1 – Functional significance of hippocampal disinhibition in schizophrenia

- Hippocampal disinhibition has emerged as a key feature of schizophrenia pathophysiology (Listman et al., 2008; Schobel et al., 2009; Heckers & Konradi, 2010). However, it is unclear to which symptoms hippocampal disinhibition contributes.
- The hippocampus is associated with rapid acquisition and use of certain types of memory, and temporal to intermediate hippocampal can modulate diverse behavioral-control processes via functional connectivity to prefrontal and subcortical sites (Bast, 2011).
- Here, we focus on the hypothesis that hippocampal disinhibition, if affecting temporal to intermediate hippocampus, may not only disrupt hippocampus-dependent memory performance, but also disturb fronto-striatal cognitive functions, such as attention, and cause dopamine-dependent psychosis-related effects (Bast, 2011).

Experimental strategy
To test this hypothesis, we combined disinhibition of temporal to intermediate hippocampus by local microinfusion of the GABA-A receptor antagonist picrotoxin with behavioral and electrophysiological analyses in Lister hooded rats.

3 – Attentional deficits

The 5-CSRTT resembles continuous performance tasks used to test for attentional and executive deficits in schizophrenia patients and is dependent on prefrontal cortex (Chudasama & Robbins, 2006).

- Hippocampal disinhibition disrupted prefrontal-dependent attention, as indicated by a selective reduction of correct responses (no other measures were affected).

2 – Locomotor hyperactivity

- Locomotor hyperactivity may often reflect dopamine hyperfunction and, for this reason, has long been used as a simple psychosis-related behavioral index.
- Subacute picrotoxin doses caused locomotor hyperactivity, providing the basis for further characterization of behavioral effects of hippocampal disinhibition in Lister hooded rats.

5 – Effects of picrotoxin infusion into temporal hippocampus on local neuron firing in vivo

Experimental set up

- Picrotoxin increases multi-unit firing rate
- In isoflurane-anesthetized rats, picrotoxin increased neuronal firing in the vicinity of the infusion site (without inducing epileptiform burst-firing pattern).

4 – Memory deficits

- The watermaze DMTP task resembles the everyday memory task of using newly learned place and route memory, with which schizophrenia patients have marked problems (Al-Uzri et al., 2006).
- Hippocampal disinhibition disrupted DMTP performance.

References