SO 01. Recent advances in Depression

SO 0101. Treating depression with anxiety
Siegfried Kasper
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Depression and anxiety have a high comorbidty and medications can be used that have the indication for depression (bauer et al, 2013) and/or anxiety disorders (Bandelow et al, 2012). Anxiety symptoms are prevalent to a large extent in patients who meet the criteria for major depression and depressive symptomatology are often observed in patients who fulfill the criteria for anxiety disorders, specifically general anxiety disorder. The comorbidity of depression and anxiety is associated with a larger degree of treatment resistance as well as higher rates of suicidality. The latter two are important implications for clinicians and indicated the importance to diagnose this comorbidity. Anxiety symptoms within depression often necessitate the addition of benzodiazepines in patients with major depression in order to overcome the time lag until antidepressants are fully effective. Interestingly pharmacological methods like electroconvulsive therapy (ECT) as well as deep-brain stimulation (DBS) are associated with a simultaneous reduction in depression and anxiety symptoms. The use of ketamine, a new pharmacological approach, is also associated with a rapid antidepressant as well as anxiolytic and anti-suicidal response. The treatment of depression with anxiety is a great challenge to clinicians since randomized controlled studies on comorbidity of these two disorders are not available and data from clinical trials can only be extrapolated for these comorbid diseases. If a patient suffers from both depression and anxiety, those medications should be used which have the indication for both disorders as well as augmentation strategies with, for instance, lithium or atypical antipsychotics that have been described to be effective.

References:


SO 0102. Treating post stroke depression (PSD)
Stuart Montgomery
Imperial College, London, UK

Depression is common following stroke and is seen in about 25% of cases. Although not recognised as part of MDD the core symptoms are the same and conventional scales in MDD are able to establish efficacy compared to placebo. SSRIs such as citalopram, sertraline and fluoxetine have demonstrated acute efficacy as well as the NARI reboxetine but the studies are mostly small. Placebo-controlled studies of long-term relapse prevention have demonstrated efficacy for fluoxetine and sertraline.

Antidepressants apparently have another function in promoting motor and functional recovery following stroke possibly by neurogenesis and encouraging brain plasticity. This appears to be independent of depression since it is observed both in those who develop depression and in those who do not (Chollet et al 2011, Lancet Neurol 10 123-130).

SO 0103. Novel mechanisms and drugs as adjunctive treatment in depression
Torgny H. Svensson
Dept of Physiology and Pharmacology Karolinska Institutet, Stockholm, Sweden

About 30% of severely depressed patients respond inadequately to antidepressants such as SSRIs, and adjunct treatment with various drugs, including α2 autoreceptor antagonists like mirtazapine as well as low doses of atypical antipsychotic drugs (APDs), have been shown to significantly augment the antidepressant effect with a rather fast onset of action. Preclinical data propose that enhanced catecholamine output, dopamine D1 receptor activation and an associated facilitation of glutamatergic, NMDA receptor-mediated transmission in the medial prefrontal cortex (mPFC) may essentially explain this clinical outcome. These mechanisms are largely similar to those underlying the rapid and potent antidepressant effect of ketamine, which has been shown to be critically dependent on activation of glutamatergic, in particular AMPA receptor-mediated, neurotransmission in the mPFC. Not surprisingly, several studies have accordingly reported an antidepressant effect of several pro-glutamatergic drugs, which will be discussed elsewhere at this meeting.

In addition, preclinical results obtained in recent years indicate that agonists at the α7 nicotinic acetylcholine receptor (α7nAChR) may also generate a significantly enhanced antidepressant effect when used as adjunctive treatment, but also, as we have observed very recently, an antidepressant-like effect in rodents even when given alone.

The above clinical and preclinical results are of considerable interest since severe depression, particularly treatment-resistant major depressive disorder (MDD) and bipolar depression, represent common recurrent diseases with a high risk of suicide and a very significant economical burden on society, largely because of lack of productivity. A major reason is the associated cognitive impairment, which represents one of the core symptoms in MDD (listed already in DSM-IV). Importantly, our experimental data show that several of the above mentioned adjunctive treatment alternatives generate activation of specific neurobiological mechanisms within the prefrontal cortex, as described above, which are directly involved with control of cognition, in particular working memory and executive functioning. In recent years adjunctive treatment with α7nAChR agonists in schizophrenic patients maintained on a stable medication with APDs has been shown to significantly improve cognition (Meltzer et al. 2011, Hoford et al. 2011, Preskorn et al 2014). Indeed, even nicotine itself has been found to improve cognition and depressive symptoms in humans and to show antidepressant-like effects in rodents.

Moreover, MDD is frequently associated with somatic co-morbidity, e.g. arthritis, thyroiditis and colitis, which probably reflects an enhanced inflammatory activity. In recent years a whole range of studies by Kevin Tracey et al. indicate a reduced effenter vagal activity in depression. This implies a reduced activation of peripheral α7 nAChRs, which in turn are known to specifically
suppress inflammatory mechanisms. Therefore, adjunctive treatment with α7nAChR agonists in depression may provide a particularly interesting novel treatment option to explore.

EXPERT CLINICAL UPDATE 1

Managing and not managing suicide risk: notes from a small island
David Baldwin
Professor of Psychiatry, Faculty of Medicine, University of Southampton, UK

This talk is based on a commissioned independent review of all suicides and open verdicts recorded on the Channel Island of Jersey between 2000/09: 145 individuals (100 men, 45 women), aged 15-93 years, died from suicide or probable suicide during this period. The full inquest files were read by two researchers. Quantitative data on risk factors and range and quality of contact with health services were abstracted from files using a standard data collection proforma. Qualitative data synthesized for each case included the field notes written whilst reading files, copies of media reports, lists of prescriptions obtained by police officers, copies of suicide notes, text messages sent in the hours before death, correspondence relating to the case, photographs from the scenes of death, and audio recordings of the inquest.

There was an overall rate of between 12.8-15.5/100,000, higher than that on the UK mainland. There was much contact with medical services in the month before the event leading to death, in primary medical care (37.9%), local secondary care mental health services (24.8%), and emergency services (19.3%), but structural problems in health service delivery were common, and maladaptive assumptions may have been important. Based on findings relating to the medical care of the 145 individuals, 15 recommendations were made to the States of Jersey Suicide Prevention Group. I will summarize findings of the review and its recommendations, consider the strengths and weaknesses of this approach to understanding suicide, and highlight potential implications for management of potentially suicidal patients in other settings.

Managing Suicide Risk
Zoltán Rihmer
Semmelweis University and National Institute of Psychiatry and Addictions, Budapest, Hungary

Suicide is a very complex, multicausal human behavior with several biological as well as psychosocial and cultural components. As it is very rare in the absence of current major psychiatric disorders, psychiatric-medical suicide risk factors, particularly current major depression with a prior suicide attempt, are the clinically most useful predictors, especially in the presence of psycho-social and demographic risk factors. However, since the vast majority of psychiatric patients never commit and more than half of them never attempt suicide, special illness features (severe bipolar depression with agitation, insomnia, hopelessness, and comorbid substance-use disorder, etc.) as well as psychosocial factors (impulsivity, isolation, adverse life events, etc.) also play a contributory role. As suicidal behavior is a complex phenomenon, its prevention should also be complex. Considering the clinically explorable suicide risk factors, in the majority of cases, suicidal behavior is well predictable. Clinical studies show that successful acute and long-term pharmacological treatment of depressive and other psychiatric disorders substantially reduces the risk of suicidal behavior, even in this high-risk population (Rihmer and Gonda, 2013). Restricting lethal suicidal methods (toxic agents, guns, barriers, etc), whenever possible, as well as multi-level community prevention programs (including also public education, gate keeper-training, appropriate media reporting of suicide, etc) and psycho-social therapies (psychoeducation, regular aftercare, targeted psychotherapeutical interventions, etc) are also effective (Fleischmann et al, 2008), particularly in combination with appropriate medical treatment.

References:

SO 02. Advances in the treatment of Anxiety

SO 0201. Pharmacologic Treatment of Obsessive-Compulsive Disorder Comorbidity
Stefano Pallanti
University of Florence, Florence, Italy

Introduction: obsessive-compulsive disorder (OCD) is clearly a heterogeneous syndrome in which comorbidity is the rule rather than the exception and is often "phase-specific". Comorbid conditions have a negative impact on OCD outcome and may clearly impact the disease trajectory. Nevertheless, in the current literature there is an impressive neglect of comorbidities in clinical trials and treatment approaches for these conditions are still not evidence-based.

Areas covered: in this paper we summarized the available data on the treatment of the main OCD comorbidities (mood and anxiety disorders, “bipolar neurosis”, tics and OCD-related disorders, addictions and impulsive disorders, eating disorders, attention deficit hyperactivity disorder, psychoses, post infective syndromes).

Expert opinion: to achieve the goals of “precision medicine” there is a critical need for deconstructing current diagnostic groups with biomarkers to predict and improve response to treatment. Despite the continuous efforts of several researchers in subtyping homogeneous samples of OCD patients (for example the comorbidity based sub-classification), current available treatments are still syndrome-based rather than network dysfunctions-based. Identifying homogenous subgroup, subtyping patients according to comorbidity patterns, symptom dimensions, clinical course, neurocognitive and neurophysiological dysfunctions, could represent an essential first step in the direction of a “precision medicine” approach.

SO 0202. The further management of treatment-resistant generalized anxiety disorder
David Baldwin
Faculty of Medicine, University of Southampton, UK

Many patients with generalized anxiety disorder (GAD) do not respond to first-line pharmacological or psychological interventions. Recent guidance from the British Association for Psychopharmacology summarizes further options when patients with GAD have not responded to first-line treatments (Baldwin et
al., 2014). There is only inconsistent evidence for a dose-response relationship with antidepressant drugs, but some patients who have not responded to an initial low dosage may respond to a higher daily dose: the efficacy of pregabalin when compared with placebo is more marked at higher daily doses (200 mg or higher). The addition of pregabalin to SSRI or SNRI antidepressant drugs is superior to continued treatment with antidepressants alone. The findings of small randomized placebo-controlled augmentation studies suggest that augmentation of antidepressants with antipsychotic drugs (olanzapine, quetiapine, risperidone) may be beneficial, but the evidence for quetiapine augmentation is inconsistent, and uncertain for ziprasidone augmentation. There is a persistent role for benzodiazepines in patients with chronic, severe, distressing and impairing symptoms which have not responded to a sequence of other treatments (Baldwin et al., 2013). Alternative treatments which have been found helpful in some patients include multi-faith spiritually based intervention; Galiphipha glauca (‘thyrallis’), Matricaria recutita extract (chamomile), ‘Silexa’ lavender oil preparation, ‘relaxing room therapy’, yoga-based breathing programme and ‘balneotherapy’ (hydrotherapy with massage): but more investigation of these approaches is needed before they can be recommended.

References:

SO 0203. Advances in the treatment of Borderline Personality Disorder
Borwin Bandelow
Department of Psychiatry and Psychotherapy, University of Göttingen, Germany

Although up to 94% of patients with Borderline Personality Disorder (BPD) receive some kind of drug treatment, no drug is approved for this indication so far. Controlled studies are hampered by high rates of placebo response, high drop-out rates, high comorbidity (eg with substance abuse), and the exclusion of patients with suicidality. Systematic reviews have converged on the effectiveness of mood stabilizers (eg, topiramate, lamotrigine and valproate) and atypical antipsychotics (aripiprazole and olanzapine). Selective serotonin reuptake inhibitors may be only be helpful in patients with comorbid MDD. The evidence for omega-3 fatty acid supplementation is preliminary. Therefore, there is room for improvement of drug treatment for BPD.

A recent theory has posed that a dysregulation of the endogenous opioid system (EOS) underlies the neurobiology of BPD (1). Neurobiological findings that support this hypothesis are reviewed: Frantic efforts to avoid abandonment, frequent and risky sexual contacts, and attention-seeking behavior may be explained by attempts to make use of the rewarding effects of human attachment mediated by the EOS. Anhedonia and feelings of emptiness may be an expression of reduced activity of the EOS. Patients with BPD tend to abuse substances that target µ-opioid receptors. Self-injury, food-restriction, aggressive behavior, and sensation-seeking may be interpreted as a desperate attempt to artificially set the body to “survival mode”, in order to mobilize the last reserves of the EOS. BPD-associated symptoms, such as substance abuse, anorexia, self-injury, dissociation, and sexual overstimulation, can be treated successfully with µ-opioid receptor antagonists, although evidence for improvement of overall BPD symptomatology is lacking (2). Large-scale double-blind studies are warranted to examine the efficacy of opioid antagonists (naltraxone, nalmefene) in BPD. Future research strategies will focus on the potential role of neuropeptide agents (oxytocin, vasopressin, neuropeptide Y and partial agonists/antagonists at δ or κ opioid receptors).

References:

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Speaker’s honorarium: AstraZeneca, Glaxo, Janssen, Lilly, Lundbeck, Pfizer, Meiji-Seika
Advisory Board: Lilly, Lundbeck, Ono, Otsuka, Pfizer
Publication honorarium: Pfizer
Grant: none

SCIENTIFIC UPDATE 1: Ketamine analogues in Depression

Is there a place for ketamine analogues in depression ?
Torgny Svensson
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Several large real-world effectiveness trials over the past 20 years have found that first-line antidepressants (ADs) and combinations thereof are unfortunately ineffective for many patients. Moreover, all currently approved antidepressants require weeks to months of daily administration to obtain maximum efficacy, placing a considerable personal, psychosocial, and professional burden on affected individuals and the health-care system.

Clinically, Berman et al. (2000) first reported that a single subanesthetic (0.5 mg/kg) dose of the glutamatergic NMDA-R antagonist ketamine very rapidly, within hours, reduced standardized depression scores in patients (maximum effect in about 2 days) with major depressive disorder (MDD), revealing a moderate-to-large effect size and lasting for about a week. Subsequently this finding was replicated and confirmed in several large studies with single as well as repeated ketamine administration, showing that ketamine also has a rapid antidepressant effects in ECT-resistant MDD and even within an hour may resolve suicidal ideation in acutely suicidal patients in the emergency room.

Preclinically, ketamine has been shown to induce a rapid antidepressant-like effect and to increase the release of glutamate in brain, e.g. in the prefrontal cortex (PFC), and in similarity with the
intravenous ketamine at subanesthetic doses produces a rapid and potent antidepressant response in patients who have failed oral antidepressant therapy.

Three phase 2 studies have been conducted to date as part of the development program for intranasal esketamine in treatment resistant depression, evaluating intravenous ketamine, intravenous esketamine or intranasal esketamine compared to placebo. In aggregate, these studies defined the dosing and frequency of esketamine treatment sessions to be utilized in phase 3 trials. The regimen for intranasal esketamine treatment to be evaluated in these studies consists of a four-week induction phase consisting of twice weekly treatments, followed by a maintenance phase during which treatment sessions will continue at a reduced frequency. Efficacy and safety data collected to date and the further plans for clinical development of intranasal esketamine will be presented.

**EXPERT CLINICAL UPDATE 2**

**Treating Bipolar Mixed States**

Eduard Viesta  
Department of Psychiatry, the Bipolar Disorders Program, and the Clinical Institute of Neuroscience, University of Barcelona, Barcelona, Spain

Bipolar mixed states are difficult to diagnose and treat. In order to improve their detection and management, the DSM-5 has substantially changed the definition of such states (1). There is some evidence that mixed states may be more responsive to anticonvulsants than to lithium. Valproate, and to a lesser extent carbamazepine, may be used either in monotherapy or as adjuncts to lithium. Use of other anticonvulsants, such as gabapentin, lamotrigine, levetiracetam, oxcarbazepine, pregabalin, tiagabine, topiramate or zonisamide, is not supported by controlled data as yet and they should not be used. The use of antidepressants is largely discouraged, as they may worsen this condition (2). Atypical antipsychotics, on the other hand, may be effective either in monotherapy or in combination with valproate or lithium. As mixed states are associated with a higher risk of switching to depression, and most antipsychotics are not very good for the prevention of depression, antipsychotic monotherapy is not advised, with the only exceptions of quetiapine and asenapine. The acute trials with olanzapine in combination with valproate or lithium enrolled a substantial number of patients to allow for statistical subanalyses on this population, showing positive results. Aripiprazole, asenapine, ziprasidone, and to a lesser extent risperidone, quetiapine, paliperidone and clozapine have also been studied in randomized clinical trials but the number of acutely ill patients enrolled was not very high. A pooled analysis of two large combination trials of quetiapine with lithium or valproate showed positive results in time to recurrence of any pole in patients with mixed episodes (3). Both evidence and clinical experience point at combination therapy of an atypical antipsychotic and an anticonvulsant, preferably valproate, or lithium as first-line therapy for severe mixed states. Mild cases could be treated with valproate or monotherapy with a second generation antipsychotic, preferably aripiprazole, asenapine (4) or quetiapine. A good alternative is electroconvulsive therapy. More research is needed in this area, and particularly in mixed states other than dysphoric mania, which have been largely neglected.

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Intravenous ketamine at subanesthetic doses produces a rapid and potent antidepressant response in patients who have failed oral antidepressant therapy.

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**EXPERT CLINICAL UPDATE 2**

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Eduard Viesta  
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References:

SO 0301. Is resistant depression a signal for bipolarity?
Zoltán Rihmer
Semmelweis University and National Institute of Psychiatry and Addictions, Budapest, Hungary

It is well documented that comparing with unipolar major depression antidepressants work less frequently in the depressive episode of bipolar I and II disorder. However, 30-40% of DSM-IV/S defined "unipolar" major depressive disorder patients show clinically significant current and/or lifetime subthreshold hypomanic symptoms. In fact, most recent findings show that the high rate of antidepressant resistance is not limited only to the classical (threshold) bipolar I and II depression as major depressives with subthreshold hypomanic symptoms respond as poorly to antidepressants as classical, (threshold) bipolar I and II depressives. In spite of this, these patients are regularly included into Phase II/III randomized controlled trials on antidepressant monotherapy in unipolar major depression probably resulting in a higher rate of antidepressant resistance than would be expected in "pure" unipolar major depression (Rihmer et al, 2013). Considering the new psychopathology of mood disorder (i.e. taking into account the subthreshold bipolarity in DSM-IV/S defined unipolar major depressive disorder) in the planning and interpretation of genetical and pharmacological studies is strongly recommended.

References:

SO 0302. Treating delusional unipolar and bipolar depression
Stuart Montgomery
Imperial College, London, UK

The term psychotic is confusing as it is used to describe both non-neurotic depression in the old ICD classification and delusional depression. The presence of delusional symptoms is associated with impaired response to antidepressants. In many studies the combination of an atypical antipsychotic and an antidepressant is seen to produce a significantly better response than the antipsychotic or antidepressant alone and the preferred treatment of delusional depression is the combination therapy.

In mania the presence of delusions also impairs response but the subanalysis of patients with delusions in studies which included both delusional and non-delusional patients shows that a variety of atypical antipsychotics are effective in both mania and delusional mania.

In bipolar depression quetiapine is the only treatment licensed in the EU but since delusional depression is usually excluded from studies on bipolar depression the data are too sparse for valid comment. Quetiapine and lurasidone remain the most likely candidates in delusional BP depression but this remains to be tested.

SO 0303. New treatments for Bipolar Disorders
Eduard Vieta
Department of Psychiatry, the Bipolar Disorders Program, and the Clinical Institute of Neuroscience, University of Barcelona, Barcelona, Spain

The main unmet need in the management of bipolar disorder is the lack of available optimal treatment options for bipolar depression. Currently, antidepressants, antipsychotics, and mood stabilizers are commonly prescribed for this condition. New agents are needed that improve remission rates and prevent new episodes, have fewer side effects than existing treatments, and are effective on the core symptoms of bipolar disorder, as well as on cognition, functioning, and physical health. Ideally, these new agents will prevent the high mortality rates associated with cardiovascular disease and suicide in bipolar disorder and promote treatment adherence through greater tolerability. Researchers are currently investigating a number of novel treatment targets, particularly the glutamatergic system (1), among others, in an attempt to develop a drug that will address these unmet needs in the management of bipolar disorder.

References:
EXPERT CLINICAL UPDATE 3

Myths and truths in treating non response in depression
Alessandro Serretti¹, Stuart Montgomery²
¹Bologna University, Bologna, Italy; ²Imperial College, London, UK

The response to antidepressant treatment is still unsatisfactory: about 40-50% of depressed patients do not respond to the first antidepressant and about 60% do not reach remission at all leading to the status of resistant depression. Several opinions having been presented in this field have not always been confirmed afterwards. Just as examples: antidepressants are useless, chronic depression is untreatable, or also high doses of SSRI are always more effective and so on.

Similarly, regarding to strategies, a number of possibilities have been suggested with variable degree of support, such as switching to another drug, to another class of antidepressants, 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.

EXPERT CLINICAL UPDATE 4

How to treat anxiety with comorbidity
Borwin Bandelow¹, Stefano Pallanti²
¹Department of Psychiatry and Psychotherapy, University of Göttingen, Germany; ²University of Florence, Florence, Italy

Epidemiology: There is a high comorbidity among the different anxiety disorders and between anxiety disorders and other mental disorders, in particular depression. In most studies, comorbid subjects with both anxiety and depression had a higher degree of impairment that pervades all aspects of life – suicidality, social and family interactions, and workplace productivity than those who had only one disorder.

Hypotheses on the causes of comorbidity assume that anxiety disorders and depression may be explained by (1) coincidence of two common psychiatric disorders by chance (2) secondary depression due to demoralization by recurring anxiety symptoms (3) two syndrome complexes sharing a common underlying pathogenic process, but presenting differently in individual patients.

A number of randomized controlled studies have investigated the efficacy of drugs including selective serotonin reuptake inhibitors (SSRIs), selective noradrenalin reuptake inhibitors (SSRIs), second generation antipsychotics, agomelatine and others in comorbid patients.

SO 04. Advances in treatment of Depression

SO 0401. Evidence Based markers and an algorithm for treatment of depression
Alessandro Serretti
Bologna University, Bologna, Italy

The available evidence suggests that biological factors contribute substantially to the variability in response to antidepressant treatments.

Among genetic variants of interest, a functional polymorphism (−5-HTTLPR) in the upstream regulatory region of the serotonin transporter gene (SLC6A4) shows replicated findings. Further, replicated results have been reported particularly for HTR2A, BDNF, and GNB3, but inconsistent findings exist as well and innovative approaches have been pursued to overcome the limitations of candidate gene studies.

New genes have been recently identified through genome-wide association studies (GWAS), such as UBE3C and UST genes. Genome-wide data provide the opportunity to perform multilocus analyses such as pathway analyses that yielded interesting findings related to early response and gene x environment interactions. Complementary research is rapidly developing, with the aim to identify epigenetic variants (i.e. DNA methylation and RNA interference) that may impact on protein level or study directly mRNA or protein level in order to unravel unknown processes of modulation. Further analyses identified a number of biomarkers from peripheral blood which may predict subjects response or tolerability.

On the basis of the abovementioned evidence, a number of clinical sites are currently applying prediction algorithms in clinical practice, however an optimal algorithm is still to be identified.

SO 0402. Glutaminergic approaches to treating depression
Ted Dinan
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Controlled clinical trials have demonstrated that the non-competitive N-methyl-D-aspartate antagonist ketamine (0.5mg/kg given intravenously (IV)) has rapid antidepressant effects in patients with treatment-resistant major depressive disorder (Berman et al., 2000; Zarate 2006; Morrough et al., 2013) with results remarkably consistent, demonstrating rapid reductions in depressive symptomatology that are maintained for approximately 1-2 weeks following a single infusion. Response rates in the open-label investigations and controlled trials have ranged from 25% to 85% at 24 hours post infusion and from 14% to 70% at 72 h. Ketamine is associated with robust and rapid anti-suicidal effects. Repeated ketamine infusions can reduce suicidality ratings (MADRS-SI) but only as long as the duration of the 12-day repeated infusion trial (Price et al., 2009). A study investigating IV ketamine in the emergency room showed beneficial results but this study was not without its flaws most notably the lack of a control group (Larkin et al., 2011). However these studies have led the way for further studies to explore this avenue.

We aimed to compare the antidepressant effect of ketamine with the established antidepressant effect of ECT in treatment resistant depression. Comparing ketamine treatment with ECT revealed that there was no significant difference in depressive symptoms between ECT post treatment and at all time points following ketamine. Thus ketamine is as effective as ECT as an antidepressant. The distinct advantage of ketamine is that the effect occurs more rapidly. A range of biomarkers were examined before and after treatment including the cortisol awaking response, tryptophan metabolism and peripheral miRNA levels. These data will be presented.
SO 0403. New treatments for bipolar depression
Allan H. Young
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The currently available licensed pharmacotherapeutic treatment options for bipolar disorder, (e.g. anticonvulsants, lithium and atypical antipsychotics), show different efficacy profiles in bipolar depression, the predominant mood state of bipolar disorder [1]. Of these, only Quetiapine is recommended for acute bipolar mania and acute bipolar I or II depression and maintenance treatment. Monoamine-based antidepressants (SSRIs and SNRIs) are recommended for first-line treatment of MDD, although they have not been adequately studied in bipolar depression. Furthermore, SSRIs and SNRIs are associated with inadequate response, slow onset of action, (long-term) tolerability issues and potential induction of mood switch to mania. New pharmacotherapies are, therefore, needed.

Alternative treatment options may arise from novel pharmacological mechanisms, e.g., N-methyl-D-aspartate receptor antagonists, glutamate-based therapies and serotonin receptor antagonists [1,2] and could potentially include medications for other indications that may demonstrate antidepressant effects in mood disorders. There is also uncertainty regarding the most appropriate treatment for depressive episodes in the various mood disorders, due in part to dispute over whether depression should be treated differently in diverse disorders [3]. For example, the process of licensing medications for depressive episodes in patients with MDD and bipolar disorder are disconnected, and effective treatment of depression with medication in one disorder does not provide evidence for its effectiveness in treating depression in another. Studies will prove to be more informative to a real-life setting if treatment of depressive episodes was comprehensively assessed transdiagnostically ab initio. This may help to guide treatment of all depressive episodes, while indicating which antidepressants are effective for which disorder [3].

References:

Keywords: ‘Antidepressants: clinical’; ‘Bipolar disorders’; ‘Drug development: basic’

Disclosures/conflicts of interest:
Allan Young has served on advisory boards for AstraZeneca, BCI, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Lundbeck, Otsuka, Pfizer, Sanofi-Aventis and Sunovion, received grant support from AstraZeneca, BCI, Eli Lilly, GlaxoSmithKline, Novartis, Sanofi-Aventis and Wyeth, and has received honoraria for giving lectures from AstraZeneca, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Janssen, Lundbeck, Novartis, Otsuka Pharmaceutical Co., Pharmaceutica, Pfizer, Sanofi-Aventis, Servier Laboratories and Wyeth.
P 01. Identifying risk factors for suicide among epilepsy patients in South Korea: A case-control study

Myung Hee Ahn1; Sung Jin Park2; Subin Park3; Eun Ju Choi4; Hoon Jin Lee5; Han Uk Ryu6; Joong Koo Kang7; Jin Pyo Hong8
1Department of Psychiatry, Asan Medical Center, Seoul, South Korea; 2Department of Psychology, Seoul National University, Seoul, South Korea; 3Department of Psychiatry, Seoul National University, Seoul, South Korea; 4Department of Neurology, Asan Medical Center, Seoul, South Korea

Background/Methods: Suicide is a major cause of premature mortality among epilepsy patients. However, few previous studies have attempted to examine risk factors in order to develop early identification of and prevention strategy for epileptic patients who are at risk for suicide. The goal of this study was to identify risk factors for suicide among epilepsy patients at a tertiary medical center in South Korea.

Methods: We conducted a matched, case-control study based on a clinical case-registry of epilepsy patients (n=35,638) treated between January 1994 and December 2011 at an academic tertiary medical center in Seoul, Korea. Cause of death by suicide during the observation period was obtained through the Korean National Statistical Office. In a one-to-two ratio the epilepsy patients who died of suicide (Suicide Group; n=74) were matched to those who didn't (Non-Suicide Group; n=148) by age, gender, and approximate time of first treatment. The two groups were compared in clinical characteristics, and multivariate analysis was conducted to identify independent risk factors for suicide.

Results: In an univariate analysis, seizure frequency during the year before suicide, use of anti-epileptic drug (AED) polytherapy, diagnosis of temporal lobe epilepsy, psychiatric co-morbidity, and use of antidepressants were significantly higher (p<.05) in the Suicide Group than the Non-Suicide Group. Lack of aura before seizure was also associated with suicide. Levitracetam was found to be marginally significant in increasing odds of suicide. According to multivariate analysis, high seizure frequency (weekly or more) during last year (OR=8.1, 95% CI=1.2-55.4), temporal lobe epilepsy (OR=3.6, 95% CI=1.4-9.6) and use of levitracetam (OR=31.4, 95% CI=1.1-944.7) were associated with higher odds of suicide. Having aura was protective of suicide. (OR=0.2, 95% CI=0.0-1.6)

Conclusion: Patients who are diagnosed with temporal lobe epilepsy, suffer seizures weekly or more, or are on levitracetam are at higher odds of suicide and should be monitored closely.

P 02. Postpartum PTSD, A bad birth experience that last a lifetime

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P 03. Frontal EEG theta activity and QEEG cordance in the prediction of treatment outcome to repetitive transcranial magnetic stimulation (rTMS) and venlafaxine in patients with depression.

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Background: Alterations in frontal theta activity and change of QEEG prefrontal cordance and their associations with treatment outcome have been described in depressive patients [1]. The aim of this double-blind study was to assess and compare the efficacy of frontal QEEG theta cordance and absolute and relative theta power in the prediction of response to 4-week, right, prefrontal, 1-Hz repetitive transcranial magnetic stimulation (rTMS) and venlafaxine (VNF) in patients with resistant depression [2].

Methods: Frontal (Fp1, Fp2, Fz electrodes) QEEG cordance and theta power values of 50 inpatients (25 subjects per group) completing the study were obtained at baseline and after the first week of treatment. Depressive symptoms were assessed using MADRS.

Results: All responders (250% reduction of MADRS, n=9) and six of 16 non-responders in rTMS group reduced cordance value at week 1 (p<0.01). The reduction of theta cordance value at week 1 was detected in all responders (n=10) to VNF but only in 4 of 15 non-responders (p=0.005). The comparison of the areas under the curve of cordance change for prediction of response between rTMS (0.75) and VNF (0.89) treated groups yielded no significant difference (p=0.27). We did not find any difference between responders and non-responders to both interventions in terms of frontal relative and absolute theta power values at baseline and week 1.

Conclusion: The QEEG cordance can be a promising tool not only for predicting the response to antidepressant, but also to rTMS treatment, with comparable predictive efficacy for both interventions.

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References

P 04. Vitamin D in anxiety and affective disorders

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Background: Vitamin D3 (cholecalciferol) after metabolism to the active form 1,25 OH2 D3 (calcitriol) acts as a neuroactive steroid and is ranked even between neurosteroids. It has its receptors (VDR) dispersed throughout the body. An indicator of the state of body saturation with vitamin D is its intermediate 25 (OH) D3 (calcidiol). In the last few years, more and more communications are dealing with the relationship between vitamin D and psychiatric and neurological disorders.

The International classification of mental disorders ICD - 10 distinguishes between the two disorders: mixed anxiety and affective (depressive) disorder. This classification is still a matter of discussion and it is criticized by many psychiatrists. With regard to the ICD 10, we decided to investigate both disorders separately.

Method: Calcidiol was detected by the ECLIA method consisting of two main steps: dissolving calcidiol from vitamin D binding protein (DBP) and following by heterogeneous electrochemiluminescent immunoassay. The levels of calcidiol were estimated in anxiety and affective females and males, 20 persons in each group and compared with the levels of calcidiol in groups of healthy controls (24 females, 12 males). The patients and control subjects were recruited throughout the whole year.

Results and Conclusions: Our work points to the fact that significantly reduced levels of calcidiol were found in both the above mentioned disorders and in both sexes in comparison with controls. In addition, we bring a brief overview of vitamin D metabolism and its therapeutic use.

The work was supported by grant IGA MZ CR no. NT 13 890-4
P 05. Cortisol awakening response profile is normalized in bipolar patients after group psychoeducation. Stability at one year follow-up.
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Background: Relapse reduction observed in Bipolar Disorder (BD) patients after group psychoeducation (PE), could depend also on other mechanisms besides improved treatment adherence. Among these an important role could be played by a reduction in stress vulnerability. To test this, we measured cortisol awakening response (CAR), a reliable index of adrenocortical activity, in a group of BD patients before and after a group PE program.

Methods: 59 BD patients under pharmacological treatment were randomly assigned to group PE (PE, N=31) or to continuation of their treatment as usual (TAU, N=28), then followed up over a 6 month period. In the TAU group patients participated to unstructured/group specific meetings. Baseline and endpoint assessments were performed with HDRS and YMRS, while treatment compliance was measured with the ARMS. CAR was assessed measuring cortisol levels in saliva samples collected upon waking, 30 and 60 min thereafter; additional samples were collected at h 13 and 20. Besides baseline and endpoint, for 16 of the 59 enrolled patients (8 in the PE and 8 in the TAU group), we also performed a follow-up evaluation 12 months after the endpoint (18 months from the baseline).

Results: At both baseline and endpoint no intergroup differences were found with regard to YMRS, HDRS or ARMS scores. While baseline salivary cortisol levels showed no significant intergroup differences over time, at the endpoint, a significant change between cortisol awakening levels over time was found within the PE group but not within TAU group. Such normalization of the CAR profile found in the PE group at the endpoint was still present also at the 12 months follow-up.

Conclusions: Since only patients of the PE group, but not those of the TAU group, normalized their CAR profile at the endpoint, with restoration of a physiological pattern, this might indicate that PE of the TAU group, normalized their CAR profile at the endpoint, with change between cortisol awakening levels over time was found significant in the PE group in terms of response rates (N=14, n=467; RR=1.98, 95% CI: 1.23 to 3.19; p=0.005) and mean change in Y-BOCS total score (N=14, n=465, SMD=0.6, 95% CI: -0.97 to -0.23; p=0.002). When analyzing the individual antipsychotics, aripiprazole as well as risperidone significantly outperformed placebo in terms of both responder rates and mean Y-BOCS change. Olanzapine, paliperidone, and quetiapine were not significantly different from the control group, whereas the findings for haloperidol were inconsistently related to the applied outcome. There was no significant heterogeneity and no evidence for publication bias.

Conclusions: Aripiprazole and risperidone augmentation of SRIs can be regarded as evidence-based treatment options in treatment-resistant OCD and showed superiority over olanzapine, paliperidone, and quetiapine. About one third of all SRI-resistant OCD subjects responded to augmentation with antipsychotics. However, further research is needed, for example in terms of the questions concerning the optimum antipsychotic doses, the ideal duration of adjunctive treatment, the long-term tolerability, and the evaluation of response predictors. Moreover, future trials should focus more on a distinction between predominant obsessions or compulsions.

P 07. Dysfunctional theory of mind and neurocognitive soft signs, but not symptom profile and clinical severity, predict psychotic transition in young adolescent patients.
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Background/Aims: Psychiatric symptoms present during prodromal phase in patients who will later develop full blown psychotic syndromes may be heterogeneous. In this study we tried to evaluate the predictive value for psychotic transitions of specific symptom profiles (e.g. schizophrenia vs. bipolar spectrum), comparing this with the predictive value of other clinical features (eg. dysfunctional theory of mind, neurocognitive soft signs, cognitive impairment).

Methods: 70 first psychiatric onset patients (age 16-32) were tested with the Comprehensive Assessment of At Risk Mental States (CAARMS). Of them 35 met Ultra High Risk (UHR) criteria and 35 did not (n=UHR group). Assessments were performed at baseline (BL) and after one year (FU), to evaluate dysfunctional theory of mind (Th.o.m.a.s.), cognitive functioning (RBANS), and neurocognitive soft signs (NES). Sociodemographic data, frequency of DSM IV-TR (SCID-I) diagnoses and illness severity (BPRS) did not differ between the two groups at BL. Psychotic transitions at FU were assessed through PANSS.

Results: At BL, UHR and n-UHR patients did not differ for severity of psychiatric symptoms and for DSM IV-TR diagnoses. Such variables did not differ also when comparison was performed between patients who had subsequent psychotic onset (OP) and those who did not (n-OP). On the contrary significant intergroup OP vs. n-OP differences were found with regard to BL NES, RBANS and Th.o.m.a.s. scores. Worsening in Th.o.m.a.s. total score was found in OP patients after psychotic transition.

Conclusions: Our findings in young patients at their psychiatric onset confirm those of previous studies and point out the strong predictive value for subsequent psychotic transitions of defectual analyzed by calculating standardized mean differences (SMD) and dichotomous outcomes by using risk ratios (RR).

Results: Fourteen DB-RCTs (n=467) investigating quetiapine (N=5, n=178), risperidone (N=3, n=72), aripiprazole (N=2, n=79), olanzapine (N=2, n=70), haloperidol (N=1, n=34), and paliperidone (N=1, n=34) were incorporated. The pooled antipsychotic augmentation group was significantly superior to the placebo group in terms of response rates (N=14, n=467; RR=1.98, 95% CI: 1.23 to 3.19; p=0.005) and mean change in Y-BOCS total score (N=14, n=465, SMD=0.6, 95% CI: -0.97 to -0.23; p=0.002). When analyzing the individual antipsychotics, aripiprazole as well as risperidone significantly outperformed placebo in terms of both responder rates and mean Y-BOCS change. Olanzapine, paliperidone, and quetiapine were not significantly different from the control group, whereas the findings for haloperidol were inconsistently related to the applied outcome. There was no significant heterogeneity and no evidence for publication bias.

Conclusions: Aripiprazole and risperidone augmentation of SRIs can be regarded as evidence-based treatment options in treatment-resistant OCD and showed superiority over olanzapine, paliperidone, and quetiapine. About one third of all SRI-resistant OCD subjects responded to augmentation with antipsychotics. However, further research is needed, for example in terms of the questions concerning the optimum antipsychotic doses, the ideal duration of adjunctive treatment, the long-term tolerability, and the evaluation of response predictors. Moreover, future trials should focus more on a distinction between predominant obsessions or compulsions.

P 06. Augmentation of serotonin reuptake inhibitors with antipsychotic drugs in obsessive-compulsive disorder: an update meta-analysis
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Background: In a previous meta-analysis investigating pharmacological treatment options in treatment-resistant obsessive-compulsive disorder (OCD) we determined a significant efficacy of augmentation of serotonin reuptake inhibitors (SRIs) with antipsychotic drugs. Because new relevant double-blind, randomized, placebo-controlled trials (DB-RCTs) evaluating new antipsychotics were conducted, we updated our meta-analysis.

Methods: Applying a systematic literature search, we included all DB-RCTs that compared augmentation of SRIs with antipsychotics to placebo augmentation in SRI-resistant OCD. Meta-analytic outcomes were treatment response defined by 35% reduction in Yale–Brown Obsessive–Compulsive Scale (Y-BOCS) total score and mean changes in Y-BOCS total score. Continuous outcomes were
theory of mind, cognitive dysfunctions or NSS, but not of the syndromal profile of the clinical presentation (schizophrenic spectrum vs. bipolar spectrum vs. axis 2 disorders) or of symptom severity. Assessments of these features could therefore facilitate identification of patients with high risk of developing subsequent psychoses and this strategy could help to reduce their duration of untreated illness.

P 08. Paliperidone Palmitate Once Monthly Injectable Delays Relapse and Maintains Functioning in Patients With Schizoaffective Disorder

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Background/Aims: The efficacy of antipsychotics in schizoaffective disorder (SCA) has been reported, but few large controlled studies have been performed. Results of the first controlled relapse-prevention study of the long-acting injectable antipsychotic paliperidone palmitate (PP) in patients with SCA are presented here.

Methods: This randomized, double-blind (DB), placebo-controlled, international study (NCT01193153) included subjects diagnosed with SCA experiencing an acute exacerbation of psychotic and mood symptoms (≥16 on the YMRS and/or HAM-D21). Subjects could continue adjunctive antidepressants (AD) or mood stabilizers (MS). After stabilization with PP (50-150 mg eq.) during a 25-week open-label phase, subjects were randomized (1:1) to PP or placebo in the 15-month, DB, relapse-prevention period (RPP). Time to relapse was examined using Kaplan-Meier estimates, and between-group comparison was performed using a log-rank test. Patient functioning was examined with the Personal and Social Performance Scale (PSP).

Results: 667 subjects enrolled; 334 subjects were stabilized and randomly assigned (PP 164; placebo 170) in the RPP. Mean (SD) age was 39.5 (10.7) years; 54% of patients were male; 45% received monotherapy and 55% received adjunctive AD/MS. During the DB period, PP significantly delayed time to relapse (P<0.001); 15% relapsed in PP arm vs 34% in placebo arm. Risk of relapse was 2.49-fold higher for placebo (HR 2.49; 95% CI, 1.55-3.99; P<0.001) vs PP. Significant difference (PP vs placebo) favoring PP was observed from week 5.95; DB baseline to 15-month endpoint in PSP (least squares means, 3.3; 95% CI, 0.68-5.95; P=0.014). Proportion of subjects with good functioning decreased from 50.6% at DB baseline to 41.1% at DB endpoint for placebo; PP group maintained good functioning (57.9%, DB baseline; 59.9%, DB endpoint; P=0.001). Adverse events occurring in <5% of patients in any group (PP vs placebo) were weight increased (8.5%, 4.7%), insomnia (4.9%, 7.1%), SSA (3.0%, 5.9%), headache (5.5%, 3.5%), and nasopharyngitis (5.5%, 3.5%).

Conclusion: PP as monotherapy or adjunctive to AD/MS significantly delayed relapse in stabilized patients with SCA and maintained patient functioning.

P 09. Management of mood and anxiety with medicinal plants

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Background: Disorders of mood and anxiety are highly prevalent, recurrent and may last for a lifetime in the absence of treatment. Currently, pharmacotherapy is the first primary treatment modality for mood and anxiety disorders. However, it has its own limitations like insufficient results, high costs and producing unwanted effects. Medicinal plants always have been a good source for developing new therapeutics for treatment of emotional disorders. This article will provide (1) a brief review of the literature on herbal remedies for the management of mood and anxiety and (2) the results of our studies in recent years on screening of medicinal plants for sedative-hypnotic activity.

Methods: Hydro-alcoholic extracts were prepared from several medicinal plants including Coriander sativum, Lactuca sativa, Lactuca Serriola, Nepeta glomerulosa, Ocimum basilicum, Pinus eldarica and Viola tricolor. Also, with solvent-solvent extraction, each extract further fractioned to water, ethyl acetate fraction and n-butanol fractions. The extracts and their fractions were administrated intraperitoneally to mice, 30 min before pentobarbital injection. Furthermore, the possible neurotoxicity of these plants was assessed using cell viability assay on PC12 neuronal cells. The quality of extracts and their fractions was also evaluated using HPLC fingerprint.

Results: Most of the above mentioned plants particularly O. basilicum potentiated pentobarbital hypnosis in mice. The sedative/hypnotic effect was comparable to that induced by diazepam. The tested medicinal plants didn’t induce neurotoxicity in cultured neuronal cells.

Conclusion: Results of our studies in recent years and other published data suggest that some medicinal plants particularly O. basilicum are good candidates to be used as complementary and alternative therapy for management of mood and anxiety disorders.

Acknowledgment: This work was supported by Mashhad University of Medical Sciences. The authors declare that they have no conflict of interests.

P 10. Neuroprotective effect of Boswellia serrata and its active constituent acetyl 11-keto beta boswellic acid

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Background: Neurons are especially sensitive to oxidative stress due to having relatively low levels of endogenous antioxidants and high rates of oxidative metabolic activity. Increased levels of reactive oxygen species (ROS) damage cellular macromolecules and are considered as important inducers of apoptosis in neurodegenerative disorders. Boswellia serrata and its active constituent, 3-acetyl-11-keto-β-boswellic acid (AKBA) have displayed a broad spectrum of pharmacological properties such as antioxidant, anti-ischemic, anticonvulsant and anti-nociceptive activities. The present work was carried out to investigate if they have a protective effect against oxygen, glucose and serum deprivation (OGSD)-induced cytotoxicity in PC12 neuronal cells.

Methods: The cells were pretreated with different concentrations of B. serrata extract (1-400 µg/mL) or AKBA (0.5-40 µg/mL) for 2 h, and then subjected to the OGSD for 6 h. Cell viability was quantified by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium (MTT) assay. Intracellular ROS and lipid peroxidation were determined by spectrophotometry. The extent of DNA damages was determined using single cell gel electrophoresis assay.

Results: Exposure of PC12 cells to OGSD condition leads to a significant decrease in cell viability. The B. serrata at concentrations of 3-12.5 µg/mL and AKBA at concentration of 1 µg/mL significantly increased the cell viability (P < 0.05) as compared to untreated cells. The OGSD also significantly increased the percentage of DNA fragmentation (P < 0.001) and a significant decrease in DNA damage was seen following treatment with both B. serrata and AKBA. The lipid peroxidation and generation of intracellular ROS were significantly increased (P < 0.001) after OGSD insult. Incubation with B. serrata and AKBA significantly decreased the OGSD-induced lipid peroxidation and ROS accumulation (P < 0.001).
Conclusion: Our data suggests that B. serrata and its active constituent AKBA have neuroprotective properties via antioxidant mechanisms. Our findings might raise the possibility of potential therapeutic application of B. serrata for managing neurodegenerative disorders.

Acknowledgment: This work was supported by grant from Mashhad University of Medical Sciences. The authors declare that they have no conflict of interest.

P 11. Citalopram pulse-loading for treatment-resistant obsessive-compulsive disorder: preliminary data from an open-label trial
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Introduction: Treatment resistance is a frequent situation in Obsessive Compulsive Disorder (OCD), occurring in 40–60% of patients. However, in the current literature there are only a few evidence-based options for treatment-resistant patients. Pulse-loading treatment consists of a rapid titration of the pharmacological agent in the first days of treatment. A few studies suggested that this kind of titration with intravenous clomipramine could result in a greater and faster response than with a standard titration in OCD resistant patients. The aim of this open-label trial was to investigate the effectiveness and tolerability of a citalopram pulse-loading protocol in severe treatment-resistant OCD patients.

Methods: We enrolled 8 severe treatment-resistant OCD patients. Patients were treated with intravenous citalopram starting with 40 mg for 3 days and increasing the dose up to 80 mg from the fourth day. The patients continued the treatment with 80 mg of intravenous citalopram for 18 days (a total of 21 days of intravenous treatment), then they switched to oral treatment (80 mg of oral citalopram). We assessed treatment response using the Yale-Brown Obsessive-Compulsive Scale (YBOCS) and the Clinical Global Impression – Improvement scale (CGI-I) at baseline, week 3 and week 12. We monitored any QTc change and sodium levels during the course of treatment.

Results: During the pulse-loading treatment no patients showed significant adverse events. No patients showed a clinically significant change of the QTc interval and/or of the sodium levels. Five out of eight patients had a partial or full response at the end-point (4 patients had a full response and 1 patient had a partial response) and two of these obtained remission. Pulse-loading treatment seemed to induce a faster improvement respect to a standard titration, since the responder patients showed a significant improvement already after 3 weeks. Three out of eight patients did not respond.

Conclusion: Taking into account the very limited sample size, this case series suggests that this treatment approach deserves further controlled studies.

P 12. The efficacy of support groups for people with depression and the possibility of self-help groups
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Background/Aims: There have been widespread community-based self-help group activities for many chronic diseases, but few self-help groups (SHG) or support groups (SG) for people with depression in Japan. Therefore, we (a group of nurses) established an SG based on the Clubhouse model in 2011. The purpose of this study is to clarify the efficacy of the SG and the possibility of an SHG for people with depression.

Methods: The data was collected by participant observation and semi-structured interviews by 10 SG members from 2011 to 2013, and started after approval from the Ethical Committee of Kanazawa University. The data was recorded with the permission of the subjects and was analyzed by qualitative methods.

Results: Subjects were suffering from feelings of isolation in daily living, such as “mental anguish due to depression” and “pain due to not being understood.” The subjects participated in the SG while feeling from these feelings and they perceived the SG as “an opportunity to share the feelings associated with depression with others with similar backgrounds.” Furthermore, they felt “fulfillment as a group member,” and learned how to “understand and accept depression” at the same time. But the subjects considered it too difficult to continue managing the SG in the long run because they felt that there are “limits to mutual aid/peer support”, because of the lack of their knowledge about depression, and/or due to their poor health condition. However, the subjects understood the importance of the SG as a place to talk and learn from each other about the pains of living with depression.

Conclusions: The study demonstrated that SG members’ autonomy can be increased via role assignment and by accommodating the members’ physical conditions. However, the results also suggested that we need to keep supporting the members and, before we can start an SHG (before developing an SG into an SHG), we need to foster leadership and self-help abilities of the members.

P 13. Quality of life in patients with depression treated with duloxetine or a selective serotonin reuptake inhibitor in a naturalistic outpatient setting
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Aims: This study compared the level of quality of life (QoL) in patients with major depressive disorder (MDD) treated with either duloxetine or a selective serotonin reuptake inhibitor (SSRI) as monotherapy for up to 6 months in a naturalistic clinical setting mostly in the Middle East, East Asia, and Mexico.

Methods: Data for this post-hoc analysis were taken from a 6-month prospective observational study involving 1,549 MDD patients without sexual dysfunction. Qol was measured using the EQ-5D instrument. Depression severity was measured using the Clinical Global Impression of Severity (CGI-S) and the 16-item Quick Inventory of Depressive Symptomatology-Self Report (QIDS-SR16), while pain severity was measured using the pain-items of the Somatic Symptom Inventory. Regression analyses were performed to compare the levels of QoL between duloxetine-treated (n=556) and SSRI-treated (n=776) patients, adjusting for baseline patient characteristics.

Results: The mean age of the 1,332 patients included in this analysis was 38.0 years (standard deviation [SD]=10.5) and 56.5% were female. On average, patients had moderately impaired QoL at baseline, and the level of QoL impairment was similar between the two groups [EQ-5D score of 0.46 [SD=0.32] in the duloxetine cohort and 0.47 [SD=0.33] in the SSRI cohort, p=0.066]. Both descriptive and regression analyses confirmed QoL improvements in both groups during follow-up, but duloxetine-treated patients achieved higher QoL. At 24 weeks, the estimated mean EQ-5D score was 0.90 in the duloxetine cohort, which was statistically significantly higher than that of 0.83 in the SSRI cohort (p<0.001). Notably, pain severity at baseline was also statistically significantly associated with poorer QoL during follow-up (p<0.001). In addition, this association was observed in the subgroup of SSRI-treated patients (p<0.001), but not in that of duloxetine-treated patients (p=0.47).

Conclusions: Depressed patients treated with duloxetine achieved higher QoL, compared to those treated with SSRIs, possibly
in part due to its moderating effect on the link between pain and poorer QoL.

P 14. The changes of psychiatric symptoms in psychiatric outpatients after indirect exposure by all day broadcasting about the sinking of the 'Sewol'

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Objectives: The purpose of this study was to investigate the effect of indirect exposure to all day broadcasting about the sinking of the 'Sewol' on changes of psychiatric symptoms of psychiatric outpatients.

Methods: This study was performed with 111 psychiatric outpatients in a university hospital. Subjects were evaluated by the change of psychiatric symptoms including depressed mood, anxiety, guilt, despair, irritability, anger, somatic symptom, loss of appetite, insomnia, loss of energy, difficulty concentrating, suicidal ideation and self-mutilation with a 7-point scale.

Results: Neurosis patients including depression and anxiety disorder had higher aggravation in despair (t=3.50, p<.001), irritability (t=2.42, p<.05), anxiety (t=2.32, p<.05), anger (t=2.66, p<.05), somatic symptom (t=3.83, p<.001), insomnia (t=3.87, p<.001) compared to psychosis patients after indirect exposure to all day broadcasting about the sinking disaster. Among the neurosis group, depressive patients showed more significant aggravation in anxiety (t=2.41, p<.05), somatic symptoms (t=3.88, p<.001) and loss of appetite (t=2.06, p<.05) compared to anxiety disorder patients. And patients who had experienced trauma had more significant aggravation in depressed mood (t=2.91, p<.05), despair (t=2.09, p<.05), irritability (t=3.38, p<.05), anxiety (t=2.36, p<.05), anger (t=3.15, p<.05), somatic symptoms (t=3.83, p<.001), loss of energy (t=2.80, p<.05) compared to patients who had not. Overall, there were no significant changes in suicidal ideation and self-mutilation.

Conclusion: This study suggested the negative effects of indirect exposure to all day disaster broadcasting on psychiatric outpatients, especially with depression and trauma history. Careful consideration will be needed to minimize these negative effects in a clinical setting.

P 15. Lamotrigine-induced neutropenia followed by drug eruption

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We present the case of a patient who became neutropenic soon followed by drug eruption while taking lamotrigine. To our knowledge, this is the first case of reporting side effects of lamotrigine for neutropenia along with drug eruption.

A 55-year-old woman was hospitalized for bipolar depression. The medication was started with lamotrigine 25 mg/day, olanzapine 10 mg/day, and lorazepam 0.5 mg/day. On day 14, her depressive episode much improved. Lamotrigine dose was increased to 50 mg/day according to a regular titration schedule, and olanzapine remained.

On day 18, hematologic test showed an abnormal neutropenic result as WBC count of 3,200 cells/mm³ and ANC of 1,755 cells/mm³. On day 22, WBC count showed further mild decrease as WBC of 2,900 cells/mm³ and ANC of 1,720 cells/mm³. At that time, lamotrigine was decided to be discontinued immediately, while the other drugs were maintained. At the same day, the patient complained of pruritus and some skin rashes on both her legs. Some oral antihistamines and steroid ointment were prescribed. WBC and ANC were soon normalized within 6 days after the discontinuation of lamotrigine. Drug eruption, however, became worse and broadened out to her entire body, particularly on both her deltoid and both thighs showing characteristic morbilliform and maculopapular manifestations.

At the next day, considering the possibility of a more severe dermatologic condition, she was transferred to the Department of Dermatology, where she had a skin biopsy and was treated with intravenous antihistamines and steroids. According to the recommendation to minimize every drug dose as low as possible, olanzapine was reduced to 5 mg/day and lorazepam was discontinued. Following a few days after the recovery from neutropenia, both her pruritus and skin rashes improved completely without any complications.

Possible explanations for this case: (a) neutropenia developed a few days after lamotrigine had been increased, (b) neutropenia began to improve soon after the lamotrigine discontinuation, (c) drug eruption improved completely after the recovery of neutropenia.

P 16. Factors influencing HAMD score in acute treatment of bipolar depression

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P 17. Effect of a case management program after suicide attempt

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P 18. Attachment quality and early maladaptive schemas affect the utilization of social support in a fearful situation

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Background: Several studies underline the direct or indirect effect of social support on mental health; buffering hypothesis states that the eligible support reduces or eliminates stressful events’ negative effects (Cohen & McKay, 1984; Cohen & Wills, 1985; Tahmasbipour & Taheri, 2012). Considering the importance of social support, discovering variables that influence the utilization of social support is necessary. Insecure attachment correlates with the perception of less social support (Florian et al. 1995; Vogel & Wei, 2005; Collins & Feeney, 2004). Early maladaptive schemas (EMSs), that are related to attachment quality (Vankó, 2013), influence information processing in social situations and affect social anxiety (Calvete et al, 2013). Aims: To examine the effect of attachment quality and EMSs on the level of fear in an imagined archaic fearful situation. While previous studies mainly focused on social support’s availability, perception of support or satisfaction with that support, the present study assessed whether individuals can profit from the presence of others in a fearful situation. Method: A self-developed scale was used to assess fear of darkness’ intensity in two conditions; alone and in the company of friends. Young Schema Questionnaire - Short Form, Experiences in Close Relationship Scale - Short Form were also applied. 120 undergraduate students (68 women, 52 men) filled out the tests. Subjects’ self-reported fear of darkness was significantly less intense in the social condition. To assess the influence of attachment quality and EMSs, typical participants have been compared to those who reported equal fear in the two situations or elevated fear in the social condition. Results: Atypical subjects were characterized by higher levels of avoidant
attachment and more intensive EMSs than typicals. Significant differences in EMSs were found in Disconnection and Rejection Schema Domain; Emotional Deprivation, Mistrust/Abuse, Social Isolation/ Alienation, Defectiveness/Shame, Emotional Inhibition and Failure schemas. Conclusions: Results highlight that the presence of significant others can influence self-reported intensity of archaic fears differently, depending on attachment quality and early maladaptive schemas.

P 19. Three-way interaction of 5-HTTLP, BDNF Val66Met and COMT Val158Met polymorphisms and its effect on regional gray matter volume in patients with Major Depressive Disorder

Milutin Kostic 1; Elisa Canu 2; Ana Munjiza 2; Federica Agosta 2; Ivana Novakovic 2; Valerija Dobricic 2; Vera Miler Jerkovic 2; Tatjana Pekmezovic 2; Dusica Lecic Tosevski 2; Massimo Filippi 2
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Background/Aims: Up to date, several genetic polymorphisms have been associated with susceptibility for major depressive disorder (MDD), but usually with inconsistent results. The aim of this study was to assess whether there is a complex three-way interaction between SERT, BDNF and COMT genes functional polymorphisms in MDD patients.

Methods: Seventy-eight MDD patients and 66 healthy controls (HC) underwent genetic testing for 5-HTTLPR, BDNF Val66Met and COMT Val158Met polymorphisms, with a 3D T1-weighted MRI scan, and a comprehensive clinical assessment. Compared with controls, patients were more BDNF-Val homozygotes (MDD=53; HC=32; p=0.013), COMT Met carriers (MDD=63; HC=47; trend of significance, p=0.058) and SERT L’ carriers (MDD=65; HC=47; trend of significance, p=0.056) . Based on these results all patients and controls were separated into three groups: 1. High risk group, i.e. patients or controls with all three susceptibility polymorphisms (SP); 2. Intermediate risk group (two SPs); and 3. Low risk group (one or none SPs). Voxel Based Morphometry (VBM) in SPM8 was performed in order to assess differences in regional gray matter (GM) volumes between patients and controls, taking into account their genetic background.

Results: The High risk group was significantly larger among the patients than the controls (MDD= 40; HC= 17; p<0.001). Compared to the Low risk control group, the High risk patient group showed reduced GM volume in the right middle and inferior orbitofrontal cortex bilaterally, and left superior frontal, inferior temporal and lingual gyri. No morphological differences were observed in Low risk and Intermediate groups when compared to controls.

Conclusions: Our data showed that the accumulation of SPs is associated with specific GM volume changes of brain regions known to be vulnerable in MDD that are not visible when comparing each SP separately. Our findings suggest that observing differences among patients based on the accumulation or interaction of genetic risk factors is necessary to obtain greater understanding of MDD pathological mechanisms.

P 20. The impact of metabolic syndrome on suicidal ideation and quality of life in the population living in community

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Background: Many studies showed that the metabolic syndrome is associated with many psychiatric disorders. The prevalence of depression is higher in subjects with metabolic syndrome than in those without metabolic syndrome, this is associated with decreased quality of life.

Aims: To investigate the impact of metabolic syndrome on suicide ideation and quality of life in community based population. We hypothesized that metabolic syndrome is related to suicide ideation and quality of life in community, when considering age, gender and depressive symptoms.

Methods: Our study was based on a cross-sectional design evaluating 318 adults living in communities without psychiatric disorder and 87 with psychotic or affective disorder. Metabolic syndrome was defined by NCEP criteria (3 of 5 criteria specified by the National Cholesterol Education Program) based on peripheral blood examination, depressive symptoms by CES-D( Center for Epidemiological Studies-Depression Scale), suicide ideation by Reynolds Suicidal Ideation Questionnaire), and Quality of Life by BREF WHOQOLL. We analyzed the difference of Quality of Life, suicidal ideation, depressive symptoms compared among individuals with and without metabolic syndrome.

Results: The frequency of metabolic syndrome was 25.8% in subjects without psychiatric disorders, 47.9% in psychotic disorders, 27.6% in affective disorders. The physical and environmental domain score of WHOQOLL was significantly lower in subjects with metabolic syndrome than those without in individuals without psychiatric disorders, but not with psychiatric disorders. Metabolic syndrome was not associated with depressive symptoms (CES-D score) statistically significantly(p-value <0.05). Suicidal ideation increased in subjects with metabolic syndrome compared with those without(0.R: 16.48, C.I:1.85-14.71, p-value=0.05).

Conclusions: This results show that metabolic syndrome is associated with suicidal ideation and Quality of Life in community population without psychiatric disorders.

* This work was approved by SMC-Institutional Review Board(IRB)
* Conflict of Interest/Disclosure: Each Authors has no commercial associations that might pose a conflict of interest in connection with the submitted article, except as disclosed on a separate attachment. This study is not supported by any profit/commercial organizations.

P 21. Job Stress, Depression, and Quality of Life among Korean Fire Fighters

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Objectives: This study was aimed to investigate the prevalence of depression and to identify demographic variables and clinical characteristics influencing depression and quality of life among fire fighters in Junbuk province.

Methods: The subjects were fire fighters in Junbuk province. 1675 data sheets were collected and among them 1217 were used in analyzing. The questionnaire covered demographic characteristics, job characteristics, Korean Occupational Stress Scales-26 (KOSS-26), Patient Health Questionnaire-9 (PHQ-9), Social support, World Health Organization Quality of Life Assessment Instrument Brief Form-Korean (WHOQOL-BREF). Independent t-test analysis, ANOVA, and multiple linear regression analysis were performed.

Results: The prevalence of depression among fire fighters in Junbuk province was 44.5%. Compared to the non-depressive, the depressive group appeared significantly higher on mean scores of KOSS-26 (p<.001) and lower of social support p<.001) and WHOQOL-BREF (p<.001). Job stress and social support were significant explanation variables for depression (30.2%). Adjusting for demographic factors, depression,
social support and job stress were additionally significant explanation variables for quality of life (43.6%).

Conclusion: Depression, social support, and job stress were significant predictor for QOL. Findings from this study indicate the importance of proper management of depression and job stress among fire fighters for improvement of QOL.

P 22. Clinical Factors Associated with Suicide in Parkinson’s disease
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1Asan Medical Center, Seoul, South Korea

Background: Parkinson’s disease (PD) is a debilitating, chronic disease frequently complicated by psychiatric disorders. Patients with PD may be at high risk for suicidal behavior but such an association was not evident in previous studies. The aim of this study is to estimate the suicide rate and to clarify the risk factors for suicide in PD.

Method: The sampling pool consisted of 4,362 patients diagnosed as PD who visited the outpatient clinic in a general hospital in South Korea, from January 1990 to December 2012. Information about whether the patients had completed suicide by December 31, 2012 was obtained from the database of the National Statistical Office (NSO). The standardized mortality ratio (SMR) for suicide was estimated. A case-control study was conducted to determine the risk factors for suicide using Chi-square test and student’s T-test.

Results: Completed suicide occurred in 29 patients (19 males, 10 females). The SMR for suicide in PD was 1.99 (95% CI 1.33-2.85). The case-control study consisted of a case group (n=29) and a control group (n=116). Depression was prevalent in 24.8% of PD patients (n=36) and in 41.4% of PD patients who completed suicide. History of depression, psychotic symptoms (delusion), history of any psychiatric disorder, antidepressant treatment, antipsychotics treatment, higher dosage of L-dopa usage was significantly associated with death by suicide in PD. Of the PD related variables, most were not significantly associated with death by suicide except the bradykinesia score, a subscale of Unified Parkinson’s Disease Rating Scale (UPDRS).

Conclusion: Results from this study suggest that psychiatric diagnosis, antidepressant or antipsychotics medication, and dosage of L-dopa used is associated with completed suicide, but PD related variables are relatively not. Outcome of this study is meaningful in that psychiatric symptoms and related medication usage is not to be overlooked in PD.

P 23. N-acetylcysteine modulates methamphetamine acute and chronic effects in mouse model of behavioural sensitization
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Introduction: The behavioural sensitization, characterised by increased response to an addictive drug and its repeated administrations, is associated with dysregulation of the brain glutamatergic signalling. Probably by influence on Xc- transporter on neuronal membrane N-acetylcysteine (NAC) modulates functions of glutamate metabotropic receptors. Although already tested in several studies, data about its effects on addictive behaviour remains limited. The aim of the study is to evaluate influence of NAC on acute and chronic behavioural effects of methamphetamine in mouse model.

Methods: Mice were allocated into 4 groups and from Days 3 to 9 were daily intraperitoneally administered with saline (a), NAC 50 mg/kg (b), MET 2.5 mg/kg (c), MET+NAC (d). On the Day 10 a challenge MET dose was administered to all groups. From Day 11 to Day 16, animals were split into subgroups and were administered with for groups a1, c1 and d2 saline; groups a2 and b2 MET; groups b1, c1 and d1 NAC. On the Days 17 and 24, a challenge MET dose was administered to all groups. Locomotor activity was measured in the Open-field test on Days 1, 3, 10, 17 and 24.

Results: NAC itself did not affect total locomotion but increased distance travelled in open-field central zone. Increased locomotion after acute MET was attenuated by co-administered NAC. After repeated administration, animals receiving MET+NAC were stimulated by MET challenge less than animals receiving MET alone. On Day 17 the only subgroup treated with MET followed by saline showed increased response to MET.

Discussion: We have fully confirmed NAC modulatory influence on MET effects. NAC inhibited acute stimulatory effect of MET. Behavioural sensitization to MET effects on locomotom development in animals receiving repeatedly MET, but animals receiving NAC before, in combination or after MET repeated treatments were not sensitized to MET challenge. Furthermore, acute doses of NAC elicited anxiolytic-like efficacy exhibited as increased mouse travelling in the open-field arena central zone.

Support: CEITEC - Central European Institute of Technology; C2.1.05/1.1.00/02.0068.

P 24. Neuroprotection of frontal cortex and hippocampus for antipsychotics used in treatment of depressive disorder (animal model)
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Background: Guidelines recommend to use a combination of antidepressants and antipsychotics for the treatment of depression with psychotic features. In our clinic this strategy was around 15%, and in outpatients setting around 40% with a high rate of cognitive deficit (Mild Cognitive Impairment (~70%), correlated with decrease of frontal cortex and hippocampus volumes. The most used antipsychotics were ziprasidone, olanzapine and aripiprazole. We have evaluated the neuroprotective qualities of these antipsychotics on animal models.

Methods: Animal model study (8 adult Wistar male rats for each study group, weight between 200-250 grams, which were kept during the study in a stress-free environment with optimal parameters of temperature, humidity and food) in order to highlight the differences between neuroprotective effects of ziprasidone, olanzapine and aripiprazole, against a control group (N0) during 14 days.

The substances were administered in intraperitoneal injections on Day 0: group N1 – ziprasidone (1.25 mg/kg), group N2 – olanzapine (0.15 mg/kg), group N3 – aripiprazole (0.6 mg/kg) and control group N0 – saline solution. The rats were sacrificed on Day 15 and biological material from the frontal cortex and hippocampus was prepared with specific histological techniques of coloration and fixation (hematoxyline-oxine, triehromGSS, PAS-hematoxyline, toluidine blue, methylten blue for Nissle corpuscles).

The study was approved by the Ethical Committee of the University and respected the regulations for animal research.

Results: In the frontal cortex a superior neuroprotection for aripiprazole compared to ziprasidone and for ziprasidone versus olanzapine was highlighted. The most often microvascular changes were observed in rats treated with olanzapine, while in rats who received ziprasidone numerous vacuolisations were present. The effect of aripiprazole was minimal against neuronal structures. In hippocampus minimal changes for all three antipsychotics were observed.

Conclusions: Vulnerability of the frontal cortex due to antipsychotic treatment may emphasize cognitive impairment in
P 25. Neurocognitive improvement in depressive patients after ECT
Christine Mohl1; Bjørn Rishovd Rund1
1Research Department, Vestre Viken Hospital Trust, Drammen, Norway; 2Department of Psychology, University of Oslo, Oslo, Norway

Background: There have been reports of retrograde amnesia and anterograde cognitive impairments in patients undergoing electroconvulsive treatment (ECT) for depressive disorders. There is a lack of longitudinal follow-up studies. Currently, we follow depressive patients for 2 years after ECT treatment, employing a comprehensive neurocognitive test battery. Here we report the results of the assessment at 6 weeks after cessation of ECT.

Method: Data from 26 participants (19 women, 7 men) with a mean age of 46.6 years (SD 10.8, range 24-67) and a current ongoing treatment-resistant depressive episode (2 had schizoaffective and 4 had bipolar type II disorder) were collected before the start of ECT and 6 weeks post ECT. The square wave brief pulse ECT procedure was not standardized, but tailored to each individual. Current depression level was assessed with the Montgomery-Åsberg Rating Scale (MADRS). Memory problems were assessed with the Everyday Memory Questionnaire (EMQ). Neurocognitive function was assessed with the MATRICS Consensus Cognitive Battery (MCCB), consisting of 10 tests: TMT-A, BACS, HVTL-R, SS-WMS, UMS, NAB Mazes, BVRT-M-R, Category Fluency, MSCEIT, and CPT-IP.

Results: After ECT, there were no statistically significant changes in self-reported memory problems, and the depression score was significantly reduced (F 48.78, p .001, η² 6). Attention/Vigilance (CPT-IP) (F 6.44, p .022, η² .29) and Visual Learning scores (F 4.60, p .042, η² .16) were significantly improved, and the improvement in the Speed of Processing of TMT-A (F 3.91, p .052, η² .14) and BACS (F 4.19, p .051, η² .14) were near significant. The other cognitive scores were not altered from baseline.

Conclusion: In contrast to much previous research, we found improved neurocognitive performance 6 weeks after ECT. This probably reflects the alleviation of depression after treatment.

P 26. The impact of pain and comorbidities on the cost of treatment of Japanese patients with major depression taking antidepressant medications
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1Eli Lilly Australia Pty Ltd, West Ryde, Australia; 2Eli Lilly and Company, Windlesham, Surrey, United Kingdom; 3RTI Health Solutions, Research Triangle Park, North Carolina, USA; 4Medical Affairs, Shionogi & Co., Ltd., Osaka, Japan; 5Eli Lilly Japan K.K., Kobe, Japan

Background/Aims: Previous research has shown that the presence of pain is associated with worse outcomes and higher costs in patients treated for major depressive disorder (MDD). Our objective is to examine factors associated with increased all-cause and MDD-related healthcare costs among Japanese MDD patients receiving antidepressants.

Methods: Data for this analysis are from the Japan Medical Data Center insurance claims database. All personal information was protected in compliance with local laws and guidelines. Patients were included if they received either a selective serotonin reuptake inhibitor or duloxetine between July 1, 2005, and March 1, 2011 (first antidepressant claim = “index date”), were aged ≥ 18 years on the index date, had ≥ 6 months pre- and ≥ 12 months post-index date continuous health plan enrollment, had an MDD diagnosis, and had no schizophrenia or bipolar disorder diagnoses or antipsychotic claims during the 6-month pre-index date period. Total all-cause and MDD-related healthcare costs were estimated during the 12-month post-index date period. Multivariable generalized linear models with a log-link function and gamma distribution provided estimates of costs adjusted for demographic and clinical characteristics.

Results: A total of 8,460 patients met study inclusion criteria. Mean total all-cause and MDD-related adjusted healthcare costs were $3,570 (284,442 JPY) and $2,362 (188,240 JPY), respectively. Higher total all-cause healthcare costs were associated with increased age, presence of pain-related disorders (28% higher costs), fatigue/sleep-related problems, and one or more comorbidities during the 6-month pre-index date period, and with antidepressant switching or initiation in the 12-month post-index date period. Similar factors were associated with higher total MDD-related costs.

Conclusions: The presence of pain-related disorders was associated with higher total and MDD-related healthcare costs in Japanese patients receiving antidepressant treatment. Antidepressant treatment switching and/or augmentation were also associated with higher total and MDD-related costs. Results are consistent with those observed in other MDD patient populations. Pain should be taken into account when treating patients with depression.

Mathew Morrison1; Walsh David2; Brodie Dallas3; Theron Margaret1
1NHS GGC Liaison Psychiatry, Glasgow, United Kingdom

Background: With data from 8618 self harm episodes over 4 years it was decided to analyse presentations retrospectively for any correlations with socio-economic factors or patient demographics, i.e. it was apparent that the incidence of referrals to our service was higher among women and those from deprived backgrounds.

Aim: The aim was to observe, if patient demographics (gender, age and employment status) varied over the 4-year study period, and secondly, if factors such as methods, contributing factors, or involvement of alcohol changed over time.

We investigated the relationship between deprivation and individuals who self-harm, using two validated deprivation measures.

Method: 8618 self-harm episodes were assessed. Patient demographic data was collected and analysed. Deprivation level was derived from the patient’s postcode, using two scoring systems: ‘Deprivation category scores as defined by Carstairs and Morris’ (DEPCAT), using 2001 Census data, and ‘Scottish Index of Multiple Deprivation’ (SIMD), 2003.

Results: We demonstrated that patients who self harm are much more likely to come from the most deprived areas of Scotland. In 2012, two-thirds (66%) of individuals who self-harm resided in the most deprived decile. Observational data, of 8618 self-harm episodes, over the 4-year study period, yielded a wealth of information. Women more commonly self-harm than men (female: male ratio was 1.39:1). However, all demographics remained static over time. Similarly, method of self-harm (poisoning/injury), substance used and alcohol use at time of self-harm remained largely unchanged. The total number of referrals for self-harm were similar (2039-2260).

Conclusions: From our data, we concluded that individuals from the areas in the most deprived category are significantly more likely to self harm and be referred to our service. Although Glasgow is a city of high socio-economic deprivation, with one-third (32%) of its population residing in the 10% most deprived areas of Scotland, individuals from this decile accounted for two-thirds (66%) of referrals.

Mathew Morrison; Brodie Dallas; Theron Margaret

1 NHS GGC Liaison Psychiatry, Glasgow, United Kingdom

Background: Each year a vast quantity of information on self harm presentations, methods, demographics and contributing factors is collected in NHS GGC. Previous research had shown that 86% of self harm presentations in GGC were from the 10% most deprived. This pattern was consistent year on year. Factors contributing to the presentation are also measured.

Aim: The UK recession ran from April 2008 to September 2009 with significantly slowed growth and wage freezes for several years to follow. The aim was to examine if financial and/or housing pressures caused direct variation in self harm rates over the 6-year study period, and secondly if these factors correlated with the economic downturn and any persisting consequences.

Method: 8420 self-harm episodes, 2006-2012, where contributing factors were definitively assessed were included. Patient demographic data was collected and analysed. The percentage of presentations in which in which financial hardship contributed to the episode were recorded and plotted over 6 years for both males and females.

Results: It was demonstrated that male self harm presentations relating to housing and finance rose to 13% and 18% in 2009 from a 2006 level of 5% and 6%. By 2012 both remained at 15%. Female presentations saw episodes relating to housing and finance rise from 6% and 7% in 2006 respectively to peaks of 13% and 12% in 2009 and remaining at 13% and 14% in 2012.

Conclusions: From the data it can be concluded that rates of self harm related to financial and housing pressures increased over the economic downturn and reached peaks in 2009. The data shows that while these pressures have decreased somewhat since the economic upturn, they remain persistently high.


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Background: It is known that children with autism spectrum disorder (ASD) have varied symptoms like frequent mood dysregulation or exhibition of anxiety. Comorbid psychiatric symptoms of children with ASD are frequently missed because of their not fully expressed skills due to a communicative disability, and therefore, we sometimes have difficulties in making a diagnosis of comorbid disorders for children with ASD. In previous studies, a clear consensus on comorbid psychiatric disorders in children with ASD has not been reached due to reasons of differences in age, intellectual level and the diagnostic approach for the subjects of studies. The purpose of this study is to identify reliable prevalence and types of psychiatric comorbidities in ASD children, who were strictly limited in terms of age and IQ scores, using the Japanese version of the Schedule for Affective Disorders and Schizophrenia for School-Age Children - Present and Lifetime version (K-SADS-PL-J), administered in semi-structured interviews.

Methods: Forty-nine children with ASD, aged 6-15 years, outpatients of the Department of Neuropsychiatry, Osaka City University Hospital, and excluding those with mental retardation, were assessed using K-SADS-PL-J by experienced psychiatrists. The interview was conducted with a parent. This study was reviewed and approved by the Human Subject Review Committee at Osaka City University.

Results: The subjects, 36 males (73.5%) and 13 females (26.5%), had a mean age of 11.2±2.5 years and a mean Full IQ score of 95.7±13.1. The findings were: major depressive disorder 18 (36.7%), anxiety disorder 28 (57.1%), obsessive-compulsive disorder 7 (14.3%), specified phobia 8 (16.3%), and panic disorder 4 (8.2%). 37 (75.5%) had multiple comorbid disorders.

Conclusions: This study shows that, as in previous studies, Japanese school-age children with ASD have high rates of anxiety disorder or mood disorder. Additional prospective studies would lead to projected prognosis. It is important to be aware of those comorbid disorders in order to provide the children with effective treatment.

P 30. Detecting and measuring functional and organic disease in general population: Validation of TOPYPS clinical scale

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Aim: To develop a clinical tool to detect and measure functional and organic diseases (TOPYPS) in the general population.

Methods: TOPYPS scale was administered to 67 adults randomly chosen from a primary care setting in Barcelona, Spain. TOPYPS yields a Cumulative Illness Rating Scale (CIRS), and also detects, with a high index of suspicion, some functional diseases (allergies, migraine, tensional headache, mitral valve prolapse, interstitial cystitis, sexual dysfunction, dyspepsia, irritable bowel syndrome, fibromyalgia, and temporomandibular joint dysfunction) by an interview according to standard diagnostic criteria. It has six sections based on body systems, each one scored 0 (absent) to 3 (severe) according to the degree of interference in daily activity, type of treatment received, and prognostic of the reported illnesses in each section. CIRS is obtained by the total sum of the scores, rated either absent, mild (1-6), moderate (7-12), or severe (13-18).

Results: Test-retest reliability was calculated in all 67 volunteers on two occasions one week apart. Validity was analysed by comparing the results with the clinical examination performed by two different specialists in general practice. This examination included both the application of the diagnostic criteria for the functional diseases mentioned before, and the use of a clinical classification based on the same parameters of CIRS ("Gold Standard").

P 31. Homocysteine as a Potential Biochemical Marker for Depression in Elderly Stroke Survivors

Michaela Pascoe1; Sheila Crewther2; Leeanne Carey1; Kate Noonan3; David Crewther1; Christian Blomstrand1; Ingmar Skoog4; Thomas Linden5

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Abstract Leaflet – 14th International Forum on Mood and Anxiety Disorders

Vieanna, 10 – 12 December 2014

Results: Repeatability (test-retest) in each of the six sections (Kappa index) was between 0.72 (musculoskeletal) and 0.968 (respiratory), with an overall average of 0.823. Inter-rater agreement was also at its lowest value in the musculoskeletal (0.6) whereas the highest was the respiratory section (0.78), with an overall average of 0.703. As for the total score, an intraclass correlation index of 0.923, and 0.858 was obtained for the intra and inter-rater agreement, respectively. Validity was acceptable both for content and construct, according to their correlation with the Gold Standard.

Conclusions: TOPYPS displayed good psychometrical properties. It appears as a suitable tool to detect and measure functional and organic diseases in general population.

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Michaela Pascoe1; Sheila Crewther2; Leeanne Carey1; Kate Noonan3; David Crewther1; Christian Blomstrand1; Ingmar Skoog4; Thomas Linden5

1Sahlgrenska Academy at University of Gothenburg, Gothenburg, Sweden; 2La Trave University, Melbourne, Australia; 3St. Blythe's Foundation, Melbourne, Victoria, Australia; 4Karolinska Institute, Stockholm, Sweden; 5Institut Universitat Parc de Salut Mar., Barcelona, Spain

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Conclusions: TOPYPS displayed good psychometrical properties. It appears as a suitable tool to detect and measure functional and organic diseases in general population.
Neuroscience Institutes, Melbourne, Australia; 4Brain Sciences Institute, Swinburne University, Melbourne, Australia

Background: Elderly stroke survivors have been reported to be at risk of malnutrition and depression. Vitamin B-related metabolites methylnalonic acid and homocysteine have been implicated in depression. We conducted a study exploring the relationship between homocysteine and post-stroke depression.

Method: Observational cohort study of elderly Swedish patients (n = 149) 1.5 years post-stroke, assessed using Diagnostic and Statistical Manual of Mental Disorders, Montgomery-Åsberg Depression Rating Scale and serum blood levels of methylnalonic acid and homocysteine. Ethics approval was granted by The Ethics Committee for Medical Research, at the University of Gothenburg.

Results: Homocysteine significantly correlated with depressive symptomatology in stroke survivors (β = .18%). Individuals with abnormal levels of methylnalonic acid and homocysteine were almost twice more likely to show depressive symptomatology than those with normal levels (depressive symptoms 22%; no depressive symptoms 12%). Comparison of methylnalonic acid and homocysteine levels with literature data showed fewer stroke survivors had vitamin deficiency than did reference individuals (normal range 66%; elevated 34%).

General Conclusions: Homocysteine is significantly associated with depressive-symptomatology in elderly Swedish stroke survivors.

Key Words: Depression, Ischemia, Nutrition, Neurodegeneration, Geriatric. The authors have no commercial interest to declare.

P 32. GSK3b, CREB, and BDNF in peripheral blood of patients with major depressive disorder
Jiri Raboch
1Department of Psychiatry, Institute of Medical Biochemistry, First Faculty of Medicine, Charles University, Prague, Czech Republic

Objectives: Glycogen synthase kinase-3b (GSK3b), cAMP-response element binding protein (CREB) and brain-derived neurotrophic factor (BDNF) play critical roles in neuronal survival, synaptic plasticity and memory and participate in the pathophysiology of depressive disorder

Design and Methods: The aim of the study was to determine the association of clinical characteristics of depressive patients with GSK3b activity in platelets, CREB activity in lymphocytes and BDNF concentration in plasma, platelet-rich plasma or platelets. 65 patients with depressive disorder (diagnosis was confirmed by structured clinical interview for ICD-10) were evaluated. The control group consisted of 96 age-matched healthy volunteers, non-depressed, and without any organic brain disorder. Severity of current depressive episode was assessed using the HRSD-21 and CGI-S; improvement of the intervention was assessed by CGI-I. Patients with depressive disorder were assayed at two different time points: before start of the treatment, and at the end of the trial (28 ±15 days).

Results: In depressive patients before treatment, a significant association was found between GSK3b activity and HRSD-21 (p = 0.013). Significantly decreased GSK3b activity was found in depressive patients after treatment (p = 0.0034); increased CREB activity was found in depressive patients after treatment (p = 0.0070). In depressive patients after treatment, a significant association was found between GSK3b and HRSD-21 (p = 0.0034). In responders (N = 49), a significant association was found between BDNF and HRSD-21 (p = 0.0025) after treatment.

Conclusions: Small alterations of the mean values of the measured blood-based biochemical parameters in patients with depressive disorder were found. Associations of these biochemical parameters with disease severity were observed. Observation of decreased phosphorylation of GSK3b in platelets of depressive patients after treatment confirms its role in the pathophysiology of depressive disorder.

P 33. Transcranial Direct Current Stimulation for Depression in a 92 Year-old Patient: A Case Study.
Ica Albuquerque Sato; Alison Paulino Trevizol; Pedro Shiozawa; Malu Enokibara da Silva; Danielle Rigueira Dias; Ana Chaves; Breno Satler de Oliveira Diniz; Quirino Cordeiro
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Background: Elderly depressed patients with an early first onset of depression are more likely to have had a greater lifetime number of relapses and an overall longer duration of illness; both of these factors are important predictors of poor prognosis.

Objective: We aim at evaluating clinical effects over depressive symptoms of a tDCS protocol regarding both safety and clinical impact. Method: Intervention protocol was as follows: 10 sessions with 2 mA with 30 minutes duration (only weekdays). Anode was placed over the left dorsolateral prefrontal cortex (F3 according to the 10/20 EEG system) and cathode was placed extracranial at the contralateral deltoid. Depressive and anxiety symptoms and cognitive function were assessed using the Hamilton Depression Rating Scale (version 17 items), Beck Anxiety inventory (BAI), and Montreal Cognitive Assessment Scale (MOCA), respectively.

Results: Mr. “J” is a 92 year-old patient diagnosed with major depression for the last 3 years. The patient presented no significant changes in complementary tests, including neuroimaging. After 10 sessions the patient presented with satisfactory clinical response. In fact, HDRS17 demonstrated a decrease of 17 points (94.4%) from baseline rates, which was maintained during the 3-week follow up. Exploratory analysis showed no significant changes for anxiety as assessed by BAI (mean change of 16% from baseline; from 6 to 5 points) or cognitive symptoms as assessed by MOCA (mean change of 3.8%, from 26 to 27 points). The intervention was well tolerated and no adverse effects were reported.

Discussion and Conclusion: While there have been a very large number of studies investigating response to pharmacological treatment of middle-aged persons, there is still a remarkably small number of studies specifically focused on assessing interventions in older persons, particularly those with late-life depression. To the best of our knowledge this condition has not been evaluated specifically for the “oldest old” population. Further controlled studies will contribute to establish the clinical relevance of this new strategy.

Key Words: Depression, NIBS, brain stimulation
optimal treatment. Regarding new interventional strategies, the development of non invasive brain stimulation techniques such as transcranial direct current stimulation (tDCS) has shown promising results. However, tDCS use has not been reported for GAD.

Objective: We hereby describe a 58-year-old woman with GAD who successfully underwent a tDCS intervention, with important ameliorating of her symptoms.

Methods: We performed 15 consecutive daily tDCS sessions (except for weekends). The cathode was positioned over the right dorso lateral prefrontal cortex and the anode was placed extracephallic over the contralateral deltoid. We used a direct current of 2.0 mA for 30 minutes per day. The 25cm2-rubber electrodes were wrapped in cotton material, which was moistened with saline as to reduce impedance. For assessment of anxiety symptoms we used the Generalized Anxiety Disorder 7-item scale (GAD-7), Beck Anxiety Inventory (BAI) and the Hamilton Anxiety Rating Scale (HARS). We also assessed depressive symptoms through the Hamilton Depression Rating Scale (HDRS) - version 17 items; and cognitive functions with the Montreal cognitive Assessment (MOCA).

Results: “Ms. C.” progressively developed anxiety symptoms during the past 3 years. Despite adequate treatment with several medicines in adequate doses such as venlafaxine, sertraline, amitriptyline and quetiapine, she presented no significant improvement of her symptoms and important adverse effects that ultimately lead her to discontinue the use of pharmacotherapy. Anxiety symptoms substantially improved during the 15-day treatment course. After one month of treatment, the patient was asymptomatic and reported significant clinical gains.

Discussion and Conclusion: These encouraging results should be seen as hypothesis-driving for further controlled, randomized trials exploring the impact of tDCS in the treatment of anxiety disorders.

Keywords: Anxiety disorders, NIBS, brain stimulation

P 35. Galactorrhea Associated With Selective Serotonin Reuptake Inhibitors And Reuptake Inhibitors Of Both Serotonin And Norepinephrine Without Increasing Prolactin Levels: Case Report

Isa Albuquerque Sato; Alisson Paulino Trevizoli; Elie Leal de Barros Calfat; Rodrigo Lancelote Alberto; Brazilio de Carvalho Tasso; Heloísa Helena de Aquino Heber Medina; Pedro Shiozawa; Quirino Cordeiro

Abstract: Hyperprolactinemia is an undesirable effect of several classes of psychotropic medications. However, there is limited awareness of this adverse effect of selective serotonin reuptake inhibitors (SSRIs) and dual-effect antidepressant reuptake inhibitors of serotonin (5-HT) and norepinephrine.

Objective: Report a case of galactorrhea after SSRIs and dual effect antidepressants.

Case report: Patient E.O.S, 39 years, female, architect, no psychiatry history started treating. After three months intaking 100mg/day of Sertraline she developed galactorrhea. Medication was ceased and symptoms disappeared 6 months after. The patient remained asymptomatic for 2 years, when she referred anxiety symptoms, being diagnosed with Generalised Anxiety Disorder by DSMV criteria. Fluoxetine was introduced and after one and a half month with 60 mg/day she developed galactorrhea in bigger amounts than before as referred by the patient. Fluoxetine was replaced by Venlafaxine 75 mg/day. The patient referred no ceasing of the galactorrhea and anxiety worsened after months. It was opted to initiate escitalopram 10mg/day and no change in galactorrhea was observed after 4 months. Treatment was interrupted and two moths after galactorrhea ceased, but anxiety worsened. During the intake of all medications laboratory exams were performed and prolactin, LH, FHS, THS, T4 DHEA and testosterone were always within normality. Magnetic Resonance of brain and sella turcica was performed without abnormalities.

Discussion and Conclusion: Hyperprolactinemia with SSRIs treatment is reportedly mediated by postsynaptic 5-HT receptors in the hypothalamus through serotonergic activation of PRL-releasing factors such as thyrotropin-releasing hormone and gamma-aminobutyric acid, and/or mediated by serotonergic inhibition of PRL inhibitor factors such as dopamine or indirectly through vasoactive intestinal peptide and oxytocin release. Euprolactinemic galactorrhea is hypothesized with indirect inhibition of tuberoinfundibular dopaminergic neurons. The peculiarity of this case lies in the fact that the patient had galactorrhea despite changes in prescription and serum PRL level was not raised throughout treatment, while earlier it was thought and proved to be the basic mechanism of galactorrhea with SSRIs and dual-effect antidepressant.

Keywords: anxiety disorders, galactorrhea, prolactin

P 36. The clinical features of patients who attempted suicide by charcoal burning in South Korea

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Background: South Korea has been the highest ranked country in suicide rates among the OECD countries for 8 years. (33.3 deaths per 100,000 populations, 2011). [1] It is related to the dramatic increase in suicide attempts using charcoal burning. Suicide by charcoal burning was relatively rare (0.7%, in 2007) however, has become one of the common methods of suicide attempts (7.9% in 2011).[2] Despite rapid increases in incidence of charcoal burning suicides within recent years, little is known about the characteristics of suicide attempters who used charcoal burning. The aim of this study is to examine the clinical features of the survivors of suicide attempts by charcoal burning and compare with those of people who attempted suicide by medicines/poisons ingestion.

Methods: We reviewed EMRs (electronic medical records) on suicide attempters who visited the emergency room at the Asan Medical Center in Seoul, South Korea between August 2013 and January 2014. In total, we enrolled 125 patients who attempted suicide by poisoning including charcoal burning, drug intoxication and toxin ingestion. We analyzed using chi-squared tests and t-test to compare people using methods.

Results: 35 of 125 patients (28%) had attempted suicide by charcoal burning. The other methods included drug intoxication (n=79, 63%) and toxin digestion (n=11, 9%). The charcoal burning method group was more likely to be men, living alone and having never visited a psychiatrist before the suicide incident. Previous suicide attempt history could be observed in the charcoal burning suicide attempters: p-value 0.052.

Conclusions: We demonstrated the demographic and clinical characters of patients who attempted suicide by charcoal burning. It is needed to follow up the patients who attempted suicide by charcoal burning because they are relatively less likely to be given psychiatric treatment and highly likely to attempt suicide again in the future. Further researches are required to clarify the spectrum of clinical features to prevent further suicide attempts. Targeted interventions from multiple levels and perspectives can then be achieved.
Table. Demographic and clinical characteristics of patients in the charcoal burning and other poisoning methods groups.

<table>
<thead>
<tr>
<th>Feature</th>
<th>Charcoal burning method group (n=35)</th>
<th>Other poisoning methods group (n=90)</th>
<th>Test Statistic</th>
<th>Test p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, (%)</td>
<td>42.9</td>
<td>49.5</td>
<td>1.00</td>
<td>0.10</td>
</tr>
<tr>
<td>Age, Mean (SD)</td>
<td>43.8 (2.19)</td>
<td>43.1 (2.97)</td>
<td>t test</td>
<td>0.05</td>
</tr>
<tr>
<td>Education, (%)</td>
<td>54.3</td>
<td>52.2</td>
<td>t test</td>
<td>0.38</td>
</tr>
<tr>
<td>Living alone, (%)</td>
<td>34.3</td>
<td>39.5</td>
<td>t test</td>
<td>0.26</td>
</tr>
<tr>
<td>Employment, (%)</td>
<td>45.7</td>
<td>55.6</td>
<td>chi-squared</td>
<td>0.13</td>
</tr>
<tr>
<td>Alcohol intake at suicide attempt, (%)</td>
<td>34.6</td>
<td>45.1</td>
<td>Fisher</td>
<td>0.05</td>
</tr>
<tr>
<td>Precipitating event, (%)</td>
<td>34.6</td>
<td>45.1</td>
<td>Fisher</td>
<td>0.05</td>
</tr>
<tr>
<td>Family psychiatric history, (%)</td>
<td>34.4</td>
<td>55.6</td>
<td>Fisher</td>
<td>0.13</td>
</tr>
<tr>
<td>Other poisoning methods, (%)</td>
<td>34.4</td>
<td>55.6</td>
<td>Fisher</td>
<td>0.13</td>
</tr>
<tr>
<td>Personality disorder, (%)</td>
<td>34.6</td>
<td>45.1</td>
<td>Fisher</td>
<td>0.05</td>
</tr>
<tr>
<td>Mental health problem, (%)</td>
<td>34.6</td>
<td>45.1</td>
<td>Fisher</td>
<td>0.05</td>
</tr>
<tr>
<td>Social and economic impairment, (%)</td>
<td>34.6</td>
<td>45.1</td>
<td>Fisher</td>
<td>0.05</td>
</tr>
<tr>
<td>Suicide attempt history, (%)</td>
<td>34.6</td>
<td>45.1</td>
<td>Fisher</td>
<td>0.05</td>
</tr>
<tr>
<td>Living alone, (%)</td>
<td>34.6</td>
<td>45.1</td>
<td>Fisher</td>
<td>0.05</td>
</tr>
<tr>
<td>Employment, (%)</td>
<td>34.6</td>
<td>45.1</td>
<td>Fisher</td>
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</tr>
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<td>54.3</td>
<td>52.2</td>
<td>t test</td>
<td>0.38</td>
</tr>
<tr>
<td>Sex, (%)</td>
<td>42.9</td>
<td>49.5</td>
<td>1.00</td>
<td>0.10</td>
</tr>
</tbody>
</table>

Conclusions: This is the first study investigating esketamine in the treatment of major depressive disorder. The results indicate that a 40-minute IV infusion of esketamine at both doses (0.2 and 0.4 mg/kg) has a rapid onset (within hours) and robust antidepressant effects in patients with TRD. Lower dose may allow for better tolerability while maintaining the robust efficacy.

P 38. Transcranial Direct Current Stimulation for Panic Disorder: A Case Study

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Background: Panic disorder (PD) is characterized primarily by the presence of recurrent and unexpected panic attacks, followed by at least one month of persistent concern about other attacks, the possible consequences of attacks and a significant behavioral change related to the attacks. The neurocircuitry of fear includes two pathways for processing sensory information. Transcranial direct current stimulation (tDCS) use has not been reported for PD. Objective: To report the results of an experimental tDCS protocol for ameliorating anxiety symptoms in a patient with panic disorder. Method: The current report is based on a single case study. We used an experimental tDCS intervention protocol as to inhibit the right dorsolateralprefrontal cortex during a period of two weeks. Symptoms were assessed by adequate clinical scales. Results: We hereby describe a 44-year-old woman with PD who successfully underwent a tDCS intervention, with important ameliorating of her symptoms. Discussion and Conclusion: To the best of our knowledge, this is the first report using tDCS for PD. Some study limitations, however, should be addressed. Our findings are based on a case study, thus having limited generalizability. Nonetheless, these encouraging results should be seen as hypothesis-driving for further controlled, randomized trials exploring the impact of tDCS in the treatment of PD and maybe other anxiety disorders.

Keywords: tDCS; Neuromodulation; Panic disorder


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Background: Major depressive disorder (MDD) is an incapacitating mental disorder associated with significant personal, social and economic impairment. Trigeminal nervestimulation is an incipient, simple, low-cost interventional strategy based on the application of an electric current over a branch of the trigeminal nerve with further propagation of the stimuli toward brain areas related to mood symptoms.

Methods: We performed an open label proof-of-concept trial using TNS for MDD. To the best of our knowledge, we present a TNS interventional protocol that has not been evaluated for MDD hitherto.

Results: A total of 11 patients were elected, with a mean age of 50.36 years (sd: 11.8 from 30 to 60). Only one patient was male. Regarding the main outcome, there was a reduction of depressive symptoms with a mean score of 5.72 (sd: 2.24) (p b 0.001) at the HDRS-17. Considering a categorical analysis, all patients presented clinical response defined as a reduction of scores of at least 50%. Only one patient did not reach remission scores (defined as an HDRS score lower than 8). Discussion: In the current neuromodulation scenario, clinical results have been working as truly hypothesis-
driven forces, i.e., empirical observation and data analysis from related studies have been highlighting possible mechanisms related to the neurobiological functioning of neuromodulation strategies. The present results, however significant, need to be taken as hypothesis-driven given the study design. Data generalization is jeopardized due to the present study lacking a control group. Our results, therefore, may be overestimated due to intrinsic characteristics such as the placebo effect and Hawthorne effect.

Conclusion: We present a proof-of-concept trial evaluating a new TNS protocol for depression. Data analysis underscores a significant participation of TNS in ameliorating depressive symptoms of patients with moderate or severe depressive episodes. Further controlled studies will contribute to establish the clinical relevance of this new strategy for MDD.

Keywords: TNS, Depression, Neuromodulation.


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Background: Generalized anxiety disorder (GAD) is characterized by a subjective sensation of uncontrollable worry and multiple physiological symptoms such as sleep disturbances, muscle tension, and difficulties in concentrating. Current treatment strategies are based on both psychological and pharmacological therapies, although treatment-resistance and low adherence due to adverse effects are some issues that compromise optimal treatment.

Objective: We hereby describe a 39-year-old woman with GAD who successfully underwent a Trigeminal Nerve Stimulation with important ameliorating of her symptoms.

Methods: We delivered electric current transcutaneously through the orbital branch of the trigeminal nerve. The protocol was as follows: frequency of 120 Hz, 148±200 μ of pulse duration, and 30 s of cycling for 30 min. The intensity was determined individually and corresponds to the intensity that each subject refers as a nonpainful mild paresthesia without muscle contraction. The electrodes were 25 cm and were wrapped with sponges soaked in saline solution to reduce impedance. A total of 10 sessions (one session a day over two weeks) were performed. For assessment of anxiety symptoms we used the Generalized Anxiety Disorder 7-item scale (GAD-7) and State-Trait Anxiety Inventory (STAI). We also assessed depressive symptoms through the Hamilton Depression Rating Scale (HDRS) - version 17 items; and cognitive functions with the Montreal cognitive Assessment (MOCA). To the best of our knowledge, we present a TNS intervention protocol that has not been evaluated for GAD hitherto.

Results: Anxiety symptoms substantially improved during the 15-day treatment course. At the end of treatment, the patient was asymptomatic and reported significant clinical gains.

Discussion and conclusion: These encouraging results should be seen as hypothesis-driving for further controlled, randomized trials exploring the impact of TNS in the treatment of anxiety disorders.

Keywords: Anxiety disorders, NIBS, brain stimulation, TNS

P 41. Transcranial Direct Current Stimulation for Treating Depression in a Patient With Right Hemispheric Dominance: A Case Study

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Background: Using positron emission tomography, resting-state studies revealed reduced cerebral blood flow and metabolism in the left dorsolateral prefrontal cortex (DLPFC) and hypermetabolism in the right DLPFC in acute major depressive disorder. This difference is also reflected in the therapeutic effects of transcranial direct current stimulation (tDCS).

Objective: Evaluate clinical effects over depressive symptoms of a tDCS protocol.

Method: The intervention protocol consisted in 10 consecutive daily tDCS sessions and was performed including the weekend. The cathode was positioned over the right and the anode over the left dorsolateral prefrontal cortex. We used a direct current of 2.0 mA for 20 minutes each session.

Results: The 66-year-old male patient diagnosed with major depressive disorder for the last 6 months had been diagnosed with dyslexia during childhood and was left-handed. After 5 days of tDCS, the patient presented intensification of depressive symptoms. It was hypothetized that the intensification of symptoms may have been due to the stimulation protocol itself. Considering the patient was left-handed and presented comorbidity with dyslexia, there was a plausible hypothesis of right hemispheric dominance. This was corroborated by the Edinburgh Handedness Scale. In fact, dyslexic patients present right hemisphere dominance more frequently. The patient also presented a single photon emission computed tomography with a hypoperfusion area over the left posteriorparietal lobe. A 10-day experimental repetitive transcranial magnetic stimulation low-frequency protocol over the left dorsolateral prefrontal cortex was started to inhibit the area, which was hypothetically hyperactivated following the rationale of right dominance. The patient presented amelioration of depressive and anxious symptoms.

Discussion and Conclusion: Given the hemispheric reversal we show in the present case study, however, it seems that therapies that are beneficial to right-handers could be detrimental to left-handers. In conclusion, the issue of hemispheric dominance should be in focus among research groups when defining interventional protocols as to optimize clinical results.

Key Words: dyslexia, depression, hemispheric dominance

P 42. Amygdaloid PKA activation is involved in anxiety-like behaviors but not social avoidance induced by social defeat stress

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It is known that social defeat (SD) stress, a social relating depression model, induces anxiety-like behaviors besides social avoidance. The key nuclei and molecular roles involved in these behavioral changes remain undefined. We found that besides a SD-induced social avoidance (assessed by the social interaction test), the stressed mice exhibited increased anxiety levels (by elevated-plus maze and open field test). Ten days of SD exposure significantly activated the amygdaloid neurons (c-Fos-immunoreactive) and astrocytes (GFAP protein level). In amygdala, the expressions of p-PKA (phosphate-PKA), p-GluR1, and p-CREB were increased after SD exposure; and they were linearly dependent on each other. Both susceptible and resilient animals to SD showed an increased p-PKA (as well as p-GluR1 and p-CREB) level, but the resilient ones exhibited even
higher. To unravel the effects of amygdaloid PKA activation on the anxiety and social avoidance in the SD model, we buried tubes into bilateral amygdala and administrated saline, H-89 (a PKA antagonist) or 8-Br-cAMP (a PKA agonist) for 4 times in the first 4 days of the SD. In the EPM test, the H-89 group showed more serious anxiety but 8-Br-cAMP improved the anxiety-like behaviors. However, no differences in the social interaction ratio (SIR) were discovered among the three groups. These findings suggest that PKA activation plays an anti-anxiety-like role in the amygdala, while amygdaloid PKA activation is not involved in changes in social interaction. Whereas the resilient animals (those with high SIR even after SD) exhibited higher amygdaloid p-PKA level, it is highly possible that amygdala is downstream of some social-avoidance-relating nuclei, which decides resiliency of the SD stress. We further examined the p-CREB level of the nucleus accumbens (Nac); comparison of the control, susceptible and resilient animals revealed a similar change with the amygdaloid p-PKA level, which suggests that Nac may be the upstream of amygdala in processes of the SD resulted behavioral changes.

Key Words: social defeat; anxiety; social avoidance; PKA; H-89; 8-Br-cAMP; GluR1; CREB.

P 43. Relationship between behavioral coping and personality in depressive patients

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Background/Aims: Personality can influence the response to stressors and coping. Previous researches were mainly focused on cognitive strategies, not behavioral coping. Cognitive characteristics for stressful situation may lead to behavioral patterns. We aimed to examine the relationship between behavioral coping and personality in depressive patients.

Methods: Sixty-five depressive patients who meet the diagnostic criteria of major depressive disorder and dystymic disorder with DSM-IV-TR were included in this study. Behavioral coping strategies were measured by self-reported behavioral checklist for stress coping. Personalities were assessed by Barratt Impulsiveness Scale (BIS), Temperament and Characteristic Inventory (TCI), and NEO Five-Factor Inventory (NEO-FFI). The relationship between behavioral coping and personalities were examined by using Pearson’s correlation.

Results: Behavioral coping with personal and inner activity was positively correlated with cooperativeness, openness, and conscientiousness, respectively (p=0.004, p=0.005, p=0.044) Coping with impulsive and pleasure-seeking activity was positively correlated with novelty-seeking and impulsivity (p=0.001, p=0.013), and negatively correlated with self-directedness and conscientiousness, respectively (p=0.033, p=0.034). Coping with social and outgoing activities was positively correlated with novelty-seeking and reward dependence, respectively (p=0.025, p=0.010) Coping with compulsive and inner activities was positively correlated with novelty-seeking and neuroticism (p=0.041, p=0.001), and negatively correlated with extraversion, respectively (p=0.001)

Conclusions: This study supports that behavioral coping may come from individual personality and characteristics. Therefore, it is important to understand the relationship between behavioral coping and personality in order to assess coping strategies for stressful situations. Consideration of personality and characteristics is needed to change maladaptive behavioral pattern into adaptive behavioral strategy.

P 44. Early onset of lithium prophylaxis as a possible good prognostic factor for staging bipolar disorder

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1San Raffaele Scientific Institute, Vita–Salute San Raffaele University, Milan, Italy

Purpose: A previous study conducted at our center (Franchini L., et al., 1999) reported that beginning lithium therapy within the first ten years of illness predicts better preventive outcome than beginning prophylaxis later, both in major depression recurrent and bipolar patients. The aim of the present study was to confirm these results considering only bipolar patients and to evaluate the clinical markers that may be associated with the response to the stabilization therapy.

Material & Methods: Two hundred fourteen subjects affected by Bipolar Disorder receiving a stabilization therapy were studied. We recorded the time of onset of the preventive therapy and divided the sample into three groups: an “Early group”, including patients who initiated the preventive therapy within the 5th year from the onset of illness, a “Late group” between the 5th and 10th year, and a “Very Late group” after the 10th year.

Results: Patients received, as main stabilization treatment, lithium salts (65%). The percentage of responders was 77% during a maintenance treatment period of 4.5 years. The variables significantly associated with the outcome of preventive therapy were the use of lithium salts as a first treatment choice (P=0.02), starting the preventive therapy within 5 years of the illness onset (P=0.0001), and the high recurrence index of the illness before treatment (P<0.0001). The presence of psychotic manifestations turned out to be the only factor that negatively influenced the response to the preventive therapy (P=0.03).
Conclusions: The present study showed that starting lithium therapy within the first five years of illness is more effective than treatments delivered later in the illness course. Our data suggests that the time of onset of lithium therapy is a new prognostic element: referring to the staging models proposed recently (Vieta E. et al., 2011), we suggest that the time of initiation of maintenance therapy is a clinically crucial information for staging (please check what this means) patients with Bipolar Disorder and, therefore, for giving an appropriate preventive treatment.