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THERAPEUTIC DRUG MONITORING (TDM) AND POPULATION PHARMACOKINETICS (PPK)

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Thymoleptic SSRIs F=fluvoxamine (introduced in Sweden in June 1990), P=paroxetine (June 1991) and C=citalopram (+ desmethylcit.; Oct. 1992) were subjected to postmarketing surveillance by introducing serum RP-HPLC (UV-detect.) analytical methods determining the F (from Oct. 1992), P (Nov. 1992), and C (April 1993) for routine use in southern Sweden (pop. 3 mill). Specifically designed TDM-request forms were used to acquire adequate clinical data. Stratification of the data made us perform traditional statistics as well as PPK modelling on this large and naturalistic clinical phase-IV cohort. By June 1994 the collection of such data amounted to 363 (F), 775 (P) and 778 (C) TDM-analyses. Eligible data were subjected to NONMEMR PPK-calculations and as an example the paroxetine estimates from two time points (Oct. 1993; 129 TDM-analyses/115 patients and June 1994; 333 TDM-analyses/268 patients) displayed: elim t1/2 to be dependent on sex and co-medication; t1/2 = males 28 h vs. females 36 h. Vd was dependent on sex; males 281 L vs. females 406 L. Oral clearance (Clo) was dependent on sex, age and co-medication::

Patient age (years)	20	40	60	80
Clo at monotherapy (L per h); Males	38	32	26	19
Females	29	24	20	15

PPK calculations for F and C will be discussed in detail in the presentation. Developing clinical trials TDM-routines for the SSRIs served several important purposes. Firstly, the physicians were assisted in optimizing their dosing strategies for each individual patient in the complex true clinical setting where these drugs are used. Secondly, as exemplified, the PPK modelling for P unravelled clearcut abberations in kinetic features in agreement with the scarce reports found in the literature. We submit that this clinically relevant postmarketing surveillance strategy has the potential to greatly improve drug safety in psychiatric practice.

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SUPERIOR TEMPORAL GYRUS VOLUME (STGV) IN SCHIZOPHRENICS

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Since precedent studies showed an association between auditory hallucinations in schizophrenia and some pathologic areas in left temporal lobe (1), we measured STGV to examine this hypothesis

We derived by MRI measurements of the anterior STGV in 15 right-handed men (mean age 27 5±7.5 SD) with a DSM-III-R diagnosis of Schizophrenia (undifferentiated, N=6, paranoid, N=5, disorganized, N=2, catatonic, N=2) and in 15-age-and-sex-matched healthy controls

Anterior SGTV was measured in three consecutive coronal 4-mm-slices (two where the amygdala was visible, plus the next anterior slice)

SGTV in the two hemispheres was almost the same size in controls, while in the schizophrenics we found a 20% reduction in the left side. As compared with controls, patients showed significant reductions in the left anterior SGTV (in the right side by 9% and in the left side by 14%) and a positive correlation between percent difference in left SGTV and SAPS-auditory-hallucinations score ($p < 0.05$)

The results suggest that a reduction of the left STGV in schizophrenic subjects appears strongly correlated with severity of auditory hallucinations

Our finding agrees with previous MRI, SPECT (2) and PET (3) studies that report a volumetric and functional reduction of the left STG in schizophrenic patients withs severe auditory hallucinations

(1) Barta P E, Pearlson G D, et al Auditory hallucinations and smaller superior temporal gyral volume in schizophrenia American Journal of Psychiatry 1990,147 1457-1462

(2) McGuire P K, Shah G M, Murray R M Increased blood flow in Broca's area during auditory hallucinations in schizophrenia Lancet 1993,342 703-706

(3) Cleghorn J M, Franco S, et al Toward a brain map of auditory hallucinations American Journal of Psychiatry 1992,149 1062-1069

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CORPUS CALLOSUM AREA (CCA) IN SCHIZOPHRENIC PATIENTS

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Since some observations in schizophrenic subjects suggest a sexual dismorfism in CCA, where "schizophrenic women account for most of the variance "(1), aim of the study was to verify whether there are some differences in MRI CCA measurements between male individuals discordant for schizophrenia. Moreover, to examine the hypothesis suggesting an association between hallucinations and a disruptes interhemispheric communication in schizophrenia (2), we investigated possible correlates between CCA and SAPS-hallucination scores

We used MRI techniques to derive CCA measurements in 18 men (mean age = 28 2±8 4 SD) meeting DSM-IIIR diagnosis of schizophrenia and in 18 age-and-sex-matched healthy controls

We measured by a 4-mm-slice midsagittal section brain area (BA), CCA and CCA to BA ratio (CCBR).

Schizophrenic patients and controls showed by the ANOVA analysis a homogeneous BA, CCA and CCBR value

In the schizophrenics CCBR correlated at a positive statistically significant level ($p < 0.05$) with SAPS-total-hallucination and SAPS-auditory-hallucination scores

The results confirm previous studies (3), indicating the existence of sexual dismortism, in some brain areas, in schizophrenia. In addition, our finding of an increase in the severity of hallucinations related to the size of CCA support the intriguing hypothesis linking an unintegration of the hemispheres potentially independent thoughts with the hallucinatory symptoms in schizophrenia.

(1) Nasrallah H.A, Andreasen N.C, Coffman J A, Olsen S C., Dunn V D, Ehrhardt J, Chapman S A controlled Magnetic Resonance Imaging study of corpus callosum thickness in schizophrenia Biological Psychiatry 1986,21 274-282

(2) Doty R., Schizophrenia a disease of interhemispheric processes at forebrain and brainstem levels ? Behavioural Brain Research 1989,34 1-33

(3) Cowell P E., Kostianovsky D J, Gur R C, Turetsky B I., Gur R E Sex differences in Neuroanatomical and Clinical Correlations in Schizophrenia American Journal of Psychiatry 1996,153 799-805

This study was supported by CNR grant (MRI-Project 1995-1997)

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A FOLLOW UP STUDY OF THE TREATMENT OF FRAGILE X SYNDROME

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A follow up study of the treatment of Fragile X patients: To show positive results in patients with fragile X syndrome, after several years of control - all patients to be included in our study underwent different treatments without positive results. In this way the patient controlled himself. Everyone had done a chromosom study, a psychiatric interview and a topographic brain tomography when needed. We made an agreement with the patients' family saying that the patient will receive a trial treatment for 4 months with a monthly evaluation. Expectatives were that clinical changes must be clear enough so that everybody could see them. Lithium, haloperidol, folic acid, vit. E, nicotinamide and GABA were given - 90% improved. In general there was an improvement in learning capacities in 67%, attention and hiperkinesia in 61%, writing in 62%, social behavior in 33%. Side effects were seen in 1.2% as slightly excited or nervous. Side effects disappear when medication was withheld for 72 Hs. and lower doses were used. Quality of life for both patients and family improved.

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