The effect of selective inhibition of inducible nitric oxide synthase on hippocampal CA1 proliferation after pentylenetrazol-induced seizures in rats

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There is abundant evidence that epileptic seizures can induce a significant increase in Nitric oxide (NO) production (Bashkatova et al., 2000) which may be involved in seizure-induced enhancement of neurogenesis(Moreno-Lopez et al., 2000). Also, NO has been suggested to mediate the enhancement of precursor cell proliferation in the hippocampus after epileptic seizures. However, the underlying mechanism remains to be elucidated.

The aim of this study was to investigate the effects of NO on the proliferation of granule cell precursors in the CA1 of hippocampus in adult male Wistar rats (250-320 g) after pentylenetrazol (PTZ)-induced generalized clonic seizures.

Using systemic bromodeoxy uridine (Brdu) to label dividing cells, quantitative analysis by optical density measurement showed that administration of inducible NOS (iNOS) inhibitor aminoguanidine (250 mg/kg, i.p.) 10 min before PTZ, significantly reduced the Brdu labeled cells in the CA1 3, 7 and 14 days after PTZ-induced seizures (p<0.001, one-way ANOVA followed by Newman–Keuls post hoc test). However, injection of AG did not cause any significant difference in seizure grades, onset and duration of seizure in comparison to the control (PTZ + saline treated) group (n = 8 in each group).

These findings provide important evidence indicating that epileptic seizures lead to increased cell proliferation in the adult rat CA1 through NO-dependent mechanisms. Furthermore, our observations support the notion that NO originating from iNOS may be involved in seizures-induced neurogenesis.
