Imagerie en psychiatrie

Rapport Hcéres

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

Section des Unités de recherche

Evaluation report

Research unit :

Imagerie en psychiatrie

Of the University Paris 11, CEA, Collège de France, INSERM

March 2009

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

Section des Unités de recherche

Rapport d'évaluation

Unité de recherche

Imagerie en psychiatrie

Of the University Paris 11, CEA, Collège de France, INSERM

Le Président
de l'AERES

Jean-François Dhainaut

Section des unités
de recherche

Le Directeur

Pierre Glorieux

mars 2009

Evaluation report

The research unit :

Name of the research unit : Imagerie en psychiatrie

Requested label : UMR_S INSERM, UMR CEA

N° in case of renewal : U797

Head of the research unit : Mr. Jean-Luc MARTINOT

University or school :

Université Paris 11

Other institutions and research organization:

INSERM

CEA

Date of the visit :

22 Janvier 2009

Members of the visiting committee

Chairman of the commitee :

Mr Olaf BLANKE (Ecole Polytechnique Fédérale de Lausanne, Switzerland)

Other committee members :

Mr Jean-François DEMONET (Université Toulouse 3)

Mrs Nouchine HADJIKHANI (Harvard Medical School, Ecole Polytechnique Fédérale de Lausanne, Switzerland)

Mr Philippe MARTIN-HARDY (Centre de Recherche de l'Institut du Cerveau et de le Moelle épinière)

Mrs Lilianne MANNING (Université de Strasbourg)

Mrs Florence THIBAUT (Faculté de Médecine de Rouen)

Mr Christoph SEGEBARTH (Grenoble Institut des Neurosciences)

CNU, CoNRS, CSS INSERM, représentant INRA, INRIA, IRD.....) representatives :

INSERM CSS representative : Mr Jean-François DEMONET, Mr Philippe MARTIN-HARDY

Observers

AERES scientific representative:

Mr Christian BARILLOT

University or school representative:

Mrs Dominique EMILIE and Jacques BITTOUN, Université Paris-Sud 11

Research organization representative (s) :

Mrs Catherine LABBE-JULLIE, INSERM

Mr Jacques NEYTON, CEA

Evaluation report

1 • Short presentation of the research unit

- Number of lab members : 31 (20 FTE) including
  - 9 (4,6 FTE) full time researchers : DR1, DR2, CR1, Ing CEA
  - 8 (2,2 FTE) researchers with clinical duties : APHP
  - 2 postdoctoral fellows
  - 8 PhD students, all with a fellowship
  - 4 (3,2 FTE) engineers, technicians and administrative assistants (2 full-time and 2 part-time)
- Number of HDR : 8
- Number of PhD students who have obtained their PhD during the past 4 years: 5
- Average lenght of a PhD during the past 4 years : 3,7
- Number of lab members with a PEDR : 0
- Number of "publishing" lab members among permanent researchers : 7 out of 8

2 • Preparation and execution of the visit

Before the site visit, the committee received the Report 2005-2008 and the Project 2010-2014 of the Unit.

During the visit, the evaluation committee had the opportunity to listen to presentations about various aspects of the unit's activities, and to ask questions and discuss with several of its scientists. The director of the Unit gave a presentation about the organization and projects of the entire group (45 minutes). This was followed by 6 presentations given by different unit members (90 minutes). A planned short visit of the local research facilities could not be carried out due to time constrains.

In a second part of the visit the committee split up into smaller groups (of 2-3 people). One group met separately with the PhD and postdoctoral students, one group with the engineers, technicians, and administrative assistants, and one group with the permanent researchers (30 minutes each). Finally, the entire committee met with the observers from INSERM, CEA, and Université Paris-11 (30 minutes). This was followed by an internal discussion among the committee members and the AERES representative (75 minutes).

The visit lasted 5 hours.

3 • Overall appreciation of the activity of the research unit, of its links with local, national and international partners

Past scientific achievements concerned three main domains: (1) neuroimaging and developmental psychiatric conditions, (2) neuroimaging of psychiatric treatment and the effects of psychotropes, and (3) methods development.

Autism: Concerning brain structure and function in autism the group has investigated a specific cortical region, the superior temporal sulcus (STS) region, and its involvement in autism. Deficits in social perception have also been investigated. The results revealed grey matter abnormalities as well as hypoperfusion and sulcus abnormalities in patients with autism in the STS area that were also found to correlate with disease severity. In addition, abnormalities in voice perception were found in this region and these results were summarized in an important international review journal. The project for the next 4 years was clear and feasible. It is planned to improve the characterization of STS abnormalities in autists using additional neuroimaging approaches such as DTI, MRI-based TMS; also eye tracking during neuroimaging experiments will be added to better control the perceptual and cognitive states of these patients during future studies. Further projects include a joint imaging-genetics approach and the study of pharmacological effects of fluoxetine treatment on PET data in autists.

Anxiety and depression in adolescents: Grey matter volume has been analyzed in this population revealing a loss of grey matter from childhood age to adulthood. Several studies have been carried out in early-onset patients bipolar disorders using a variety of brain imaging techniques (i.e. fMRI, DTI).

Psychotropic drugs: This research has investigated the role of dopamine in psychiatric disease using high-resolution PET. Preliminary data were presented on dopamine transporter availability in the case of tobacco and cannabis addiction. This work also included work in cocaine dependant patients as well as the report of increased dopamine transporter availability in schizophrenic patients, localized to the limbic system. For the 4-year project, it is planned to study the links between PET and fMRI based imaging during the processing of facial emotions (as well as DTI and anatomic MR analyses).

Methods: Data basing for large groups of psychiatric patients (autism and a new patient group [teenagers with increased risk-taking]) and multimodal neuroimaging within an ANR and EU project were presented. The usability of neuroimaging based prediction of disease and severity of disease will be tested in these patient populations. The project plans to investigate links between genetic and neuroimaging data.

Overall, the **scientific production** in the past four years was excellent and consisted of 36 peer-reviewed papers in international journals ranging from excellent neuroscience and neuroimaging journals to top clinical journals including American Journal of Psychiatry, Nature Neuroscience, Trends in Neuroscience, NeuroImage, Human Brain Mapping, Cerebral Cortex to name just a few. 6 further articles are in revision or submitted. The group also participated in a large number of other publications in collaboration.

Several important grants were obtained including one EU- and one ANR-grant.

The overall impression of the commission of the unit's past and future research activities was excellent including highly original neuroimaging research (especially in the domain of autism) and cutting edge projects. The review committee was very impressed by the strong and exceptional translational research.

The review committee noted that the attachment of unit to the CEA may be problematic given the recent installation of Neurospin at Saclay whereas the unit has remained at the SHFJ center.

Concerning the new research project the committee was sceptical whether the unit will have enough manpower for the computational neuroimaging and genetic aspects of the project IMAGEN.

It was also felt that the Unit may embark on several ambitious neuroimaging projects and scientific questions for which the existing local methodological expertise is not internal to the group.

4 • Specific appreciation project by project

Autism: The group's research in this field is remarkable and unique in France. The autism work is well-known internationally and published in top international journals. The past and future work was well presented to the committee and was very interactive. The project for the next 4 years is clear and feasible.

Psychotropic drugs: Most of the presented data were prliminary using high-resolution PET and applied to dopamine transporter availability in addiction and schizophrenia. The 4-year project was discussed clearly, is feasable, and plans to extend the previous PET work in schizophrenic patients to MRI based imaging and different cognitive procedures.

Anxiety, risk taking, and methods in adolescents: The group plans to fuse previous expertise in child psychiatry on anxiety and depression with their neuroiamging expertise and apply this to neuroimaging in teenagers with increased risk taking behavior. The project is very ambitious.

Methods: Concerning the new research project the committee was sceptical whether the unit will have enough manpower for the computational neuroimaging and genetic aspects of the project IMAGEN.

5• Appreciation of resources and of the life of the research unit

— Management :

The organization of research is excellent linking bedside evaluations (network of psychiatrists in the larger Paris area) to behavioral paradigms and state-of-the-art neuroimaging (at Orsay). This is a major strength of this well known research unit. The unit sucessfully shares research ressources, equipment, and expertise across its different teams. Young teams have emerged in the unit as for example the prominent autism research axis.

— Human ressources :

The permanent staff of the laboratory should be reinforced so that full-time dedicated engineers join the team to secure data handling and processing. This seems especially important with respect to some aspects of future research projects.

— Communication :

The members of the unit are present at many national and international conferences and have published their data in international journals ranging from excellent neuroscience and neuroimaging journals to top clinical journals. The unit organizes weekly research seminars that are well appreciated by the younger researchers and students. The unit is attractive to young researchers and teaches and educates many doctoral and postdoctoral students from various academic backgrounds.

6• Recommendations and advice

— Strong points :

The translational character of the research is remarkable and unique in France. Internationally, the group is very well-known in the field of psychiatry and neuroimaging of psychiatric conditions. This is especially the case for the research projects focussing on autism by which the review committee was particularly impressed.

The committee felt that the excellence of the unit's translational research is also due to the unique access to the technological and methodological platform at Orsay allowing for the application of state-of-the-art multimodal neuroimaging to a wide range of patient populations.

The committee was impressed by the unique and essential integration and efficiency of several unit members performing clinical work that is crucial for carrying out the subsequent neuroimaging work in carefully selected patient populations including schizophrenia, autism, substance abuse, etc.

— What needs to be improved :

The commission felt that the research may not be focussed enough. With a somewhat limited number of permanent staff it covers a wide range of clinical and cognitive questions as well as methodological and neuropharmacological issues. This concern was somewhat more apparent in the research project for 2010-2014 than in past research.

It was also noted that there were differences in scientific performance between the different projects that were presented.

— Recommendations :

Concerning the vast on-going program on neuroimaging, cognition and genetics of developmental psychiatric disorders, the committee recommends that the permanent staff of the laboratory should be reinforced so that full-time dedicated engineers join the team to secure data handling and processing.

Note de l'unité	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	A	A	A	A

L'Administrateur Général

Monsieur Pierre GLORIEUX
Directeur de la Section des Unités

AERES
20, rue Vivienne
75002 Paris

Saclay, le 24 avril 2009

Objet : Observations du CEA sur le rapport d'évaluation du Laboratoire « Neuroimagerie et psychiatrie », U797
(Référence : EVAL-0911101C-S2100012405-UR-RPRELIM)

N/Réf. : DPG/RM/mos/2009-127

Monsieur le Directeur,

Je remercie tout d'abord l'AERES pour la qualité du rapport d'évaluation et pour la pertinence des recommandations qui ont été faites.

Vous trouverez, ci-joint, les commentaires faits par Monsieur Jean-Luc Martinot, directeur du Laboratoire « Neuroimagerie et psychiatrie » (UMR CEA, INSERM, U797), sur ce rapport d'évaluation.

En tant qu'Administrateur Général de l'Etablissement CEA, ce rapport n'appelle pas de commentaires particuliers de ma part. Je prêterai la plus grande attention à la mise en œuvre des actions qui permettront de répondre aux recommandations formulées par l'Agence.

Je vous prie d'agréer, Monsieur le Directeur, l'expression de mes meilleures salutations.

Bernard BIGOT

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Direction des sciences du Vivant

Unité de Recherche U. 797
« Neuroimagerie & Psychiatrie »
04 22 2009

Mr Pierre GLORIEUX
Directeur de la section des unités de recherche
Agence d'évaluation de la recherche
et de l'enseignement supérieur
20, rue Vivienne 75002 Paris

Dear Sir,

We appreciated the genuine commitment of the evaluators of our research unit, and there are only two comments we would like to add to the report from the visiting committee, with respect to points we might not have detailed during their visit.

The committee suggested 1/ to improve the focus of the research, and 2/ to specify the attachment of the unit with respect to the recent installation of Neurospin at Saclay.

1. We are aware of the necessity to keep research sufficiently focused as regards the ratio between the number of research lines and the human resources.
This is why, for instance, we do not aim to address many ambitious issues related to the Imagen european project resources (presently including imaging, genetic, and psycho-behavioural data from > 600 adolescents, and 1000 are foreseen by fall 09) that could only be fully analyzed through international collaborations gathering the required manpower and expertise. Rather, we will use this database for selected psychopathology issues where we already have an established expertise and previously have performed research in adults, and the analyses will be performed synergistically with the other international partners as planned by the exploitation committee of which we are members. In addition, this adolescent database will serve as a normative reference in order to further investigate in juvenile patients the few developmental psychiatry disorders which are at the core of our research program (e.g. adolescents with autism, or at risk for a mental disorder we previously studied in adults). Thus, we hope to maintain a focused research and translation towards clinical issues.

2. The attachment to CEA is effective with both research platforms SHFJ-Orsay and Neurospin-Saclay located 5min. drive apart. Indeed, three permanent research staff with part-time activity within the Unit are located in the new installation, and in charge of granted projects involving the Unit. In addition, convention between INSERM and CEA is being set up as regards local facilities, data acquisition, analysis and storage in Neurospin.

Sincerely,

Jean - Luc Martinot, MD, PhD
Director of research INSERM, AIHP, ACCA, psychiatrist.

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