

MASTER 2 Fundamental and Clinical Neurosciences

Internship proposal 2025-2026

(internship from January to June 2026)

Host laboratory: Lyon's Neurosciences Research Center (U1028/UMR5292)

Host team : Translational Group in Epilepsy Research (TIGER)

Internship supervisors :

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Project title : Assessment of cortical reactivity to respiratory stress in epileptic animals.

Project summary :

This project is integrated within the framework of the ERC-funded EPIAROUSAL project.

Both seizures and their complications are modulated by patients' vigilance states. Several epilepsy complications are associated with sleep, including Sudden and Unexpected Death in Epilepsy (SUDEP). SUDEP primarily results from a fatal postictal central apnea after a nocturnal generalized convulsive seizure. Reducing the severity of postictal respiratory dysfunction has thus appeared as one of the most promising ways to prevent SUDEP. However, no encouraging result has been reported yet, suggesting that epilepsy-related respiratory dysfunction may only be the tip of the iceberg. Given the numerous interconnections between the network that regulates arousal and sleep and the respiratory network, one might make the hypothesis that some patients with drug-resistant epilepsy might combine this well-known seizure-related respiratory dysfunction with a chronic alteration of arousal regulation, resulting in abnormal asphyxia-induced arousal.

The aim of this project is to focus on the voluntary control of breathing, which is localized in the cortical region. Indeed, patients who die following a SUDEP are often found in the prone position, with their head in the pillow. It is possible to hypothesize that, following a nocturnal epileptic seizure, cortical default occurs. During the respiratory distress associated with the epileptic seizure, reactivity to wakefulness would thus be impaired, and could explain SUDEP.

The objective is to study inspiratory endurance (characterized as the time to fatigue following the application of an inspiratory load) in epileptic rats (temporal lobe epilepsy model). This inspiratory endurance studied by plethysmography will be characterized under acute sleep deprivation conditions or after "normal" sleep, monitored by an EEG/EMG telemetry system. During the internship, the student will be involved in *in vivo* experiments. He/she will also take part in the analysis of respiratory and EEG/EMG data during sleep and the plethysmography test, and in the post-mortem investigation of brains by RTqPCR and/or immunohistochemistry.

3-5 recent publications :

Boglietti E, Haddad D, Bezin L, Rheims S. Pathophysiology of SUDEP: How far are we from understanding? Rev Neurol (Paris). 2025 Apr 8:S0035-3787(25)00491-6.

Kouchi H, Smith J, Georges B, Cracknell F, Bezin L, Rheims S. Serotonin 2C receptor in a rat model of temporal lobe epilepsy: From brainstem expression to pharmacological blockade in relation to ventilatory function. Epilepsia. 2024 Jul;65(7):e125-e130.

Kouchi H, Ogier M, Dieuset G, et al. Respiratory dysfunction in two rodent models of chronic epilepsy and acute seizures and its link with the brainstem serotonin system. Scientific Reports 2022;

Rault C, Sangaré A, Diaz V, Ragot S, Frat JP, Raux M, Similowski T, Robert R, Thille AW, Drouot X. Impact of Sleep Deprivation on Respiratory Motor Output and Endurance. A Physiological Study. Am J Respir Crit Care Med. 2020 Apr 15;201(8):976-983.

Salgueiro-Pereira, A, Duprat, F, Pousinha, PA et al. A two-hit story: Seizures and genetic mutation interaction sets phenotype severity in SCN1A epilepsies. Neurobiology of Disease 2019; 125:31-44.

Ryvlin, P, Rheims, S, Lhatoo, SD. Risks and predictive biomarkers of sudden unexpected death in epilepsy patient. Curr Opin Neurol 2019; 32:205-212.

Rheims, S, Alvarez, BM, Alexandre, V et al. Hypoxemia following generalized convulsive seizures: Risk factors and effect of oxygen therapy. Neurology 2019; 92:e183-e193