EFFECTS OF NITRIC OXIDE INFLUENCE ON EXPERIMENTALLY-INDUCED HYPEREXCITABILITY OF THE HIPPOCAMPUS: IN VIVO AND IN VITRO COMPARATIVE ELECTROPHYSIOLOGICAL STUDY IN THE RAT

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Introduction: NO is supposed to have an important role in the genesis and/or the maintenance of several diseases of the central nervous system (CNS). In the last decade a strong influence of NO in various experimental models of epilepsy has been documented, however its role remains controversial.

Aim: The present study investigated the role of nitric oxide on two models of experimental hippocampal hyperexcitability. In particular, the experimental design compared the data in vivo, in maximal dentate gyrus activation (MDA), considered a model of complex partial seizure and in vitro in recurrent hippocampal seizures.

Methods: In vivo experiments were performed on urethane-anaesthetized male Wistar rats (B.W.: 280-320g) in which reverberatory seizure discharges were obtained in the context of hippocampal-parahippocampal circuit through the stimulation of the angular bundle. In vitro experiments were executed on rat brain slices (Age: 4 weeks) in which the epileptiform activity was induced reducing the calcium and magnesium levels in the artificial cerebrospinal fluid (aCSF). In both experimental sets NO levels were modified administering L-arginine, a NO precursor, and 7-NI or L-NAME, NO-synthase (NOS) inhibitory drugs.

Results: L-arginine administration caused an increase of the epileptiform activity (decrease of latency associated with a significant increase of MDA duration) in MDA paroxystic activity. On the contrary, 7-NI i.p. administration, a selective inhibitor of neuronal NO synthase, caused a reduction of paroxystic phenomena (increase of onset time and decrease of MDA duration). Similarly, in in vitro experiments, L-Arginine applied to the aCSF induced a significant increase of the paroxystic discharge of hippocampal neurons, antagonised by the NOS inhibitory L-NAME.

Conclusion: Despite the extremely different experimental sets, very high analogies were highlighted in the pro-convulsive effect induced by nitrergic neurotransmission. In fact, all the data suggest a strong pro-convulsant influence exerted by NO excluding any sort of interference due to the anaesthesia and/or the experimental model of epilepsy.