P45.39

P300 Brain Microstate in deficit and nondeficit schizophrenia

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Topographic abnormalities of the auditory P300 in schizophrenia have been found in several studies, usually indicating an impairment of the left hemisphere regions. However, both negative and conflicting results have also been reported. It has been suggested that discrepancies in findings might be related to the heterogeneity of the syndrome. Thus, the investigation of more homogeneous subgroups of schizophrenic patients may represent a valuable strategy in the study of topographic characteristics of P300 in patients with schizophrenia.

In the present study, we investigated the topography of the auditory P300 in 10 deficit (DS) and 13 nondeficit (NDS) stabilized schizophrenics, and 12 sex-, age- and education-matched healthy controls (HC), by means of the so-called 'Brain Microstates' technique.

P300 field strength was significantly reduced in NDS with respect to both HC and DS, and was inversely correlated with psychopathology and duration of illness. A rightward shift of the P300 field was observed only in NDS, and was associated with higher scores for positive symptoms.

Our findings suggest abnormal left hemisphere functioning in subjects with nondeficit schizophrenia.

P45.40

Neurological soft signs (NSS) in schizophrenia

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The study of the presence and severity of Neurological Soft Signs (NSS) in schizophrenic patients (N= 94) has been object of a line of research that investigated demographic, clinical and neurological variables of the illness. NSS have been assessed by the Neurological Evaluation Scale (NES) of Buchanan et al. (1989). Some preliminary meaningful results of the can be presented:

Epidemiological variables (N=94). Significant correlations emerged between Mean Age and Complex Motor Acts (p=.05) as well as between Educational Level and NES total score (p=-.02).

Seasonality of birth (N= 86). No significant correlations emerged.

Obstetric Complications (Presence N= 14 vs Absence N= 18). Mirror Movements to the left (p= .034) and Finger Nose Opposition to the left (p= .034) are higher in patients group without OC; Left-Handedness is higher in the group with presence of OC (p=.032).

Family history (positive N= 45 vs negative N= 49). Sequencing of Complex Motor Acts (p= .05) and Sensory Integration (p= .016) are significantly prevalent in patients without family history of schizophrenia.

Psychopathology (N= 94). Significant correlations emerged between: SANS total score and Motor Coordination (p= .02 1); Alogia and Motor Coordination (p= .026); Flat affect and Motor Coordination (p= .046); SANS total score and Sensory Integration (p= .017); Alogia and Sensory Integration (p= .007); Apathy and Sensory Integration (p= .037); Thought Disorder and Sequencing of Complex Motor Acts (p= .048).

CT measures of cortical and subcortical brain structures (N= 36). No significant correlations emerged.

Conventional and atypical neuroleptic treatments (Haloperidol N= 34; Risperidone N= 18; Clozapine N= 32; Olanzapine N= 10). Romberg test is higher in the haloperidol treated patients group (p = .028) and Tremor to the right is higher in the olanzapine treated patients group (p= .037).

Cannabis use (Consumer patients N= 25 vs No-consumer patients N= 25). NES total score (p=.009), Motor Coordination (p=.002), Complex Motor Acts (p=.005) and Sensory Integration (p=.05) are higher in the group of no consumer patients. The results suggest a substantial independence of NSS from considered variables. The evidence of the correlations with negative symptoms could be considered as a dysfunctional finding of structural alterations in deficit syndrome.

P45.41

Biochemical origin of the schizophrenia and of the behavioral pathologies of schizoid type

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The complexity of the pathological mechanism of the schizophrenia is due to the diversifies biochemical expression. Nevertheless a common factor exists. It is identified in the enzymatic deficit, for genetic defect, in the biochemical formations and transformations, along the way to cascade of the signals of hormonal nature from the NSC to the final hormone. The NSC receives signals from the external surrounding and/ or from the internal "milieu", it analyzes them and orders triggering the system to cascade, for the secretion of the hormone from the organism required. The pathology is characterized from the deficit and/or from the alteration of one or more cerebral neurotransmitters among which the catecholamines, the serotonin and of the glucocorticoid cortisol hormone. Such deficit originates from an alteration or scarceness of genes that codify the synthesis of the enzymes delegated to their production and transformation (this is the common factor, the scarceness of enzymes synthesized from the genes, with the ambivalent consequence of a deficit, in comparison to that requirement of the organism, and of an inopportune production of abnormal metabolites might be produced: The adrenochrome that causes psychotic states and the dimetoxiphenylethylamine, a substance from the intermediate chemical structure between epinephrine and mescaline that has been found in the urines of schizophrenic patients (Piergiorgio STRATA 1991). The mescaline, whose property psicodislettiches are well known, besides, might be produced by chemical alteration of the dopamine and norepinephrine, similar substances structurally. The alteration of the epinephrine, of the norepinephrine, might to give place to the LSD or to a substance from the similar chemical structure. The synthesis of epinephrine might to remain blocked for scarceness of one or more enzymes in the followings biochemical transformations: 1) Tyrosine-dopa for scarceness of enzymes tyrosine hydroxylase 2) Dopa-dopamine for scarceness of enzymes L-aromatic amino acid decarboxylase 3) Dopamine-norepinephrine for scarceness of enzymes dopamine-β-hydroxylase 4) Norepinephrine-epinephrine for scarceness of enzymes phenylethanolamine N-methyl transferase.To follow of the deficit and/or altered productions of epinephrine, the NSC warns an inadequacy to the stress and orders to the adenohypophysis, by electrical/ chemical signals to the limbic system and from this to the hypothalamus, the production of ACTH. Besides, the removal of the feed negative back constituted from the scarceness of epinephrine causes an increase of ACTH production to leave out of consideration of the signal from the NSC induced. It is produced so in the organism an inopportune increase of hormones along the system of biochemical transformations beginning from the tyrosine, up to that hormone that cannot be synthesized for scarceness of the enzyme delegated to its synthesis, and a scarceness of the

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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

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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

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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

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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

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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.

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