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Core Symposium: New Perspectives in Negative Symptoms: A Transnosographic Approach to Diagnosis and Treatment

CS0001

Treatment of negative symptoms across diagnostic categories: Achievements and challenges

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Negative symptoms can be observed in a variety of neuropsychiatric disorders and are not specific to a diagnostic category. The dimensional approach aims at developing specific treatments for negative symptoms independent of categorical diagnoses. Although there is no clear evidence for transdiagnostic treatments so far, this approach has stimulated the discussion on potential target mechanisms. Here we provide a selective review of pharmacological and psychosocial treatment approaches targeting negative symptoms in at least two diagnostic groups of patients.

Pharmacological treatments include modulators of the monoamergic systems. Antidepressants have been employed in different disorders, but they have only limited effects against negative symptoms without concurrent depression. Stimulants have proven to be effective against negative symptoms in neurological disorders, but clear evidence for efficacy in schizophrenia and affective disorders is lacking. Newer approaches including the use of memantine and anti-inflammatory drugs will be briefly discussed.

Psychosocial treatments have rarely targeted negative symptoms as primary outcome. Nevertheless, cognitive behaviour therapy seems to be a valid treatment option for negative symptoms, but will also have to take into account the diagnostic context. Cognitive impairment has been linked to negative symptoms and recent studies suggest a positive effect of cognitive remediation that is not restricted to patients with schizophrenia. Finally, an increasing number of studies shows a beneficial effect of physical exercise on negative symptoms, although these symptoms have rarely been defined as the primary outcome.

Future development of transdiagnostic treatment approaches should aim at a better integration of pharmacological and psychosocial treatment approaches. A truly dimensional approach to the treatment of negative symptoms will eventually require transdiagnostic treatment studies, which employ the same treatment protocol across diagnostic categories.

Disclosure of interest.– SK receives royalties for cognitive test and training software from Schuhfried (Austria).

Core Symposium: Brain Mechanisms of Resilience to Mood and Psychotic Disorders

CS0002

Brain volume abnormalities in different types of first degree relatives of schizophrenia and bipolar disorder: An ENIGMA study

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Background.– First-degree relatives of schizophrenia (SZ) and bipolar disorder (BD) patients show brain abnormalities. Through the ENIGMA consortium, we compare different types of SZ or BD first-degree relatives (i.e. co-twins, siblings, offspring, parents) to healthy controls (HC) on global and subcortical brain measures.

Methods.– To date, 6235 individuals (of which 1177 SZ relatives and 868 BD relatives) from 27 independent studies were included. MRI scans were processed with FreeSurfer. Linear mixed model analyses were performed comparing each type of relative to HC, while taking family relatedness into account. Cohen's d effect sizes were obtained at each site and then pooled using an inverse variance-weighted random-effects meta-analysis for all relatives combined.

Results.– First-degree relatives of BD patients had a significantly larger intracranial volume (ICV) than controls (Cohen's $d = 0.16$), which was not the case for SZ relatives ($d = -0.03$). See figures. Fur-

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thermore, first-degree relatives of BD patients showed significantly larger volumes of cortical and cerebellum GM ($d = 0.14$, $d = 0.12$), total surface area ($d = 0.14$), and lateral ventricle volume ($d = 0.13$) as compared with controls, which no longer reached significance after correction for ICV. After ICV correction only a smaller thalamus volume ($d = -0.13$) was found in BD relatives.
First-degree relatives of SZ patients showed significantly smaller volumes of the total brain ($d = -0.11$), cerebral WM (Cohen's $d = -0.09$), cerebellar GM ($d = d0.10$) and WM ($d = -0.09$), mean cortical thickness ($d = -0.14$), accumbens ($d = -0.09$), putamen ($d = -0.09$) and thalamus ($d = -0.12$), and a larger third ventricle volume ($d = 0.13$) relative to controls. After correction for ICV, the pattern of findings for SZ relatives remained largely similar or effect sizes increased, and additionally included a smaller cortical GM volume ($d = -0.13$).
Conclusions.– The main finding is that BD relatives have a larger ICV as compared with controls, which was not the case in SZ relatives. In contrast, smaller global and subcortical brain volumes were present in SZ relatives. This may implicate that the familial risk for SZ and BD differentially associates with structural brain measures, possibly reflecting different neurodevelopmental pathways. We are currently expanding the analyses to investigate whether having a DSM diagnosis other than SZ or BD in the relatives explains the differences in intracranial and other brain volumes, and whether there are differences between the different types of relatives.
Disclosure of interest.– The authors have not supplied their declaration of competing interest.

CS0003

Polygenic risk profile score increases schizophrenia liability mostly through cognition pathways: Mathematical causation models with latent cognition and polygenic risk

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Objective.– Cognition shares substantial genetic variance with schizophrenia, with recent evidence from cross diagnosis genome-wide association study (GWAS) data and from statistical modeling of twin data suggesting direct causality from the former to the latter. However, it is not clear how much of the genetic component of schizophrenia is mediated through cognition. Thus, we included in causation models direct measurements of the genetic risk (e.g. schizophrenia polygenic risk scores) to quantify the genetic component of schizophrenia that is mediated by cognition and captured by the polygenic risk score.
Method.– Data were from 1313 members of 1078 families, and included 416 schizophrenia patients, 290 unaffected siblings, and 607 controls. Polygenic risk scores (PRS) were based on the latest data from the schizophrenia working group of the Psychiatric Genomics Consortium (PGC) and represented the sum of genotypic scores for all common genetic variants associated with schizophrenia at p-value thresholded to 0.05 (i.e. PRS6). Cognition (L-COG) was extracted through common pathway models and captured the common variance across measurements in six cognitive domains: processing speed, verbal memory, visual memory, span, working memory, and executive function.
Results.– Of the genetic component of schizophrenia, 2.71% was through PRS pathways mediated by L-COG, 3.93% by PRS covariation pathways that included L-COG, and 26.87% by L-COG pathways not captured by the PRS. The remaining variance in schizophrenia liability was through pathways other than cognition and PRS.
Conclusions.– Cognition pathways captured by the PRS score mediated a significant part of genetic risk for schizophrenia. However, the evidence suggests that other cognition pathways not captured by PRS mediate an even greater part. We anticipate that when schizophrenia PRS include all possible variants associated with risk, more than 25% of the variants' cumulative effect will first influence variation in cognition.
Disclosure of interest.– The authors have not supplied their declaration of competing interest.

Core Symposium: Forcibly Displaced People and Mental Health in Europe: Challenges and Needs

CS0004

Dimensions of the problem and the psychosocial context

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Warfare, armed conflicts, persecution and human rights violations, in different parts of the world have led to an humanitarian disaster: forced displacement of millions of people, especially in the last decade. There has been an increase in the number of refugees by about 1/3 over the last 10 years, over half of whom were under the age of 18. Hence, this is not only a disaster of today but will have serious impact on our future.
Forcibly displaced people are under threat in all areas of attachment, mastery, and survival. Almost all attachments are left behind, degree of mastery is decreased; the nutrition of the self and the self-image are devastated. Basic needs for survival maintained mostly in the mercy of others. Refugees fleeing with few possessions leading to neighbouring or more developed countries face many life-threatening risks before, during and after displacement, and they have nowhere to return. A refugee is a person who has lost the past for an unknown future. Experiences of loss and danger are imprinted in their selves.
There is increasing evidence that about 60% of refugees and asylum seekers residing in Europe suffer from mental disorders in the short/medium term. In the long term, evidence suggests that mental disorders tend to be highly prevalent in war refugees even many years after resettlement. This increased risk may not only be a consequence of exposure to wartime trauma but may also be influenced by post-migration socio-economic factors.
This presentation aims to review the current situation of the forcibly displaced people (refugees and asylum seekers) living in Europe. The dimensions of the problem and the psychosocial context in which the mental health problems develop will be further discussed.
Disclosure of interest.– The authors have not supplied their declaration of competing interest.

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CS0005

Mental health situation of forcibly displaced people

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It is well known that migration is one of the risk factors for developing mental disorders, and that traumatized migrants, in particular, may face psychological distress and even serious psychiatric illness as they have been exposed to adverse conditions before, during and after migration. Prior to migration, migrants may have been exposed to deprivation, persecution, violence, imprisonment, human rights violation, including sexual harassment, even torture. Particularly, it is recognized that the transition phase which often includes a temporary residence can also be perceived as very stressful as well as the post migratory phase in the new host country. Data from studies on risk for psychosis show that stress factors in the post migratory stage over all have more impact on mental health than those in the pre-migratory stage.
Furthermore, it is well known that the loss of loved ones/caregivers and/or livelihood, the destruction of property, deprivation, persecution, insecure living conditions, war, torture, imprisonment, terrorist attacks, abuse and sexualized violence have high impact on the mental health situation of refugees and asylum seekers. Experiences, e.g. defencelessness and disorientation, conditions of cold or heat, hunger and thirst, lack of medical care, robbery, assault and discrimination during the process of flight are often. Additionally, many women may be subjected to different kinds of sexual assaults and violations.
In this talk data from representative studies on the mental health situation of forcible displaced people will be presented and discussed.
Disclosure of interest.– The authors have not supplied their declaration of competing interest.

Core Symposium: Setting Priorities for Mental Health Research in Europe

CS0006

The ROAMER project: A roadmap for mental health research in Europe

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Developing priorities for mental health research across Europe: methods, priorities and developing impacts.
Mental disorders represent potentially the greatest health burden to Europe – not only for directly affected individuals, but also for caregivers and wider society. This burden has increased during the last decades and the predictions are that this increase has not finished. However, funding for research to mitigate these effects lags far behind the cost to society. This is despite the fact that the return to society from mental health research is similar to the return from other areas such as cancer or cardiovascular diseases. These linked presentations describe the ROAMER project, funded by the European Commission, which established a comprehensive, coordinated mental health research agenda for Europe and the world that might reduce these costs and burdens.
This paper leads on from the description of Consortium and a comparison of methods for achieving consensus by Professor Josep Maria Abad Haro, the ROAMER consortium lead. This presentation concentrates on how each work package produced their list of priorities and how these led to consensus on the gaps in current research and priorities for future research. These priorities were integrated and revised through surveys and consensus decision-making by more than 1000 scientists and affected stakeholders including individuals with mental health problems and their families, healthcare workers as well as policymakers and funders to produce 6 high-level priorities for mental health research in Europe which if answered would have substantial impact in the next five to 10 years.
In a further joint presentation Professors Wykes and Haro will describe how these priorities have been adopted in Europe and the UK and the management of this process as an example of moving research priorities into policy and then into funding.
Finally, Professors Wykes and Haro will discuss the current European scenario in mental health research and the impact of the ROAMER project.
Disclosure of interest.– Josep Maria Haro has received honoraria for participating in advisory boards or giving educational lectures from Eli Lilly and Co., Lundbeck and Otsuka.

CS0007

Priorities for mental health research in Europe: A survey among National Stakeholders' Associations within the ROAMER project

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Discontent towards our profession is increasingly reported by patients with mental disorders and their relatives. Criticisms by patients are mainly related to the existing divergences between the goals of clinicians and those of users and carers. Recent arguments suggest that opinions of people who use mental health services are fundamental to set priorities in mental health research field.
Within the ROAMER project, funded by the European Commission, an online survey was carried out with the European associations of all stakeholders involved in mental health (psychiatrists, other mental health professionals, users and carers, psychiatric trainees) with the aim to identify the priority areas for mental health research.
One hundred and eight associations/organizations compiled the questionnaire. The most frequently reported research priorities were early detection and management of mental disorders, quality of mental health services, prevention of mental disorders, rehabilitation and social inclusion, new medications for mental disorders, and stigma and discrimination. These results seem to support the recent argument that some rebalancing in favour of psychosocial and health service studies may be needed in psychiatric research.
The stakeholders' views are being progressively considered in the process of developing clinical guidelines, public health recommendations and research protocols. In particular, users' and carers' direct involvement in research development can lead to a "better" quality of the research itself.
Disclosure of interest.– The authors have not supplied their declaration of competing interest.

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CS0008

Defining research priorities for mental health: An integrated and comprehensive ROADMAP

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Developing priorities for mental health research across Europe: methods, priorities and developing impacts.
Mental disorders represent potentially the greatest health burden to Europe – not only for directly affected individuals, but also for caregivers and wider society. They incur substantial economic costs through direct (and indirect) healthcare and welfare spending, and via productivity losses – all of which significantly affect European development. Funding for research to mitigate these effects lags far behind the cost to society. These linked presentations describe the ROAMER project which established a comprehensive, coordinated mental health research agenda for Europe and the world that might reduce these costs and burdens.
This paper leads on from the description of Consortium and a comparison of methods for achieving consensus by Professor Josep Maria Abad Haro, the ROAMER consortium lead. This presentation concentrates on how each work package produced their list of priorities and how these led to consensus on the gaps in current research and priorities for future research. These priorities were integrated and revised through surveys and consensus decision-making by more than 1000 scientists and affected stakeholders including individuals with mental health problems and their families, healthcare workers as well as policymakers and funders to produce 6 high-level priorities for mental health research in Europe which if answered would have substantial impact in the next five to ten years.
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Finally, Professors Wykes and Haro will discuss the current European scenario in mental health research and the impact of the ROAMER project.
Disclosure of interest.– The authors have not supplied their declaration of competing interest.

Core Symposium: Cyberbullying, Cybersuicide and Novel Psychoactive Substances: Mental Health Needs in Young People

CS0009

Cyberbullying: A new challenge for mental health care

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Internet has facilitated communication and dissemination of information worldwide, at little or no cost. Internet and related technologies are not inherently "good" or "bad", but they are rather tools that can be used for a variety of purposes, with a variety of consequences. There is no doubt that the Internet and related technologies are posing new challenges to mental health professionals, such as the development of new forms of psychopathologies, including cyberbulling and cybersuicide.
Cyberbullying is a repeated hostile or aggressive behaviour against others, performed by an individual or a group of individuals using electronic or digital media. This activity can take many different forms, including email, blogs, chat rooms, and text messaging.
Cyberbullying is different from "traditional" bullying, since it is not based on physical direct violence, the perpetrator remains anonymous and the violent behaviour can happen anywhere and at any time.
Although prevalence rates vary considerably across countries from 1% to 60%, a significant association between cyber victimization and depressive disorders and suicidality has been observed. In a recent study carried out in an Italian sample of students from secondary schools, we found that 30% of participants reported to have been victimized and 6% of them suffered from cyber victimization. The long-term consequences of being cyber victimized are not yet completely understood, but it seems that these traumatic events are pathoplastic for the development of mental disorders during adulthood.
A better identification of the new forms of Internet-related mental disorders in young adults, including a clinical and therapeutic characterization, is needed.
Disclosure of interest.– The authors have not supplied their declaration of competing interest.

CS0010

Youth space and youth mental health

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Background.– Services to young people in the city of Birmingham have been transformed from a traditional CAMHS-AMS framework to a 0–25 framework with an early intervention ethos. This includes collaboration with schools in the early detection of emerging mental health problems, including the subject of this presentation: emergent eating disorders. It is known that long duration of untreated eating disorders, leads to a low recovery rate such that those with an eating disorder over 10 years duration have a very low chance of LT recovery. This study aims to identify the earliest stages of emergent eating disorders in adolescence and to predict early transition.
Research questions.– (1) What is the period prevalence of partial or full ED in 13/14 year olds? (2) How many incident cases are there? (3) Can we predict transition to these incident cases?
Method.– Over 600 school students age 13–14 years were followed-up for 2 years in 4 6-monthly waves, using computer aided data collection. We used the Eating Disorder Examination (self-report) EDE-Q (Fairburn, Cooper, and O'Connor, 2008), a widely used validated measure together with measures of affective dysregulation, self-esteem and BMI.
Results.– The two year period prevalence of partial ED syndromes in 13/14 year olds was 15%. During this period 8% transitioned to de novo partial ED syndromes. The best predictor of transition was raised level of eating/weight concerns on EDQ. Within the EDQ, moderate or severe dieting raises risk of transition to ED by factor of 10 and 23 respectively. Using a ROC curve it was found that and EDQ value of >2.9 best predicted transition.
Conclusion.– Using relatively non-intrusive screening in schools the earliest stages of eating disorders could be identified including those with prodromal features including moderate or severe dieting. The results justify an early intervention approach to screening and early intervention as a realistic method of preventing the early entrenchment of eating disorders in young people. We are now developing an early intervention trial.
Disclosure of interest.– The authors have not supplied their declaration of competing interest.

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Core Symposium: Revision of the International Classification of Diseases – State of the art in ICD-11 Field Studies

CS0011

Current developments in overall ICD-revision on mental, behavioural or neurodevelopmental disorders

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In June 2018, the World Health Organization (WHO) will have released the ICD-11 for implementation by WHO member states. The Clinical Descriptions and Diagnostic Guidelines (CDDG) developed by the WHO Department of Mental Health and Substance Abuse, the diagnostic manual designed for use by mental health professionals in clinical settings, will also be published near the same time published. This session will present an overview of the extensive programme of international and multilingual field studies that have been used to text major innovations in the new system. The initial focus of the field studies was large international surveys of psychiatrists' and psychologists' views of mental disorders classification and the features that would make it maximally useful. This was followed by formative field studies of the structure of clinicians' conceptualization of mental disorders. A systematic program of case-controlled field studies was then implemented using experimental methodologies to evaluate the specific impact of proposed changes to the diagnostic guidelines on clinicians' diagnostic decision-making. Case-controlled field studies were implemented over the internet with members of the Global Clinical Practice Network, consisting of more than 14,000 psychiatrists and other health professionals from more than 150 countries who agreed to participate in field studies related to the ICD-11. Finally, ecological implementation field studies focusing on the reliability and clinical utility of the diagnostic guidelines for ICD-11 mental and behavioural disorders have been implemented in clinical settings in 17 countries, including every WHO region.
Overall, results of the case-controlled field studies indicated significant improvements in the consistency of clinical judgments and clinical utility of the proposed diagnostic guidelines for ICD-11 as compared to ICD-10. Results for specific aspects of the guidelines that did not perform as expected were used as a basis for making improvements in the guidelines. Preliminary data from clinic-based field studies indicate very high reliability and clinical utility for the ICD-11 guidelines across global settings.
Disclosure of interest.– The authors have not supplied their declaration of competing interest.

CS0012

ICD-11 and the future of diagnosis in psychiatry

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The ICD-11 chapter on mental disorders will be the only one in the new diagnostic system – along with those on sleep-wake disorders and conditions related to sexual health, which were part of it in the previous editions of the classification – whose title will not contain the term "disease". As a matter of fact, at the current state of development of our discipline, we are not assuming anymore that all the conditions we are dealing with are discrete disease entities. What we know is that they are patterns of reported experiences and observed behaviours which derive their clinical utility from their ability to allow non-trivial inferences about further course and response to treatment. Indeed, clinical utility has been the organizing principle underlying the ICD-11 chapter on mental disorders and the main focus of the relevant field studies. Are current ICD-11 categories the most clinically useful tools to describe the "patterns" that are the subject of our discipline? This is the key question about the future of psychiatric diagnosis. The two main alternatives to the ICD-11 approach that can be identified at the present are: (a) the one assuming that the domain of psychopathology can be more efficiently described in terms of dimensions; and (b) the one assuming that the neurobiological underpinnings of psychopathology should be the major drivers of psychiatric classification. These two alternatives are currently exemplified by the projects named Hierarchical Taxonomy Of Psychopathology (HiTOP) and Research Domain Criteria (RDoC). Both these approaches, in order to emerge in the future as real alternatives to the ICD-11 classification, will have first of all to prove being at least equally clinically useful, which means equally applicable in ordinary clinical practice, with an acceptable degree of inter-clinician reliability, and at least equally able to guide the choice of treatment and predict outcomes. This will have to be documented in different clinical settings and in the hands of different relevant categories of health professionals. However, a different, much more likely, scenario is that those projects will not turn up to be a basis for a reclassification of psychopathology, but that elements of them will be gradually incorporated in the clinical characterization of individual cases, a step which should always follow that of classification, and which is indeed the other, even more decisive, element of diagnosis intended in its proper meaning. Several pieces of evidence suggest that this is indeed what we are going to witness in the years to come.
Disclosure of interest.– The authors have not supplied their declaration of competing interest.

Core Symposium: ADHD and Addiction, Towards a Consensus

CS0013

Epidemiology of ADHD and SUD

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Attention-deficit/hyperactivity disorder (ADHD) has been primarily considered, for a long time, a childhood condition. Despite it, recent data suggest that symptoms of ADHD continue into adulthood in up to 50% of people diagnosed as affected by ADHD during their childhood. Accurate diagnosis of ADHD in adults is challenging and requires attention to early development and symptoms of inattention, distractibility, impulsivity and emotional liability. Currently, it does not exist a "gold standard" for its diagnosis, and we demonstrated a low reliability of screening test such as the Brown ADD Scales in populations at risk (e.g. acute psychiatric inpatients and parents of children affected by ADHD). Moreover, diagnosis is further complicated by the overlap between the symptoms of adult ADHD and the symptoms of other common psychiatric conditions such as depression and substance abuse. While stimulants are a common treatment for adult patients with ADHD, they are often used as a self-treatment, especially in patients who lack of a correct diagnosis and treatment. Antidepressants may also be effec-

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tive, while cognitive-behavioural skills training and psychotherapy are useful if adjuncts to pharmacotherapy. Addiction thus embodies a key point in differential diagnosis as well as it might be considered an adverse effect of a long duration of untreated illness. As a consequence, it should be accurately checked and weighted during the diagnostic process.
Disclosure of interest.– The authors have not supplied their declaration of competing interest.

CS0014
International statement on ADHD in patients with SUD
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Adult attention deficit/hyperactivity disorder (ADHD) and substance use disorders (SUD) are often co-occurring, and are associated with early onset and more severe development of SUD and with reduced treatment effectiveness. Screening tools allow for a good recognition of possible ADHD in adults with SUD, and should be used routinely, followed by an ADHD diagnostic process initiated as soon as possible. Simultaneous and integrated treatment of ADHD and SUD, using a combination of pharmaco- and psychotherapy, is recommended. Long-acting methylphenidate, extended-release amphetamines, and atomoxetine with up-titration to higher dosages may be considered in patients unresponsive to standard doses. This consensus statement includes evidence- and eminence-based recommendations developed to provide guidance in the screening, diagnosis and treatment of patient with ADHD-SUD comorbidity.
Disclosure of interest.– The authors have not supplied their declaration of competing interest.

CS0015
Treatment of ADHD in patients with SUDs: new evidences
F. Matthys
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The treatment of ADHD in patients with SUD is a delicate matter. Previously caregivers thought SUD had to be under control firstly, but now we know that the treatment of ADHD is best integrated into the addiction treatment. Pharmacologically there are a number of options which, however, need to be adapted. Recent research shows that higher doses of stimulants may be needed.
In addition, psychotherapy is important and effective. This is more difficult to prove through a randomized trial. But there is evolution in that area too.
The existing programs for addiction must be adapted to the limitations of ADHD. Specific skills training is necessary and will be presented.
Disclosure of interest.– In the last 12 months, I have received fees for the following activities:
Advisory boards: Lundbeck, Johnson & Johnson.
Lecturing: Eli Lilly Benelux.
Research funding: Johnson & Johnson.

Core Symposium: Combination of Biomarkers and Epigenetic Signatures: Impact on Psychiatric Disorders and Treatment Response

CS0016
Cortisol secretion and specific methylation profiles: Biomarker of conversion to schizophrenia?
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The effect of stress on brain pathways could participate to the mechanisms underlying the onset of psychotic symptoms, both as a precipitating factor and as a marker of a predisposing vulnerability. This dysregulation fits into the gene × environment model: in subjects with genetic predispositions, stressful environmental factors can modify biological pathways implicated in psychiatric disorders, promoting the emergence of symptoms. However, many confounding factors obscure the literature, and further studies are needed in schizophrenic patients, ultra-high-risk (UHR) and first episode patients (FEP) to clarify the precise role of stress in psychotic transition.
The onset of psychosis is the consequence of complex interactions between genetic vulnerability to psychosis and response to environmental and/or maturational changes. Epigenetics is hypothesized to mediate the interplay between genes and environment leading to the onset of psychosis. We believe we performed the first longitudinal prospective study of genomic DNA methylation during psychotic transition in help-seeking young individuals referred to a specialized outpatient unit for early detection of psychosis and enrolled in a 1-year follow-up. We used Infinium HumanMethylation450 BeadChip array after bisulfite conversion and analysed longitudinal variations in methylation at 411,947 cytosine-phosphate-guanine (CpG) sites.
Here, we report findings from the first French cohort of young help-seekers (ICAAR) including UHR, FEP and non at-risk help seekers controls (HSC), followed by a meta-analysis of all available reports on salivary basal cortisol levels in early psychosis (UHR and FEP). We discuss the main methylomic findings from the same longitudinal cohort.
Disclosure of interest.– The authors have not supplied their declaration of competing interest.

CS0017
Neuropeptide concentrations and epigenetic profiles of patients who remitted from anorexia nervosa: Prognostic biomarkers?
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Introduction.– Anorexia nervosa (AN) is the most severe disorder in terms of morbidity psychiatric illness with the highest mortality rate increased by 23-fold. Treatments have a limited effectiveness. Only one-third of the AN patients evolve to the remission. Deregulations of peripheral control of food intake, hunger signals (ghrelin and obestatin) and satiety signals (leptin and insulin), have been

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reported. These differences could be a consequence or risk factors of the disease due to genetic or epigenetic factors, such as DNA methylation. They could represent useful biomarkers to prognostic the evolution of the disorder to the remission.

Objectives.– We are currently investigating genotyping of polymorphisms and DNA methylation of candidate genes, and we have measured the concentration levels of the neuropeptides encoded by these genes in current AN patients, subjects in remission and healthy control women. Our goal is to replicate the differences of concentration levels between AN, remitters and controls, and to identify in link the differences of genetic variants or in the levels of DNA methylation that affect the gene expression, to characterize biomarkers of prognosis of AN.

Methods.– 100 anorexic patients, 50 remitters, and 200 control women were recruited at CMME (Sainte-Anne Hospital, Paris). They arrived at 8:30 am, fasting since the day before, to take a blood sample, in order to carry out genetic, epigenetic and physiologic analyses. Dosage of ghrelin, obestatin, and leptin were done by EIA or RIA. Single nucleotide polymorphisms of candidate genes were genotyped by Taqman assay. DNA methylation levels were extracted from the data of the Infinium® Human Methylation chip.

Results.– We have confirmed that peripheral control mechanism of food intake is deregulated in AN patients compared to controls. We also report a significant intermediate concentration for remitters. No genetic association was observed. We have identified differentially methylated sites located among candidate genes. We are currently comparing methylated-sites and concentrations between remitters and AN patients to identify prognostic biomarkers.

Conclusions.– At least, leptin and ghrelin dosages might be prognostic biomarkers to remission of anorexia nervosa.

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Disclosure of interest.– The authors have not supplied their declaration of competing interest.

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