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25th European Congress of Psychiatry

## Joint Symposia

### Joint symposium: How long do we have to wait for the antidepressant effect?

JS001

#### Joint symposium: How long do we have to wait for the antidepressant effect? Mechanisms of action for delay of onset response to antidepressants

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Major depressive disorder (MDD) is a severe psychiatric syndrome with very high prevalence and socioeconomic impact. Monoamine-based antidepressant drugs (AD) display slow onset of action and limited efficacy. Preclinical studies show that ADs trigger a series of slow adaptive mechanisms that limit the clinical response. These mechanisms result from the pharmacological blockade of monoamine transporters (SERT, NET) and involve presynaptic, such as autoreceptor desensitization (e.g., 5-HT<sub>1A</sub> and 5-HT<sub>1B</sub> for serotonin neurons) as well as postsynaptic mechanisms, such as increased neurogenesis and expression of trophic factors, increased dendritic complexity, etc.

Given the strong homeostasis of serotonin and noradrenaline neurons, a way to improve antidepressant action is to prevent self-inhibitory presynaptic mechanisms mediated by auto- and heteroreceptors after reuptake blockade. This strategy was used in the past with the non-selective 5-HT<sub>1A</sub> antagonist pindolol and has been incorporated by two recently developed AD (vilazodone and vortioxetine). Likewise, new molecular strategies using RNA interference (RNAi) show that the modulation of gene expression in serotonin neurons offers a great potential. Hence, local or intranasal administration of small interfering RNA (siRNA) molecules targeting SERT or 5-HT<sub>1A</sub> autoreceptors evokes rapid and robust antidepressant-like effects in rodents.

Moreover, glutamatergic drugs such as the non-competitive NMDA receptor antagonist ketamine, offer a potential for the development of fast-acting AD due to its rapid and persistent antidepressant effects in treatment-resistant unipolar and bipolar patients after single i.v. infusion, an effect that likely involves the activation of AMPA receptors in ventral areas of the cingulate gyrus and the subsequent fast activation of serotonergic function.

**Disclosure of interest** F.A. has received consulting honoraria on antidepressant drugs from Lundbeck and he has been PI

of grants from Lundbeck. He is also co-author of the patent WO/2011/131693 for the siRNA and ASO (antisense oligonucleotides) molecules.

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JS002

#### What do clinical trials tell us about antidepressant delayed onset of action?

J. Rabinowitz

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Response to antidepressants in major depressive disorder is highly variable and determinants are not well understood. Presentation will provide clinical trial data on time to response and determinants of response to antidepressant treatment. Data is from the Innovative Medicines Initiative funded NEWMEDS collaboration, a large public-private collaboration which assembled the largest dataset of individual patient level information from randomized placebo-controlled trials of antidepressant drugs. Studies were conducted by four large pharmaceutical companies. Dataset includes placebo-controlled trials of citalopram, duloxetine, escitalopram, quetiapine and sertraline in adults with MDD. We examined patient and trial-design-related determinants of outcome as measured by change on Hamilton Depression Scale or Montgomery–Asberg Depression Rating Scale in 34 placebo-controlled trials (drug,  $n=8260$ ; placebo,  $n=3957$ ). While it is conventional for trials to be 6–8 weeks long, data presented will show that drug-placebo differences were observable at week 4 with nearly the same sensitivity and lower dropout rates. Having any of these attributes was significantly associated with greater drug vs. placebo differences on symptom improvement: female, patients being middle aged, increasing proportion of patients on placebo, excluding all patients from centers with high placebo response regardless of active treatment response, using active run in periods and including self-report measures. Proof of concept trials can be shorter and efficiency improved by selecting enriched populations based on clinical and demographic variables, ensuring adequate balance of placebo patients, and carefully selecting and monitoring centers. In addition to improving drug discovery, patient exposure to placebo and experimental treatments can be reduced.

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## Joint symposium: The value of treatment for brain and mental disorders

### JS003

#### Closing the treatment gap: The EPA case study of schizophrenia

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**Introduction** Schizophrenia still ranks among the first 10 leading causes of disability worldwide. Recent analyses show that there is a considerable treatment gap in schizophrenia in Europe and worldwide.

**Objectives** To provide evidence-based information and give a concise overview of what is needed to overcome the treatment gap in schizophrenia.

**Methods** Using a combined approach of systematic review and health economics was used to assess the socioeconomic impact of medical interventions (or the lack of thereof) for schizophrenia.

**Conclusions** The case study analysis demonstrates socioeconomic impact and health gains of best practices in specific healthcare interventions for schizophrenia in comparison with the cost burden of current care or non-treatment.

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- Lundbeck International Neuroscience Foundation (LINF), Denmark

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### JS004

#### The cost of non-treatment

M. Knapp

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There are large treatment gaps in relation to schizophrenia across all European countries, either because the illness is not recognised or because the response from treatment and care services is inadequate - not evidence-based. This could be because of resource or other constraints. The consequence can be very damaging indeed for individuals with schizophrenia, their families and for the wider society. In this talk I will set out the economic consequences of not identifying or responding appropriately to schizophrenia. Evidence will be drawn from a number of studies, but will be channelled to show new findings in relation to both England and Czech Republic. These figures add to the argument for earlier and better treatment, to benefit everybody including public and private budgets.

**Disclosure of interest** The author has not supplied his declaration of competing interest.

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## Joint symposium with the Italian psychiatric association: Early intervention in psychotic disorders: Comparing models and experiences

### JS005

#### Assertive interventions for first episode psychoses: The Danish experience

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Early Intervention services with team-based intensive case management and family involvement are superior to standard treatment in reducing psychotic and negative symptoms and comorbid substance abuse and improving social functioning and user satisfaction. The results of the OPUS-trial will be presented together with meta-analyses based on similar trials. The implementation of OPUS all over Denmark will be presented together with the Danish OPUS-fidelity study. Specialized elements are being developed such as inclusion of new methods in CBT for psychotic and negative symptoms, neurocognitive and social cognitive training programs, interventions for supported employment and focus on physical health. Results of long term follow-up studies indicate that the prognosis of first episode psychosis is very diverse with the extremes represented by one group being well functioning and able to quit medication without relapse; and another group having a long term chronic course of illness with a need for support to maintain daily activities. The Danish TAILOR-trial—testing dose reduction versus maintenance therapy will be presented. It will be of immense value to be able to intervene in risk groups identified in the premorbid phase, and there are few examples of ongoing trial for children of parent with schizophrenia and bipolar disorder.

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

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### JS006

#### Assertive interventions for first episode psychoses: The Italian experience

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In Italy, despite the favourable conditions created by the 1978 reform law and the community psychiatry, at the end of the past century there were no culture or initiatives oriented to innovative and evidence-based interventions in early psychosis. The watershed was the setting up in the MHD of Niguarda (Milan) of Programma 2000, addressed to FEP and HR mostly inspired by the knowledge of existing studies and experiences and with the recommended characteristics of specificity, multicomponentiality, assertiveness and doctrinal orientation. From the very start, one fundamental aim was to disseminate information, training, supervision, and to raise consensus and initiatives throughout Italy, as well as to improve international links. In many ways, the consequences have been extremely positive. In 2005, Angelo Cocchi and Programma 2000 team founded the AIPP (Italian Association for Early Intervention in Psychosis), now named Italian Association for Prevention and Early Intervention in Mental Health. Over the