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

Department for the evaluation of research units

AERES report on unit:

Neuroplasticité et thérapies des addictions

Under the supervision of the following institutions and research bodies:

Université Paris Descartes

Centre National de la Recherche Scientifique

November 2012

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

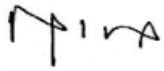
Research Units Department

President of AERES

Didier Houssin

Research Units Department

Department Head



Pierre Glaudes

The president of AERES "signs[...], the evaluation reports, [...]countersigned for each evaluation department by the relevant head of department (Article 9, paragraph 3, of french decree n°2006-1334 dated 3 november 2006, revised).

Grading

Once the visits for the 2012-2013 evaluation campaign had been completed, the chairpersons of the expert committees, who met per disciplinary group, proceeded to attribute a score to the research units in their group (and, when necessary, for these units' in-house teams).

This score (A+, A, B, C) concerned each of the six criteria defined by the AERES.

NN (not-scored) attached to a criteria indicate that this one was not applicable to the particular case of this research unit or this team.

Criterion 1 - C1: Scientific outputs and quality;
Criterion 2 - C2: Academic reputation and appeal;
Criterion 3 - C3: Interactions with the social, economic and cultural environment;
Criterion 4 - C4: Organisation and life of the institution (or of the team);
Criterion 5 - C5: Involvement in training through research;
Criterion 6 - C6: Strategy and five-year plan.

With respect to this score, the research unit concerned by this report and its in-house teams the following grades:

- Grading table of the unit: Neuroplasticité et thérapies des addictions

C1	C2	C3	C4	C5	C6
A	A	A	A	A	A

Evaluation report

Unit name:	Neuroplasticité et thérapies des addictions
Unit acronym:	
Label requested:	UMR mono organisme
Present no.:	
Name of Director (2012-2013):	
Name of Project Leader (2014-2018):	Ms Florence NOBLE

Expert committee members

Chair:	Ms Martine CADOR, Bordeaux Segalen University
Experts:	Ms Catherine HEURTEAUX, CNRS, Nice-Sophia Antipolis University, (CoNRS representative)
	Mr Beat LUTZ, Mainz University, Germany
	Ms Guylène PAGE, Poitiers University, (CNU representative)

Scientific delegate representing the AERES:

Mr Pierre VIERLING

Representative(s) of the unit's supervising institutions and bodies:

Ms Nathalie LERESCHE, CNRS

Mr Stefano MARULLO, Paris Descartes University

1 • Introduction

History and geographical location of the unit

The new project unit "Neuroplasticité et Traitements des Addictions » to be reviewed is presently the preclinical team named "Neurochimie et Neurobiologie des Addictions », nowadays part of the unit "Neuropsychopharmacologie des addictions", which is directed by Mr Jean Michel SCHERRMANN and labelised both by the CNRS (UMR8206) and INSERM (U705) within the Paris 5 René Descartes and Paris 7 Denis Diderot Universities in the 2010-2013 contract. The future principal investigator (PI) of this future unit is Ms Florence NOBLE, who is currently the deputy director of the UMR and the responsible for team "Neurochimie et Neurobiologie des Addictions ".

This new unit will move from the Pharmacy Faculty to the Biomedical Faculty rue des Saints Pères (another location of the Paris 5 University) where it plans to establish collaborations with chemists and where technical platforms will be available for further developments.

The general theme of the former team/future unit to be reviewed was linked to the research topic of addiction with preclinical and clinical approaches. It involves presently 9 permanent positions, 1 PhD student and 2 ERASMUS students (Italy, UK). For the next period (2014-2018), four permanent members of the present team will leave.

Management team

As a reminder, in the former unit, the team is headed by Ms Florence NOBLE , who will be the director of the future unit. Specifically regarding this team, the management appears to be fine as 6 PhD theses and one HDR were defended in the 2010-2013 contract and financial ressources were found (an ANR is starting in 2013, several contracts with industrial partners are reported).

AERES nomenclature

SVE1_LS5

Unit workforce

Unit workforce	**Number as at 30/06/2012**	**Number as at 01/01/2014**	2014-2018 **Number of project producers**
N1: Permanent professors and similar positions	2	1	1
N2: Permanent researchers from Institutions and similar positions	3	2	2
N3: Other permanent staff (without research duties)	4	2	
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)			
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)		1	1
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	**9**	**6**	**4**

Percentage of producers	***100 %***

Unit workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended	6	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	2	1

2 • Assessment of the unit

Strengths and opportunities

1. The unit has a good level of funding both from academic and private sources.

2. The potential of the research conducted is very timely and might provide new therapeutic strategies.

3. The unit has strong support from the CNRS, and from the Biomedical Faculty (rue des Saints-Pères location) and the Paris Descartes University, who all confirm the moving to the Saints-Pères location of the Paris Descartes University with the advantages of getting help of different technical platforms of the two SFR (structure fédérative de recherche) in Chemistry, Toxicology, Cell Signalisation, Therapeutic Targeting (C2T2S), and in Neurosciences and Pharmacology of the Biomedical Faculty.

4. More space in the Saints-Pères location (180 m^2 for the new unit) should allow recruitment of researchers and post docs.

Weaknesses and threats

1. In terms of human resources, the project involves very few people for very time-consuming and diverse sub-projects raising questions about the feasibility of the whole proposal. The number of HDR should be increased to welcome more students (one researcher of the team should get his HDR as soon as possible). The number of post-docs from abroad should also be increased. A clearer identification of who is responsible of the different sub-projects will be welcome.

2. In terms of scientific project, the unit should focus more on some original and timely aspects of the project for which they have already gathered data and find their own “niche” in the context of the large number of highly competitive teams working already in the field of addiction in France and abroad, which have already investigated the issue of vulnerability and variability in drug addiction. This very competitive field needs highly innovative concepts and techniques to make a breakthrough. Hence, again regarding the small number of people, the team should find a way to make each sub-project more in coherence and potentiate one to another instead of being completeley independent as they have been presented in the document and during the visit.

3. Regarding the technological feasability of the project, the Saints-Pères location will provide access to the new technologies that are going to be developed in the future project. Therefore, the moving to the Biomedical Faculty appears a crucial step (and therefore a threat if not fulfilled) for the feasability of the project.

4. Regarding the potential therapeutic outcomes of the project, the loss of the clinical surrounding provided by the present UMR is detrimental.

Recommendations

Due to the very small size of the unit, the project should be more focused. Based on the grounds of previously acquired data, the member of the unit should put their forces and competences together to study in depth the questions raised by previously acquired data. The unit should be more involved in international networks, which regarding the project should be of interest for most of these networks.

3 • Detailed assessments

Assessment of scientific quality and outputs

The main objectives of the team since 2010 were aimed at (1) increasing the knowledge on the neuropathological mechanisms of addiction focusing mainly on psychostimulants (MDMA and cocain) and opiates, and (2) optimizing the existing treatments and developing new therapeutic strategies. The scientific production over the last 4 years (2007-2012) is presented over 4 themes Polyconsommation, Substitution treatment, Mechanisms of action of opioids, Psychostimulants.

The general impression is a dispersion of projects according to the low number of researchers involved, with difficulties to dress a leading link between these different sets of data. Four themes are investigated in the team with no evident link betweem them though that there are all related to addiction. It is therefore quite difficult to envisage which one among these results can be efficiently pursued for therapeutic applications.

Despite this remark, the overall level of scientific publication of the permanent members of the former team is good both qualitatively and quantitatively, with a mean of 2.24 publications per person per year, 35 international peer-reviewed publications since 2007 (among which 4 review articles), and 4 book chapters. Out of the 35 articles, 63% of the production results from a major contribution of the team/unit. Most of the papers were published in good or even leading journals in their specific research fields, such as 1 Translational Psychiatry, 1 Plos One, 2 Addiction Biology, 1 Journal of Neuroscience, 3 Psychopharmacology, 1 Pain, 2 Neuropharmacology, 1 Neuropsychopharmacology and others with a large part of them having an impact factor (IF) between 4 and 8, but none above an IF of 9. Of the 35 articles, 91% of them have an IF superior to 2, 57% with an IF>4, 5.7% with an 7<IF<9 and 0% with an IF>9. The head of the team demonstrates a high number of invitations in national and international conferences (26/27 in total with 5 international and 21 national). Collaborations are active and productive as evidenced by many papers (10 of 35) based on collaborative work. Of the 3 future permanent lab members, all are producers.

Assessment of the unit's academic reputation and appeal

The academic reputation is very good in regards to the number of collaborative projects (2 national with one ANR whose coordinator is the PI of the team and 2 international Erasmus projects (with Italy/Bologne and USA/Baltimore), the participation to a GDR network, the implication in a Labex (resistance to medicine and toxicity. The team has also organized some colloques and symposia among which 6 were abroad. The PI is a member of the editorial board of the Journal of Addiction and of the committee of “Le Courrier des Addictions”. The team has collected prizes such as the « Coup d’Elan pour la Recherche française (250 000 euros) and some travel grants and poster prizes. The team was a member of the IFR 71 “Institut Médicament, Toxicologie, Chimie, Environnement” and will join the new SF C2T2S at the Biomedical Faculty of the Paris Descartes University.

In terms of attractiveness, the team has welcomed 2 post-docs in the past 5 years and will welcome a new post-doc on an ANR project in the next three years. One of these former two post-docs was recruited (as professor) in 2010.

Assessment of the unit's interaction with the social, economic and cultural environment

The team interactions with the social, economic and cultural environment are excellent. The team has indeed been implicated

1. in articles published in professional journals such as Le Flyer (Bulletin de Liaison des Centres de Soins Spécialisés pour Toxicomanes et Médecins Relais, Réseaux de Soins, Pharmaciens d’Officine, ECIMUD et structures de soins auprès des usagers de drogues)
2. in several expertises (Ministère de la Santé, INSERM, SFN)
3. has participated to numerous debates organized for professionnals
4. has obtained many contracts with industrial companies and academic agencies (MILDT, ANR)

Furthermore, the PI was nomitated as Directeur-adjoint scientifique at the INSB of the CNRS.

Assessment of the unit's organisation and life

The organisation and life in the team/unit is very good. The UMR to which belongs the present team organizes 2 or 3 "conseils de laboratoire" per year. The team has further organized monthly meetings as well as specific meetings to discuss data and projects. Its members have several responsabilities (Web master for instance and others). They look in good harmony with the team leader and report to appreciate the team's organization and to attend conferences on a regular basis. The PI confirms that the two technical persons belonging to INSERM will stay in the team and these two confirm that they want to stay in the team.

Assessment of the unit's involvement in training through research

The team provides very good PhD training (7 theses between 2006 and 2012, which were all affiliated to the Ecole doctorale ED 436 "Médicament Toxicologie, Chimie, Environnement » from the Paris Descartes and Paris Diderot Universities) and a good follow-up of PhD students for their post-doc and a good level of scientific production per student (despite the fact that the team has only 1 HDR). There were 4 thesis defended by pharmacy students who all got the "Médaille de l'Internat" to be 100% in research for one year and then 50% of their time in the lab. They have all published articles from their PhD works. Importantly, there is a training programme for PhD supervisors in the university. Nine master 1 and master 2 students have been trained in the lab and 2 Erasmus students have been working in the lab.

The MCU in the team (MCU since 2010) has several responsibilities in the M1 Santé and L2 Pharmacy. There is a lack of involvement in teaching units related to addiction research. Researchers of the team are involved at the M2 level in Pharmacology (a few hours/year). The PI of the team has been a member of various PhD (17) and HDR (5) defences mostly in neuroscience. In conclusion, the training through research is fine though the teaching aspect could have been better developped.

Assessment of the five-year plan and strategy

At a scientific level, for the next 5 years (2014-2018), the team proposed to develop a project with 3 independent aims of research:

Aim 1: *(financed by ANR (2012-2016)) "longitudinal study in rats of vulnerability and variability in the different stages of drug self-administration and in the response to pharmacological treatment"*. This new project is aimed at characterising behaviourally animals on anxiety, hedonia, stress response before, during and after self-administration of drugs inducing different level of drug dependence and see whether correlations can be found between these behavioural markers and response to substitutive treatments during abstinence. Hence a very ambitious transcriptomic, (including miRNA) and biochemical analyses will be implemented to find both peripheral markers and new candidates for therapeutic approaches. This transcriptomic study will be out sourced to a specialized company.

Aim 2 : "*Neurochemical memory : what are the cellular and molecular mechanisms involved?".* This theme is in line with previous data obtained and is aimed at determining whether the increase in dopamine, enkephalin and BDNF observed in the nucleus accumbens is specific to drugs, dependent on Rack1 and dopamine D1 receptors for BDNF, and involved in the vulnerability to relapse.

Aim 3 : "*mGluR7 and addiction : regulation of receptor and fonction ?".* This new theme aimed at deciphering the role of mGluR7 in heroin and cocaine behavioural responses will be using new selective molecules designed in collaboration with the chemical group located at the Biomedical Faculty of the Paris Descartes University.

Aim 1, which is already financed by ANR, is going to be tremendously time and energy consuming and very risky as it is. The team has to think very carefully which strategy will be followed once hundred of genes will be fished. Nevertheless this project was selected by ANR and the financial support given by ANR will allow paying the transcriptomic analysis and hiring a new post-doc, giving the opportunity to increase the forces of the team.

Aim 2 is the project which is more in line with previous team researches and requires technologies that the team has already used (intra cerebral dialysis).

Aim 3 is a completely new one and aims at showing that mGLUR7 receptor is a good candidate for drug addiction therapeutic. It is again a very ambitious and risky project since everything has to be done from start and no preliminary data are presented demonstrating the opportunity to follow such a project.

Each of these projects in itself is interesting but does not synergize with the others. Hence, these projects are quite risky, time and energy consuming and regarding the small size of the unit (4 persons), one can question whether the team will be competitive.

In conclusion, the committee is questioning the adequacy between large, very ambitious, time-consuming and diverse projects with the very small size of the unit.

4 • Conduct of the visit

Visit date:

Start: Monday, 5, november, 2012, at 10h30

End: Monday, 5, november, 2012, at 18h

Visit site :

Institution: Faculté de Sciences Pharmaceutiques et Biologiques, Université de Paris 5 Descartes

Address: 4 avenue de l'Observatoire, 75270 Paris Cedex 06

Conduct or programme of visit:

10h30-11h	Presentation of the AERES by the AERES delegate to the visiting committee (closed doors)
11h-11h15	Presentation of the committee and the AERES by the AERES delegate to the unit
11h15-13h00	General presentation of the unit (results and project) by the head then discussion
14h-14h30	Meeting with the representative of the institution (University of Paris 5) and body (CNRS) *Public: committee members, AERES delegate*
14h30-14h45	Meeting with the technical and administrative staff *Public: committee members and AERES delegate, only (in the absence of institution representatives and the unit head)*
14h45-15h00	Meeting with the PhD students and post-docs *Public: committee members and AERES delegate, only (in the absence of institution representatives and the unit head)*
15h-15h15	Meeting the permanent researchers and assistant-professors *Public: committee members and AERES delegate, only (in the absence of institution representatives and the unit head)*
15h15-15h30	Debriefing *Public: committee members, AERES delegate*
15h30-16h00	Meeting with the unit head (in case) *Public: committee members, AERES delegate*
16h00-18h00	Meeting of the committee (closed doors) *Public: committee members, AERES delegate*

5 • Statistics by field: SVE on 10/06/2013

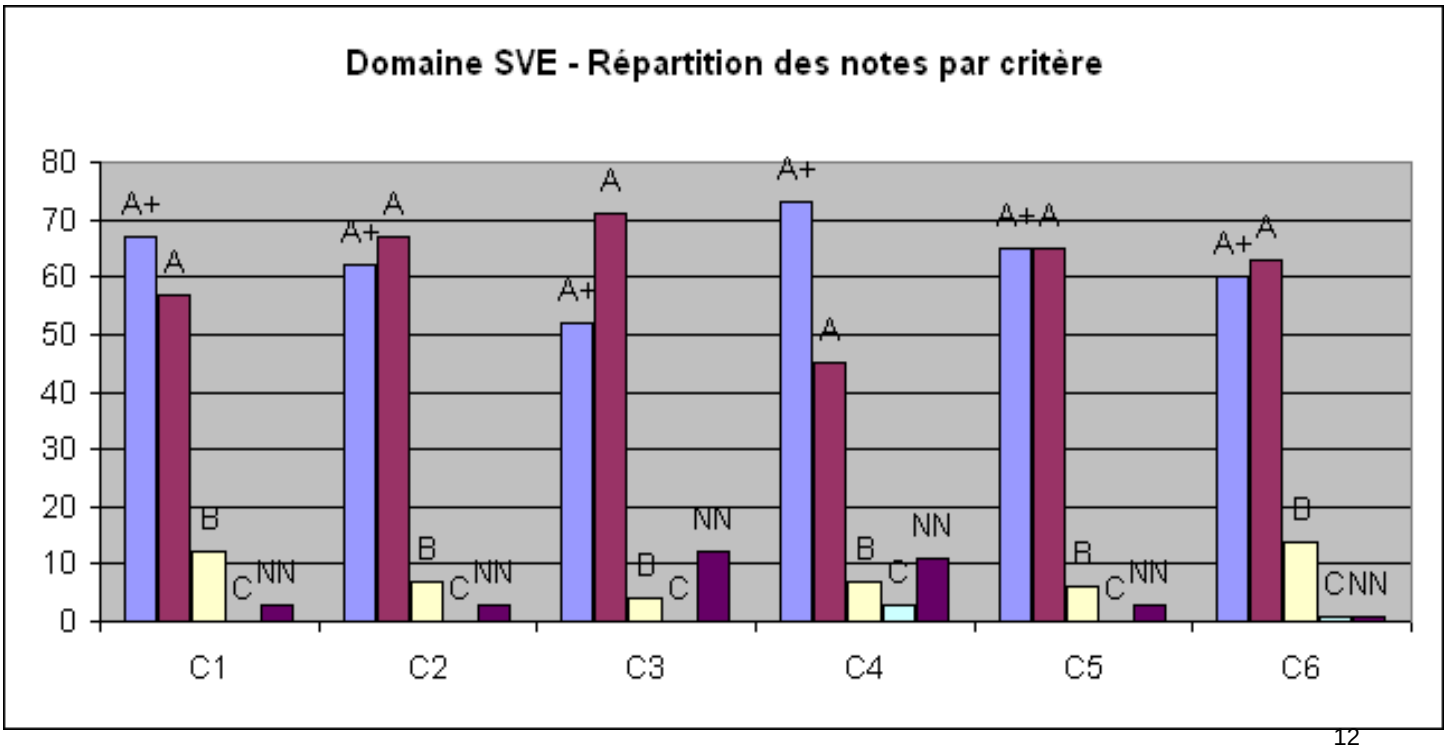
Grades

Critères	C1 Qualité scientifique et production	C2 Rayonnement et attractivité académiques	C3 Relations avec l'environnement social, économique et culturel	C4 Organisation et vie de l'entité	C5 Implication dans la formation par la recherche	C6 Stratégie et projet à cinq ans
A+	67	62	52	73	65	60
A	57	67	71	45	65	63
B	12	7	4	7	6	14
C	0	0	0	3	0	1
Non Noté	3	3	12	11	3	1

Percentages

Critères	C1 Qualité scientifique et production	C2 Rayonnement et attractivité académiques	C3 Relations avec l'environnement social, économique et culturel	C4 Organisation et vie de l'entité	C5 Implication dans la formation par la recherche	C6 Stratégie et projet à cinq ans
A+	48%	45%	37%	53%	47%	43%
A	41%	48%	51%	32%	47%	45%
B	9%	5%	3%	5%	4%	10%
C	0%	0%	0%	2%	0%	1%
Non Noté	2%	2%	9%	8%	2%	1%

Histogram



6 • Supervising bodies' general comments

UNIVERSITÉ PARIS DESCARTES

Vice Président du Conseil Scientifique

Paris le 3 Janvier 2012

Vos ref : S2PUR140006259-
Neuroplasticité et Traitement des
Addictions-0751721N

Monsieur Pierre GLAUDES
Directeur de la section des unités de recherche
Agence d'Evaluation de la Recherche et de
l'Enseignement Supérieur
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 « Neuroplasticité et Traitement des Addictions »

Vous trouverez ci-joint les réponses du Directeur de l'unité, Florence NOBLE.
Concernant la critique sur la perte de l'équipe Clinique, comme je l'avais moi-même exposé aux membres du comité de visite, en raison du contexte local il vaut effectivement mieux privilégier des interactions externes (avec les cliniciens) qui fonctionnent plutôt que des internes qui manifestement ne sont pas satisfaisantes.

Le Président et moi-même n'avons pas d'autre remarque particulière à formuler.

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

Le Vice Président du Conseil Scientifique

Stefano Marullo, DM, DesSci

Université Paris Descartes, Vice-présidence du conseil scientifique, 12 rue de l'école de médecine, 75170 PARIS cedex 06
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NEUROPSYCHOPHARMACOLOGIE DES ADDICTIONS
Vulnérabilité et variabilité expérimentale et clinique

U 705 INSERM – UMR 8206 CNRS

Réponses au rapport:

Le rapport mentionne que la perte de l'équipe Clinique pour ce nouveau contrat est préjudiciable. Le rattachement des cliniciens dans l'Unité pourrait effectivement paraitre plus rationnel vu les thématiques que nous développons. Néanmoins comme nous l'avons mentionné, nous avons établi depuis de nombreuses années des contacts forts avec plusieurs cliniciens dans plusieurs régions françaises et avec lesquels nous sommes très régulièrement en contact. La présence à l'organigramme de cliniciens ne nous semble donc pas être essentielle, les contacts étant déjà très fortement ancrés.

Le comité de visite souligne dans son rapport des projets trop larges et dispersés au regard de la composition de l'Unité. Dans le projet présenté pour les 5 prochaines années, nous avons effectivement 3 axes de recherche, qui peuvent paraitre indépendants, mais qui sont tous les trois tournés vers la pharmacologie des addictions, et les traitements, qui sont des axes de recherche originaux par rapport aux autres laboratoires français et étrangers travaillant dans le champ des addictions. Les projets ayant été réfléchis sur plusieurs années, ils apparaissent à l'écriture obligatoirement large, mais naturellement en fonction des données que nous obtiendrons, peu à peu ils se focaliseront sur les résultats les plus pertinents, et tout naturellement seront en interconnexions les uns avec les autres, tournés vers les pharmacothérapies. De plus nous avons déjà été contactés par des Chercheurs et Ingénieurs-Techniciens qui souhaiteraient pouvoir rejoindre l'Unité après sa création.