

P11 THE EFFECT OF VALPROIC ACID AND ITS AMIDE DERIVATIVE ON EXTRACELLULAR GLUTAMATE AND GLUTAMINE LEVELS IN THE CEREBRAL CORTEX OF FREELY MOVING RATS: AN IN VIVO MICRODIALYSIS STUDY

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ABSTRACT

The effect of intraperitoneal administration of the anticonvulsant valproic acid (VPA) on the extracellular levels of glutamate and glutamine in the cerebral cortex as a reference of its amide derivative, (N-Hydroxymethyl)-2propylpentamide (HPP) was studied in freely moving rats. Male Wistar rats were implanted with microdialysis probes into the cerebral cortex. The experiments were performed in conscious rats 24 h after surgery. The microdialysis probe was perfused with an artificial cerebrospinal fluid at a flow rate of 2 μ l/min. Following an initial 60-min equilibration period, 12 consecutive 20-min dialysates were collected. Injection of either saline, PEG-400, VPA (220 and 440 mg/kg) or HPP (80 and 160 mg/kg) were made intraperitoneally in a volume of 1 ml/kg of body weight. Dialysates were analyzed for glutamate and glutamine content by HPLC with Electrochemical detection (ECD). Samples mixed with homoserine, an internal standard, were automatically injected by HPLC autosampler. Dialysates were pre-column derivatised with *o*-phthalodialdehyde (OPA). The mobile phase consisted of 70% 0.1M phosphate buffer solution and 30% methanol with flow rate 1 ml/min. VPA (220 mg/kg) did not alter basal glutamate level but in high dose (440 mg/kg), there was significant decrease on basal glutamate level. In contrast, HPP (80 mg/kg and 160 mg/kg) caused reduction in basal glutamate level. Similarly, basal glutamine level after HPP administration has been changed significantly by both low and high doses, whereas only the high dose of VPA has affected the basal glutamine level. These results suggest that HPP induced a decrease in the basal release of glutamate and glutamine in cerebral cortex may underlie the mechanism of anticonvulsant of HPP.

Key words : Valproic acid, (N-Hydroxymethyl)-2propylpentamide, glutamate, glutamine, microdialysis