FC65-7

TARDIVE DYSKINESIA AND DOPAMINE 3 RECEPTOR GENE MUTATION

Harald N. Aschauer[1]*, J. Scharfetter[1], K. Fuchs[2], E. Gerhard[2], C. Gebhardt[1], E. Lenzinger[1], K. Meszaros[1], K. Hornik[3], W. Sieghart[2], S. Kasper[1]. *[1]Department of General Psychiatry; [2]Division for Biochemical Psychiatry, University Hospital for Psychiatry, 1090 Vienna; [3]Department of Statistics and Probability Theory, University of Technology, Vienna, Austria*

Genetic variability of neurotransmitter receptor genes is hypothesized to play an important role for interindividual differences in treatment response and side effects. The presence of tardive dyskinesia was found to be associated with a specific dopamine D3 receptor gene (DRD3) polymorphism (Ser9Cys substitution).

We set out to test this finding in a sample of schizophrenic patients treated chronically with neuroleptic drugs. After giving written informed consent a structured psychiatric interview was made, applying the Schedule for Affective Disorders and Schizophrenia, lifetime version (SADS-L). A consensus diagnosis blind to the identity of the patients was performed. More than 50 patients who met the DSM-III-R diagnostic criteria for schizophrenia were selected. The DRD3 Ser9Cys polymorphism was genotyped with polymerase chain reaction (PCR). Patients were rated for tardive dyskinesia using the Tardive Dyskinesia Rating Scale. The diagnosis of stable tardive dyskinesia was established following the research criteria for tardive dyskinesia.

The results did not show an association between tardive dyskinesia and DRD3 genotype, as well as tardive dyskinesia with allele 1 oder allele 2 of the DRD3 mutation.

Our results do not replicate an earlier report in the literature. Because this study was a retrospective pilot study we are preparing now a prospectivly designed study investigating possible molecular genetic contributions in the development of tardive dyskinesia.

FC65-8

THERAPEUTIC DRUG MONITORING ROUTINE IN GENERAL PSYCHIATRY

J.A.J. Boermans[1], S. Tuinier[1], W.M.A. Verhoeven[1]*, J.B.G.M. Noten[2], T.M. Jagmont[2], Y.W.M.M. Van den Berg[1]. *[1]Vincent van Gogh Institute for Psychiatry, Venray, 5800 AA; [2]ZALV Pharmaceutical Laboratories, Venray, 5800 AA, The Netherlands*

In man a great inter-individual variability exists in the oxidative capacity to metabolize drugs. A major factor contributing to this phenomenon, is the genetically determined hydroxylation capacity of the cytochrome P450 enzyme system, comprising several isozymes. In this respect, a bimodal clearence distribution has been demonstrated indicating subjects with poor and extensive metabolization rates.

Applying standard dosing schemes of compounds that are predominantly metabolized by these isozymes, a considerable number of patients will be intoxicated because of poor metabolism. Henceforth, cytochrome P450 isozymes are likely targets for pharmacokinetic interactions.

In order to estimate inter- and intrapatient serum concentration variance and hence clearence as a function of metabolic rate, sex, age and comedication in a clinical setting, the total database of our pharmaceutical laboratories over the past five years was evaluated with special reference to: clozapine and SSRI's, TCA's and neuroleptics, monotherapy with SSRI's and ratio's between parent compound and metabolites.

It was found that plasmalevels of clozapine increase substantially by concomitant use of SSRI's, that adding low potency neuroleptics like thioridazine and levomepromazine to the TCA's clomipramine and amitriptyline induces disturbances in biotransformation of both classes of compounds and that the E-hydroxymetabolite of nortriptyline may contribute significantly to the antidepressant efficacy.

It is concluded that routine therapeutic drug monitoring is mandatory not only to reduce toxicity, but also to enhance efficacy and to disclose unexpected abnormalities in biotransformation.

FC66. OCD and eating disorders: biology and epidemiology

Chairs: P Munk-Jørgensen (DK), G Bersani (I)

FC66-1

AUDITORY EVENT RELATED POTENTIALS AND OBSESSIVE COMPULSIVE SYMPTOMS

G. Bersani*, T. Arcangeli, P. Venturi, A. Valchera, I. Taddei. *Department of Psychiatry Science and Psychological Medicine University of Rome "La Sapienza", Italy*

There are few studies in literature about the use of event-related potentials in OCD. The previous studies are often not comparable, as regards methodology, and incomplete or contraddictory in the results. Aim of the study was to investigate a possible relationship between the severity of OC symptoms measured by Y-BOCS (Yale Brown Obsessive Compulsive Scale) and EP (Evoked Potentials) latencies and amplitudes.

We examined 8 male patients (mean age 31.62 ± 13.76 SD) meeting DSM IV diagnostic criteria for OCD, by measuring auditory event-related potentials (ERPs) during a selective attention task.

Event-related potentials were measured in an auditory "oddball" task. We examined N1, N2, P2, and P3 amplitudes and latencies recorded after binaural click stimulation. The evaluation of OC symptomatology was performed by Y-BOCS.

OC subjects were found to have a significantly negative correlation between latencies on N1 ($p < 0.01$), N2 ($p < 0.01$), P2 ($p < 0.002$) and P3 ($p < 0.005$) of the AEP (Auditory Evoked Potentials) and the Y-BOCS item score "time spent on compulsions".

The results are consistent with the current neurobiological models of OCD. The model of an overactive cortical-striatal-thalamic-cortical circuit was proposed in the OCD pathophysiology after the findings by functional neuroimaging. This hypothesis could be confirmed by electrophysiological data. These are the first data about the clinical dimensional aspect of this pathology related to the electrophysiological level, leading to an indirect confirm of the neuroanatomic results.

This study was supported by CNR Grant (MRI-Project years 95–97).

FC66-2

EPIDEMIOLOGY OF OBSESSIVE-COMPULSIVE DISORDER IN YOUNG ADOLESCENTS — A POLISH PERSPECTIVE

A. Bryńska, T. Wolańczyk*, B. Goszczyńska. *Department of Child Psychiatry, Warsaw Medical Academy, 00-576 Warszawa, Poland*

Obsessive Compulsive Disorder (OCD) in childhood and adolescence has been considered a rare and maybe underdiagnosed