

# LES CONFÉRENCES DE L'ICM



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*Antoine DEPAULIS - february 6, 2012 at 11:00*

## Initiation of absence seizures in a genetic model of epilepsy in the rat : an anomaly of the cortical glial network ?

Absence epilepsy is a prototypic form of childhood generalized epilepsy which is characterized by behavioural arrest and loss of consciousness, associated with 3-Hz spike-and-wave discharges in human patients. We have characterized a rat model of this form of epilepsy, the Genetic Absence Epilepsy Rat from Strasbourg (GAERS) in which we initially described the critical role of the thalamo-cortical loop in the generation of absence seizures. More recently, using different methodologies (fMRI, intracellular recordings, multielectrode-arrays, synchrotron X-rays microbeams), we have demonstrated the existence of a population of neurons in the barrel field of the somatosensory cortex that initiate spike-and-wave discharges and show a different dynamics compared to other cortical areas, or to the homologous region in non-epileptic animals. Furthermore, in this “seizure initiating” cortical region, abnormal oscillations occur, as soon as 15 days postnatal that become spike-and-wave discharges around the age of 25 days. Because glial cells are suggested to be involved in the synchronization of cortical neurons during the onset of epileptic seizures, we hypothesized that the organization and/or maturation of the cortical glial network could be different in the somatosensory cortex of GAERS, during the first 4-5 postnatal weeks (i.e., epileptogenesis). Indeed, a higher expression of Glial Fibrillary Acidic Protein (GFAP) was reported in adult and young rats, as compared to non-epileptic controls. Using immunohistochemical labeling, our preliminary data showed in the GAERS (i) an anomaly in the maturation state of GFAP+ astrocytes in the somatosensory cortex and (ii) the presence of radial glia-like cells at P7, whereas they have almost disappeared in controls. Using a non-invasive, specific and ubiquitous method that we developed to stain astrocytes *in vivo* via iv injection of sulforhodamine dyes, we measured the number of astrocytes in P15 rat pups by two-photon microscopy and showed that there is a quite equivalent number of astrocytes between strains. However, the morphology of the astrocytes appeared different in GAERS, suggesting a difference in their functioning during brain development. This hypothesis is currently examined using intravital and endoscopic two-photon microscopy and calcium imaging. Our expected findings should provide important knowledge on the mechanisms of cortical epileptogenesis and may provide new targets for the development of prophylactic therapeutic strategies in epilepsies.