

Neuroanatomical substrates for recurrent epileptic limbic seizures

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Epilepsy is a neurological disorder characterized by the recurrence of spontaneous, unprovoked epileptic seizures. Mesial temporal lobe epilepsy (more briefly, MTL) is a very common form of epilepsy which is featured by the occurrence of focal limbic seizures, and associated to a specific neuropathological alteration, the so-called Ammon's horn sclerosis, whose main features are a selective loss of the CA1 and CA3/4 section of the Ammon's horn (CA, from Latin Cornu Ammonis, abbreviated as CA), a selective cell loss of inhibitory interneurons in the hilus of the dentate gyrus (DG), and the abnormal sprouting of granule cells mossy fibers (the so called mossy fiber sprouting, MFS). The onset of spontaneous

seizures (SRS) is the hallmark of a good model of epilepsy. For temporal lobe epilepsy (TLE), the most used models consist in administering systemically chemoconvulsants inducing limbic status epilepticus (i.e. seizures lasting for more than 30', SE) and evaluating the occurrence of SRS. However, in these models, the widespread involvement of different structures which complicates the interpretation of experimental findings: limbic seizures and status epilepticus (SE) can be triggered by focal infusion of chemoconvulsants within anterior piriform cortex (abbreviated as APC) This brain region is densely innervated by noradrenergic fibers arising from the locus coeruleus (LC), and we recently showed that a lesion of LC (induced by a selective neurotoxin, DSP-4, i.p.), induces SE. LC plays a critical role in modulating several models of seizures, and it plays a critical role in plastic mechanisms and neuroprotection in the brain. Thus, we compared the group DSP-4+bicuculline and cyclothiazide+bicuculline, to evaluate whether the focal SE evoked from the APC is capable of inducing SRS and AHS, and whether LC plays a significant role in this phenomena.

We found that: the loss of LC induced: (i) a higher incidence of SRS; (ii) cell loss in the hippocampal DG hilus and CA3 (iii) the loss of parvalbumin-positive neurons.

In conclusion, our study confirms that focal induction of SE from the APC represents a good model of TLE, and that NE released from the fibers originating from the LC plays a significant role both in the hippocampal damage occurring after SE, and in the incidence of SRS.

Keywords: epilepsy, limbic system, hippocampus, Cornu Ammonis