SCIENCES SORBONNE UNIVERSITÉ

Master de Sciences et Technologies
Mention Biologie Intégrative et Physiologie
Parcours : Neurosciences
Responsable : Professeur Régis Lambert

Internship Proposal
Academic Year 2018-2019

1. Host team :

Research Unit (e.g. Department or Institute) :
Matières et Systèmes Complexes UMR 7057 CNRS
Service de Physiologie – Explorations Fonctionnelles, Hôpital Bichat, AP-HP,

Research Unit Director :
UMR 7057 CNRS : Laurent Limat
Explorations Fonctionnelles, Hôpital Bichat : MP d'Ortho
Research Team Director : Laurence Mangin
Team name: Theory of complex systems

Address : Bâtiment Condorcet , 10 rue Alice Domon et Léonie Duquet, Université Paris 7 Diderot, 72 205 Paris cedex 13

Supervisor of the Research Intern for this project: Laurence Mangin
Telephone: 01 40 25 84 01
E-mail : laurence.mangin@php.fr

2. Internship project title: BreathnetworkAC

3. Internship Description :

Central sleep apnea (CSA) or central sleep apnea syndrome (CSAS) is a sleep-related disorder in which the effort to breathe is diminished or absent, typically for 10 to 30 seconds either intermittently or in cycles, and is usually associated with a reduction in blood oxygen saturation. CSA is usually due to an instability in the body's feedback mechanisms that control respiration. The neural networks direct muscles that form the walls of the thorax and abdomen and produce pressure gradients that move air into and out of the lungs. The respiratory rhythm and the length of each phase of respiration are set by reciprocal stimulatory and inhibitory interconnection of these brain-stem neurons.

Chaos in the rhythmic activity is a major issue that has been discussed in many studies of neuroscience and physiology, and especially in the respiratory air flow. The team has previously compared the activity and the connectivity of the respiratory neural network in healthy humans and patients with obstructive lung disease. Our results show an increase in the dynamic chaos of airway flow in patients, focusing on expiratory flow. The reasons for this augmentation were explored by analyzing the activity of neural centers involved in respiratory rhythmogenesis, using functional brain imaging of the automatic neural networks, the first group generating inspiration (pre-Bötzinger complex) and the second in charge of expiration (the parafacial group). Brain imaging reveals in healthy humans a significant activation of the pre-Bötzinger complex linked to a high active inspiration while patients have a higher expiratory parafacial excitability leading to an active expiration. We also proposed a theoretical model of respiratory rhythmogenesis which reproduces the synchronized respiratory neural network from two chaotic pacemakers, the first modelling the pre-Bötzinger complex and the second modelling the expiration. Our model reveals how the synchronized chaotic activity of this network reproduced the experimental data of the activity of the respiratory nerve centers both in healthy humans and the patients. Besides, the respiratory neural network comprises the automatic brainstem and voluntary cortical network. The extension of the study to other important aspects as functional connectivity and Granger causality allow to better understand the communication within the network with the future perspective to develop new therapeutic strategies involving the modulation of brain oscillation.

The aim of the present study is to extend this study to patient with central apnea, hypothesizing that neural network would be different from patients with COPD in one hand, and from normal subjects in another hand.

Methods
The respiratory neural network is characterized from the brain to the output of the system (ventilatory flow). High density electroencephalography (EEG_hd, 64 electrodes) and electromyograms of the respiratory muscles (diaphragm and intercostal) are performed with active unipolar electrodes. Other synchronous acquisitions related to the network include ventilatory flow, mouth pressure, oxygen saturation and partial pressure of end-tidal carbon dioxide (PeTCO2). All the biological signals are acquired on a laptop.
The experimental paradigm lasts 20 minutes and comprises three randomized sequences: breathing with inspiratory resistance, breathing without inspiratory resistance, breathing during a hand motion task. Twenty control subjects have already been recorded.
EEG_hd processing includes filtering, noise removal with independent component analysis and source reconstruction with Loreta (low resolution brain electromagnetic tomography).
Wavelet and cross wavelet analyses characterize the frequency dynamics of the network elements (time-frequency and instantaneous phase difference relationships).
During the internship, the student will perform the neurophysiological experiments in patients. He will process EEG_hd and perform 3D brain source reconstruction of the cortex and deep cerebral structures.
The student will learn to use key software in the field of neuroscience for EEG processing and statistics: MATLAB, EEGLab, Brainstorm, Fieldtrip.

References:
1/ Monti A, Medigue C, Mangin L. Instantaneous parameter estimation in cardiovascular time series analyses by harmonic and Time-frequency analysis. IEEE Trans Biomed Eng 2002;49:1547-1556
2/ Hess A, Yu L, Klein I, et al. Neural mechanisms underlying breathing complexity. PLoSONE 2013;8;e75740.
3/ Yu L, De Mazancourt M, Hess A, et al. Functional connectivity and information flow of the respiratory neural network in chronic obstructive pulmonary disease. Hum Brain Mapp 2016; DOI: 10.1002/hbm.23205