[3] Margolese, H.C., Chouinard, G., Beauclair, L., et al., 2002. Therapeutic tolerance and rebound psychosis during quetiapine maintenance monotherapy in patients with schizophrenia and schizoaffective disorder. J Clin Psychopharmacol, 22: 347–352.

P.5.017 Use of valproate in treatment of behavioural and psychological disturbances of dementia

M. Perini*, A. Carnicelli, F. Bollini. *S.Antonio Abate Hospital, Neurology, Gallarate, Italy*

Purpose: The major objective was to pharmacologically control the behavioural and psychological symptoms of dementia (BPSD) without the use of neuroleptic agents, which are well known for their extrapyramidal, hypotensive, and cognitive effects. In this way, the use of atypical antipsychotic (AAP) drugs should be avoided, which are undesirable in geriatric patients due to increased cerebrovascular risk [1]. The authors report their experience in the treatment of BPSD using a sustained release valproate formulation (VPA-SR).

Methods: During the period from May 15, 2004 to Feb 28, 2005, the incidence of BPSD in patients affected with dementia of various origin was evaluated. All patients were either in therapy with AAPs for early diagnosis of BPSD or were newly diagnosed with BPSD and therefore had never undergone therapy with sedative agents. Selected patients underwent treatment with, or switched to, VPA-SR and were observed for a period of three months. BPSD was evaluated using the Neuropsychiatric Inventory (NPI) scale described by Cummings.

Results: Of a total of 507 patients affected by dementia, 60 cases with BPSD (11.8%) were treated with VPA-SR (500 mg/day), including 32 females and 28 males with an average age of 78 years. Of these 60 patients, 35 switched treatment from AAP to VPA-SR, while 25 took VPA-SR as first-line therapy for BPSD. Of those switching therapy, all had good control of behavioural symptoms with AAPs. After three months of therapy with VPA-SR, seven patients (11.7%) suspended therapy due to inefficacy, although no collateral effects were observed. For the remaining 53 cases, the NPI score indicated that the BPSD were stabilized in those previously treated with AAPs, and were reduced in those cases in first-line therapy with VPA-SR, with the exception of items related to hallucinations and delirium.

Conclusions: Improvement in BPSD after treatment with valproate were previously reported and this drug is especially well-tolerated in geriatric patients [2,3]. The present report confirms the therapeutic effectiveness of VPA-SR in patients newly-diagnosed with BPSD. Moreover, the therapeutic efficacy of VPA-SR and AAPs was similar in patients subjected to a therapeutic switch, with the exception of symptoms related to psychosis (delirium, hallucination). Only in patients with these symptoms, even though present in only a minority of cases, treatment with antipsycotic drugs is preferred. This is the first report on an indirect comparison between VPA-SR and AAPs.

References

[1] Risperdal (risperidone) and Cerebrovascular Adverse Events in Placebo-Controlled Dementia Trials: Letter to Healthcare Professionals. 2004.Toronto, Janssen-Ortho. http://www.janssen-ortho.com/JOI/en/.
[2] Porsteinsson AP et al, 2001, Placebo-controlled study of divalproex sodium for agitation in dementia. Am J Geriatr Psychiatry 9(1): 58–66.
[3] Sival RC et al, 2002, Sodium valproate in the treatment of aggressive behaviour in patients with dementia: a randomized placebo-controlled clinical trial. Int J Geriatr Psychiatry. 17(6): 579–85.

P.5.018 Nicotinic agonist RJR-2403 improves cognitive performance in old female rats with experimental dementia of Alzheimer's type

N. Platonova*, J. Fedotova, N. Sapronov. *Institute for Experimental Medicine, Neuropharmacology, St. Petersburg, Russian Federation*

Statement on the purpose of the study: Estrogen is thought to enhance cognitive functions by modulating the production of acetylcholine in basal forebrain neurons, a system that projects to the cerebral cortex and hippocampus and plays a central role in learning and memory. The present work was devoted to the comparative analysis of the cognitive status in intact and ovariectomized (OVX) old female rats with experimental dementia of Alzheimer's type chronically receiving either selective nicotinic agonist – RJR-2403 or nicotinic antagonist – mecamylamine alone or in a combination with 17b-estradiol.

Methods: The OVX old females have been treated with RJR-2403 (1.0 mg/kg, i.p.) or mecamylamine (1.0 mg/kg, i.p.) alone or in a combination with 17b-estradiol (0.5 mkg per rat, s.c.) during 14 days. The acquisition of passive avoidance response (PAR) and active avoidance response (AAR) were assessed. Statistical processing of the received data was carried out with use of one-way ANOVA test and post-hoc test at $p < 0.05$.

Results: RJR-2403 alone or in combination with significantly ($p < 0.05$, ANOVA) improved 17b-estradiol PAR and AAR in old OVX female rats receiving β-amyloid. On the contrary, mecamylamine administration failed to increase PAR and AAR in old OVX female rats receiving β-amyloid. Thus, these data indicate the role of the brain N-cholinergic system in the control of the cognitive functions status in old ovariectomized female rats with experimental dementia of Alzheimer's type.

Conclusions: These findings could have important implications for the effective use of hormone replacement and cholinotherapy strategies in the prevention and treatment of Alzheimer's disease and age-related cognitive decline in imbalance of estrogen.

Supported by RFBR grant 04–04–49025.

P.5.019 Plasma levels of tumor necrosis factor-alpha (TNFα) in first-episode bipolar disorder and schizophrenia patients

A. Palomino[1]*, A. Aldama[2], M.O. Rojas-Corrales[3], J.A. Micó[3], F. Mosquera[2], A. González-Pinto[2], C. Matute[1]. [1]*University of the Basque Country, Neurosciences, Zamudio (Bizkaia), Spain;* [2]*Santiago Apostol Hospital, Psychiatry, Spain;* [3]*University of Cádiz, Neuroscience, Spain*

Introduction: Immunological dysfunction at different structural and functional levels of the immune system has been suggested to play a role in the psychosis pathophysiology. However, current evidence remains controversial. We have analysed the plasma levels of TNFα, a hallmark pro-inflammatory cytokine, in first-episode bipolar disorder and schizophrenic patients.

Method: We studied TNFα plasma levels in 40 patients with a first-psychotic episode in the health catchment area of Vitoria in 2002–2004. In accordance with DSM-IV, 8 were diagnosed of bipolar disorder, 20 of schizophrenia, and remaining 12 of other psychotic disorders. Blood samples were taken upon arrival into the emergency room and processed following standard procedures. In addition, samples were taken from healthy volunteers that were

matched for sex and age. Plasma levels of TNFα were measured by ELISA, using the sandwich technique.

Results: Levels of TNFα in both controls and patients typically ranged between 5 and 25 pg/ml. Bipolar disorder patients showed large variability and a non-statistically significant TNFα increase of about 50% in average. Instead, schizophrenic patients displayed a significant reduction of 30% in the plasma levels of TNFα. Finally, no changes were measured in patients with other psychotic disorders. Comment: These preliminary results point to immunological alterations at the onset of bipolar disorder and schizophrenia. Ongoing studies on a larger sample will definitively clarify whether blood levels of TNFα are dysregulated in these diseases. The well established role of TNFα as a cell survival and death factor as well as a regulator of gene expression in the CNS may be relevant to the etiology of major mental disorders.

P.5.020 Plasma levels of brain-derived neurotrophic factor (BDNF) in first-episode bipolar disorder and schizophrenia patients

A. Palomino[1]*, A. Aldama[2], F. Mosquera[2], G. González-García[1], A. González-Pinto[2], C. Matute[1]. [1]*University of the Basque Country, Neurosciences, Zamudio (Bizkaia), Spain;* [2]*Santiago Apostol Hospital, Psychiatry, Spain*

Introduction: Impaired brain development is implicated in the etiology of schizophrenia and other psychotic disorders. Brain-derived neurotrophic factor (BDNF), the most abundant neurotrophin in the brain, promotes growth and maintenance of connections, serves as a neurotransmitter modulator, and participates in plasticity mechanisms such as long-term potentiation and learning. Consequently, abnormal signaling of BDNF can influence neuronal differentiation and synaptic function leading to altered brain development and functioning. Here, we have analyzed the plasma levels of BDNF in first-episode bipolar disorder and schizophrenic patients.

Method: We studied 36 patients with a first-psychotic episode in the health catchment area of Vitoria, Spain, in 2002–2004. In accordance with DSM-IV, 8 were diagnosed of bipolar disorder, 18 of schizophrenia, and the remaining 10, of other psychotic disorders. Blood samples were taken upon arrival into the emergency room and processed following standard procedures. In addition, samples were taken from healthy volunteers that were matched for sex and age. Plasma levels of BDNF were measured by ELISA, using the sandwich technique.

Results: Levels of BDNF in both controls and patients typically ranged between 1.5 and 20 ng/ml. Bipolar disorder patients showed large variability and a non-statistically significant BDNF decrease of about 30% in average. Schizophrenic patients displayed a significant reduction of 35% in the plasma levels of BDNF. Finally, a non-statistically reduction of about 15% were measured in patients with other psychotic disorders. In addition, a follow-up study of 11 schizophrenic patients showed that BDNF plasma levels remained similarly low at 4 weeks after the first psychotic episode and rose thereafter at six months and 1 year to control values.

Comment: These preliminary results show that plasma levels of BDNF are decreased at the onset of schizophrenia and possibly also in bipolar disorder. In addition, these findings point to neurodevelopmental impairments, driven at least in part by BDNF, at the onset of these psychiatric diseases. Ongoing studies on a larger cohort of patients will definitively clarify whether plasma levels of BDNF are dysregulated in these diseases and if specific treatments after the first psychotic episode normalize the synthesis of this growth factor.

P.5.021 Semax treatment effects in patients with postradiation brain lesion

L. Zhavoronkova[1]*, N.B. Kholodova[2], O.A. Krotkova[3], N.V. Gogitidze[4]. [1]*Inst. of Higher Nervous Act. & Neurophysiology RAS, Clinical Neurophysiology, Moscow, Russian Federation;* [2]*Rentgenoradiological Center, RAMS, Dept. of Radiology, Russian Federation;* [3]*Burdenko Neurosurgical Institute, RAMS, Dept. of Rehabilitation, Russian Federation;* [4]*Burdenko Neurosurgical Institute, RAMS, Dept. of Neuropsychology, Russian Federation*

Introduction: It is known that patients with consequences of exposure to radiation suffered a lot from immunodeficiency, psycho-emotional and memory impairment (Zhavoronkova et al., 1995, 2002). Previous experimental and clinical studies showed that Semax (synthetic ACTG analogue, Russia) treatment proved to be an effective CNS status regulator, adaptogen and a modulator of memory processing (Kaplan et al., 1996). The purpose of the present study was to evaluate the efficacy of Semax treatment in patients with remote consequences of exposure to radiation accompanied by psycho-organic and memory disorders.

Methods: Open randomised case-controlled clinical, EEG and neuropsychological study of Semax effect was performed in 45 Chernobyl patients (aged 47.3+6.5) who gave consent to participate in this trial. For 7 days Semax was administered intranasally (dosage – 0.030–0.050 mg/kg). Ten persons from patients group took part in placebo experiment. The other patients entered studies without any treatment. Data of 25 healthy persons were used as a control. EEG, neuropsychological and clinical examination was performed before and after drug treatment. Neuropsychological study included evaluation of memory, mental and emotion functioning. Psycho-neurological status was examined during clinical examination. EEG study was based on visual inspection, power and coherence mapping and dipole source localisation analysis.

Results: EEG examination showed that before treatment all patients had low level of power and EEG coherence (intra- and interhemispheric) in all deviations ($p < 0.01$, ANOVA). After treatment course values of interhemispheric EEG coherence demonstrated the increase of EEG coherence in central and frontal leads the most evident in theta- and alpha-bands ($p < 0.05$) and had a tendency to normal values approximation. These EEG coherence data most corresponded to the results of neuropsychological study and demonstrated improvement of memory processing (87.5%) and psycho-emotional functions (90.5%). The clinical study showed decrease of headache (75.5%), increasing of capacity for work (87.5%). In general, an improvement in neurological, psychological and physical status and EEG signs after Semax treatment was observed in 93.3%. Results of placebo and longitudinal examinations without any treatment showed no sufficient changes in status and EEG of patients.

Conclusion: The obtained results showed that Semax might be recommended for treatment of patients in remote terms after irradiation. Our investigations and literature data permitted us to propose that Semax influenced brain functions, probably diencephalic and limbic structures and cortical-subcortical interaction as well as provide improvement of patients' quality of life.