LNCA - Laboratoire de neurosciences cognitives et adaptatives

Rapport Hcéres

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

Research Units Department

AERES report on unit:

Laboratoire de Neurosciences Cognitives et Adaptatives (LNCA)

Under the supervision of the following institutions and research bodies:

University of Strasbourg and CNRS

February 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

Unit

Name of unit:	Laboratoire de Neurosciences Cognitives et Adaptatives
Acronym of unit:	LNCA
Label requested:	UMR CNRS
Present no.:	7237
Name of Director (2009-2012):	Mr Christian KELCHE
Name of project leader (2013-2017):	Mr Jean-Christophe CASSEL

Members of the committee of experts

Chair:	Mr Bruno POUCET, Marseille
Experts:	Mr Aldo BADIANI, Rome, Italy
	Ms Muriel DARNAUDERY, Bordeaux (CNU representative)
	Mr Rémi GERVAIS, Lyon (CoNRS representative)
	Mr Shane O'MARA, Dublin, Ireland
	Ms Carla SANCHIS-SEGURA, Castello de la Plana, Spain
	Mr Maurits VAN DER Molen, Amsterdam, The Netherlands

Representatives present during the visit

Scientific Delegate representing AERES:

Ms Thérèse JAY

Representatives of the unit's supervising institutions and bodies:

Mr Bernard POULAIN, CNRS

Mr Eric WESTHOF, University of Strasbourg

Report

1 • Introduction

Date and conduct of visit:

The visit was conducted on February 22nd, 2012. The documents sent before the visit proved to be very useful to get a clear view of the structure of the lab, as well as of its goals, achievements and projects. The oral presentations complemented the documents very nicely. After a closed-door meeting with the AERES committee members, the general presentation of the unit started with the presentation of the past activity of the group by the director and the presentation of the project by the future director. These talks were followed by 30 min discussion. Then, each group leader presented the past activities and projects for 20 min followed by 20 min discussion in front of the director, the team members and the AERES committee members. The director and team members left the room 5 min before the end to allow a "private" discussion between the AERES committee members and each group leader. Half an hour exchange with the representatives of the research organization (CNRS) and the University of Strasbourg took place. The committee was split into three groups each having one hour discussion with i) the PhD students and post-doctoral fellows, ii) the researchers with permanent position, excluding the team leaders, and iii) the technicians, engineer staff and administrative assistants. The AERES committee members had a private discussion with the future director of the unit. Then, there was the final closed-door meeting with the AERES committee members.

History and geographical location of the unit, and overall description of its field and activities:

The proposed unit "Laboratoire de Neurosciences Cognitives et Adaptatives" results from the split of the former "Laboratoire d'Imagerie et de Neurosciences Cognitives" (UMR 7191, then UMR 7237), jointly administered by the University of Strasbourg and the CNRS. This unit, created in 2007 by the merging of three formerly separate research units, comprised initially 13 research teams which were then reorganized in 5 groups: Group 1 "In Vivo Imaging", Group 2 "Biopathology of Myelin and Imaging", Group 3 "Neuroadaptations to Psychostimulants", Group 4 "Neuropsychology and Perception", Group 5 "Cognitive and Behavioural Neurobiology".

The present project, which is built on a further reorganization concerning only the last three groups of the former unit, will be structured in four research teams: 1) "Interactive Dynamics of Memory Systems", 2) "Neurobiological bases of cognitive decline", 3) "Neuroadaptations to psychostimulants", 4) "Normal and Pathological Aging: Neuropsychological and Neurophysiological Investigations". The first two teams result from the split of Group 5 of the former research unit, while the other two teams stem from Group 3 and Group 4 respectively.

This dramatic reorganization has three important consequences. First, it allows the re-focusing of the research activity on a smaller number of scientific issues. Second, it is accompanied by a strong reduction in the number of permanent personnel involved in the project (from more than 60 permanent positions in the past unit to about 30 permanent positions in the project). Third, it reduces the number of geographical sites of implantation of the unit from four to two (Faculté de Psychologie at Strasbourg centre and CNRS campus of Cronenbourg). These two sites are about 6 km apart from each other.

The LNCA is part of the Research Federative Institute (IFR) in Neuroscience, a larger consortium of research units all located in Strasbourg. Research performed in this Institute primarily concerns fundamental research in cognitive psychology and cognitive and integrative neuroscience, but also importantly clinical research, and involves a wide variety of techniques including those of molecular biology. The LNCA also participates in the Neurex Network, which gathers several neuroscience research institutes in Germany, France and Switzerland all located near Strasbourg.

The overall research aim of the LNCA is three-fold: 1) understanding the neurobiological mechanisms of memory, 2) deciphering the cognitive processes altered during normal and pathological aging, and 3) the epigenetic mechanisms of behavioural deregulations with a focus on drug addiction. These various issues are addressed with a wide methodological approach that allows neural activity to be either manipulated (lesions, inactivations, pharmacology, transcranial magnetic stimulation – TMS) or measured in both animals (e.g., brain imaging using early genes) or in humans (e.g., fMRI, EEG), single unit recordings, local field potentials – LFP. The new unit will be divided into four teams.

Management team:

The head of the unit is Mr Jean-Christophe CASSEL. For important decisions, he will be assisted by a direction committee composed of the leaders of each research team. He will be assisted by an administrative secretary.

Unit workforce:

Workforce	Number on 06/30/2011	Number on 01/01/2013	2013-2017 Number of producers**
N1: Professors or assistant professors	24	11	11
N2: EPST or EPIC researchers	13	9	8
N3: Other professors and researchers	5	1	1
N4: Engineers, technicians and administrative staff *on a permanent position	19,4	9,4	
N5: Engineers, technicians and administrative staff * on a non-permanent position	-		
N6: Postdoctoral students having spent at least 12 months in the unit	4		
N7: Doctoral students	33		
N8: PhD defended	25		
N9: Number of Habilitations to Direct Research (HDR) defended	2		
N10: People habilitated to direct research or similar	27	11	
TOTAL N1 to N7	**98,4**	**30,4**	**20**

* If different, indicate corresponding FTEs in brackets.

** Number of producers in the 2008-2011 period who will be present in 2013-2017.

2 • Assessment of the unit

Overall opinion on the unit:

After several successive reorganizations between 2005 and 2011, the unit project has been resized so as to focus on a smaller number of scientific issues. The overall production of its members is good, even though it is uneven from one team to another. The publication output could be improved however by targeting high impact factor journals more frequently. The focus on fundamental questions varies a lot between teams. The new recruitments are excellent with regard to quality and potential. Many members of the unit are assistant professors and therefore have heavy teaching duties. One team also has a strong involvement in applied research. Therefore, long-term viability of some research teams would greatly benefit from additional arrivals, both in terms of research and technical assistance. Finally, all members of the proposed unit strongly support the project and are enthusiastic about upcoming collaborations with other teams. Some of these collaborations already exist. Others will have to be encouraged through an active scientific policy. Overall, the committee is optimistic that the new unit will be successful if it is supported by the University of Strasbourg and the CNRS.

Strengths and opportunities:

The project brings together a group of investigators with interests in the study of cognition and behaviour from the cellular to the behavioural level, which allows a real multidisciplinary approach. There are various existing and natural links between the groups working on the animal and there are possible interactions with the group working with humans. A feature of this laboratory is also that more than half of investigators have teaching duties. Although this has drawbacks (see below), it has the advantage of providing a good knowledge of the undergraduate student population, making it easier to identify those more likely to be successful in research. Through its participation to the Federative Institute, the unit has access to excellent facilities (e.g., fMRI), some of them being administered by members of the unit themselves (human platform at Cronenbourg site). Finally, the different meetings with the technicians, the students, and the postdocs and researchers of the LNCA left the committee with the strong feeling that the unit is a supportive and collegial environment in which facilities and know-how are shared.

Weaknesses and risks:

The visibility of the proposed unit is not as high as it could be and therefore needs to be improved. The detailed review of the projects suggests that this unit wishes to compete in research areas in which there is already a substantial international presence with laboratories tending to be larger, better funded and interdisciplinary in nature. In this competitive field, focusing on a restricted set of hot topics may be the solution for middle size research groups. In addition, while most participants of the proposed unit do have a common past history, it appears to the committee that it would be useful and even necessary to strengthen the proposed connections between the teams working on animals, but also to tie the links with the team working with humans. This is perfectly feasible given the convergence of the scientific issues raised by the latter and one of the animal research teams. A last concern is that investigators who carry heavy teaching duties have less time and opportunity for research, which makes it more difficult for them to participate in the research community. More generally, although the unit currently has a reasonable number of permanent administrative and technical members as compared to the number of permanent scientists (ratio is about 0.5), retirements during the coming years will make the situation very difficult.

Recommendations:

Recommendations are in direct relationship with the observed points of weakness at the level of the whole research unit but more specific recommendations for individual teams may also provide useful directions.

First, it may be necessary for some teams to reduce the number of operations and to establish priority so as to be more competitive in the fields that will be judged the most important.

Second, it is necessary to increase the international visibility of the teams. This can be achieved through various ways (e.g., organizing seminar series with international-level scientists, increasing the participation of lab members to international meetings, etc.)

Third, it is recommended to tighten the scientific links between the teams. Some of these links were alluded to by the future head of the unit and should be strongly supported and encouraged.

Fourth, the workforce devoted to fundamental research can be improved by finding any meaningful method to decrease the consequences of the teaching and administrative load of some team members. This also may rely on the support provided by non-teaching scientist. The recruiting of new researchers to consolidate some teams is mandatory.

Fifth, the unit will have soon too low administrative and technical support, which requires hiring the appropriate positions in anticipation of the departures.

3 • Detailed assessments

Assessment of scientific quality and production:

The former head of the LINC (from which the LNCA originates) made a very good job in managing this large consortium of teams which, in addition, were located in widely separated areas of Strasbourg. The overall achievements of the LINC are also very good. The production of those teams, which are joining the LNCA project, though uneven, is very good as suggested by the number of primary papers in scientific journals and other numerical indices calculated over the period 2007-2011 (98 articles, with 17 in journals with IF > 5; 8 chapters; 81 proceedings in international meeting; 13 PhD theses defended). There are two "non-producers" in the unit. One is playing a significant role in its team according to his colleagues whereas the other will retire in 2013.

Assessment of the unit's integration into its environment:

The unit has a special interest in the valorisation and socio-economical aspects of its research: about 20% of its activity is devoted to these points. This is largely caused by two factors. The first factor is the focus on age-related alterations, which is a major concern of our societies. The second factor is that the unit is coupled with a technical platform for analysis of human behaviour and brain activity. This platform, located at Cronenbourg CNRS site, is a joint service unit of the CNRS and is administered by the head of one of the research teams of the proposed unit. Although this association ensures regular financial incomes through industrial contracts with this team, it also has the drawback of increasing the team's workload in a domain not directly related to fundamental research. The number of grants is quite different among the teams. Most of them come for the Cronenbourg technical platform. The number of national or international grants obtained by the other teams is small but significant however (e.g., one ANR and one ERA-Net Neuron).

Assessment of the research unit's reputation and drawing power:

The reputation of the unit is good at national level but could be improved at international level. The number and the reputation of the awards obtained by staff members, including invitations to conferences and symposia (n=27) is significant but could also be improved. It should be noticed that some members were involved in the foundation of an international scientific society (IDARS) and the organization of several Neurex workshops. One member of the proposed unit was nominated as an adjunct professor at Pennsylvania State University and is also a member of editorial boards of online scientific journals (e.g. The Open Geriatric Medicine Journal).

The unit has attracted many PhD students over the past four years. It recently recruited several high levels young scientists. Two of them will reinforce the working potential of the newly created research team #2 while two others have joined existing teams. It is to be noticed that there are currently discussions about the coming of two additional high-level researchers (one with teaching duties) who would participate in the consolidation of research team #3 in which several members are expected to retire from 2013.

The unit has several international collaborations with foreign partners. However a recommendation would be to seek more National (e.g., ANR) and European grants so as to be in a better position to attract foreign postdocs. Finally the LNCA is heavily involved in teaching and many of its members participate actively in the diffusion of science (e.g. Semaine du Cerveau).

Assessment of the unit's governance and life:

The scientific and administrative organization of the unit and the rules for decision-making are well thought. The rules of laboratory governance are well defined in the documents.

The committee split to meet the personnel of the proposed unit in parallel sessions. Committee members listened and questioned researchers and assistant professors. The overall life of the research unit seems good, with good interaction between people and general overall good and reasonable management of the lab. Many of those present hoped to have postdoctoral experience at labs abroad, preparatory to returning back to France - and in general wanted to return to Strasbourg. This is a clear indicator of the general degree of satisfaction that the staff has when considering the work in the unit. Each week, lab seminars are organized and journal clubs are also made within each team. Publication strategy seems to proceed in a collegiate and reasonable fashion, with a clear expectation of who should be the first/lead author and last/senior author. Several Assistant Professors have what appear to be, by any reasonable standard, heavy to excessive teaching and administrative duties and mentioned the difficulty in reducing these activities in order to free up time to engage in research. The committee encouraged them asking for reduction of duties from the university and/or CNU to help them to increase their research activities.

The committee also met the technical and administrative staff (CNRS ITA and University BIATOS) who first presented their main duties and how they were dispatched in the present and future organization. From 2011 to 2013, 9 on 24 of the personnel of the former unit have or will retire. In the new laboratory configuration, the technical/administrative staff would include 8 persons (4 from CNRS and 4 from Strasbourg University; one additional technician is about to be hired) while the remaining will join another project. Importantly, those who are concerned by the new project are enthusiastic in joining it. They also welcome the introduction of new techniques such as electrophysiology and molecular biology. As a whole, the visiting committee is confident that this staff will fit well with the project and encourages the new director to discuss with CNRS and University of Strasbourg in order to optimize the staff according to new needs and future retirements.

Finally, the committee met with the PhD students and was impressed with their enthusiasm, maturity, and competence. All PhD students are funded and receive reliable support and assistance from their supervisors. Their future is discussed with the permanent staff. The policy of authorship for publications resulting from PhD's work is well defined and is coherent (see above). Their participation to one national or international meeting per year is financially supported by the unit. Finally, they profit from an in-house seminar series where seminars are given by permanent researchers. Clearly, the unit is a great place to make research for these young colleagues.

Finally through its participation to the Neuroscience Federative Institute of Strasbourg and the Neurex Network, which brings together neuroscientists of the Swiss and German universities of Basel and Fribourg, the unit is well implanted at the local and regional level.

Assessment of the strategy and 5-year project:

The overall project is in the logical continuation of the research previously conducted by the former groups of the LINC (e.g., neurobiological mechanisms of memory and neurobiology of addiction) but offer new perspectives by including an interest shared by several teams for epigenetic mechanisms and for age-related alterations. Its feasibility is high given the existing structure of the current unit and the fact that most facilities are well thought. The policy for allocation of means is well defined and takes into account the performance of each research team. Such performance will be assessed yearly using a methodology which is accepted by the members of the unit.

Mid-term and long-term prospects concern the development of in vivo electrophysiology and molecular biology in combination with the research conducted by two of the research teams. Longer-term plans include the possibility to use optogenetics, and collaboration has already been initiated in this perspective. All of these projects however are time-consuming and carry the inherent risk of a dilution of the workforce in too many methodologies. To be successful, they certainly would require either the arrival of new scientists possessing the appropriate skills or the intensification of national or international collaborations.

Assessment of the unit's involvement in training:

More than half of members of the unit, including the director, are researchers with teaching duties (2 professors and 9 assistant professors) therefore ensuring involvement of the unit in training in several university degrees (License and Master in Neurosciences, Psychology, Pharmacology) of the University of Strasbourg. As said above, the doctoral students are actively participating to the life of the unit and its research teams. Similarly, the policy of the unit with regard to the hosting, financing and monitoring of the students is clear and appropriate. The staff of the unit is concerned with the future development of the doctors who have been trained in the unit.

4 • Team-by-team analysis

Team 1: Interactive Dynamics of Memory Systems

Team leader: Ms Anne-Laurence BOUTILLIER and Mr Jean-Christophe CASSEL

Workforce

Workforce	Number on 06/30/2011	Number on 01/01/2013	2013-2017 Number of producers**
N1: Professors or assistant professors	5	2	2
N2: EPST or EPIC researchers	5	3	3
N3: Other professors and researchers	1	1	1
N4: Engineers, technicians and administrative staff * on a permanent position	4,5	1	
N5: Engineers, technicians and administrative staff * on a non-permanent position	0		
N6: Postdoctoral students having spent at least 12 months in the unit	1		
N7: Doctoral students	9		
N8: PhD defended	10		
N9: Number of Habilitations to Direct Research (HDR) defended	2		
N10: People habilitated to direct research or similar	6	4	
TOTAL N1 to N7	**25,5**	**7**	**6**

* If different, indicate corresponding FTEs in brackets.

** Number of producers in the 2008-2011 period who will be present in 2013-2017.

• Detailed assessments

Assessment of scientific quality and production:

Team 1 originates from the split of a group working on Cognitive and Behavioural Neurobiology from the former unit (see below team 2 of the project). One of their main achievements is to have demonstrated that enriched conditions during the whole life shapes cognitive reserve by preventing attention and memory deficits in rats (Neurobiol Aging). The involvement of transcriptional events depending on H2B and H4 histone acetylation in spatial learning is the other main line of research of the team (Neuropsychopharmacol). They have also provided evidence for the contribution of the intralaminar thalamic nuclei (J Neurosci), septal GABAergic and cholinergic neurons to remote spatial memory in rats (Hippocampus) and the direct activation of HAT enzymes in adult neurogenesis and remote memory formation in mice.

The new team will be co-headed by two senior investigators (including the future head of the overall research unit) and will involve four other permanent researchers. The two team leaders' "h-index" are respectively 26 and 17 and their citations/year have risen over the last years. This group has had a complex evolution over the past number of years and appears to be working towards a more settled state. In spite of its small size, the team has a substantial publication record over the past 4-year period (more than 50 articles, mean impact factor: 4.05; all but 1 resulting from direct work of the team). The overall level of research being conducted, relative to international standards, is very good.

Assessment of the research team's integration into its environment:

The team seems comfortably embedded within the Strasbourg context. It manifests a relatively limited ability to attract research funding from the greater French system and from the European Union, or from commercial sources, for example, the pharmaceutical industry. It appears that the group has participated in a relatively limited number of international networks, and that it could make a greater effort in this regard.

Assessment of the research research team's reputation and drawing power:

The team overall has a modest number of prizes and distinctions awarded to the members. It is difficult from the documentation provided to understand to what extent the team has been invited to participate in international events. It appears from the documentation provided that the team principally relies on recruits from within France for its membership and has relatively few recruits from abroad. The recent recruitment of one young CNRS researcher is a very positive point however.

Assessment of the strategy and 5-year project:

The team will have to compete in an area of research in which there is already a substantial international presence, with laboratories throughout Europe, North America, and to an increasing extent, Asia, participating in this area. These laboratories tend to be larger, better funded and interdisciplinary in nature. A group of this size, therefore, if it wishes to avoid "me too" research, needs to be very focused in terms of the research programme that it undertakes. The group suggests a focus on the thalamic nuclei and on the lateral habenula, as well as an exciting and relatively new area of research, which is the role of epigenetic factors in memory. There is the basis, therefore, of a programme of research which can have a greater international impact than is currently present. For this goal, the groups should work together to focus on higher level scientific questions, and ensure that they deliver research of the appropriate scale and quantity. The feasibility of the long-term scientific objectives presented is no doubt reasonable. To do so, however, the group is going to have to undertake a greater degree of risk, in terms of the scientific programme, with the possibility that certain of the research programme components will yield relatively little by way of experimental results.

Conclusion:

Overall opinion of the team: Team 1 has a reasonable start on attempting to devise a coherent and consequential research programme. A focus on a relatively limited number of areas, but which embraces multi-level analysis, is warranted.

Strengths and opportunities: The team clearly is cohesive and this is both strength and a weakness. It is strength in the sense that close colleagues working together on difficult scientific programmes can make rapid progress.

Weaknesses and risks: The team clearly is cohesive but this is a weakness in the sense that close colleagues can become too comfortable with each other, and each other's modes of thinking. In this regard the overall team needs to address a specific weakness in the area of benchmarking and internationalising its focus.

Recommendations: Overall, there is the basis for a strong and successful research program, in an area which brings together research that will have international visibility. The team, however, needs to spend more time reflecting on their own internal scientific strategy, focusing on work that is likely to differentiate them from other laboratories. The team needs to spend time benchmarking itself relative to other research groups, so that it achieves within its own work a level of research excellence that allows it to focus on being the best that it can. The team should not focus in the short-term on importing new and complex techniques, for example, optogenetics, merely because these are the latest techniques in the field. A consideration of the adoption of new technologies should only be made after it has been determined that the scientific questions to be investigated require them. It may also be the case that, through appropriate networks of internationalization, difficult new techniques can be incorporated with ease as a result of the collaborative network, rather than establishing it on the ground in Strasbourg.

Team 2

Neurobiological Basis of Cognitive Decline

Team leader: Ms Chantal MATHIS

Workforce

Workforce	Number on 06/30/2011	Number on 01/01/2013	2013-2017 Number of producers**
N1: Professors or assistant professors		3	3
N2: EPST or EPIC researchers		3	3
N3: Other professors and researchers		-	-
N4: Engineers, technicians and administrative staff * on a permanent position		0.8	
N5: Engineers, technicians and administrative staff * on a non-permanent position			
N6: Postdoctoral students having spent at least 12 months in the unit			
N7: Doctoral students			
N8: PhD defended			
N9: Number of Habilitations to Direct Research (HDR) defended			
N10: People habilitated to direct research or similar		2	
TOTAL N1 to N7		**7**	**6**

* If different, indicate corresponding FTEs in brackets.

** Number of producers in the 2008-2011 period who will be present in 2013-2017.

a ; this is a newly formed team, thus those figures are not relevant.

• Detailed assessments

Assessment of scientific quality and production:

This team originates from a split of the group 'Cognitive and Behavioural Neurobiology" working in the former unit (see analysis of team 1 of the project). Beyond its participation to some studies conducted by team 1 (e.g., on the effects of enriched environments), the main achievements of this team include the behavioral characterization of several lines of transgenic mice (APPSWE, apoE4 TR, GASP1 mice) as models of Alzheimer's disease. Thus, this team has demonstrated that activation of neprilysin, a zinc-dependent metalloprotease enzyme, prevents memory deficits in the APPSWE mouse model of Alzheimer's disease (patent currently under evaluation). Furthermore, spatial memory in this transgenic model as well as in human apoE4 TR mice (published in Behavioural Brain Research) has been shown highly sensitive to basal forebrain cholinergic lesion.

A close inspection of the previous research of this former group reveals a progressive expansion of its members' research interests and helps to understand the need of this strategic scission. In this way, the research of the new team will benefit of a simpler organizational management and more focused objectives/ resources allocation. Also, it must be noticed that several of the senior researchers of the new team come from separate fields and that several of them have never joined a previous publication with the principal researcher. Therefore, the integration of researchers coming from different topics in a common project might be one important challenge for the team.

This group has published 20 peer-reviewed articles during the previous contract without counting the 16 articles published over the same period by the two new members. The team leader's "h-index" is 17, with a steep increase of citations/year over the last years. In spite of this productivity, the publication list also points out two of its possible weaknesses: 1) the lack of a clear network of collaborators at the international level (at least for the main topics of the project); 2) the absence of a common history among most of the researchers composing this group, which is obvious since this is a new team, but makes it difficult to predict which level of performance will be achieved. In terms of scientific quality, several researchers of this group (including those more recently arrived) have published in very highly rated journals (IF >5). This fact, together with the complementary expertise provided by those researchers seems to provide an optimal basis for developing comprehensive and multi-leveled projects on aging and aging-related diseases. The synergy created by these different expertises is a major strength of this group in the near future whereas the teaching duties of several of its members might be a significant drawback. Thus, in order to keep this level of productivity, a reduction of teaching duties or the arrival of additional team members should be considered.

The results reveal the originality, relevance and applicability of the research conducted by this group. A weakness is related to the international visibility of the team, as reflected by the lack of reference to international research conferences, editorial boards of international scientific journals and similar indicators. The head of the team participated as reviewer for 8 scientific manuscripts.

Finally, the team members have been involved in students' scientific formation as supervisor or co-supervisors of 4 PhD theses (1 of them, already defended). The head of the team is a member of the Special Admission Committee of the Doctoral School ED414. Another member is the training officer of the Master of Neurosciences at the UdS and still another was an expert on the creation of a subsidiary of the University S. Freud (Vienna, Austria) in Paris.

Assessment of the research team's integration into its environment:

This group has several contracts with the pharmaceutical industry, two patent applications and has developed two original protocols. Through its links with the pharmaceutical industry, this group is financially autonomous for most of its research.

However, the group leader has not yet been awarded with any ANR grant and some of the other senior scientists do not have experience in obtaining financial support. Most of the funding was obtained in collaboration with other teams. Therefore, although this might be a competitive research team able to attract funding from private and public scientific agencies, the quality and continuity of contractual relationships of this team is difficult to assess.

Finally, there are clear opportunities for collaboration with other research teams within the laboratory as well as from other local scientific institutions (e.g. IFR des Neurosciences, NEUREX). The ambience of the newly created laboratory and the personality of its head appear to ensure an effective and regular collaboration by the different teams included in this new laboratory. Such a collaboration spirit will result not only in a fruitful exchange of ideas but also in the mutualization of efforts and resources as well as in real possibilities for obtaining fundings. It is less clear if the team will be able to establish collaborations beyond this local level so as to obtain funding from international agencies such as the EU.

Assessment of the research team's reputation and drawing power:

The different members of the team have been prized (e.g., one has received a NARSAD young investigator award) or recognized as international experts. Other similar activities were conducted at the local or national level. The group is attractive for young researchers, as shown by the recent arrival of two young French researchers who have a very good track record and are competitive at the international level.

The head of the team was invited to 2 international conferences, both of them in relation to its collaboration with the pharmaceutical industry. There is a significant number of non-invited participations in international meetings. The team members have developed a more intense activity at the national (e.g. information dissemination and education) than at the international level. Therefore, the attractiveness of this team must be highlighted as one of its major strengths and might result in the incorporation of additional students and researchers that would enhance the overall productivity.

Regarding collaborations with other research teams, and beyond the links with the pharmaceutical industry, most connections are at the local and national level, but this might change with the recently incorporated scientists. Finally, collaboration with other teams of the LNCA seems to be ensured by its thematic coherence and shared history.

Assessment of the strategy and 5-year project:

Most team members were members of the team "Cognitive and Behavioural Neurobiology" of the former unit. The research of the new team will have a clearer focus: cognitive decline, both normal and pathological (Alzheimer disease). Both topics are complementary and the use of different rodent models and the various expertises of the researchers provide a promising start point, even though these topics are highly competitive and some of the team members have only marginally contributed to them in the past.

The scientific project is relevant and extensive. The workload might be excessive for the size of the team, specially considering that most of its members have significant teaching and educational duties. On the other hand, the proposed models and theoretical framework are solid and adequate. Some parts of the project are not particularly novel, but the intended work plan includes very interesting and original elements such as testing the "cognitive reserve" hypothesis (which is the focus of intense research in human cognition but is almost unprecedented on aging studies in rodents) as well as the use of a novel whole hippocampus in vitro preparation that will allowing studying this structure preserving its original connections. The inclusion of these two novel elements might be of special relevance given the competitivity of Azheimer's disease research. Finally, the attempt of the team to adopt a translational perspective on its own research is laudable. Although at present it still remains at the speculative level, the group has tried to see how some of their scientific questions and methodological approaches might result in a better and earlier diagnosis of Alzheimer's disease.

Conclusion:

Overall opinion of the team: This is a newly created team, therefore making it difficult to establish a prognosis on its evolution. The team combines experienced and young scientists whose past activity proves their expertise in a variety of methods and experimental approaches that, if properly merged, will provide information at different levels that might result in a more integrated knowledge of an important topic: Cognitive decline associated to aging and to some of its disturbances.

Strengths and opportunities: There is a clear potential strength and the research project has a great opportunity to develop (together with other LNCA groups, especially teams 1 and 4) a solid cluster of researchers focused on cognition-related processes and their disturbances.

Weaknesses and risks: The team seems burdened with excessive teaching duties and diffusion of knowledge. In fact, only 40% of research activity will be allocated to the production of new knowledge whereas 30% will be devoted to its dissemination (table 1.2.3 of the project).

Recommendations: The team should find a way to address this issue of excessive teaching, e.g., by incorporating new members or by reducing the duties not directly related to the project. Another minor concern is that some team members have been working separately or in topics that only partially overlap the objectives of this project. The effective engagement of all members must be a priority to minimize the impact of the first concern. Other recommendations include the need for the team to increase its international visibility with the creation of a wider collaborative network and an active involvement in meetings and activities of scientific societies. The scientific cluster derived through the LNCA creation and its privileged geographical location might be an attractive platform to develop initiatives that could highlight this center as a reference point of cognitive research at the European level. Finally, this team has strong links with the pharmaceutical industry, ensuring funding for most of the proposed projects. However, it is necessary that the team attracts funding from other sources, especially from international organizations, since most of the previous contracts were obtained by scientists who will belong to other teams in the proposed unit.

Team 3: Neuroadaptations to psychostimulants

Team leader: Mr Jean ZWILLER

Workforce

Workforce	Number on 06/30/2011	Number on 01/01/2013	2013-2017 Number of producers**
N1: Professors or assistant professors	2	1	1
N2: EPST or EPIC researchers	3	3	1
N3: Other professors and researchers	1	0	0
N4: Engineers, technicians and administrative staff * on a permanent position	1	1	
N5: Engineers, technicians and administrative staff * on a non-permanent position	0		
N6: Postdoctoral students having spent at least 12 months in the unit	1		
N7: Doctoral students	2		
N8: PhD defended	2		
N9: Number of Habilitations to Direct Research (HDR) defended	0		
N10: People habilitated to direct research or similar	3	3	
TOTAL N1 to N7	**10**	**5**	**2**

* If different, indicate corresponding FTEs in brackets.

** Number of producers in the 2008-2011 period who will be present in 2013-2017.

• Detailed assessments

Assessment of scientific quality and production:

This team has shown that changes in gene transcription underlie many of the neuroadaptations resulting from chronic exposure to drugs of abuse. These findings provide plausible mechanisms for how the environment might influence vulnerability to drug addiction. There are several mechanisms of epigenetic regulation, including histone tail modification and DNA methylation. These studies have contributed in a significant manner to link these two types of epigenetic adaptation to cocaine exposure. In particular, the team has shown that prolonged inhibition of the co-repressors known as class II histone deacetylases (HDACs) decreases cocaine but not sucrose self-administration (published in Journal of Neuroscience), thus identifying an epigenetic mechanism specific to drug reward but not to natural rewards. Furthermore, this team has linked DNA methylation to drug exposure, by showing that cocaine self-administration increases MeCP2 expression in the nucleus accumbens, a brain area thought to play a critical role in drug reward and addiction (Neurobiology of Disease). In short, this team has contributed in a pioneering manner to the investigation of the epigenetic mechanisms associated to drug abuse.

Over the 2007-2011 period, team 3 published 10 papers in peer-reviewed journals (mean impact factor: 4.0). Although the quality of these papers is satisfactory (2 papers in high impact factor journals in 2007 and 2008), the quantitative production is modest. In fact, the team includes only 3 "producers" out of 3 HDRs. The team produced 13 communications (only 5 at truly international meetings, FENS). Two PhD students defended their dissertation in 2009 and 2010, respectively. One patent ("Serotonin reuptake inhibitors for the treatment of Rett syndrome") was deposited by the head of the team in 2008, and was extended internationally in 2009.

Assessment of the research team's integration into its environment:

The head of the team has held several conferences on the theme of drug addiction before high school students, teachers, and the general public, both at a local and national level. Thus the team has a satisfactory performance in terms of cultural relations. The team has been involved in two relatively small research contracts (AFSR, 2011-2013; IREB, 2011-2012). It appears that no external funding has been obtained other than the contracts detailed above.

Assessment of the research team's reputation and drawing power:

Although the research conducted by this team is of good quality, no prize or distinction was listed in the report for the 2007-2011 period and no invited lectures were delivered at major universities or research centres in the same period. In contrast, the head of the team received several invitations to give oral presentations at meetings, including a major international meeting (CINP 2010, Hong Kong, 2010). Two researchers and one technician will retire soon and no new recruit has been hired for the present project. However, the research project of the unit acknowledges this weakness and mentions the possibility of hiring 2 additional members for this team. Although this is still in discussion, the likelihood that it happens is apparently high according to the representatives of the institutions. The team has been able to attract and retain 1 foreign post-doc from Brazil. Thus the drawing power is satisfactory. The team has 2 national and 4 international collaborations for the period 2007-2011, which resulted in 4 joint publications in the 5-year period. The scope and productivity of collaborations is therefore relatively modest, but must be levelled to the overall productivity of the team.

Assessment of the strategy and 5-year project:

The scientific objectives of this team are reasonable and the research strategies are sound with respect to cellular and molecular techniques. One particular matter of concern is represented by the stated aim of running drug self-administration in the mouse, which is an extremely tricky procedure. The present structure of the team does not appear to be suitable to develop such a procedure in-house. No team-specific policy of allocations of means is described in the applications. It is not clear how the team, under its present configuration, might accomplish the scientific objectives described in the application. Overall, the research project is sound and original. It may require, however, some revisions in the design of the behavioural procedures and a more sophisticated approach to the theoretical issues concerning drug reward, drug abuse, and drug addiction.

Conclusion:

Overall opinion of the team: Team 3 has great potential and might represent a crucial component of the unit's research project. The working environment of the team appears to be excellent with optimal interactions between team members. There is a considerable degree of enthusiasm concerning the research project and the possible arrival of new recruits.

Strengths and opportunities: The field of epigenetics in conjunction with drug abuse/addiction is still a relatively original area of research.

Weaknesses and risks: Members of this research team are not particularly productive since two of them are "non-producers". An unspecified number of team members (likely two) will retire in the next few years. The risk therefore is that the research objectives will not be achieved in the 5-year span of the project, unless the structure of the team is considerably strengthened.

Recommendations: The recommendations are in line with the weaknesses addressed above. First the project requires some revisions in the design of the behavioural procedures and a more sophisticated approach to the theoretical issues concerning drug reward, drug abuse, and drug addiction. Furthermore, it is mandatory that, given the expected leaves for retirement, the composition of this team be strengthened in order to achieve the research objectives detailed in the research project of the unit.

Team 4

Neurophysiology and Neuropsychology of Normal and Pathological Aging

Team leader: Mr André DUFOUR

Workforce

Workforce	Number on 06/30/2011	Number on 01/01/2013	2013-2017 Number of producers**
N1: Professors or assistant professors	7	5	5
N2: EPST or EPIC researchers	2	-	-
N3: Other professors and researchers	2	-	-
N4: Engineers, technicians and administrative staff * on a permanent position	5	1	
N5: Engineers, technicians and administrative staff * on a non-permanent position	2		
N6: Postdoctoral students having spent at least 12 months in the unit	-		
N7: Doctoral students	13		
N8: PhD defended	6		
N9: Number of Habilitations to Direct Research (HDR) defended	1		
N10: People habilitated to direct research or similar	5	2	
TOTAL N1 to N7	**31**	**6**	**5**

* If different, indicate corresponding FTEs in brackets.

** Number of producers in the 2008-2011 period who will be present in 2013-2017.

• Detailed assessments

Assessment of scientific quality and production:

Team 4 originates from a previous team 'Neuropsychology and Perception' which has been split between different projects. The research of the latter team has been concerned with four major themes, 'Mechanisms of sensorial integration', Neurophysiology of verbal learning', 'Investigations of memory in normal subjects and neurological patients', and 'Neurophysiology of attention and vigilance'. Each theme consisted of several research topics (17 topics in total). The diversity in themes and the large number of topics present a serious challenge to conceptual coherence and organizational framework. Nevertheless, the team has made important contributions to the field. For example, their results suggest that age-related impairment of spatial memory is related to an alteration of the fronto-parietal loop and that the elderly over solicits the frontal cortex for compensation. They also made the counter-intuitive finding that one year after temporal lobectomy, patients with right temporal lobe epilepsy show enhanced autobiographical memory (published in Epilepsia).

The team generated 51 peer-reviewed articles (mean impact factor: 3.8) in international journals during the review period (2007-2011). However, this very good output is severely skewed across team members. The team generated 4 completed doctoral theses, while 9 theses are in progress. Positions in scientific organizations (e.g., societies, national or international research boards) are not listed. Apparently, none of the team members is included in (or associate to) an editorial board. Team members have been asked as ad-hoc referee for journal publications. Finally, the team has several national and international collaborations but the status of these collaborations is difficult to evaluate (e.g., in terms of shared funding or publications, exchange of personnel).

Assessment of the research team's integration into its environment:

The team conducted applied research in addition to examining fundamental issues. The results that emerged from this applied research have been published in several reports (n=8). The reports dealt with thermoregulation or thermal processing (3), environmental issues (3), psychophysiology of emotional states (1), and sleep deprivation (1). Throughout the years of the evaluation period, the team attracted funding from several sources. It should be noted, however, that the funding for applied work relates to research that is external to the primary mission of the team. The benefit of this external applied work is that it may generate funds for primary research but the obvious cost is taking away time to be invested in the primary research.

Assessment of the research team's reputation and drawing power:

The self-evaluation does not list invited addresses or similar invitations. It does provide a list of conference contributions (n=27; i.e., .5 contributions per team member / per year). Half of the contributions (13) were to international conferences; 8 were co-authored by members who will participate in the new team. The self-evaluation does not list prizes or other distinctions. Although the 'attraction power' of the team is difficult to assess given the overall re-organization of the team, the hiring of a new associate professor in 2008 is a positive aspect. The team does not seem to participate in international or national programmes and its collaborations with other laboratories or partners (e.g., hospitals, industry) is difficult to evaluate given the weight of its participation to applied programs.

Assessment of the strategy and 5-year project:

The members of the new team 'Neurophysiology and Neuropsychology of Normal and Pathological Aging' are all members of the previous team 'Neuropsychology and Perception'. But the new team will be reduced considerably; it will consist of only 1 professor, 4 assistant professors and 1 engineer. All researchers have teaching duties. The research of the new team will have a much stronger focus: cognitive aging. The cognitive aging research will be organized around four themes; 'Aging and alteration of fronto-cortical and fronto-subcortical networks', 'Alteration in attention and vigilance systems', 'Aging and sensorial systems', and 'Aging and expertise'. The first two themes are related, both from a conceptual and methodological perspective. The two other themes seem to stand apart. It is difficult to envisage how a relatively small team might significantly contribute to each of these four research themes and be able to establish cross-connections between themes. This is all the more surprising given the strong bias towards applied research (30% according to table 1.2.1 of the proposal). Moreover only 30% of the team's effort will be devoted to the production of knowledge (fundamental and applied; see the project). In conclusion, the research programme seems to be a heavy burden for a limited sized team and new recruitment is not envisioned in the project description.

Conclusion:

Overall opinion of the team: The team is active and has considerable experience in a variety of methods that can be used in the study of cognitive aging.

Strengths and opportunities: The technical infrastructure seems well suited; it includes EEG/ERP, Infrared, and fMRI facilities.

Weaknesses and risks: The team is small relative to its research ambitions (i.e., fundamental research in four domains of cognitive aging and applied research aimed at developing diagnostic tools). Moreover, the team consists of only part-time researches who invest only 30% of their time in fundamental research. The limited effort presents a serious risk. The objective of the team is to develop neurocognitive assessment procedures that can be used to examine dementia and other diseases related to aging. Most of the efforts will be devoted to establish relations with institutions involved in the care for the elderly and in the dissemination of knowledge. The track record of the team does not testify of its ability in this regard. Finally, the team has to operate in a context that is dominated by animal research. In this regard, the team stands apart from the three other teams. This applies not only to (a) use of subjects (animals vs. human), but also to physical location (campus Centre vs. campus Cronenbourg), and funding (CNRS/U. Strasbourg vs. autonomous). The limited efforts that can be invested in the research program and its isolation from the other programs carry the risk that this team will be dissolved in the near future.

Recommendations: They are threefold: (a) more time should be invested in fundamental research, (b) the focus of this research should be tightened even further, and (3) the team should establish joint research projects with the other teams (in this regard themes 1 and 2 provide conceptual links with the animal research conducted by the other teams). Most importantly, the team should reconsider its involvement in applied research extrinsic to their focus on cognitive aging. This involvement may generate extra funding but the costs may well be larger than the benefits (in particular vis-à-vis the current teaching load of the team members).

5 • Grading

Once the visits for the 2011-2012 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 four criteria defined by the AERES and was given along with an overall assessment.

With respect to this score, the research unit concerned by this report (and, when necessary, its in-house teams) received the overall assessment and the following grades:

Overall assessment of the unit [Laboratoire de Neurosciences Cognitives et Adaptatives]:

Unité dont la production, le rayonnement et le projet sont très bons. L'organisation et l'animation sont excellentes.

Grading table:

C1 Scientific quality and production.	C2 Reputation and drawing power, integration into the environment.	C3 Laboratory life and governance.	C4 Strategy and scientific project.
A	**A**	**A+**	**A**

Overall assessment of the team [Interactive Dynamics of Memory Systems]:

Équipe dont la production et le rayonnement sont très bons. Le projet est excellent.

Grading table:

C1 Scientific quality and production.	C2 Reputation and drawing power, integration into the environment.	C3 Laboratory life and governance.	C4 Strategy and scientific project.
A	**A**	**-**	**A+**

Overall assessment of the team [Neurobiological Basis of Cognitive Decline]:

Équipe dont la production ne peut être évaluée, le rayonnement et le projet sont très bons.

Grading table:

C1 Scientific quality and production.	C2 Reputation and drawing power, integration into the environment.	C3 Laboratory life and governance.	C4 Strategy and scientific project.
NN	**A**	**-**	**A**

Overall assessment of the team [Neuroadaptations to psychostimulants]:

Équipe dont la production est bonne mais pourrait être améliorée. Le rayonnement et le projet sont très bons.

Grading table:

C1 Scientific quality and production.	C2 Reputation and drawing power, integration into the environment.	C3 Laboratory life and governance.	C4 Strategy and scientific project.
B	**A**	**-**	**A**

Overall assessment of the team [Neurophysiology and Neuropsychology of Normal a nd Pathological Aging]:

Équipe dont la production, le rayonnement et le projet sont très bons.

Grading table:

C1 Scientific quality and production.	C2 Reputation and drawing power, integration into the environment.	C3 Laboratory life and governance.	C4 Strategy and scientific project.
A	**A**	**-**	**A**

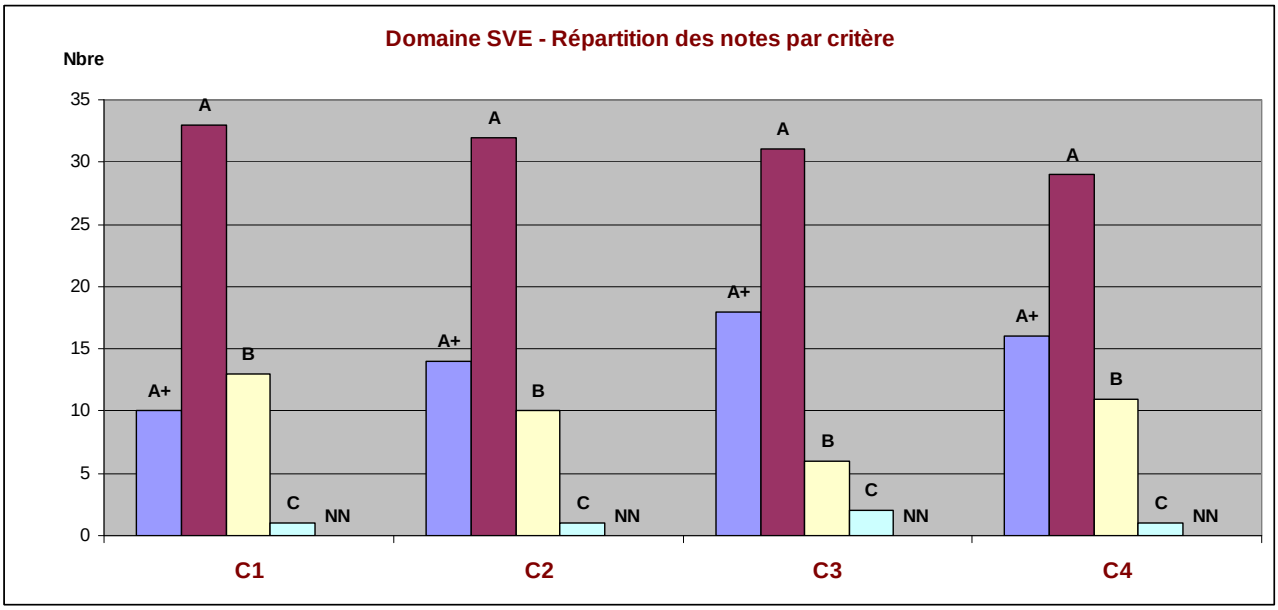
6 • Statistics per field: SVE au 10/05/2012

Notes

Critères	C1	C2	C3	C4
	Scientific quality and production	Reputation and drawing power, integration into the environment	Laboratory life and governance	Strategy and scientific project
A+	10	14	18	16
A	33	32	31	29
B	13	10	6	11
C	1	1	2	1
Non noté	-	-	-	-

Pourcentages

Critères	C1	C2	C3	C4
	Scientific quality and production	Reputation and drawing power, integration into the environment	Laboratory life and governance	Strategy and scientific project
A+	18%	25%	32%	28%
A	58%	56%	54%	51%
B	23%	18%	11%	19%
C	2%	2%	4%	2%
Non noté	-	-	-	-



UNIVERSITÉ DE STRASBOURG

Monsieur Pierre GLAUDES
Directeur de la Section des Unités de recherche
Agence d'évaluation de la recherche et de
l'enseignement supérieur (AERES)
20 rue Vivienne
75002 PARIS

Alain BERETZ
Président

Strasbourg, le 11 mai 2012

Objet : Rapport d'évaluation du projet d'UMR « Laboratoire de neurosciences cognitives et adaptatives » (réf. S2PUR130004539-RT)
Réf. : AB/EW/N° 2012-237

Affaire suivie par
Eric WESTHOF
Vice-président Recherche
et formation doctorale
Tél : +33 (0)3 68 85 15 80
eric.westhof@unistra.fr

Direction de la recherche

Cher collègue,

Je vous remercie pour l'évaluation du projet d'unité mixte de recherche « Laboratoire de neurosciences cognitives et adaptatives » (LNCA) porté par Monsieur Jean-Christophe Cassel.

Vous trouverez ci-joint les réponses du porteur de projet concernant les erreurs factuelles et les remarques et appréciations du comité d'experts.

Je confirme le soutien de l'Université de Strasbourg à ce projet d'unité qui succèdera à l'actuelle UMR 7237 Laboratoire d'imagerie et de neurosciences cognitives (LINC) actuellement dirigéé par Monsieur Christian Kelche.

Le comité d'experts mentionne à plusieurs reprises les charges d'enseignement pesant sur les membres de l'unité de recherche. En matière répartion des charges des enseignants entre enseignement et recherche, l'Université a mis en place plusieurs actions. Une mesure d'attractivité est ciblée sur les nouveaux maîtres de conférences : une décharge de service d'enseignement de six mois leur est accordée afin de faciliter leur insertion dans les unités de recherche. Cette décharge peut être utilisée dans les cinq années suivant leur recrutement. En outre, l'Université a mis en place un référentiel des activités des enseignants-chercheurs ciblant un certain nombre de responsabilités dans le domaine de la recherche qui permet une modulation des services. De plus, en phase avec le CNRS et l'INSERM, nous encourageons les demandes de délégation qui permettent de dégager des moyens en heures supplémentaires pour permettre des décharges d'enseignement. Des efforts importants sont faits également pour encourager aussi bien les présentations à l'IUF et aux CRCT.

La question des futures vacances d'emplois de personnels ingénieurs et techniciens (BIATS) a été abordé dans le rapport. Ces emplois feront l'objet, comme tous les emplois, d'un arbitrage au niveau de l'Université. Le dialogue de gestion instauré

4 rue Blaise Pascal
CS 90032
F-67081 STRASBOURG cedex
Tél. : +33 (0)3 68 85 15 80
Fax : +33 (0)3 68 85 12 62
www.unistra.fr

avec les composantes et les unités de recherche permettra de dégager les priorités en terme de maintien d'emplois.

Je vous prie d'agréer, Cher Collègue, l'expression de mes sentiments distingués.

Alain BERETZ

P.J. :

- **Une première partie corrigeant les erreurs factuelles**
- **Une seconde partie comprenant les observations de portée générale**

Laboratoire
d'imagerie et
de neurosciences
cognitives
UMR 7237

IFR 37 en neurosciences

Christian KELCHE
Directeur

LNCA
Laboratoire de Neurosciences Cognitives et Adaptatives

Observations générales en réponse au rapport de l'AERES à propos du projet d'unité

Les membres de l'unité se joignent à moi pour remercier le comité de l'AERES pour le temps qu'il nous a accordé, le rapport qu'il a établi ainsi que les recommandations qu'il y a formulées. En particulier, nous avons apprécié l'urgence que le comité d'évaluation souligna à recruter des personnels techniques et chercheurs pour compenser les nombreux départs à la retraite qui doivent intervenir dans un futur proche. Ces recrutements doivent garantir une bonne vitesse de croisière au projet que nous voulons développer. Au nom de l'ensemble du groupe, je souhaite également faire un certain nombre d'observations sur quelques points du rapport évoqués à propos de l'unité dans son ensemble ou des équipes en particulier et de leur projet.

1) Evaluation de l'unité.

Parmi les forces mises en exergue, le rapport souligne une adhésion enthousiaste et sans faille au projet de la part de tous les acteurs de l'unité, un bon (à quelque endroit très bon) niveau de publication laissant toutefois une marge de progression à exploiter impérativement, des recrutements récents d'excellente qualité qui doivent en appeler d'autres, notamment sur le plan de l'assistance technique, et un optimisme de la part du comité d'évaluation par rapport au succès du projet (sous condition toutefois d'un soutien par le CNRS et l'Université de Strasbourg). L'ensemble de l'unité en prend acte et se réjouit que ces éléments aient été perceptibles dans la présentation écrite comme orale du projet. L'Unité relève également que le comité de l'AERES a souligné le très bon travail de management de l'actuel directeur de l'UMR, un point de vue auquel tous les membres de l'UMR 7237 et les acteurs impliqués dans le futur projet souscrivent sans réserve.

Faculté de psychologie
12 rue Goethe
F-67000 Strasbourg
Tél. : (33) 03 68 85 19 06
Fax : (33) 03 68 85 19 58
http://neurochem.u-strasbg.fr
fre3289@linc.u-strasbg.fr

Plusieurs faiblesses sont identifiées, et notamment celle d'une visibilité à améliorer. Conformément aux recommandations, l'amélioration de cette visibilité passera par une définition plus fine des axes prioritaires de recherche de certaines équipes au regard de la compétition internationale, une incitation plus affirmée à la recherche de financements, notamment dans le cadre de programmes internationaux, des liens renforcés entre les équipes autour de thèmes fédérateurs, au minimum connexes, mais aussi de compétences complémentaires, et une politique plus incitative en matière aussi bien de participation à des événements internationaux que de publications dans des journaux à fort facteur d'impact, et tout cela dans le contexte économique que chacun connaît. Il est à noter qu'en ce qui concerne certains thèmes de recherche, la compétition internationale par rapport à des unités plus solides et mieux dotées n'a pas empêché le groupe de publier une partie de ses travaux dans des journaux de spécialité éventuellement acceptables (par ex., Biological Psychiatry, Journal of Neuroscience, Cortex, Neuropsychopharmacology, Neurobiology of Aging, Hippocampus).

Une autre faiblesse évoquée dans le rapport, et cela à plusieurs endroits, concerne le nombre important d'enseignants-chercheurs impliqués dans le projet (11 des 20 chercheurs et enseignants-chercheurs permanents sont des enseignants-chercheurs). Du fait de leur charge d'enseignement ou/et des tâches administratives qu'ils assument, ceux-ci ne peuvent pas s'engager dans la recherche au niveau de leurs ambitions, et donc de celles des attentes de l'institution. Bien que tous les enseignants-chercheurs soient considérés comme des personnels qui publient, et ce sans exception, le comité propose que tous les efforts possibles soient faits pour leur dégager davantage de temps de recherche. Malheureusement, au-delà de l'indiscutable légitimité d'une telle recommandation, une telle perspective apparaît, irréaliste, la charge de 192 h ETD/an étant une obligation statutaire. Nous prenons acte du fait qu'il existe une possibilité pour les enseignants-chercheurs de demander une délégation dans un EPST. Cette possibilité est fréquemment présentée comme LA solution. Mais d'une part le nombre de ces délégations reste faible, d'autre part elles sont limitées dans le temps. A cela se rajoute un problème conjoncturel que l'Institution occulte presque systématiquement : le volume des enseignements dont une délégation soulage transitoirement certain(s) enseignant(s)-chercheur(s) forme un numérateur constant pour un dénominateur diminué du nombre de délégataires ! Autrement dit, la décharge transitoire de l'un conduit souvent à une charge transitoirement plus lourde pour tous les autres. En conséquence, si le bénéfice de ce type de mesure est évident au plan individuel, le bilan en temps de recherche dégagé pour une unité est quasi nul.

Une troisième "faiblesse" porte sur le nombre important de prochains départs à la retraite, notamment parmi les personnels techniques (mais pas uniquement, puisque deux chercheurs, un DR1 et un CR1, sont également concernés). Le terme de "faiblesse" (au sens où il pourrait renvoyer à une insuffisance) nous semble inapproprié. En effet, ces départs à la retraite sont inévitables et représentent un handicap ou un problème pour lequel existent des solutions. Le comité invite explicitement le directeur à se rapprocher des tutelles pour aborder la question d'une optimisation rapide des remplacements à des fins de recrutements appropriés. Il ne manquera pas de le faire. En ce qui concerne le départ des chercheurs, comme le souligne le rapport, des discussions sont en cours depuis plus d'un an pour l'intégration d'un chercheur et d'un enseignant-chercheur (maître de conférences) en poste dans une autre ville/université/unité. Ces discussions peuvent à présent se poursuivre en direction d'une arrivée espérée prochaine, peut-être dès 2013, de ces renforts. Ce mouvement de personnels nécessitera, lui aussi, un appui substantiel des tutelles puisqu'il faudra optimiser les conditions de la mutation d'un enseignant-chercheur, donc, à terme, envisager la création d'un poste de maître de conférences.

Le futur directeur regrette que le manque de visibilité soulevé par le comité de l'AERES à propos des acteurs du projet n'ait pas fait l'objet d'une analyse plus fouillée au regard des nombreuses réorganisations intervenues entre 2005 et 2011, et dont les dernières en date (entre 2008 et 2011) sont davantage imputables à des approximations et hésitations des tutelles dans un cadre politique tâtonnant qu'à des facteurs relevant de l'inadéquation ou de l'insuffisance scientifique des acteurs des projets d'unités ou d'équipes antérieures, voire de l'actuelle UMR.

2) Analyse des Equipes

A partir d'ici, le futur directeur se fait le porte-parole de chaque responsable(s) d'équipe.

2.1. Equipe 1

Pour ne pas en rester aux points forts évoqués dans le rapport – à savoir que le projet d'équipe, qui est porté par un groupe cohésif, apparaît cohérent, relativement focalisé bien que fourni, réaliste, et s'appuie sur une très bonne [*"very good"*] recherche au regard des références internationales –, l'équipe a la ferme volonté d'appliquer toutes les recommandations faites par le comité de l'AERES. Cette application visera avant tout à atteindre une différenciation marquée des champs de compétences et d'intérêts par rapport à la concurrence nationale et internationale. Par conséquent, la priorité de l'équipe ne

sera pas de développer de nouvelles techniques complexes (comme l'optogénétique ; au passage, il n'en était pas question !) ou de s'engager dans les sentiers d'une *"me too research"* (!), contrairement à ce qui semble avoir été compris par le comité de l'AERES. Pour cette équipe, il s'agira au contraire d'édifier des objectifs essentiels de recherche sur ses points novateurs les plus récents, dont, par exemple, la mise en évidence d'une implication du diencéphale dans la persistance à long terme d'une trace mnésique (par ex., J. Neurosci. 29, 2009, p3302 ; un manuscrit actuellement en révision pour le même journal) et celle d'une construction de plusieurs types de mémoires dépendant d'événements transcriptionnels impliquant l'acétylation des histones H2B et H4 dans l'hippocampe (par ex., Neuropsychopharmacology 35, 2010, p 2521). Le réseau international dans lequel l'équipe est invitée à s'engager pour éviter que le confort fourni par sa cohésion n'en endorme la dynamique de pensée sera seulement développé davantage, donc renforcé, car ce réseau existe déjà, ainsi que le mentionnait le dossier fourni au comité. Au sujet dudit risque d'uniformisation de pensée entre collègues proches, il est encore à rajouter que deux chercheurs "issus d'autres berceaux" ont très récemment rejoint cette équipe (AL Boutillier, DR2 CNRS, en 2011 par voie de mutation, et L Lecourtier, CR1 CNRS, en 2010 par voie de recrutement), et non un seul comme l'indique le rapport du comité. Les craintes du comité ne semblent donc que partiellement fondées. Enfin, pour terminer sur ce sujet et clore cette série d'observations, cette équipe aurait apprécié que le comité se demandât au moment de la rédaction du rapport comment des enseignants-chercheurs et chercheurs qui s'engagent dans leur travail à raison de 50 à 65 heures hebdomadaires allaient décrypter ce type de réflexion au sujet du risque qu'une synergie de pensée devienne négative par excès de proximité entre collègues. Ce n'est pas très grave en soi, mais comme les écrits ont la meilleure endurance temporelle…

2.2. Equipe 2

Les recommandations faites comme les critiques formulées par le comité de l'AERES ont été notées et intégrées. L'équipe souhaite cependant apporter des précisions en ce qui concerne certaines d'entre elles.

1. L'intégration de chercheurs travaillant dans des domaines différents: TOUS les membres seniors de l'équipe ont contribué de façon significative aux travaux sur l'enrichissement et le vieillissement (CK, MM et AB : 1er et derniers auteurs sur + de 30 ans de publications) et sur les modèles Alzheimer (CM avec + de 15 ans sur Alzheimer, CH avec la pathologie tau, RG avec le découplage thêta-gamma chez les souris CRND8). Ces deux groupes de chercheurs ont peu publié ensemble, car chacun a développé une expertise très poussée sur

deux aspects complémentaires du vieillissement et sur deux espèces différentes. C'est précisément pour cette raison qu'ils forment aujourd'hui une seule équipe. Des interactions entre leurs domaines respectifs seront faciles à mettre en place dans de nouveaux projets, notamment grâce aux deux jeunes chercheurs (RG et CH) qui maîtrisent de nouvelles approches (électrophysiologie et biologie moléculaire) sur les deux espèces. Ils sont déjà impliqués dans des travaux recouvrant les deux domaines et espèces. Lorsque des modèles satisfaisants de rats transgéniques Alzheimer seront disponibles et que le modèle de la souris âgée sera développée (projet Interreg IV Rhin Supérieur), cet apparent décalage entre sous-groupes de chercheurs disparaîtra. Les interactions mises en place sur des projets fédérateurs en cours et sur ceux en préparation déboucheront nécessairement sur des publications communes.

2. Le réseau de collaborateurs internationaux: les collaborations internationales de CM avec l'industrie ne sont pas uniquement orientées sur du contrat de service, mais également sur une base scientifique dans deux projets en cours (C Zerbinatti, Merck, USA "réorganisation synaptique et apoE"; A. Marti et C Dorner-Ciossek, Boehringer Ingelheim, Allemagne " inhibiteurs de PDE9 et cognition chez les tg2576"). De plus, notre projet de réseau européen trinational soumis à Interreg IV est en phase finale d'évaluation après avoir été classé dans le top 7 des sélectionnés (sur plus de 50). Par ailleurs, RG and CH ont d'excellents contacts (établis en postdoc) qui sont intégrés dans des projets en cours (S Williams, McGill, Canada " thêta-gamma et souris CRND8 ") et en préparation (JP Brion, Université de Bruxelles, Belgique, "interactions pathologies tau et amyloïde "). Néanmoins, il est vrai que l'établissement de nouvelles collaborations internationales permettrait d'augmenter la visibilité internationale de l'équipe. Celle-ci sera également stimulée par la participation à des congrès internationaux, à des comités de rédaction et à l'organisation de symposium.

3. Lourdes charges d'enseignement des trois enseignants-chercheurs: Le rapport propose de diminuer cette charge et de recruter de nouveaux membres pour compenser le manque de productivité attenant à ces charges. Il est à noter que deux membres (CH and MM) bénéficient déjà d'une demi-charge d'enseignement sur un an et que un tiers de l'équipe vient tout juste d'être recruté. Malgré cela, nous tenterons encore d'augmenter nos capacités par le biais des demi-charges (AB dans un an) et en favorisant de nouveaux recrutements.

4. Continuité des relations contractuelles difficiles à évaluer: Pourtant, ce type de financement est plus facile à renouveler (grâce à la qualité du travail fourni) que d'obtenir des subsides publics et associatifs. Deux nouveaux contrats ont été signés ces dernières semaines. Par ailleurs, nous avons aussi obtenu des subsides publics

et associatifs ces derniers mois (RG: Fyssen, CIG Marie Curie ; CH : Alsace Alzheimer 68). De plus, nous avons soumis plusieurs projets dont 2 ANR (RG PI, CM responsable local), 1 au LECMA (CM PI), 1 à France Alzheimer (CM PI, lettre d'intention retenue), 1 au programme Interreg IV (CM responsable local, sélectionné 7/50) et d'autres demandes sont en préparation (Neurex, FRM, ANR). Le succès déjà rencontré et nos efforts soutenus dans ce sens devraient porter ses fruits même dans un milieu aussi compétitif que celui du vieillissement.

5. Certaines approches ne sont pas particulièrement nouvelles (sauf réserve cognitive chez les rongeurs et hippocampe isolé): D'autres approches, bien que très originales, ne semblent pas avoir été considérées. Tout d'abord, et non des moindres, l'étude du couplage des ondes thêta-gamma au cours du déclin cognitif chez la souris Alzheimer et le rat âgé (en cours), puis chez l'Homme (en projet). C'est une nouvelle approche, à la fois conceptuelle et technique, qui parait très prometteuse pour la mise au point d'un biomarqueur du déclin cognitif. L'organisation du projet et des collaborations (équipe 4 et F Blanc, neurologue aux Hôpitaux de Strasbourg) est plus longue à mettre en place chez l'Homme, mais cela fera l'objet d'une demande d'ANR l'année prochaine. La relation entre apoE/réorganisation synaptique ET performances mnésiques n'a jamais été abordée à ce jour. Ce projet intègre désormais une approche translationnelle avec une étude parallèle lancée sur des cerveaux de patients Alzheimer grâce à un accord obtenu auprès du GIE Neuroceb en collaboration avec F Blanc.

2.3. Equipe 3

Nous apprécions que le comité ait reconnu le rôle pionnier qu'a joué cette équipe dans le domaine des régulations épigénétiques en rapport avec le mode d'action des drogues. Nous sommes aussi très satisfaits de l'analyse faite concernant l'organisation, le travail et la thématique de l'équipe. Certains points mineurs demandent néanmoins des éclaircissements.

Nous avions mentionné dans le rapport écrit, et cela a été repris lors de la présentation du porteur de projet, que le nombre de personnes partant à la retraite durant le prochain quinquennat était de 2 chercheurs.

A propos des deux chercheurs non-publiants : s'il faut comprendre que l'un d'eux est JB Dietrich (dont le départ à la retraite est prévu pour octobre 2013), l'information n'est pas exacte. D'après les critères de l'AERES, « *un chercheur en sciences du vivant devra publier quatre fois durant le quadriennal* ». C'est bien le cas de ce chercheur (cf. la copie *PubMed* ci-dessous). Cette statistique du rapport est d'autant plus surprenante que le tableau récapitulatif de la page 4 ne fait état que d'un seul non-publiant parmi les chercheurs.

1. Cocaine induces the expression of MEF2C transcription factor in rat striatum through activation of SIK1 and phosphorylation of the histone deacetylase HDAC5. **Dietrich JB**, Takemori H, Grosch-Dirrig S, Bertorello A, Zwiller J. Synapse. 2012, 66:61-70. Epub 2011 Nov 3.
2. Cocaine self-administration alters the expression of chromatin-remodelling proteins; modulation by histone deacetylase inhibition. Host L, **Dietrich JB**, Carouge D, Aunis D, Zwiller J. J Psychopharmacol. 2011, 25:222-9.
3. Alteration of blood-brain barrier function by methamphetamine and cocaine. **Dietrich JB**. Cell Tissue Res. 2009, 336:385-92.
4. Cocaine induces the expression of homer 1b/c, homer 3a/b, and hsp 27 proteins in rat cerebellum. **Dietrich JB**, Arpin-Bott MP, Kao D, Dirrig-Grosch S, Aunis D, Zwiller J. Synapse. 2007, 61:587-94.

Le deuxième non-publiant, P. Anglard, est auteur des publications suivantes :

1. Histone deacetylase inhibitors upregulate MMP11 gene expression through Sp1/Smad complexes in human colon adenocarcinoma cells. Barrasa JI, Olmo N, Santiago-Gómez A, Lecona E, **Anglard P**, Turnay J, Lizarbe MA. Biochim Biophys Acta. 2012, 1823:570-81. Epub 2011 Dec 29.
2. CDKL5 is a brain MeCP2 target gene regulated by DNA methylation. Carouge D, Host L, Aunis D, Zwiller J, **Anglard P**. Neurobiol Dis. 2010, 38:414-24.
3. Inhibition of histone deacetylases in rats self-administering cocaine regulates lissencephaly gene-1 and reelin gene expression, as revealed by microarray technique. Host L, **Anglard P**, Romieu P, Thibault C, Dembele D, Aunis D, Zwiller J. J Neurochem. 2010, 113:236-47.

Enfin, nous sommes tout à fait conscients de la difficulté, principalement d'ordre technique, à réaliser des expériences d'auto-administration intraveineuse de cocaïne chez la souris. Compte-tenu du fait que cette approche permettrait de tester le comportement de souris transgéniques, donc d'obtenir sans nul doute des résultats extrêmement significatifs dans notre domaine de recherche, ces expériences seront tentées malgré tout. A noter qu'une recherche croisant *"cocaine self-administration"* et *"mouse"* dans PubMed ne recense pas moins de 108 travaux originaux. Cette technique est donc maîtrisée par un nombre substantiel de chercheurs dans le monde.

2.4. Equipe 4

Trois principales critiques et recommandations ressortent du rapport du comité de l'AERES :

1. Le projet semble trop ambitieux eu égard au temps pouvant être consacré à la recherche par ses membres (5 enseignants-chercheurs) en raison de leur lourde charge d'enseignement.

Nous prenons acte de ce constat. Toutefois, il nous semble important de souligner que malgré le faible pourcentage de temps que les membres de l'équipe peuvent consacrer à la recherche, la productivité scientifique de l'équipe n'en est pas moins respectable puisque, pour la seule année 2011, l'équipe compte près de 10 publications dans des journaux internationaux ayant un facteur d'impact supérieur à 5. Cela correspond à une moyenne annuelle de 2 publications par enseignant-chercheur.

2. Les thématiques scientifiques de l'équipe sont trop nombreuses et, bien qu'un resserrement ait été initié autour de la thématique du vieillissement normal et pathologique, la réduction du nombre de thèmes est fortement conseillée.

Nous sommes d'accord avec cette observation et nous allons travailler à un rapprochement/resserrement des thématiques scientifiques de l'équipe. Cependant, cela devra se faire progressivement par le biais de collaborations intra-équipe pour ne pas ralentir la productivité scientifique d'un ou plusieurs chercheurs.

3. Un temps trop important est consacré à la recherche appliquée.

Comme ce point était encore en discussion au moment de la rédaction du projet, il ne ressortait pas clairement de la lecture de ce dernier que la recherche appliquée est très étroitement liée à l'exploitation de la plate-forme de physiologie et d'électrophysiologie humaine, qui génère de nombreux contrats avec des partenaires industriels et se doit de respecter un principe d'autonomie fonctionnelle. Ces contrats sont gérés par le responsable de l'équipe, les autres membres ne participant pas à ces projets. Afin d'identifier clairement ce qui relève de l'activité de la plate-forme d'une part et des recherches menées par l'équipe d'autre part, il a été décidé avec les tutelles (CNRS & Université de Strasbourg) de créer une Unité Mixte de Service. Cette UMS sera dirigée par le responsable de l'Equipe 4. Les projets de recherche industriels seront réalisés par du personnel contractuel, alors que l'Equipe 4 du LNCA sera simplement utilisatrice de la plate-forme. Cette organisation permettra d'identifier clairement les ressources humaines et financières qui seront allouées à la recherche fondamentale de l'Equipe 4.

Conclusion

Dans son ensemble, ce rapport nous encourage dans notre dessein de créer une structure de recherche qui nous permette de mobiliser nos forces et nos efforts, notamment de créativité, pour les mettre au service de notre projet scientifique. Nous espérons vivement que nos tutelles partageront notre optimisme et nous permettront, par des moyens humains et financiers, de nous engager dans une expédition quinquennale en marche vers l'excellence.

Strasbourg, le 23 avril 2012

Jean-Christophe Cassel