Joint Master in Neuroscience, M1:

Training in anatomo-electrophysiological approaches (from single-cell to EEG) in an in vivo LTP protocol.

**Background:** N-methyl d-aspartate-type glutamate receptor (NMDAr) antagonist ketamine induces, in cortical-related networks of the rat, abnormal persistent hypersynchrony in γ frequency (30-80Hz) oscillations, a potential neurophysiological marker of psychosis (Pinault, 2008). Ketamine-induced aberrant γ oscillations are correlated with abnormal behaviour but are not the consequence of the motor activity and of conscious sensorimotor processing (Hakami et al., submitted). The present findings suggest that NMDAr-related persistent γ hypersynchrony in cortical circuits, interconnected with the thalamus (Guillery and Sherman, 2002), is a network noise that might cause cognitive dysfunction and acute psychosis. Ketamine-induced pathophysiological hypersynchrony in ongoing γ oscillations is reminiscent of findings in schizophrenic patients, revealing disorders of cognition-related coherences of γ oscillations between cortical areas (Spencer et al., 2003; Uhlhaas and Singer, 2006). Ketamine is used at a single non-anesthetic dose, equivalent to that that induces, in humans, cognitive deficits and a wide spectrum of behaviours relevant to schizophrenia (Hetem et al., 2000). The symptoms of schizophrenia, including cognition deficits, are underlain by neuronal mechanisms that remain to be deciphered. It is currently thought that they result, at least to some extent, from functional disconnections in cortical-related networks, which denote the disintegration of psychic processes (Friston 2002).

**Hypothesis:** Ketamine-induced pathophysiological γ oscillations are a neurophysiological marker of functional disconnections in corticothalamocortical (CTC) systems.

**Task (postdoc project; M1 training):** To test the hypothesis requires the synaptic plasticity in intact CTC systems in our ketamine model to be assessed in vivo, at the cellular and integrative level. NMDAr-dependent long-term potentiation (LTP) of thalamocortical transmission is measured in the cortex of anesthetized adult rats, treated with NaCl (0.9%) or ACSF then with ketamine (systemic injection or local cortical application). The LTP is assessed with the physiological and selective stimulation of the natural pathways.

**Expected results:** This project should give further evidence in favor of the hypothesis that functional disconnections in CTC systems underlie dysfunctions of conscious integration, including cognitive deficits, in schizophrenic patients. Indeed, ketamine-induced pathophysiological γ oscillations are expected to be associated with a decrease of the NMDA-dependent LTP at least of the thalamocortical transmission. This work is also interesting when it comes to measure the impact of deep brain stimulation in the spatiotemporal dynamics of oscillating CTC networks, which are disturbed during psychiatric disorders.