Comportements et noyaux gris centraux

Rapport Hcéres

agence d'évaluation de la recherche
et de l'enseignement supérieur

Section des Unités de recherche

AERES report on the research unit

Behavior and basal ganglia

from the

University of Rennes 1

February 2011

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Le Président de l'AERES

Didier Houssin

Section des unités de recherche

Le Directeur

Pierre Glorieux

February 2011

Research Unit

Name of the research unit: Behavior and basal ganglia

Requested label: EA

N° in the case of renewal: 425

Name of the director: M. Marc VERIN

Members of the review committee

Committee chairman

Mrs. Christine TRANCHANT, University of Strasbourg, au titre du CNU

Other committee members

M. Pierre BURBAUD, University of Bordeaux, France

M. Luc DEFEBVRE, University of Lille, France

M. Antonio PISANI, University Tor Vergata, Rome, Italy

M. Marc SAVASTA, University of Grenoble, France

Observers

AERES scientific advisor

M. Bruno BONTEMPI

University, School and Research Organization representatives

M. Claude LABIT, Université de Rennes 1

M. Xavier MORANDI, Université de Rennes 1

M. Yves RAYER, CHU de Rennes

Report

1 • Introduction

- Date and execution of the visit

The visit took place in Rennes on February 16, 2011 from 8.30 am to 5.00 pm. The scientific program included an overall presentation of the Unit by its director, followed by scientific presentations of the past activity and projects organised into three main research themes. Meetings with PhD students, administrative and technical staff and researchers were also organized before a final door-closed meeting during which the members of the committee exchanged their opinions

- History and geographical localization of the research unit, and brief presentation of its field and scientific activities

The research unit, titled "Behavior and basal ganglia, is located in the Faculty of medicine, at the University of Rennes 1. It has been recognized as "Unité de Recherche Universitaire-Equipe en emergence" (URU-EM425) in October 2006. Its topic is the study of non motor functions of the basal ganglia in humans, and it has developed three research themes: Emotions, Motivation and neuropsychiatric therapeutic applications.

- Management team

The unit is directed by Marc VERIN, Neurologist, PUPH. Each of the 3 research themes is headed by one of the 3 PUPHs of the team: Emotion and basal ganglia (Marc VERIN); Motivation and basal ganglia (Dominique DRAPIER); and Neuropsychiatric therapeutical applications (Bruno Millet).

- Staff members (on the basis of the application file submitted to the AERES)

N1: Number of researchers with teaching duties (Form 2.1 of the application file)	6	6
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)		
N3: Number of other researchers including postdoctoral fellows (Forms 2.2, 2.4 and 2.7 of the application file)	2	2
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)		
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)		
N6: Number of Ph.D. students (Form 2.8 of the application file)	6	
N7: Number of staff members with a HDR or a similar grade	3	3

2 • Overall appreciation on the research unit

- Summary

This unit has been judged excellent particularly in regard of the originality of its research and its pluridisciplinary. It was the first French team to focus its research in the field of behavioral and basal ganglia. It has obtained interesting findings within the three main axes envisioned, that are "Emotion and basal ganglia"; "Motivation and basal ganglia", and "Therapeutic applications". Its research activity has led to very good publications in Brain, Neurology, PloS One, and Movement Disorders, and to the creation of a startup called "Syneika", which offers technical innovations in the field of transmagnetic stimulation (rTMS). The management team appeared very dynamic and efficient in developing new projects and raising funding (University, PHRC, Industry…).

- Strengths and opportunites

The topic of the research developed, which focuses on the role of basal ganglia in emotion and motivation in humans, and the scientific approach used (centered on deep brain stimulation data) are very original and very specific to this unit.

The numerous medical and scientific domains (neurology, psychiatry, neuropsychology, neuroradiology, functional imaging, neurophysiology, neuropharmacology, biostatics…) which are actively explored allow to establish a solid ground for this original and creative approach.

The third research theme of the unit has led to technical innovation and to the creation of a startup called "Syneika".

The team has demonstrated a great ability to collect funds [University (78kE), PHRC (974kE), Industry (518kE), France Park (18kE), Bourse AXA (120KE)].

The team has developed pertinent collaborations and partnerships.

Students benefit from very good training, and availability of the scientific staff.

- Weaknesses and threats

Despite the fact that this unit is not associated with any research agency, the absence of full time researchers and its small size could become a handicap in the near future. However, one of the researchers, Julie PÉRON, will postulate in 2011 for a CR2 INSERM position and the objective of the unit is to merge with the INSERM units 642, 746 and 936 for the next "quinquennal plan".

Absence of dedicated administrative or technical supports in the unit

- Recommendations

The team should focus on a fewer neurological and therapeutic aspects of its research

Recruitment of full time researchers

- Production results

Despite the youth of the unit (it has been created only in 2006) and research themes dedicated to the clinical research field, the level of publication is high with a good progression of the citation index over the last five years.

A1: Number of permanent researchers with teaching duties (recorded in N1) who are active in research	6
A2: Number of permanent researchers without teaching duties (recorded in N2) who are active in research	2
A3: Ratio of members who are active in research among staff members [(A1 + A2)/(N1 + N2)]	1
A4: Number of HDR granted during the past 4 years (Form 2.10 of the application file)	1
A5: Number of PhD granted during the past 4 years (Form 2.9 of the application file)	4

3 • Specific comments

- Appreciation on the results:

This unit proposes a very original, multi- and transdisciplinary clinical research in the field of behavioral and basal ganglia. It was the first team in the French community of Neuroscience to focus on behavioral aspects rather than motor aspects of the subthalamic nucleus, and to emphasize its role in emotions and apathy. Its multidisciplinary composition, including neurologists, psychiatrics, neuropsychologists, neuroradiologists and neurophysiologists constitutes one of its strengths.

Taking advantage of observations in Parkinson's disease and obsessive compulsive disorders patients treated by Deep Brain Stimulation (DBS), this group has chosen to develop three main complementary research themes: » emotion and basal ganglia"; "motivation and basal ganglia", "therapeutic applications". It has demonstrated a very high level of creativity in clinical research. The main findings of the team are:

- The role of the subthalamic nucleus in the recognition of negative emotions
- The role of the orbitofrontal cortex and amygdala in fear recognition
- The causal link between disruption of mood monitoring and apathy
- The correlation between posterior cortex activation and apathy

Members of this research unit participate in most French multicenter studies using DBS in the field of Neurology and Psychiatry. They are leaders in an ambitious project dealing with the treatment of depression with DBS.

Consequently, research activity of the group has led to several therapeutic innovations including the use of a neuronavigator to select anatomic targets for transmagnetic stimulation (rTMS), and the development of novel DBS electrodes.

Since its creation in 2006, this unit has published 70 papers among which 24 were original papers and 14 published in reviews with an impact factor >4 (Brain 2008, Neurology 2009 (X2), PLOS one 2010, Mov Disord 2009 (X2), Neuropsychologia 2008, 2009, 2010, Neuropsychology 2010, Psychiatry research 2006, 2010, European Journal of Nuclear Medicine and Molecular Imaging 2010; Biological psychiatry 2011).

The committee wishes to state that the impact factor of these publications is not fully representative of the quality of the work accomplished since clinical journals do not benefit from very high impact factor compared to other journals in the field of Neuroscience. In the field of basal ganglia however, and of behavioral disorders, these papers are very important as demonstrated by the exponentially growth of the index citation of the unit for the last 4 years (from less than 50 citations in 2006 to more than 200 in 2010).
Four PHD thesis have been produced since 2006, and 6 other are in progress.
Besides its multidisciplinary approaches, this unit has developed interactions and contact with several other laboratories at the University of Rennes, and also at the national and international levels (Switzerland, Belgium, and USA).

At the University of Rennes, the unit:

- Has very good interactions with other local research groups, with the project of fusion to create a bigger IMSERM unit within the next three years.
- Is a member of the GIS "Cerveau-Comportement- Society" directed by Martine Hauberger, and has collaborations with INSERM U74 (IRMf), INSERM U642 (electrophysiology), UMR CNRS 6552 (ethology).

Several projects have been realized in collaboration with the National center of competence in the affective sciences (Pr K Scherer) in Genève, with the "Unité de Neuroscience cognitive" of the Catholic University of Louvain la Neuve in Belgium (Pr. PHILIPPOT), and with the Sobell Department of motor neurosciences and movement disorders (Pr. BROWN) in London (UK).

New models of DBS electrodes and stimulators are tested in collaboration with industries in the USA (Boston Scientific and Medtronic)

- Appreciation on the impact, the attractiveness of the research unit and of the quality of its links with international, national and local partners:

The number of national and international communications is good (16 oral communications among which 7 international) considering the topics and the youth of the unit. The unit is very attractive for medical fellows implicated in research: 6 PhD students are now working in the laboratory: 4 psychiatrists, 1 neurologist and 1 neuropsychologist. The unit is also quite young (created in 2006) which might explain why it has not yet recruited post-doctoral researchers.

This research unit has demonstrated an excellent capacity to raise funds and numerous grants has been obtained: University (78kE), PHRC (974kE), Industry (518kE), France Park (18kE), Bourse AXA (120KE). It is actively implicated in the French DBS network. Its members are co investigators in several national projects (STOC, STOC uni/bil), and main leaders in two programs of DBS related to depression (PréSTHYM, STHYM).

Research activity of this group has led to the creation of one startup named "Syneika", which proposes the use of a neuronavigator to select anatomic targets for transmagnetic stimulation (rTMS). A collaboration with the CIC and the department of medical computing has allowed the elaboration of a multimodal data base for patients with DBS.

Newly developed DBS electrodes and a "clever" adaptable stimulator are now being tested in the unit (collaboration with industrial partners and CIC-IT).

- Appreciation on the management and life of the research unit:

Organization and communication as well as training and availability of the director are attested by all members and partners of the unit. The research themes which are developed are very original and denote a high level of creativity. Several unit members have made a post-doctoral or research stay in one of the foreign collaborators of the unit to import new techniques and new approaches (fMRI, electrophysiological recordings, signal analyses).

Translational research and therapeutic applications are successfully developed (technical innovation in DBS; brain-machine interface for TMS).

Six members of the unit are implicated in teaching (M1, M2, medical studies). Marc VERIN is co-director in the Master "Human and animal behaviour".

- Appreciation on the scientific strategy and the project:

The project is in direct continuity with the past activity of the unit and will rely on multi- and transdisciplinary approaches. The main research theme listed in the project will tackle the fascinating question of the role of basal ganglia in emotion and motivation processes in a variety of physiological and pathological situations. New approaches and new tools of investigation such as sEEG, signal analyze, PET new tracers and rTMS coupled with neuronavigation will be used to provide significant advances in the field. All these techniques are already mastered by local teams in Rennes and no problem of feasibility are to be envisioned.

The section of the project dealing with experimental therapeutic is particularly interesting and innovative. The development of clever stimulators (with modulation of stimulation according to biological brain signals) is a totally new concept but appears also very challenging at the technical level. Success will require efficient collaborations which are already in progress.

This unit has an exceptional ability to get funding. Consequently, the current search of funding for the project is not an issue.

Intitulé UR / équipe	C1	C2	C3	C4	Note globale
COMPORTEMENTS ET NOYAUX GRIS CENTRAUX	A+	A	A	A	A

C1 Qualité scientifique et production

C2 Rayonnement et attractivité, intégration dans l'environnement

C3 Gouvernance et vie du laboratoire

C4 Stratégie et projet scientifique

Statistiques de notes globales par domaines scientifiques

(État au 06/05/2011)

Sciences du Vivant et Environnement

Note globale	SVE1_LS1_LS2	SVE1_LS3	SVE1_LS4	SVE1_LS5	SVE1_LS6	SVE1_LS7	SVE2 _LS3 *	SVE2_LS8 *	SVE2_LS9 *	Total
A+	7	3	1	4	7	6		2		30
A	27	1	13	20	21	26	2	12	23	145
B	6	1	6	2	8	23	3	3	6	58
C	1					4				5
Non noté	1									1
Total	**42**	**5**	**20**	**26**	**36**	**59**	**5**	**17**	**29**	**239**
A+	16,7%	60,0%	5,0%	15,4%	19,4%	10,2%		11,8%		12,6%
A	64,3%	20,0%	65,0%	76,9%	58,3%	44,1%	40,0%	70,6%	79,3%	60,7%
B	14,3%	20,0%	30,0%	7,7%	22,2%	39,0%	60,0%	17,6%	20,7%	24,3%
C	2,4%					6,8%				2,1%
Non noté	2,4%									0,4%
Total	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%

*** les résultats SVE2 ne sont pas définitifs au 06/05/2011.**

Intitulés des domaines scientifiques

Sciences du Vivant et Environnement

- **SVE1 Biologie, santé**
  - **SVE1_LS1 Biologie moléculaire, Biologie structurale, Biochimie**
  - **SVE1_LS2 Génétique, Génomique, Bioinformatique, Biologie des systèmes**
  - **SVE1_LS3 Biologie cellulaire, Biologie du développement animal**
  - **SVE1_LS4 Physiologie, Physiopathologie, Endocrinologie**
  - **SVE1_LS5 Neurosciences**
  - **SVE1_LS6 Immunologie, Infectiologie**
  - **SVE1_LS7 Recherche clinique, Santé publique**
- **SVE2 Ecologie, environnement**
  - **SVE2_LS8 Evolution, Ecologie, Biologie de l'environnement**
  - **SVE2_LS9 Sciences et technologies du vivant, Biotechnologie**
  - **SVE2_LS3 Biologie cellulaire, Biologie du développement végétal**

PRÉSIDENCE

Guy Cathelineau
Président

UNIVERSITÉ DE RENNES 1

Rennes, le 22 avril 2011

Vos réf. : S2UR120001337
Comportements et noyaux gris centraux – 0350936C

Monsieur Pierre GLORIEUX
Directeur de la section des unités de recherche
Agence d'Evaluation de la recherche et de l'Enseignement Supérieur (AERES)
20, rue Vivienne
75002 PARIS

Monsieur le Directeur,

Je vous adresse mes remerciements pour la qualité du rapport d'évaluation fourni à l'issue de la visite du comité d'expertise concernant l'unité de recherche **«Comportements et noyaux gris centraux ».**

L'université de Rennes 1 sera particulièrement attentive à ce que les recommandations formulées par le comité de visite soient prises en compte.

A la lecture de ce rapport, vous trouverez ci-joint, les réponses du directeur de l'équipe d'accueil auxquelles nous souscrivons en totalité, en y ajoutant quelques précisions sur les deux éléments suivants :

L'émergence de cette thématique a été accompagnée par l'université de Rennes 1 tout au long du contrat quadriennal actuel 2008-2011. L'établissement appuie donc logiquement la demande de création de cette nouvelle EA et se voit conforter avec satisfaction dans cette stratégie par l'évaluation très positive du projet scientifique proposé.

De manière plus large et au-delà de cette seule EA, la thématique des neurosciences prend beaucoup d'essor et d'intérêt interdisciplinaire tant au sein de l'université de Rennes 1 que chez son partenaire CHU. Au travers d'autres unités de recherche (telle que l'unité VISAGES en neuro-imagerie) ou le GIS « Cerveau, comportement, société » qui associe également des éthologues, des sociologues, des psychologues, etc..., il apparaît évident que cette problématique de recherche est en forte croissance et la nouvelle EA du professeur Vérin y trouvera toute sa place pour son développement futur.

Je vous prie d'agréer, Monsieur le Directeur, l'expression de ma considération distinguée.

Le Président de l'Université de Rennes 1

Guy CATHELINEAU

2, RUE DU THABOR
CS 46510
35065 RENNES CEDEX
www.univ-rennes1.fr

TÉL. 33 (0)2 23 23 36 36
FAX 33 (0)2 23 23 36 00

president@univ-rennes1.fr

Rapport de l'AERES concernant l'URU-EM 425

« Comportement et noyaux gris centraux »

Observations et réponses aux recommandations

Pr Marc Vérin - Directeur

Cette réponse est divisée en deux parties : la première comporte les commentaires généraux sur le rapport du comité d'évaluation, la seconde est la réponse aux recommandations issues du même rapport.

Commentaires généraux sur le rapport

Les experts ont accueilli très favorablement notre souhait de création d'Equipe d'Accueil intitulée « Comportement et noyaux gris centraux » en jugeant excellent le bilan de 2006 à 2010 de l'URU-EM 425 et le projet de l'équipe pour le contrat quinquennal 2012-2017.

Ils ont particulièrement apprécié l'originalité de sa recherche et de sa pluridisciplinarité. Ils ont souligné qu'il s'agit de la première équipe française à focaliser sa recherche dans le champ du comportement et des noyaux gris centraux.

Ils ont souligné les avancées intéressantes d'ores et déjà réalisées dans les trois axes envisagés : « Emotion et noyaux gris centraux » ; Motivation et noyaux gris centraux » et « Applications thérapeutiques ».

Ils ont jugé très bon le niveau des publications auquel a mené l'activité de recherche et ont noté positivement la création de la startup « Syneika » qui apporte des innovations thérapeutiques dans le champ de la stimulation magnétique transcrânienne.

Ils ont jugé la gestion de l'équipe très dynamique et très efficiente pour développer de nouveaux projets et lever des fonds auprès du Ministère, de l'Université et de l'Industrie.

Au-delà de ces observations très positives qui confortent l'équipe dans ses choix stratégiques pour les années à venir, des remarques constructives et des recommandations ont été faites visant à améliorer le projet. Elles sont discutées point par point dans le paragraphe suivant.

Réponses aux recommandations

Weaknesses and threats

Despite the fact that this unit is not associated with any research agency, the absence of full time researchers and its small size could become a handicap in the near future. However, one of the researchers, Julie Péron, will postulate in 2011 for a CR2 INSERM position and the objective of the unit is to merge with the INSERM units 642, 746 and 936 for the next "quinquennal plan".

Réponse : Julie Péron a été classée 17ème sur 60 au concours de CR2 INSERM en avril 2011 (pour 6 postes disponibles). Elle candidatera de nouveau en 2012. La qualité du classement obtenu pour une première présentation, alors que son stage postdoctoral à l'étranger n'est pas encore achevé, est très encourageante. Nous confirmons par ailleurs notre volonté très ferme de participer au projet fortement soutenu par l'Université Rennes 1 de regroupement des unités INSERM 642, 746 et 936 sur le site rennais autour de la thématique générale des nouvelles technologies de la santé. Nos thématiques cliniques utilisant les outils de haute technologie autour de la stimulation cérébrale profonde (tomographie par émission de positon, IRM fonctionnelle, enregistrement neuronal) y trouveront naturellement leur place.

Absence of dedicated administrative or technical supports in the unit.

Réponse : Comme l'ont souligné les experts, notre développement dans le cadre de la labellisation nécessitera de bénéficier de temps de secrétaire et d'ingénieur de recherche (analyse des images et des signaux neurophysiologiques, gestion du parc informatique, création de logiciels dédiés). Cette demande légitime sera transmise aux autorités de l'Université Rennes 1 dès la labellisation confirmée.

Recommendations

The team should focus on a fewer neurological and therapeutic aspects of its research.

Réponse : Notre objectif fondamental est de comprendre le rôle émotionnel et motivationnel des noyaux gris centraux, en particulier le noyau subthalamique, en nous servant du modèle de la stimulation cérébrale profonde allié à l'exploration neuropsychologique, métabolique et neurophysiologique. L'objectif thérapeutique découle directement des avancées obtenues. Il vise à la fois à développer de nouvelles indications neuropsychiatriques de la stimulation cérébrale profonde et à améliorer la tolérance comportementale du matériel et des indications actuelles.

C'est sur ces objectifs que nous focaliseront notre recherche puisque le comité de visite a clairement souligné leur excellente adéquation avec le savoir faire multidisciplinaire de l'équipe et les collaborations développées.

Nous n'utiliseront que secondairement d'autres outils comme la stimulation magnétique transcrânienne et la stéréo-électro-encéphalographie dans l'objectif de préciser l'articulation fonctionnelle des structures corticales avec les noyaux gris centraux dans le champ des émotions et de la motivation.

Recruitment of full time researchers

Réponse : Comme indiqué plus haut, nous comptons sur la candidature de Julie Péron au concours de CR2 INSERM l'an prochain, sachant que son premier classement est très encourageant.

Notre volonté d'obtenir la labellisation d'Equipe d'Accueil avec la meilleure lisibilité possible procède également de notre souhait de renforcer l'équipe grâce à notre attractivité dans un champ de recherche très novateur et fort peu développé en France.

Appreciation on the results

The committee wishes to state that the impact factor of these publications is not fully representative of the quality of the work accomplished since clinical journals do not benefit from very high impact factor compared to other journals in the field of Neuroscience.

Réponse : En parallèle de la structuration de l'équipe depuis 2006, ses publications ont vu leur facteur d'impact s'élever considérablement pour atteindre celui de Brain (IF 2009 = 9.49), de Biological Psychiatry (IF 2009 = 8.926) et de Neurology (IF 2009 = 8.172).

La maîtrise désormais conjointe au sein de l'équipe des outils tels que la neuropsychologie expérimentale, l'imagerie métabolique et l'enregistrement neuronal alliée à l'originalité des thématiques, soulignée par les experts, devraient nous permettre dans un futur proche de publier des résultats très novateurs bénéficiant de l'approche intégrée multimodale et multidisciplinaire. La soumission à des revues de Neurosciences à très haut facteur d'impact, telles que Neurone et Nature Neurosciences, pourra désormais être légitimement envisagée.