



## PhD Offer

**Title:** [Post-stroke sleep apnea : impact of intermittent hypoxia on cerebrovascular recovery](#)

**Laboratories :** HP2 (Hypoxie et Physiopathologie cardiovasculaire) and GIN (Grenoble Institute of Neurosciences) team Barbier. INSERM and UGA laboratories.

### Abstract

**Stroke** affects up to 15 million people / year worldwide and is associated with impaired quality of life, functional impairment and accelerated decline of cognitive functions. Acute stroke treatment reduces stroke-associated mortality and disability, however, cognitive and sensitive-motor impairments may remain in up to one third of patients. Cerebrovascular recovery is lengthy and can be delayed by some comorbidities, such as **sleep apnea syndrome (SAS)**. SAS is a respiratory pathology with systemic deleterious consequences affecting up to 1 billion people in the world, and up to 30% of post-stroke patients. Indeed, SAS and its main component **intermittent hypoxia (IH)** can independently induce cognitive dysfunction and physio-pathological mechanisms (*e.g.* inflammation, oxidative stress) that could be deleterious by aggravating stroke-induced alterations and slowing recovery processes.

Emergent data suggests that treating SAS after stroke by pressure support (PS) may promote cognitive recovery. However, the impact of SAS treatment on cerebrovascular function remains unknown. Moreover, physio-pathological processes controlling cerebral repair are complex and largely understood. Finally, there is a crucial need for identification of biomarkers to better monitor the impact of SAS on post-stroke recovery. In humans, however, identification of these physio-pathological processes and biomarkers is complicated due to poor access to cerebral tissue samples.

Thus, we propose a pre-clinical study using a model of stroke in rats (transient middle cerebral artery occlusion, tMCAO) associated with intermittent hypoxia exposure. Our objectives are :

- 1) To decipher physio-pathological mechanisms of stroke-IH interaction
- 2) To test treatments targeting these mechanisms in order to reduce the deleterious consequences of IH on post-stroke recovery
- 3) To identify biomarkers monitoring IH impact post-stroke to optimize treatment follow-up and adaptation.

Rats will be submitted to tMCAO then exposed to intermittent hypoxia or normoxia for 2 to 8 weeks, to allow short- and middle-term impact of IH on stroke recovery. MRI imaging will be used to evaluate cerebrovascular structure and function, together with histological and biochemical analysis of brains. Finally, metabolomics study will be performed on the brain and blood of rats.

Our preclinical study will identify mechanistic insights and therapeutic targets that will then be translated to and validated in human patients, based on a large prospective cohort study (currently

recruiting patients). This cohort is a clinic-based cohort, which includes first-ever ischemic stroke or transient ischemic attack patients. All included patients are referred to the Sleep Laboratory for a full-night polysomnography, to screen SAS and, if needed, treat them according to current standard of care. A unique biobank of sera levied at multiple time points following stroke is being constituted and will serve at identifying blood-based biomarkers of the detrimental impact of SAS on stroke recovery and secondary cardiovascular morbidity and mortality. The PhD student will participate in this biomarker identification and characterization, with the aim of identifying new tools for clinical follow-up of patients.

**PhD supervision.** PhD co-directors will be Dr Anne Briançon-Marjollet (HP2 lab, [anne.briancon@univ-grenoble-alpes.fr](mailto:anne.briancon@univ-grenoble-alpes.fr)) and Dr Claire Rome (GIN, [Claire.rome@univ-grenoble-alpes.fr](mailto:Claire.rome@univ-grenoble-alpes.fr)).

### **Applicant profile**

Applicants should hold a Master of Sciences in biology with knowledge and interest in brain and/or vascular patho-physiology. Previous experience in animal experimentation and interest for *in vivo* imaging techniques will be appreciated.

**Application :** Send CV, motivation letter, recommendation letters and Master grade transcripts to [anne.briancon@univ-grenoble-alpes.fr](mailto:anne.briancon@univ-grenoble-alpes.fr) and [Claire.rome@univ-grenoble-alpes.fr](mailto:Claire.rome@univ-grenoble-alpes.fr)