The role of nitric oxide in glutaric acid-induced convulsive behavioural

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Glutaric acidemia type I (GA-I) is a cerebral organic disorder characterized by accumulation of glutaric acid (GA) and seizures. It is known that GA-I can lead to the development of seizures in children but the mechanisms underlying this disorder are not well established. Therefore, this study investigated the role of nitric oxide in GA-induced convulsive behavioural in pup rats. Pup male Wistar rats (18 days-old) were anesthetized and placed in stereotaxic apparatus for cannula insertion into the striatum (coordinates relative to bregma: AP, 0 mm; ML, 3.0 mm; V, 3.0 mm from the dura). The experiments were performed 3 days after surgery (pup rats 21 days-old) when animals did not show any sign of pain, infection or discomfort. Arginine (80 or 250 mg/kg), L-NAME (40 mg/kg) or saline (vehicle) were administered intraperitoneally (i.p.) 30 min before the intrastriatal injection of GA (1 µL, 1.3 µmol/striatum) or saline. Immediately after the intrastriatal injections we recorded the latency and duration of seizures for 20 min. The administration of L-NAME reduced significantly the duration of seizures induced by GA in pup rats [H(3) = 32.92; p< 0.05]. Besides, pre-treatment with arginine (80 and 250 mg/kg, i.p.) reversed the protection of L-NAME in the duration of seizures in pup rats injected with GA [H(3) = 22.13; p< 0.05]. These results are experimental evidence that nitric oxide plays a role in the seizures induced by GA in pup rats. Thus, these findings may be of value in understanding the physiopathology of neurological signs observed in children with this organic acidemia and may represent new strategies for the treatment of seizures in this disorder.

Word Keys: glutaric acid, seizures, pup rats, L-NAME, arginine, nitric oxide.
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