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

Rizzo Valerio[1], Ferraro G[1], Sardo P[1], Carletti F[1], D'Agostino S[1], La Grutta V[1] and Cannizzaro G[2]

[1] Dip. Medicina Sperimentale, Sez. Fisiologia umana, Università di Palermo, Italy. [2] Dip. Scienze Farmacologiche, Università di Palermo, Italy

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.