S6 *Neurophysiology in psychiatry: ..*

## P300 ABNORMALITIES IN SCHIZOPHRENIC SUBGROUPS: CLINICAL IMPLICATIONS AND PERSPECTIVE

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P300 amplitude reductions and right lateralized peaks have been repeatedly described and are considered to be typical for schizophrenia. However, the clinical implications and the relations with schizophrenic subgroups have been delineated only recently. In a series of studies, our group has shown that stable and characteristic alterations of the P300 component are found at remission of the psychotic episode in schizophrenia. Furthermore, it was shown that a subdivision of DSM-III-R schizophrenia based on Leonhard's classification was necessary to obtain reliable results. Cycloid psychoses showed a significantly higher global field strength of the P300 component while core schizophrenics had slightly lower amplitudes than controls and right lateralized P300 peaks. In a dimensional approach, the field strength was inversely correlated with cross-sectional negative symptoms, and longitudinally with the global social impairment. Manic patients, on the other hand, had normal field strength and topography after remission of the episode. The findings show that there are specific P300 features in schizophrenic subgroups which appear to be useful for diagnostic and prognostic purposes.

S7 *Parental pharmacological treatment of depression: ...*

## Intravenous treatment of depressive patients with antidepressants

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Intravenous application of antidepressant drugs is a well established procedure, especially for so-called therapy-resistant inpatients (Kielholz et al. 1982). As advantages of infusion therapy the following factors have been reported: a more rapid onset of action, an increased therapeutic effect due to higher plasma levels (avoiding first-pass effects and incomplete absorption), fewer side effects by using lower doses, assured compliance and psychological factors. Remarkably few controlled, double-blind studies comparing drip infusion therapy with oral antidepressant treatment have been published, however (Laux et al. 1997 for review). A review is given regarding the drugs available and the data base of efficacy and tolerability. The WHO collaborative study (Gastpar et al. 1986, Kielholz et al. 1990) and a double-blind study comparing doxepin i.v. vs. oral including determination of plasma levels (Laux et al. 1989) are referred as the extensive studies available in this topic.

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S7 *Parental pharmacological treatment of depression: ...*

## PHARMACOKINETIC AND PHARMACODYNAMIC RATIONALE FOR PARENTERAL ADMINISTRATION OF ANTIDEPRESSANTS

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The major consequence of administering a drug parenterally instead of orally is that the first passage of the drug through the intenstine mucosa, the portal vein and the liver in avoided. For many antidepressants, a substantial fraction of an oral dose will be metabolised during this first pass. The metabolism may lead to elimination of active compounds (e.g., hydroxylation and glucuronidation) or to formation of active metabolites (e..g, through demethylation). AS shown for imipramine, the hydroxylation process is saturated during the first pass causing a shift towards demthylation (formation of desipramine). Parenteral administration of imipramine thus, compared with oral administration, results in relatively higher ratio of imipramine vs desipramine in blood. This may have qualitative pharmacodynamic consequences if the parent compound and the desmethyl metabolite have different effects. For imipramine and clomipramine, the parent compound has a strong serotonergic effect whereas the desmethyl metabolite is largely adrenergic. Parenteral administration of these compounds thus will result in a relatively strongly serotonergic effect. For venlafaxine (V) with 4 active compounds (R and S V and R and S O desmethyl V) all with dual serotonergic/adrenergic effects, the picture is even more complex. The relative importance of serotonergic and adrenergic effects for the antidepressant response is currently debated, and the possible advantages of using parenteral administration ought to be rigorously tested in randomised trials.

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## Intravenous treatment of depressive patients with an SSRI, citalopram: Clinical and pharmacokinetic aspects

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The psychological and potential psychotherapeutic effects of a slow drop infusion procedure in the initial phase of pharmacological treatment of severely depressed patients still needs to be the subject of systematic and controlled investigations (1). Citalopram (CIT), a SSRI (2), is available for infusion.

A multicentre, double blind, double dummy, parallel group, fixed dose study was carried out in two groups of 30 depressive patients to compare efficacy and tolerance of CIT. The drug was given either intravenously (placebo orally) or orally (placebo intravenously) for 10 days (40 mg/day) and then orally till day 42. CIT was measured in plasma (days 10, 21, 42) of the CYP2D6/CYP2C19 phenotyped patients.

On day 11, 33.3% of those patients receiving infusion had a >50% reduction in their baseline HDRS-17 score compared to 17.9% of patients receiving oral medication. At the end of the trial (day 42), there were similar levels of responders (IV-PO: 66.7%, PO-PO: 63.3%). There were no obvious differences with regard to the side effects profile of CIT, between the groups.

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