following hormones up to the epinephrine. An excess of tyrosine and a scarceness of epinephrine are always present. the deficit of Epinephrine is measurable instanteneously only, in the moments of failure adaptation to the stress when the fits from schizophrenic symptomatology reach their peak because the enzymes have the function of to catalyze the biochemical transformation making her around 200 times faster. For this reason the historical searches around the alterations of the epinephrine, strongly suspect of to be the cause of the schizophrenia, they have given negative result always. The techniques that we can use for centering the diagnosis are two: The first one consists in to effect under stress an opportune test: 1) – test of the enzymes of synthesis of the epinephrine beginning from the Tyrosine: tyrosine-hydroxylase, L-aromatic amino acid decarboxylase, dopamine-α-hydroxylase, phenylethanolamine-N-methyl transferase; while the second, since the geniuses that synthesize the aforesaid enzymes have been already isolated, to use the same procedure to verify the deficit and/or the alteration of such geniuses. The treatment consists in to replacing such geniuses with healthy geniuses and introducing such cells cloned in the human organism to cure.

P46. Psychopharmacology – clinical

P46.01

Pharmacokinetics of psychotropics

S. Tuinier*, W.M.A. Verhoeven, A.E.S. Sijben. *Vincent van Gogh Institute for Psychiatry, Venray, The Netherlands*

Therapeutic Drug Monitoring (TDM) is a well recognized instrument to enhance therapeutic efficacy of psychotropics and to detect pharmacokinetic factors involved in treatment resistance. Over a period of 5 years the results of TDM were analysed yielding a total of 4000 samples.

The first objective was to establish a relationship between dosage and plasma concentration, the second to evaluate the effects of age and sex. From the total group, data were available on the antidepressants: amitriptyline (n=271), clomipramine (n=584), fluvoxamine (n=515), imipramine (n=165) and nortriptyline (n=253), and on the antipsychotics: clozapine (n=93), haloperidol (n=30) and thioridazine (n=41). For the other psychotropics only small groups were present.

With respect to sex, a male-female difference was found for clozapine and nortriptyline in that females appeared to have higher plasma concentrations. Concerning the dose-plasma concentration, a relationship was observed for nortriptyline, fluvoxamine, amitriptyline and clomipramine, but not for clozapine.

Preliminary analysis showed that about 20 percent of the values are outside the more or less established therapeutic range. In addition, major effects of age on the plasma concentrations of various compounds were observed.

P46.02

Valproic acid in unstable mood disorder

S. Tuinier*, W.M.A. Verhoeven. *Vincent van Gogh Institute for Psychiatry, Venray, The Netherlands*

Since the beginning of the last century, cyclic changes in behaviour and mood that do not meet the criteria for bipolar affective disorder, have been reported in patients with developmental disorders. Based on data from factor analytical studies, we recently postulated the concept of unstable mood disorder in mentally retarded patients that is characterized by a cyclic alteration of behaviour associated with an episodic pattern of disturbed mood and/or anxiety.

In the present study including 28 mentally retarded patients with a long history of episodic changes in behaviour and affect, a diagnosis of unstable mood disorder was established. Following a baseline controlled design treatment with valproic acid was started with dosage adjustments according to plasma levels. Treatment period comprised six months (n=7) to one year (n=21). As assessed with the CGIS moderate to marked improvement was observed in 19 patients that included stabilization of behaviour and mood as well as reduction of symptoms belonging to the mood, anxiety and motor domains.

It is concluded that valproic acid is an effective treatment in unstable mood disorder.

P46.03

Atypical antipsychotics in schizophrenia; efficacy and effect on serotonergic parameters

S. Tuinier*, W.M.A. Verhoeven, F.M.M.A. van der Heijden, A.E.S. Sijben. *Vincent van Gogh Institute for Psychiatry, Venray, The Netherlands*

In an ongoing research project the atypical antipsychotics risperidone, olanzapine, sertindole and quetiapine were investigated in patients with an acute episode of schizophrenia. For the various atypical antipsychotics, groups of at least 20 patients who completed the experimental period of 14 weeks were analysed.

The studies followed an open baseline-controlled, prospective design. The compound was administered in a flexible dose during the first 6 weeks to achieve optimal individual dosages and thereafter doses were kept unchanged. As response criterium served in all substudies a reduction of at least 40% on the BPRS total score.

Secondary efficacy measures were PANSS and CGI. Analyses were performed on a intent-to-treat basis and were calculated with a repeated measurement procedure (MANOVA).

For all four atypical antipsychotics a modest treatment response was observed. No specific effects on affective or negative symptoms could be demonstrated.

With respect to serotonergic parameters, at baseline no differences were found between responders and non-responders. In the non-responding group, however, a significant increase of these parameters emerged suggesting the presence of a pre-existing down regulation of the serotonergic receptor system.

P46.04

Citalopram in mentally retarded patients with depression

W.M.A. Verhoeven*, S. Tuinier. *Vincent van Gogh Institute for Psychiatry, Venray, The Netherlands*

Affective disorders in patients with mental retardation should be considered when an episode occurs with changes in affective equivalents, motivational behaviour, motor activity or vital signs. Although the efficacy of several antidepressants in this patient group has been established, various specific risk factors have to be considered such as higher vulnerability for anticholinergic and motor side effects.

In the present study following a baseline controlled, long-term open design, the effect of citalopram was investigated in 20 mentally retarded patients suffering from a depressive disorder characterized by alterations in the domains of affectivity, motivation, motor activity and vital signs. Citalopram was started in a daily dosage of 20 mg that was kept unchanged for six weeks. Thereafter dosage was adjusted to maximally 60 mg per day. Treatment effects were assessed with the CGIS after at least six months.

https://doi.org/10.1016/S0924-9338(02)80809-4 Published online by Cambridge University Press