LIST OF PROJECTS (7)

INTERNATIONAL CO-SUPERVISED PHD SCHOLARSHIPS

MARCH 2020

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*** NeuroSchool's PhD program (EUR nEURo*AMU) finances up to 50% of the thesis. The co-financing proposed by the foreign partners is not all confirmed yet.**

PROJECT C1

Title : Modelling of Physiological Signals and Early Prediction of Epileptic Seizures

Supervisor (Monastir, Tunisie) : BEN ABDALLAH Asma (assoumaba@yahoo.com - +33 (0)2 16 73 46 20 19)

Laboratory : Laboratory of Technology and Medical Imaging (TIM, LR12ES06)

http://www.labtim.org/

Co-supervisor (Marseille) : CARRERE Marcel (marcel.carrere@univ-amu.fr - +33 (0)4 91 32 42 54)

Laboratory : Institute of System Neurosciences (INS, UM_S1106)

http://ins-amu.fr/

Duration : 60% TIM, 40% INS

SUJET : Epilepsy is a disease which various pathologies, some of which are serious due to their symptoms evolution which are difficult for their family and lead to socio-economic repercussions. It is a common disease, affecting more than 70 million people worldwide [1]. It is a chronic pathology which manifests itself by different recurrence of seizures. These seizures result from generalized or focused brain dysfunction due to an abnormal electrical discharge [2]. These discharges are measured by significant electrical variations at the level of electroencephalogram (EEG) signal [1]. Other work suggests the possibility of detecting these attacks from the electrocardiogram (ECG) [3]. The goal of the thesis will be to use signals in order to prevent, or detect seizure before their appears. The applicant will have to improve the mathematical prediction of crisis and realize that an apparatus to prevent seizure could be done , this could also enrich the socio-economic world. Moreover when electrocardiogram (ECG) and electroencephalogram are simultaneously recorded , a relationship between these two signal has to be studied.

MAIN ISSUE AND OBJECTIVES : main issues will 1. realize an build a new mathematical treatment to detect seizure. 2. Distinguish between real crisis and “false seizure” which are present mainly with young epileptic patients. The proposed approach is based on real-time analysis of electrocardiogram (ECG) and electroencephalogram (EEG) [4]. The first intermediate objective is to model EEG and ECG signals based on the method of Vector auto regression (VAR) and Vector Error Correction (VEC) [5, 6] and to seek a causal relationship between these two types of signals. The second intermediate objective follows from the first and consists in predicting the advent of seizures by going through two stages: extraction of significant characteristics representing the different stages of crises, before, during and after these crises and the use of connectionist methods with supervised and unsupervised learning for decision-making. The method will be implemented with real signals and compare with mathematical signals generate by a phenomenological model (TVB) epileptor.

METHODOLOGY AND FIRST STEP FOR THIS THESIS : •The thesis work will follow: study deeply the state of the art about EEG et ECG in literature and also what is done in both laboratories. Study the work previously done by thesis on this topics (for example the one done by Inès Assali) Apply new tricks to reduce the signal to noise ration in order to improve the quality of signals before treatments. Study the stability index versus distances RR. Study the effect of distances RR during epileptic seizure. Model ECG and EEG signals based on VAR and VEC[5, 6] and exhibit a relationship between the two signals as a new causality[8]. suggest a new method to detect crisis based on causality between the two signals ECG and EEG.

BEN ABDALLAH / NAMES AND DATES OF THE CURRENTLY SUPERVISED PHD STUDENTS :

- Sofien Ben SAYADIYA
- Manef ben Mbarek
- Souhir Khessibaa

BEN ABDALLAH / NAMES AND DATES OF THE PREVIOUSLY SUPERVISED PHD STUDENTS :

- Hamdi Salah, Thesis defence: 27/12/2016
- Asma kerkeni, Thesis defence: 09/05/2016.
- Rym Ayari, Thesis defence: 22/10/2015.
- Ibtihel Nouira, Thesis defence: 13/05/2015.
- Hanen Akkari, Thesis defence: 14/12/2012.

BEN ABDALLAH / PUBLICATIONS OF THE PREVIOUSLY SUPERVISED PHD STUDENTS :

- Salah Hamdi, Asma Ben Abdallah, Mohamed Hédi Bedoui. "A robust QRS complex detection using regular grammar and deterministic automata". *Biomedical Signal Processing and Control*. 2018, vol. 40, p. 263-274.
- Salah Hamdi, Asma Ben Abdallah, Mohamed Hédi Bedoui. "Real time QRS complex detection using DFA and regular grammar". *Biomedical engineering online*. 2017, vol. 16, no 1, p. 31.
- Salah Hamdi, Asma Ben Abdallah, Mohamed Hedi Bedoui. "Using Grammars in Medical Imaging: A Comprehensive Overview". *2016 13th International Conference Computer Graphics, Imaging and Visualization (CGiV)*. IEEE, 2016. p. 343-348.
- Salah Hamdi, Asma Ben Abdallah, Mohamed Hedi Bedoui. "Grammar Formalism for Computed Tomography and Angiography Image. Segmentation and 3D Carotid Artery Reconstruction". *2016 13th International Conference Computer Graphics, Imaging and Visualization (CGiV)*. IEEE, 2016. p. 339-342.
- Salah Hamdi, Asma Ben Abdallah et Mohamed Hedi Bedoui. "Deterministic Automata and Lexical Analysis for Normalized ECG Signals Diagnosis". *TAIMA'2015*. Mai 2015, p. 411-419. Hammamet, Tunisie.
- Salah Hamdi, Asma Ben Abdallah et Mohamed Hedi Bedoui. "Two-Dimensional Parser: A New Tool of CTA Image Segmentation Based on Grammar". *TAIMA'2015.* Mai 2015, p. 531-539. Hammamet, Tunisie.
- Salah Hamdi, Asma Ben Abdallah, Mohamed Hédi Bedoui*. "Grammar Formalism for ECG Signal Interpretation and Classification". Applied Medical Informatics*. 2014, vol. 35, No. 4, p. 21-26.
- Salah Hamdi, Asma Ben Abdallah, et Mohamed Hédi Bedoui. "Novel Technique for Image Segmentation Based on Grammar Parsing and Hilbert Transform". In: *International Conference on Image Analysis and Recognition (ICIAR 2013)*. Póvoa de Varzim, Portugal Springer Berlin Heidelberg. 2013, p. 346-353.
- Asma Kerkeni, Asma Ben Abdallah, Antoine Manzanera and Mohamed Hedi Bedoui. "Automatic Bifurcation Detection in Coronary X-Ray Angiographies". 2016 13th

International Conference Computer Graphics, Imaging and Visualization *(CGiV)*. *IEEE.* 2016. p. 333-338.

- Asma Kerkeni, Asma Ben Abdallah, Antoine Manzanera and Mohamed Hedi Bedoui. "A coronary artery segmentation method based on multiscale analysis and region growing". *Computerized Medical Imaging and Graphics*, 2016, vol. *48*, p. 49-61.
- Asma Kerkeni, Asma Ben Abdallah et Mohamed Hedi Bedoui. "Reconstruction 3D de l'arbre coronaire à partir de deux images angiographiques non calibrées". *TAIMA'2015*. Mai 2015, Hammamet, Tunisie, pp : 497-504.
- Asma Kerkeni, Asma Ben Abdallah and Mohamed Hedi Bedoui. "Comparison of Multiscale Filters for the Coronary Vasculature Enhancement". *Traitement et Analyse de l'Information Méthodes et Applications (TAIMA 2013). Mai 2015*, Hammamet, Tunisie.
- Asma Kerkeni, Asma Ben Abdallah and Mohamed Hedi Bedoui. "Coronary Artery MultiScale Enhancement Methods: A Comparative Study". In : *Image Analysis and Recognition (ICIAR 2013)*. Póvoa de Varzim, Portugal Springer Berlin Heidelberg, 2013. p. 510-520.
- Rim Ayari, Asma Ben Abdallah, Mohamed Hédi Bedoui. "Global and regional deformation analysis of the myocardium: MRI data application". *RFMI'2017.* 17-20 December 2017. France.
- Rim Ayari, Asma Ben Abdallah, Faouzi Ghorbel, Mohamed Hédi Bedoui. "Analysis of regional deformation of the heart left ventricule". *IRBM*. 2017, vol. 38, no 1, p. 90-97.
- Rim Ayari, Asma Ben Abdallah, Faouzi Ghorbel, Mohamed Hédi Bedoui. "Analysis of regional deformation of the heart's left ventricle using curvature values with Hotelling T2 metric". *2016 13th International Conference Computer Graphics, Imaging and Visualization (CGiV)*. *IEEE.* 2016. p. 115-118.
- Rim Ayari, Asma Ben Abdallah, Faouzi Ghorbel and Mohamed Hédi Bedoui. "Analyse régionale des déformations dans le ventricule gauche du cœur". *TAIMA'2015.* Mai 2015. Hammamet, Tunisie, p. 441-450.
- Rim Ayari, Asma Ben Abdallah, Faouzi Ghorbel, Mohamed Hédi Bedoui. "Segmentation of 3D object according to the AHA standard". *Journal of Biosciences and Medicines, 2015 Spring World Congress on Engineering and Technology (SCET)*. Avril 2015. Pekin, Chine.
- Rim Ayari, Asma Ben Abdallah, Faouzi Ghorbel, Mohamed Hédi Bedoui. "Analysis of regional deformation of the heart's left ventricle using invariant SPHARM descriptors". *IRBM*. 2014, vol. 35, no 5, p. 226-232.
- Rim Ayari, Asma Ben Abdallah, Faouzi Ghorbel, Mohamed Hédi Bedoui. "Regional curvature analysis in the left ventricle of the heart using Hotelling T2 metric". *Journal of Computers (JCP)*. Juin 2014, vol. 9, no. 7.
- Rim Ayari, Asma Ben Abdallah, Faouzi Ghorbel, Mohamed Hédi Bedoui. "Local deformation analysis of the heart left ventricle using SPHARM descriptors and modified Hotelling T2 metric". *The 37th International Conference on Telecommunications and Signal Processing (TSP)*. Juillet 2014, Berlin, Germany.

- Rim Ayari, Asma Ben Abdallah, Faouzi Ghorbel, Mohamed Hédi Bedoui. "Local deformation analysis in the heart left ventricle using the regional volume evolution". *The 4th International Conference on Multimedia Computing and Systems (ICMCS'14)*. Avril 2014, Marrakech, Maroc.
- Rim Ayari, Asma Ben Abdallah, Faouzi Ghorbel, Mohamed Hédi Bedoui. "Analysis of local deformation for left ventricle of the heart using spherical harmonics descriptors". *Traitement et Analyse de l'Information Méthodes et Applications (TAIMA 2013)*. Mai 2013, Hammamet, Tunisie.
- Rim Ayari, Asma Ben Abdallah, Raja Sfar, Faouzi Ghorbel, Mohamed Hédi Bedoui. "Analyse régionale de la déformation d'objets 3D par utilisation des harmoniques sphériques". *Traitement et analyse de l'information méthodes et applications (TAIMA 2011).* Octobre 2011, Hammamet, Tunisie.
- Ibtihel Nouira, Asma Ben Abdallah, Siham Layouni, Mohamed Hédi Bedoui, Mohamed Dogui. "Spectral density variation mapping of cerebral waves by three-dimensional interpolation techniques". *International Journal of Imaging Systems and Technology.* 2015, *25*(3), p. 191-198.
- Ibtihel Nouira, Asma Ben Abdallah, Mohamed Hédi Bedoui. "Three-dimensional interpolation methods to spatiotemporal EEG mapping during various behavioral states". *Signal, Image and Video Processing.* 2015, p. 1-7.
- Ibtihel Nouira, Asma Ben Abdallah, Mohamed Hédi Bedoui, Mohamed Dogui. "Spectral density variation mapping of cerebral waves by three-dimensional interpolation techniques". *International Journal of Imaging Systems and Technology, International Journal of Imaging Systems and Technology.* 2015, vol. 25, no 3, p. 191-198.
- Ibtihel Nouira, Asma Ben Abdallah, Mohamed Hédi Bedoui, Mohamed Dogui. "Cartographic mapping of alpha brain wave by 3D Spline interpolation". *Journal of Biosciences and Medicines, 2015 Spring World Congress on Engineering and Technology(SCET).* 14-16 avril 2015. Pekin, Chine.
- Ibtihel Nouira, Asma Ben Abdallah, Mohamed Hédi Bedoui. "EEG Potential mapping by 3D interpolation methods". *The 4th International Conference on Multimedia Computing and Systems (ICMCS'14)*. Avril 2014, Marrakech, Maroc.
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- Ibtihel Nouira, Asma Ben Abdallah, Mohamed Hédi Bedoui, Mohamed Dogui. "Détection des pics R par la transformée en ondelette dyadique". *Applications Médicales de l'Informatique : Nouvelles Approches (AMINA 2012).* Décembre 2012, Monastir, Tunisie.
- Ibtihel Nouira, Asma Ben Abdallah, Ibtissem Khouja, Mohamed Hédi Bedoui. "Comparative Study of QRS Complex Detection in ECG". *International Conference on Medical Image and Signal Computing* (*ICMISC 2012)*. Novembre 2012, 28-29, pp. 1447-1451, Paris, France.

- Hanen Akkari, Asma Ben Abdallah, Imen Bhouri, Patrick Dubois, Mohamed Hédi Bedoui. "Classification of Objects Using 3D Q-structure Functions". *ICMSC'10.* Novembre, 2010, Cairo, Egypte.
- Hanen Akkari, Imen Bhouri, Asma Ben Abdallah, Patrick Dubois and Mohamed Hédi Bedoui. "Multifractal modelling and 3D lacunarity analysis". *Physics letters A*. September 2009, volume 373, Issue 40, 28, p. 3604-3609.
- Hanen Akkari, Imen Bhouri, Asma Ben Abdallah, Patrick Dubois and Mohamed Hédi Bedoui. "Lacunarity estimation for analysis of 3D images of trabecular bone". *The Fifth International Symposium on Fractals in Biology and Medicine*, 2008, Suisse.
- Hanen Akkari, Imen Bhouri, Asma Ben Abdallah, Patrick Dubois and Mohamed Hédi Bedoui. "Analyse tridimensionnelle des volumes par mesure de la lacunarité : Etude comarative". *AMINA'08*, 2008, Monastir.

PROJECT C2

Title : Multi-modal analysis of the relationships between mechanical, structural, connectivity and functional alterations of the spinal cord in cervical spondylotic myelopathy and central canal syndrome

Supervisor (Marseille) : CALLOT Virginie (virginie.callot@univ-amu.fr) - +33 (0)4 91 38 84 65)

Laboratory : Center for Magnetic Resonance in Biology and Medicine (CRMBM, UMR 7339)

http://crmbm.univ-amu.fr/

Co-supervisor (Montréal) : PETIT Yvan (yvan.petit@etsmtl.ca) - + 1 514 396 8691

Laboratory : Canada Research Chair in Biomechanics of Head and Spinal Trauma, École de Technologie Supérieure (ETS)/Hôpital du Sacré-Coeur, Montréal, Canada

www.crc-trauma.etsmtl.ca

Duration : 50% AMU lab, 50% partner lab

Project

STATE OF THE ART : The spinal cord (SC) is an important signal-processing center that is critical to many functions. It can be severely impaired following injury (SCI) and be devastating in terms of quality of life. Considerable research efforts are thus conducted to restore impaired SC and assess objective quantifiers of functional impairment/recovery. In this context, thanks to recent methodological advances, functional Magnetic Resonance Imaging (fMRI) can now be considered to study SC neural activity. Ultra-high field MR systems have especially demonstrated huge potentials for such investigations. Coupled with microstructural MRI and existing biomechanical SCI model, such functional information could be very valuable to build a virtual platform that could be used to further increase understanding, prevention and treatment of SC trauma..

OBJECTIVES : To identify how injury alters connectivity in compressed SC. To quantify structuro-functional alteration in patient with cervical spondylotic myelopathy (CSM) and central canal syndrome (CCS). To integrate these data to refine the current biomechanical model of cervical spine and spinal cord (Spine Model for Safety and Surgery). To study, using this refined virtual model, the mechanisms of SCI in CSM (strain and stress distribution) and their relationships with the structuro-functional alterations in local circuit integrity seen by MR.

METHODS : To implement a robust 7T SC fMRI protocol that will complement already implemented morpho-structural methodologies and hence identify resting-state functional connectivity networks in normal and compressed conditions. To simulate the mechanisms of SCI associated with CSM and CCS and investigate the relashionships between MRI-based structure and neural activity level changes and biomechanical SC alterations (residual stresses, deformation).

EXPECTED RESULTS : Mechanico-structuro-functional biomarkers and thresholds of spinal cord injury. Refined simulation tools of the mechanisms of spinal cord injury in cervical spondylotic myelopathy. New perspectives to further classify the patients and evaluate regenerative strategy.

FEASABILITY : Strong expertise of the teams in : SC imaging (V. Callot), rs-fMRI (JP.Ranjeva), spine biomechanics and simulation (Pr. Y. Petit), clinical management of SCI (Pr. Pr. JM.MacThiong, Hôpital Sacré-Coeur Montréal, Pr. PH. Roche, Hôpital Nord, Marseille). Established and fruitful collaboration within the iLab-Spine consortium. Preliminary works together.

COMPLEMENTARITY OF THE 2 LABS : While CRMBM-CEMEREM dedicates its researches to MR developments and new biomarker identifications, the ETS / Chaire Neurotrauma is deeply involved in experimental and numerical developments for spine trauma management and prevention. Both labs belong to the iLab-Spine international laboratory, which gathers 8 institutions, and provides original and complementary approaches directed toward a multi-physics approach for a better understanding and management of spinal cord injuries.

EXPECTED CANDIDATE PROFILE : Strong knowledge in Computational Neuroscience, signal processing, MR experimentation, numerical simulation. Strong basic knowledge on computational mechanics, ideally applied to the spine. Able to develop/optimize/validate proof-of-concept methodology for MR investigations and biomechanical simulations of SCI. Willingness to study and interact in a multidisciplinary and international team, ability to work on an interdisciplinary project, highly motivated.

CALLOT / NAMES AND DATES OF THE CURRENTLY SUPERVISED PHD STUDENTS :

- Simon Lévy (oct 2017- sept 2020)
- Arash Forodighasemabadi (oct 2018– sept 2021)

CALLOT / NAMES AND DATES OF THE PREVIOUSLY SUPERVISED PHD STUDENTS :

- Henitsoa Rasoanandrianina (oct. 2015 – janv 2019)
- Manuel Taso (oct 2013 – april 2016)
- Slim Fellah (april 2009 – dec 2012)

CALLOT / PUBLICATIONS OF THE PREVIOUSLY SUPERVISED PHD STUDENTS :

- H. Rasoanandrianina, S. Demortière,, A. Trabelsi, M. Guye, JP. Ranjeva, O. Girard, G. Duhamel, M. Guye, J. Pelletier, B. Audoin, V. Callot, Sensitivity of inhomogeneous Magnetization Tranfer to Spinal Cord damage in Multiple Sclerosis, AJNR,accepted with revision 2020
- S.Lévy, S. Rapacchi, T.Troalen, M. Guye, V. Callot, Intra-Voxel Incoherent Motion at 7T to quantify human spinal cord microperfusion: pitfalls and promises, MRM, 2020 Feb 14. doi: 10.1002/mrm.28195
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- H. Rasoanandrianina, AM. Grapperon, M. Taso, OM. Girard, G. Duhamel, M. Guye, JP. Ranjeva, S. Attarian, A. Verschueren,V. Callot , Region-specific impairment of the cervical spinal cord (SC) in amyotrophic lateral sclerosis: a feasibility study using SC templates and quantitative MRI (DTI/ihMT)), *NMR Biomed*,2017, 30(12):doi:10.1002/nbm.3801
- B. De Leener, S. Lévy, V.S. Fonov, N. Stikov, L.D. Collins, V. Callot, J. Cohen-Adad SCT: pinal Cord Toolbox, an open-sourcesoftware for processing spinal cord MRI data, *euroimage,*2017, 145, 24-43
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- M. Taso, L. Fradet, V. Callot, PJ. Arnoux, Anteroposterior compression of the spinal cord leading to cervical myelopathy: a finite element analysis. *Comput Methods Biomech Biomed Engin*. 2015 Oct;18 Suppl 1:2070-1. doi: 10.1080/10255842.2015.1069625
- S.Lévy, M. Benhamou; C. Naaman, P. Rainville, V. Callot, J. Cohen-Adad White matter atlas of the human spinal cord with estimation of partial volume effect, *Neuroimage, 2*015;119:262-71. doi: 10.1016/j.neuroimage.2015.06.040
- M. Taso, A. Le Troter, M. Sdika, J. Cohen-Adad, PJ. Arnoux, M. Guye, JP. Ranjeva, V. Callot, A reliable spatially normalized template of the human spinal cord - Applications to utomated white matter/gray matter segmentation and Tensor-Based Morphometry (TBM) mapping of gray matter alterations occurring with age, *Neuroimage,* 2015, 117:20-8. doi: 10.1016/j.neuroimage.2015.05.
- V. Fonov, A. Le Troter, M. Taso, G. Leveque, M. Benhamou, M. Sdika, H. Benali, PF. Pradat, L. Collins, V. Callot, J. Cohen-Adad, Framework for integrated MRI average of the spinal cord white and gray matter: the MNI-Poly-AMU template, *Neuroimage* 2014, 102 Pt 2:817-27, doi: 10.1016/j.neuroimage.2014.08.057

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- S. Fellah, D. Caudal, A. Maues de Paula, P. Dory-Lautrec, D. Figarella-Branger, O. Chinot, P. Metellus, PJ. Cozzone, S. Confort-Gouny, B. Ghattas, V. Callot, N. Girard, Multimodal MRI (Diffusion, Perfusion and Spectroscopy): Is it possible to predict oligodendroglial tumors grade and genotype in the pretherapeutic diagnosis, AJNR Am J Neuroradiol, 34: 1326-1333, 2013
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PETIT / NAMES AND DATES OF THE CURRENTLY SUPERVISED PHD STUDENTS :

- Brieg Lecoublet (Phd defence on 08/2020; codirection)
- Marie-Hélène Beauséjour (Phd defence on 12/2020; codir)
- Florian Guillaume (Phd defence on 08/2020)
- Marion Fournely (Phd defence on 06/2020; codir)
- Jean-Michel Desrosiers (expected Phd defence on 04/2021)
- Caroline Lecours (Phd defence on 08/2020)
- Jawad Dahmani (Phd defence on 04/2020)
- Sophie Labat (Phd defence on 08/2022; codir)
- Sajjad Rastegar (expected Phd defence on 04/2022; codir)

PETIT / NAMES AND DATES OF THE PREVIOUSLY SUPERVISED PHD STUDENTS :

- Annie Levasseur (2020)
- Yann Facchinello (2015)
- Hedayeh Mehmanparast (2015)
- Luc Cloutier (2014
- Martin Brummund (2014)
- Léo Fradet (2013)
- Dominic Boisclair (2012)

PETIT / PUBLICATIONS OF THE PREVIOUSLY SUPERVISED PHD STUDENTS :

- Lecoublet B, Boisclair D, Evin M, Wagnac E, Petit Y, Aubin CE, Arnoux PJ. (2019). Assessing the Global Range of Motion of the Helmeted Head Through Rotational and Translational Measurements. International Journal of Crashworthiness. DOI: 10.1080/13588265.2019.1593288.

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- Mac-Thiong JM, Levasseur A, Parent S, Petit Y. (2016) Experimental Model of Proximal Junctional Fracture after Multilevel Posterior Spinal Instrumentation. BioMed Research International. 2016: 8058796.
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- Mehmanparast NH, Petit Y, Mac-Thiong JM. (2015) Comparison of Pedicle Screw Loosening Mechanisms and the Effect on Fixation Strength. J Biomech Eng. 137(12).
- Brummund M, Sgard F, Petit Y, Laville F (2014) A threedimensional finite element model of the human external ear for simulation of the occlusion effect, Journal of the Acoustical Society of America, 135(3): 1433-1444.
- Cloutier LP, Laflamme GY, Menard J, Petit Y. (2014) Anterior locking plate reduces trochanteric fracture migrations during hip extension. Clin Biomech. 29(8):930-5.
- Facchinello Y, Brailovski V, Petit Y, Mac-Thiong JM. (2014) Monolithic superelastic rods with variable flexural stiffness for spinal fusion: modeling of the processing-properties relationship. Med Eng Phys. 36(11):1455-63
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PROJECT C3

Title : Deciphering the impact of long-range projecting interneurons in the temporal lobe epilepsy pathology

Supervisor (Marseille) : CREPEL Valérie (crepel.valerie@inserm.fr - +33 (0)4 91 82 81 15)

Laboratory : Mediterranean Institute of Neurobiology (INMED, UMR 1249

http://www.inmed.fr/en/integrative-properties-of-plastic-neuronal-circuits-in-health-and-disease-en

Co supervisor (Genève) : MICHEL Christoph (christoph.michel@unige.ch - + 41 (0) 22 37 95 457)

Laboratory : Department of Basic Neurosciences, University Medical Centre/NEUFO

https://www.unige.ch/medecine/neuf/en/research/grecherche/christoph-michel/

Duration : 50% AMU lab, 50% partner lab

Project

STATE OF THE ART : Temporal Lobe Epilepsy (TLE) is the most prevalent type of epilepsy in adults. The disease manifests as the occurrence of unpredictable and recurrent seizures, associated with severe disorders of mood and cognitive functions. Using mouse models, it has been pointed out several alterations of the temporal lobe circuits, including a degeneration of both inhibitory and excitatory neurons, accompanied by the acquisition of aberrant intrinsic properties by survivor cells, as well as a reorganization of the synaptic network. We are particularly interested in the dysfunctions of some peculiar temporal lobe inhibitory interneurons subsets such as somatostatin-expressing long-range projecting interneurons, which are thought to "orchestrate" neuronal physiological activity within the interconnected temporal lobe structures and with extra-temporal brain regions, therefore modulating the behavior and cognitive functions (Farrel et al., 2019; Melzer et al., 2012). We hypothesize that an impairment of long-range projecting inhibitory neurons properties could play a key role to the pathological mechanisms of temporal lobe epilepsy. An alteration of those interneurons' features could not only contribute to the detonation and the propagation of epileptic seizures, but also interfere with the neural coding, and consequently disrupt the functions that are normally handled by the temporal lobe structures. If the latter hypothesis were true, the selective manipulation of those interneurons' properties would be a valuable approach for reducing epileptic activities and reinstating the correct neural functions in the hippocampus.

OBJECTIVES : The objectives of the prospective PhD student will be 1) to study the morpho-functional properties of somatostatin-expressing long-range projecting neurons using reliable mice models of TLE that reproduces the symptoms displayed by the patients, and 2) to specifically manipulate those neurons using genetic and/or pharmacological strategies with the aim to reduce the generation of seizures and to restore normal cognitive functions.

FEASABILITY : The feasibility of the project within the duration of a PhD (3 years) relies on the extreme complementarity of the two hosting groups, which are both renowned for their numerous publications in the field of temporal lobe epilepsy (Epsztein et al. 2007, Peret et al., 2015; Sheybani et al., 2018; 2019, etc).

EXPECTED CANDIDATE PROFILE : Expected candidates should have a background in neuroscience and should be familiarized with methods such as experimentation on mice, in vitro and in vivo electrophysiological recordings (patch-clamp, EEG, and/or multitrode recordings), neuronal manipulation techniques (using optogenetic and/or chemogenetic approaches) and behavioral testing. Every tool necessary for the project is routinely used by one or the other hosting lab, and projects using similar methodologies were already conducted in the last years (Marissal et al., 2018; Sheybani et al., 2018; 2019). The prospective PhD student will be mentored by Drs. Valérie Crépel and Thomas Marissal (INMED INSERM1249, Marseille) for the study at the cellular level (patch-clamp, specific neuronal manipulation, etc.), and by Dr. Charles Quairiaux and Prof. Christoph Michel (Department of Basic Neuroscience, CMU, Geneva) for the experiments at the macroscopic level (in vivo local and large-scale neuronal recordings, etc.). Other team members with compatible expertise (histological analysis, electrophysiology, programming, etc.) will participate to the project when necessary. As the two labs developed several collaborations with clinical setting and companies, the project has the potential to slide into translational aspects. In summary, that ambitious project aims at unravelling a key mechanism of temporal lobe epilepsy pathology, and ultimately identifying a target for novel therapy for that disease.

CREPEL / NAMES AND DATES OF THE CURRENTLY SUPERVISED PHD STUDENTS :

- Lucas Goirand-Lopez
- Alexandre Vigier

CREPEL / NAMES AND DATES OF THE PREVIOUSLY SUPERVISED PHD STUDENTS :

- Claire Pléau, PhD – November 2019
- Shu Xian Ho, PhD – December 2018
- Angélique Peret, PhD – November 2014
- David Ouedraogo, PhD – September 2013
- Julien Artinian, PhD – December 2012
- Jérôme Epsztein, PhD – December 2005
- Patrice Congar, PhD – December 1998

CREPEL / PUBLICATIONS OF THE PREVIOUSLY SUPERVISED PHD STUDENTS :

- Peret A, Pléau C, Pearlstein E, Scalfati T, Marti G, Michel F, Crépel V. Mature dentate granule cells show different intrinsic properties depending on the behavioural context of their activation. BioRxiv, 2018
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- Congar P, Leinekugel X, Ben-Ari Y, Crépel V. A long-lasting calcium-activated nonselective

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MICHEL/ NAMES AND DATES OF THE CURRENTLY SUPERVISED PHD STUDENTS :

- Selected PhDs: in animal epileptic models' studies
- co-supervised with Dr. Charles Quairiaux: Guru Padmasola and Fabien Friscourt

MICHEL / NAMES AND DATES OF THE PREVIOUSLY SUPERVISED PHD STUDENTS :

- Selected PhD: in animal epileptic models' studies
- co-supervised with Dr. Charles Quairiaux: Laurent Sheybani, 2016

MICHEL / PUBLICATIONS OF THE PREVIOUSLY SUPERVISED PHD STUDENTS :

- Sheybani, L., Birot, G., Contestabile, A., Seeck, M., Kiss, J.Z., Schaller, K., Michel, C.M., and Quairiaux, C. (2018). Electrophysiological Evidence for the Development of a Self-Sustained Large-Scale Epileptic Network in the Kainate Mouse Model of Temporal Lobe Epilepsy. J. Neurosci. 38, 3776–3791.

- Sheybani, L., van Mierlo, P., Birot, G., Michel, C.M., and Quairiaux, C. (2019). Large-Scale 3–5 Hz Oscillation Constrains the Expression of Neocortical Fast Ripples in a Mouse Model of Mesial Temporal Lobe Epilepsy. ENeuro 6.
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PROJECT C4

Title : The mechanisms underlying the generalization and propagation of epileptic activity in the neonatal brain in vivo

Supervisor (Marseille) : LEINEKUGEL Xavier (xavier.leinekugel@inserm.fr - +33 (0)6 09 55 53 39)

Laboratory : Mediterranean Institute of Neurobiology (INMED, UMR 1249

http://www.inmed.fr/en/integrative-properties-of-plastic-neuronal-circuits-in-health-and-disease-en

Co supervisor (Kazan, Russie) : MINLEBAEV Marat (minlebaev@mail.ru - +79600387001)

Laboratory : Department of Physiology of Human and Animals, Kazan Federal University

Duration : 25% AMU lab (2visits to INMED 6 months each, 12months/ 4 years), 75% partner lab

Project

STATE OF THE ART : Epilepsy is a neurological disease involving recurrent seizures, which affects up to 1.5% of the human neonates (Sheth et al., 1999; Plu and Fred, 1983). Neonatal seizures often propagate and degenerate into generalized seizures, even though starting in a local circuit (Pisani et al., 2012). However, in mature brain the interictal activity triggers the epileptic surround inhibition (ESI) that limits the interictal-to-ictal transition and spread of epileptic activity (Prince and Wilder, 1967). ESI arise from the various mechanisms such as modulations of blood flow, oxygen delivery, long-range and local inhibitory circuitry. On the other hand neonatal nervous system is characterized by the low level of the neurovascular coupling maturation (Kozberg et al., 2013; Zehendner et al., 2013) and immaturity of the interneuronal based inhibition (Daw et al., 2007; Doischer et al., 2008; Minlebaev et al., 2011). ***Our hypothesis*** *is that immature neurovascular coupling and inhibitory circuits are inefficient to generate surround inhibition resulting in easily propagating epileptic discharges and their degeneration into the epileptic activity in the developing cortex.* Our PhD project is to test this hypothesis using a combination of sophisticated imaging and electrophysiological recordings from rodent models of epileptic activity *in vivo*.

OBJECTIVES : Our first objective is to characterize the changes in blood flow and oxygenation of the neuronal tissue, both in the epileptogenic focus and in the surrounding regions. This will be performed in the laboratory of Neurobiology (Russia), which has already showed the efficiency of the intrinsic optical signal imaging (IOSi) in detection and characterization of the evoked neuronal activity and associated changes in local blood flow and oxygenation (Sintsov et al., 2017; Suchkov et al., 2018). The result of the first objective will be (i) ameliorated IOSi technique in order to detect the position of the epileptic focus and (ii) detailed description of the hemovascular changes and oxygenation of the neuronal tissue over extended cortical surface during epileptic activity in the immature nervous system. Our second objective is to combine the imaging techniques, providing spatio-temporal information about seizure dynamics, with a direct evaluation of inhibitory function within the epileptic focus and in the surrounding cortical tissue.

Extra- and intracellular in vivo recordings of neuronal activity are the main speciality of the INMED group (France), and will provide a direct assessment of the intracortical recruitment and functional efficacy of distant and local GABAergic inhibition in local and distant cortical sites. Monosynaptic interactions between pyramidal cells and interneurons will be also quantified with single cell resolution using spike sorting technique. All the resources required for realization of this objective are available in INMED.

METHODS : These complementary sets of expertise will therefore allow us to explore the mechanisms underlying the generalization and propagation of epileptic activity in the neonatal brain in vivo.

CANDIDATE PROFILE : The PhD student to be recruited should be highly motivated and versatile, with a background in experimental biology, especially in neuroimaging in vivo using IOSi. The candidate should be interested in network dynamics and image analysis. Background in electrophysiological recordings in vivo would be a significant plus

LEINEKUGEL/ NAMES AND DATES OF THE CURRENTLY SUPERVISED PHD STUDENTS :

- Arnaldo Ferreira Gomes Da Silva

LEINEKUGEL / NAMES AND DATES OF THE PREVIOUSLY SUPERVISED PHD STUDENTS :

- Aude Retailleau (2008 - 2011)
- Maria Isabel Carreno (2014 - 2017)
- Olivier Dubanet (2015 - 2019)

LEINEKUGEL / PUBLICATIONS OF THE PREVIOUSLY SUPERVISED PHD STUDENTS :

- M.I. Carreno-Munoz, F. Martins, M.C. Medrano, E. Aloisi, S. Pietropaolo, C. Dechaud, E. Subashi, G. Bony, M. Ginger, A. Moujahid, A. Frick & X. Leinekugel (2018). Potential Involvement of Impaired BKCa Channel Function in Sensory Defensiveness and Some Behavioral Disturbances Induced by Unfamiliar Environment in a Mouse Model of Fragile X Syndrome, Neuropsychopharmacology, 43 492-502.
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- Beyeler,A., Retailleau,A., Molter,C., Mehidi,A., Szabadics,J. & Leinekugel,X. (2013). Recruitment of Perisomatic Inhibition during Spontaneous Hippocampal Activity In Vitro.PLoS One 8(6), e66509.

MINLEBAEV/ NAMES AND DATES OF THE CURRENTLY SUPERVISED PHD STUDENTS :

- Sharipzyanova Lyailya

INLEBAEV / NAMES AND DATES OF THE PREVIOUSLY SUPERVISED PHD STUDENTS :

- Mitrukhina O, 12/10/2017
- Suchkov D, 24/12/2019

LEINEKUGEL / PUBLICATIONS OF THE PREVIOUSLY SUPERVISED PHD STUDENTS :

- Suchkov D, Sharipzyanova L, Minlebaev M. Horizontal Synchronization of Neuronal Activity in the Barrel Cortex of the Neonatal Rat by Spindle-Burst Oscillations. Front Cell Neurosci. 2018 Jan 19;12:5.
- Sintsov M, Suchkov D, Khazipov R, Minlebaev M. Developmental Changes in Sensory-Evoked Optical Intrinsic Signals in the Rat Barrel Cortex. Front Cell Neurosci. 2017 Dec 12;11:392. doi: 10.3389/fncel.2017.00392. eCollection 2017.
- Sintsov MY, Suchkov DS, Minlebaev MG. [DETECTION OF OPTICAL INTRINSIC SIGNAL IN SOMATOSENSORY CORTEX OF NEONATAL RATS USING PRINCIPAL COMPONENT ANALYSIS]. Ross Fiziol Zh Im I M Sechenova. 2017 Feb;103(2):152-60. Russian.
- Khazipov R, Zaynutdinova D, Ogievetsky E, Valeeva G, Mitrukhina O, Manent JB, Represa A. Atlas of the Postnatal Rat Brain in Stereotaxic Coordinates. Front Neuroanat. 2015 Dec 23;9:161.
- Mitrukhina O, Suchkov D, Khazipov R, Minlebaev M. Imprecise Whisker Map in the Neonatal Rat Barrel Cortex. Cereb Cortex. 2015 Oct;25(10):3458-67.
- Tsintsadze V, Minlebaev M, Suchkov D, Cunningham MO, Khazipov R. Ontogeny of kainate-induced gamma oscillations in the rat CA3 hippocampus in vitro. Front Cell Neurosci. 2015 May 20;9:195

PROJECT C5

Title : Oculomotor decision-making in health and Parkinson's disease

Supervisor (Marseille): MONTAGNINI Anna (anna.montagnini@univ-amu.fr - +33 (0)4 91 32 40 43)

Laboratory : Timone Institute of Neurosciences (INT, UMR 7289)

http://www.int.univ-amu.fr/MONTAGNINI-Anna?lang=en

Co supervisor (Columbia, Canada): SPERING Miriam (mspering@mail.ubc.ca - +1 604 822 3511)

Laboratory : Department of Ophthalmology & Visual Sciences, University of British Columbia (UBC)

http://www.visualcognition.ca/spering/index.html

Duration : 18 months AMU lab, 18 months partner lab

Project

STATE OF THE ART : Voluntary eye movements provide a dynamic readout of ongoing perceptual and cognitive processes and they are often taken as a model of sensorimotor decision-making. Our two laboratories have previously investigated, both jointly and independently, the role of retinal and extraretinal (predictive and reward-related) information for gaze tracking behaviour (e.g Spering and Montagnini 2011), with a complementary approach, toward the clinical aspects for the UBC partner (Ming et al., 2016; Fooken et al., 2018) and the computational aspects for the AMU lab (Bogadhi et al. 2013, Damasse et al. 2018a, Pasturel et al. 2020). Parkinson's Disease (PD) is mostly known for its dramatic effects on motor performance. However, few previous studies suggest that visual and memory-guided eye movements are largely spared in PD, whereas predictive eye movements undergo specific impairments (Helmchen et al. 2012). In addition, severe impairments in decision-related cognitive functions have been documented in PD patients (and related to their L-Dopa medication). For instance, their performance is suboptimal when they have to learn a probabilistic associative rule between a choice and the delivered reward, or when they have to learn a *Prior* about the occurrence of a perceptual feature (Perugini et al. 2018). Deficient frontal dopaminergic circuits are believed to be at the origin of several motor and cognitive impairments in PD. However, the evidence in this sense is multifaceted, with positive, negative and even null effects of dopamine abundance on specific PD-related deficits reported (Perugini et al. 2018), and typically addressed in independent, thus hardly comparable studies.

OBJECTIVES : With this project we aim at elucidating the pattern of deficits in sensorimotor decision-making in PD patients and healthy age-matched controls, addressing its multiple facets with novel oculomotor experiments. These experimental paradigms will globally target all aspects of decision behavior at once, including efficient use of prior experience, analysis of noisy sensory evidence, reward outcome-based correction, and choice selection under risk. Data will be analyzed and modeled within the theoretical framework of Bayesian statistical inference for decision-making (at AMU). Importantly, we

will systematically correlate decision-making deficits with patients' motor performance and with a number of clinical and neuropsychological assessments, with a particular focus on risk-taking behavior (at UBC, with clinical collaborators in Neurology). In addition, we will investigate the role of L-Dopa medication on the integration of experience-based information about contextual contingencies.

FEASABLITY : The feasibility of this project is high, as supported by the long-lasting collaboration of the partners, as well as by a set of preliminary results, obtained in a recent AMU-UBC study on visual target selection in presence of a stochastic target-reward association. These promising results were presented at international conferences (VSS and SfN; Damasse et al. 2018b; Montagnini et al., 2018). The first part of the PhD project will be devoted to finalizing and publishing this study. In a second time, the student will compare obtained results with data obtained in a new group of PD patients and a cohort of patients with schizophrenia, another documented dopaminergic dysfunction (Spering et al.; 2013; Bansal et al., 2018). To conclude, we expect that, by leveraging on a well-known sensorimotor system and on a high-resolution behavioral measure, this PhD project will shed new light on the multifaceted and yet poorly understood pattern of sensorimotor and cognitive deficits of Parkinson's Disease.

EXPECTED CANDIDATE PROFILE : The selected PhD student will design, implement and analyze a set of experiments to test eye movements and visual perception in Parkinson's Disease patients, both ON and OFF medication, as well as in age-matched healthy controls and young healthy adults. She/he will also run simulations to fit the data with different decision models.

References

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- Damasse J-B., Perrinet L.U., Madelain L. and Montagnini A. (2018a). Reinforcement effects in anticipatory smooth eye movements. *Journal of Vision* 18(11):14
- Damasse J-B., Mann G., Jones C., McKeown M., Spering M. and Montagnini A. (2018b) Reinforcement contingencies affect pursuit target selection in healthy and Parkinson's disease participants. Poster presented the *Vision Science Society Meeting*, Abstract published on Journal of Vision, Vol.18, 599. doi:10.1167/18.10.599
- Fooken J., Mann G.K., Jones C.B., McKeown M.J., and Spering M. (2018). Eye and hand movement characteristics during rapid go/no-go decisions in Parkinson's disease. Poster presented at the Society for Neuroscience meeting, San Diego, CA: Society for Neuroscience, Online.
- Helmchen C., Pohlmann J., Trillenberg P., Lencer R., Graf J., and Sprenger A. (2012). "Role of anticipation and prediction in smooth pursuit eye movement control in Parkinson's disease". In: *Movement Disorders* 27.8, pp. 1012–1018.
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•Montagnini A., Damasse J-B., Mann G., Jones C., McKeown M. and Spering M. (2018) Smooth pursuit eye movements as dynamic readout of reward-based target selection in healthy and Parkinson's Disease participants. Poster presented at the Society for Neuroscience meeting, San Diego, CA: Society for Neuroscience, Online.
• Pasturel C., Montagnini A. and Perrinet L. (2020). Humans adapt their anticipatory eye movements to the volatility of visual motion properties. Plos Computational Biology, *in press.*
•Perugini A., Ditterich J., Shaikh A.G., Knowlton B.J., Basso M.A. (2018). Paradoxical Decision-Making: A Framework for Understanding Cognition in Parkinson's Disease. Trends in Neuroscience 41(8):512-525
•pering M., and Montagnini A. (2011). Do we track what we see? Common versus independent processing for motion perception and smooth pursuit eye movements: A review. Vision Research 51: 836–852
•Spering, M., Dias, E.C., Sanchez, J.L., Schütz, A.C., & Javitt, D.C. (2013). Efference-copy failure during smooth pursuit eye movements in schizophrenia. *Journal of Neuroscience, 33*, 11779-11787

MONTAGNINI / NAMES AND DATES OF THE CURRENTLY SUPERVISED PHD STUDENTS :

- Federica Conti
- Vanessa Carneiro-Morita (co-supervised by Guillaume Masson)
- Nicolas Orlando-Dessaints (co-supervised by Laurent Goffart)

MONTAGNINI / NAMEES AND DATES OF THE PREVIOUSLY SUPERVISED PHD STUDENTS :

- Jean-Bernard Damasse (2014-2018)
- Kiana Mansour-Pour (2015-2019, co-supervision)
- Mathieu Servant (2011-2015, co-supervision)
- Claudio Simoncini (2008-2013, co-supervision)
- Amarender Bogadhi (2008-2012, co-supervision

MONTAGNINI / PUBLICATIONS OF THE PREVIOUSLY SUPERVISED PHD STUDENTS :

- Mansour-Pour, L.U.Perrinet, A.Montagnini and G.S. Masson, under review for Journal of NeuroscienceJ-B. Damasse, L.U. Perrinet, L. Madelain and A. Montagnini (2018) Journal of Vision 18(11):14
- M.Servant, C.White, A.Montagnini and B.Burle (2016). Journal of Cognitive Neuroscience 28(10):1501-21
- M.Servant, C.White, A.Montagnini and B.Burle. (2015). The Journal of Neuroscience, 35(28): 10371-10385.
- M.Servant, A.Montagnini and B.Burle. (2014). Cognitive Psychology, 72: 162-195.
- AR Bogadhi, A Montagnini & GS Masson (2013), Journal of Vision, 13(13):5, 1–26.
- C.Simoncini, L.U. Perrinet, A.Montagnini, P.Mamassian and G.S. Masson (2012). Nature Neuroscience 15(11):1596-603.

SPERING / NAMEES AND DATES OF THE CURRENTLY SUPERVISED PHD STUDENTS :

- Xiuyun Wu (2017
- Philipp Kreyenmeier (2018

SPERING / NAMEES AND DATES OF THE PREVIOUSLY SUPERVISED PHD STUDENTS :

- Jolande Fooken (2015 – 2019)

SPERING / PUBLICATIONS OF THE PREVIOUSLY SUPERVISED PHD STUDENTS :

- Rothwell A.C., Wu X., and Spering M. (2020). On the relation between anticipatory ocular torsion and anticipatory smooth pursuit. Journal of Vision 20(20):4.
- Murch W.S., Limbrick-Oldfield E.H., Ferrari M.A., MacDonald K.I., Fooken J., Cherkasova M.V., Spering M., and Clark L. (2020). Zoned in or zoned out? Investigating immersion in slot machine gambling using mobile eye tracking. Addiction in press.
- Wu X. and Spering M. (2019). Ocular torsion is related to perceived motion-induced position shifts. Journal of Vision 19(12):11.
- Rolin R., Fooken J., Spering M. and Pai D.K. (2019). Perception of looming motion in virtual reality egocentric interception tasks. IEEE Transactions on Visualization and Computer Graphics 25:3042-3048.
- Fooken J. and Spering M. (2019). Decoding go/no-go decisions from eye movements. Journal of Vision 19(2):5.
- Fooken J., Lalonde K.M., Mann G.K., and Spering M. (2018). Eye movement training is most effective when it involves a task-relevant sensorimotor decision. Journal of Vision 18(4):18, 1-18.
- Kreyenmeier P., Fooken J., and Spering M. (2017). Context effects on smooth pursuit and manual interception of a disappearing target. Journal of Neurophysiology, 118:404-415.
- Palidis D.J., Wyder-Hodge P., Fooken J., and Spering M. (2017). Distinct eye movement patterns enhance dynamic visual acuity. PLoS ONE 12(2):e0172061.
- Fooken J., Yeo S.H., Pai D.K., and Spering M. (2016). Eye movement accuracy determines natural interception strategies. Journal of Vision 16(14):1, 1-15

PROJECT C6

Title : Neural regulation of feeding. A translational approach from mouse to human

Supervisor (Singapore, Asie) : YU Fu (fu_yu@sbic.a-star.edu.sg)

Laboratory : Agency for Science, Technology and Research

https://www.a-star.edu.sg/sbic

Co supervisor (Marseille) : RANJEVA Jean-Philippe (jean-philippe.ranjeva@univ-amu.fr - +33 (0)4 91 38 8463)

Laboratory : Center for Magnetic Resonance in Biology and Medicine (CRMBM, UMR 7339)

http://www.crmbm.univ-amu.fr/

Duration : 1 year AMU lab, 2 years partner lab

Project

STATE OF THE ART : One of the biggest challenges of the modern society is the conflict between the feeding regulation echanisms shaped by evolution to survive under food-scarcity and the food abundance in majority of the world brought by technological revolution. Such challenge led to rapid growing epidemic of obesity and many other metabolic diseases. Feeding is critical for energy homeostasis and its deregulation is related with not only metabolic diseases but also mental health issues. Feeding is tightly regulated by brain and especially by hypothalamus. Several hypothalamic nuclei, including lateral hypothalamus, zona incerta (ZI), arcuate (Arc), have been found to regulate feeding. Recent research from SBIC (Luo et al. Science 2018) revealed the critical role of yet another region, tuberal nucleus (TN), in feeding regulation. Despite revealing multiple brain regions in feeding regulation, how these different nuclei communicate with each other and influence each other's function to orchestrate proper feeding behavior is still unclear. More importantly, even though feeding is a conserved behavior from mouse to primates, whether the knowledge obtained from mouse research can be translated into understanding human feeding regulation is still debatable. With strong imaging and systems neuroscience expertise of both Singapore and French teams, we propose to systematically study the neural regulation of feeding in both mouse and human, in both control and obese subjects, to explore the potential neuronal targets for treating obesity.

OBJECTIVES AND METHODS : 1: Functional imaging of different hypothalamic nuclei in control and obese mice (To be conducted by SBIC team during the two first years). SBIC team has established strong capability in systems neuroscience research, including cutting-edge optogenetic tools, in vivo calcium imaging, and advanced viral tools, to investigate the neural circuits of mouse (Luo et al., 2018). Combining viral tools and different transgenic mice, we can specifically label defined subpopulation of neuronal cells in different mouse hypothalamic nuclei and perform in vivo imaging of neuronal calcium dynamics in free moving mice, so that the temporal profile of neural dynamics can be precisely analyzed in accordance with the feeding behavior (i.e. start of food consumption, termination of food consumption, food foraging, etc.) (Jennings et al., 2015). Endpoints: 1) Calcium response of GABAergic neurons in ZI, somatostatin neurons in TN, lateral hypothalamus GABAergic neurons and somatostatin neurons in Arc, during approaching and consumption of normal chow diet and high fat diet in lean wild type mice; 2) Calcium response of GABAergic neurons in ZI, somatostatin neurons in TN, lateral hypothalamus GABAergic neurons and somatostatin neurons in Arc, during approaching and consumption of normal

chow diet and high fat diet in high-fat diet induced obese mice. 2: Functional and quantitative anatomical high resolution MRI of hypothalamic nuclei in control, obese and anorexic patients (To be conducted by CRMBM team during the third year). Integrated clinical 7T MRI protocols will be used at CRMBM to characterize human hypothalamic nuclei in vivo. Endpoints 1) Comparison of morphometrics of hypothalamic nuclei between patients and controls; 2) Activation patterns of hypothalamic nuclei during palatable and non-palatable food; 3) Comparisons of functional/structural connectivity of hypothalamus between patients and controls.

EXPECTED RESULTS : Combining the work at two sites will help us to understand how the feeding regulation neural circuits evolve from mouse to humans and will lead to better identification of the key neural nods in developing eating disorders, and thus provide the foundation for better treating these diseases.

EXPECTED CANDIADTE PROFILE : During the whole period of the PhD work (the 2 first years in Singapore followed by at least one year in Marseille), monthly skype meetings will be organized with the student and the two supervisors. Through the Merlion project, two face-to-face meetings are organized each year (one in Singapore, one in Marseille).

RANJEVA / NAMES AND DATES OF THE PREVIOUSLY SUPERVISED PHD STUDENTS :

- 12 PhD supervisions or co-supervisions since 2006, (Audoin, Au Duong, Reuter, Bettus, Rico, Gour, Faivre, Lecocq, Wirsich, Maarouf, Donadieu)

RANJEVA / PUBLICATIONS OF THE PREVIOUSLY SUPERVISED PHD STUDENTS :

- At least 4 common publications with each of the PhD students (PhD students as first authors)

PROJECT C7

Title : Adaptive plasticity of interactive somatosensory and motor cortical networks underlying recovery of forelimb skills following cortical ministroke in rats

Supervisor (Marseille) : XERRI Christian (christian.xerri@univ-amu.fr - +33 (0)4 13 55 09 55)

Laboratory : Sensory and Cognitive Neuroscience Laboratory (LNSC, 7260)

https://lnsc.fr/

Co Supervisor (Montréal, Canada) : DANCAUSE Numa (numa.dancause@umontreal.ca - + 1 514 343 6317)

Laboratory : Cortical plasticity and motor recovery laboratory

www.numadancause.com

Duration : 18 months AMU lab, 18 months partner lab

Project

STATE OF THE ART : Sensory contribution to the recovery of movement is currently neglected in the vast majority of stroke tudies which mainly focus on the motor component of movements and most often assess deficits and recovery of movement execution that do not require a fine somatosensory feedback. Therefore, there is a need to evaluate the contribution of somatosensory function to the recovery of motor skills and to provide a neural basis to the optimization of somatosensory feedback in the rehabilitation procedures following stroke. It is well established that cortical map remodeling is a substrate of adaptive changes in the post-stroke recovery of skilled movement. A way of searching for the neural underpinning of this recovery is to track postlesion changes taking place in a global interactive network that includes motor and somatosensory cortical areas which have so far been investigated independently of each other in the animal stroke studies.

OBJECTIVES : We will investigate the postlesion remodeling of sensory and motor somatotopic maps in parallel with the spontaneous recovery of impaired somatosensory-guided distal movements following a ministroke targeting the forelimb areas in S1 or M1 in rats. In addition, we will search for the effects of a rehabilitative training procedure on the time course of both cortical changes and behavioral recovery.

METHODS : In a rat model of cortical stroke, we will use a combination of micro-electrode array covering somatosensory and motor area and cortical mapping techniques complemented by voltage-sensitive-dye (VSD) imaging as well as behavioral assessment of deficits and recovery of fine sensorimotor skills (manual dexterity, fine locomotor adjustments). A forced-locomotion carrousel will be used as a rehabilitative sensorimotor training procedure. In addition, we will use GABA-mediated (muscimol) cortical inactivation to explore the causal relation between cortical changes and behavioral recovery.

EXPECTED RESULTS : Following stroke in the forepaw area in S1, we expect both a reinforcement of thalamocortical tactile inputs converging to M1 on the ipsilesional side and a motor map remodeling as the functional recovery develops. Reciprocally, a lesion targeting M1 is expected to remodel the S1 forepaw map through an increased contribution of somatosensory feedback in the recovery of sensorimotor abilities. Moreover, we hypothesize that reinforcing sensorimotor experience as a rehabilitative training will improve and shorten the functional recovery through adaptive changes in sensorimotor
cortical networks.

COMPLEMENTARITY OF THE 2 LABS : Both partner teams have a strong experience in stroke-induced cortical plasticity, cortical mapping and behavioral assessment of sensorimotor recovery. The team in Montreal has had a focus on the motor cortex plasticity and currently uses the chronic implantation of electrode arrays, whereas the team in Marseille on somatosensory cortex plasticity and uses both electrophysiological mapping and VSD imaging. Therefore, this collaboration is a unique pportunity to explore the postlesion adaptive remodeling of sensorimotor cortical networks by sharing scientific expertise and transferring technical skills.

FEASABILITY : All the technical skills (electrophysiological, VSD imaging, behavioral methods…) required to carry out this project successfully are well mastered by the collaborative teams, each having its own expertise.

EXPECTED PROFILE : The PhD candidate will acquire or improve skills in cortical mapping (motor and somatosensory), VSD imaging and behavioral assessment in rats.

XERRI / NAMES AND DATES OF THE CURRENTLY SUPERVISED PHD STUDENTS :

- No formal PhD direction currently, but co-supervision of Justine Facchini's doctoral research with Yoh'i Zennou-Azogui (director).

XERRI / NAMES AND DATES OF THE PREVIOUSLY SUPERVISED PHD STUDENTS :

- 2011-2015 Sandie THOMATY (codirection with J-M. Jean-Michel Brezun)
- 2014-2017 Julien CORBO (codirection with Nicolas Catz)
- 2016-2020 Jeanne CARON-GUYON (codirection with Nicolas Catz until 2018, then I handed over to Anne Kavounoudias, as a fRMI project was included in the doctoral research)

XERRI / PUBLICATIONS OF THE PREVIOUSLY SUPERVISED PHD STUDENTS :

- THOMATY S, PEZARD L, XERRI C, BREZUN J-M (2017) Acute granulocyte macrophage-colony stimulating factor treatment modulates neuroinflammatory processes and promotes tactile recovery after spinal cord injury. Neuroscience, 349: 144-164.
- CORBO J, ZENNOU-AZOGU Y, XERRI C, CATZ N (2017) Cortical merging in S1 as a substrate for tactile input grouping. ENeuro; doi: 10.1523/ENEURO.0342-17.

- CARON-GUYON J, CORBO J, ZENNOU-AZOGUI Y, XERRI C, KAVOUNOUDIAS A, CATZ N (2019) Heteromodal motion coding in the associative parietal cortex in rats. (submitted to Cerebral Cortex).
- CORBO J, ZENNOU-AZOGU Y, XERRI C, CATZ N Spatiotemporal ntegration of cutaneous inputs in primary somatosensory cortex in relation

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DANCAUSE/ NAMES AND DATES OF THE CURRENTLY SUPERVISED PHD STUDENTS :

- Sandrine Cote
- Ian Moreau
- Boris Touvykine

DANCAUSE / NAMES AND DATES OF THE PREVIOUSLY SUPERVISED PHD STUDENTS :

- Meghan Watson (2012/05 – 2015/09)

DANCAUSE / PUBLICATIONS OF THE PREVIOUSLY SUPERVISED PHD STUDENTS :

- Touvykine M, Elgbeili G, Quessy S, Dancause N. Interhemispheric modulations of motor outputs by the rostral and caudal forelimb areas in the rat. (R1 submitted; J Neurophysiol).
- Côté SL, Quessy S, Dancause N. Modulatory effects of the supplementary motor area (SMA) on primary motor cortex outputs and comparison to those of the dorsal and ventral premotor cortex. J. Neurophysiol. 2020 Jan 1;123(1):407-419.
- Côté SL, Hamadjida A, Quessy S, Dancause N. Contrasting modulatory effects from the contralateral dorsal and ventral premotor cortex on primary motor cortex outputs. J Neurosci. 2017 May 23. pii: 0462-17.
- Quessy S, Côté S, Hamadjida A, Deffeyes J, Dancause N. Ipsi and interhemispheric interactions of the ventral premotor cortex (PMv) with the primary motor cortex (M1) in cebus apella. Cerebral Cortex. 2016 Oct;26(10):3905-20.
- Watson M, Sawan M, Dancause N. The Duration of Motor Responses Evoked with Intracortical Microstimulation in Rats Is Primarily Modulated by Stimulus Amplitude and Train Duration. PLoSOne. 2016 Jul 21;11(7):e0159441.
- Watson M, Dancause N, Sawan M. Intracortical Microstimulation Parameters Dictate the Amplitude and Latency of Evoked Responses.Brain Stimul. 2016 Mar-Apr;9(2):276-84.
- Watson M, Dancause N, Sawan M. Efficient Microstimulation of the Brain: A Parametric Approach. Conf Proc IEEE Eng Med Biol Soc. 2015 Aug; 2015:2155-8.