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Symposium

Clinical/Therapeutic: Symposium: Adolescents' Non-Suicidal Self-Injury

S001

Treating adolescents with suicidal and non-suicidal self-injury - what works?

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Suicide attempts and non-suicidal self-harm are important public health problems increasing strongly in prevalence in middle and late adolescence and they are robust risk factors for adult suicide attempts. Repetitive self-harm is, furthermore, associated with severe mental health and behavioral problems requiring emergency room visits and repeated hospitalizations. Emergency interventions are, however, costly, and there is no evidence that they lead to reductions in suicidal and self-harming behaviors. There is, thus, a strong need to develop and make available affordable, specific and effective treatments for self-harming adolescents and their families. Over recent years the first few randomized control trials of interventions specifically designed for self-harming and suicidal adolescents have shown that this patient group may indeed be successfully treated. These interventions include adaptations for adolescents of mentalization-based therapy (MBT-A) (Rossouw and Fonagy 2012)and dialectical behavior therapy (DBT-A) (Mehlum et al., 2014), replicated by McCauley et al. (2018), and two interventions based on cognitive behavioral approaches; the integrated cognitive- behavioral therapy (I-CBT) (Esposito-Smythers et al., 2011)and the Safe Alternatives for Teens and Youths (SAFETY) (Asarnow et al., 2017). In addition, a very brief, structured family intervention (RAP-P) was found to significantly reduce suicidal behaviors in adolescents both posttreatment and at 6 months follow-up (Pineda and Dadds 2013). This presentation will review the current research on what works in the treatment of adolescents with suicidal and non-suicidal self-injury and highlight what mechanisms therapeutic change seem to work through. Whereas treatment research with suicidal and self-harming adolescents and their families remains one of the most complex and demanding tasks clinical researchers can undertake, a lot of progress has been made over recent years that gives reason for treatment optimism provided we are able to disseminate the new knowledge into routine clinical practice in the many contexts self-harming adolescents are encountered.

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Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Clinical/Therapeutic: Symposium: Anti-Inflammatory Treatments: the Next Generation of Antipsychotic Drugs?

S002

From conventional to novel immune markers guiding novel therapy development in psychiatry?

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There is a considerable body of data that inflammatory and oxidative pathways, impaired neurogenesis, apoptosis and mitochondrial dysfunction are involved in the aetiology and progression of diverse psychiatric disorders. Elevated levels of inflammatory markers, oxidative stress and mitochondrial dysfunction have deleterious sequelae that include lipid peroxidation, DNA fragmentation, telomere shortening, protein carbonylation, reduced

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neurogenesis and vulnerability to apoptosis. This leads the consequence of structural and cognitive changes that are observed in many individuals across the major psychiatric disorders. These pathways form potential novel treatment targets, and open the door to novel therapeutic opportunities. Many of the agents that have potential in these disorders are repurposed, and thus have established tolerability and safety profiles. Options include N acetylcysteine, aspirin, minocycline, infliximab, celecoxib and statins. Mitochondrial dysfunction is also amenable to therapeutic intervention. A recent trial in bipolar disorder has been completed. Anti-inflammatory agents including cox inhibitors and aspirin have treatment potential and also may have as preventive potential as part of integrated preventive programs targeting non-communicable disorders. This presentation will focus on these novel treatment targets and the new treatment findings directed at these targets, which augment existing approaches and may contribute to better outcomes.

Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S003

Effect of antidepressant treatment on peripheral inflammation markers

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However numerous studies report significant influence of antidepressants on pro-inflammatory/anti-inflammatory cytokines balance, the available data is often inconsistent with regard to specific cytokines and drugs used. This heterogeneity of results is reflected in the conclusions from meta-analyses that have been conducted so far. One paper reported that pharmacotherapy with antidepressant drugs decreases concentrations of C-reactive protein (CRP) and IL-6, especially in outpatients and males. They stated a lack of influence on IL-10. Other meta-analysis demonstrated that antidepressant therapy decreases IL-1β whereas it does not have significant effect on IL-6 iTNF-α. The decrease in IL-6 levels was however significant with a small effect size when calculated specifically for studies with the use of SSRI drugs.

Our group performed a comprehensive meta-analysis of the effect of antidepressant treatment on a wide array of cytokines.

A systematic search of 6 databases was performed, which yielded 32 studies measuring the levels of selected cytokines before and at a second time-point during antidepressant treatment. For meta-analysis of selected studies with a continuous measure we analysed variables containing the number of cases, mean and standard deviation of the level of IL-1ß, IL-2, IL-5, IL-6, IL-8, IL-10, CRP, TNF-α, IFN-γ levels observed in the different studies, in the intervention groups before and after antidepressant treatment.

Statistical analysis revealed significant decreases of IL-4, IL-6, and IL-10 in MDD subjects after antidepressant treatment. In case of IL-1ß the decrease was significant exclusively for SSRI drugs. We did not find any significant effect of antidepressant medication on IL-2, TNF-α IFN-γ and CRP.

Antidepressant treatment affects the levels of cytokines in depression. The immunological imbalance in MDD is complex and seems to be mediated by other factors yet to be elucidated. The credibility of our results is limited by high heterogeneity among studies and very few studies with a placebo-controlled design. Research with MDD subtypes, response to treatment status and cytokine associations with the kynurenine pathway taken into account pose a promising target for future studies.

Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Clinical/Therapeutic: Symposium: Bipolar Disorder: from Prediction to Intervention

S004

Prediction of mood recurrence

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Bipolar Disorder (BD) is a recurrent disease and a significant part of its prognosis and direct and indirect costs depends on the frequency and severity of mood recurrences. The prediction of mood recurrences in BD is a challenge to individualize the risk for a subsequent episode, then to adapt the care plan including more intensive follow-up, choice of (combinations of) drugs and psychosocial interventions. We will present here new data from the FACE-BD cohort that was used to describe the time to first mood recurrence in a large sample of patients with BD-I or BD-II and to explore whether clinical predictors of mood recurrences are shared or specific to BD subtype. The samples consisted in 1135 patients with a mean duration of follow-up is 14.6 (9.5) months. Patients with BD-II have a higher risk of recurrence during the follow-up as compared to patients with BD-I. The univariable analysis showed that a high number of baseline characteristics was associated with the time to first mood recurrence. In patients with BD-I, the time to a first mood recurrence was mainly associated with higher level of depressive symptoms, lifetime history of rapid cycling, history of substance misuse and a higher level of emotional reactivity. In patients with BD-II, the time to a first mood recurrence was mainly associated with a higher level of mood symptoms and a younger age at onset of BD-II. These results will be discussed according to the previous studies available in the literature.

Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S005

Using affective lability to predict suicide

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Background.– Affect lability defined as the degree to which affects fluctuate over time, is a core feature of bipolar disorder . It is one of the strongest prodromal symptoms of thymic recurrence in bipolar disorder . It has been associated to suicidal ideation in several cross-sectional studies. However, longitudinal studies exploring the relationship between intensity and subtype of affect lability, and suicidal ideation occurence in bipolar patients are lacking.

Method.– A total of 319 euthymic or mild depressed bipolar outpatients recruited in the French FondaMental Advanced Centres of Expertise for Bipolar Disorder were divided into two subgroups according the occurrence of suicidal ideation during a 2-years follow up: 121 patients without suicidal ideation (non-SI), and 198 patients with suicidal ideation (SI). Affect lability was assessed by the French version of the Affect Lability Scale. To investigate if affective lability could predict occurrence of suicidal ideation, we took into account potential confounding factors, e.g. demographic characteristics, psychiatric comorbidities, rapid cycling, lifetime history of suicide attempt (SA), current depressive symptoms, family history of SA or completed suicide, and psychotropic medication.

Results.– Bipolar patients with high affect lability were more likely to report suicidal ideation, during follow up even after adjustment for age, study level, rapid cycling, current depression level, anxiety

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disorder, lifetime history SA (OR = 2.47; 95% CI [1.15–5.30], $p = 0.01$). The risk of suicidal ideation increased with level of affect lability.
Conclusion.– Affect lability predicts occurence of suicidal ideation, independently of other clinical suicidal risk factors. Therapeutic interventions should target this dimension in bipolar patients.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Clinical/Therapeutic: Symposium: Diagnosis and Management of Treatment-Resistant Psychiatric Disorders

S006

Can a better classification of psychiatric drugs reduce treatment resistance?

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How the Neuroscience based Nomenclature (NbN) can help in the treatment of refractory patients?
In the recent years the Neuroscience based Nomenclature (NbN) of psychopharmacological medications was developed by the key international psychopharmacological societies under the guidance of ECNP. The mission was to avoid the problems of an indication related terminology (like e.g. "antidepressants"), but to use terms describing key aspects of the pharmacological mechanisms.
This was more complicated as initially thought and is still work in progress. But meanwhile the first NbN book as well as two revisions, the latest one NbN2R (2018), are published. For most colleagues even more attractive are the respective Apps. The NbN is more and more accepted in the psychiatric community, by many of the relevant psychiatric journals, and recently also by some guidelines. In the context of the treatment of refractory patients the avoidance of indication related terms helps to overcome confusions and misinterpretations, especially on the side of the patients. Thus we must not offer anymore a patient with a refractory depression an "antipsychotic" as augmentation therapy. Also the stepwise approach in treating refractory depression becomes more understandable in its pharmacological sense: starting with an SSRI, than switching or combining with a more complex serotonin/noradrenalin reuptake inhibitor, than combining with a D2-5HT2 receptor antagonist etc. The indication of the different mechanisms explains the theoretical framework for the intervention in the sense of a "rational site-directed pharmacotherapy" (Blier 2014).
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S007

Evaluating and managing treatment-resistant schizophrenia

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Treatment-resistant schizophrenia (TRS) is a frequent, difficult-to-manage clinical problem; up to 30% of patients show little or no response to treatment. Several definitions of TRS have been proposed, typically requiring a non-response to minimum of two antipsychotics (AP) with different mechanism of action. Data indicate the existence of two types of TRS, primary (present from the onset) and secondary (developed later). First step in the management of TRS is to rule out pseudoresistance, i.e., failure to respond from different reasons (non-adherence, poor metabolizers, incorrect diagnosis, comorbidity, insufficient dosage or duration of trial, masking side effects). Therapeutic drug monitoring is useful in this stage. Various strategies have been proposed: switch to AP with different mechanism of action, combination of AP, higher doses of AP or their reduction, other drug formulations (LAI), augmentation of AP with other psychotropics (lithium, carbamazepine, valproate, lamotrigine, pregabaline, SSRI, benzodiazepines). In combination of AP, only co-administration of drugs with different pharmacodynamic profiles is justified. Drug of choice for TRS is clozapine. In contrast to other AP, improvement with clozapine can be observed even after longer duration of treatment. Recent data suggested that many patients can benefit from clozapine treatment much earlier than is current practice. Non-response to clozapine can be managed by augmentation with antidopaminergic AP (amisulpride, aripiprazole), antiepileptics (valproate, lamotrigine), antidepressants (SSRI, mirtazapine), unsaturated fatty acids, etc. Both clozapine and non-clozapine AP can be augmented with glutamatergic agents, in order to improve negative or cognitive symptoms. There is a solid evidence for efficacy of electroconvulsive therapy (ECT) in TRS. In addition to ECT, other non-pharmacological interventions are used for refractory auditory hallucinations or negative symptoms: transcranial magnetic stimulation, direct current stimulation. Specific symptoms resistant to drug treatment (delusions, hallucinations, depression and anxiety, thought disorder) can be targeted with psychotherapy, e.g., cognitive-behavioral therapy.
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S008

Progress in the treatment of treatment-resistant depression

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The group for the study of resistant depression (GSRD) is a European collaborative project between eight centres in Belgium, France, Greece, Italy, Israel and Austria. A staging model that distinguishes between "non-responders" (patients who failed to respond to one form of treatment, a condition which is now termed "insufficient response" by the European (EMA) as well as by the US health authorities (FDA), "treatment resistant depression" (TRD patients that failed to respond to two or more adequate antidepressant trials), as well as "chronic resistant depression" (CRD, patients being treated with several antidepressants for more than12 months) have been characterised. Clinical findings of the GSRD provide a set of variables associated with treatment resistance, among them co-morbid anxiety disorders, as well as melancholic features. The group set out not only to elucidate clinical variables but also conducted prospective studies that indicated for instance, that switching the mechanism of action is less beneficial than continuing the same medication. The GSRD European multicentre project encompasses now more than 2700 patients for which clinical, pharmacological as well as a molecular biological variables are documented and analysed. Genetic findings, combined with clinical characteristics might help to uncover a patient type in the future which is responsive to specific treatment modalities, pointing towards a precision medicine approach.
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Clinical/Therapeutic: Symposium: Eating Disorders, Anorexia Nervosa, Novel Clinical Features and Biomarkers for Diagnosis

S009

Physical activity, an obsessive compulsive disorder or one consequence of the addictive behavior in anorexia nervosa

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Patients with anorexia nervosa (A) restrict their energy intake even though they are underweight, (B) with irrational fear of becoming fat and (C) a distorted view of their body shape. Interestingly, there is no mention in these three diagnostic criteria of one of the way one can lose weight, namely excessive physical exercise. One of the main prognostic markers in anorexia nervosa (AN) is nevertheless physical hyperactivity, its frequency ranging between from 31% and 80% [Gümmer et al., 2015]. If physical hyperactivity is a triggering and maintaining factor in AN, it could also be used as a tool for prevention strategies and even constitute a therapeutic target [Bewell et al., 2010].
Physical exercise dysregulation could also be a vulnerability factor for AN, potentially related to other already known related traits such as negative emotions (Godart et al., 2015), poor cognitive flexibility and impaired decision making (Oltra et al., 2012) or negative self-evaluation (Dalle et al., 2008).
We therefore studied three sets of 20 subjects (with anorexia nervosa, healthy controls, healthy relatives of patients with anorexia nervosa) in order to assess the cognitive and emotional impact of a standardized physical effort (based on each physical capacity). Among other aspects, we detected that for the first 10 minutes of "cycling for pleasure", patients and healthy relatives produced an effort which was closer to their maximum than controls, and an equivalent physical effort created more positive emotions, lowered cognitive flexibility and worsened body image in patients and healthy relatives more than in healthy controls ($p < .05$).
In another protocol comparing the informativity from self-questionnaires, real life assessments and standardized efforts, we concluded that objectively and experimentally assessed physical activity appears to be the best marker, associated with cognitive rigidity in anorexia nervosa (Di Iodovico et al., *in prep)*. In this protocol we found an addictive attitude towards physical exercise, statistical correlated with poor cognitive flexibility, and detected an exercise-related worsening of body image perception.
These different findings strengthen the role of excessive physical activity as a core aspect of anorexia nervosa.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S010

Socio-emotional and neurocognitive functioning predictors of AN and therapeutic outcomes

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Introduction.– There has been much interest in socio-emotional and neurocognitive aspects of functioning in anorexia nervosa as potential risk and/or illness maintaining factors. The classical neuropsychological profile of anorexia nervosa is thought to include impaired set-shifting, excessive detail focus and poor central coherence. Reward-related decision making is also uniquely impaired in anorexia nervosa with a preference for 'larger later' over 'smaller sooner' rewards in delay discounting tasks, whereas in most other psychiatric disorder the preference is typically altered in the direction of 'smaller sooner' rewards. In regards to the socio-emotional processing stream, in anorexia nervosa all aspects of this are impaired, from emotion recognition, regulation and expression, to theory of mind, social perception and social problem solving.
Method.– In this paper I will review how functioning in these areas relates to clinical symptoms, illness duration, comorbidity and treatment outcomes and how these impairments might be ameliorated through specific interventions.
Results.– In cross-sectional studies, illness stage (early stage vs enduring), severity and recovery status affect neurocognitive and socio-emotional impairments. Much less is known about the impact of these impairments on treatment outcome and whether they can be ameliorated through specific targeted interventions.
Conclusion.– Both state and trait factors seem to be implicated in socio-emotional and neurocognitive impairments in anorexia nervosa.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S011

Specific epigenetics biomarkers of the physiology and emotions in AN patients and remitters

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Introduction.– Anorexia nervosa (AN) is a severe psychiatric disorder, leading to the highest rate of mortality, with no medication treatment. The epigenetic mechanisms are strongly suggested to be involved in AN. They include DNA methylation, histones and chromatin modifications but also the dysregulation of non-coding microRNAs. These mechanisms modify the regulation of the gene expression. We and other teams have mainly focused in DNA methylation of candidate genes or of the whole-genome methylation study (methylome) in AN patients versus controls. We found that the differentially methylated CpG sites are located around genes involved in biological processes playing a role in brain development and its plasticity. However, little is known in the AN remitters.
Objectives.– This presentation will show the recent epigenetic biomarkers in AN patients and remitters.
Methods.– This work is based on the literature and databases on results obtained from anorexia nervosa studies. Several works use the measure of the DNA methylation by carrying out of whole-genome analyses of the methylone with Infinium HumanMethylation450 BeadChip technology.
Results.– Analysis showed significant differences of methylation levels in AN compared to controls or remitters. It appears also that for some genes, remitters present an intermediate profile between AN and controls. One of the most promising epigenetic biomarker is the DNA methylation of the BDNF (brain-derived neurotrophic factor gene) whose the blood circulating level is also altered.
Conclusions.– Correlations and associations between epigenetic biomarkers and clinical features in AN patients and remitters could be made to propose precise medicine and a better care.
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Clinical/Therapeutic: Symposium: Female Gender, Reproductive Events and the Expression of Selected Mental Disorders

S012

Menopause and mental health

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Menopause is a natural event, which women on average experience around age 50. It is defined as the final menstrual period and is preceded by many years of "menopausal transition" associated with marked biological, especially hormonal, changes. Although it is a physiological process, especially the fluctuations and final loss of estrogen activity may have a negative impact on mental wellbeing, lead to vasomotor symptoms, sleep disturbances, sexual problems, cognitive decline, and depressive symptoms. In addition to the biological changes, for women this phase of life is often burdened with numerous psychosocial stressors, role changes, losses and the experience of aging. Altogether those factors may even contribute to an upsurge in the incidence of severe mental disorders such as depressive disorders or schizophrenic psychoses.
This has many implications for the clinic and for research. In the clinic the specific diagnostic and therapeutic needs of women of this age group have always to be taken into account. Appropriate treatment strategies should not only include specific psychotherapeutic and psychosocial interventions but also consider estrogen replacement where indicated in addition to standard psychiatric care. The latter of course has always to be based on a thorough individual risk-benefit assessment and decided on in close cooperation with a gynecologist and the well-informed woman herself.
While many studies suggest a benefit in perimenopausal *depression*, there still is a lack of well-designed studies on the indications and contraindications of estrogen replacement in perimenopausal women at risk for or suffering from other mental disorders. Further research is needed, especially regarding perimenopause and schizophrenic psychoses, the relative risk of hormone replacement as compared to treatment with psychotropic drugs or the best augmentation strategies. Last but not least, we need more research on psychotherapies addressing the specific needs of women of this age group.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S013

Mood changes related to reproductive events in women with ADHD

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ADHD in women and hormonal mood changes during the lifespan,
Introduction.– Many aspects of the female presentation of ADHD are still understudied, and the typical symptoms of ADHD in women deserve more attention in clinical practice. This is especially true for the hormonal mood changes during the menstrual cycle, and their effects on the severity of ADHD and sleep problems. In clinical practice, women with ADHD often complain about severe mood changes in the last week of the menstrual cycle: they are down, irritable, agressive, and sometimes even suicidal. The severity of these symptoms diminishes after menstruation, only to return the next month.
Method.– We used a selfreport version of the MINI-5 plus questionnaire to assess Premenstrual Dysphoric Disorder symptoms, the Edinburgh Postnatal Depression Scale (EPDS) to assess life-time PPD symptoms, and the Greene Climacteric Scale (GCS) for mood symptoms during menopause, to compare 200 women with ADHD with 200 controls.
Results.– Our study showed that women with ADHD indeed suffered more often from premenstrual depressive symptoms, and that these symptoms were more severe than in controls. Women with ADHD also met more often criteria for PMDD, premenstrual dysphoric disorder (Dorani et al, submitted). A similar pattern was found for postnatal depression in women with children, and for depressive symptoms in the climacteric period.
Conclusion.– The pathophysiology of these results may be understood using the literature on the interaction of dopamine and estradiol in women in general, and the few studies that have been performed in this field. Plans for future research, as well as current treatment options for women with ADHD and severe hormonal mood changes during the lifespan will be discussed.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Clinical/Therapeutic: Symposium: Implementing Cognitive Behavioral Therapy as a Standard Method to Treat Insomnia in Psychiatric Practice

S014

Current guidelines for the diagnosis and treatment of insomnia

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Problems to fall asleep, to maintain sleep and early morning awakening in association with daytime complaints are termed insomnia. Insomnia can occur as a symptom, a syndrome or an independent disorder - then called Insomnia Disorder according to DSM-5. Insomnia as a disorder afflicts approximately 6-10% of the population in European countries. Pathophysiological models of insomnia stress hyperarousal on a cognitive, emotional and physiological level as a main factor involved in the condition. Just recently, several professional and scientific societes have published guidelines for the diagnosis and treatment of insomnia. Here to mention are the guidelines of the American College of Physicians (ACP, 2016), the American Academy of Sleep Medicine (AASM, 2017) and the European Sleep Research Society (ESRS, 2017). All of these guidelines agree that a proper and thorough diagnostic and differential-diagnostic process should be conducted before any kind of therapy is started. With respect to treatment, all guidelines agree that Cognitive-Behavioral Treatment for Insomnia (CBT-I) should be considered as first-line treatment. Evidence for the effectiveness of pharmacological treatment is considered as weaker, especially with respect to long-term-effectiveness. CBT-I encompasses relaxation techniques, sleep hygiene, stimulus control, sleep restriction and cognitive techniques to reduce nocturnal ruminations. At present an initiative within the European Sleep Research Society is working on establishing a European CBT-Academy, as a body to teach and disseminate CBT-I on a European level.
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S015

Adjusted CBT-i for sleep problems in bipolar and psychotic disorders

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Introduction.– Sleep problems are highly prevalent in psychiatric populations, and often prodromal to psychiatric symptom deterioration. Despite strong evidence for cognitive behavioral therapy for insomnia (CBT-I), pharmacological treatment is most commonly used, and the use of CBT-I in psychiatric populations is poorly studied.
Objectives.– The larger project Better Sleep in Psychiatric Care aims to evaluate and disseminate CBT-I to psychiatric clinics with different patient groups within Stockholm County Council. Manuals for CBT-I-based group-interventions have been developed for patients at psychiatric specialist out-patient clinics with e.g. bipolar or psychotic disorders, and here we investigate treatment acceptability and effects on sleep problem severity.
Methods.– A regular CBT-I protocol was adjusted to needs of patients with bipolar disorders and psychotic disorders respectively. Patients at involved clinics were invited to participate in the preliminary evaluations with a pre-post design. Inclusion was generous, and required only self-reported sleep difficulties and ability to attend to and function during group sessions.
Results.– Therapists found treatment manuals credible, and patients were interested in participating. Though drop-out rates were relatively high, insomnia severity in patients who did not drop out improved from pre- to post treatment. Additional adjustments to the treatment manuals, mainly to address non-compliance and treatment drop-out, may be beneficial.
Conclusions.– CBT-I-based group treatments adjusted for patients with bipolar and psychotic disorders, seem acceptable for patients and therapists, and promising to ameliorate insomnia symptoms in theses patient groups with psychiatric disorders. Lessons from the studies in psychiatric specialist out-patient clinics will be discussed.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S016

Diagnosing and treating insomnia in ambulatory mental health care services

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Introduction.– Insomnia is one of the most frequent disorders of the brain and a common symptom of many mental illnesses. Its treatment is challenging in psychiatric practice and a mental disorder comorbid with insomnia usually requires more complex interventions than the standard treatment.
Objectives.– The aim of this presentation is to summarize data on diagnosing and treating insomnia in mental health care services at our institute. Followed by a discussion on how current guidelines on treating insomnia can be implemented in daily psychiatric practice.
Methods.– Sleep and daytime symptoms were assessed with actigraphy, clinical rating scales and sleep diaries in a group of over 130 patients (mean age 48 +/– 17 years, females 59,8%) referred to Sleep Medicine Center for diagnostic evaluation of chronic insomnia. The patients were divided into four quartile subgroups based on results from actigraphy and sleep diaries. The means between the groups were compared with one-way ANOVA.
Results.– The most consistent findings in the majority of the patients were excessive time spent in bed and low physical activity. There were large discrepancies between subjective (sleep diaries) and objective (actigraphy) evaluation of sleep continuity in both directions, some patients were under- and the others overestimating their sleep duration.
Conclusions.– Treatment of insomnia in mental disorders requires behavioral interventions to strengthen the homeostatic sleep need and circadian sleep rhythm. Low daytime physical activity is a major problem in a majority of the patients.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Clinical/Therapeutic: Symposium: Ketamine in Psychiatry: Beyond Depression

S017

Ketamine for unipolar and bipolar depression

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A substantial proportion of patients with major depressive disorder do not to respond to multiple trials of antidepressants, augmentation therapy or other forms of therapy. These patients with treatment-resistant depression (TRD) have to undergo significant delays until symptomatic recovery. This underscores the need for new therapies for this subgroup. Of the novel pharmacotherapeutic strategies seeking to rapidly alleviate depressive symptoms, glutamatergic modulators such as ketamine have shown rapid and relatively sustained antidepressant efficacy in treatment resistant uni- and bipolar depression. I will present results of a clinical trial recently conducted at the NIMH investigating biomarker of ketamine's treatment response and remission. This study implemented a variety of techniques such as structural, functional neuroimaging, MRS, EEG, MEG as well as proteinomics an genomics in 33 patients with TRD as well as 25 matched healthy controls. Results indicate that one dose of the rapid-acting antidepressant ketamine is associated with lasting changes in functional connectivity as measured with functional MRI. In addition, this study found that ketamine significantly increased HAM-D values of healthy controls, potentially indicating a U-shaped curve of ketamine's action on cerebral function, i.e. normalizing brain function in TRD, while tipping homeostatic plasticity outside of normal levels in healthy subjects. Finally, I will present implications from a current guideline paper on how to implement ketamine treatment in daily clinical practice.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S018

Antidepressant efficacy and tolerability of ketamine and esketamine

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Ketamine and esketamine are promising candidates in the search of a rapid-onset antidepressant effect in treatment-resistant depression. A range of mechanisms beyond unspecific N-methyl-

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D-aspartate receptor antagonism, some of which will be reviewed, may mediate their antidepressant effects. Clinical proof-of-concept studies of ketamine and esketamine will be reviewed, mainly showing a rapid, significant antidepressant effect and a possible specific antisuicidal effect. The duration of those effects will be discussed (transient when limited to a single administration), together with the published strategies to maintain longer effects. Tolerability seems acceptable in the short term, with transient elevation of blood pressure and mild and transient dissociative and psychotomimetic effects, but there are major concerns regarding the safety of the long-term use of ketamine or esketamine. Some of the unresolved issues and limitations of the current evidence of these drugs will also be discussed.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Clinical/Therapeutic: Symposium: Lifestyle Modifications for Treatment of Major Psychiatric Disorders: Current and Future Perspectives

S019

Non-pharmacological treatment options in schizophrenia: beyond psychotherapy

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Beside the established pharmacological treatments in schizophrenia, psychoeducation is well established as a second independent column for improving the acute and especially long-term outcome of schizophrenia. There are several well controlled studies demonstrating that psychoeducation in inpatients and their relatives reduces the likeliness of a relapse and improves the long-term outcome of schizophrenia in terms of positive and negative symptoms. One of the underestimated areas of treatment is the use of Cognitive Behavioural Therapy (CBT) and lately also the Metacognitive Training (MCT) in resistant schizophrenia, especially if positive symptoms prevail. Another fruitful way to augment the treatment of schizophrenia is non-invasive brain stimulation: For rTMS the literature is non-conclusive but overall hints at a significant improvement of negative symptoms in small-scale studies. TDCS, another recent development based on a few pilot studies reveals a good option in treatment resistant positive as well as negative symptoms. A third way to improve the long-term outcome of schizophrenia is the modification of lifestyle including nutrition and physical exercise. Several meta-analyses demonstrate the beneficial effect of exercise on function, positive as well as negative symptoms and brain structure in multi-episode schizophrenia. Finally, the question arises whether the targeted substitution of the daily nutrition might be a way to improve the neuronal plasticity conveying cognitive dysfunction in schizophrenia.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S020

Dietary factors in the treatment of major psychiatric disorders: focus on essential fatty acids and gluten

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A growing body of evidence indicates that nutrition may be a crucial factor affecting mental health. Nutritional psychiatry as a new paradigm offers a promising avenue for the prevention and co-treatment of psychiatric disorders. Dietary components relieving the symptoms of mental illness and easy to implement are particularly needed.
Omega-3 polyunsaturated fatty acid (n-3 PUFAs) supplementation has been proposed as an adjuvant treatment of mood disorders. PUFAs play a profound role in the brain structure and physiology, with particular importance of their anti-inflammatory properties responsible for PUFAs anti-depressant effect. Although n-3PUFA supplementation has shown inconclusive results, studies on the use of PUFAs that take into account their type (EPA/DHA) and inflammation are most promising. Patient stratification dependent on their genetic predispositions, inflammatory state and nutritional deficiencies offers more tailored therapeutic interventions.
Gluten is a cereal-derived protein composite with highly immunogenic properties. Its intake could trigger gut-brain axis dysfunction, leading to immune-inflammatory cascade initiating or aggravating psychiatric symptoms. Meta-analyses have shown elevated levels of gluten sensitivity biomarkers in schizophrenia patients although the immune response is different than in coeliac patients. While the number of clinical trials on the effects of a gluten-free diet on schizophrenia patients is insufficient to formulate recommendations, the results of the first RCT focused on patients with an abnormal immune response to gluten are optimistic and suggest AGA IgG antibodies as possible markers of treatment efficacy.
Patients stratification according to the results of biochemical and genetic biomarkers appears to be the first step to an individualized therapy including dietary intervention.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S021

The role of gut microbiota in major psychiatric disorders: future perspectives

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Evidence is accumulating to suggest that gut microbes are involved in neural development and function, both peripherally in the enteric nervous system and centrally in the brain. While evidence is still limited in psychiatric illnesses, there are rapidly coalescing clusters of evidence which point to the possibility that variations in the composition of gut microbes may be associated with changes in the normal functioning of the nervous system.
The brain-gut-microbiota axis provides a bidirectional route of communication between the gut microbes and the brain. The axis involves the vagus nerve, short chain fatty acids, tryptophan, cytokines and the hypothalamic-pituitary-adrenal axis.
There are marked differences in the gut microbiota between patients with major depression and healthy controls. Patients with major depression show decreased microbial diversity. We conducted a faecal microbiota transplant in rats with faeces from depressed patients or healthy controls. Those rats receiving a transplant from depressed patients developed a depressive phenotype with alteration in corticosterone release and tryptophan metabolism. They also developed a pro-inflammatory phenotype.
That bacteria might have a positive mental health benefit is now becoming clear. Such bacteria may influence the capacity to deal with stress, reducing anxiety, perhaps positively impacting on mood and are now called psychobiotics. Whether, they are capable of acting like and in some circumstances replacing antidepressants remains to be seen.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

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Clinical/Therapeutic: Symposium: Management of Mood Disorders: Current Treatments and the Potential of GABA-A Receptor Positive Allosteric Modulators in Postpartum Depression and Major Depressive Disorder

S022

An overview of depression: disease burden and treatment history

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Depression poses a substantial public health challenge, at the personal, social and economic level. It is a leading cause of years of life lost to disability (YLD) in World Health Organization (WHO) member states and corresponds to 10.3% of the total YLD across all diseases (Smith, 2014). Several psychological and pharmacological treatment options are available although, regardless of type, their efficacy compared to "placebo" is generally of moderate effect size (Cuijpers et al., 2016; Cipriani et al., 2018). Psychological therapies, and particularly cognitive behavioral therapy, are currently recommended as first line treatment for less severe depression and as adjunct treatment for recurrent cases (NICE, 2009); there is emerging evidence that increasing physical activity may also be beneficial in mild depression (NICE, 2009). Antidepressants are the standard pharmacological interventions for depression and they typically target monoaminergic neurotransmission. Compared to placebo, the odds ratio of response or remission following antidepressant treatment is 1.66 and 1.56 respectively (McCormack and Korownyk, 2018). However, approximately 30–40% of patients with depression do not benefit from antidepressant treatment (Ionescu and Papakostas, 2017). This proportion may be higher in actual clinical practice, as research studies typically exclude more complicated or severely ill patients. Additional concerns include delayed onset of action, increased suicidality, particularly in the youth, and high rates of relapse following discontinuation. The use of ketamine as an antidepressant reflects a shift towards fast-acting agents that involve pathways other than the monoamines system. The current focus of drug development in depression focuses on identifying novel molecular targets and therapeutics with potential to deliver fast and safe relief.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S023

Postpartum depression epidemiology and diagnosis

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Introduction.– Postpartum depression (PPD) is the most common complication of pregnancy. The onset of PPD symptoms may occur during pregnancy or up to one year postpartum. PPD is considered under-recognized, and left untreated, PPD symptoms can have long-term negative impacts on mother, baby, and family.
Objective.– At the end of this presentation, participants will understand the essential symptoms of the "Baby Blues" versus antenatal depression and postnatal depression (collectively PPD), with or without co-morbidities, and the potential consequences of these symptoms for pregnancy, newborns, and parent-infant interactions.
Methods.– The most recent recommendations for the screening and diagnosis of PPD and for the differentiation of PPD from other perinatal psychiatric disorders will be discussed, including appropriate screening frequency and tools. The identification of PPD in women in context with other co-morbid conditions will also be examined. Finally, the burden of illness and potential long-term impacts of PPD on the mother and child will be presented.
Results.– Recent studies have demonstrated deficiencies in PPD screening and significant underdiagnosis of PPD. In addition, PDD has been shown to be heterogenous, further indicating the importance of appropriate screening and diagnosis. PPD has a clearly demonstrated impact on public health. Personal experience with implementation of PPD guidelines for screening, recognition, assessment, and diagnosis and the implications for PPD case management in the peripartum period will be discussed.
Conclusions.– Although PPD is common, it is underdiagnosed. Multiple societies and organizations support the implementation of PPD screening.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S024

GABAergic mode of action and GABA-A receptor positive allosteric modulators in postpartum depression

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Introduction.– The etiology of postpartum depression (PPD) is not completely understood and is likely multifactorial. Perinatal alterations in GABAergic signaling, due to changes in levels of $GABA_A$ and endogenous $GABA_A$ receptor ($GABA_AR$) positive allosteric modulators (PAMs), such as allopregnanolone, have been proposed as one potential mechanism underlying PPD. The GABAergic hypothesis is supported by mouse studies demonstrating perinatal changes in $GABA_AR$ subunit composition and that deletion of the $GABA_AR$ δ subunit results in phenotypes mimicking PPD.
Objective.– Previous findings implicating GABAergic signaling in PPD have supported the development of $GABA_AR$ PAMs, such as brexanolone injection, SAGE-217, and ganaxolone, as potential PPD therapeutics. Following this presentation, participants will understand the GABA hypothesis of PPD and the current state of $GABA_AR$ PAM development in PPD.
Methods.– Brexanolone injection, an investigational, intravenous formulation of allopregnanolone, has been evaluated in three pivotal, double-blind, randomized, placebo-controlled studies in PPD conducted under an umbrella protocol to allow a pre-planned analysis of an integrated dataset. The investigational, oral $GABA_AR$ PAM SAGE-217 is also being evaluated in a Phase 3 PPD study. Two placebo-controlled Phase 2 studies are investigating oral or intravenous formulations of ganaxolone in PPD.
Results.– Brexanolone injection achieved its primary endpoint of a significantly larger reduction from baseline in mean Hamilton Rating Scale for Depression total scores versus placebo at the end of a 60-hour infusion in all three studies. Studies of SAGE-217 and ganaxolone are ongoing.
Conclusions.– Completed and ongoing clinical studies are exploring the potential of $GABA_AR$ PAMs in the treatment of PPD.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S025

GABAergic mode of action and GABA-A receptor positive allosteric modulators in major depressive disorder

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Introduction.– Gamma-aminobutyric acid (GABA) signaling has been implicated in major depressive disorder (MDD). Lower GABA concentrations have been reported in plasma, cerebrospinal fluid (CSF), and cortical brain tissue from depressed patients. Additionally, reduced CSF levels of allopregnanolone, an endogenous positive allosteric modulator (PAM) of $GABA_A$ receptors ($GABA_A$Rs) are normalized following conventional antidepressant treatment; such treatments support remission in some patients after extended exposures of up to 8 weeks.
Objective.– The GABAergic hypothesis of depression has supported the development/exploration of $GABA_A$R PAMs, such as SAGE-217 and ganaxolone, as potential depression pharmacotherapies. After this presentation, participants will understand the potential role of GABA dysfunction in MDD etiology and the current state of development of $GABA_A$R PAMs for depression.
Methods.– SAGE-217, an investigational, synthetic, orally-bioavailable $GABA_A$R PAM, was evaluated in a pivotal, double-blind, 1:1 randomized, placebo-controlled trial in 89 subjects of both sexes with MDD and a Hamilton Rating Scale for Depression (HAM-D) total score $\geq$22. SAGE-217 30 mg or placebo was administered once daily for 14 days, with 4 weeks follow-up. An open-label trial of oral ganaxolone (8 weeks dosing, 2 weeks taper) as an adjunctive therapy in treatment-resistant depression has been conducted in 10 post-menopausal women.
Results.– SAGE-217 achieved its primary endpoint of a significant reduction in depressive symptoms, by HAM-D total score change from baseline versus placebo, at Day 15. The results of the ganaxolone study have not yet been reported.
Conclusions.– Completed and ongoing clinical studies are evaluating $GABA_A$R PAMs as potential therapies for depression.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Clinical/Therapeutic: Symposium: Metabolic Syndrome in Psychiatry: Recognition and Management of Psychotropic Drug-Induced Metabolic Effects

S026

Metabolic syndrome in psychiatry: an overview

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Introduction.– Metabolic syndrome and its components, such as obesity, dyslipidemia, hyperglycemia and hypertension, are on the rise in the general population, but both more common and less well treated in people with severe mental illness, adding to a growing mortality gap.
Objectives.– To review data on the interface between metabolic syndrome and severe mental illness.
Methods.– Summary of the current knowledge about the epidemiology, characteristics, correlates and proposed underlying mechanisms related to metabolic syndrome in people with severe mental illness. In addition to the traditional components of the metabolic syndrome, elements, such as inflammation and oxidative stress markers, are discussed. Data from meta-analyses are reviewed to provide clinically relevant background knowledge to the monitoring, risk evaluation and management of people with mental illness in need of psychotropic medications.
Results.– Metabolic syndrome and its components, such as obesity, dyslipidemia, hyperglycemia and hypertension, are more common in people with severe mental illness than in the general population. Large meta-analyses found little differences in the magnitude of these cardiovascular risk factors and adverse health states between patients with schizophrenia, bipolar disorder and unipolar depression. Data point to a multifactorial pathophysiology, including mechanisms related to the underlying disorders, nonspecific "stress" and related hypercortisolemia, unhealthy lifestyles, and different psychotropic agents that have predictable differential risk profiles, which are modified by patient factors.
Conclusions.– To optimize outcomes in people with severe mental illness, clinicians need to keep the body in mind and balance psychiatric and physical outcomes that interact via several detectable mechanisms with each other.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S027

Clinical determinants of metabolic syndrome induced by psychotropic drugs

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Introduction.– Weight gain and obesity are important health problems associated with psychiatric disorders and/or with psychotropic drug treatment. Obesity can lead to the development of other components of the metabolic syndrome such as dyslipidemia, hypertension and type 2 diabetes, which may lead to the development of cardiovascular diseases, reducing a patient' quality of life and increasing the risk of mortality. Many psychotropic drugs increase the risk of cardiometabolic disorders with considerable inter-individual variability.
Objectives.– To review data on clinical risk factors for metabolic worsening during psychotropic treatment, and on the monitoring, prediction and/or identification of patients at risk for weight gain and/or cardiovascular disorders.
Methods.– Results from meta-analyses and from recent studies will be used to summarize current knowledge.
Results.– In addition to the well-known clinical risk factors for metabolic worsening (e.g. young age, first episode status and/or low initial BMI), we will present some recently identified risk factors including the intake of high doses of caffeine and socio-economic factors. Data will be shown demonstrating the usefulness of monitoring early increase of weight and/or modifications of blood lipid levels following the prescription of psychotropic drugs, and of predicting important weight gain, dyslipidemia and/or the metabolic syndrome in adult and adolescent patients
Conclusions.– When starting treatment with psychotropic drugs known to induce weight gain and/or metabolic disturbance, the choice of drugs should consider important clinical risk factors for evaluating the risk/benefit ratio (e.g., worsening of metabolic parameters/drug effectiveness). The prospectively monitoring of metabolic parameters is essential.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S028

Genetic determinants of metabolic syndrome induced by psychotropic drugs

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Background.– Antipsychotic (AP) medications are the first line of treatment for schizophrenia but most are conferring risk for antipsychotic-induced weight gain (AIWG). The objective of this investigation was to conduct a genome-wide association study (GWAS) of AIWG, followed by comprehensive, post-GWAS approaches.
Methods.– We investigated $n = 201$ schizophrenia or schizoaffective disorder patients of European and African American ancestry who were treated mostly with clozapine or olanzapine. We conducted genome-wide association analysis for AIWG defined primarily as a percentage of weight change from baseline.
Results.– In the entire sample, we observed the genome-wide significant association between rs1525085 ($\beta = 0.411$, $p = 3.15 \times 10^{-9}$) variant of the DGKB gene and AIWG. The association was nominally significant in Europeans ($\beta = 0.271$, $p = 0.002$) and African Americans ($\beta = 0.579$, $p = 5.73 \times 10^{-5}$) with the same risk allele. When examining Europeans exclusively ($n = 147$), the top variant rs7720513 ($\beta = 0.406$, $p = 1.26 \times 10^{-6}$) was located upstream of the STC2 gene. Our top genes ($p < 5 \times 10^{-5}$) were enriched in the GWAS catalog for the risk of obesity and schizophrenia. Top genes for the whole sample also interacted with the known risk factors for obesity (G6PD) and schizophrenia (NDEL1) and are targeted by miRNAs related to schizophrenia (mir-34a) and obesity (mir-19b). However, our polygenic risk score analyses did not provide support for major genetic overlap between obesity and the risk of AIWG.
Conclusions.– Our findings suggest that rs1525085 variant in DGKB is associated with AIWG across two populations and that the G6PD and NDEL1 related pathways might be involved in AIWG.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Clinical/Therapeutic: Symposium: Negative Symptoms: New Challenges and Perspectives

S029

Negative symptoms in schizophrenia: evolution of their conceptualisation and relationships with real-life functioning

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Negative symptoms of moderate severity are present in more than 50% of people with schizophrenia, have a significant impact on real-life functioning, and pose a substantial burden on the affected people and their families.
The dearth of effective therapeutic interventions and the inconsistency of research findings relevant to the neurobiological underpinnings of negative symptoms have highlighted the need for a reconceptualization of this dimension.
Several studies demonstrated that negative symptoms might be primary to schizophrenia or secondary to other factors. The presence of primary and enduring negative symptoms seems to identify a disorder that differs from schizophrenia without primary and enduring negative symptoms in terms of pathogenesis, outcome and response to treatment.
Neither primary nor secondary negative symptoms represent a unitary construct and factor analyses on many different data sets reported that these symptoms tend to group in at least two domains, showing distinct associations with functional outcome measures, cognitive impairment and neurobiological abnormalities.
Recent studies indicate that the 5 factor solution is preferable with respect to the two factor structure, and data from the Italian Network Follow-up Study show a high temporal stability of the 5-domains, identified by the network analysis, in a group of 617 clinically-stable subjects with chronic schizophrenia, assessed twice with a 4-year interval. These domains predicted different aspects of real-world functioning at follow-up.
External validation of these domains is still in progress and will be instrumental to research progress on negative symptom pathophysiology and treatment.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S030

Support for the five consensus domains of negative symptoms: evidence from computational modeling

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Negative symptoms have been considered a core component of psychopathology in schizophrenia since the earliest conceptualizations of the disorder. Modern empirical evidence confirms that negative symptoms are distinct from other aspects of the illness (e.g., positive and disorganized symptoms), and associated with a number of poor clinical outcomes (e.g., risk for illness onset, low rates of recovery, poor quality of life). Unfortunately, attempts to remediate negative symptoms using pharmacological and psychosocial treatments have been largely ineffective. One reason for the limited progress in developing effective treatments is that there is a lack of conceptual clarity regarding the latent structure of negative symptoms. Latent structure refers to how the universe of behaviors that comprise negative symptoms relate to underlying traits, factors, or domains. Practically, it indicates how many aspects of negative symptoms should be evaluated in clinical rating scales and diagnostic systems like the DSM and ICD, as well as how the pharmaceutical industry should approach targeted treatment development. In this presentation, I will present data from a series of studies indicating that early unidimensional models and current two-dimensional models (consisting of motivation and pleasure and diminished expression) offer poor fit for data on the 3 most contemporary negative symptom scales (CAINS, BNSS, SANS), whereas more complex five-factor and hierarchical models provide excellent fit. This pattern of findings is replicated across a diverse range of cultures (Italy, Spain, China, Switzerland, USA), across prodromal and chronic phases of illness, with alternate mathematical approaches (e.g., network analysis), and using novel ecological momentary assessment measures. Furthermore, the 5 domains have unique external correlates that are masked when broader one and two factor structures are considered (e.g., reward processing, brain function, cognition, functional outcome). Collectively, these findings provide strong evidence that the recent trend toward conceptualizing negative symptoms in relation to two dimensions reflecting diminished expression and motivation and pleasure is not statistically or theoretically justified. Rather, negative symptoms are best conceptualized in relation to the 5 domains identified in the NIMH Consensus Development Conference: anhedonia, avolition, asociality, alogia, blunted affect. These

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findings have ramifications for DSM and ICD diagnosis, exploring pathophysiological mechanisms, and the search for novel treatment targets.
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S031
Pharmacological treatment of negative symptoms: new findings and perspectives
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Most secondary negative symptoms (caused e.g. by depression, extrapyramidal symptoms) respond well to pharmacological treatment, however the treatment of enduring primary negative symptoms remains an unmet need. The European Medicines Agency's guideline recommends studies in patients with *predominant and persistent negative symptoms* for investigating the efficacy of a compound for the treatment of negative symptoms. A number of compounds tested for the treatment of primary/predominant and persistent negative symptoms in schizophrenia failed to show efficacy. The objective of this short presentation is to show examples of successful or promising clinical research with new compounds in this field.
One approach is to develop a single antipsychotic drug with efficacy both against positive and negative symptoms. Two *dopamine D_3-receptor-preferring partial agonists*, F17464 (it is in Phase II) and cariprazine (it is already on the market) showed efficacy against positive symptoms, cariprazine has been found also effective against predominant and persistent negative symptoms as compared to risperidone.
Another approach is to develop an "add on" treatment for negative symptoms, i.e. add a second drug to the ongoing antipsychotic drug treatment. An example is pimavanserin, which is an inverse agonist and antagonist at serotonin 5-HT2A receptors with high binding affinity and at serotonin 5-HT2C receptors with lower binding affinity. Pimavanserin is being tested in ongoing studies for the treatment of negative symptoms. This drug has already been approved by the FDA for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis.
An interesting further approach is to discontinue antipsychotic drugs in stable schizophrenia patients with negative symptoms and start a drug for the treatment of negative symptoms, such as MIN-101, a 5HT2 and Sigma 2 antagonist, which demonstrated statistically significant efficacy as a monotherapy; and Lu AF11167 (an inhibitor of a phosphodiesterase enzyme) which is being tested as monotherapy on negative symptoms in patients with schizophrenia with persistent prominent negative symptoms.
While it is beyond the topic of this presentation, it is important to emphasize the combination of psychosocial interventions, physical exercise and drugs for a better outcome in the treatment of negative symptoms in schizophrenia.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S032
Genetically modified animal models of negative symptoms: future challenges for drug development
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Schizophrenia is a complex and multifactorial disorder, which is caused by the complex interplay of both genetic and environmental factors. Diagnostic symptoms of schizophrenia, which typically emerge during early adulthood, comprise positive symptoms, cognitive deficits, and negative symptoms, the latter including motivational deficits, anhedonia, blunted affect, poverty of speech, and decreased social functioning. Negative symptoms (and cognitive deficits) have proven resistant to both first- and second-generation antipsychotic drugs. Alongside cognitive dysfunction, severity of negative symptoms has also been shown to significantly predict functional outcome in schizophrenia, heightening the necessity to develop more effective treatment strategies. Improved pharmacotherapeutic strategies requires a greater understanding of the mechanisms underlying such symptoms, as well as enhanced precision around measurement of features which mimic negative symptomatology in animal models. This presentation will provide a selective summary of recent developments in this field, with a particular focus on phenotypic data arising from preclinical genetic models for negative symptoms. Recent findings will be discussed in the context of the search for potential new directions for therapeutics which will address the negative symptoms of schizophrenia.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Clinical/Therapeutic: Symposium: New Treatment Targets in Addiction Psychiatry: Translating Neuromodulation to the Clinic

S033
Transcranial magnetic stimulation to reduce cognitive bias in alcohol addiction
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Introduction.– High Frequency Repetitive Transcranial Magnetic Stimulation (HFrTMS) is a promising new treatment modality to target craving and relapse in a variety of substance use disorders. In this study we focus on its effects in patients with alcohol use disorder (AUD). These patients have an attentional bias towards alcohol related cues. During the process of recovery this attentional bias shifts towards normalization and can therefore be used as a neurobiological marker of recovery of AUD.
Objectives.– To study the effectiveness of HFrTMS treatment on attentional bias in patients with AUD.
Methods.– 22 patients received active HFrTMS on the right dorsolateral prefrontal cortex in 10 sessions (3000 pulses per session), 27 received sham. On three moments (at the beginning, halfway and at the end of the treatment) an approach-avoidance task was executed, in which patients were asked to pull or push a joystick directly on seeing a picture tilted to the left or to the right. These pictures could contain alcohol or non-alcohol related images. Reaction times were measured and analyzed.
Results.– Average D-scores of alcohol bias reduced after 10 sessions of HFrTMS, compared with baseline ($F = 5.842$, $p = 0.20$). There was no significant difference between active HFrTMS and the sham-group.
Conclusions.– This study revealed that 10 sessions of HFrTMS over two weeks on the right DLPFC might have some effect on approach tendencies in recently detoxified outpatients with severe alcohol use disorders.
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S034

Modification of substance intake and craving through tDCS in substance use disorder

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Craving and reduced inhibitory control are relevant clinical features of any substance use disorder (SUD). Both of these symptoms have previously been linked to a hypoactivation in the frontal lobe. Research using neurostimulation has, in the last years, been able to reduce this hypoactivation and – in turn – reduce substance craving. Indeed, applying transcranial direct current stimulation (tDCS) over the dorsolateral prefrontal cortex (DLPFC) is considered probably effective in reducing substance craving by the European Medial Agency (Level B efficacy). The effects of tDCS on inhibitory control or risky behavior in SUD have been studied with mixed results, so far. It seems that effects are highly dependent on task design and stimulation current direction. It remains to be investigated, which stimulation setup can affect craving as well as inhibitory control in the most positive way to decrease relapse rates.
Our current work aims to detect how tDCS affects smokers' inhibitory control, craving and tobacco consumption. In this ongoing study, participating smokers are to receive anodal transcranial direct current stimulation of the right DLFPC or a sham stimulation for 20 minutes on five consecutive days. Neuropsychological tests on inhibitory control and interviews on smoking habits and craving will be applied before and after the first stimulation as well as after the fifth stimulation. Results will be presented in this talk.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S035

Deep brain stimulation treatment for alcohol use disorders

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Next to genetic, social and contextual factors, a substance-induced dysfunction of the brain's reward system is considered a decisive factor for the consolidation and maintenance of a substance use disorder. Under the hypothesis of modulating substance- induced dysfunctions of the brain reward system, single-case and small scalestudies serve to discuss the procedure of Deep Brain Stimulation (DBS) in substance use disorders since the early 2000s. Unfortunately, an immense difficulty in the recruitment of patients was the reason for most studies being prematurely terminated in the past. Yet, this talk nevertheless aims at reporting the current state of knowledge on therapeutic DBS in patients with long time substance addiction, but will also point out the many difficulties associated herewith.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Clinical/Therapeutic: Symposium: Should We Include Exercise in the Regular Treatment of Psychiatric Disorders?

S036

The effects of continuous endurance training on brain structure and function in multi-episode schizophrenia patients

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Schizophrenia is a severe brain disorder characterised by positive, negative, affective and cognitive symptoms and can be viewed as a disorder of impaired neural plasticity. Aerobic exercise has a profound impact on the plasticity of the brain of both rodents and humans such as inducing the proliferation and differentiation of neural progenitor cells of the hippocampus in mice and rats. Aerobic exercise enhances LTP and leads to a better performance in hippocampus related memory tasks, eventually by increasing metabolic and synaptic plasticity related proteins in the hippocampus. In healthy humans, regular aerobic exercise increases hippocampal volume and seems to diminish processes of ageing like brain atrophy and cognitive decline.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S037

Physical activity and cardiorespiratory fitness in schizophrenia and the associations with mental and physical health

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Low physical activity and cardiorespiratory fitness in people with schizophrenia: a comparison with matched healthy controls andassociations with mental and physical health
Introduction.– The aim of this study was to objectively assess time spent in physical activity (PA) and sedentary behaviour (SB) in patients with schizophrenia compared to healthy controls matched for age, gender and socioeconomic status. Associations between both PA and cardiorespiratory fitness (CRF) and mental and physical health parameters in patients with schizophrenia were examined.
Materials and Methods.– Moderate and vigorous PA (MVPA), moderate PA, vigorous PA, total and active energy expenditure (TEE and AEE), number of steps, lying down and sleeping time was assessed with SenseWear Pro-2 body monitoring system for three 24-h bouts in patients with schizophrenia ($n = 63$) and matched healthy controls ($n = 55$). Severity of symptoms (Positive and Negative Syndrome Scale and Montgomery and Åsberg Depression Rating Scale), CRF (peak oxygen uptake, VO2peak), body mass index (BMI), and metabolic syndrome were assessed.
Results.– Patients with schizophrenia performed less MVPA and moderate activity had lower TEE and AEE, spent more time per day lying down and sleeping, and had poorer CRF compared to healthy

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controls. The amount of MVPA, but especially CRF was associated with severity of negative symptoms in patients with schizophrenia. Only CRF was associated with BMI.
Discussion: The current data offer further evidence for interventions aiming to increase physical activity and decrease sedentary behaviour. Given strong associations of CRF with both negative symptoms and BMI, treatment aimed at CRF-improvement may prove to be effective.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S038

Randomized controlled trial of psychical activity as an add-on intervention in depressive adolescent inpatients - preliminary results

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Background and aims.– Physical activity (PA) has therapeutic effect an depressive symptoms. However PA efficacy has not been studied in adolescent inpatient sample.
Aim of the study is assessment of PA efficacy on depressive symptoms in adolescent inpatients.
Methods.– Consecutive adolescent inpatients with depression confirmed by Child Depression Inventory and/or Hamilton Depression Scale were included to the study. All participants have been treated according to the state-of-art recommendations with the add-on study intervention. Each patient has been randomly assigned either to physical activity (PA) or occupational therapy (OC) group. The intervention was administered three times a week during four weeks. At the baseline and after four weeks psychopathological symptoms were assessed with composite battery, including Kutcher Adolescent Depression Scale (KADS), Children Depression Inventory (CDI), Clinical Global Impression Scale-Severity (CGI-S) and Improvement (CGI-I) and self-rated Global Impression Scale (PGI). Improvement was defined as the difference between baseline and final score.
Results.– The project is in progress. By now 10 patients in the PA group and 6 in the OC group completed the study. For the whole group $n = 16$ statistically significant improvement in all scales was observed ($p < 0.05$). In group comparison statistical analysis was not performed due to small sample sizes. Mean improvement in PA and OC groups was respectively: CDI 12.7 ± 7.4 versus 3.4 ± 5.0; KADS 6.9 ± 4.4 versus 3.8 ± 2.6; PGI $2,3 \pm 2.3$ versus $1,2 \pm 0.8$; CGI 1.1 ± 0.6 versus 1.3 ± 1.0 and CGI-I score was 2.3 ± 0.7 and 2.3 ± 0.5.
Conclusions.– Physical activity is non-invasive intervention easy to administer in inpatient setting. Preliminary results, although promising, should be interpreted with cautious. Larger sample is needed.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S039

Cerebral blood flow during exercise in schizophrenia and depression – fNIRS study

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Functional near-infrared spectroscopy (fNIRS) is a relatively new method of neuroimaging allowing to observe blood flow, and indirectly the neuronal activity in the cerebral cortex. The method is based on the principle that light in the NIR-spectrum is capable of penetrating superficial biological tissues (up to 5cm), and is absorbed to different degrees by oxygenated and deoxygenated hemoglobin. Despite several limitations, fNIRS in contrast to other methods may allow assessing the cerebral blood flow (CBF) during real-life situations such as physical activity. The study aimed to assess the effect of the single bout of exercise on the hemodynamic response in the prefrontal cortex during the neurocognitive testing. We recruited 47 individuals, age 18-65 years of both sexes: 15 patients with schizophrenia, 18 patients with depression and 14 healthy controls. Patients with somatic illnesses and cognitive impairment (MMSE < 23) were excluded from the study. The experimental paradigm consisted of continuous measurement of CBF during 1-minute rest, Stroop Color and Word Test, 5-min rest, 10-min cycling on a stationary bicycle, 5-min rest and repeat of Stroop Color and Word Test. Preliminary results may suggest, that single bout of physical activity increases the activity in the prefrontal cortex during the subsequent cognitive task in both psychiatric patients and healthy controls. The obtained results suggest that exercise may facilitate the activation of the relevant brain areas during the specific task. The confounding effects of systemic blood flow during exercise cannot be excluded.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Clinical/Therapeutic: Symposium: Social Evaluation and Emotion Regulation in Eating Disorders: Advances in the Management of Anorexia and Bulimia Nervosa

S040

A multilevel approach to the effects of social evaluation exposure: which responses in eating disorders?

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Introduction.– Vulnerability to acute interpersonal stress is either a risk or a maintenance factor for Eating Disorders (EDs). Indeed, social evaluation sensitivity precedes ED onset and exposure to an acute social challenge promotes emotional deregulation in ED patients. However, literature studies did not enough explore the possible interplay among biological, emotional and behavioral responses to an acute social challenge in EDs.
Objectives.– We aimed to investigate these relationships according to a multilevel study approach.
Methods.– Women with Anorexia Nervosa (AN) or Bulimia Nervosa (BN) and healthy subjects were exposed to the Trier Social Stress Test (TSST), an acute social challenge. Emotional and biological responses to the stressor as well as thoughts and perceptions related to the eating behavior were measured.
Results.– Compared to healthy women, AN subjects showed increased TTST-induced cortisol secretion while both AN and BN people exhibited heightened anxiety levels in response to the acute stress. In the AN group the amount of desired food was significantly reduced after the stress exposure. Moreover, in both ED groups post-stress anxiety predicted body dissatisfaction. Finally, a relationship between cortisol increase and hunger perception was found in both AN and healthy controls with opposite directions.
Discussion.– Present data confirm that sensitivity to social evaluation is a key characteristic of ED subjects implying a complex interaction between emotional/biological responses to social stressors and eating attitudes and behaviors. These findings have potential clinical implications.

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S041

Novel neuropeptides in eating disorders

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The aetiology of eating disorders is complex and remains unclear. It has been postulated that centrally and peripherally synthesized proteins, which are responsible for regulation of food intake contributing to homeostatic control of feeding, are involved. While it is unclear whether alternations in these proteins are primary or secondary dysfunction, even the latter may probably modify the course of the disease. Furthermore, many are not only involved in the maintenance of energy homeostasis but also in non-homeostatic regulation of food intake processes.
The aim of this lecture is to present the latest findings on the role of already known proteins such as BDNF, oxytocin, selected adipokines, gut-secreted peptides and more recently identified peptides such as neuropeptide B, vaspin, omentin, kisspeptin, spexin, phoenixin and others associated with eating disorders. The results of our longitudinal studies examining many proteins in serum and saliva in adolescent patients with anorexia nervosa will also be presented. Most of the proteins were examined at different phases of the disease – during malnutrition and after normalization of body weight. Moreover, their correlation with selected somatic and psychopathological symptoms of diseases was analyzed.
We found that some of the proteins were statistically significantly different in the group of patients with eating disorders compared to healthy persons. Moreover, over the course of anorexia nervosa, they do not stabilize despite normalization of body weight. It is suggested that some peptides may be useful biomarkers of eating disorders and may modify the course of the disease. In addition, some of the proteins correlate with the intensity of psychopathological symptoms, which indirectly points to their participation in the regulation of food-related behaviors and emotions. Due to the constant lack of effective methods of treating eating disorders, it is worth considering whether the tested proteins may be a potential target for pharmacological intervention.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S042

The improvement of social cognitive and neurocognitive functioning in anorexia nervosa throughout the integrative model of psychotherapy

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Introduction.– Patients with anorexia nervosa (AN) show disturbances of social cognition and neurocognition, which may impede grossly daily functioning. Objectives. The present study was to evaluate the social cognition and neurocognition in AN before and after a 12-week inpatient treatment including Social Cognitive and Neurocognitive Training (SCNT). Methods. Participants were 60 healthy subjects and 60 AN patients aged 18–35. Half of them was offered treatment as usual (TAU) while the other half - TAU plus SCNT. The clinical variables were measured using: The Eating Attitude Test, The Beck Depression Inventory II, The State-Trait Anxiety Inventory, and The Toronto Alexithymia Scale. Social cognition was assessed using the Penn Emotion Perception Battery and the Reading the Mind in the Eyes Test. Cognitive deficits in attention, visuospatial ability, memory, executive functions, abstract thinking, and cognitive rigidity were measured using: The Ruff Figural Fluency Test, The Trail Making Test, The Stroop Test, The Rey-Osterrieth Complex Figure Test, and The Verbal Fluency Test. Results. Results as hypothesized, at the beginning both groups of patients presented a high level of clinical psychopathology and deficits in emotional and neurocognitive functioning which decreased significantly during the hospitalisation. The group on TAU plus SCNT showed significantly higher improvement compared to TAU group alone, however most of the measured variables did not reach the level presented by controls. Moreover, greater improvement in functioning co-occurred with greater improvement of clinical variables. Conclusion. The more targeted treatments appeared efficacious in reducing examined deficits in AN.
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Clinical/Therapeutic: Symposium: Somatic Treatments of Perinatal Mental Disorders in Pregnancy

S043

The use of ECT in childbearing women

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During the perinatal period, women are at increased risk of onset or recurrence of any psychiatric disorder, and especially of mood disorders. So the prescription of psychotropic treatments is mandatory in many cases, but remains challenging during pregnancy. In such situations, clinicians have to weigh the risk for maternal relapse vs the risk associated with antenatal exposure to the treatment. Electroconvulsive therapy (ECT) is a rapid and effective treatment option in case of severe mood disorder, especially in case of suicidal risk and can be an appropriate intervention in some women during pregnancy. This talk will explore the very few available data on the topic, especially regarding the wide variation between the papers on patient characteristics, illness characteristics, ECT characteristics, confounder characteristics, and outcome characteristics, adverse maternal and/or fetal outcomes. Finally, we will present and discuss the current guidelines.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

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Clinical/Therapeutic: Symposium: The New Tools for the Assessment of Negative Symptoms in Schizophrenia

S044

Construct validity of the Brief Negative Symptom Scale (BNSS) and relationship with outcome in ENI schizophrenia Pan-European study

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Negative symptoms are frequent, strongly associated with functional outcome and represent one of the unmet needs of treatment in schizophrenia.
One of the obstacles to the development of effective treatments are the limitations of negative symptom assessment with established, validated rating scales.
This study represents a large European, multicenter, multinational validation study of a second-generation negative symptom assessment instrument, the Brief Negative Symptom Scale (BNSS), promoted by the ECNP Schizophrenia Network.
Two hundred and forty-nine clinically-stable subjects with schizophrenia (SCZ) were recruited in 12 Centers from 10 European Countries. Apart from BNSS, subjects with SCZ were assessed using the Positive and Negative Syndrome Scale (PANSS), the Calgary Depression Rating Scale for Schizophrenia, the St. Hans Rating Scale for extrapyramidal syndromes and the Personal and Social Performance scale (PSP).
Results showed an excellent convergent and discriminant validity of BNSS and replicated a two factor-structure (with expressive deficit and avolition/apathy factors). A larger number of subjects with predominant negative symptoms of moderate severity, i.e. the target population for clinical trials, was identified by using the BNSS than the PANSS. Regression analysis showed that BNSS-avolition, a key negative symptom poorly assessed by PANSS, explained 23.9% of the total model variance of the PSP, while no combination of the PANSS core negative symptoms showed the same impact on functioning. The study validated the BNSS in the context of a multicenter, multinational large European study and demonstrated that the scale has substantial advantages with respect to the PANSS for the identification of the avolition domain.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S045

Self-assessment of negative symptoms: interest and validity in schizophrenia

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Negative symptoms can be present at any stage of schizophrenia but their detection and evaluation remain challenging. Recent tools including the Brief Negative Symptoms Scale (BNSS) and the Clinical Assessment Interview for Negative Symptoms (CAINS) have improved negative symptom evaluation. However these scales, based on observer ratings, do not allow patients self-assessing their feelings and experiences even if ratings of internal experiences regarding asociality and avolition are considered.
Here, we want to present a new scale, the Self-assessment of Negative Symptoms (SNS) that has several advantages. It is a short 20 item scale with short and easily understandable sentences, and the three response choices allow a fast self-evaluation in under five minutes. The five negative dimensions are self-evaluated and patients are able to express their deficits in motivation and pleasure as well as their loss of emotion independently of depressed mood. Moreover, the first validation study for the SNS revealed a good test-retest reliability, good internal consistency, tight convergent and divergent validities. The SNS also appears to be an appropriate screening tool for distinguishing negative symptoms in patients with schizophrenia and healthy subjects with a threshold value of 7; the sensitivity and specificity being 92.7% and 85.9% respectively. The results coming from several studies support that SNS is a valuable tool for screening and rating negative symptoms in clinical practice. Further studies using SNS in subjects at high risk for psychosis or with a first psychotic episode would be useful in the detection of negative symptoms.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S046

Negative symptoms and cognitive deficits in schizophrenia in the ENI schizophrenia pan-European Study

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Introduction.– Neurocognitive impairment is considered a core aspect of schizophrenia and is strongly associated with functional outcome. Negative Symptoms (NS) and Social Cognition (SC) were also shown to predict functional outcome but with a smaller impact than neurocognition (NC). According to some evidence, NS and SC can mediate the impact of NC on functional outcome. The mediating role of the two negative symptom domains "Avolition-Apathy" (AA) and "Expressive deficit" (ED) has not been investigated, yet.
Objectives.– The aims of this study were: (1) to evaluate correlations of NC, AA, ED, and SC with functional outcome, and (2) to analyze, whether AA, ED and/or SC mediate the relationship between NC and functional outcome.
Methods.– 149 clinically stable subjects with schizophrenia were recruited. NS were assessed by the Brief Negative Symptom Scale. NC and SC were assessed by the Trial Making Test (TMT) A and B, the Symbol CodingTest, and the Facial Emotion Identification Test, respectively. Functional outcome was assessed by the Personal and Social Performance scale (PSP).
Results.– Between the several neurocognitive variables, only TMT-A and the neurocognitive composite score showed a moderate correlation with ED ($r = -.367$ and $r = -.324$, respectively). TMT-A, TMT-B, and the neurocognitive composite score were moderately correlated with the PSP global score ($r = .329$, $r = .359$, and $r = .302$, respectively). ED significantly mediated the relationship between TMT-A and functional outcome (Sobel test: $p < .05$). No other significant mediation was found.

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Conclusions.– Our results confirm the hypothesis that ED might at least in part mediate the relationship between neurocognition and functioning.
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S047

Polish experiences with the BNSS and SNS scales

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Objectives.– The Brief Negative Symptom Scale (BNSS) and Self-evaluation of Negative Symptoms (SNS) scale have been introduced in the recent decade for the assessment of negative symptoms of schizophrenia. The Polish versions of both scales were validated in the Department of Adult Psychiatry and Department of Psychiatric Nursing, Poznan University of Medical Sciences. The preliminary results with using both these scales are presented.
Methods.– The study included 40 patients with paranoid schizophrenia (20 men, 20 women) aged 44 ± 13 years, with illness duration of 17 ± 10 years, and severity of symptoms on the Positive and Negative Syndrome Scale (PANSS) 56 ± 16 points, receiving unchanged pharmacological treatment in the last three months.
Results.– In the population studied, the BNSS and its subscales showed meaningful correlation with the total PANSS score and with the PANSS negative symptom subscale, both original and modified. Significantly greater scores were obtained in men compared to women in asociality, avolition, and alogia. All BNSS subscales highly correlated with the Facial Emotion Recognition Test, and distress, emotional blunting and alogia - with a theory of mind assessment by the Reading the Mind in the Eyes Test. The SNS in its subscales showed significant correlations with the total BNSS score and with the scores of the BNSS subscales. No gender differences in the evaluation of negative symptoms by the self-assessment SNS scale were observed.
Conclusion.– The results obtained with the Polish version of both BNSS and SNS tests confirm their validity and usefulness in investigating negative symptoms of schizophrenia and related factors.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Clinical/Therapeutic: Symposium: The Promise and Challenges of Drug Repurposing in Psychiatry

S048

Can gene discovery in schizophrenia provide clues for repurposing drugs for antipsychotic treatment?

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Mental illnesses, including psychotic disorders, are leading global causes of morbidity and among the most costly human disorders. Identifying the underlying pathophysiology is imperative and can lead to major health benefits, through better treatment and prevention strategies.
The heritability of schizophrenia is high, and recent discoveries of genetic risk factors in schizophrenia have provided large opportunities for development of novel therapeutic alternatives. Recent large international genome-wide association studies and innovative analytical approaches have enabled us to identify more of the genetic architecture of schizophrenia. Mathematical modelling and bioinformatics analysis have improved our understanding of the underlying neuropathology and disease mechanisms. Recent experimental findings also indicate functional implications of these gene variants, suggesting opportunities for novel drug development. There are two main areas of interest, immune factors and neuronal excitability, both highly interesting for re-purposing pharmacological agents.
New understanding of the polygenic architecture has a large potential for development of prediction tools and opportunities for treatment stratification in a personalized medicine framework. Together, these developments have large potential for improving health care in mental illness in general, and schizophrenia in particular.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S049

Non-dopaminergic mechanisms and negative symptoms in schizophrenia: opportunities for repurposing?

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Introduction.– Negative symptoms in schizophrenia are challenging to treat. Antipsychotics generally are not effective in treatment primary negative symptoms.
Objectives.– Review studies of treatments for negative symptoms in schizophrenia.
Methods.– A comprehensive review of 72-unique registered negative symptom studies since 2005, when registering clinical trials became mandatory, will be presented.
Results.– Five major compounds that had cognition and negative symptoms as main targets, were abandoned, four failed to provide significant superiority over placebo (encenicline, TC-5619, bitopertin, pomaglumetad methionil) and one was withdrawn due to safety concerns (AMG 747). In contrast, there have been some initial favorable results in registered robust trials of other compounds which need to be replicated. These include MIN-101, a novel cyclic amido derivative, cariprazine, a D2 and D3 receptor partial agonist, with high selectivity towards the D3 receptor, minocycline, a broad-spectrum tetracyclic antibiotic displaying neuroprotective properties, and raloxifene, a selective estrogen receptor modulator for post-menopausal women. In addition, primvaserin a non-dopaminergic antipsychotic, which has recently been approved for Parkinson's disease psychosis, is being tested in a large trial for adjunctive treatment of patients with negative symptoms of schizophrenia. Also, being tested non-invasive electromagnetic neurostimulation. Favorable results of psychosocial approaches will also be discussed.
Discussion.– The conclusions from almost a decade ago of Patient Outcomes Research Team schizophrenia guidelines, that no treatment for negative symptoms has proven to have enough evidence to support a treatment recommendation, remain intact.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

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Clinical/Therapeutic: Symposium: Virtual Reality in the Assessment and Treatment of Psychotic Disorders

S050

Virtual reality in the assessment and treatment of paranoid ideation

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Introduction.– Recently, Virtual Reality (VR) has been introduced in psychosis research and treatment. The defining characteristic of VR is the experience of a sense of presence in an interactive, computer-generated, three-dimensional world. This experience elicits psychological and physiological responses remarkably similar to those in the real world. The ecological validity offers a unique possibility to explore and train interactions between individual and social situations in an experimental, controlled way. Psychosocial mechanisms are tested in a way that has not been possible before, and novel treatments are developed.
Objective.– To present and discuss diagnostic and therapeutic VR applications for psychosis.
Methods.– (1) 170 participants with different psychosis liability were exposured to virtual social stressors in VR experiments, and reported paranoid ideations and distress after each experiment. (2) Randomized controlled trial (RCT) of VR cognitive behavioral therapy, compared to treatment as usual, including 116 patients, primary outcome level of paranoid ideations in social situations.
Results.– Level of paranoid ideations about avatars was associated with psychosis liability and number of virtual social stressors. Effects were moderated by affective symptoms and history of childhood trauma. VRcbt was effective for reducing paranoia (effect size 1.49) and anxiety (0.75) in social situations, which enabled people with psychotic disorders to participate in daily life. The effect of this VRcbt was partly mediated by reducing cognitive biases.
Conclusions.– VR applications for assessment and treatment of psychotic disorders appear to have a great potential for increasing our understanding of psychosis and expanding the therapeutic toolbox.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S051

AVATAR therapy for distressing voices

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AVATAR therapy forms part of the digital revolution in healthcare, in that it uses novel technology to create a digital representation, an Avatar, of the entity which is the source of a person's distressing voice. The therapist's voice is digitally transformed so that the therapist is enabled realistically to voice the Avatar. In this talk the creation of the Avatar will first be described. Even though the Avatar software does not create an immersive Virtual Reality set up, data will be presented showing that participants report a good match with their own experience of their voices and a high 'sense of presence' when communicating with their Avatar. Therapy proceeds as a trialogue between the voice hearer, the Avatar and the therapist, and, through dialogue, aims to change the relationship of the voice hearer with their voice, reducing the voice's power. The overall aim is to reduce the distress and frequency of the voices. A summary of the results of a recent randomised controlled trial for people with psychosis who hear distressing voices will be presented (Craig et al, 2018).
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Educational: Symposium: DSM, ICD, and RDoC: Quo Vadis Classification?

S052

Why the clinical utility of DSM and ICD is intrinsically limited and how we can use new approaches to complement them

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The vast majority of DSM and ICD diagnostic categories are unlikely to represent "natural kinds" (i.e., discrete disease entities marking a real division in nature), and the minority which may approximate that model are likely to be heterogeneous from the etiopathogenetic viewpoint. Therefore, the information conveyed by "diagnosis" (i.e., the "type" to which the individual patient can to a variable extent be reconducted) is in itself insufficient for therapeutic and prognostic purposes. Hence the need for a more detailed psychopathological characterization of each case, as well as for an exploration of what is behind the "pattern" we have applied, in that specific case, with respect to vulnerability and protective factors. We should start to promote the construction and validation – in addition to structured or semi-structured interviews leading to a given diagnosis – of tools guiding the clinicians systematically in the characterization of the individual case, with a special focus on the assessment of psychopathological dimensions, the reliable evaluation of the severity of the clinical picture, and the exploration of a series of antecedent and concomitant variables. We should try to incorporate in this effort elements of the approaches that are currently presented as alternative to the ICD/DSM, that is: (a) those focusing on psychopathological dimensions, either at the level of the entire domain of psychopathology (e.g., the Hierarchical Taxonomy of Psychopathology, HiTOP) or at the level of specific areas of psychopathology (e.g., the "transdiagnostic psychosis spectrum model"); and (b) those looking for the neurobiological underpinnings of mental disorder, once again either at the level of the entire domain of psychopathology (e.g., the Research Domain Criteria, RDoC) or at the level of specific areas of psychopathology (e.g., the neurodevelopmental gradient model). These approaches, rather than being considered a real alternative to the ICD/DSM, should be used to improve the detailed characterization of the individual case that should always complement in clinical practice the act of diagnosis.
Reference.–
Maj M. World Psychiatry 2018;17:121–2.
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S053

What is the role of clinical psychopathology in future classification?

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Clinical psychopathology has its roots in the late 19th century with the main purpose to understand, describe and explain mental and behavioral disorders in an objective and scientific approach. The spectrum of scientific clinical psychopathology is broad, ranging from clinical symptom assessment in multifaceted domains, the definition and classification of mental disorders as well as a basic tool in psychiatric research. Descriptive psychopathology, which includes the classification of mental disorders, serves as a tool for standardized and objective assessment of clinical diagnoses. Most commonly used are the Diagnostic and Statistical Manual (DSM-5) and the International Classification of Diseases (ICD-10, actually in revision to ICD-11). Since their creation these classification systems have been revised constantly in order to optimize their application. However, there are also claims for a paradigm shift in these categorical classification systems towards a more dimensional approach or to relate diagnoses more strictly to a genetic or neuro-biological basis. To promote this attempt, novel assessment systems have been developed to enable a more modular approach. The aim of this lecture is to present the development and state of the art of current classifications and take a look at developments beyond the established systems into possible future classification approaches.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Educational: Symposium: E-Mental Health Approaches to Prevention and Early Intervention in Affective Disorders

S054

Preventing the onset of depressive disorders: meta-analytic findings

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In the past decades several dozens of randomised trials have examined the effects of preventive interventions in participants without a current depression on the incidence of major depressive disorders. In this presentation an overview of these trials is given with meta-analytical summaries of the evidence. The results will be given for unievrsal, selective and indicated prevention, as well for specific target groups, including adolescents, pregnant women and patients with comorbid general medical disorders. Overall, it is found that the effects are clearest for indicated prevention.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Educational: Symposium: Effective Prevention and Assessment of Risk of Suicidal Behaviour in Different Populations with Special Focus on Young People

S055

Universal suicide prevention in schools

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Suicide is one of the leading causes of death among young people globally. It has become a serious global public health concern with severe societal implications. Due to the magnitude of the problem, recognising the need for suicide prevention among youths is imperative.
The design and evaluation of suicide preventive interventions for young people is particularly challenging, due to methodological difficulties related to the study group, the outcome measures, ethical aspects and confounding factors. It is known that establishing and maintaining controlled conditions is difficult in population-based suicide preventive studies when conducted in natural field settings, such as schools. Population-oriented universal suicide prevention focuses on building up supportive networks and strengthening the life skills that protect people in difficult situations and also on providing close-range support to counteract the isolation felt by susceptible people.
In spite of those difficulties there are randomized controlled studies showing significant effects on diminishing suicide attempts and ideation in intervention groups, where mental health literacy, suicide risk awareness and coping skills were the focus of the program. *Good Behaviour Game* (GBG), an evidence-based intervention that helps primary school pupils to learn how to work together to create a positive learning environment, *Signs of Suicide* (SOS), a school-based prevention program that teaches youths action steps to take if they encounter a situation that requires help from a trusted adult, and *Youth Aware of Mental health* (YAM), an evidence-based mental health promotion programme for pupils from 14 to 17 years old, will be presented.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S056

Verbal Suicide Scale (VSS) – measuring attitudes toward suicide – new diagnostic approach

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The assessment of suicidal risk is one of the most difficult diagnostic challenges in psychiatry. Determining attitudes toward suicide has been a subject of numerous studies and analyses. There are many research methods, but most of them have a limited reliability and validity. The Verbal Suicide Scale (VSS) takes a different form to other diagnostic tools available. The method is based on modified mechanism used in the free association technique, which implies that the mental apparatus decomposes conflict contents. The aim of such approach is to limit the resistance and therefore omit what is consciously declared by an individual, for the sake of what is more primitive and unconscious and, hence, secret

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In the VSS construction and validation process the Varimax factor analysis validated the three factor structure. Cronbach's alpha reliability for each factor was satisfactory: 0.881 for suffering avoidance subscale, 0.772 for internalized aggression subscale and 0.723 for hopelessness subscale. In order to enable the application of the VSS tool in the clinical practice, the researchers specified sten norms for each of the subscales and the total result.
In terms of VSS validity the group of patients with the diagnosis of F10-F19 attracts most attention. In this group the tool shows the highest diagnostic suicide risk validity. The achieved data confirms the validity of the VSS in terms of diagnosing risk factors related to volitional stage of suicide.
The clinical use of the method supports the clinicians in defining the affect typology which is helpful in the therapeutic process. Due to the simplicity of the tool and possibility of a repetitive measurement, it can be applied in the clinical practice of psychiatrists, psychologists, physicians and psychiatric nurses.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S057

Suicidal behaviour related to psychoactive substance use - genetic and clinical risk factors

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Introduction.– The neurobiological model of suicide assumes that this behavior results from the dual presence of a biologically-based diathesis and an activating psychosocial stressor. The large body of studies suggests that the most important risk factor for suicide is alcohol and other psychoactive substances dependence.
Objectives.– The objectives of the conducted study were:
- to estimate the prevalence of the suicide attempts and completed suicides among substance-dependent patients,
- to analyze the clinical and genetic risk factors for suicide.

Methods.– The study was based on a sample of:
- individuals with alcohol use disorder ($N = 122\,427$),
- opioid-dependent individuals ($N = 240$),
- suicide victims ($N = 520$).

Genetic markers of interest were selected to assess the genetic vulnerability to suicide.
Results.– The lifetime prevalence of suicide attempt was 27.6% in alcohol-dependent participants, and 36.3% in opioid-dependent patients. Participants with alcohol use disorders had over three times greater hazard of dying (HR = 3.29). The most important risk factors for suicide attempts in opioid-dependent individuals were: childhood sexual abuse (OR = 4.6) and somatic comorbidity (OR = 2.6).
The studies on genetic vulnerability to suicide behaviors revealed the association between:
- rs2738888 *DISC1* and suicide attempts in opioid-dependent individuals,
- rs1386483 *TPH2* and suicide under the influence of alcohol,
- *FKBP5* alleles and completed suicide.

Conclusions.– There are specific clinical and genetic risk factors for different phenotypes of suicide behavior associated with psychoactive substance use. It is advisable to include detailed diagnosis of the experience of childhood sexual abuse as an indispensable part of the psychiatric examination of opioid-dependent patients.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Educational: Symposium: Epigenetic and Neuroendocrine Alterations Mediating the Association Between Exposure to Stress During Ontogenic Windows of Development and Risk for Psychiatric Disorders

S058

Stress during pregnancy and its role for the Toddler's neurodevelopment

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Early life stress, especially prenatal stress, is associated with an untoward development of the Infant. We studied longitudinally a cohort of 410 women and their offspring from late pregancy, birth, 6 month post partum to 45 months after birth. We analyzed birth outcome, mother-Infant interaction, regulation of the child's activity of the pituitary-adrenal system as well as cognitive and emotional development. Our findings indicate that prenatal social stress is related to birth outcome, especially birth weight. Prenatal stress is also associated with mother-Infant interaction, e.g. better interaction in women with moderate prenatal stress. Moreover, prenatal stress was found to be related with a dampened pituitary-adrenal activity at the age of 45 months.
Taken together, our study confirms that perinatal stress is strongly related to childhood development. Perinatal stress may have unadvantageous (e.g. birth weight) as well as advantageous consequences.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S059

Preterm behavioural epigenetics: DNA methylation and telomere length regulation as biomarkers of early adversities and developmental risk in very preterm infants

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Very preterm (VPT) infants (gestational age < 32 weeks) require long-lasting hospitalization in the Neonatal Intensive Care Unit (NICU), even in absence of severe morbidities. During NICU stay, life-saving interventions occur and include invasive and painful skin-breaking procedures (NICU-related stress), which constitute a major early adverse experience for VPT infants. Epigenetic mechanisms (e.g., DNA methylation and telomere length (TL) regulation) are highly susceptible to early stress exposures. In previous research, we documented that NICU-related stress associates with increased methylation of a stress-related gene (i.e., serotonin transporter gene, *SLC6A4*) and reduced TL at discharge. At 3-months corrected age (CA) increased *SLC6A4* methylation predicted temperament and stress regulation during a socio-emotional stress-inducing laboratory task (i.e., Still-Face Procedure, SFP). Moreover, infants' salivary cortisol reactivity to SFP was predicted by shortened TL from birth to discharge. Here, we present new longitudinal evidence on the long-term association between NICU-related epigenetic biomarkers (*SLC6A4* methylation and increased rate of TL shortening) and behavior development and stress regulation at 4 years in VPT children and in a group of age-matched full-term (FT) children. At 4 years VPT and FT children were followed-up and assessed for behavior and stress regulation using

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the Preschooler Regulation of Emotional Stress (PRES) task, which is an observational laboratory procedure derived from the Laboratory Temperament Assessment Battery (Lab-TAB) and designed to provide similar indexes of behavior and stress regulation to those obtained with the SFP in young infants (i.e., negative emotionality and social engagement). VPT children reacted to the PRES task with increased negative emotionality and reduced social engagement compared to FT counterparts. Notably, increased birth-to-discharge *SLC6A4* methylation and TL shortening were both predictive of increased negative emotionality and reduced social engagement in VPT children, compared to FT ones and controlling for post-discharge life events. These findings suggest that early exposure to stress is not only associated with short-term behavioral and stress regulation outcomes, but also contributes to the long-lasting programming of phenotype in VPT children. Implications for behavioral epigenetics methodology, further research programs and clinical practice will be discussed.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S060

Proximal exposure to severe childhood maltreatment and HPA axis deregulation in young individuals

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Both childhood maltreatment and exposure to life events during early life stages have been associated with an increased risk for the development of a wide range of complex disorders, including those of a metabolic, cardiovascular and psychiatric nature, both in the short- and the long-term. Nevertheless, whether specific types of childhood trauma are associated with specific psychiatric conditions remains unknown.
Likewise, exposure to stress in early life stages has been suggested to deregulate the human stress response, i.e. hypothalamic-pituitary-adrenal (HPA) axis functioning. Nevertheless, long-term modulation of HPA axis in response to early life stress remains a controversial issue with inconsistent findings. Disparity of findings has been suggested to partly rely on the psychometric instruments used to assess and measure such exposures to stressful events. Specifically, the accurate measurement of the type, chronicity, severity, accumulation and timing of the trauma experienced remains a challenging task. Furthermore, the genetic background can also modulate stress responsivity and dictate to a certain degree the establishment of trauma-associated epigenetic signatures; integration of all these environmental, clinical and biological layers will be crucial in the understanding of psychopathological physiopathology.
Remarkably, most studies regarding the association between early life stress and psychopathology vulnerability have been developed in adult populations. Such study designs have several limitations due to the latency between the exposure to stress and the onset of the disorder. Thus, the study of childhood trauma in young subjects may be crucial to disentangle its role in both HPA axis modulation and contribution to psychiatric morbidity.
Hence, our research group has recruited a sample of 161 subjects (age range between 7 and 17 years old), including 91 cases affected by psychiatric disorders, and 70 age-matched control subjects. Exposure to childhood trauma was thoroughly assessed by means of several questionnaires and interviews including: the widely used childhood trauma questionnaire, CTQ; a newly validated instrument for measuring life events, life events inventory for adolescents (LEIA); the Childhood Experience of Care and Abuse (CECA-Q2); and a tailored interview for the accurate recording of any experienced trauma including the timing, type, frequency and severity of the event along with its perpetrator.
Furthermore, all subjects were exposed to an experimental stress task, the Trier Social Stress Task (TSST) in order to appropriately measure HPA axis reactivity, by means of salivary cortisol, in front of psychosocial stress. The aim of this study was to elucidate the relevance of appropriately defining and quantifying exposure to trauma prior to testing its association with alterations in HPA axis reactivity.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S061

Embedding of chronic stress in the epigenome

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Psychosocial stress triggers a set of behavioral, neural, hormonal, and molecular responses that can be a driving force for survival when adaptive and time-limited, but may also contribute to a host of disease states if dysregulated or chronic. The effects of stress - whether beneficial or detrimental- are in large part mediated by the hypothalamic-pituitary axis, a highly conserved neurohormonal cascade that culminates in systemic secretion of glucocorticoids. Cortisol, the primary glucocorticoid in humans, activates the glucocorticoid receptor, a ubiquitous nuclear receptor that not only causes widespread changes in transcriptional programs, but may also induce epigenetic modifications in target tissues. Here I will propose two key principles that may govern the epigenetics of stress and glucocorticoids along the human lifespan: the presence of distinct life periods, during which the epigenome shows heightened plasticity to stress exposure, such as in early development and with advanced age; and the potential of stress-induced epigenetic changes to accumulate throughout life both in select chromatin regions and at the genome-wide level. These principles have important clinical and translational implications, and they show striking parallels with the existence of sensitive developmental periods and the cumulative contribution of stressful experiences to the development of stress-related conditions.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Educational: Symposium: From Clinics to Neurobiology: Bridging the Gap in Bipolar Disorders

S062

Lithium revisited: investigating clinical and neuroimaging predictors to lithium

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Bipolar disorder is a recurrent illness affecting about 2% of the world population. Lithium is perhaps the most effective evidence-based treatment for relapse prevention of bipolar disorder and several studies have shown that Lithium could improve different aspects of long-term illness activity. A substantial minority of individuals remain asymptomatic for years on Lithium, but many partially respond and up to one third do not respond well. This

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variability is currently poorly understood, and response cannot be predicted before treatment is started (and sometimes for many months afterward). Despite recent advances in identifying new biomarkers capable of predicting response to treatments, few studies have evaluated Lithium response using these methodologies, particularly for sufficient durations of treatment. The R-LiNK* study has therefore been designed using a new ("multimodal") approach which will provide valuable information using these new methodologies alongside a close follow-up of participants taking Lithium over 24 months. This study will recruit 300 individuals with bipolar disorder type I, across 15 European specialist bipolar centres. Patients will be recruited in a naturalistic setting; before commencing Lithium based on their clinicians' assessment and their agreement. Thus, R-Link is a pragmatic cohort trial of lithium initiation, the results of which could help patients and clinicians to have better and more accurate predictions when considering Lithium prescribing. At present, it is still difficult for clinicians to reliably personalize and provide information to people starting Lithium about how effective the medication will be, prospectively. The R-Link findings have the potential to finally enable personalization of Lithium treatment, which would lead to prevention of unnecessary side effects and ineffective treatments while improving long-term management and prognosis for individuals with bipolar disorder.
*N.B. Chief Investigator Prof Frank Bellivier, Paris Diderot University
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S063

Structural correlates of illness progression and neuroprotection in bipolar disorder: a clinical perspective

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The course of bipolar disorder (BD) is characterized by progressive reduction of free interval duration, increase rates of suicide, anxiety, comorbidity, drug resistance, cognitive impairment and death. Premorbid impairment, age at onset, episode polarity, cycle pattern, frequency and length, and the prophylactic effect of mood stabilizers have been classically addressed as key clinical variables influencing such progression. In the last decades, the surge of the structural magnetic resonance imaging (sMRI) techniques prompted the formulation of comprehensive frameworks linking illness course to brain alteration. However, to date, results from sMRI are not always consistent, possibly because the impact of some of the aforementioned longitudinal course predictors are not extensively investigated. Therefore, interpreting neuroimaging findings from a clinical perspective could represent an alternative point of evaluation of the available evidence, possibly addressing the several issues related to the neurobiology of illness evolution. To this extent, Illness outbreak appears to influence frontal, temporal and limbic structure volumes, as demonstrated by the greater consistency in the evidence of volumetric shrinking in early vs late age of onset. Progressive structural shortenings in fronto-lateral and temporal areas appear to be related to the number of episodes, with slight greater consistency for manic, rather than depressive. The effect of cyclicity has not been evaluated yet. However, indirect evidence suggests that contraction in free intervals duration, as well as depression-mania-free interval cycle in BD type II are related with volumetric medial prefrontal shrinking. Conversely, the effect of mood-stabilizing drugs has been clearly evaluated, even though the vast majority of the studies has mainly focused on lithium. The "neuroprotective" effect of lithium appears to be confirmed by consistent findings linking its use with gray matter increase mainly in prefrontal areas, amygdala and hippocampus. However, it is still not clear if this effect is related to its anti-cycling properties or represent an independent mechanism.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S064

Investigating heterogeneity in bipolar disorder using multimodal imaging

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Bipolar disorder (BD) is considered etiologically and phenotypically heterogeneous. The presence of disorder-related heterogeneity at the level of brain organization is poorly defined. Here we tested whether patients with BD show greater variation in structural morphometry and resting-state functional magnetic resonance imaging (fMRI) signal than those expected in healthy individuals. Clustering based on the individual-patient deviation in fMRI signal coherence variance (but not mean) was able to separate symptomatic and remitted patients with high accuracy (77%). Separate regression analyses showed that individual-patient deviation in signal coherence variance in the posterior default-mode network was the best predictor of symptom severity, explaining 29% of the variance in overall symptom severity. Our results suggest that functional rather than structural measures are useful in providing a mechanistic understanding of the pathophysiology of bipolar disorder.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Educational: Symposium: Problematic Use of the Internet - What the Psychiatrist Needs to Know

S065

Exploring PUI's determinants, assessment and clinical course

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Problematic Internet Use (PIU), is an umbrella term incorporating a range of repetitive impairing behaviours which are conducted in the online milieu. Gaming Disorder is being considered for inclusion as a mental disorder in diagnostic classification systems, and was listed in the ICD-11 version released for consideration, however, disorder definitions, validation of clinical tools, prevalence, clinical parameters and neurobiology are not well understood. In this presentation we will explore PIU determinants, assessment tools and clinical course of what is known up-to-date about PIU. We will explore the neurobiological determinants with a focus on cognitive findings, discuss the difficulties and advances in regards to the development of valid tools for the assessment of the disorder and describe what is known about its clinical course and symptomatology.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S066

Diagnosis and conceptualization of gaming disorder

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There is substantial clinical and public health evidence that video gaming, particularly online gaming, can become excessive and lead to psychological distress and functional impairment. This has led to the inclusion of Gaming Disorder (GD) as an official mental condition in the International Classification of Diseases, 11th Edition (ICD-11; World Health Organization, 2018). Recognition of gaming disorder as a psychiatric condition was supported by a variety of scientific evidence (e.g., epidemiological, psychological and neurobiological data), including clinical studies documenting individuals seeking treatment. In the ICD-11, gaming disorder is defined as a pattern of gaming that is characterized by (1) impaired control (e.g., onset, frequency, intensity, duration, termination, context); (2) increasing priority given to gaming to the extent that gaming takes precedence over other life interests and daily activities; and, (3) continuation or escalation of gaming despite the occurrence of negative consequences. Furthermore, to be considered as a disorder, the gaming pattern must be associated with distress or significant impairment in personal, family, social, and/or other important areas of functioning. In the this talk, I will shortly review the evidences having led to the inclusion of GD in the ICD-11 and discuss some keys aspects that have to considered when it comes to identify or diagnose GD (e.g., the crucial distinction between "high involvement" and "addictive involvement"; the risks associated with the recycling of Substance Use Disorder criteria).

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S067

Introducing a COST action on PUI: aims, network and activities results

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The EU under Horizon 2020 recently founded a 4-year European Cooperation in Science and Technology (COST) Action Programme to promote a better understanding of Problematic Use of the Internet (PUI). The network (currently 109 participants, 37 countries) aims to connect multidisciplinary and geographically diverse group of experts to ensure the generalizability of the results. The main goals are: conceptualisation of PUI, the development of diagnostic criteria and related reliable tools, investigating etiological factors, brain-based mechanisms and potential biomarkers, quantifying the clinical and health economic impact and development of effective prevention and treatment strategies. The project aims to involve not only scientists and clinicians across different fields but also information-technology industry, health economists, policy makers, service planners, and people with the lived experience of PUI. Dissemination tools include not only websites, social media and blogs but also seminars, workshops, webinar and exchange visits between researchers. The COST EU-PUI started with the initiation meeting held in October 2018 and, over the last 18 months, there have been periodic european and american update meeting (ACNP Palm Springs, COLOGNE COST MEETING, APA New-York, ECNP Barcelona and ACNP Hollywood). More recently, the EU-PUI published a Manifesto article in european neuropsychopharmacology and an International Training School and Conference on PUI in Cambrige. In conclusion, the european PUI Network aims to investigate biological, psychological, clinical and therapeutic aspects of PUI through networked research, which brings together individuals with different knowledge, skills or even lived experience. The EU-PUI COST Actions and deliveries will be presented at the Symposium.

Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Educational: Symposium: The Language System in the Major Psychoses – Psychopathological Structure, Neurobiology and Treatment Options

S068

Formal thought disorders: from phenomenology to neurobiology

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Formal Thought Disorders: From Phenomenology to Neurobiology. Speech and language disorders, such as concretism and formal thought disorder (FTD) are core symptoms of Schizophrenia, but do occur to a similar extent in other diagnoses such as bipolar disorder and major depression. We will review clinical rating scales of FTD and introduce a new, validated scale, the TALD. Further, structural and functional brain imaging data will be reviewed and own novel findings presented, relating speech and language dysfunctions to neural networks, within schizophrenia and across the "functional psychoses". The impact of genetic variance and glutamatergic pathways (NMDA receptor blockage) on brain function will be addressed with a particular focus on speech and language (dys-)function. We demonstrate, from the genetic to the brain structural and functional level, that particular aspects of the neural language system is disrupted in patients with FTD across traditional diagnoses.

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Educational: Symposium: Translational Approaches to Study Early Adversity

S069

Effects of inflammational activation in early states of schizophrenia

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Maternal infection during pregnancy enhances the offspring's risk for severe neuropsychiatric disorders in later life such as schizophrenia. Recent attempts to model this association in animals provided further experimental evidence for a causal relationship between in-utero immune challenge and the postnatal emergence of a wide spectrum of behavioral and neurobiological dysfunctions implicated in schizophrenia. However, it still remains unknown what is the exact mechanism of the early immunological activation and these tremendous effects in later life of an organism, and which treatment strategies and preventive intervention are suitable at best to stop or to diminish this development. It will present evidence that prenatal infection mimicked by poly I:C administration prenatally in pregnant mice will cause significant activation of microglia cells in puberty and release of nitrit monooxid (NO) which might be one of the major neurotoxic agents inducing further

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neurodegenerative processes. This is accompanied by the release of specific cytokines and activation of further immunological processes. Recent data in cell culture, how activated microglia interact with neuronal cells reducing their plasticity properties, will be presented. In conclusion, this potential animal model will help in elucidating the mechanisms responsible for pathogenesis of schizophrenia, involving activated microglia.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S070

Immune activation via maternal milk leads to sex-specific phenotypes via identical developmental trajectories of inflammation, structural damage and behavioral abnormalities

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Injection of the viral mimic poly-I:C to nursing dams on PND 4, leads in the adult offspring to sexually dimorphic behavioral endophenotypes, with schizophrenia-like cognitive inflexibility (persistent latent inhibition [LI] and impaired reversal) in males, and affective/hedonic deficit (increased immobility in the FST and decreased sacharine preference) in females, recapitulating the known sex bias in these disorders.
Objectives.– To delineate and compare the developmental trajectories of behavioral, brain inflammatory, and brain structural abnormalities in male and female offspring exposed to lactational polyI:C or saline.
Methods.– Nursing dams received polyI:C (4 mg/kg/ml) or saline injection on PND4. Three cohorts of male and female offspring were tested. One cohort was tested in behavior on PNDs 30, 50, 70 and 90. Males were tested in LI, while females were tested in FST. The second cohort was imaged repeatedly on the same PNDs. Offspring of the third cohort were sacrificed on PNDs 4, 21, 30, 50, 70 and 90 for bran cytokines and microglia assessment.
Results.– Lactational poly-I:C altered the developmental trajectories of hippocampus, prefrontal cortex and striatum, with volume reductions that began post-pubertally, from PND50. Behavioral abnormalities were preceded by hippocampal and striatal reductions and emerged on PND70, in parallel to maximal overall volumetric abnormalities. Inflammatory abnormalities (increased cytokine levels and microglia) were evident from PND4.
Conclusion.– Lactational poly-I:C exposure exerts widespread and long-term influence. However, in contrast to sex-specific (non-overlapping) behavioral deficits, neither structural nor inflammatory abnormalities show strong sex differences. Thus, structural and inflammatory abnormalities are sex- and disorder-nonspecific processes.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S071

Epigenetic mechanisms in a rodent model of early life stress

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Introduction.– More than a quarter of adults state being physically maltreated during childhood and the numbers for sexual abuse are even higher. At the same time, early life stress can have lifelong consequences for mental and physical health. One of the factors mediating disturbances in development might be epigenetic changes after early life stress (ELS). A gene that has recently been associated with stress and depressive-like behavior after ELS is the transcription factor Orthodenticle homeobox 2 (Otx2).
Objectives.– In animal model of ELS the gene Otx2 was further examined.
Methods.– Spraque-Dawley rats were subjected to maternal separation (4 h/day, P2- P21) and/or social isolation (P21–P40) or served as controls. During adulthood ($P > 60$), all animals were examined in two different anxiety tests, followed by realtime PCR analysis of Otx2 mRNA levels in the ventral tegmental area.
Results.– There were no group differences in anxiety but a significant effect of sex with males being more anxious. First results furthermore indicate no group nor sex effect in Otx2 RNA levels. However, anxiety levels in the maternal separation group depended on litter while controls showed no litter effect. Furthermore, a significant correlation was found between anxiety-like behavior and Otx2 mRNA levels in the control group ($n = 14$) but not in the stress exposed group ($n = 15$). It seems that low levels of Otx2 mRNA correlate with high anxiety but this correlation is disturbed after ELS.
Conclusions.– Genetics or maternal behavior might influence the effect of early life stress on Otx2 and behavioral outcome.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

European: Symposium: A Humanitarian Disaster: Mental Health Needs of Forcibly Displaced People in Europe

S072

Mental health consequences of forced displacement

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Research on forcibly displaced people mental health is fraught with practical obstacles. Populations are often physically, linguistically, and culturally inaccessible to researchers, and humanitarian aid usually has higher priority than scientific investigation. Studies are often exploratory and methodologically compromised, and the specificity of local circumstances makes it difficult to draw generalized conclusions. As a result, research synthesis is needed to establish the magnitude of the mental health consequences of forced displacement and the variables that moderate these consequences. Adverse impacts of migration on mental health are well-established and are compounded in these situations by the traumatic events typically precipitating migration, as well as by the social disadvantages which follow. Causation may be complex due to pre-migration health and social environment, varied nature of stressors (e.g. conflict exposure) giving rise to migration, the stress of the migration episode itself, and that arising from the post-migration environment. Even after displacement, they continue to face substantial stressors, such as problems with food, shelter, education, healthcare, finances, employment and discrimination which may become perpetuating factors for mental disorders. It is highly likely that the risk of developing mental disorders such as depression, anxiety, post-traumatic stress disorder (PTSD) and psychoses are greater among displaced populations than that of stable populations. In this talk an overview will be given and results from

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across-sectional study on female refugees will be presented and discussed.
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S073
Mental health services for asylum seekers and refugees
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From a social psychiatric perspective an important public health issue is the increasing number of asylum seekers and refugees with a traumatic background requiring mental health services. In a European context, incentives should be encouraged that result in reducing inadequate access to services for this population.
On service level it is recommended to review "refugee friendly" institutions and experiences in Europe, serving as a role model for others. Further it is important to review e-mental health initiatives to overcome the shortage of resources as well as any health promotion activities, psycho-educational interventions, resilience and/or resource – oriented interventions.
On training level courses should be initiated on cultural awareness and cultural competence and encourage such initiatives in all European countries. Further to develop recommendations to be included in the training curricula suited to different levels and offer different educational modules directed towards psychiatrists, and take initiative to develop exchange programs, in collaboration with the early career psychiatrists and national psychiatric associations. There is also a need to evaluate treatment outcome of asylum seekers and refugees cared for by the different kind of services offered. Despite the increasing focus on and need to provide documentation that services work, and that facilities provide the best and most efficient care, research related to this has made slow progress.
On the organizational level it is important to lobby at the national levels for more resources and better mental health services to the refugees and asylum seekers. But also in collaboration with other professional organizations of psychiatrists and mental health workers, service users and service providers lobby at a European level for more resources to and better mental health services to the refugees and asylum seekers.
On research level it is important to support, and/or encourage a review of existing scientific evidence on the mental health aspects of the problem and prepare guidelines to support researchers in implementing "refugee and migrant sensitive" issues in their clinical and community researches.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Mental Health Needs of Forcibly Displaced People in Europe

S073A
A humanitarian disaster: forcibly displaced people in Europe
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Warfare, human rights violations and persecution have led to a humanitarian disaster: forced displacement of millions of people. By 2017 there are 68.5 million forcibly displaced people worldwide, the highest number since World War 2. Among these, 40 million are Internally Displaced Persons, 25.4 million refugees, and 3.1 million are asylum seekers. Furthermore, 51% of all refugees are under the age of 18, thus the magnitude of the current humanitarian disaster will impact us for generations.
A forcibly displaced person is experiencing a human made psychosocial disaster. Almost all attachments are left behind, degree of mastery over one's own life is decreased, the nutrition of the self and the self-image are devastated. Hence, their basic needs for survival are maintained mostly in the mercy of others. Forced displacement challenges five core adaptive systems subserving the functions of safety, attachment, justice, identity-role, and existential-meaning. A forcibly displaced person is a person who has lost the past for an unknown future. Experiences of loss and threat are imprinted in their selves; they are in a situation of 'die or fly'.
Once more, psychiatry and mental health workers are facing the mental health consequences of persecution, general violence, wars, and human rights violations caused by the current prevailing economy-politics and socio-politics. So, a serious challenge here is both consolidating the psychiatric/medical help and avoiding the medicalization of social phenomena at the same time.
This presentation aims to discuss the dimensions of this humanitarian disaster and its psychosocial context on a European level.
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S073B
Displacement process: traumas faced on the way
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In recent years the political situation in the Middle East and some African countries led to a big wave of refugees to Europe. A significant number of these refugees underwent traumatic events in their home country (e.g. war, loss of relatives, torture) and on their way to Europe (concrete fear of dying through nature or people). Additionally, most of the refugees face a situation of existential uncertainty in the receiving country like insecure residence permit status, fear of deportation, unstable future perspectives and worries about relatives back in the home country. Refugees hence constitute a psychologically vulnerable population whose special needs should be considered.
Transcultural research provides some studies on mental health of refugees which mostly show that this population suffers more often from certain mental disorders than the local population in the receiving countries. Elevated prevalence rates of affective, anxiety disorders and PTSD were found among refugees. The prevalence rates differ by up to four times from each other between the various studies and appear to be four to ten times higher compared to local populations. Moreover, there are moderating effects of postmigration factors and possible links between premigration trauma and postmigration psychological distress.
However, there are no current systematic reviews or meta-analyses on this issue. Hence, there is an urgent need to analyse and review transcultural research on mental health of refugees deepen our understanding of premigration trauma and postmigration impact to improve mental health care across Europe according to up to date evidence.
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Mental Health Policy: Symposium: Advancing Partnership in Mental Health Care

S074

Advancement of partnerships in Germany

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The German Alliance for Mental Health is an anti-stigma initiative led in trialogue fashion to promote mental health. It maintains a nationwide network of over 100 alliance partners, including experts from self-help groups and psychiatry, health promotion and politics. Founded in 2006 by the anti-stigma initiative "Open the Doors" and the German Association for Psychiatry and Psychotherapy (DGPPN), which is also the funding organisation, scientific project activities are funded by the German Federal Ministry of Health.
The Alliance implements and evaluates nationwide anti-stigma campaigns, it also conducts seminars on "Mental Health at the Workplace" for managers. Furthermore the Alliance promotes non-stigmatising reporting in the media and coordinates nationwide awareness weeks around WHO World Mental Day on Oct 10th. The DGPPN together with the Alliance is providing an annual anti-stigma award endowed with 10.000 Euros. Since 2016 focusing on young adults, various awareness building activities via social media having reached over 3 million users so far.
The Alliance is constantly expanding its national and international partnerships: The Alliance itself is a growing network including all relevant expert groups from psychiatry and psychology, family and consumer organizations as well as self-help groups and grass-root organizations advocating for people with mental illness. Furthermore the Alliance is connected with all relevant national stakeholders like foundations, political institutions and partnering with networks like the Berlin Suicide Prevention Network or the initiative psyGA ("Mental Health in the Workplace"). Internationally the Alliance partners with advocacy groups like GAMIAN and is an active partner in the EU-financed project "eMEN" supporting the promotion of eMental-health in Europe.
Reference.–
Ramge A, Becker H (2017) The German Mental Health Alliance. In: Gaebel W, Rössler W, Sartorius N (eds) The Stigma of Mental Illness - End of the Story? Springer International Publishing Switzerland, pp 405–16
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S075

Programmes to assist persons with mental illness acquire and/or retain jobs among stakeholders in Japan

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Introduction.– Peer supporters can motivate others and complement with professional staff in their support for people with mental illness to obtain job. Training courses to help peer supporters to partner with professional staff can be important. Also a program to help working patients to build resilience and avoid relapse after return-to-work is necessary, and such a program should partner with corporations.
Objective.– The objective of this presentation is to report the progress of peer supporter training and Re-Work program in Japan.
Methods.– Peer supporters and professionals created basic, advanced and follow up training course for peer supporters. Knowledge questions, Burn-out scale and Mor Barak inclusion/exclusion scale were examined pre- and post- basic and advanced training courses, and at a time of follow-up course for 34 peer supporters. Re-Work program receives information about job from corporation and send the assessment by 23 items Re-Work Readiness Scale to corporations. The relapse after return-to-work was compared between 51 Re-Work program participants and treatment as usual (TAU) group with propensity score matching.
Results.– The correct answer rates to knowledge questions were significantly improved. There was no significant effect for Burn-out scale and Mor Barak scale. Re-work group had significantly less relapses than TAU group.
Conclusions.– Training courses were effective to improve basic knowledge about partnership. To improve burn-out and organizational culture, other measures seem to be necessary. Re-Work program is effective to prevent relapse in partnership with corporations.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S076

Rehabilitation of people with mental illness: a paradigm which needs re-examination

N. Sartorius
Some hundred years ago it became generally accepted that there should be life after mental illness and that people who have experienced a mental disorder should be given a chance to continue their life in a manner worth living. Rehabilitation – returning to one's position before illness was considered as a goal as worthy as the treatment of the illness.
In the course of years that followed it became clear that this goal can be achieved in some forms of disease and not in others and that many people who suffered from mental illness came from backgrounds which were contributing to the occurrence of their illness so that returning to the pre-illness state was not necessarily an acceptable goal.
It also became clear that many of the interventions which were introduced to facilitate rehabilitation did not contribute to it. People with mental illness were often exposed to therapy by work which did not contribute to their employability nor to their capacity.
The concept of recovery gradually made its way into practice. It replaced the goal of rehabilitation and made a realistic appreciation of one's capacity central to the search of best ways to re-enter society and define an existence that was satisfactory to the individual and to society. The application of the paradigm of recovery requires considerable change in the methods of treatment of mental illness. These changes in turn will require changes of education of psychiatrists and of other professions as well as of carers.
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Mental Health Policy: Symposium: All Psychiatrists Are Medical Doctors. . . Hope That They Have Not Forgotten Their Hippocratic Pledge

S077

The 2017 revised version of the declaration of Geneva

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Ever since the days of Hippocrates medical doctors took an oath by which they pledged to abide to the ethical and professional rules of their guild. Some of the basic Hippocratic rules were dropped. As for a long time, medical doctors did not take on them to care for their teachers and mentors until the end of their lives. Other points of view evolved especially where shared decision-making and informing the patient were concerned. Basic notions as "to do the patient no harm" and the "medical secrecy" that ensures free and secure access to medical care for all, strongly remain. These were formulated in the modern version of the Hippocratic oath, when the World Medical Association (WMA) accepted it, in 1948 under the title "Declaration of Geneva". In some countries that oath is mandatory for all physician to take when entering the profession, other countries had, have adapted versions. In the past years the WMA has undertaken a process of revision of the Declaration of Geneva. The result was adopted by the WMA in 2017 and is now the golden standard under the title "Physicians Pledge". For some Basic notions, named here above, the language has been adapted for the sake of clarity. The doctor-patient relationship has been reformulated in more equivalent terms. An important new notion has been introduced namely the responsibility of doctors to take care of and promote their own health!

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S078

Situations in which physicians should take the stand of opposition

N. Sartorius

Physicians are increasingly often before the dilemma of accepting moral or ethical rules or objecting to their application. The examples which illustrate such situations are rules of prescriptions linked to the price of medications, limitations linked to early diagnosis of specific conditions, prescriptions concerning assistance to dying, disclosure of medical information on grounds of security concerns, maintenance of confidentiality in family-based cultures, diagnosis of mental disorder when there is none, making a diagnosis which leads to poor/good treatment, participation in torture by prolonging life of those tortured and numerous others.

In many of these situations the maintenance of principles of physician's behaviour may lead to grave consequences for the physicians involved. Three possible lines of action seem open – stepping out of practicing the medical profession, stepping out of the society in which rules are broken and fighting for observation of rules at the level of practice, level of education and level of law. Other ways of resolving conflicts can also be of importance e.g. the acceptance the hierarchy of human rights, of breaking of rules if this does not bring immediate harm and administrative manoeuvres are compromise solutions which have also to be considered.

Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Mental Health Policy: Symposium: Burn-Out Amongst Students and Health Professionals: a Matter of Great Concern

S079

Burn-out. . . an underestimated psychopathology

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In today's most commonly applied classification systems, the ICD-10 and DSM-5, dysphoria and/or irritability is mentioned mostly in the context of diagnostic criteria of personality and affective disorders (Musalek et al., 2000). Summarizing the various publications on the nosological position, dysphoria is a nosological non-specific syndrome, which may occur in the course of all psychiatric disorders and illnesses.

According to the results of our psychopathological analyses, the pathogenesis of dysphoria has to be considered as a multidimensional circular process in which various mental, physical, and social factors act as predisposing, triggering and disorder-maintaining factors. Stressors as experienced in the development of burn-out constellations, e.g. work overload and/or unfairness and value-conflicts in working situations, lead to the occurrence of dysphoric symptomatology resulting in a detoriation in the mental and physical state and show a clear impact on the patient's social network. Following a dimensional diagnostic approach based on a dynamic model of vulnerability, a precise differential diagnosis of the complex constellations of conditions and their interactions becomes necessary in order to develop effective treatment strategies.

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S080

The doctor is a stubborn, a difficult patient that might not get the treatment he needs

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Medical doctors are in general better at treating and helping patients, than at taking care of their own health and at being a patient themselves. In addition doctors are often unprofessional when their patient is a colleague! The result can be dramatic: drop-out at the least, health deterioration at the worst. The pitfall often is a lack of critical self-reflection on one's own ill health on one side and a curious overestimation on the other side. The latter refers to the fact that many doctors over estimate the colleague-patient. They overestimate them in two ways: first they suppose that the patient knows as much as they themselves regarding a disease that often is well out of the scope of the speciality of the patient. Secondly both the treating doctor and the doctor in treatment underestimate the fact that one's perspectives as a patient are very different from those of the health professional treating patients.

These considerations will be illustrated with case reports. 'The overall conclusion is that the possibility that one may succumb to stress as a doctor or become a patient oneself is a matter that needs attention within the medical curriculum. Taking this possibility seriously is a safeguard that will help doctors to seek help an advice in a sound manner, in due course.

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Mental Health Policy: Symposium: Development and Implementation of Quality Indicators for Mental Health Care in the Danube Region (Daqumeca)

S082

The eMEN Interreg Project – introduction and first results

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eMEN: making e-mental health work; from research to practical implementation
The demand for mental health care is increasing globally as a result of societal challenges such as automation, more competition and the growing impact of climate change. In Europe, the current mental health care systems will not be sustainable and must become more efficient in order to absorb this increased demand. E-mental health can contribute to keeping mental health services, accessible, affordable and patient-centred. The eMEN project is about implementing e-mental health technology in Europe and setting up a European cooperation platform (network) to promote effective and safe use of this technology.
Developments in the field of e-mental health are very promising but there are many implementation barriers. The research to practice gap remains large. The eMEN project started in May 2016 and has, by using a multidisciplinary approach, implemented several actions focused on finding and promoting practical solutions for scaling up e-mental health technology. The main activity in the project has been the selection, modification and piloting of 7 e-mental health applications - 2 for depression, 2 for anxiety and 3 for PTSD. Quality, co-creation with SMEs, efficient validation, skills, reimbursement, 'blended care', policy, organisational requirements and acceptance are all taken into account. Pilots are conducted in the 6 eMEN partner countries in different mental health care settings.
Other project actions focus on developing a European policy recommendations for e-mental health implementation and organising 18 seminars and 6 conferences. This session will present the results achieved so far, with a specific focus on the product pilots.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S083

E-mental health – experiences from Ireland

K. Cullen
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Overall, there has been significant progression of the eMental health field in Ireland during the past year or two. We can see a growing coherence in activity focusing on leveraging eMental health's potential to address specific challenges in the mental healthcare system, and also in supporting broader improvement in the quality, range and reach of mental health services and supports. This involves an increasing coming-together of 'top-down' initiatives (from the Minister of State for Mental Health, Department of Health, HSE and other players) and 'bottom-up' activities (including development/deployment of eMental health by third sector mental health providers, as well as clinician-led eMental health innovation). The presentation will outline some of the key developments, as well as the contribution of the eMEN project in supporting this.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S084

eMEN – focus on transnational policy solutions

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So far, there is great variance with regard to e-mental health developments among North-West European countries and e-mental health implementation often lacks a structured approach. Lack of quality and safety standards, no legal clarity and missing implementation strategies are only a few factors that hamper the successful implementation of e-mental health products and services.
The eMEN work package "Transnational policy solution for e-mental health implementation" aims to facilitate the uptake of e-mental health through the development and active promotion of a Transnational Policy Solution with effective and feasible political suggestions.
In order to develop the Transnational Policy Solution, relevant national and European policy documents as well as information about e-mental health projects and initiatives were gathered, and the respective levels of e-mental health development and related challenges in the NWE countries were analyzed. In addition, each participating country selected national and European experts and interviewed them with regard to technological, policy, organizational and legal issues. Last, political recommendations on how to master those challenges were developed.
Several country-specific and transnational barriers and facilitators for e-mental health implementation were identified. Effective e-mental health implementation requires a comprehensive, multidisciplinary and strategic approach that considers the wide variety of challenges. The eMEN Transnational Policy Solution aims to advocate such a structured approach through outlining priority actions, policy recommendations and a practical action plan in order to guide EU and national policy makers on how to deal with challenges and enhance the effective and sustainable implementation of e-mental health.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Mental Health Policy: Symposium: Early Intervention in Psychoses: the State of the Art

S085

European status and perspectives on early detection and intervention in at-risk mental state and first episode psychosis

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Over the last two decades psychiatry has taken an important and overdue step, which other medical disciplines had taken much earlier, by recognizing the chances of early detection and intervention – in a first step mainly regarding emerging psychosis. It could be shown that early detection and intervention not only

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in first episode psychoses, but also in the at-risk mental state for psychosis, bears a great potential for improving the mental health of many people.
Especially early detection shows very promising results. Duration of untreated, frank psychosis could be reduced. Identification of individuals at risk and prediction of transition to psychosis is in the meantime possible with an excellent accuracy comparable to other preventive approaches in medicine and there is growing evidence of how this accuracy can be even more improved. Regarding early intervention, staged interventions according to the degree of risk seem feasible.
Long-term studies now show that we have even underestimated the magnitude of the problem, i.e. that only a minority of those at risk make a full clinical and functional recovery, and that there is quite a number of patients with a late transition to psychosis even after many years.
Thus, we urgently have to take action. There is now enough evidence to justify the implementation of early detection and intervention services with low threshold access for all patients all over Europe. However, implementation of such services is very unevenly distributed over European countries, and a lot of effort will have to be taken to establish early detection and intervention for all European patients.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S086

Dynamic symptom networks for the prediction of onset and progression of psychosis: Mapping Individual Routes of Risk and Resilience (MIRORR) study

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Course and outcome of early psychotic symptoms are difficult to predict, hampering timely intervention. Research relies heavily on diagnostic categories, group-level comparisons and assessment of static symptom levels. However, symptoms may wax, wane, change individually or cross diagnostic borders. Clinical staging has been an important first step towards. Adding a more personalized as well as a more transdiagnostic dimension to the model may provide a valuable step forwards.
The new Mirorr study investigates this. Mirorr follows $N = 100$ individuals (age 18–35), divided over four subgroups with increasing psychopathological severity (i.e. subsequent clinical stages). Mirorr is a diary study, assessing a broad range of transdiagnostic symptoms for 90 consecutive days that are then mapped into individual networks of interacting symptoms. Comparison of these networks across different stages as well as within-person comparison of symptom networks over time are investigated. Network characteristics will be used to predict clinical and functional outcome after one, two and three years. Mirorr is currently running and results of the study so far will be presented.
Preliminary results indicate differences in symptom dynamics between individuals and between subgroups. Characteristics of these symptom networks of individuals in different clinical stages will be presented, and associations with psychopathology and functioning. Of particular interest are structure (e.g. density) of the symptom networks, differences therein and the specific role of psychotic experiences.
Research and clinical practice may benefit from a more personalized, dynamic, transdiagnostic perspective. Mirorr exemplifies how this may help to capture the complex nature of psychopathology and its development.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Mental Health Policy: Symposium: Mass Violence, Radicalisation and Terrorism: Relation with Mental Health and Role of Psychiatric Professionals

S087

Systematic litterature review on mass violence, radicalisation and mental health

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Introduction.– Extreme political, social and religious beliefs are being developed in a multi-step process, termed radicalization. Emerging evidence suggests that certain mental health characteristics might make individuals more prone to develop radical ideations.
Objectives.– The aim of this study was to perform a systematic review of studies investigating the relationship between mental health and radicalization.
Methods.– Independent online search was performed by two reviewers and covered the period from database inception until 8th April 2018. The search strategy followed the PRISMA guidelines.
Results.– Out of 2768 records identified, 12 studies met the eligibility criteria. Three most important limitations were identified in the majority of studies: (1) low sample representativeness; (2) the use of diagnostic procedures without personal psychiatric examination or the use of standardized tools and (3) a cross-sectional study design. Representative cross-sectional studies demonstrated that depressive symptoms might be associated with higher risk of radicalization. In addition, a number of personality traits increasing the risk of radicalization were identified. Finally, there are studies, indicating that lone-actor terrorists might be a specific group of radicalized individuals, characterized by high rates of psychotic and mood disorders.
Conclusions.– There is no compelling evidence for a predefined profile of mental health or personality characteristics that make individuals more prone to engage in radicalization. Lone-actors might be a group of radicalized subjects with more severe psychopathology compared to group terrorists. More representative cohort studies are needed to address findings reported in this systematic review.
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S088

The danger of radicalisation of refugees, asylum seekers and displaced persons: cultural influence

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Since 2004, the term 'radicalisation' has become central to terrorism studies and counter-terrorism policy-making. The concept of radicalisation has become the master signifier of the late 'war on terror' and provided a new lens through which to view Muslim minorities. According to Hörqvist and Flyghed (2012) Additionally, in the following years a sudden interest in the phenomenon of radicalisation was seen. Terrorism was treated as the end result of a process of radicalisation as well as a reflection of broad social changes. In the literature two fundamentally different perspectives were identified. One of these perspectives locates the causes of terrorism in alien cultures and identity clashes, while the other proceeds from socio-economic conditions and sees the threat as coming from increasing levels of social exclusion. Both perspectives are not compatible but co-exist in practice, making terrorism a projection screen for an array of ambitions and fears. The emphasis on radicalisation has further become tied to policy preferences which have affected the Muslim community in quite different ways. In this talk an overview of cultural influences will be undertaken and discussed.

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S089

Mental illness and terrorism

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Although the UK security services have been largely successful in preventing the loss of life in Britain since 7/7 as a direct result of terrorism, there is evidence that those being radicalised by extreme political groups are significant and possibly increasing. From 11 September 2001 to the end of December 2017, 1,043 individuals were charged with terrorism offences in Britain (not including Northern Ireland); of these, 845 were taken to court and 716 (85%) found guilty. Despite high conviction rates and the introduction of lengthy prison sentences for such crimes, young people remain vulnerable to appeals from extreme groups at either end of the political spectrum. Why young men and women find such organisations attractive despite the penalties of membership is analysed. Vulnerabilities that recruiters seek to exploit will be examined not only to understand the process of radicalisation better but also to suggest possible interventions based on these findings. It will draw upon previous research that shows that depression is correlated with sympathies for violent protest and terrorism, whilst forms of political engagement may serve as protective factors. Although considerable resources have been devoted to protecting people and identifying terrorist activities, less attention has been given to the root causes of radicalised protest. This presentation explores the process of becoming sympathetic to extreme political or ideological beliefs and measures.

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S090

Migration, violence, and the role of psychiatry in Europe

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In recent times there have been increasing discussions about the role of mental illness in violent attacks as well as radicalisation especially among migrants whether they are first generation or second or third generation. Among migrants, changing personal values, extreme religious ideas; peer pressure and acceptance of ideas of hatred and prejudice and of martyrdom may contribute to the risk of violence the actual processes of acculturation in response to migration may occur at a group and at an individual level. The processes of radicalisation needs to be seen and studied both at personal and social levels. It is possible to apply public health models to understand the process and its consequences. An understanding of micro-identities as well as both vertical and horizontal identities can be helpful. A model is presented linked with a three-stage process – pre-migration, migration and post-migration – more emphasis needs to be paid to the post-migration period, which may well last for several generations. Public health interventions can be used to disrupt the pathways into violent radicalisation. Preventive paradigms and interventions should be applied as early as possible and before there is progression along the pathway towards terrorist actions. Indeed, in the UK, classroom teaching on extremism for school children is now mandated, and mental health and health professionals are asked to play a role in preventive interventions, and to help identity those vulnerable to radicalising influences. These issues raise ethical and professional dilemmas given we have no sure ways of screening and identifying people who are likely to commit crime, murder someone, or indeed be involved in terrorist incidents. The science of prediction for rare events is poor in adults and even weaker in adolescents and school children. Small groups may feel that they face existential uncertainty. Violent behaviours may result from personal, social and cultural levels such as grievances and social as well as health inequalities, sense of being discriminated against whether that is real or perceived, poor education and poor employment, poor political engagement, along with a sense of alienation leading to vulnerability to a number of adverse health outcomes. Why should this be of interest to psychiatrists and mental health professionals? Because their expertise can be usefully applied to rule out underlying psychiatric disorders. They may be called upon as expert witnesses and to provide treatment and intervention when needed.

Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Mental Health Policy: Symposium: Modern Challenges for Social Psychiatry in a Transition World

S091

New challenges for psychiatrists

N. Sartorius

Challenges for psychiatry in the early 21st century will include at least the following:

i. Enhance the prevention of mental and neurological disorders
ii. Organize care for people with comorbid mental and physical disorders
iii. Develop a greater variety of options for mental health care
iv. Acquire and use of professional skills

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To respond to these challenges it will be necessary to consider legal and administrative changes as well as radical reform in training in psychiatry for all stake holders in mental health care.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S092

From epidemiology to social psychiatry: the impact of new risk factors on the development of mental disorders

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Introduction.– Migrant or minority status and urbanicity have been strongly associated with greater psychosis risk for decades. We are still yet to fully elucidate the reasons underpinning this variance, but new studies and methods in epidemiology are providing insight into the possible mechanisms underpinning these paradigms.
Objectives.– We aimed to investigate the influence of social risk factors for psychosis over the life course by reviewing recent findings and data from the PsyLife group, UCL.
Methods.– We employed data from the Social Epidemiology of Psychosis in East Anglia [SEPEA] study, the Avon Longitudinal Study of Parents and Children [ALSPAC] study, the EU-GEI study and Psychiatry Sweden, a large longitudinal population register linkage of psychiatric disorders in Sweden. We used traditional and causal inference methods in epidemiology.
Results.– The incidence of psychosis varies substantially by place and ethnicity. In the SEPEA study, rates increased in both rural and urban populations with greater social deprivation, and in ethnic minority groups independently of urbanicity. Data from SEPEA and Sweden showed migration during early years predicted later psychosis, specifically on psychotic rather than affective pathways. Risk amongst migrants extended into very late-onset psychosis. Data from the EU-GEI study suggested sociocultural distance may explain elevated risk in migrant and minority groups, and data from ALSPAC and Sweden reveal urbanicity predicts later psychosis independently of genetic risk for disorder, and may be mediated by cognitive impairments.
Conclusions.– Data and causal inference methods allow us to delineate risk factors underpinning variation in psychosis risk by ethnicity and place.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S093

Reducing the mortality gap in patients with severe mental disorders

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In the last decade, the need to improve physical health in patients with severe mental disorders has been repeatedly highlighted by several international scientific bodies and reported in several guidelines. Nevertheless, physical health care of people with several mental disorders is often neglected by the patients themselves, as well as by their caregivers and health professionals. Patients with severe mental disorders die on average 20 years prior to the general population and have a significantly higher risk of obesity, hyperglycaemia and metabolic syndrome. This risk is strongly associated to modifiable risk factors, such as heavy smoking, poor physical activities, and inappropriate unhealthy diet, which can be improved through lifestyle changes. It is an ethical and a clinical priority to develop and implement effective strategies for modifying and eliminating those risk factors.
Several psychosocial interventions - including behavioural, educational and psychological components - have been developed worldwide for improving dietary patterns or smoking habits or improving physical inactivity, unhealthy dietary habits and smoking. These lifestyle psychosocial interventions - that are different in format, setting, duration and involved professionals - have been found to be effective in improving patients' physical health. However, in order to understand if these lifestyle psychosocial interventions reduce the mortality gap with the general population, there is the need to implement them in routine care on large scales and to evaluate their efficacy on the long-term. Recent evidences on the topic of physical health in patients with severe mental disorders will be discussed an Italian multicentre study on the development of a lifestyle psychosocial intervention will be described.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Mental Health Policy: Symposium: New Challenges in the Prevention and Treatment of Mental Disorders in the Peripartum Period

S094

New challenges in the prevention of mental disorders in the peripartum period

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Mental disorders, especially mood and anxiety disorders are very common during the perinatal period. About ten percent of all mothers suffer from depression in pregnancy and the first post-natal year. Bipolar and psychotic disorders have a very high rate of relapse postnatally. This confronts us with specific needs regarding prevention, early detection and early intervention.
Unfortunantly, help-seeking is often delayed due to shame and stigma, and diagnosis is often missed due to misinterpretation of symptoms. Women in the fertile age group as well as professionals should therefore be educated about the symptoms of mental disorders and possibilties of early intervention. Women with a history of mental disorders and a wish for pregnancy should get special counselling. Services should meet the needs of the women concerned and take into account their specific situations, problems and fears. Mental disorders in the perinatal period need special attention and special treatments with modifications of the classical pharmacological, non-pharmalogical and psychotherapeutic approaches. All non-pharmacologcial therapies including psychotherapy or light-therapy should be used. In more severe disorders also psycho-pharmacotherapy is needed, as the risk of ongoing disorder is higher than the potential risk of carefully chosen medication. A good mother-infant bonding should be a main concern from the start and fathers should be integrated as much as possible. Therapy should be interdisciplinary, including not only psychiatrists/psychologists but also gynaecologists/obstetricians, paediatricians, midwives and social workers. This does not only concerns the period of pregnancy but also the planning of delivery and the postpartum.
Untreated, peripartum disorders can have severe long-term consquences, not only for the mother, but also for the whole family and can adversely influence a child's early and later development.

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Prevention and early intervention in this area is therefore essential in the interest of the whole Society.
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S095
New challenges in the psychopharmacology of mental disorders in the peripartum period
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During the perinatal period, women are at increased risk of onset or recurrence of any psychiatric disorder, but especially of mood disorders. So the prescription of psychotropic drugs is mandatory in many cases, but is challenging during pregnancy. In such situations, clinicians have thus to weigh the risk for maternal relapse vs the risk associated with antenatal exposure to the drug that is, should the treatment be interrupted or modified against the teratogenic or fetotoxic risk of antenatal exposure to the drug. Women and their partner must also be informed of the potential influence of the pregnancy on the course of their disorder and consider whether the benefits outweigh the risk through a specific counselling.
This talk will explore the actual knowledge on the topic and discuss the current guidelines as well as some new therapeutic options.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S096
New challenges in the treatment of addiction in the peripartum period
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World Federation of Societies of Biological Psychiatry - International Association for Women's Mental Health Guidelines for the treatment of alcohol use disorders during pregnancy.
Practice guidelines for the treatment of Alcohol Use disorders (AUDs) in pregnant women were developed by members of the international Task Force of the World Federation of Societies of Biological Psychiatry (WFSBP) and the International Association for Women's Mental Health (IAWMH). The guidelines will be presented by the first author during this session. There is very little evidence based on the literature for the screening and management of alcohol use and treatment of AUDs in pregnant women and further research is urgently needed. Raising public awareness about the risks of alcohol, tobacco and illicit drug use during pregnancy is also crucial.
Reference.–
Thibaut F, Chagraoui A, Buckley L et al., WFSBP* and IAWMH** Guidelines for the treatment of Alcohol Use Disorders in pregnant women. World J Biol Psychiatry in press 2018.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Mental Health Policy: Symposium: Psychiatric Malpractice: Twists and Turns Through Regulatory Systems

S097
The drama of the German wings pilot: medical secrecy and lessons to be learned
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On 24 March 2015, the co-pilot of a Germanwings Airbus A320 caused the aircraft to crash, allegedly in a deliberate act of suicide, resulting in the deaths of 150 people. The subsequent discussion about the cause of the crash also revolved around the subject of medical confidentiality.
The co-pilot had already been diagnosed with and was receiving medical treatment for depression. Fear of losing his job led him to regularly switch from physician to physician for treatment in order to conceal his medical condition. In addition, the co-pilot failed to pass along medical certificates of incapacity for work to his employer. As a result of this, civil aviation accident investigation authorities, to cite one example, called for clearer rules regarding the requirements for reporting pilots with mental health issues in the aftermath of the crash. The German Medical Association had expressed its opposition to any premature relaxation of the medical confidentiality requirements enshrined in the Professional Code and Criminal Code, as this is fundamental to the relationship of trust between patient and physician. Only in the case of imminent danger to life and limb should a doctor be required to inform the competent authorities, but not the individual's employer. Since the obligation to maintain medical confidentiality also extends beyond the death of the patient, the German Medical Association has criticised the fact that the practices of the physicians treating the co-pilot were searched by the prosecution and the co-pilot's medical records confiscated in the course of the investigation into the cause of the crash. As a result of this tragic accident, the German Aviation Act was amended to require airlines, as of April 2016, to monitor aviation personnel before the start of work, e.g., for the influence of medications or psychoactive substances. In addition, the law introduced an electronic database of aeromedical examinations.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S098
Risk management: groupthink, hindsight-bias, or misalignment?
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Risk-Prediction is a perilous science, liable to political manipulation for popular purposes or discarded to the wind as an impossible dream. In the UK a Court censured a psychiatrist for the death of a patient with epilepsy and learning difficulty for taking what many may regard as a reasonable therapeutic risk. The ripples of this decision still spread with a concerning effect on our understanding of how others regard risk and whether we have stepped too fa rout of line with societies expectations of what we can do. We shall discuss the risks, the realities and some possible strategies to mitigate how an overzealous system concerned with its reputation might otherwise hinder autonomy, development and eventually innovation and patient well-being.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

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S099

Why a European professional card? A sad story of malpractice in the Netherlands and German Länder: lessons to be learnt

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Cross border practice in the EU opportunities and hazards. The European Professional Card procedure.
Free circulation of persons is one of the basic principles within the European Union. When it comes to professionals this includes mutual recognition of diplomas in all member states and the freedom to exercise one's profession in all EU countries. With regard to medicine and other health professions there are minimal restrictions including language skills in the host country. But to limit the eventual hazards the EU is considering a procedure of checks and balances regarding ones professional capacities and skills, misleadingly named the European Professional Card (EPA). The importance of this procedure for patient's security will be illustrated by a case description: this case is about a brilliant Dutch neurologist that became addicted to opiates after a car accident leaving him with great pain. He started misdiagnosing patients with dementia, MS and other severe medical conditions and was eventually suspended for malpractice in the Netherlands. Nevertheless he managed to work as a neurologist for an odd eight years in .different German federal lander. His case illustrates the weakness of the cross-border information flow when countries do not check for the professional status of health professionals wanting to work across the borders within the EU. The pros and cons of the EPC will be discussed.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Mental Health Policy: Symposium: Suicidal Behaviour in Immigrants, Refugees, Asylum Seekers and Ethnic Minorities

S100

Suicidal ideation - are displaced people more at risk?

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The relationship between place of birth and attempted suicide is of growing importance in view of the increasing number of migrants, refugees, and displaced people in the world. In June 2018, the United Nations High Commission for Refugees reported the existence of 25,4 million refugees and other displaced persons of concern. Refugees and labor migrants have an increased risk of psychological distress, an established risk factor for attempted suicide. Thus, suicidal behavior in displace people is a debated issue in the scientific literature, and current reports are inconsistent. Displace people seem to 'bring along' their suicide risk, at least for the initial period they spend in the immigration country. Concerns about increased suicide rates in displace people have been raised, and their relation with trauma and stressful life events has been underscored. It should be considered that, apart from the possible exposition to severely stressful life events in the native country, the process of migration itself entails several stressors. These include difficulties in the acculturation and integration process and discrimination and marginalization in the host country. Within this talk, an overview of literature about this topic will be undertaken and results from different sudies on refugees and asylum seekers will be presented and discussed.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S101

Suicidal behaviour among black and minority ethnic groups in London

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Suicidal behaviour appears to be a ubiquitous human behaviour that has occurred and been reported on throughout human history and across a range of different cultures. For decades it has been known that rates of suicide and attempted suicide and self-harm are greater in minority ethnic groups in London. In the 1990s, several studies showed that rates of self-harm were higher in south Asian groups but not in black groups. This appears to have changed in recent times. The decision to harm oneself in an intentional way is a common public health issue in the UK, with self-poisoning, the commonest form of this behaviour presenting to secondary health care services. The intent behind the behaviour can indeed be complex with a range of what have been described as possible 'functions' of the act to the person, which can include both suicidal and a range of non-suicidal motives. The concepts and notions of the 'self' vary across cultures and have to be negotiated across cultures. The act of self-harm may be seen as a cry for help but carries with it a high degree of stigma. This is almost certainly due in part to the fact that is judged by many as a challenging response to crisis, resulting as it does, reflecting as some form of mental distress requiring psychological assessment and interventions. As such, types of suicidal behaviours offer an interesting and important point at which to investigate aspects of self-identity. Recent data have demonstrated that rates among black women have increased and among south Asians gone down. Suicidal behaviour has gone up in the past decade attributed to economic downturn and is a major public health issue. These variations will be discussed with potential explanations.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Research: Symposium: Biomarkers - the Future of Diagnosis in Psychiatry?

S102

Can we diagnose schizophrenia with a blood test?

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Biomarker is a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes or pharmacologic responses to an intervention. It has capability to discriminate ill from healthy persons – it has its specificity (ability to discover positive cases as positive) and sensitivity (ability to discover negative cases as negative) and accuracy – more or less combining both measures
Early recognition and intervention in mental disorders may prevent or at least postpone disease onset. May reduce illness severity

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and/or improve its course and outcome and response to antipsychotic treatment. Biomarkers seem to be critically needed for diagnosis, predicting treatment response and follow-up outcomes of mental disorders.
Biological – especially biochemical and metabolomic markers in association with clinical assessment may in future find a practical application in early psychosis management.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S103

Sterile inflammation of brain, due to activation of innate immunity, as a culprit in psychiatric disorders

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Evidence has accumulated that the occurrence of psychiatric disorders is related to chronic inflammation. In support of this linkage, changes in the levels of circulating pro-inflammatory cytokines and chemokines in the peripheral blood of psychiatric patients as well as correlations between chronic inflammatory processes and psychiatric disorders have been described. Furthermore, an inflammatory process known as "sterile inflammation" when initiated directly in brain tissue may trigger the onset of psychoses. It will be presented hypothesis that prolonged chronic activation of the complement cascade directly triggers inflammation in the brain and affects the proper function of this organ. Based on the current literature own work on mechanisms activating the complement cascade (ComC) it is hypothesized that inflammation in the brain is initiated by the interplay between purinergic signaling and ComC activation. This activation is triggered by an increase in brain tissue of danger-associated molecular pattern (DAMP) mediators, including extracellular ATP and high-mobility group box 1 (HMGB1) protein, which are recognized by circulating pattern-recognition receptors (PRRs), including mannan-binding lectin (MBL), that activate the ComC. An important link between purinergic signaling and complement cascade plays NRLP3 inflammasome. On the other hand, this process is controlled by the anti-inflammatory action of heme oxygenase 1 (HO-1). Moreover, during ComC activation subsets of stem cells are mobilized into peripheral blood from bone marrow that are potentially involved in repair or brain remodeling mechanisms.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S104

Understanding heterogeneity and variability in brain imaging phenotypes of psychosis

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Psychiatric disorders such as schizophrenia (SCZ) and bipolar disorder (BD) are considered etiologically and phenotypically heterogeneous. The presence of disorder-related heterogeneity at the level of brain morphometry is poorly defined. We developed and validated the Person-Based Similarity Index (PBSI) in which all individual morphometric as features of a single vector. This measure provides an estimate of intra-group similarity in global and regional brain morphometry using data derived from parcellation of structural magnetic resonance images. We calculated PBSI measures to measure global and regional intra-group morphometric similarity in three independent samples of patients with schizophrenia, bipolar disorder and healthy individuals (total number of participants = 479). We found that in terms of global intra-group morphometry patients with schizophrenia showed greater heterogeneity than that of healthy individuals; conversely patients with bipolar disorder were comparable to healthy individuals. The regional coefficient of variation was greater for most cortical measures in patients with schizophrenia compared to healthy individuals while it was lower for patients with bipolar disorder. Our results suggest that greater morphometric heterogeneity is a feature of schizophrenia but not bipolar disorder.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S105

Genetic markers and stem cells in psychiatry

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Linkage and candidate gene studies of schizophrenia have not yet produced a definite genetic association. GWAS methods have produced around 50 very strong genetic association findings in many complex disorders. The heritability (80%) and relative risk (RR = 10) values for schizophrenia compare very favorably to the diseases for which strong associations have been found.
In modern psychiatric nosology, genetics operationalized criteria have proven reliable but current psychiatric diagnoses cannot yet be guided by biological data (blood test etc.). Operationalized criteria are constructs and thus subject to change.
For almost half a century, successful application of hematopoietic stem cells in hematopoietic transplants has encouraged attempts to employ stem cells in treating and diagnosing clinical problems.
It is well known that low numbers of stem cells circulate continuously in peripheral blood and lymph and undergo a circadian rhythm.
A new area of research in psychiatric disorders is concerned with abnormal regeneration processes. The role of brain neurogenesis has been studied for decades. New discoveries, concerned with the pluripotency of VSEL cells and the role of factors involved in stem cell trafficking in peripheral blood create hope that it will be possible to develop a better understanding of the processes of neuroregeneration/neurodegeneration.
The presentation will contain data on stem cells in: a/psychotic disorders b/in anxiety disorders c/n affective disorders d/and effect of lithium on the presence of stem cells.
The data will cover the concentrations of: sphingosine -1-phosphate, SDF-1, elements of complement cascade, and stem cells in peripheral blood, including their possible connection to psychiatric disorders. All collected data, suggesting an abnormal course of regeneration processes in psychiatric disorders, raises hope of finding new potential markers of psychotic and anxiety disorders.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

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Research: Symposium: Current Developments in Psychiatric Epidemiology: Evidence from Population-Based and Clinical Studies

S106

Antecedents and risk factors of mood disorders in children of affected parents

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Objectives.– Using prospective data on the offspring of patients with unipolar and bipolar mood disorders as well as clinical controls, our aims were to identify disorders preceding the onset of bipolar disorder (BPD) and major depressive disorder (MDD) in these offspring and to determine the risk factors related to the onset of these disorders including personality traits and adverse life-events.
Methods.– Clinical information was collected on 160 offspring of parents with BPD, 127 offspring of parents with MDD and 158 offspring of comparison probands. Children were 6-17 years old at study entry (mean age: 10.0 years). Offspring and their parents were directly interviewed every 3 years with a mean duration of follow-up of 11.9 years.
Results.– Our major findings were that, compared to the other offspring, those who developed manic or hypomanic episodes reported major depressive and minor hypomanic episodes prior to the onset of the first manic or hypomanic episode more frequently. However, by far the strongest predictor of the onset of manic or hypomanic episodes in offspring was a parental BPD with an onset earlier than 21 years. Neuroticism and life events were not associated with the onset of mania/hypomania, whereas Neuroticism, sexual abuse and witness of violence were the strongest predictors of the onset of MDD in offspring.
Conclusion: Our results support distinct antecedents of MDD and BPD and distinct risk factors involved in the development of these two mood disorders.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S107

The role of Ambulatory Assessment (AA) phenotypes in mental health reserach

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Ambulatory Assessment (AA) allows to measure micro-processes during daily life which are gaining increasing attention with regard to their potential to for the understanding of risk factors for the development, psychopathology, and course of mental disorders. While current research predominantly focuses on the role of affective AA phenotypes, cognitive vulnerability factors have rarely been investigated during daily life. The current talk will give an overview on AA-studies in which we investigated daily life ruminative processes and their interplay with affective processes, as well as their neurobiological correlates (peripheral stress measures, fMRI) in clinical (Major Depression, Premenstrual Dysphoric Disorder) and nonclinical samples. Our studies show that ruminative processes during daily life have predictive value for the course of illness. Furthermore, they appear to be more closely linked to biological parameters, such as a neuroimaging phenotype of cognitive reactivity and peripheral cortisol activity, than retrospectively assessed traits and psychiatric symptoms. Cognitive together with affective micro-level processes during daily life may therefore also be ideally suited to contribute to the further understanding of transdiagnostic endophenotypes in psychopathology. Furthermore, they can contribute to the identification of specific intervention-related mechanisms in therapy research.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S108

Psychiatric epidemiology of old age: from brain imaging to society

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Introduction.– With ageing populations worldwide, we need to learn more about mental disorders among older people.
Objectives.– To study mental disorders of old age using a combination of social, psychological and biological measures
Methods.– The Gothenburg H70 Birth Cohort studies are longitudinal population studies on representative samples of older people. The studies have been on-going since 1971, when a birth cohort of 70-year-olds born 1971–72 were examined and thereafter followed over three decades. Thereafter birth cohorts of 70-year-olds born 1906–7, 1911–12, 1922, 1930 and 1944 have been examined longitudinally. The studies include include psychiatric, somatic, psychosocial, genetic, functional, personality and cognitive examinations, and blood, plasma, serum, and cerebrospinal fluid, MRI and PET scan of the head, and body composition.
Results.– Using CSF data, we found that 25% of healthy 70-year-olds have amyloid pathology and 44% have amyloid or tau-pathology. We also found similar risk factors for dementia and depression, such as ischemic white matter lesions on brain imaging and genetic factors. The life-time prevalence was 44% for major depression and 67% for any depression based on evaluations by psychiatrists over 44 years follow-up. Depression with onset before age 40 years was related to increased risk for dementia after age 70. Among late-life depression, only one third had late-onset.
Conclusions.– It is important to consider silent disorders, which can only be detected by detailed biological measures (e.g. preclinical Alzheimer's disease), and also have a life course perspective, which is important in relation to risk factors, and the diagnosis of late-onset disorders.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Research: Symposium: In Search of Biomarkers for Mood Disorders

S110

Biomarkers of bipolar mood disorder in relation to staging of the illness

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Abstract: The purpose of the study was to analyze changes in serum activity of cytokines, oxidative stress markers (TBARS), and trace elements (Copper and Zinc) associated with both – inflammation

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and oxidative stress in particular phases of bipolar disorder, taking into account specific clinical features, intensity of symptoms and degree of advancement of the disease (staging). As we have shown: TBARS levels were influenced by: an episode of disease (higher concentration of TBARS in the acute episode in comparison to remission), BD stage (higher concentrations in the more advanced, late stages – stage 3 plus 4). Zinc concentration in the subgroup of patients with more advanced stage of bipolar disorder (stage 3 and 4), during the episode of depression was significantly lower than in healthy volunteers and in patients in remission. It has been also found that the copper concentration in serum of patients in BD stage 1 was significantly higher comparing to other stages of the disease treated jointly (2 + 3 + 4). More advanced stages of bipolar disorder (stage 3 and 4 by Kapczinski) were characterized by significantly higher level of sTNFR80, lower sIL-2R level compared to patients, who were in less advanced form of the disease (stage 1 and 2). The concentration of sIL-1RA and sTNFR-80 kDa was significantly higher in patients diagnosed with bipolar disorder in comparison to healthy volunteers. Additionally, there various relationships between cytokine concentration and clinical features and the severity of the depressive episode were observed.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S111
Stem cell and pluripotency markers of lithium treatment in bipolar mood disorder
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Objectives.– In bipolar disorder (BD) various changes reflecting low-grade inflammation occur which can be attenuated by lithium treatment. The effect of such treatment on very-small embryonic-like stem cells (VSELs) and the mRNA expression of pluripotency markers (Oct-4, Sox 2 and Nanog), in peripheral blood, was studied in patients with BD of long duration.
Methods.– Fifteen BD patients treated with lithium for 8–40 years were compared with 15 lithium-naïve BD patients, with duration of illness >10 years, and 15 control subjects. The groups were matched for age.
Results.– In lithium-treated BD patients, the number of VSELs was similar to controls and correlated negatively with the duration of lithium treatment and serum lithium concentration. The mRNA levels of Oct-4, Sox-2 were not different from controls and these of Nanog were higher and correlated with the number of VSELs. In lithium-naïve BD patients, the number of VSELs was significantly higher than in control subjects and correlated with the duration of illness. The expression of pluripotency markers was significantly higher than in the controls and correlated with the number of VSELs.
Conclusion.– In lithium-naïve BD patients, the VSELs may provide a potential marker of the illness and its clinical progress, and the higher expression of peripheral mRNA markers may be due to an ongoing low-grade inflammatory process. Long-term treatment with lithium may suppress the activation of regenerative processes by reducing the number of circulating VSELs and attenuate inflammatory processes, reflected by the higher mRNA expression of the transcription factors Oct-4 and Sox-2.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S112
Biomarkers for treatment-resistant depression identified in the whole genome sequencing
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Treatment resistant depression (TRD) is a common complication (∼1/3 of patients) of major depressive disorder (MDD) that contributes to the huge personal and socio-economic burden of the disease. Genetic variants are key modulators of antidepressant efficacy, but previous genome-wide association studies (GWAS) have generally failed to identify the polymorphisms involved. Whole exome sequencing and network analysis represent promising and innovative strategies.
47 patients with diagnosis of MDD with current episode of at least moderate severity were selected if they satisfied the definition of TRD or were optimal antidepressant responders. TRD was defined as lack of response to at least two antidepressant trials while optimal responders satisfied remission criteria after the first antidepressant trial. Next generation exome sequencing was performed from whole blood. After quality control (fastqc) and aligment to the reference human genome (ENSEMBL, release 83), gene-based tests were performed by PlinkSeq and enrichment analysis was performed using the Cytoscape GeneMania plugin to identify networks involved in TRD. Replication of results in the STAR*D study was attempted using a comparable phenotype (remission to the first antidepressant trial ($n = 583$) vs. non-remission to the fourth antidepressant trial ($n = 48$)).
24 TRD patients and 23 good responders were included in the study. 967,208 variants were available. Initial pathway analysis based on known gene product interactions identified some networks that were associated with TRD status, including the neurotrophin signalling pathway and other pathways involved in cell growth. Particularly a group of genes belonging to a network involved in metaphase-anaphase transition of mitotic cell cycle was replicated in STAR*D. Final analyses will be presented at the meeting.
Genes involved in cell growth and in metaphase-anaphase transition of mitotic cell cycle may have a relevant role in the risk of TRD. Components of this network (the CDC20/APC complex) were demonstrated to have a pivotal role in controlling dendrite growth in post-mitotic neurons, a process that is essential for antidepressant response. Future directions include whole exome sequencing in a larger sample to replicate these findings.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Research: Symposium: Innovations in Forensic Psychiatry: 2019

S113
Innovations in treatment of offenders diagnosed with personality disorders in forensic setting
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Personality disorders are common and disabling conditions. Yet, a sufficient evidence base regarding their effective management is lacking. The best evidence exists for borderline and antisocial personality disorders (BPD and ASPD) were psychotherapy is regarded as first-line treatment. However, pharmacotherapy is also widely used in personality disorders.

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This presentation will focus on two main topics: 1. The evidence from findings of systematic literature reviews on pharmacological and psychological interventions for personality disorders will be presented, based on Cochrane reviews on the subject. 2. Recent service developments for patients with PD in forensic settings as well as adaptations of PD treatments for this specific group will be discussed.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S115
Variety of forensic psychiatry in Europe
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Political, cultural and systemic changes during the last 25 years in several European countries resulted in the significant modification of psychiatric care, including forensic psychiatric care. It concerned the legislative issues and legal framework (e.g. Italy, Poland), the new infrastructure development (e.g. Belgium, Italy), implementation of the modern diagnostic and treatment procedures (e. g. East European countries) and innovative approach to cognitive impairment, neuro-cognitive and social cognitive deficits coexistent with mental disorders. But the systemic basis of forensic psychiatric care across European countries still differs significantly. During this talk, the main differences and convergences of the forensic care systems across Europe will be presented, considering its strengths and weaknesses, as the basic for further discussion. The objectives of multinational research project EU-VIORMED will be discussed, as the example of European research-network aiming to provide detailed data on the organization of forensic psychiatric care.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Research: Symposium: New Targets to Improve Real-Life Functioning of People with Mental Disorders

S116
New targets in the treatment of schizophrenia
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Schizophrenia is a severe brain disorder characterised by positive, negative, affective and cognitive symptoms and can be viewed as a disorder of impaired neural plasticity. Pharmacotherapy, psychotherapy and social therapy form a multi-facetted treatment for schizophrenia has helped considerably to improve the outcome of schizophrenia.
Despite this fact we are left with a substantial proportion of partial- or non-remitting patients who demonstrate a bad vocational outcome and who are unable to keep up a long-term relationship.
Reasons for this unfavourable outcome are the residual symptoms, mainly negative symptomatology and cognitive dysfunction. Reduced residual symptoms targeted add-on therapies are needed to improve the efficacy of the antipsychotics.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S117
New targets in the treatment of eating disorders
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Background and aims.– The pathophysiology of eating disorders (EDs) is not clearly understood, and there is a lack of effective treatments. A better understanding of ED pathophysiology could improve the effectiveness of treatments and minimize the relapse risk. In the last years, the gut microbiota is emerging as a factor influencing behaviour and brain regulation.
The assessment of fecal microbiota and metabolomic profiles of AN patients may lead to the characterization of possible biomarkers able to guide new treatment strategies.
Methods.– In this study we analyzed the fecal microbiota and the metabolomic profile of 21 AN women, before treatment (T0) and after weight-restoration (T1), and compared them with those of 20 healthy control women (HC).
Results.– AN subjects had a less diverse microbiome and a lower rarefaction measure than HC when underweight.
At taxonomic levels, underweight AN subjects exhibited decreased abundance of Lachnospiraceae, Clostridiales and Bacteroidaceae compared to HC. Moreover, Coprococcus gene was significantly reduced in AN at T0 compared to both T1 and HC.
In AN patients, cadaverine, cycloserine, N-acetyl ethylenediamine, steric acid, coprostanol, propionic acid, linoleic acid, lactic acid, methyl ketobuthyric acid were higher at T0 compared to T1 and HC while fucose, xylose, rhamnose, arabinose were lower at T0 compared to T1 and HC.
Conclusions.– These findings suggest that a specific microbiome and metabolomic signature is present in AN. The extent to which these characteristics represent possible biomarkers of AN and may promote new treatment strategies (such as the use of pro- and pre-biotics) remains to be determined.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Research: Symposium: Paternal Depression in the Postpartum and Beyond: Diagnosis, Risk Factors and Consequences for Child Development

S118
Depression and parental stress among swedish fathers in the postnatal period: screening and working through the help-seeking barriers
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Introduction/Objectives.– The meta-analytical prevalence of paternal postnatal depression (PPND) is 8.4% (Cameron et al., 2016). However, measures for PPND are scarce and the commonly used *Edinburgh Postnatal Depression Scale* (EPDS) has low sensitivity, as many men express depression with somatization and/or externalizing symptoms. Recent studies show higher prevalences, indicating that affected men conceal their symptoms and underscoring the lack of knowledge concerning adequate PPND screening. We addressed these issues in three studies.
Methods/Results.– By assessing fathers of infants 0–18 months old (study 1, $N = 447$) with multiple measures (*Beck Depression Inventory-II* (BDI-II), *Gotland Male Depression Scale* (GMDS), EPDS), we found that a combination of depression items from EPDS and depressive-equivalent symptom items from GMDS yields a

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highly sensitive screening instrument for PPND. Structural equation modelling (study 2, $N = 395$) revealed a strong mediating role of parental stress, but not relational variables, between fathers' attachment anxiety/avoidance and depressive symptoms. Finally, fathers' (study 3, $N = 172$) widespread tendency to conceal depressive symptoms comprises convictions that negative feelings/symptoms are normal and best managed privately, desires to fulfill expectations of being happy and to be perceived as a 'good father', and fears of not being taken seriously by healthcare professionals.
Conclusions.– In all studies, 25%–35% of fathers reported symptom levels indicative of PPND, with unchanged prevalences for the 18-month period; 90% of affected fathers had no treatment/support professional contact, underscoring the usefulness of our highly sensitive screening instrument for PPND and the importance of exploring also alternative routes for screening to support the developing father role.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S119

Identifying risk factors for paternal depression in the perinatal period: data from the ELFE cohort study

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Introduction.– Lack of social support is a well-known risk factor of postpartum depression (PPD) in mothers. However, knowledge about informal and professional dimensions of social support during pregnancy and paternal PPD is very limited.
Objectives.– The aim of this study was to identify whether lack of informal and professional social support factors during pregnancy are associated with elevated paternal depressive symptoms in the year following the child's birth.
Methods.– Using the nationally representative French ELFE cohort study (N = 12,350), we studied the associations between lack of informal support (sufficient support from the spouse and frequent quarrels) and professional support (access to a mental health professional, prenatal psychological screening and parenthood class) during pregnancy and paternal only PPD using multi imputed and weighted multivariate multinomial regression.
Results.– In 702 (5.7%) out of 12,350 couples, only the father was depressed. Lack of informal support during pregnancy was significantly associated with an increased probability of paternal only PPD. Results regarding professional support were less clear: access to a mental professional and parenthood classes were associated with decreased probability of paternal only PPD. Prenatal psychological screening attendance was associated with increased probability of paternal only PPD.
Conclusions.– These results suggest that prevention of PPD in fathers should focus on increasing both Informal and professional support (at least access to mental health care and parenthood classes) during pregnancy. Interventions could have benefits for paternal PPD, by improving father's knowledge of PPD and maintaining good relationships within expectant couples.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

S120

Paternal depression and emotional and behavioural problems in middle childhood - the role of father involvement

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Introduction.– Children of parents with psychopathology are at a higher risk of developing mental health problems in adulthood. The pathways of transmission from maternal mental health to childhood symptoms are well researched, but the effects of paternal psychopathology on children are less understood.
Objectives.– This study examined the possible moderating role of the level of father involvement in the association between paternal depression and childhood emotional and behaviour problems.
Methods.– Behaviour of 875 children from the French EDEN cohort was assessed when they were 8 years old using the Strengths and Difficulties Questionnaire (SDQ). Paternal depression was assessed using the CESD. Father involvement scores were derived by factor analyses, resulting in three variables: Playing, Helping and Talking. To measure the 'Accessibility' aspect of father involvement a binary indicator was used to identify if the father lived with the child or not at the age 8 wave. Multiltiple linear regression was used, adjusted for inverse probability weights (IPW), with multiple imputations to account for missing data. Analysis were stratified by child sex to investigate potential sex differences.
Results.– Father's depression was associated with children's total difficulties scores in both boys and girls, with a larger impact for boy's internalising behaviours. While girls internalising symptoms were related to paternal involvement, in particular accessibility, there was little evidence that involvement moderated the effects of paternal depression on child outcomes.
Conclusion.– Father's depression should be included in research on children's difficulties in middle childhood. Given the increasingly important roles modern fathers play in their children's lives, future research should continue to investigate the impact of their day to day involvement on children's social and emotional development.
Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Research: Symposium: Personalised Psychiatry: Novel Neuroimaging Tools for Clinical Translation

S121

Clinical implications for big data approaches to mental health research

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Over the past decades, the neuroimaging field has had very limited impact on clinical routines in psychiatry, partly grounded in the complexity of brain imaging phenotypes, the large heterogeneity of findings for patients with similar diagnosis, and a lack of a mechanistic understanding of the underlying pathophysiology. However, with recent advances in data sharing and large-scale cohort studies, the neuroimaging psychiatry field has entered the era of big data, which paves the way toward robust mapping of brain imaging findings to the genetic architectures, clinical symptoms and cognitive traits. This talk will cover two recent large-scale brain

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imaging genetics studies. In one study we estimated the relative age of the brain compared to chronological age using imaging data from 36,891 individuals. We provide evidence for an apparent aging of the brain in a range of brain disorders and show that genes involved in apparent brain aging in healthy individuals overlap with genes identified in the genetic architectures of brain disorders. In a second study, we map the genetics of psychiatric disorders onto the brain using data from 16,612 individuals, yielding brain maps that highlight areas associated with the genetics of the respective disorders. We use these maps to inform prediction models for detecting deviations from normal brain development in 1,467 children and adolescents, aiming toward biology-informed, early detection of psychiatric illness in the developing brain. The talk will discuss the potential and limitations of such big data approaches to mental health research and will pinpoint future directions toward clinical application.

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S122

Parsing heterogeneity in healthy individuals and patients with psychosis: clinical implications

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The characterization of the functional significance of inter-individual variation in brain morphometry is a core aim of cognitive and clinical neuroscience. Prior research has focused on inter-individual variation at the level of regional brain measures thus overlooking the fact that each individual brain is a person-specific ensemble of interdependent regions. To expand this line of inquiry we introduce the Person-Based Similarity Index (PBSI) for brain morphometry. The conceptual unit of the PBSI is the individual person's brain structural profile which considers all relevant morphometric measures as features of a single vector. In two independent cohorts (total of 1756 healthy participants), we demonstrate the foundational validity of this approach by affirming that the PBSI scores for subcortical volume and cortical thickness in healthy individuals differ between men and women, are heritable, and robust to variation in neuroimaging parameters, sample composition, and regional brain morphometry. Moreover, we identified regions that show significant contribution to the PBSI namely hippocampus/parahippocampal gyrus, anterior cingulate and occipital cortex. Investigation of PBSI in patients with schizophrenia and bipolar disorder showed that increased heterogeneity was in global and regional cortical morphometry was present only in schizophrenia. In both disorders, the intra-group similarity was associated with cognitive but not clinical measures.

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