group versus I group (by 232.2% and 310.5% accordingly). All the drugs (especially pramiracetam) increased its level in a varying degree (table 1).

**Conclusion:** Course administration of neuroprotective drugs piracetam, pramiracetam and Ginkgo biloba extract in conditions of experimental alloxan diabetes was established to promote reduction of endothelial dysfunction indices and to inhibit platelet aggregation. Piracetam possesses the most positive endotheliotropic and antiaggregative properties.

**References**


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**P1.c.054 Genotype–phenotype correlations between the CYP2C19 polymorphism and pharmacokinetic parameters in Romanian epileptic patients**


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**Introduction:** The polymorphisms of the genes involved in the metabolism of AEDs can potentially modify the activity of the coded enzymes. The CYP2C9 and CYP2C19 genes belong to the P450 (CYP) enzymatic system, being involved in the metabolism of the main AEDs. Valproic acid/Sodium valproate (VPA) is an AED with a broad spectrum, and it is extensively metabolized in the liver, the enzymes of the P450 system being involved in the process [1]. The polymorphism of the CYP2C9 and CYP2C19 isoenzymes represent a potentially determinant factor in the alteration of some drug’s metabolism [2]. There are relatively few studies investigating the influence of the CYP2C9 and CYP2C19 polymorphisms over VPA pharmacokinetics.

The aim of the study: The aim of the study was to evaluate the influence of genetic status on the metabolism of valproic acid (VPA) and the correlation between the genotype and the plasma levels of it.

**Materials and Method:** 80 patients with a mean age of 39.25±1.59 years, either with idiopathic or secondary epilepsy, evaluated in the Neurology Clinic of Cluj-Napoca, Romania were included into the study. Steady state plasma concentration of VPA were determined using the GC/FID technique to all patients under a stable treatment for at least a month. We considered therapeutic level of VPA between 50–100 μg/mL. According to steady-state plasma concentration of VPA the patients were divided into three groups: patients with subtherapeutic (<50 μg/mL), supratherapeutic (>100 μg/mL) or normal (50–100 μg/mL) therapeutic levels. Genotyping was conducted using DNA extracted from lymphocytes of peripheral blood. Using the PCR-RFLP method for each patient we have determined allelic variant CYP2C19*2 and CYP2C19*3. We correlated the plasmatic level of VPA with CYP2C9 and CYP2C19 polymorphisms. The statistical evaluation was performed, using a Chi-square test, with a significance at p < 0.05, with SPSS version 17.

**Results:** 58.25% were female patients and 43.75 male patients, sex ration F:M = 1.33. 60% of the patients presented idiopathic epilepsy, while 40% of them had a secondary form of the disease. The mean plasma level of VPA was 71.18±30.87 μg/mL. 62% of the patients had therapeutic level of VPA, while 20% had subtherapeutic and 18% of the patients supra-therapeutic level of it. 22.5% of the patients were heterozygous for CYP2C9*2, and 1.25% were homozygous, while 21.25% of the patients were heterozygous for CYP2C9*3. None of the patients were homozygous for CYP2C9*. Regarding CYP2C19*2 16.25% of the patients were heterozygous and 7.5% of them homozygous. The polymorphism of CYP2C19*3 was absent. There were no significant correlation between the presence of CYP2C9*2 (p = 0.9) and CYP2C9*3 (p = 0.52) polymorphism and the plasma concentrations of VPA. The same observation was noticed in case of CYP2C19*2 polymorphisms (p = 0.77).

**Conclusions:** The different allelic expression of CYP2C9 and CYP2C19 have no statistically significant influence on plasmatic level of VPA.

**References**


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**P1.c.055 Metadoxine: a novel 5HT-2B receptor antagonist with a possible therapeutic role in treating ADHD**

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Metadoxine (pyridoxol 1-2-pyrrolidone-5-carboxylate), an ionpair salt of pyridoxine and pyrrolidone carboxylate, is approved in some countries for use in the treatment of acute and chronic alcohol intoxication and for treatment of related chronic liver diseases. In a preliminary clinical trial, Metadoxine demonstrated improvements in cognitive performance in alcohol impaired individuals, as demonstrated by results obtained from the Test of Variables of Attention (T.O.V.A), a computerized test of attention. Therefore, a subsequent 40-person adult (32.1±6.9 yrs) study was conducted in Geha Medical Center in ADHD diagnosed subjects, in which all participants were dosed with a single1400 mg dose of Extended-Release Metadoxine. A cognitive improvement in a T.O.V.A. test (mean score increase of −4.9 to a mean range of −1.8, SE=2.1, p < 0.001) was seen suggesting that Metadoxine could indeed improve ADHD symptoms. Pre-clinical (in vitro and in vivo) studies were conducted in order to elucidate the mechanism of action of Metadoxine in cognitive function.

Data obtained from a panel of in vitro receptor binding assays suggest that Metadoxine affects the Serotonin receptor family; in an agonist radioligand assay, it was shown that Metadoxine binds
Serum brain-derived neurotrophic factor (BDNF) is an important mediator of neuronal development, survival, and function. In addition, BDNF modulate and regulate immune functions. BDNF is associated with the pathogenesis of several neuropsychiatric diseases [1] but there are few studies [2] evolving systemic lupus erythematosus (SLE). Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by the production of antibodies against various cell components leading to a spectrum of clinical findings ranging from lesions confined to the skin to multisystem organ involvement [3]. Between 10% and 70% of SLE patients exhibit central nervous system involvement, which is associated with inflammatory features in the brain.

Objective: To investigate if the serum BDNF levels were associated with disease activity in SLE patients with neuropsychiatric (NPS) and no-neuropsychiatric (no-NPS) manifestations.

Methods: A total of 141 SLE subjects were evaluated: 72 patients presenting NPS-SLE (42 with active disease), and 71 patients with no-NPS-SLE (27 with active disease). NPS-LES patients presented psychosis (n = 22), major depression (n = 12), seizures (n = 11), stroke (n = 10), vasculitis (n = 4), panic disorder (n = 3), transverse myelitis (2), peripheral neuropathy (n = 2), corea (n = 10), and aseptic meningitis (n = 1). All patients were diagnosed according to criteria set by the American College of Rheumatology. Lupus activity was assessed using the disease activity index (SLEDAI), being active SLE defined with SLEDAI >5, and inactive SLE with SLEDAI <2. We also evaluated 36 out of 42 patients with active SLENPS in two different moments: one with active disease and other six months after the improvement of neuropsychiatric symptoms (inactive state). All blood samples were collected in the morning, and the plasma was separated and frozen at -70°C until BDNF assessment. BDNF was measured by sandwich ELISA according to the protocol provided by the manufacturer (R&D Systems, USA). Parametric analysis was performed using the ANOVA test or paired t-test for comparison of unpaired and paired data, respectively. The p value was set at 0.05.

Results: Serum BDNF levels were significantly reduced in active NPS-SLE (mean±SE = 2.87±0.33 ng/mL) compared with inactive NPS-SLE (mean±SE = 4.39±0.33 ng/mL, p <0.0001). We observed similar findings in active no-NPS-SLE (mean±SE = 2.25±0.28 ng/mL) when compared with inactive no-NPS-SLE (mean±SE = 2.25±0.69, p <0.0001). When we analyzed 36 active SLENPS patients during NPS manifestation and after six months, we observed an increased in serum BDNF levels in parallel with the improvement of neuropsychiatric symptoms (mean±SE = 2.89±0.24 ng/mL versus mean±SE = 4.01±0.30 ng/mL, p <0.05).

Conclusions: Serum BDNF levels were reduced in active SLE, irrespective of neuropsychiatric manifestations. In addition, serum BDNF levels increased in parallel with the improvement of neuropsychiatric symptoms, suggesting that BDNF could be a biological marker for SLE disease activity.

References