 2012 (KMAP-DD 2012). We aimed

to compare KMAP-DD 2012 with other recently published treatment guidelines for depressive disorder.

Methods: We reviewed a total of five treatment guidelines for depressive disorder that included American Psychiatric Association Practice Guideline, Canadian Network for Mood and Anxiety Treatments Clinical Guidelines, The National Institute for Health and Clinical Excellence Guideline, Texas Medication Algorithm Project Procedural Manual, and World Federation Societies of Biological Psychiatry Guidelines. We compared the recommendations of these five guidelines to those of KMAP-DD 2012.

Results: In terms of recommendations for initial treatment strategies, KMAP-DD 2012 is not significantly different from the other five guidelines. However, in case of non-response or partial response to initial treatment, the recommendations varied across treatment guidelines. For the maintenance therapy, the duration of maintenance therapy, and the doses of antidepressants and antipsychotic agents differed among the treatment guidelines. There are some discrepancies in the recommendations for each subtype of depressive disorders across treatment guidelines. For the treatment among special population such as child-adolescent depression, geriatric depression and postpartum depression, there are no significant differences in overall recommendation across guidelines. However, most guidelines other than KMAP-DD 2012 describe the potential risk of antidepressant such as increased suicidality among young population.

Conclusion: This comparison identified that, by and large, the treatment recommendations of KMAP-DD 2012 are similar to those of other treatment guidelines, and reflect current changes in prescription pattern for depression based on accumulated research data. Further studies will be needed for several issues that the treatment guidelines reviewed here cannot draw a definitive conclusion because of lack of evidence.

P 06. Mixed-state bipolar I and II depression: Time to remission and clinical characteristics

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Background: We compared the time to achieve remission and the clinical characteristics of patients with bipolar depressive mixed state and those with bipolar depressive non-mixed state.

Methods: The subjects (N = 131) were inpatients diagnosed between 2006 and 2012 with bipolar I or II disorder, depression and were classified into the following three groups: "pure depressive state" (PD, n = 70), "sub-threshold mixed state" (SMX, n = 38), and "depressive mixed state" (DMX, n = 23). Diagnosis of a DMX was in accordance with Benazzi's definition: three or more manic symptoms in a depressive episode. The subjects' charts were retrospectively reviewed to ascertain the time to achieve remission from the index episode and to identify other factors, such as demographic and clinical characteristics, specific manic symptoms, and pharmacological treatment, that may have contributed to remission.

Results: The time to achieve remission was significantly longer in the DMX ($p = 0.022$) and SMX ($p = 0.035$) groups than in the PD group. Adjustment for covariates using a Cox proportional hazards model did not change these results. Clinically, subjects with a DMX were more likely to have manic symptoms in the index episode, especially inflated self-esteem and psychomotor agitation than those in the PD.

Conclusion: These findings showed that sub-syndromal manic symptoms in bipolar depression had different clinical characteristics and a more severe illness course, including a longer time to achieve remission, than did a pure depressive state.

P 07. The differences in the clinical characteristics and treatment pattern between bipolar disorder patients with and without psychiatric comorbidity

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Background: We aimed to identify the differences in the treatment pattern and clinical characteristics between bipolar disorder patients with and without psychiatric comorbid condition.

Methods: We retrospectively reviewed the medical records of patients who discharged with the diagnosis of bipolar disorder from the Department of Psychiatry, Yeouido St. Mary's hospital from 2006 to 2010. Data on disease-related, sociodemographic variables and treatment pattern were analyzed.

Results: A total of 161 patients were included for the analysis, and among them, 34 patients had psychiatric comorbidity. We divided the subjects into two groups (with-comorbidity group and without-comorbidity group) according to whether they had psychiatric comorbidity or not. Comparing sociodemographic variables, there were no variables that were significantly different between with-comorbidity group and without-comorbidity group. With-comorbidity group showed higher rate of being single than without-comorbidity group. However, this difference did not reach statistical significance. Comparing disease-related variables and treatment pattern, there also were no variables that showed significant difference between two groups. With-comorbidity group showed higher rate of mixed episode at admission, while without-comorbidity group showed higher rate of manic episode. However, this difference did not reach statistical significance, neither.

Conclusion: There found to be no difference in various clinical characteristics and treatment pattern between without-comorbidity and with-comorbidity groups. We think further studies with large sample size and prospective

designs will be needed to confirm the difference in the clinical characteristics and prescription pattern between bipolar patients with and without psychiatric comorbidity.

P 08. The differences in the clinical characteristics and treatment pattern between major depressive disorder patients with and without psychiatric comorbidity

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Background: This study aims to identify the differences in the clinical characteristics and treatment pattern between major depressive disorder patients with and without psychiatric comorbidity.

Methods: The medical records of patients who discharged with the diagnosis of major depressive disorder from the Department of Psychiatry, Yeouido St. Mary's hospital from 2008 to 2010 were reviewed. Data on sociodemographic, disease-related variables and treatment pattern were analyzed.

Results: A total of 142 patients were enrolled, and among them, 61 patients had psychiatric comorbidity. We divided 142 patients into two groups (with-comorbidity group and without-comorbidity group) according to whether they had psychiatric comorbidity or not. Comparing sociodemographic variables, with-comorbidity group showed younger age, higher rate of male, longer educational years, and higher rate of being single, divorced or separated than without-comorbidity group. Comparing disease-related variables, with-comorbidity group showed younger age at onset, longer duration of index hospitalization, and higher number of previous hospitalization than without-comorbidity group. For psychotropic medication at discharge, without-comorbidity group was more likely to be prescribed with antidepressant monotherapy, while with-comorbidity group was more likely to be prescribed with the combination therapy of antidepressant, mood stabilizer, and antipsychotic agent. But this difference did not reach statistical significance.

Conclusion: Various sociodemographic and disease-related variables were found to be different between depression patients with and without psychiatric comorbidity. Further studies with large sample size and prospective study designs will be needed.

P 09. The safety and tolerability of vortioxetine (Lu AA21004) in the treatment of adults with major depressive disorder (MDD): A pooled analysis

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Background/Aims: To assess the safety and tolerability of vortioxetine in adult patients with MDD.

Methods: Tolerability was based on the nature, incidence and severity of adverse events (AEs) during 6–8 weeks of treatment in 10 randomised, double-blind placebo-controlled short-term studies in MDD (NCT00672958, NCT00672620, NCT00735709, NCT01153009, NCT01163266, NCT01179516, NCT00839423, NCT00635219, NCT00811252, NCT01140906), 6 with active reference, and 5 long-term studies including relapse prevention (NCT00761306, NCT00694304, NCT01323478, NCT00707980, NCT00596817). Symptoms following discontinuation were specifically assessed through the Discontinuation-Emergent Signs and Symptoms (DESS) checklist.

Results: In the short-term studies, patients were treated with placebo (n = 1621), vortioxetine (5–20mg/day) (n = 2616), venlafaxine (225mg/day) (n = 113), or duloxetine (60mg/day) (n = 753). The overall AE withdrawal rate with vortioxetine (5–20mg/day) was 4.5–8.4%: compared to placebo (3.5%), venlafaxine (14.2%) or duloxetine (8.8%). Common AEs (incidence ≥ 5% and > 2x placebo) with vortioxetine (5–20mg/day) were nausea (20.9–31.2%), *versus* placebo (8.6%), venlafaxine (33.6%) and duloxetine (34.1%) and vomiting (2.9–6.5%): compared to placebo (1.2%), venlafaxine (3.5%) and duloxetine (4.1%). Nausea was dose-related, mild to moderate, and most commonly occurred in the initial weeks of treatment with vortioxetine (median duration: 10–16 days). The incidence of insomnia-related AEs was 2.0–5.1% for vortioxetine (5–20 mg/day): compared to placebo (4.4%), venlafaxine (15.9%), and duloxetine (8.1%). The incidence of sexual dysfunction-related AEs was 1.6–2.6% for vortioxetine (5–20 mg/day): compared to placebo (1.1%), venlafaxine (12.4%) or duloxetine (4.5%). The mean DESS total score was 1.55 and 1.58 (vortioxetine 10–20mg/day), 0.96 and 1.19 (placebo), and 1.33 and 2.85 (duloxetine) in the first week and second week following abrupt discontinuation. There were no clinically significant trends within or between treatment groups regarding clinical laboratory values, ECG or vital sign parameters, or new safety or tolerability findings arising uniquely during long-term treatment with vortioxetine. The mean weight increase from baseline to last assessment was < 1 kg for patients treated with vortioxetine for up to 1 year.

Conclusions: Vortioxetine (5–20mg/day) appears safe and generally well tolerated in short- and long-term treatment for MDD. *[319 words– max 320]*.

Commercial support: This analysis and the component studies were sponsored by H Lundbeck A/S and the Takeda Development Center Americas, Deerfield IL, USA.

DSB has received honoraria for educational presentations from H. Lundbeck A/S, and has acted as a paid consultant to Eli Lilly, GlaxoSmithKline, Grunenthal, Lundbeck, Pfizer, Pierre Fabre and Servier, and currently holds research grants (on behalf of his employer) from Lundbeck and Pfizer. He has accepted paid speaking engagements in industry-supported satellite symposia or other meetings hosted by Eli Lilly, Glaxo-SmithKline, Lundbeck, Pfizer, Pierre Fabre and Servier.

MS was an employee of Takeda Development Center Americas.

WP is an employee of Takeda Development Center Americas.

SL is an employee of H. Lundbeck A/S.

JM is an employee of H. Lundbeck A/S.

P 10. The prevalence of bipolar spectrum disorder in the Korean college students according to the K-MDQ

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Background: The purpose of this study was to assess the prevalence of bipolar spectrum disorder (BSD) in the general Korean population.

Methods: A sample of college students (n = 1026) was stratified to reflect geographical differences accurately in Korean college students. The Korean version of the Mood Disorder Questionnaire (K-MDQ) was administered and an epidemiological survey carried out between November 2006 and February 2007. BSD was defined as a score of at least seven K-MDQ symptoms that co-occurred and resulted in minimal or more functional impairment.

Results: The prevalence of BSD was 18.6% (95% confidence interval [CI] 16.2–21.0) in total, being 19.8% (95% CI 16.3–23.2) in men and 17.5% (95% CI 14.2–20.8) in women. The prevalence of BSD was more common in rural dwellers than in urban dwellers (P = 0.008, chi-square test). Univariate and multivariate regression models showed that rural residence was a significant factor associated with BSD. There were no significant relationships between BSD and gender, age, and socioeconomic status.

Conclusion: The prevalence of BSD found in the present study is higher than that reported by other epidemiological studies in Korea and in international studies.

P 11. Effect of polymorphisms in tryptophan hydroxylase 2 Gene on suicide risk in Korean patients with major depressive disorder

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Background: The tryptophan hydroxylase gene (TPH2) encodes the rate-limiting enzyme in the serotonin biosynthesis in brain. Despite suicide attempt is strongly associated with major depressive disorder (MDD), not all patients with MDD attempt suicide. We hypothesized variation at the TPH2 gene and its 5' upstream region may predispose to attempt suicide in depressed patients. We also investigated associations between haplotypes in the TPH2 gene and suicide attempts.

Methods: We examined the association between three SNPs polymorphisms (rs11178997, rs4570625, rs7305115) of 5' upstream region and the TPH2 and suicide attempts. The genotypes of the polymorphisms in the TPH2 were compared in 190 patients with MDD, who either had made a suicide attempt (82 suicide attempters, 34 males and 48 females) or had never made a suicide attempt (108 non-attempters, 37 males and 71 females). We also analyzed associations between haplotypes (TGA, TGG, TTA, TTG, ATA, ATG) in TPH2 gene and suicide attempts.

Results: There were significant differences in the distribution of the three genotypes (GG, GA, and AA) of rs7305115 between suicide attempters and non-attempters ($X^2 = 10.7$, $p = 0.005$). There was an excess of GG genotypes in the suicide attempter group compared with the non-attempter group. We found a significant association between the distribution of haplotypes and suicide attempts ($X^2 = 14.3$, $p = 0.010$). Controlling for suicide risk factors, logistic regression analysis showed GG genotype significantly predicted suicide attempts in patients with MDD (OR = 2.55, 95% CI = 1.31–4.96, $p < 0.01$).

Conclusions: The TPH2 gene variants may be associated with the biological susceptibility for suicide attempts in MDD. If replicated, the genotypes of the polymorphisms in the TPH2 may shed light on the biological basis of this potentially dangerous adverse event and help identify depressed patients at increased risk of suicide.

P 12. Generalized poststroke anxiety disorders: clinical and radiological correlation

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Background: Generalized poststroke anxiety disorders (GPAD) is one of the important and often unrecognized sequela of stroke.

Purpose: The purpose of the study was the assessment of anxiety disorders prevalence after stroke at acute stage

neuroradiological correlation and in association with post-stroke depression.

Patients/Methods: A prospective study of the 294 stroke patients were conducted. Stroke severity was assessed by NIHSS. CT/MRI were performed. Diagnosis of GPAD was performed according to DSM-IV criteria: presence of a sustained worrying state associated with at least three anxiety symptoms (including restlessness, decreased energy, difficulties in concentration, irritability, muscle tension, and sleep disturbances).Depression symptoms were assessed Hamilton Depression Scale. Patients were divided into the three groups: I-patients with GPAD, II- patients with poststroke depression(PD), II-patients with poststroke depression and GPAD.MMSE and ADL Index were recorded.

Different statistical tests were performed by SPSS.

Conclusion/Discussion: Of the 294 stroke patients 57(19.3%) patients had GPAD, 96 (32.6%) PD, and 34(11.5%) GPAD+ PD.

Group I patients more often had damage of the left hemisphere, prevalence of ischemic this cortical lesion. Group II patients had no lateralized effect, but in the acute stage correlated with thalamic stroke, group III patients revealed prevalence of left cortical lesion.

Multiple linear logistic regression analysis revealed a significant share of hypertension, age, previous history of stroke and female gender in the development of GPAD. Comparison of this three groups revealed that group II patients had a lower MMSE, higher NIHSS score, and worse ADL Index.

P 13. Efficacy and tolerability of escitalopram and pregabalin in patients with generalized anxious disorder (GAD)

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Aim: The aim of investigation was to compare the efficacy and tolerability of escitalopram, pregabalin and combination of two psychotropic medications in treatment of patients with generalized anxiety disorder.

Matherial: The sample count of 87 out patients with diagnosis of G.A.D., according to ICD-X. Patients were treated with escitalopram, pregabaline or in combination in patients treated with escitalopram, mean daily dosage was 15 mg/day. Pregabaline was administrated in daily dosage of 225 mg/day. In the third group of patients, escitalopram was prescribed in a dosage of 7.5 mg/day with pregabalin in a dosage of 75 mg/day. Patients were monitored during 10 weeks. Effectiveness was measured by reducing the total score on Hamilton Anxiety Scale (HAMA) from baseline to endpoint. At baseline the total score on HAMA was >20.

Results: The efficacy of treatment in patients suffering from GAD with escitalopram and pregabaline was similar, but treatment in combination with escitalopram and pregabalin was superior compare to this psychotropic separately. The most common effect in the group of patients treated with escitalopram was nausea (in 4.2%). Among patients treated with pregabalin it was dizziness (in 6.1%). In patients treated with a combination of escitalopram and pregabalin the most common adverse event was dizziness (in 3.1%).

Conclusion: Escitalopram and pregabalin confirmed well efficacy and tolerability in patients with GAD. Combination of escitalopram and pregabalin was superior in efficacy with less adverse events. As adverse events are partly dose-related, it is possible that lower doses of both medicaments accounted for a such result.

P 14. Survey about headache in patients with obstructive sleep night apneas and anxiety disorders

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Introduction: We enrolled 254 subjects, 173 men and 81 women, mean age 56.8 + 15.0, suffering from obstructive sleep night apneas syndrome associated with anxiety disorders to evaluate the prevalence of headache to then put in place a series of preventive measures also in view of preventing complications.

Materials and methods: The subjects were recruited in a period of 2 years at the Department of Pneumology of Teramo Hospital. Apneas were graded as mild (AHI between 5–10), moderate (AHI between 11–20), severe (AHI greater than 20). Anxiety was graded as mild (HAM–A <17), moderate (HAM–A between 18–24), severe (HAM–A greater >25). Headaches were classified according to the ICHD-II criteria. Twenty patients (8.1%) referred a history of primary headache: 3 were affected by migraine (1.2%) and 17 (6.9%) by headache. One hundred and eighty (70.9%) had headache on awakening, with a greater frequency of breathing pauses during sleep, insomnia of central type and episodes of sweating and anxiety. All were underwent an interview with a standardised questionnaire on anxiety disorders, on sleep features, on related conditions, on the type of headache, and on risk factors for headache.

Results: The clinical severity is related to the frequency of morning headache (frequency greater than in patients with insomnia), suggesting the relevant role of the hypercapnia consequential vasomotor phenomena.

Discussion: The strength of our study is the large sample size assessed, and the detailed information collected on sleep disorders, anxiety disorders and other risk factors for headache.

Conclusions: Our study suggests the need for patients with morning headache to undergo careful screening for sleep disturbances and anxiety disorders related to breathing disorders.

P 15. TINER: a new strategy in disorder of sleep-wakefulness sphere associated with mild depression

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Introduction: We studied 60 patients suffering from sleep-wakefulness sphere associated with mild depression, of which 30 with reported episodes of Insomnia of type terminal, was submitted to TINER, relaxation technique, assessing the possible psycho-corporeal positive role on affective state.

Materials and methods: The patients are subjects suffering from depression that results, with HAM-D, a psychological assessment, having average rating between 8 and 17 and none of them has been subjected to any treatment with antidepressants. Then the group study of thirty people, including 10 episodes of Insomnia of type terminal, was submitted to sessions of TINER specifically, weekly, for a period of three months, with subsequent maintenance sessions every fortnight for three months, while the control group of equal number not effected any therapy. At the end of six months, both the studio and the control group, have been subjected to clinical and psychological re-evaluation.

Results: The scores obtained between the HAM-D start and retest, showed a decrease of 40% 6 points, 4 points in 25% and 2 points in 35% for the subjects submitted to TINER; of course only for persons subjected to TINER emotional state.

Patient group	HAM-D baseline	HAM-D 9 Months
40%	8-17	6 points
25%	8-17	4 points
35%	8-17	2 points

Discussion: Clinically, we observed a reduction in episodes of insomnia of type terminal, into the study group within the first six months.

Conclusions: In the study group, we observed a significant reduction in episodes of insomnia of type terminal and enhance emotional state. TINER, play a positive role in patients suffering from mild disturbance related to sleep-wakefulness sphere.

P 16. Manic vs mixed; the evaluation of anxiety, depression and global assessment of functioning in bipolar patients

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Aims: To compare two samples of bipolar patients presenting in mixed and manic episodes to assess their differences in terms of anxiety, depression and functioning.

Methods: The sample included 94 patients who were admitted to the Shahid Beheshti Mental Hospital of Kerman Iran during autumn, winter (2007) and spring (2008) and were diagnosed suffering from bipolar disorder type-I based on DSM-IV framework. Then they were grouped under the two categories of manic episode (48 Patients) and mixed episode (46 Patients). All patients were evaluated by the Hamilton's Rating Scale for Depression (HRSD) and the Hamilton's Anxiety Rating Scale (HARS). The patients' functionality was rated during their illness and for the period of 6 months prior to their admittance using "Global Assessment of Functioning" (GAF) scoring system.

Results: The average of both Hamilton's Depression and Anxiety rates in bipolar mixed patients were significantly higher than manic patients. The patient's functionality rate at the time of admission was reduced noticeably for both groups but the functionality between both groups while they were admitted to the hospital did not show a significant difference.

Conclusion: Mixed patients may suffer from anxiety and depression more than manic ones but both of these groups have impaired functionality. The co morbidity of anxiety in mixed patients may result in incorrect diagnosis of this disorder .It seems that further improvement in classification of Mixed bipolar diagnosis in DSM IV is required.

P 17. Predictors and consequences of post-stroke depression in a sample of Egyptian patients

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Background and objectives: In spite of its high incidence, post-stroke depression (PSD) is still under diagnosed and the risk factors for its development have not been clearly delineated. The present study was set to detect different predictors for the development of PSD and assess potential risk factors influencing the occurrence of the condition while also examining the consequences of its severity.

Patients and methods: 120 Egyptian stroke patients were administered the Mini International Neuropsychiatric Interview (M.I.N.I.) and a thorough neurological examination and CT scan or MRI for localization of the lesion. Other measurements were Hamilton Rating Scale for Depression (HAM-D), Barthel Index (B.I) for activity of daily living assessment, Quality of Life Depression Rating scale (QLDR) and Caregiver Strain Index (CSI) for assessment of the stress level.

Results: We report that the main risk factors for the development of PSD in the study sample were male gender (63%), younger age group, frontal lesions irrespective of the side (35%), presence of stressful life events (22%) and presence

of post-stroke functional impairments (73%), whereas the main factors affecting the severity of PSD included female gender (77.2%), lower socioeconomic class (70.4%) and the severity of post-stroke functional impairments (90.9%). We also report that the main consequences of PSD encountered were significant impairment of the quality of life (QOL) and significant increase of caregiver stress compared to a non PSD group ($p < 0.001$).

Conclusion: We conclude that PSD should be carefully evaluated in all stroke patients and recommend further prospective studies targeting the immediate and remote complications of PSD.

Declaration of interest: none.

P 18. Dialectical behavior therapy in bipolar disorder: clinical applications in outpatient population at Tripler Army Medical Center- a proposed treatment

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Background: DSM 5 defines Borderline Personality Disorder (BPD) as periods of pervasively unstable mood, affect, self image, relationships and self injurious behavior. Bipolar Disorder (BD) is characterized by sustained periods of pathological moods and marked impulsivity, irrational behavior, and neurovegetative symptoms. Both disorders are characterized by negative self talk and cognitive distortions. Dialectical Behavior Therapy (DBT) is an evidence based treatment proven to be effective in the treatment of BPD. Given the parallels in symptom cluster of BD and BPD, we propose a treatment protocol to implement formal DBT as an adjunct to the biological management of BD in outpatient population at Tripler Army Medical Center (TAMC).

Objectives: Develop theoretical treatment in patients with BD in Outpatient Population at Tripler Army Medical Center.

Describe the clinical course of the disease.

Propose DBT as a valid model and an effective treatment protocol in combination with biological management of BD.

Methods: Implementation of DBT in outpatients with BD at TAMC who have been previously stabilized of index episode with an inclusion YMRS score of < 7, and a HAM-D score < 7, but are now experiencing residual symptoms, in combination with a psychopharmacological plan during the study period of 12 months. We will describe observed changes, report changes in objective scores and make conclusions based on this data.

Results: The DBT therapist enables the patient to effectively cope and act in a more realistic and adaptive manner in relation to their symptoms. A protocol inclusive of psychopharmacological and behavioral interventions is intuitively likely to be more effective in the outpatient population. Implementation and objective measure of such a protocol will quantify whether this observation is correct.

Conclusions: In looking at similarities between BPD and BD, including challenges in the psychological and behavioral aspects of the disease, we can design a novel treatment protocol for BD at Tripler AMC that incorporates pharmacological, psychological and social interventions that is quantifiable and based on evidence.

P 19. Transcranial light alters the expression of brain encephalopsin and plasma monoamine concentration in the mouse

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Encephalopsin (OPN3) belongs to the light sensitive transmembrane receptor family mainly expressed in the brain and retina. The function of OPN3 can be divided into two parts; light absorption and G protein activation. It is believed that light affects mammalian circadian rhythmicity through the retinohypothalamic tract, which transmits light information to the suprachiasmatic nucleus in the hypothalamus and entrains the animals according to the solar day. Blind mice were randomly assigned to three different groups: control group, morning-light group and evening-light group. Test animals were illuminated transcranially five times a week eight minutes per animal for four weeks and samples of hypothalamus, cerebellum, retina, adrenal gland, liver and plasma were taken. Amount of OPN3 in hypothalamus and cerebellum samples were investigated by western blot and monoamine concentrations in plasma and adrenal gland by HPLC. Transcranial light treatment increased the amount of OPN3 in hypothalamus, as well as dopamine and noradrenaline concentrations in plasma with morning-light group. Furthermore, the amount of OPN3 decreased in hypothalamus for evening-light group and in cerebellum for morning-light group. The activation of OPN3 is caused by either the straight activation of OPN3 by skull penetrating light or via molecules regulating circadian clock, such as melatonin. The deactivation is possibly caused by the activation of GABA, which is an inhibiting molecule and compete binding sites in G protein with opsins. The changes in monoamine concentrations can be caused by the phase shift change caused by the light treatment or the stimulation of hypothalamus by light. These results provide new information on the effects of light on transmitters mediating mammalian rhythmicity and possibly help to understand the basis of mental disorders, such as seasonal affective disorder.

P 20. Eye movement desensitization reprocessing, posttraumatic stress disorder, and trauma: a review of randomized controlled trials with children and adolescents

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The current literature review examines the methodological rigor of randomized controlled trials (RCTs) of eye movement

desensitization reprocessing (EMDR) conducted specifically with children and adolescents who had a diagnosis of post-traumatic stress disorder and history of trauma. A thorough search for RCTs of EMDR with children and adolescents that were published between 1998 and 2010 was conducted utilizing several databases. A total of five studies were identified. Following an extensive review of the literature, it became apparent that the number of RCTs conducted with EMDR with children and adolescents was negligible, though initial results suggest that it is a promising practice. Although current EMDR studies have been conducted with children and adolescents, and have indicated that EMDR is a promising practice, the state of knowledge at this point is insufficient. EMDR tends to produce less positive results when compared to other trauma-focused interventions, although some research indicates the opposite.

P 21. Age-dependent memory impairment is improved by Vortioxetine in old female mice

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Background/Aims: Altered neurogenesis has been proposed as a possible mechanism underlying cognitive decline during aging and a mechanism by which antidepressants may affect cognition. Antidepressants increase neurogenesis in young adult rodents, but it is not clear if this also occurs in old mice (> 12 months). The aim of this study was to compare effects of antidepressants with different modes of actions (i.e. vortioxetine, an investigational antidepressant with a multimodal mechanism of action and the selective serotonin reuptake inhibitor fluoxetine) in old mice with respect to cognitive function, neurogenesis and BDNF levels. Vortioxetine is a 5-HT_3, 5-HT_7 and 5-HT_{1D} receptor antagonist, 5-HT_{1B} receptor partial agonist, 5-HT_{1A} receptor agonist, and an inhibitor of the serotonin transporter in transfected cell lines.

Methods: We examined cognitive function, BDNF levels and neurogenesis in old (> 12 months) female C57BL/6 mice treated chronically (1 month) with vortioxetine (10 mg/kg/day in food), fluoxetine (16 mg/kg/day in drinking water) or vehicle (tap water and normal rodent chow). Visuospatial memory was evaluated in the novel object placement task. Neurogenesis was measured by counting bromodeoxyuridine (BrdU) labeled cells in the hippocampal region. Brain-derived neurotrophic factor (BDNF) was quantified by ELISA in cortical and hippocampal samples.

Results: Vortioxetine, but not fluoxetine, significantly improved the visuospatial memory deficits of old mice and increased BDNF levels in the cortex. Neither vortioxetine nor fluoxetine improved the low level of neurogenesis in old mice.

Conclusions: The observed memory improving effect of vortioxetine in aged mice model is independent of neurogenesis but accompanied by an increase in BDNF level.

P 22. The prevalence of depression among resident doctors working in a teaching hospital in Karachi, Pakistan

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The study aimed to look at the prevalence of depression among the trainee resident doctors in Ziauddin Hospital, Karachi.

Methodology: 285 trainee doctors were included in the study from the three campuses of Ziauddin Hospital in Karachi. We looked at the prevalence of depression, any gender differences and differences in prevalence during the levels of training. The Beck Depression Inventory (English version) was used to assess depression. During data collection, complete anonymity of the doctors was maintained.

Results: Out of the 285 surveys distributed, we had response a rate of 30%. The mean ($\pm$ SD) score was 7.88 ± 5.93 with a range of 0 to 30 for the entire population. When analyzing the different training levels for depressive symptoms no significance was found ($p = 0.670$). On comparing the genders the mean ($\pm$ SD) score was 9.37 ± 10.52 (males) and 8.52 ± 7.55 (females) with no significant ($p = 0.718$) differences in the prevalence of depression between them. Prevalence of depression among the different campuses also remained non-significant ($P = 0.337$).

Conclusion: Despite statistically insignificant results, we believe that these results portray the wellbeing of our trainees and a structured training program.

Author Contributions: Sobia Haqqi conceived the study and design, interpreted the data and drafted the article. Areeb Sohail, Abdul Haseeb, Harris Hashim and Nisreen Ali contributed to the design of the study, collected and analyzed the data, and drafted the article.

Competing interests: No competing interests were disclosed.

Grant information: The authors declared that no grants were involved in supporting this work.

P 23. The questioning of the efficacy of antidepressants is based on the use of an inappropriate measure of improvement

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Background: The recent questioning of the efficacy of antidepressant drugs is to a large extent based on the assumption that the true effect can be assessed by comparing groups with respect to the summation of the 17 items on the Hamilton scale (HRSD-17). There are however reasons to question this view; that many of the listed symptoms are absent at baseline in many patients, and/or can be reported by non-depressed subjects, and/or can be present in recovered patients as side effects of treatment, are thus all aspects that might render HRSD-17 too blunt a measure for this purpose. In this vein, previous studies have shown subscales focusing on a few symptoms to be considerably more sensitive than HRSD-17.

Methods: We performed a post-hoc analysis of thirteen phase II-IV trials comprising twenty-one drug-placebo comparisons and including patient-level data from 5249 cases (*1642 placebo, 2303 paroxetine, 710 citalopram, 594 fluoxetine*), the aim being to assess what the outcome would have been if the single item *depressed mood,* rather than the HRSD-17 sum, had been used as measure of improvement.

Results: While 9 out of 21 comparisons (43%) failed to reveal a significant superiority of drug over placebo when the HRSD-17 sum was used as measure, only one out of 21 comparisons (5%) turned out negative when the effect was assessed using the *depressed mood* item. Moreover, while the average effect size for all comparisons was 0.30 when based on HRSD-17, it was 0.45 when based on the *depressed mood* item.

Conclusions: Our results support the notion that the use of HRSD-17 sum score is likely to result in a gross underrating of the actual efficacy of antidepressants. The use of this instrument may partly explain why many studies comparing an SSRI with placebo have failed to reveal a significant difference, as well as the outcome of recent meta-analyses questioning the efficacy of SSRIs as a group.

P 24. Childhood trauma and adult interpersonal relationship problems in patients with depression and anxiety disorder

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Background/Aims: Although a lot of studies have delineated the relationship of childhood trauma and onset, symptom severity and course of depression and anxiety disorder, there is little evidence that childhood trauma continues to the interpersonal problem in adulthood in patient with depression and anxiety disorder. Based on this background, we aimed to investigate characteristics of adulthood interpersonal problem in patients having various types of childhood abuse and neglect.

Method: A total of 311 outpatients diagnosed with depression and anxiety disorder completed questionnaire measuring socio-demographic, different kinds of childhood trauma and current interpersonal problems. Childhood Trauma Questionnaire (CTQ) was used to measure five different kinds of childhood trauma (emotional abuse, emotional neglect, physical abuse, physical neglect and sexual abuse) and current interpersonal problem was measured by the short form of the Korean version Inventory of Interpersonal Problems Circumplex scales (KIIP-SC). We dichotomized patients into two groups (abused group vs non abused group) based on CTQ score and investigated the relationship of five different kinds of childhood trauma and adulthood interpersonal problem in depression and anxiety disorder using multiple regression analysis.

Result: In the final regression model, emotional abuse and neglect were associated with general interpersonal distress and several specific areas of interpersonal problem. No association was found between childhood physical trauma and current general interpersonal distress. However, patients who experienced physical abuse appeared to be dominant position rather than submissive position in interpersonal relationship. Depressive symptom appeared to be related with all kinds of childhood trauma except physical neglect and elevated anxiety sensitivity was observed in patients having all kinds of childhood trauma except emotional neglect.

Conclusion: Childhood emotional trauma has more influence on adult interpersonal problem than childhood physical trauma. Physical abuse is related with dominant interpersonal pattern rather than submissive interpersonal pattern. These findings provide valuable evidence that childhood trauma might continue to adulthood interpersonal problem.

P 25. An auditory time reproduction task in bipolar disorder

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Background: The author's last study proved that experience of time in bipolar patients varies according to their mood states. But it was demonstrated during a visual task. So we tried to investigate it during a auditory tasks.

Methods: 20 patients with bipolar disorder (manic episode) were included. They were presented with a time reproduction task at two phases - manic phase and euthymic phase. Subjects were asked to listen two separated click sounds for 11, and 29 seconds. After that, they were asked to reproduce the same length of time of two click sounds.

Results: The short and long time intervals reproduced in manic phase were shorter than in euthymic phase in the same subjects. They reproduced 9539.1 ± 1110.5 msec in manic phase, 11100.0 ± 754.1 msec in euthymic phase in the case of 11 seconds stimuli. They did 27867.2 ± 2148.9 msec in manic phase, 30890.2 ± 2180.5 msec in euthymic phase in the case of 29 seconds stimuli.

Conclusions: Remembering and reproducing time intervals are shorter in the manic phase than in the euthymic phase. Eventually, Bipolar patients in manic phase experience faster flow of time than in euthymic phase. This results is similar to the visual time reproduction task.

P 26. Transcranial light exposure acutely alleviate anxiety symptoms in moderately depressed participants - A randomized, sham-controlled, double-blind trial

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Background: Bright light exposure has been found to have acute anxiolytic effects in patients suffering from Seasonal Affective Disorder (SAD) and subjects reporting low anxiety

symptoms.[1,2] In addition, data from a sham-controlled study with high-anxious young adults showed favorable results when comparing the bright light treatment with an inactivated negative ion generator, although statistically not significantly.[3] Transcranially administered bright light seems to alleviate anxiety symptoms of depressed patients suffering from SAD.[4] Since anxiety commonly co-occurs and has neurochemical similarity with depression, it is reasonable to expect that transcranially administered bright light might also have anxiolytic effects.

Methods: Twenty-eight participants (F = 19, M = 9, mean age ± SD: 44 ± 14 years) with anxiety symptoms (Beck Anxiety Inventory, BAI total score = 19 ± 9) were randomly assigned to either 12 minutes of acute transcranial bright light or sham exposure (double blind) under laboratory conditions in the morning between 9am and 12am. Anxiety symptoms were measured using the Spielberger State-Trait Anxiety Inventory (STAI, form Y1) self-rating questionnaire 5 minutes prior and 10 minutes after the exposure.

Results: Mean anxiety symptoms (STAI-Y1 score) in the transcranial light group decreased by 12.1 ± 7.3% from 43.7 ± 2.0 to 38.1 ± 1.4 ($p < 0.001$), whereas symptoms in sham-control group reduced non-significantly by 3.7 ± 11.3 % from 45.6 ± 2.2 to 43.4 ± 1.7 ($p = 0.115$). P-values for relative and absolute difference between groups regarding mean STAI-Y1 scores were 0.024 and 0.048, respectively.

Conclusions: This is the first randomized and sham-controlled bright light study, which shows that bright light alleviates mood symptoms acutely when it is administered transcranially. Further clinical studies on long-term efficacy of transcranial bright light treatment on anxiety symptoms are called for.

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P 27. Autonomic panic disorders after stroke

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Background: Autonomic Panic Disorders (APD) after strokes is one of the important types of Chronic Autonomic Failure, which may have a negative effect on the recovery of motor and social functioning, life quality of stroke survivors. Establishing the radiological correlates of neuropsychiatry after stroke might be helpfull to prevent it in early stages of disease.

Objectives: The aim of the present study was the assessment of prevalence, clinical and MRI correlates of APD.

Methods: We prospectively identified and examined 168 stroke patients. Stroke severity symptoms were assessed according to NHISS. Type, side and site of stroke was evaluated by conventional MRI. Diagnosis of APD was performed according to DSM-IV: A discrete period of intense fear or discomfort, in which four (or more) of the following symptoms developed abruptly and reached a peak within 10 minutes: palpitations, pounding heart, sweating, trembling, sensations of shortness of breath, feeling of choking, chest pain or discomfort, nausea or abdominal distress, feeling dizzy, derealization or depersonalization, fear of losing control or going crazy, fear of dying, paresthesias (numbness or tingling sensations),chills or hot flushes.In acute stage and 3 month later PA symptoms were evaluated with Panic Disorder Severity Scale.

Risk factors, clinical, demographic and radiological variables were set to multiple linear regression and binary logistic regression analysis to find independent correlates of Panic Disorders.

Results/Conclusion: From 168 patients APD was established in 29(17.2%). The study did not differ significantly between stroke side, type, size and location, but APD in acute stage and 3 month later correlated with anterior subcortical and basal ganglia stroke in the right hemisphere. Multiple linear regression analysis revealed a significant share of hypertension in the development of APD.

P 28. Hypertension and multiple brain damage integrity in late-life depression

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Background: Aged patients with the long lasting history of hypertension often complain of multiply silent ischemic damage, state that can lead to cognitive retardation, which is due to the injured microvasculature of frontal-subcortical areas, basis, vascular, mood circuit. Hypertension, which causes the lipohyalinosis of small cerebral vessels, may become the main risk-factor for vascular depression.

Goal: The aim of the study was to establish the impact of the hypertension on the induction of depression.

Material and methods: 136 hypertensive patients, aged 68,5 ± 7,5 years, have been investigated. Global cognitive function was evaluated by MMSE. Executive function was researched by neuropsychological test battery (letter fluency, Stroop Test, Wisconsin Card Sorting Test, digit span, letter member sequencing). Hamilton depression scale (HAM-D) was applied. Due to data patients were divided into two groups: I group- 68 patients with treated hypertension and II group,-66 patients with untreated and uncontrolled

hypertension. CT or MRI scan were performed in MCI patients to exclude another cause of cognitive decline. Two groups were compared in regard of hypertension and its treatment, vascular risk factors, demographic and radiological variables. Statistical evaluation was performed by SPSS-11.0.

Results and Conclusion: In a 1st group, depression was established in 11(16,1.8%) of hypertensive patients. In a 2nd group, depression was established in 17(25,7%) patients. Comparison of these two groups revealed that patients with untreated hypertension have significantly higher incidence of depression, and the more damage from multiple brain lesions, especially in frontal lobe ($p > 0.5$). Multiple linear logistic regression analysis revealed the significant share of untreated hypertension on development of mild cognitive impairment in late life ($p > 0.05$).

Detection of prehypertension state and treatment of hypertension in early state may prevent the depression and mild cognitive impairment in late life and improve the quality of life in elderly

P 29. Use of antipsychotics in management of depression, anxiety disorder with depression and OCD

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Objectives: Patients diagnosed with depression, depression with anxiety or OCD can be prescribed a combination of medications that include antipsychotics, antidepressants or one of each. In this audit, we will review the prescribing pattern of antipsychotics to this group of patients that were admitted.

Methods: 100 medical records were collected. Data included age, diagnosis, length of stay, number of relapses/new diagnosis and medications prescribed upon discharge. Data were collected using a questionnaire that were analyzed for patterns in prescription of antipsychotics. All patients involved were male who required admission and were discharged when stable.

Results: 45% of patients were found to be on an antipsychotic and antidepressant. Out of this group, 61% diagnosed with depression followed by 22.2% with OCD and 16.7% with anxiety disorders.

50% of these patients were between 31–50 years old, followed by 27.8% being more than 50 years of age.

Antipsychotics used were divided into typical and atypical antipsychotics. 55.6% were prescribed atypical antipsychotics and quetiapine most commonly prescribed, dominating 60% of the pool. As for the typical antipsychotics prescribed, sulpiride most commonly used at 75%.

Antidepressants prescribed with the antipsychotic medications consisted mainly of SSRIs at 66.7%, followed by others such as SNRIs and NaSSAs which were used at 33.3%.

Time at which antipsychotic was added to their prescription was pronounced most during the second admission at 77.8%, followed by first admission at 16.7%.

The length of stay was mostly in the 1–5 Day period at 38%.

Readmission figures for this group of patients showed that 66.7% of them ranged between 1–5 readmissions.

Conclusion: Most depression guidelines recommend the use of an antidepressant as first line treatment. This audit reveals that depressed patients that were admitted require prescription of an antipsychotic in combination with the antidepressant. It is most beneficial in the ages 31 to 50 years who have relapses of up to 5 readmissions.

P 30. Relative frequency of unipolar mania among hospitalized patients and its associate features: a multicenter study in Iran

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Background/aim: Considering the few studies made in the field of unipolar mania in the world, contradiction of current information, difference of its incidence in different studies and a lack of multicenter studies in this field in Iran, this study can be a manifest of preliminaries of this disorder in Iran.The goal of this study is to investigate the frequency of unipolar mania among patients suffering from unipolar mania in some mental health centers and to compare demographic and health variables among these patients as well as patients suffering from bipolar mania.

Methods: This multicenter study was made by reviewing of the files of patients suffering from bipolar mood disorder. Sampling method was made using available and simple sampling method. Finally, a number of 697 files were included. Main variables were the frequency of unipolar mania, demographic, course and treatment variables which were compared among patients suffering from unipolar mania and patients suffering from bipolar mania.Those patients were included into this study who had suffered from the disorder at least for 10 years. Average comparison of quantitative variables was made between the two groups using Man – Whitney test and comparison of qualitative variables was made between them using Chi-square test. Fischer test was used where necessary and the significant level of $p < 0/05$ was considered.

Results: Frequency of unipolar mania among patients suffering from bipolar disorder was 15.7%. Number of mania attacks, total number of mood episodes, lack of any dominant seasonal pattern, existence of psychosis in the first mania attack, existence of mood-congruent psychosis, and record of nicotine use between the two groups showed a significant difference.

Conclusions: Unipolar mania is prevalent in Iran and can be a distinct type of bipolar mood disorder. We recommend prospective studies in this field.

P 31. depression and suicidal ideation in community dwelling elderly

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Objectives: This study aims to investigate depressive symptom and suicidal ideation according to socioeconomic state in community dwelling elderly.

Method: We investigated 835 elderly subjects including 445(53.3%) which were home-visit service group and 390(46.7%) attending at senior center group, from April 2013 to May 2013. We investigated their demographic and socioeconomic data. Depressive symptoms were evaluated by the Geriatric Depression Scale (KGDS) and suicide ideation was evaluated by the Beck's Scale for suicide ideation (SSI). Using these data, we analyzed associated factor with depressive symptom and suicide ideation.

Result: The elderly with depressive symptoms amounted to 41% in a total elderly group. The depressive symptom in home-visit service group (59.3%) were significantly higher than that of senior center group (22.0%) ($P < 0.01$). The suicidal ideation in home-visit service group (15.3%) was significantly higher than that of senior center group (3.3%) ($P < 0.01$). In a factor analysis, depressive symptom (odd ratio: 8.59, 95% CI: 4.49–16.40), living alone (odd ratio: 1.72, CI: 1.01–2.94), no exercise (odd ratio: 1.69, 1.01–2.83), no current occupation (odd ratio: 3.41, CI: 1.16–10.07) were associated with suicide ideation significantly.

Conclusion: In this study the home-visit service group of the elderly patients in a low socioeconomic status had a higher rate of suicidal ideation and depressive symptoms than that of standard elderly group. We suggest future mental health care policy should be focused on a low socioeconomic community dwelling elderly.

P 32. Modulation of prefrontal-cingulate connectivity in affective processing of ostracized children

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Objective: In both circumstances of social exclusion and affective processing, the anterior cingulate cortex (ACC) and ventrolateral prefrontal cortex (VLPFC) have been shown to be involved. Here, we examined alterations in effective connectivity between these regions in response to emotional stimuli in children with experiences of ostracism in their everyday life.

Method: In functional magnetic resonance imaging (fMRI) experiments, 10 ostracized children and 11 control children were provided visual emotional feedback inducing negative or positive affective states. Using dynamic causal modelling, connectivity structure explaining the fMRI data was searched for and modulatory effects of the affective stimuli on the connections between VLPFC to ACC were estimated.

Results: The modulations of the connection from VLPFC to ACC were different between negative and positive emotional feedback contexts in ostracized children as compared to healthy children.

Conclusions: The findings suggest that the neural basis of ostracism can be revealed in terms of prefrontal-cingulate connectivity in the context of affective processing.

P 33. Behavioural effects of acute agomelatine doses in male mice social interaction model

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Background: Agomelatine is the antidepressant drug with agonistic melatonergic (MT1/MT2) and antagonistic serotonergic ($5HT_{2C}$) activity. Results of clinical studies show efficacy comparable with other classes of antidepressants with low risk of adverse effects. However, there is still a lack of information on agomelatine influence on affectivity. The aim of this study is to describe effects of acute agomelatine doses on singly-housed male mice on paired agonistic interactions with the non-aggressive group-housed partners.

Methods: The model is based on observation of ten behavioural acts performed during social interaction. While partners exert standard social behaviour, singly-housed animals can be divided into aggressive and timid phenotype according to control interaction under the vehicle treatment. All singly-housed mice were orally administered agomelatine at the doses of 2, 10 or 50 mg/kg or water, 30 minutes before interaction. Doses were administered according to Latin square design always one week apart. Animal behaviour was recorded and evaluated using the "Observer" system (Noldus Technology, Holland) by experimenter blind to application design. Frequency of sociable, timid, aggressive and locomotor/exploratory behavioural acts was evaluated.

Results: In timid animals ($n = 7$), there was a significant increase in aggressivity after the dose of 2 mg/kg. They also showed a dose-dependent inhibition of sociable behaviour, although on insignificant level. In aggressive animals ($n = 43$), there was significantly increased frequency of Defence posture after the dose of 50 mg/kg.

Conclusion: The most important findings of this study are increase of aggressive behaviour and inhibition of sociable behaviour in timid mice. Together with increased timidity in aggressive mice these results do not correspond with anxiolytic agomelatine effects described in the literature. Reason may probably lay in just acute dosing regimen used. It would be worthwhile to evaluate also changes of agonistic behaviour after the repeated drug treatment.

This work was supported by the project "CEITEC-Central European Institute of Technology" (CZ.1.05/1.1.00/02.0068).

P 34. Differences in frontal cortex vulnerability due to antipsychotics used in treatment of depressive disorder (animal model)

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Background/Aims: Antipsychotics substances are often used in the pharmacological therapy of depressive disorders. Preserve of neuroprotection in the frontal cortex represent an important target in the psychopharmacology of depression. The main objective of present study is represented by the assessment of differences in cerebral vulnerability realized by first and second generation antipsychotics.

Methods: Animal model study, on four lots consisting of 10 Wistar rats each, male adults, weight 200–250g, held during the study in temperature, humidity, food and ambient stressless conditions: N0 – control lot; N1 – dexamethasone (saline solution equivalent to 0.20mg/kg/day) administered intraperitoneally daily, for 14 days; N2 – haloperidol administered intraperitoneally (saline solution equivalent to 0.20 mg/kg/day); N3 – aripiprazole administered intraperitoneally (saline solution equivalent of 2 mg/kg/day). In the day 15, the rats were sacrificed.

The sample brain (frontal cortex) was histopathologically processed: formalin (10%) and ethyl alcohol (96%) fixation and paraffin embeded. Microtome slices were stained in hematoxyline-eosine, trichromicGS, PAS-hematoxyline, toluidine blue, methylen blue for Nissle corpuscles and argentic impregnation for neurofibriles. The obtained slices were studied with optical microscope.

Results: We observed that in the frontal cortex, dexamethasone conduced to a high level of neuronal apoptosis and pinocytosis, while haloperidol has a medium level of neuronal destruction. Second generation antipsychotic class, represented by aripiprazole, has a minimum number of cellular abnormalities for neurons and glial cells from this cerebral area.

Conclusions: Our study confirmed the existence of differences between neuroprotective skills of antipsychotic substances. Haloperidole has a significant decrease in neuroprotection, while second generation antipsychotics (aripiprazole) proved a superior neuroprotective on animal model.

P 35. Depression in first episode schizophrenia patients – data from Romanian cohort of EUFEST Study

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Introduction: Depression in schizophrenia is highly prevalent (25%) and an important risk factor for increasing mortality or relapse in schizophrenia patients. Besides the efficacy of antipsychotics, the EUFEST study has brought important information about first episode schizophrenia patients, which have a high prevalence of depression.

Objective: The purpose of our paper is to evaluate the prevalence and the socio demographic and psychopathologic correlates of depression of schizophrenic first episode patients and the outcome of initial depressed patient in the Romanian cohort of EUFEST study.

Methods: Data presented here are are a secondary analyses of Romanian patients included into the European First Episode Schizophrenia Trial. Depression was measured by the Calgary Depression Scale for Schizophrenia scale, using the cut-off of 6. Data were analysed with standard descriptive function, chi square for categorical data, t-test for continuous data and Cox regression function.

Results: Data were available for 111 patients with FES, from which 37 (33.3%) met the criteria for depression. At the beginning of the study there were statistical differences between depressed and non-depressed patients, regarding negative symptoms ($p = 0.01$), general psychopatology ($p = 0.001$) and total PANSS score ($p = 0.001$), however no differences were to be found at 1-year evaluation. There were no differences between duration in treatment in depressed vs non-depressed patients, after controlling for treatment arms, Exp (B) 1.281, CI 95%: .563-2.918, $p = .555$. There are no differences between depressed vs non-depressed patients who finished the study (1 year): $N = 32$ (86.5%), $N = 60$ (81.1.7%) with $p = .597$.

Conclusions: First episode schizophrenia patients (FES) in the Romanian cohort of EUFEST study presented depression in 33.3% of the cases. Psychopathological correlates were found only at the beginning at the study, regarding depression and negative, general and total PANSS scores. The 1-year outcome and retention of patients with FES and depression did not differ significantly from those without

P 36. Social class and depression risk

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Background: Lower social class represents a well established risk factor for depression.[1]

Aims: The purpose of our study was to observe the relationship between social class and risk for depression (age 30 years), while controlling for putative confounders or other

risk factors for both depression and social class: parental socioeconomic status (ses), maternal depression (data were not collected for paternal depression), childhood cognitive functioning.

Methods: Data for this paper originated from the cohort study "British Cohort Study 1970" which enrolled 16135 newborn infants.[2] Data about childhood cognitive functioning, parental ses and maternal depression were evaluated age 5 and data about subjects' social class and depression age 30.

Depression was evaluated with The Malaise Inventory and childhood cognitive functioning with English Picture Vocabulary Test. Parental educational level was used as a proxy for parental ses.

Results: The proportion of depressed people aged 30 by social classes was: professional 4.7% (N = 27) (reference group), managerial-technical 9.2% (N = 290)-p = .006, skilled (manual and non manual) 10.5% (430)-p = .001, partly skilled 14% (N = 138)-p = .001, unskilled 14.5% (N = 27)-p = .002, the proportion of depression increasing as social class decreases.

When we analyzed for current (30 years) social class assessing the parental socioeconomic status, maternal depression and childhood cognitive functioning, present social class (data presented above), paternal educational level (p = .038) and childhood cognitive functioning (p = .010) appear as risks factors for the onset of depression at the age of 30.

Conclusions: The results seem to imply the fact that lower social class represent an important risk factor for adult depression, but childhood cognitive functioning and paternal educational level also play a role.

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P 37. Characteristics of elderly suicide attempters in Korea; distinction between "Young-old" vs "Old-old"

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Background/Aims: Suicide amongst the elderly showed different patterns which were unlike other age groups in physical, mental, and economic aspects, and there were also insufficient empirical researches. This study focused on the characteristics of the elderly suicide attempts.

Methods: Participants were suicide attempters aged 45 years old and over who visited an Emergency Medical center, from March 2009 to December 2012, and who agreed to psychiatric interview. All subjects were classified into three groups according to their age (middle age: 45–59 years old, young old: 60–74 years old, old-old: 75–100 years). Sociodemographic, clinical information was obtained through interviewing the subjects and care-givers.

Results: Of the 384 individuals, 56.4% of middle age (N = 214), 38.4% of young-old age (N = 100) and 18.2% of old-old age (N = 70). Proportion of living alone was higher in Old-Old group compared than other groups. The use of alcohol at the time of suicide attempt was higher in the middle age group. While interpersonal problem is a major motivation in the middle age group, physical illness is in the elderly. Although old-old group had a higher rate of depression, they tend not to receive psychiatric evaluation.

Conclusion: Suicides amongst the elderly is related to a higher level of living alone and physical vulnerability than in other age groups, and so risks of suicide attempts increase according to age. Therapeutic approaches or preventive strategies for suicide attempts in the elderly are required.

P 38. An integrated model to improve access to psychiatric treatment in homebound elderly with depression

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Background/Aims: The prevalence of depression amongst U.S. adults 50 years or older is 8%. Despite the burgeoning cohort of elders with multiple medical comorbidities and depression, only 3% of adults over 65 years old receive care from a mental health provider. Furthermore the time between referral to a mental health specialist and evaluation may be as long as 3 to 4 months. In 2004, Montefiore Home Health Care, Bronx, NY and the Department of Psychiatry at Montefiore Medical Center, an accountable care organization, created a program to integrate a geriatric psychiatrist into the home care team. The purpose of this study is to assess if this program improves access to psychiatric care in homebound patients by providing home visits and decreasing the time between referral to evaluation.

Methods: New York Cornell Westchester trained clinical staff on recognition of depression. Patients who screen positive for depression on the PHQ 9 or present with depressive symptoms are referred to the psychiatrist. She completes an evaluation in the home and shares recommendations with the primary care doctor, social worker and visiting nurse. Charts were reviewed from July 1 to August 31, 2013.

Results: 37 patients were referred to the geriatric psychiatrist between July 1 and August 31, 2013. 30 in-home psychiatric evaluations were completed. 2 refused. 1 was discharged and 4 were pending evaluation. 73.3% were female. 63.3% were Hispanic, 20% were Black/African American, and 16.7% were White/Non-Hispanic. The mean and mode time from referral to evaluation were 7.1 days and 1 day, respectively.

Conclusions: This model to integrate a geriatric psychiatrist into home care effectively improves access to psychiatric care in homebound elders with depression by completing home-based evaluations and diminishing time between referral to evaluation. Future implications include investigating how this model of psychiatric care may improve care and decrease spending within different health systems such as accountable care organizations.

P 39. A study of phenomenology of anxiety disorders in children and adolescents from India

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Introduction: Anxiety disorders represent one of the most common forms of psychopathology among children and adolescents, but they often go undetected or untreated. The phenomenology of anxiety disorders in children and adolescents differs from that of adults.

Aim: The aim of this study was to assess the phenomenology of anxiety disorders in children and adolescents along with psychiatric co morbidities.

Methods: Patients between age group 6 to 16 years attending child and adolescent psychiatry clinic were screened for anxiety disorders by Screen for child anxiety related emotional disorders (SCARED) scale. Screen positive patients for anxiety disorders were assessed for the phenomenology of anxiety disorders by using Kiddie – Schedule for Affective disorders and Schizophrenia– present and lifetime version (K-SADS-PL).

Results: Out of 1465 screened patients 42(2.86%) patients had different anxiety disorders. Out of which 16(38.1%) patients had obsessive compulsive disorder, 10(23.81%) patients with specific phobias, 6(14.29%) patients with generalised anxiety disorder, 4(9.52%) patients with social anxiety disorder and 3(7.14 %) patients each with separation anxiety disorder and panic disorder.Mean age of patients with anxiety disorders was 12.5 ± 2.34 years. Anxiety disorders were more in females patients 26(62%). Co morbidities were found in 22 (54%) of patients with anxiety disorders. Dissociative disorder 8(36.36%), specific phobias 5(22.73%) and social anxiety disorder 4(18.18%) were the common co morbidities. Impairment due to anxiety disorders was more in obsessive compulsive disorder (Mean C-GAS score -46 ± 6.21) while it was less in panic disorder (Mean C-GAS score -64).

Conclusion: Anxiety disorders are the most common psychiatric disorder in children and adolescents. Still it is less commonly found in clinic settings (2.86%). No case of post-traumatic stress disorder or acute stress reaction was found in this study.

P 40. First year depression data from a treatment resistant clinic

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Background: Singapore has a population of 5.3 million residents. A recent epidemiological study has found the lifetime prevalence rate of depression to be 5.8%. It is likely that a significant number will be treatment resistant and will require a higher intensity of intervention.

In late 2010, a mood disorder service specializing in the management of treatment resistant depression and bipolar disorder was set up in the Institute of Mental Health in Singapore. The service offered a multidisciplinary approach with a fixed and experienced team of psychiatrists, pharmacists, social worker and psychologist.

Methods: Patients were accepted to the clinic by referral from a psychiatrist only. Upon acceptance to the clinic, patients would undergo close and intensive follow-up until stable. The initial contracted period of follow-up would be for a year.

Scales were administered at the first visit, 3, 6 and nine months. They were also assessed at their final visit (between 12–14 months). The following scales were used: HAMD, GAF and CGI. The same interviewer administered all the scales.

Results: Of the patients presenting to the clinic with treatment resistant major depressive disorder ($N = 19$) and had completed treatment, the initial mean HAMD was 16.1, GAF was 54.3 and the CGI was 4.4.

At the end of the follow-up with the service, the 12 month mean HAMD was 4.9, GAF was 68.7 and CGI 3.1.

Conclusions: Although the service was only in its infancy, patients with treatment resistant depression were able to obtain different interventions, which has resulted in an improvement in their symptoms.

Of course, the greatest benefit of this service would be the rekindling of hope and optimism as many have tried many treatments and interventions prior to being referred to the service.

P 41. Lithium intoxication within normal therapeutic blood level: a case report

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Background: Lithium is primarily used in treating bipolar disorder. Major side effects occur in chronic use or acute overdose, which result in CNS toxicity.

Case: A 45-year-old male patient has been suffering from bipolar disorder. He has a history of hypertension, intracranial hemorrhage, alcohol dependence. The patient had been on the maintenance treatment of lithium 600 mg/day, quetiapine 100 mg/day, and other minor medications at the other institution for the treatment of bipolar disorder. On May 14th, 2012, due to hypomanic episode, lithium and quetiapine were increased to 900 mg/day and 200 mg/day and a week later to 1200 mg/day and 400 mg/day, respectively. The patient was found lying down and continuously shaking extremities, was transferred to ER on June 8th, 2012. Lithium was stopped for a week, and tremor disappeared with conservative treatment at ICU. 14 days after the discharge,

the patient revisited other institution and prescribed with reduced dose of Lithium 600 mg/day and valproic acid 600 mg/day and quetiapine 400 mg/day. When the medication was restarted, the patient show reoccurring of the symptoms. After readmission to our hospital, all the medications were discontinued, were normalized with conservative therapy.

Discussion: Lithium toxicity is manifested as CNS toxicity according to its blood concentration. Despite the fact that blood concentration of Lithium is within the safety range, resolution of CNS toxicity, symptoms of which may last more than 7 to 10 days. In addition, after complete recovery, symptoms of toxicity reoccur even within the therapeutic range of its concentration when treatment with Lithium was restarted.

P 42. Treatment of neuroleptic malignant syndrome in child and adolescent: a case report

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Background: Neuroleptic Malignant Syndrome is a rare clinical syndrome occurring due to idiosyncratic reaction after the use of neuroleptics. Recently, the use of antipsychotics has been increasing in the field of child and adolescent psychiatry especially in psychosis, mood disorder, and destructive behavior disorders.

Case: A 14-year-old male patient, diagnosed with schizophrenia. He was prescribed with 6mg/day of risperidone in combination with 300 mg/day of quetiapine. The 3 days before the onset of neuroleptic malignant syndrome, all oral medications were stopped along with NPO for treatment due to manifestation of paralyticileus from worsening of underlying constipation; in addition, IM injection of haloperidol was only allowed for the symptom control. The day before the onset, an IM injection of 15 mg of haloperidol and 10 mg of lorazepam resulted in vomiting, headache, fever of 39°C, systemic tremor and stiffness, confusion, tachycardia and sweating. Blood work-up performed on the day of admission at ICU indicated CPK 2836 IU/L and myoglobulin 337.2 ng/ml, and CPK, after peaking at 4493 IU/L, continuously decreased and was normalized by the 18th day at ICU. Diazepam, dantrolene, domperidone, L-Dopa/benserazide and cold blanket were applied. Normalization of hematologic abnormalities were followed by stabilization of tremor, stiffness, and high fever on the 18th day.

Discussion: Neuroleptic malignant syndrome is an exigent condition which may cause fatal outcomes in the field of psychiatric treatment. Cautious pre-evaluation of risk factors in patients requiring neuroleptics are critical in order to prevent fatal complications.

P 44. Frequency and impact of pain symptoms in patients with depression in Taiwan

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Objectives: This study aimed to examine the proportion of depressive patients with painful physical symptoms (PPS) in Taiwan and its influence on the outcomes of depression.

Methods: 198 in- and out-patients from Taiwan presenting with a new or first episode of major depressive disorder (DSM-IV/ICD-10) were enrolled in a 3-month prospective observational study. Patient demographics, depressive symptoms (Hamilton Depression Rating Scale, HAMD-17), overall severity (Clinical Global Impression-Severity, CGI-S), somatic symptoms (Somatic Symptom Inventory, SSI) and quality of life (Euro QOL-5D, EQ-5D) were assessed at baseline and at three months. The presence (PPS+) or absence (PPS-) of PPS was defined as a mean score of ≥ 2 or < 2, out of a rating from 1 to 5, on the pain-related items of the SSI (abdominal, lower, joint, neck, heart and chest pain, headache and muscular soreness) at baseline. Multiple linear regression analyses were used to analyze the influence of PPS at baseline on the outcomes of depression, adjusting for baseline patient characteristics.

Results: The mean age of the sample was 46.47 years (SD 14.35); 69% were women. Approximately 69% of the sample had PPS at baseline. Compared with PPS- patients, PPS+ patients had higher depression severity (HAMD-17 rating 27.53 (SD 6.18) vs. 22.45 (SD 5.74)) and lower quality of life (EQ-5D score 0.30 (SD 0.33) vs. 0.65 (SD 0.31)) at baseline. This pattern remained the same at three months. The adjusted HAMD-17 rating at three months was higher in PPS+ patients than PPS- patients by 2.93 points (95% CI: 0.17, 5.68). The adjusted differences in quality of life (EQ-5D VAS rating) between the two cohorts at three months was -9.95 (95% CI -18.87, -1.04) .

Conclusions: The presence of PPS in a depressive episode was associated with a higher level of depression severity and a lower level of quality of life at three months.

P 45. Frequency and impact of pain symptoms in patients with depression in Malaysia

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Aims: This study aimed to examine the proportion of depressive patients with painful physical symptoms (PPS) in Malaysia and its influence on the outcomes of depression.

Methods: 95 in/out-patients from Malaysia presenting with a new or first episode of major depressive disorder (DSM-IV/ICD-10) were enrolled in a 3-month prospective observational study. Patient demographics, depressive symptoms (Hamilton Depression Rating Scale, HAMD-17), overall severity (Clinical Global Impression-Severity, CGI-S), somatic symptoms (Somatic Symptom Inventory, SSI) and quality of life (EuroQoL-5D, EQ-5D) were assessed at baseline and at three months. The presence (PPS+) or absence (PPS-) of PPS was defined as a mean score of ≥ 2 or < 2, out of a rating from 1 to 5, on the pain-related items of the SSI (abdominal, lower, joint, neck, heart and chest pain, headache and muscular soreness). Multiple linear regression analyses were used to analyze the influence of PPS at baseline on the outcomes of depression, adjusting for baseline patient characteristics.

Results: Mean age was 41.6 years (SD 12.42); 67% were women. Approximately 63% of the sample had PPS at baseline. Both PPS+ and PPS- patients had similar depression severity at baseline (HAMD-17 24.13 (SD 4.90) vs. 23.23 (SD3.51). PPS+ patients had lower quality of life at baseline (EQ-5D 0.38 (SD 0.28) vs. 0.70 (SD 0.22). PPS+ patients had higher depression severity at three months. The adjusted HAMD-17 rating at three months was higher in PPS+ patients than PPS- patients by 2.38 points (95% CI: 0.24, 4.52). The level of quality of life (adjusted EQ-5D VAS rating) at three months was also lower in PPS+ patients than PPS- patients by 18.76points (95% CI: -28.20,-9.31).

Conclusions: The presence of PPS in patients with a depressive episode was associated with a higher level of depression severity and a lower level of quality of life at three months.

P 46. Treatment effectiveness for patients major depressive disorder treated with either duloxetine or selective serotonin reuptake inhibitors in Middle East

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Objectives: The aim of the study was to compare treatment effectiveness in patients with major depressive disorder (MDD) treated with either duloxetine or a selective serotonin reuptake inhibitor (SSRI) as a monotherapy for up to 6 months in a naturalistic setting in the Middle East.

Methods: Data in this *post hoc* analysis were taken from a 6-month prospective, non-interventional, observational study that included a total of 1,549 MDD patients without sexual dysfunction at baseline in twelve countries ($n = 314$ from the Middle East). Depression severity was measured using the Clinical Global Impression (CGI) and the 16-item Quick Inventory of Depressive Symptomatology Self-Report ($QIDS\text{-}SR_{16}$). Pain was measured using the pain related items of the Somatic Symptom Inventory (SSI). Probabilities of initiating duloxetine (vs. SSRIs), expressed as propensity scores, were first constructed using logistic regression. Mixed effects modelling with repeated measures (MMRM) analysis was then used to compare treatment effectiveness between the duloxetine ($n = 160$) and SSRI ($n = 134$) groups, controlling for the propensity scores and other patient characteristics.

Results: The severity of depression and pain was comparable between the two groups at baseline. Both descriptive and MMRM regression analyses, however, showed that patients treated with duloxetine had better outcomes during follow-up, compared with patients treated with SSRIs. At 6 months, duloxetine-treated patients had lower levels of CGI (2.17 vs. 2.66, $p < 0.01$), $QIDS\text{-}SR_{16}$ (2.63 vs. 4.26, $p < 0.001$), and SSI-pain related (10.71 vs. 13.10, $p < 0.001$) (MMRM results).

Conclusions: Duloxetine-treated patients had better 6-months outcomes in terms of depression severity and pain, compared with SSRI-treated patients.

P 47. Impact of anxiety symptoms on outcomes of depression. A study in patients from Asia

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Introduction: Anxiety symptoms are frequent in patients with depression and appear to be associated with worse depression outcomes. The aim of this study is to investigate the impact of anxiety symptoms on depression outcomes in patients from Asia.

Methods: 909 in- and out-patients from Asia, presenting with a new or first episode of Major Depressive Disorder (DSM-IV/ICD-10) were enrolled in a 3-month prospective observational study. Patient demographics, depressive symptoms (Hamilton Depression Scale-HAMD-17), overall severity (Clinical Global Impression Severity–CGI-S), somatic symptoms (Somatic Symptom Inventory) and quality of life (Euro QOL-5D) were assessed. Anxiety symptoms were measured using items 10 and 11 from the HAMD-17. Patients with baseline and 3-month assessments were included in the this analysis ($N = 714$). Remission was defined as a HAMD17 total score ≤ 7. Linear, tobit and logistic regression models were used to analyze the impact of anxiety symptoms on depression severity, remission and quality of life at three months, adjusting for age, sex, and country and other significant covariates. Path analysis was employed to study the role of anxiety symptoms as mediators of the effect of pain on quality of life.

Results: The mean age of the sample was 45.9 years (SD 14.2) and 69% were women. Level of anxiety symptoms at

baseline was correlated with levels of depression and quality of life at three months. Regression results confirmed these findings Patients with a higher level of anxiety symptoms at baseline were less likely to have remission at 3 months (odds ratio 0.83 95% CI 0.72, 0.95). They also had a lower level of quality of life at three months (EQ5D -0.023 95% CI -0.045,-0.001).

Conclusions: The presence of anxiety symptoms in patients being treated for a depressive episode negatively impacts the outcomes of depression.

P 48. Adverse cutaneous effects of mood stabilizers

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Background/Aim: Mood stabilizers can be associated with adverse cutaneous reactions ranging from mild reactions to severe and potentially life-threatening reactions. The aim of this review is to explore the skin reactions associated with use of mood stabilizers including lithium, valproic acid, carbmazepine and lamotrigine.

Methods: We conducted a PubMed literature search using the key words; mood stabilizers, cutaneous reactions, skin reactions, lithium, valproate, carbamazepine, lamotrigine.

Results: Mild cutaneous reactions, such as pruritus, urticaria, hair loss and fixed drug eruptions, can occur with mood stabilizers. Hair loss is one of the common side effects of valproate which can occur in up to 28% of cases. Toxic alopecia secondary to lithium and valproate may occur with diffuse hair loss which usually resolves after stopping medications. Some primary skin conditions, such as acne and psoriasis, may be triggered or exacerbated by mood stabilizers, particularly lithium compounds. Life-threatening cutaneous drug reactions include erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, exfoliative dermatitis, drug hypersensitivity vasculitis, and Drug hypersensitivity syndrome which is also known as drug eruption with eosinophilia and systemic symptoms (DRESS) syndrome. Use of carbamazepine and valproate is associated with significant risk of erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis. Use of lamotrigine is associated with risk of developing angioedema, Stevens-Johnson syndrome and toxic epidermal necrolysis.

DRESS syndrome commonly occurs with aromatic antiepileptic drugs. Carbamazepine-induced DRESS syndrome may present with maculopapular eruption, exfoliative erythroderma, fever, and lymphadenopathy. Leukocytosis, atypical lymphocytes and hepatic failure can also occur.

Conclusion: Adverse cutaneous effects can occur with all types of mood stabilizers with varying severity. Careful monitoring for possible cutaneous reactions, particularly life-threatening conditions, should be considered when starting treatment with mood stabilizers.

P 49. Trauma informed care survey of psychiatrists and primary care physicians in the Middle East

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Background: Trauma has become an almost near universal experience due to violence, war, social and political instabilities. The physical and psychological consequences are highly disabling.

Aim: In this study we aim to sensitize mental health professionals and primary care practitioners to the extent and impact of trauma. Methods: The study is part of a partnership global mental health project between the Zayed Institute for Public Health at the United Arab Emirates University (UAEU) and the Harvard Program in Refugee Trauma (HPRT). This is an online survey of psychiatrists and primary care physicians from 20 countries with items focusing on trauma related clinical strengths and weaknesses of Middle Eastern Region mental health centers and primary health care.

Results: There were 85 completed responses. Almost half of the respondents reported that primary health care practitioners in their country are not trained to provide basic mental health services to the general population affected by trauma (47.2%) nor to persons with serious mental illness (45.2%). few respondents were completely confident to Identify and treat teenage (27.1%) or children (15.7%). Only 21.7% were completely confident to identify and treat victims of domestic violence. Most common types of reported traumas were; divorce/separation, the recent death of a close relative or friend, domestic violence and the psychological effects of war and refugees/internally displaced persons (28.8%, 27%, 21.3, 17.8% & 12.5%).

Conclusions: Our study highlights the need to develop awareness in Primary Health Care and Mental Health- and training programs in the area of the identification and treatment of traumatized persons of different age groups. We hope to expand this leading effort in the United Arab Emirates to develop a global mental health alliances for excellence in research and training in trauma informed mental health services.

P 50. Prevalence and sociodemographic correlates of premenstrual dysphoric disorder symptoms in the Gulf city of AlAin

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Background: Approximately 50–80% of women of reproductive age will experience premenstrual symptoms of varying

severity. The increased number and severity of symptoms is reported to have direct correlation with greater impairment across life domains. The prevalence of premenstrual dysphoric disorder which is clinically relevant is reported between 13–18% of women of reproductive age. Aim: This epidemiologic survey studied the prevalence and impact of premenstrual dysphoric disorder (PMDD) among adult women attending the primary care clinics in AlAin.

Methods: Five hundred and eight (n = 508) women in their reproductive years were selected at random from 5 clinics and were administered two screening instruments for PMDD.

Results: The prevalence of severe forms of PMDD was 4.3%. Moderately severe cases were 8.1%. There was significant association between the disorder (PMDD) and several socio-demographic factors. There was no statistical difference in prevalence of the disorder between UAE national and non-nationals. The resulting disability was assessed using the Sheehan Disability Scale (SDS). Logistic regression analysis revealed a significant association between the presence of the disorder and four specific life stressors reported over the past 12 months.

Conclusions: The prevalence of PMDD is consistent with the lower reported international rates and is higher among the highly educated and single. UAE nationals report less disability in association with the disorder. There was a strong association between major past life stressors in those women with the disorder compared with those without. These points to a specific vulnerability that requires further study. The study suggests co-morbidity with other psychiatric conditions.

P 51. Polarity index in bipolar disorder maintenance treatment: A naturalistic study

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Background/Aims: Predominant polarity is among the strongest predictors of recurrence into a specific episode and should be considered when implementing maintenance therapy.

Recently we have developed Polarity Index (PI), a metric depicting the relative antimanic versus antidepressive prophylactic efficacy of drugs and psychotherapies.

This study aimed to determine the role of PI in clinical decision-making and to assess differences between predominantly manic and depressed patients.

Methods: The study sample was composed of 604 BD patients. Patients who fulfilled criteria for Manic (MPP) or depressive (DPP) polarity were compared regarding sociodemographic, clinical and therapeutic characteristics.

The PI, a numeric expression of the efficacy profile of a given drug, derives from Number Needed to Treat (NNT) for prevention of depression and NNT for prevention of mania ratio, as emerging from the results of randomized placebo-controlled trials [1]. Treatments with PI > 1 have stronger antimanic prophylactic properties, while treatments with PI < 1 are predominantly antidepressive. The PI of drugs for maintenance treatment of BD was: risperidone 12.09, aripiprazole 4.38, ziprasidone 3.91, olanzapine 2.98, lithium 1.39, quetiapine1.14, and lamotrigine 0.40. PI for patients' current treatment was calculated as mean value of all prescribed drugs in each patient.

Results: 257/604 (43%) of patients fulfilled criteria a predominant polarity. 143 patients (55.6%) presented DPP.

Total PI, as well as Antipsychotics' PI and Mood Stabilizers PI were higher, indicating a stronger antimanic action, in MPP.

MPP group presented more BD-I, male gender, younger age, age at onset and at first hospitalization, more hospitalizations, primary substance misuse and psychotic symptoms. DPP correlated with BD-II, depressive onset, primary life events, melancholia and suicide attempts. The twogroups presented different treatment pattern.

Conclusions: Clinical differences among MPP and DPP groups justify differential treatment approach. PI may guide treatment choice in the context of personalized patient care and its external validity was shown in this naturalistic study.

P 52. Trait impulsivity and clinical characteristics in bipolar disorder

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Background: Bipolar disorder is associated with high levels of trait impulsivity, and previous research suggests that there are certain key clinical correlates of high trait impulsivity, such as suicide attempts, rapid cycling, presence of substance misuse and younger age of illness onset. However, further detailed exploration of clinical correlates in large, well-characterised, independent samples is required.

Methods: We examined a broad range of lifetime clinical features in 1266 individuals with bipolar disorder recruited by the UK Bipolar Disorder Research Network (bdrn.org) who had high (n = 428) and low (n = 848) trait impulsivity as assessed by the Barratt Impulsiveness Scale (BIS, version 11).

Results: Multivariate analysis revealed that even after controlling for participant age at time of completing the BIS, education level and current mood state (Beck Depression Inventory and Altman Mania Scale scores), individuals with bipolar disorder and high trait impulsivity were significantly more likely to have attempted suicide (OR = 1.65, 95% CI = 1.10–2.46, p = 0.015), have a rapid cycling course of illness (OR = 1.74, 95% CI = 1.13–2.67, p = 0.012) and have never been admitted as a psychiatric in-patient, (OR = 0.470, 95% CI = 0.298–0.741, p = 0.001) than those with bipolar disorder and low trait impulsivity.

Conclusions: Clinicians should be vigilant for high levels of trait impulsivity in their patients with bipolar disorder. Such patients may be at higher risk of suicidal behaviour and an unstable (rapid cycling) illness course, yet be less likely

to have episodes severe enough to warrant in-patient observation and treatment. These significant associations require further investigation in prospective longitudinal studies to improve understanding of the role of impulsivity in the complex aetiology of bipolar disorder.

Conflict of Interest/Disclosure: No conflicts of interest to report.

Ethical approval: This study had all relevant national and local ethical approval, and written, informed consent was taken from each participant.

P 53. The effect of self esteem and social support on suicidal ideation among elderly in a city of Korea: focused on the mediating effect of depressive symptoms

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The purpose of this study was to examine the relationship among self esteem, social support and suicide ideation as well as the mediating effects of depressive symptoms. The data of this study were collected from over 65 year old subjects located in Ik-san, Jeollabuk-do province, Republic of Korea. 320 data sheets were collected, and among them, 300 were used in analyzing. All the subjects were evaluated for depression, suicidal ideation, self esteem, social support with Geriatric Depression Scale Short Form-Korean (GDSSF-K), Scale for Suicidal Ideation (SSI), Rosenberg Self-Esteem Scale, and Scale of Social Support (SSS). The data were analyzed by factor analysis, descriptive statistics, correlation and structural equation modeling. The major findings of this study were as follows: First, suicidal ideation was negatively related to self-esteem($r = -.467$, $p < .01$), social support($r = -.355$, $p < .01$) but, positively related to depressive symptoms($r = .482$, $p < .01$). Second, self esteem and social support had direct effects on their suicidal ideation. Third, depressive symptoms mediated the process of developing suicidal ideation in the elderly. These results showed that the social support and self esteem directly influenced suicidal ideation and depressive symptoms mediated self esteem, social support and suicidal ideation.

P 54. Prevalence of depression and correlated psychosocial factors of married immigrant women in a city of Republic of Korea

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Objectives: The purpose of this study was to investigate the prevalence of depression of immigrant women in Korea and to understand its correlated factors such as acculturative stress, social support, proficiency in Korean, depression, somatic symptom and pain.

Methods: 119 immigrant women in Korea were assessed their depression, acculturative stress, social support, proficiency in Korean, somatic symptoms and pain by Acculturative Stress Scale, the Multi-dimensional Scale of Perceived Social Support(MSPSS), Beck Depression Inventory(BDI), Patient Health Questionnaire-15(PHQ-15) and Visual Analog Scale(VAS) of pain.

Results: The prevalence of depression of married immigrant women was 29%. The level of acculturative stress, social support and somatic symptom and degree of pain in depressive group were significantly higher than the non-depressive group. There were positive correlations between BDI and acculturative stress, somatic symptom and degree of pain. There was a negative correlation between BDI and social support. The level of acculturative stress has a negative correlation with proficiency in Korean.

Conclusion: The depression has correlated with acculturative stress, less social support, somatic symptom, and pain. These results suggest that mental health programs might be needed for married immigrant women and the psychosocial factors could be considered for the treatment program.

P 56. Mental disorders in offspring of parents with bipolar disorders

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Objectives: There is limited information on the specificity of associations between parental bipolar disorder (BPD) and the risk of psychopathology in their offspring. The chief aim of this study was to investigate the association between BPD in the parents and mental disorders in the offspring in Korea.

Methods: A total of 72 offspring (aged 6.0–18.9 years; mean = 13.4 years) of 48 patients with BPD, 50 offspring (aged 6.0–18.9 years; mean = 11.5 years) of controls participated in a family study. Parents with BPD were recruited primarily through inpatient and outpatient clinics between January 1, 2012, and August 31, 2013. Probands, offspring, and biological co-parents were interviewed by psychologists, using a semi-structured diagnostic interview.

Results: 29 subjects (40.3%) in offspring of parents with bipolar disorders had a psychiatric disorder, most commonly (31.9%) a mood disorder. Rates of mood and anxiety disorders were elevated among offspring of BPD probands (31.9% any mood; 22.2% any anxiety) as compared to those of controls (10.0% any mood; 18.0% any anxiety).

Any bipolar spectrum disorders was more frequent among offspring of BPD probands (12.5%) than those of controls (2.0%). Any depression was more frequent among offspring of BPD probands (19.4%) than those of controls (8.0%).

28 subjects (38.9%) had at least one comorbid disorder such as ADHD (n = 9, 12.5%), disruptive behavior disorders (n = 10, 13.9%) and anxiety disorders (n = 16, 22.2%). Parental concordance for BPD was associated with a further elevation in the rates of mood disorders in offspring (40.0% both parents versus 31.3% one parent).

Conclusions: Offspring of parents with BPD are at high risk for psychiatric disorders and specifically for early onset BP spectrum disorders. These findings further support the familiarity and validity of BPD in youth and indicate the need for early identification and treatment.

P 57. Psychotic symptoms in a sample of Albanian immigrants – correlation between sociodemografic factors and psychosys

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Introduction: These data are part of a wider research on Albanian immigration and factors influencing psychosis. The experience of migration can negatively influence mental health (Furnham & Bochner, 1986) and immigrants may have an increased risk for mental health disorders and distress when compared to non-immigrants (Breslau, et al., 2007).

Aim: How it is the correlation between immigration factors and most frequent psychotic symptoms manifested of the participants in the study.

Methods: The study sample was made up of 41 Albanian individuals (M:F = 4.9:1), presenting at University Hospital Center "Mother Teresa" Tirana during six months, with psychotic symptoms and a history of Immigration. Mean age of the subjects was 33.7 years. Semi-structured interviews that utilized several cross culturally validated questionnaires were conducted with all participants, Personal and Psychiatric History Schedule and Structured Clinical Questionnaire for DSM-IV. Non-parametric statistics (Kruskal Wallis) tests were used to determine if the immigration factors were associated with type of psychotic symptoms.

Results: The most commonly reported type of trauma was material deprivation (73%), followed by death or disappearance of family members (55%), witnessing violence (43%). Greater numbers of immigration factors were significantly associated with higher levels of persecutory delusions ($\chi 2 = 168.4$, $p = .001$), auditive commanding hallucinations ($\chi 2 = 42.1$, $p = .001$), and intrusive thoughts ($\chi 2 = 34.1$, $p = .001$). Acculturation factors were significantly negatively correlated ($r = -0.29$, $p < .001$) as well as language acculturation ($r = -0.31$, $p < .001$) and social acculturation ($r = -0.24$, $p < .001$).

Conclusions: Results of this study, as the first study on mental health of Albanian immigrant people in Albania, are very important for recommendations in future research and mental health of this target group.

P 58. Typical emotional states of adolescents with serious progress of a chronic disease

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For the purpose of study of emotional state of adolescents with serious progress of a chronic disease, 120 children (aged 12 to 17) that are getting therapy in "Scientific Center of Children's Health" of the RAMS with the diagnoses of nonspecific ulcerative colitis (29%), Crohn's disease (33%), and chronic glomerulonephritis (38%) have been examined. The average disease duration is 3.5 years.

Methods: observation, clinical interviews, projective tests.

Results: Children with a heavy chronic course of disease, according to a psychological condition, were divided in three groups.

Patients with exacerbations of the disease (I group) were in the poor emotional state. They had the following actual emotions: depressed mood background, serious anxiety because of their health, expressed feeling of loneliness, narrowing of the incentive sphere to the "recovery" incentive. The emotional state of the adolescents of this group (33%) primarily depended on the tactics and strategy of drug therapy.

Increased emotional strain and thymopathy are typical of the adolescents with the light progress of a disease (II group). Patients of this group tended to have long negative depressive emotions on the basis of asthenia. The emotional state of the children with a light progress of the disease (42%) depended and was determined by physical feelings, their sharpness and continuity, as well as with the conditions of their social environment.

A more stable emotional state was found in adolescents with a disease at the stage of remission (25%). It is characterized with internal personal strain associated with the active formation of psychological achievements of this age (development of personal and professional identity and etc).

Conclusion: The emotional state of adolescents primarily depended on the physical state of the child and stage of the disease. Prevention of emotional disturbances among the adolescents in treatment in the in-patient department is one of the most important tasks and requires the work of a team of professionals.

P 59. Psychosocial dimensions of chronic rheumatoid diseases

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Background: A growing body of research indicates that the stress system and its interactions with the immune system play a pivotal role in the aetiology and progression of chronic rheumatoid diseases. These patients experience chronic pain when compared with those with other medical conditions suffer dramatic reduction in physical, psychosocial and social well being. Chronic pain, as a major symptom of chronic rheumatic diseases, plays an important role in the occurrence of depression.

Methods: Our study aim was to evaluate the relationship between chronic pain and affective disorders (depression and anxiety). We had evaluated 60 patients aged across 20–75 years, diagnosed with chronic rheumatoid disease. All subjects underwent clinical psychiatric examination. Hamilton Depression Rating Scale (HAM-D-17) and Hamilton Anxiety Rating Scale (HAM-A) were applied to evaluate the severity of depression and anxiety. We also applied DAS28 to evaluate the severity of rheumatoid disease and to make a correlation with psychiatric symptoms.

Results: Depression was found in all patients diagnosed with chronic rheumatoid disease as a coexisting disorder. There is a statistically significant correlation between depression level and some somatic predictors found in patients with chronic rheumatoid disease. The most important predictors found by our study were: physical functioning decrease, chronic somatic pain, and decrease of vitality (according to standardized beta coefficients). Lower scores in these predictors are correlated with higher depressive scores. The same predictors were correlated with anxiety level as well and there was a statistically significant correlation between them and anxiety level.

Conclusions: In our study we found a higher risk for depression and anxiety among patients with rheumatoid diseases. Due to chronic pain the risk to develop a psychiatric disorder is higher mainly in early days after diagnosis.

P 60. Association between symptoms of posttraumatic stress disorder and blood pressure in the elderly

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Objective: Several studies have reported the association between posttraumatic stress disorder (PTSD) and hypertension (HTN). The aim of this study was to evaluate the impact of PTSD symptoms on blood pressure.

Methods: Korean veterans of the Vietnam War with (n = 62) or without PTSD (n = 87) participated in this study. The clinician administered PTSD scale (CAPS) and alcohol use disorder identification test (AUDIT) were applied. Blood pressure, pulse rate, risk factors of HTN and demographic data of the subjects were collected. Effects of potential explanatory variables on HTN were analyzed with logistic regression.

Results: Diastolic blood pressure was significantly higher in PTSD group ($p = 0.015$). However, PTSD subjects showed significantly lower pulse rate than non-PTSD subjects ($p = 0.004$). Logistic regression analysis showed that avoidance symptom might be a predictor for hypertension (OR = 1.065, $p = 0.030$).

Conclusion: These results suggest that PTSD, especially avoidance symptom, might be a risk factor on HTN in the elderly with PTSD. Further studies are needed to evaluate the change of blood pressure according to the clinical improvement of PTSD.

P 61. The efficacy and safety of milnacipran in patients with major depressive disorder following initial treatment failure with a selective serotonin reuptake inhibitor: a pragmatic 24-week, multicentre, open-label study

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Background/Aims: We investigated the long-term effectiveness and safety of switching from a selective serotonin reuptake inhibitor (SSRI) to the serotonin and noradrenaline reuptake inhibitor (SNRI), milnacipran in patients with major depressive disorder (MDD), and identified biomarkers for the response and tolerability of milnacipran treatment.

Method: We examined 30 patients with MDD, who had residual depressive symptoms after initial SSRI treatment (sertraline, paroxetine, and fluvoxamine). Switching to milnacipran was accomplished with cross-titration and tapering. We performed assessments at baseline and weeks 4, 8, 12, and 24 to determine the safety and effectiveness of the switching to milnacipran. At each assessment, we collected blood samples and administered the 17-item

Hamilton Depression Rating Scale (HDRS), Quick Inventory of Depressive Symptomatology-Self-Report, Japanese version, and Social Adaptation.

Self-evaluation Scale. Efficacy was quantified by remission rate (HDRS score ≤ 7), whereas safety was determined by the adverse events, requiring milnacipran discontinuation or symptomatic treatment. From each blood samples, we investigated the plasma levels 5-hydroxyindole acetic acid, 3-methoxy-4-hydroxyphenylglycol (MHPG), and homovanillic acid (HVA); serum levels of brain-derived neurotrophic factor, IL-6, IL-8, and MIP-1β; and whole blood serotonin.

Results: Ten participants dropped out of the study during the first 8 weeks because of noradrenergic-related adverse events, such as tachycardia and dysuria. Finally, 17 patients completed 24 weeks of this study. Remission rate were 20.0% (4 weeks), 26.7% (8 weeks), 33.3% (12 weeks), and 23.3% (24 weeks). MHPG and HVA plasma levels at baseline were significantly higher in the 10 patients that dropped out of the study for the first 8 weeks (MHPG: 5.9 ± 4.1 ng/mL, HVA: 13.6 ± 6.8 ng/mL) than in the remaining participants (MHPG: 3.5 ± 1.1 ng/mL, HVA: 9.3 ± 3.6 ng/mL): MHPG: $p = 0.017$, HVA: $p = 0.038$.

Conclusion: Milnacipran is a potentially effective and tolerated treatment for SSRI-resistant MDD that can be evaluated with MHPG and HVA.

P 62. NIDS (Neuroleptic-induced deficit syndrome) in bipolar disorder with psychosis: three cases of prolonged treatment course

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Introduction: The term neuroleptic-induced deficit syndrome (NIDS) was proposed to promote interest in the adverse mental effects of neuroleptics by Lader (1993) and Lewander (1994). We describe three patients with psychotic bipolar disorder who exhibited NIDS.

Case reports: 1. A 50-year-old man had had recurrent depression and psychotic mania since his thirties. He was admitted to a hospital at age 48 and took antidepressants and haloperidol at 9mg/day and risperidone at 12mg/day. Apathy and blunted affect only added to his symptoms. After two years of no improvement, he transferred to us and was successfully treated with nine sessions of electroconvulsive therapy (ECT). Neuroleptics were greatly reduced. He remains under remission with lithium and valproate.

2. After a month of extravagance, a 49-year-old woman turned depressive and psychotic, and was admitted to a hospital. Five sessions of ECT improved her psychosis but not depression. Diagnosed with schizoaffective disorder, she was given blonanserin at 12mg/day. Apathy and blunted affect only added to her depression. Eight months passed unchanged, and she transferred to us to undergo 12 sessions of ECT and stop blonanserin. Lithium and quetiapine have maintained her remission.

3. A 52-year-old man had depression and partial psychosis at age 45. He was diagnosed with schizophrenia, and olanzapine and fluphenazine were started. His condition was unchanged, and was considered natural as negative symptoms of schizophrenia. At age 51, after reconsideration of his diagnosis, he took mirtazapine at 45mg/day and neuroleptics were tapered. All of his symptoms remarkably improved. A year later, he became engaged in unrestrained business activities, and quetiapine has been added.

Discussion: Neuroleptics for bipolar disorder can cause NIDS including lack of initiative, emotional indifference and reduced insight into disease. When unrecognized, NIDS often prolongs patients' illness. It sometimes makes bipolar disorder resemble chronic schizophrenia. Psychiatrists should pay attention to NIDS in the pharmacotherapy of bipolar disorder for psychosis or mania and as augmentation.

P 63. Efficacy of asenapine in manic episodes with depressive symptoms: a review of post-hoc analyses

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Background: Manic episodes with depressive symptoms represent a severe presentation of bipolar disorder. The efficacy of drugs shown useful for pure mania is largely unproven in the subset of patients with depressive symptoms. We reviewed different post-hoc analyses evaluating asenapine's effects in patients experiencing depressive symptoms during manic episodes.

Methods: Different post-hoc analyses have been conducted using pooled data of two 3-week, randomized, placebo-and olanzapine-controlled trials.[1,2] Different definitions have been used to ascertain the presence of clinically relevant depressive symptoms at baseline: MADRS total score ≥ 20, CGI-BP-D scale severity score ≥ 4, DSM-IV mixed episode;[3,4] DSM-IV mixed episode with MADRS total score ≥ 20;[5] DSM-5 mixed features using different severity cut offs.[6] For each population, asenapine and olanzapine were compared with placebo on different depression endpoint (remission rates: MADRS ≤ 12, mean change in MADRS total score). Effect on manic symptoms was also assessed in some populations (remission rates: YMRS ≤ 12, mean change in YMRS total score) end points.

Results: In all populations, asenapine was significantly superior to placebo at days 7 and 21 in reducing depressive symptoms and significantly superior to olanzapine at day 7. In a few populations, olanzapine also tended to improve depressive symptoms at day 21. Asenapine significantly improved manic symptoms as compared to placebo as early

as day 2 in patients with DSM-IV mixed episodes or DSM-5 mixed features, and was significantly superior to olanzapine at day 2 in patients with the most severe depressive symptoms. Olanzapine did not separate from placebo in reducing manic symptoms severity.

Conclusion: In all post-hoc analyses asenapine significantly improved both manic and depressive symptoms in bipolar patients experiencing manic episodes with depressive symptoms. Anti-manic agents appear to have differential efficacy in people who experience depressive symptoms during a manic episode.

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P 64. Effects of tianeptine on mTOR signaling in rat hippocampal neurons

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Objectives: The aim of the present study was to find out whether alterations in mTOR signaling could be observed following treatment with tianeptine. Additionally, we investigate whether this drug affect the synaptic proteins and neurite outgrowth via mTOR signaling.

Methods: For purposes of western blotting and neurite assay, cells were cultured for 4 days and 5 days, respectively, with tianeptine (50 and 100 μM). Control cells were cultured without tianeptine under the B27-deprived condition (for western blotting) or normal condition (for dendrite outgrowth aasay). Using Western blotting, we measured changes in the phosphorylation of mTOR, its well-known downstream regulators [eukaryotic initiation factor 4E (elF4E)-binding protein-1 (4E-BP-1) and p70S6 kinase (p70S6K)], and its upstream regulators [Akt and extracellular signal-regulated kinase (ERK)] under toxic conditions induced by B27 deprivation in rat hippocampal neuronal cultures. Dendritic outgrowth of hippocampal neurons was determined by dendrite outgrowth aasay. Dendrites were visualized by immunostaining with microtubule-associated protein 2 (MAP2) known as a dendritic marker. Aditionally, the synaptic proteins, postsynaptic density protein-95 (PSD-95) and synaptophyin (SYP), were also examined by Western blotting.

Results: In this study, tianeptine significantly elevated the levels of phospho-mTOR (Ser2448), phospho-4E-BP-1 (Thr37/46), and phospho-p70S6K (Thr389) in a concentration-dependent manner ($p < 0.05$ or $p < 0.01$). Moreover, tianeptine elevated the phosphorylation of Akt (Ser473) and ERK (Thr202/Thr204) ($p < 0.05$). Additionally, increased mTOR phosphorylation induced by tianeptine was significantly blocked by the specific PI3K (LY294002, 1 μM), MEK (PD98059, 50 μM), or mTOR (rapamycin, 1 μM) inhibitors, respectively (all $p < 0.01$). Tianeptine also provocated hippocampal dendritic outgrowth ($p < 0.01$) and simultaneously increased levels of the synaptic proteins, PSD-95 and SYP (all $p < 0.01$).

Conclusions: In this study, authors observed novel -in vitro evidence indicating that tianeptine promoted dendritic outgrowth and increased synaptic protein levels through mTOR signaling. mTOR signaling may be a promising target for discovery of new antidepressant drugs.

P 65. Diagnostic stability in major depressive disorder according to DSM-IV: 4-year retrospective study in a university hospital

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Background: The aim of the study was to determine the stability of a diagnosis of major depressive disorder (MDD) according to the DSM-IV by means of retrospective reviews of medical records.

Methods: Retrospective chart review of patients admitted to a university hospital with a primary diagnosis of MDD in a period from January 2005 to August 2008 was conducted. We reviewed DSM-IV diagnoses and detailed clinical information at the index admission with assessments made every 6 months for 4 years after discharge to determine diagnostic stability.

Results: There were 440 patients diagnosed with MDD at the first contact. The data showed that 88.6% of the patients maintained their initial diagnosis of MDD during follow up periods. A total of 227 patients were diagnosed MDD at subsequent period. Among these, 218 (96.0%) were diagnosed with MDD at the first contact.

Conclusion: When the DSM-IV diagnoses are used in clinical practice, the diagnostic stability of MDD has a low stability over time. The results demonstrated that a longitudinally based diagnostic process is needed.

P 66. Differentiating between bipolar disorder types I and II: focusing on depressive symptoms

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Background: Bipolar I disorder (BD I) and bipolar II disorder (BD II) may differ in symptomatology, management and prognosis. However, when patients with depression visit outpatient clinics, the distinction between BD I and BD II is not always apparent. Examining the differences in clinical features between BDI and BD II during their depressive episodes may assist in distinguishing between these two conditions.

Methods: BD I (n = 79) and BD II (n = 39) patients were included in the study, based on DSM-IV-TR criteria. We assessed demographics, clinical features, depressive symptoms, and comorbid conditions of the patients using t-tests and chi-square analyses. For the significant variables after the aforementioned statistical analysis, logistic regression analysis was implemented to verify the predictors when diagnosing BD I or BD II.

Results: BD II patients were more likely to be unemployed (BD II: 71.8% vs. BD I: 46.8%) and were more frequently accompanied by comorbid personality disorder (BD II: 30.8% vs. BD I: 10.1%). When comparing symptom profiles of depressive episodes, irritability, indecisiveness and atypical symptoms such as weight gain and hypersomnia were more frequently observed in BD II patients. In the regression analysis, variables predictive of BD II were depressive symptoms including irritability (OR = 2.766) and indecisiveness (OR = 9.834). Unemployment (OR = 2.414) was also predictive of BD II.

Conclusion: BD I and BD II showed differences in clinical features and depressive symptom profiles. Our results may provide additional evidence supporting the distinction of BD I and BD II.

P 68. Clinical predictors of family accommodation in obsessive-compulsive disorder: a study from India

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Background: Obsessive-compulsive disorder (OCD) is a chronic and debilitating anxiety disorder with a higher degree of family accommodation. However, there is a paucity of data on the factors that engenders accommodation. This study aims to identify clinical predictors of family accommodation of obsessive-compulsive symptoms.

Methods: The sample included 100 adults (mean age 27.8 ± 8.5 years, 57 males) with a DSM-IV OCD and the primary caregiver of each patient. Assessment was done using standardized tools like Yale Brown Obsessive-Compulsive Scale (Y-BOCS), Family Accommodation Scale (FAS), Work and Social Adjustment Scale (WSAS).

Results: The family accommodation was a common phenomenon within the sample with 72 families reporting accommodating OC symptoms (occurring at-least daily among 43 families). The total score on FAS had a significant positive correlation with the following patient characteristics- symptom severity, age, global functioning, total score on WSAS and washing dimension. In the regression model, score on WSAS ($p < 0.001$) and being a washer ($p = 0.003$) predicted family accommodation.

Conclusions: Family accommodation is a common phenomenon in OCD. This study highlights the need to design specific interventions to reduce family accommodation for a better outcome for patients with OCD.

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