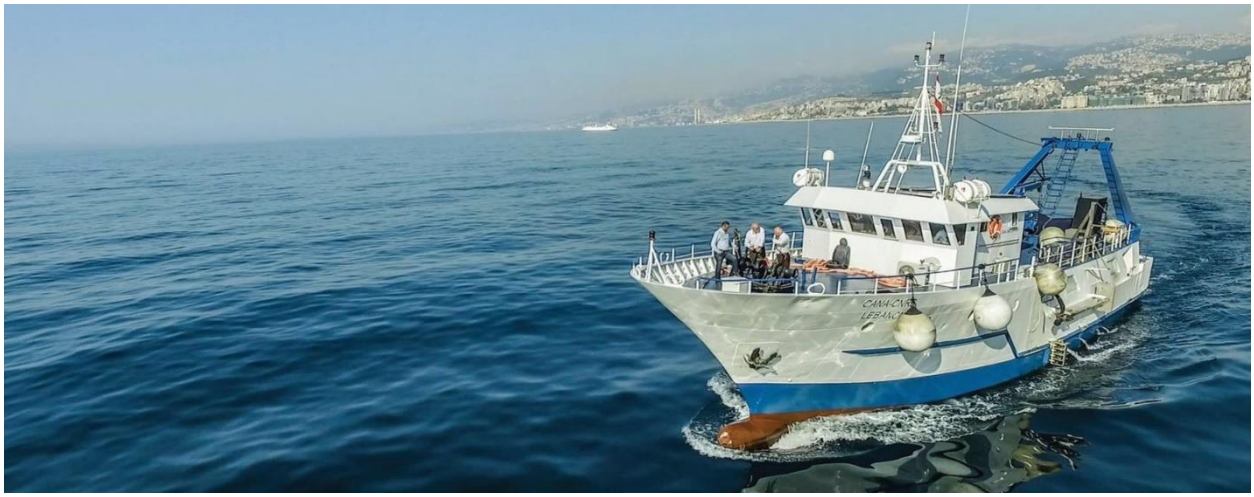
Propositionde sujet de thèse CNRS-L/UPD

2017-2018



CANA-CNRS pour la recherche marine au Liban

Dans le cadre de l'accord entre le Conseil National de la Recherche Scientifique de la République Libanaise (CNRS-L) et l'Université Paris Descartes (UPD) pour le co-financement des thèses de doctorat dans des thématiques d'intérêt commun, des contrats de recherches doctorales pour l'année 2017-2018 seront mis en place. Ces thèsessont proposées conjointement par un laboratoire de recherche de l'UPD et un laboratoire de recherche libanais dans le cadre d'une convention de co-tutelle ou de co-direction. Ainsi, les équipes souhaitant proposer des thèses de doctorat pour l'année 2016-2017 sont priées de compléter ce formulaire de proposition de sujet de thèse et de l'envoyer par courriel avant le 25 mai2017 à l'adresse suivante : tamara.elzein@cnrs.edu.lb. Les sujets retenus seront diffusés pour l'appel à candidature et la sélection finale des lauréats se fera par un comité mixte des deux institutions. **Il est à noter que le laboratoire libanais partenaire s'engage à verser durant les 3 ans de thèse 3000 euros par an comme contribution annuelle à la bourse accordée au candidat retenu.**

Pièces à joindre :

- CV du co-directeurlibanais
- CV du co-directeurfrançais

II.Fiche de Renseignementssur le laboratoired'accueilau Liban (à compléter)

Université ou centre de recherche : Université Libanaise – Faculté des Sciences – Section II

Laboratoire d'accueil : Physiopathologie Cellulaire et Moléculaire

Nom du Directeur du laboratoire : Myrna Hachem

Adresse : Université Libanaise – Faculté des Sciences II – Campus Fanar, Jdeidet, P.O. Box 90656, Liban

Ville : Fanar

Tél./Fax/Mél : 009611686981 / myrnahachem@ul.edu.lb

Faculté ou organisme auquel est affilié le laboratoire d'accueil : Université Libanaise – Faculté des Sciences II

Nom du Directeur de thèse : **Rita Nabout**

Le Directeur de thèse fait-il partie du laboratoire d'accueil : **X** Oui / Non

Si non, précisez son rattachement et ses coordonnées :

- Principaux thèmes de recherche de l'équipe où sera effectué le travail de thèse :
  - Pathologies autoinflammatoire et autoimmune
  - Désordres cognitifs et comportementaux
- Liste des publications récentes de l'équipe (pertinentes au sujet proposé) :
  - A. Hamade, S. Bhanini, T. Saade, Y. Fakih, C. Fakih, **R. Nabout –Azzi**, M. Hazzouri, F. Rizk. Vitamin D levels in serum, vitamin D receptor polymorphisms and semen quality correlations in Lebanon : a pilot cross-sectional study. *Universal Journal of Public Health. 2 (4): 118-124,*. DOI : 10.13189/ujph.2014.020402, 2014.
  - Medlej-Hashim M, Jounblat R, Hamade A, Ibrahim JN, Rizk F, Azzi G, Abdallah M, Nakib L, Lahoud M, **Nabout R.** Hypovitaminosis D in a Young Lebanese Population: Effect of GC Gene Polymorphisms on Vitamin D and Vitamin D Binding Protein Levels. *Ann. Hum. Genet.* 79, 394–401, 2015.
  - Haddad Chadia, Zoghbi Marouan, Hallit Souheil, , Bou-Assi Tarek, **Nabout Rita** ,Azar Jocelyne. Vitamin D levels in Lebanese patients with schizophrenia: a case- control study. *Annals of Nutritional Disorder&Therapy. Vol 4 (1) ISSN : 2381-8891*, 2017

- La thèse sera-t-elle effectuée en co-tutelleou co-direction: **Co-direction**

III. Fiche de Renseignementssur le laboratoire d'accueil à l'UPD

Université ou centre de recherche : Université Paris Descartes

Laboratoire d'accueil : Laboratoire de Psychologie de la Perception (LPP, UMR 8242)

Nom du Directeur du laboratoire : Andrei Gorea

Adresse : 45 rue des Saints Pères

Ville : 75006 Paris

Tél./Fax/Mél :

Faculté ou organisme auquel est affilié le laboratoire d'accueil :

Nom du Directeur de thèse : **Sylvie Chokron**

Le Directeur de thèse fait-il partie du laboratoire d'accueil : **X** Oui / Non

Si non, précisez son rattachement et ses coordonnées :

- Principaux thèmes de recherche de l'équipe où sera effectué le travail de thèse :
  Etude des processus cognitifs impliqués dans la perception et l'action chez le bébé, l'enfant et le sujet adulte, typique et atypique ainsi que de leurs bases cérébrales.

- Liste des publications récentes de l'équipe (pertinentes au sujet proposé) : **(3 dernières années)**

1. Peyrin, C., Ramanoël, S., Roux-Sibilon, A., **Chokron, S**. & Hera, R. (in press) Scene perception in age-related macular degeneration: Effect of spatial frequencies and contrast in residual vision. ***Vision Research***.

2. Tordjman, S., **Chokron, S**., Delorme, R., Charrier, A., Bellissant, E., Jaafari, N., and Fougerou, C. (2016). Melatonin: pharmacology, functions and therapeutic benefits. ***Neuropharmacology***, in press.

3. **Chokron, S.** and Dutton, G.N. (2016). Impact of cerebral visual impairments on motor skills:implications for developmental coordination disorders. ***Frontiers in Psychology.****In press**

4. Dutton, G.N., **Chokron, S**., Little, S., Mc Dowell, N., (2016). Difficulty seeing one's feet, 'clumsiness', and seeing only part of the scene at a glance: posterior parietal dysfunction, a common form of cerebral visual impairment. Visual Development and Rehabilitation. In press.

5. **Chokron, S.**, Perez, C. and Peyrin C., (2016) Behavioural consequences and cortical reorganization in homonymous hemianopia ***Front Syst.Neurosci.*** *In press*

6. Petkovic M, **Chokron S**, Fagard J. (2016). Visuo-manual coordination in preterm infants without neurological impairments.***Res Dev Disabil*****.** 51-52:76-88

7. Cavézian, C., Perez, C., Peyrin, C., Gaudry, I., Obadia, M., Gout, O. & **Chokron, S**. (2015). Is there an ipsilesional deficit in hemianopia? The question of *sightblindness*in the 'intact' visual field. ***Cortex,*** 69:166-74.

8. Perez, C. and **Chokron S.**(2014) Rehabilitation of homonymous hemianopia: insight into blindsight.***Front. Integr. Neurosci*****.*** 8:82-88.

9. Fayel A, **Chokron S**, Cavézian C, Vergilino-Perez D, Lemoine C, Doré-Mazars K. (2014). Characteristics of contralesional and ipsilesional saccades in hemianopic patients. ***Exp. Brain Res***. 232(3):903-17. *IF 2.168*

10. **Chokron S,** Helft G, Perez C.(2014). Effects of ageandcardiovasculardisease on selective attention.***Cardiovasc Psychiatry Neurol.*** 185385. doi: 10.1155/2013/185385. Epub 2013 Dec 25.

11. Graignic-Philippe R, Dayan J, **Chokron S**, Jacquet AY, Tordjman S. (2014). Effects of prenatal stress on fetal and child development: a critical literature review.***Neurosci. Bio. Behavioural Reviews***, Jun; 43:137-62.

12. Raz N, **Chokron S**, Cavézian C, Ben-Hur T, Levin N (2013), Temporal reorganization to overcome monocular demyelination. ***Neurology****.* Aug 20; 81(8):702-9.

13. Viret, AC, Cavezian C, Coubard OA, Vasseur V, Raz N, Levin N, Vignal C, Gout O, &**Chokron S**. (2013), Optic neuritis: from magnocellular to cognitive residual dysfunction. ***Behav. Neurol.*** Apr 25, in press.

14. Musel B, Bordier C, Dojat M, Pichat C, **Chokron S**, Le Bas JF, Peyrin C. (2013). Retinotopic and lateralized processing of spatial frequencies in human visual cortex during scene categorization. ***J. Cogn. Neurosci***., 25(8):1315-31.

15. Dulin D., Hatwell Y., &**Chokron S.** (2013), Haptic Learning of Spatial Concepts: Can Raised-Line Drawings Improve Blind People's Spatial Capacity? ***Imagination, Cognition and Personality***, 32, 3, 239 - 272.

16. Perez, C., Peyrin, C., Cavézian C., Coubard, O., Caetta,F., Raz, N., Levin, N., Doucet G., Andersson, F.,Obadia M., Olivier Gout O., Héran, F., Savatovsky, J., and **Chokron, S.**(2013), An fMRI investigation of the cortical network underlying detection and categorization abilities in hemianopic patients. ***Brain Topography***, 26(2):264-77.

17. Cavezian, C,Vilayphonh M, Vasseur V, Caputo, G., Laloum L, **Chokron S**, (2013). Ophthalmic disorder may affect visuo-attentional performance in childhood. ***Child Neuropsychology***, 19(3):292-312.

- La thèse sera-t-elle effectuée en co-tutelle ou co-direction: **Co-direction**

IV. Sujet de thèse

A faire signer obligatoirement par tous les co-directeurs

IV.1. Titre

Clinical features associated with visual information deficits in Parkinson's disease

*La thèse fait-elle partie d'un projet de recherche financé par le CNRS-L : □ Oui / **X** Non

Si oui, précisez :

*La thématique sous laquelle s'inscrit la thèse fait-elle partie des priorités du CNRS-L pour l'année 2017-2018 (voir Annexe) : **X** Oui / □ Non

Si oui, précisez (possibilité de choisir plus qu'une) :Neurophysiology and Brain Research

Si non, définir une:

IV.2. Résumé (ne pas dépasser 200 mots)

The population of the developed world is aging. This has led to increased risk and prevalence of late onset neurodegenerative disorderssuch as Parkinson's disease (PD). Parkinson's disease has no satisfying cure or treatment. Based on recent literature and our own preliminary data, we hypothesize that chronic increased activation of astrocytes (the most numerous non-neuronal brain cell type) may contribute to the alteration of S100B protein levels and visual information processing found in PD patients. The goals of this Ph.Dproposal are to investigate (i) whether the astrocyte-secreted biomarker S100B is found in the serum, and (ii) whether its concentrations correlate with the development of visual deficits of PD patients. Our hypothesis is, to our knowledge, new in the field of PD research. When completed, these studies will allow us to (i) identify news biomarkers of the disease, (ii) better understand the role of astrocytic S100B in the neurophysiopathology of PD, and (iii) to determine whether a novel cell type (astrocytes)isof translational relevance to treatment of PD.

IV.3. Contexte et problématique (ne pas dépasser 200 mots)

PD is one of the most widespread neurological disorders (with Alzheimer's disease), with degeneration of cognitive and motor functions due to malfunction and loss of neurons in the central nervous system (CNS). The main feature that has been studied so far is the loss of dopaminergic neurons of the *substantianigra*.

However, other areas of the brain, such the neocortex, are also affected. Accumulating evidence indicates also that PD patients suffer from sensory problems including oculo-visual dysfunction and deficits of visual information processing. Visual impairments in PD, if specifically and precisely screened, could thus be an important marker of the disease. However, some questions remain open regarding the link between the presence of visual deficits and the dynamic evolution of PD. Indeed, more work is called for to understand (1) what visual symptoms are characteristic of the prodromal phase of PD, (2) how these visual deficits evolve in parallel to PD dementia and (3) how these visual deficits as well as PD signs are linked to biological modifications such as the blood level of the astrocyticS100beta protein.This Ph.Dprojectaddressesthese 3 questions.

IV.4. Descriptif des objectifs et de l'impact(ne pas dépasser 200 mots)

The main goal of this project is to first determine whether or not OCT(Optical Coherence Tomography) and VEP (visual-evoked potential) impairments and S100B levels are robust biomarkers in PD patients, and the relationship between these markers during the evolution of the disease. Such knowledge could have profound implications for researchers in the areas of PD, but also and importantly, in the clinic, since this work has the potential to lead to better treatments of PD, or other neurodegenerative diseases such as AD

The two specific aims of this project over the 3 next years are the following:

●**Aim1**: To measure anatomical, biological and functional markers, and determine their relationship, in a cohort of PD patients

●**Aim 2**: To document visual deficits and hallucinations and their evolution in PD patients, and to study the correlation between such deficits and anatomical and functional markers

IV.5. Aspect appliqué et/ou aspect innovateur (ne pas dépasser 200 mots)

Sylvie Chokron and Florian Waszak have already been conducting research that is highly relevant for the current project; they have been conducting behavioral studies investigating the impairment of the prediction of visual stimuli in Parkinson patients.

In the current project, we will use similar paradigms meant to assess visual processing deficits at several stages of the processing stream. In humans, although patients with PD have been described as suffering from ocular as well as more cognitive visual impairments, the link between the different visual impairments (retinal dysfunction, visual processing deficits, visual hallucinations), anatomo-functional markers (OCT and VEP) as well as biological markers, remains poorly understood. The originality of the present project is both to understand the dynamics of the visual deficits in PD as well as to identify biological (S100B mevels) as well as anatomo-functional markers of visual impairments in order to better understand, prevent, treat and follow PD. Indeed, from a clinical point of view, identifying such markers would be very helpful in order to measure the positive effects of a specific treatment.

IV.6. Etat des recherches dans le domaine avant la thèse (ne pas dépasser 200 mots)

Deficits of visual information processing have been reported in PD patients, with dysfunction at several levels of the visual system. This includes psychophysical, electrophysiological and morphological evidence of disruption of retinal structure and function, in addition to disorders of "higher" (cortical) visual processing.Recently, several studies measured the thicknesses of retinal layers with high-resolution OCT and record VEPs in PD patients in an attempt to find biomarkers of the disease. Although there is a possibility that the retina could be a biomarker for disease progression and risk of visual hallucination in PD, further research is required to establish the validity of using OCT and VEP measurements as the anatomic and functional biomarkers for the evaluation of retinal and visual pathways in PD patients, as well as regarding the development of the disease. Additionally, there is increasing evidence that the astrocytic protein S100B acts as a cytokine and has a role in the pathophysiology of PD. Elevated cerebrospinal fluid or serum S100B levels have been found in several acute and chronic brain pathologies, such as traumatic brain injury, stroke or Alzheimer's disease. However, it is not yet known whether S100B levels are increased in the serum or CSF from PD patients.

IV.7. Programme de recherche prévu pour la thèse et contribution des différents partenaires (ne pas dépasser 200 mots)

20 adult patients with PD will be examined twice at 1 year interval in order to study the correlation between anatomical, biological, and functional markers throughout the evolution of the disease.

1.1. Task 1: Anatomical or visual impairment: Measure of RNFL with OCT

Peri-papillary RNFL, macular thickness and volume will be made using a commercially available OCT device (Zeiss Stratus 3000TM) in the Department of Ophthalmology (FondationOphtalmologique Rothschild).

1.2. Task 2 : Biological marker of visual impairment : Measure of S100B

The serum S100B concentrations will be measured using commercial S100 assay from Roche (Roche Diagnostics, Rotkreuz, Switzerland), with an interassay coefficient of variation <2.8% according to the manufacturer'smethods. Serum will be tested 3 times (once a year) and potentially 6 times (twice a year) in order to determine whether serum S100B levels increase over time for each PD patient.

1.3. Task 3 : Functional marker of visual impairment : VEP, visual processing and measure of visual hallucinations

Functional markers will consist of (1) visual-evoked potential (VEP) recording, (2) evaluation of visual hallucinations, (3) neurovisual examination, (4) visual detection and categorization tasks of low and high spatial frequency stimuli (for methodological details, see Cavezian et al, 2015).

Date 01/06/2017

Noms et signatures (directeurs de thèse)

Pr. Rita Nabout ***Dr Sylvie Chokron***

Annexe:thématiques prioritaires pour les bourses doctorales 2017-2018

Cultural heritage - Archaeology - Protection, conservation and restoration of artifacts and ancient manuscripts - Archaeometry
Arabic language and History - Arabic linguistics, dynamism, and history - Cognitive linguistics (in Arabic) - History of Science in Arabic civilization - Arabization of softwares
Sociology and political science - Migrationsociology - Conflict resolution and Post-conflict societies - Gender and feminist studies - Gender diversity - Ethics in media coverage of conflicts (conventional and social medias)
Business, Economics and Finance - Entrepreneurial University and innovation - Economy of conflict areas - Lebanon as potential destination for offshoring - Actuarial science and Financial risk management - Mathematical and computer modeling applied to finance and economy - Business information decision systems - International finance and emerging markets - Entrepreneurship - Corporate governance - Cross-cultural management - Digital marketing - Internal and external control - Consumer behavior - Enhancing work conditions

- Asset pricing, risk management and volatility modeling
- Banking policies in the MENA region

Environment, natural resources
- Valorization of Lebanese coastal zones
- Petroleum studies
- Sustainable water management
- Renewable energy
- Biodiversity and speciation
- Mitigation & management of natural risks
- Sociology of risk
- Air quality
- Urban planning in the age of climate change
- Environmental law

Agriculture and food
- Challenges of agricultural activities
- Food Security
- Food safety & food industry
- Veterinary medicine
- Pest and Alien species

Medical sciences
- Addictive Diseases
- Cancer Research
- Cardiovascular diseases
- Clinical pharmacology. Pharmacy
- Clinical Immunology and Immunopathology
- Clinical Biochemistry
- Clinical Genetics
- Radiotherapy
- Diseases of Bones and Joints
- Endocrinology
- Geriatrics
- Infectious Diseases
- Medical Microbiology
- Mental Disorders, Psychosomatic Diseases
- Metabolic Disorders
- Methods of Epidemiology and Preventive Medicine
- Psychiatry
- Neurophysiology and Brain Research.
- Public Health and Health Services
- Respiratory Diseases
- Ethics in medicine and medical research

Basic science
- Theoretical&Particlephysics
- Peaceful use of nuclear energy and technics
- Forensicchemistry
- Green chemistry
- Biomedical engineering
- Molecular & Cellular Biology
- Genetics
- Architecture and Design

- Civil and Environmental Engineering
- Chemical Engineering
- Ergonomy
- Electrical and Computer Engineering
- Industrial Engineering and Management
- Modern Imaging and vision
- Mechanical Engineering