S45.02

Dysfunction of the neuroendocrine system: Implications for the treatment of schizophrenia

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There is large evidence that stress plays a crucial role in the pathophysiology and course of many psychiatric disorders. The stress-vulnerability model has been widely accepted for many years. Hypothalamic-pituitary-adrenal (HPA) axis dysregulation has been previously reported in schizophrenia. Patients in the acute phase of the disease seem to have an activated HPA axis (Holsboer-Trachsler et al. 1997) compared to patients who are clinically stable. Results from studies on ACTH regulation are inconsistent. abnormal dexamethasone suppression test (DST) results have been shown in normal aging, depression and schizophrenia. DST non-suppression was associated with cognitive impairment, ventricular enlargement and poorer prognosis (for review: Yeap and Thakore, 2005). Long-term hippocampal exposure to excessive levels of glucocorticoids can induce cognitive dysfunctions due to reduced neuronal volume of this limbic structure. the pharmacological reduction of glucocorticoid excess may help to improve cognitive functioning in schizophrenia.

S45.03

Therapeutic Drug Monitoring and its implications on acute and long-term treatment with neuroleptics

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Therapeutic Drug Monitoring (TDM) is a useful tool to survey individual patients for the correct prescription and dosing of neuroleptic drugs. Confounders for causal drug effect relations are both patient-related and drug-related. An example of a patient-related confounders is problems with compliance to prescribed medication that can be objectively identified or ruled out by TDM in cases of non-response or partial but insufficient clinical response. This problem may arise both in the acute phase of treatment as well as during long-term treatment. Examples of combined patient-related and drug-related confounders are the very individual pharmacokinetic (PK) handling of the drug once the patent has ingested a neuroleptic compound. All such drugs undergo significant metabolism in the body, which is subjected to major inter-individual variability to a large extent due to existence of polymorphic genetic expressions among enzymes responsible for drug detoxification processes in the liver. Moreover, each separate neuroleptic compound, whether its is a classical or an atypical agent, has different affinities for these drug catabolic enzymes. The entire picture of PK-variability existing for antipsychotic drugs is therefore in healthy young male volunteers about one order of magnitude. In real life, i.e. in the everyday naturalistic clinical setting where for example also polypharmacy is a common feature, this variation in the PK between individuals increase 10-fold to be about two orders in magnitude.

This presentation focus TDM-studies where PK-variability and drug PK-effect relations for traditional as well as atypical antipsychotic agents are scrutinized.

S45.04

Pharmacogenetics in first-episode patients with schizophrenia

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Uncertainties in individual response to specific antipsychotics are a major limitation in improving treatment. Pharmacogenetics offers the opportunity to help the clinical decision process by allocating individuum-specific odds for response versus non-response. Pharmacogenetics in schizophrenia has up to now produced only a very limited number of valid results. A main reason might be the heterogeneity of samples under study and lack by standardization of treatment (e.g. mixture of first onset and chronic patients).

The German Competence Network of Schizophrenia has completed a long-term treatment protocol in first-episode patients with schizophrenia (double-blind randomized study with risperidone versus haloperidol). We explored the predictive power of disease-associated variants in disposition genes and modifier genes for schizophrenia. We detected predictive markers in the genes for dysbindin, neuregulin 1 and COMT. These variants were also associated with neuropsychological correlates of schizophrenia.

Thus we can be confident that time has come to improve the tools for prediction of response to antipsychotics.

S46. Symposium: THE 5-HT — ADRENERGIC INTERACTION IN THE PATHOPHYSIOLOGY AND TREATMENT OF DEPRESSIVE DISORDERS

S46

Contemporary approaches for an optimal treatment of major depression

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The pharmacotherapeutic approach to the treatment of major depression consists in giving an optimal dose of an antidepressant medication for a sufficient time. Using this conventional strategy in standard medication trials, approximately half the patients present a response, defined as a 50% improvement, but only about 30-40% generally achieves remission. This is a poor treatment outcome and these numbers have been questioned the patient population tested may be different from those in regular ambulatory conditions. The STAR*D project addressed the latter concern by treating patients all comers, including patients with physical and psychiatric co-morbidities, first with a SSRI and then with switch and combination approaches. Not covered in STAR*D was the strategy of adding an atypical antipsychotic in SSRI-resistant patients. Finally, a novel strategy consists in using two antidepressant medications from treatment initiation.

Wednesday, 21 March 2007
CS08. LONG TERM TREATMENT IN PSYCHIATRY

CS08.01

Long-term treatment of schizophrenic patients

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