EFFECT OF GAMMA-HYDROXYBUTYRATE IN TWO RAT MODELS OF FOCAL CEREBRAL DAMAGE

Ottani A., 4° anno di corso del Dottorato in Tossicodipendenze, XIV ciclo. Durata del dottorato in anni: 5. Sede di servizio: Dipartimento di Scienze Biomediche - Sez. di Farmacologia, Università di Modena e Reggio Emilia, via G. Campi 287, 41100 Modena.

Protective effects of GHB in animal models of cerebral ischaemia/hypoxia, as well as in human conditions of head injury-induced coma, have been described. Aim of our present work was to evaluate the effect of GHB on the behavioural and histological consequences of focal cerebral damage, either induced by ischaemia or by excitotoxicity. Adult male Wistar rats were used. Brain damage was induced by injecting 1 µl of either endothelin-1 or kainic acid (ischaemic or excitotoxic lesion, respectively) in the right striatum. Two hours later animals received GHB at the dose of 300mg/kg, i.p., followed by 100mg/kg twice daily for the following 10 days. Control-ischemized and sham-operated rats received 2ml/kg of saline, with the same schedule. Nineteen and thirty-nine days after endothelin-1 injection animals were submitted to the Morris water maze test to evaluate learning ability and to Bjorklund test to score sensory-motor activity; ten days after kainic-acid injection, animals were observed for circling behaviour induced by 2mg/kg apomorphine, s.c. Behavioural tests were followed by histological examination. The ischaemic lesion produced a significant impairment in sensory-motor activity (scores: 82 and 74, in the first and second trial, respectively) and in cognitive processes (seconds: 182.5±17.5 and 90.5±11.61); GHB significantly attenuated the phenomenon (scores:36 and 32; seconds: 110.3±22.6 and 71.3±14.5). In kainite-lesioned rats, apomorphine induced 275.67±59.86 ipsilateral turns/h; GHB significantly reduced this behaviour (28.17±8.65). Both models of damage produced areas of necrotis, demyelination and gliosis, which appeared much reduced after GHB. These results indicate that GHB provides significant protection against neurodegeneration in both experimental models.