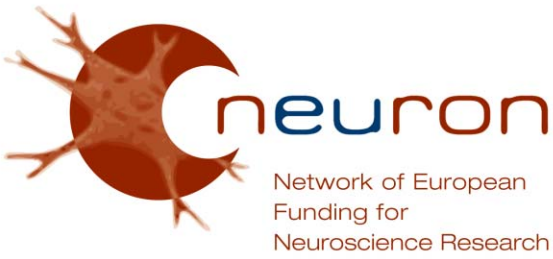

Report on the assessment of the funded projects from the JTC2013

'Mental Disorders'

by Anabela Isidro

August 2019

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Introduction

Brain-related diseases and disorders of the nervous system impose a heavy burden on society. In Europe alone more than 38% of the population is affected,[1] suffering from a considerable loss of quality of life. Moreover, according to the European Brain Council, the annual cost of brain disorders is close to 800 billion €[2]. Apart from the suffering of the individual patients, these numbers highlight the impact on economies and health care systems. In many cases the underlying disease mechanisms are still not well understood and no curative treatments are available.

To face this challenge most European countries invest considerable resources into research, leading to major advancements in science. Nevertheless, many important questions remain unanswered and major societal challenges need to be solved. Such societal challenges cannot be confronted on a national level alone. To pool resources effectively in a concerted effort to address these issues NEURON (Network of European Funding for Neuroscience Research; www.neuron-eranet.eu) was initiated and funded in 2003 by the European Commission (EC) as a pilot Specific Support Action. It was later developed into an ERA-NET with three phases: NEURON I (2007 – 2011), NEURON II (2012 – 2015) and NEURON Cofund (2016-2020), continuously funded by the EC. To date, NEURON is the result of the coordinated efforts from 27 funding organisations from 19 countries engaging in a joint effort to promote excellent research in disease-oriented neuroscience.

The overarching aim of NEURON is to support the translation of results from fundamental research into improved prevention, diagnosis, therapy and rehabilitation for the patients, their family, and carers. Therefore NEURON main activity is the coordinated transnational funding of basic, clinical, and translational research projects dedicated to the nervous system (Joint Transnational Calls - JTC). To date 14 JTCs were launched which aimed at supporting transnational research projects in neurosciences related disorders.

The report herein presented assesses the recently finished JTC2013 granted projects and is part of the work carried out in task 6.3: Monitoring of JTCs, of the work programme of ERA-NET NEURON Cofund (hereinafter abbreviated to NEURON for simplicity).

The ex-post analysis of the NEURON funded projects is considered as most relevant for the following reasons:

- The projects are funded through public funding, and thus a maximal surveillance on the outcome of the use of resources should apply.
- Assessing the impact of the NEURON research projects is important to define new priorities and adjust strategies for future calls.
- The communication on research progress for any specific neuroscience related topic is crucial for all stakeholders, patients, and health professionals.
- Promotion of NEURON achievements is primary for increase of interest within the international scientific community.
- Promotion of NEURON achievements is essential to raise awareness and inform policy makers on the developments of this initiative.

Joint Transnational Call for Research Proposals 2013

Mental disorders are a major cause for morbidity, mortality and impaired quality of life in Europe. According to the World Health Organisation one in four people in the world will be affected by mental or neurological disorders at some point in their lives. Around 450 million people currently suffer from such conditions, placing mental disorders among the leading causes of ill-health and disability worldwide. The funding of research focussing in mental

[1] Wittchen HU,, Jacobi F et al. (2011): The size and burden of mental disorders and other disorders of the brain in Europe 2010. Eur Neuropsychopharmacol, 21(9): 655-679

[2] Olesen J, Gustavsson A, Svensson M, Wittchen HU, Jönsson B; CDBE20 10 study group; European Brain Council (2012): The economic cost of brain disorders in Europe. Eur J Neurol, 19(1):155-62

disorders is therefore of utmost importance and will help improving diagnosis, therapy, and rehabilitation procedures. Such an enormous challenge calls for joint efforts worldwide. Having this into consideration 17 funding organisations from 16 countries (table 1), partners in NEURON, aligned their efforts to launch a Joint Transnational Call for research proposals on the topic of mental disorders with a total of 10.39 M€ of committed funds. The call applied a virtual common pot model in the distribution of available funds in which each country funds its national teams, participating in a winning transnational consortium. It was a two-stage process with a pre-proposal and proposal phase.

Country	Funding Organisation (acronym)
Austria	Austrian Science Fund (FWF)
Belgium	Research Foundation – Flanders (FWO)
Canada	Canadian Institutes of Health Research (CIHR)
Canada	Fonds de recherche du Québec-Santé (FRQS)
Finland	Academy of Finland (AKA)
France	French National Research Agency (ANR)
Germany	Federal Ministry of Education and Research (BMBF)
Iceland	The Icelandic Centre for Research (RANNIS)
Israel	Chief Scientist Office, Ministry of Health (CSO-MOH)
Italy	Ministry of Health (MOH)
Latvia	Latvian Academy of Sciences (LAS)
Luxembourg	National Research Fund (FNR)
Poland	National Centre for Research and Development (NCBiR)
Portugal	Foundation for Science and Technology (FCT)
Romania	Executive Agency for Higher Education, Research, Development & Innovation Funding (UEFISCDI)
Slovakia	Slovak Academy of Sciences (SAS)
Sweden	Swedish Research Council (SRC)

Table 1: Funding organisations participating in JTC2013

The aim of JTC 2013 was to enable multinational and multidisciplinary, collaborative research projects that addressed important questions related to **Mental Disorders**. Proposals could range from understanding basic mechanisms of disease through proof-of-concept clinical studies in humans, including research on affective disorders, stress-related and anxiety disorders, schizophrenia and delusional disorders, substance use disorders, and other mental disorders. Research on dementia was not accepted in JTC2013. Researchers were encouraged to submit translational research proposals that combined basic and clinical approaches, and to include young researchers as independent PIs. Clinical studies were eligible up to the point of proof of concept.

Research proposals had to cover at least one of the following areas:

a) Fundamental research on the pathogenesis and/or aetiology of mental disorders. This could include the development of innovative or shared resources and technologies. The relevance of the research to disease needed to be clearly indicated;
b) Research to develop new strategies for (early) diagnosis, therapy, and rehabilitation procedures for mental disorders.

The JTC2013 mobilised 369 principal investigators around Europe and Canada organised in 91 consortia of researchers submitting pre-proposals. After evaluation by 58 international mental health experts, 39 of these were invited to submit full-proposals, and 12 (implicating 46 principal investigators) of the latter selected for funding (Table 2). The success rate was 13%, when considering the pre-proposals submitted. The selected proposals covered a variety of mental disorders being the most common anxiety related and mood disorders as detailed in Table 2. Each proposal was evaluated by at least 2 but most proposals by 3 different reviewers. The full proposals and their reviews were further discussed in a peer review panel meeting.

Acronym	Proposal title	Coordinator in Bold and Partens	Country	Pathology
AnxBio	Novel molecular pathways and biomarkers of anxiety disorders	**I. Hovatta**	**Finland**	Anxiety Disorders
		C. Turck	Germany	
		A. Erhardt	Germany	
		A. Chen	Israel	
BrainCYP	Role of genetic polymorphisms in drug metabolizing cytochrome P450 enzymes expressed in the brain for affective disorders	**J. Stingl**	**Germany**	Affective Disorders
		R. Viviani	Germany	
		M. Ingelman-Sundberg	Sweden	
		R. Tyndale (CA)	Canada	
CBGC	Discovering genetic risk factors for neuropsychiatric disorders and their consequences using dogs, humans and mice	**H. Lohi**	**Finland**	Anxiety Disorders
		P. Arnold	Canada	
		R. Costa	Portugal	
COCACE	VGLUT3 and vulnerability to addiction	**S. El Mestikawy**	**Canada**	Substance use disorders
		F. Bellivier	France	
		S. Jamain	France	
		C. Rosenmund	Germany	
		A. Mackenzie	Sweden	
COCADDICT	Cocaine addiction: a translational study to identify and characterize dysfunctional neural networks	**V. Deroche-Gamonet**	**France**	Substance use Disorders
		R. Spanagel	Germany	
		M. Leyton	Canada	
		C. Herry	France	
HYPZITRP	HYPerforin analogues, ZInc and TRPC6 channels – a new antidepressant concept?	**K. Leuner**	**Germany**	Affective Disorders
		A. Bouron	France	
		G. Nowak	Poland	
IMFLAME-D	Role of inflammation and related processes in the development, phenomenology and treatment of depression	**M. Schaefer**	**Germany**	Affective Disorders
		L. Capuron	France	
		A. Cattaneo	Italy	
		A. Friebe	Germany	
		M. Leboyer	France	
MecTranGen	Biological Mechanisms of Transgenerational Transmission of Early Life Stress	**C. Buss**	**Germany**	Stress-related disorders
		E. Binder	Germany	
		K. Räikkönen	Finland	
		M. Meaney	Canada	
		P. Wadhwa	USA	
mTOR-DIDS	Molecular Mechanisms of Brain Function in mTOR-Deficient Intellectual Disability Syndromes	**V. Kalscheuer**	**Germany**	Various
		V. Broccoli	Italy	
		S. Schweiger	Germany	
		R. Schneider	Austria	
RD_aDBS	Development of feedback-controlled neuromodulation strategies for the treatment of intractable repetitive hyperkinetic movement disorders	**C. Winter**	**Germany**	Anxiety Disorders
		K. Meletis	Sweden	
		A. Priori	Italy	
TAO2	The role of TAO2 in brain connectivity and Autism Spectrum Disorders	**F. Calderon de Anda**	**Germany**	Autism
		C. Bagni	Belgium	
		K. Singh	Canada	
		S. Scherer	Canada	
TYMON	Uncertainty monitoring vs. inhibition of action in obsessive-compulsive disorder: role of the subthalamic nucleus and effects of stimulation in humans and rodents	**L. Mallet**	**France**	Anxiety Disorders
		L. Wojtecki	Germany	
		R. Costa	Portugal	

Table 2: JTC2013 funded consortia

All the selected projects in JTC2013 started between February and August 2014 for a period of three years. The date set by the Joint Call Secretariat to collect the final reports was three months after completion of the projects. Nevertheless, considerable delays were observed either due to extension of the project's duration by the researchers or due to the lack of response from some coordinators. In consequence, the whole monitoring and assessment process was delayed. The collection of final reports from JTC2013 was spread over more than one year as the consortia did not have the same ending dates or did not reply to the several contacts from the secretariat. Despite these hurdles it was possible to collect all final reports.

More than half of the funded projects (7 in 12, table 2) carried out research focussed on two types of mental disorders: Anxiety and Affective related disorders; both very important themes for our society and its challenges.

A variety of methodological approaches were applied as for example: (epi)genetic approaches, "omics" approaches, imaging techniques, electrophysiological approaches, gene targeting in the brain, electrical and magnetic brain stimulation, behavioural methodologies, pharmacology, therapy, clinical trials, and many others.

Analysis of JTC2013

In 2013, NEURON developed a series of key performance indicators to evaluate different aspects of the impact of the finalised projects. The list of key indicators resulting from this exercise is depicted in Table 3 and were declined in a list of questions sent to the coordinators of funded consortia together with the final report template (see Annex A). With the intention of being able to homogeneously evaluate the impact of the projects a similar analysis is done for each call since 2008. These analyses provide support for short- and long-term strategic planning for NEURON's funding activities. The number of the respective question in the questionnaire is given in brackets.

Objective of the Funding Programme	Key performance indicators	Measures (i.e. items in the questionnaire)
1. Enhance excellent cooperation between scientists working in the field of neuroscience	Communication of funded research results	List of publications and communications - level of co publication, bibliometric indicators. (**Question 1.2**)
	NEURON JTC as starter of new collaboration	Have the partners participating in the NEURON project collaborated before applying for the NEURON JTC2012? (**Question 3.1**)
	New research groups from other countries joining the consortium	During the life time of the project has the consortium established collaboration(s) with other teams (not already participating in the JTC 2012 project)? (**Question 3.2**)
	Sustainability of the collaboration (obtaining further funding for the same consortium)	Have the results led to new initiatives in other types of funding programmes? (**Question 3.3**)
	Intensity of collaboration, young researchers participation (mobility)	List of meetings, young researchers involved in the project, lab visits/exchange of researchers, and training within the consortium (**Question 3.4**)
2. Promote multi-disciplinary consortia and to encourage translational research proposals (from bench to bedside)	Composition of the consortium	List of research groups
	Involvement of patients	Analysis of full proposals and final reports
	List of patents and other outcomes with impact to health	Patents and other outcomes with impact to health (**Question 2**)
3. Support development of innovative or shared resources and technologies	Evaluation of the development and the use of new resources	Has the consortium created a new or further developed an existing transnational patient registry, database or biobank? Have the consortium partners exchanged biomaterials (DNA, tissues, cells, animals)? (**Questions 4**)
4. Support research to develop new strategies for diagnosis, therapy, and rehabilitation procedures	Evaluation of the development of new strategies for diagnosis, therapy, and rehabilitation procedures for cerebrovascular diseases.	Have the results of the NEURON research projects allowed the development of new strategies for: diagnosis, therapy (preparation of clinical trials), and rehabilitation procedures for cerebrovascular diseases, prevention or anything else? (**Question 5.1**)
	Major achievements	Please list the major achievement of the consortium. (**Question 5.2**)

Table 3: Key performance indicators in relation to the objectives of the funding programme.

In the following section, the present analysis shows the outcomes of the funded projects in relation to NEURON objectives. In addition to the indicators used for this analysis, NEURON constantly monitors the progress of the funded research projects through annual and final reports summarising the most important scientific results and consortium achievements. On the other hand coordinators of the funded projects are invited to present interim results at a mid-term symposium, subjected to evaluation. This continuous interaction between the consortia coordinators and the call secretariat was established from the beginning ensuring the appropriate development and completion of the planned work.

Projects outcomes in the context of NEURON objectives

Objective 1: Enhance Excellent Cooperation between Scientists Working in Neuroscience

One of the main goals of NEURON is to boost scientific cooperation beyond countries. This section evaluates the outcomes related to the communication of project results in joint scientific publications, the consortium composition in terms of history and sustainability of collaboration, the interactions with other research teams, the participation of young researchers and their mobility between partner laboratories.

Indicator: Communication of funded research results

This indicator was measured in the impact questionnaire (Q1.2).

The project results were communicated in scientific journals, thesis dissertations, books, scientific meetings and other supports. Table 4 presents a summary of the total number of such communications. It is important to notice that the time lag between the production of data and their publication can dramatically impact the productivity of a research group, and introduce a bias in our analysis. Thus these numbers are most likely underestimated. Indeed, we had the indication from several consortia coordinators that many publications resulting from the work carried out in the framework of NEURON JTC2013 funded project were just submitted or were in preparation.

Type of publication	Total (No)	Consortia (No)
Peer Reviewed Articles	66	8
Books or Book Chapters	3	3
Reviews	24	5
Dissemination Articles	3	2
Communications in Scientific Meeting	151	10
Dissertations	13	6
Others	11	2
Total	**266**	NA

Table 4: Total publications JTC 2013

As depicted in table 4 most communication of the results was done through scientific meetings (n=151) followed by peer reviewed articles (n=66). The publication rate is quite variable amongst the consortia and ranges between 0 and 14 peer reviewed articles. These publications were mainly published by only one of the partners in the consortium (77% of the cases); nevertheless 23 % of the publications were authored by more than 1 partner belonging to a given consortium (Figure 1). The co-authored publications are considered a good indicator of effective collaboration.

Figure 1 – Mono and multi-partner published peer reviewed articles.

For a deeper analysis we used bibliometric data to evaluate the scientific productivity of the funded projects in this call, summarised in Figure 2. 15% of the published papers were in high ranked journals with an Impact Factor

(IF) above 10, 36.5 % of the papers in journals with IF between 5-10, and 48.5% of the papers in journals with IF below 5 (figure 2).

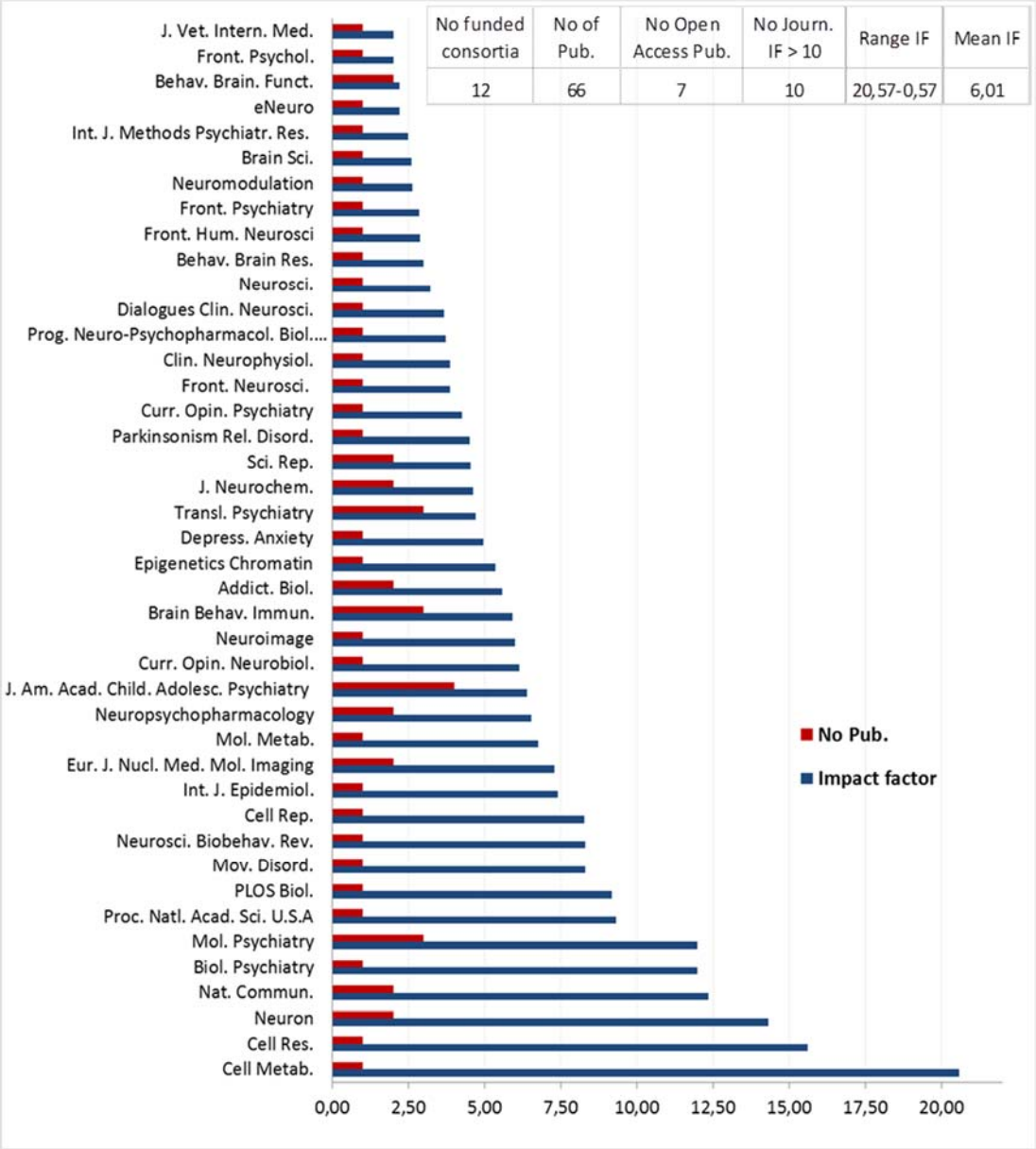

Figure 2 – Publication profile of JTC2013. Pub.-Publication. Journ.-Journal. IF-Impact Factor.

Noteworthy is the fact that the papers resulting from work under the umbrella of the funded project were in a variety of journals not always dedicated specifically to the Neurosciences field. Thus, demonstrating its interdisciplinary character, and the wider interest and impact.

Indicators: The NEURON JTC as a Starter of New Collaboration; New research groups from other countries joining the consortium; Sustainability of the collaboration

The indicators were measured in the impact questionnaire (Q3.1; Q3.2; Q3.3).

Triggering new transnational research collaborations is one of the goals of NEURON. In JTC2013, 25% of the consortia never had collaborated before, 58 % were formed by a mixture of old and new collaborators, and 17% were composed of only old collaborators (Figure 3; table). The most frequent number of partners collaborating before the JTC2013 funded project was n=2 (Figure 3; chart). When enquired about further applications to national or

transnational joint calls, 10 out of 12 responded positively, with 3 out of the 10 claiming to have applied jointly (part of the consortium) to other transnational calls launched under the umbrella of NEURON (n=2) or E-Rare-3 (n=1).

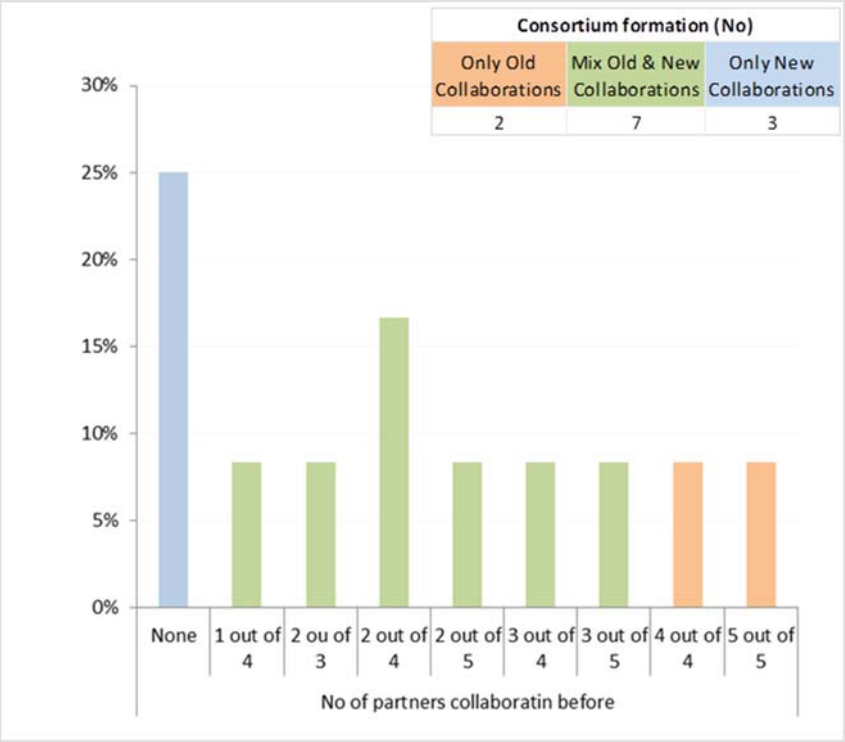

Figure 3 – Composition of the funded consortia. Percentage of consortia *versus* No of partners collaborating before (chart). Percentage of consortia with new and/or old collaborations (table).

Noteworthy are the 21 new collaborations 10 out of the 12 consortia claimed to have started in the framework of the JTC2013 funded projects (data not shown), confirming the high potential of this kind of projects to enhance collaboration and reduce the fragmentation in the European Research Area (ERA).

Indicators: Intensity of collaboration, young researchers' participation (mobility)

The indicators were measured in the impact questionnaire (Q3.4).

Networking and knowledge exchange are very important factors to improve the skills of individual researchers, to increase the impact of the research produced, and to strengthen the ERA. To gather data on these categories, we questioned the coordinators of funded projects about personal exchange and events' organisation (meetings/conferences/congresses). All consortia responded that they had meetings, ranging from 2 to 14 meetings per consortium, resulting in a total of 65 meetings for the 3 years of the funded projects (not accounting for eventual extensions of the projects). These results indicate a close collaboration between partners and in some cases even an intense collaboration as the case of COCACE project reporting 14 meetings in 3 years.

Regarding mobility there were also exchanges of personnel between laboratories, a total of 15 individuals, most of them PhD students. The mobility was mainly associated to the training in new techniques or methodologies. A non-exhaustive list of specific tasks developed during these exchanges is given below:

- Learning AGO2 immunoprecipitation methodology;

- Bioinformatics' analysis of proteomic experiments, followed by integrated multi-omics analysis of both human and mouse data sets;
- Exchange data;
- Development of genome-wide association studies in addiction;
- Learning synaptosome preparation from mouse brain tissue.

Training, education, and the support to young researchers are of utmost importance in mental disorders as the future of this area will be in the hands of the young generation of scientists. In JTC2013, NEURON continued playing an important role in training high level scientists and building bridges among them (Figure 4). Indeed, within JTC2013 a total of 79 individuals were trained. Most of them were PhD Students (n=24), followed by Post Docs (n=22) or PhDs (n=10), but also research assistants (n=3), Early Career Researcher (n=2), and others (Figure 4). Although the gender balance is not a main objective for NEURON it is a significant goal in the ERA, and therefore we have also analysed the proportion of females and males in the young fellows involved. The data shows that the gender was slightly unbalanced with 61% of females to 39% of males.

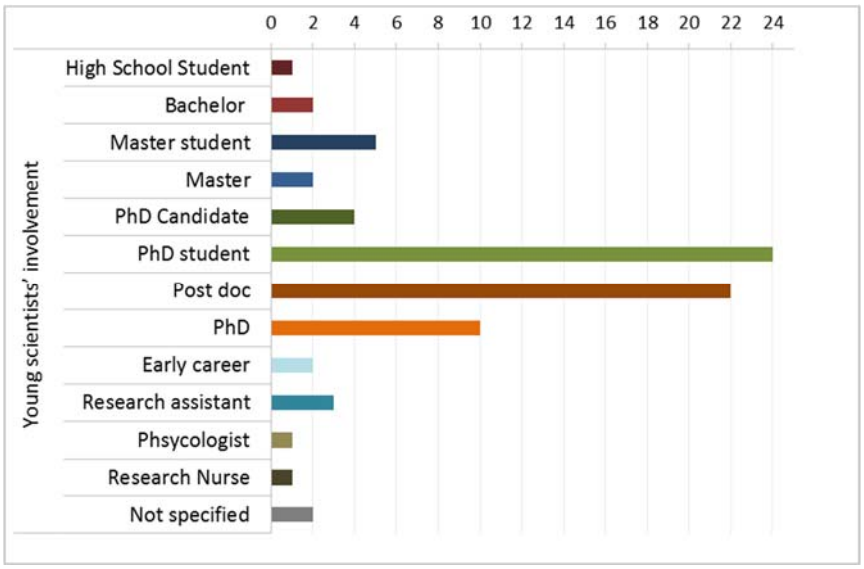

Figure 4 – Young scientists' involvement in the JTC2013 funded projects

We believe that there are many ways to evaluate productivity of research groups, besides the methods (presented in objective 1 of this report). In this context, objectives 2-4 present other outcomes of the JTC2013 funded projects with impact on knowledge, research, and with a probable future impact on health.

Objective 2: Promote Multi-disciplinary Consortia and Translational Research Proposals (from Bench to Bedside)

NEURON aims to contribute to fill the existing gap in the translation of scientific research results into useful outcomes for the treatment of mental disorders. To understand whether the JTC2013 funded projects fulfilled this NEURON expectation it was evaluated the interaction between clinicians and basic researchers, on one side, and on the other side the involvement of patients in these projects

Indicator: Composition of the Consortium

This indicator was measured using the list of research groups involved.

The majority of partners in the funded consortia were either from the academia or research institutions, 49% and 34 %, respectively, with the clinicians accounting only for 17% of the partners (Figure 5). Nevertheless, a clinical partner was found in 6 out of the 12 consortia, ensuring the critical mass required for a bench to beside approach. The other 6 projects not involving a clinician had a more fundamental approach based on the study of mechanisms, pathways and/or genes, and others.

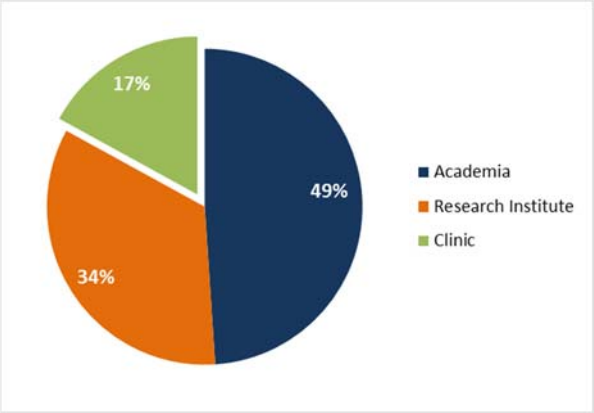

Figure 5 – Proportion of fellows from academia, research institutions or clinic in the funded consortia.

Indicator: Involvement of Patients

This indicator was measured in the impact questionnaire (Q6).

For a successful bench-to-bedside approach and translation of research results into clinical application, it is crucial to combine research in animal models with research in patients.

In the JTC2013 call only one consortium, COCADDICT, claimed to have involved patients directly in the research project. In this specific example, patients were involved in designing the research project, conducting the research project (e.g., patient committee / advisory board), and Participation in the Research Ethics Board with opportunity to comment on the research design and execution. Two other consortia contacted occasionally relevant associations of patients with very specific issues (ex. Ethical related questions).

Those consortia not involving patients presented several reasons which are listed below:

- Project in animal studies or healthy volunteers (human brain neuroimaging data), no clinical study or patient data was involved;
- Patients with substance use disorders even when they are involved in care exhibit high impulsivity and less treatment adherence than in other disorders. Thus they are not usually involved in research design and interpretation.
- Project is a collection of different “proof of concept” projects, with relatively new concepts with a focus on basic research combined with clinical research. As the clinical trial was only an observational and not an interventional trial, patients were not involved;
- Basic research project, therefore, patients and patient representatives were not directly involved.

Indicator: Patents and Other Outcomes with Impact to Health

This indicator was measured in the impact questionnaire (Q2).

The translation of scientific results is of high importance. Therefore, our final questionnaire also aimed at evaluating the valorisation of the outcomes of research projects. One out of the twelve consortia submitted a licence and obtained it, and the same consortium – CBGC – has created a SME - **Petsofi Ltd.** (described below). Another consortium submitted a database: **ChemNetDB –** http://www.chemnetdb.org, a neurochemical connectivity database, freely available resource for systems analysis of motor, sensory, emotional and cognitive information processing, that has integrated over five decades of neuroanatomical investigations into a multi-scale, multi-layer neurochemical connectome of the rat brain.

In addition, other outcomes with impact to health resulting from the JTC2013 funded projects were also reported, summarised in Figure 6 and listed below.

Figure 6 – Number of consortia reporting outcomes with potential impact to health.

List of other outcomes:

Creation of a platform available to a community

- **Petsofi Ltd** - digital animal platform: will include canine behavioural questionnaire as a part of the service to increase research participation, and to bring a multitude of service providers together to help identify and treat neuropsychiatric canine patients;
- Developing an economic **high throughput NMR platform** covering ~200 biomarkers for dogs;
- **Contribution to validate key OptoPath's** technological developments (OptoPath is a R&D platform dedicated to instrumental and procedural innovations in experimental psychopathology in rodents and humans).

New project or contract

- New Academy of Finland - funded project on myelin plasticity in chronic stress and anxiety disorders;
- ERANET-NEURON Joint Transnational Call for 'European Research Projects on Mental Disorders' 2017- acronym - ADIKHUMICE
- Brain Labex funded MAD project (2015)

Creation of a firm

- **Petsofi Ltd** - digital animal platform.

Other

- **Open Data** - RNA-seq., miRNA-seq., and proteomics data from BNST and blood, from two mouse strains and panic disorder patients submitted to publicly available databases.

Objective 3: Support Innovative or Shared Resources and Technology

In addition to the intellectual exchange the projects outcomes depend on the exchange of materials as well as the creation of new shared resources and technologies, which usually outlast the projects. The following section presents the level of biomaterial exchange as well as the development of Biobanks, Patient Registries or Patient Databases.

Indicator: Evaluation of the Development and the Use of New Resources

This indicator was measured in the impact questionnaire (Q4.1 and Q4.2).

Project's outcomes depend also on the exchange of materials and the latter represents an indicator of the level of collaboration. Apart from three consortia - COCADDICT, HYPZITRP, and TYMON - all others reported the exchange of a variety of biomaterials and clinical data between partners (Figure 7). The type of material that was mostly exchanged within the different consortia was: DNA and Tissue in 5 out of the 12 consortia; and Animals and Clinical Data in 4 out of the 12 consortia.

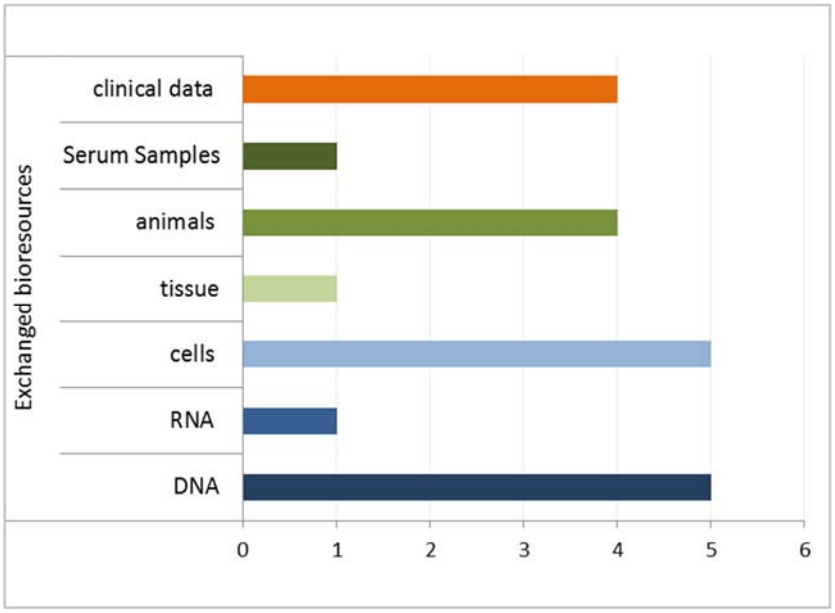

Figure 7 – Number of consortia reporting the exchange of bioresources within the group.

The setup of common platforms/resources is another way to evaluate the synergy and added value of a research consortium. More than an isolated initiative, the development of shared resources strengthens the ERA. Within the JTC2013 projects 2 patient databases and 2 biobanks were created by compiling national sources. As for the patient recruitment, it was done through already existing networks of clinicians in all cases. The question on sustainability of the databases and biobanks was only answered by one of the coordinators who claimed that it will be supported by other sources, not specifying which.

Objective 4: Develop New Strategies for Diagnosis, Therapy, and Rehabilitation Procedures

The ultimate goal of NEURON is to fund research that will have an impact on health and brings new discoveries and possibilities for patients. The following section summarises the reported outcomes contributing to this goal.

Indicators: Development of New Strategies for Diagnosis and Therapy, and Rehabilitation Procedures

This indicator was measured in the impact questionnaire (Q 5.1).

In the JTC 2013 six out of the twelve consortia declared having produced new knowledge that may translate in the future in new healthcare strategies of potential use for the diagnosis, therapeutics, or prevention of mental disorders, detailed in Figure 8.

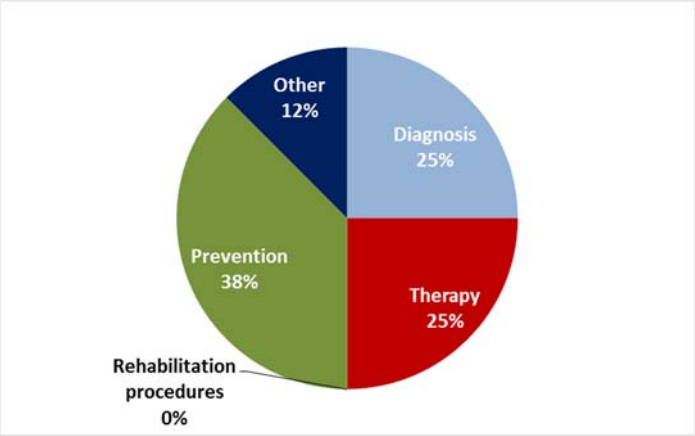

Figure 8 – Percentage of consortia developing new strategies.

These take - among others - the form of:

- New understanding of drug effects and risks during neurodevelopment;
- Specified neuromodulation of Tourette-Syndrome (clinical trials currently ongoing);
- TAO2 is likely a significant contributor to the brain size and connectivity issues in patients with 16p11.2 microdeletion.

Indicators: Major Achievements of the Funded Consortia

These indicators were measured in the impact questionnaire (5.2).

In this section several different categories of results were analysed to complement the information and outcomes reported above and know more about the achievements of the funded JTC2013 projects. In this context, we identified 9 categories of achievements shown in Figure 9.

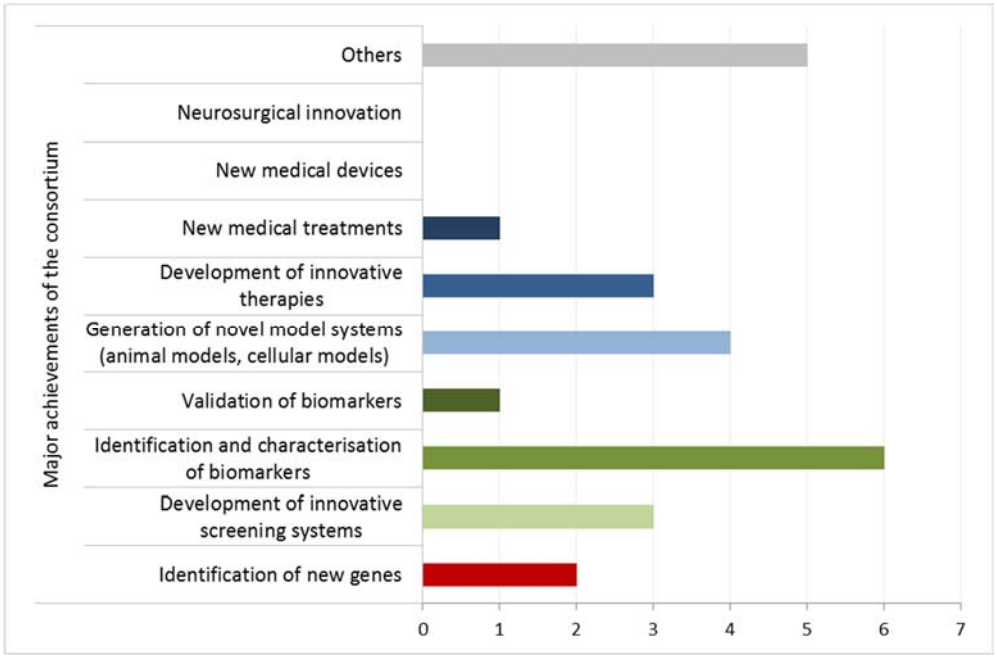

Figure 9 – Achievements reported by JTC2013 funded consortia.

The JTC2013 achievement that stands out is the "Identification and characterisation of new Biomarkers", with 6 out of the 12 consortia claiming to have carried out such type of studies. In addition, the "Development of innovative screening systems", the "Generation of novel model systems (animal models, cellular models)", and the "Development of innovative therapies" were also reported in 4, 3, and 3 out of the 12 consortia, respectively (Figure 9).

As the aforementioned categories may not provide sufficient details, a non-exhaustive list of specific examples of achievements by JTC2013 consortia is shown below:

Identification of new genes:

- Identification of the first genome-wide significant SNPs in PTPRD and NPAS2 for obsessive-compulsive traits in human and new candidates also in dogs.
- Identification of SLC17A8 (VGLUT3); SLC18A3 (VAChT); - related to substance use disorders.

Development of innovative screening systems:

- Human CYP2D6 mouse model developed so that the effects of variable metabolism by human CYP2D6 in the brain (versus liver) can be tested for drug and endogenous compound metabolism and effects.
- Online behavioural survey for canine anxiety "Identification of novel players in the TSC2 pathway like Cend1, and Frrs1l.

Identification and characterisation of biomarkers:

- Candidate protein biomarkers from mouse BNST and blood;
- Genome-wide association study of a cognitive heritable biomarker of ADHD, response inhibition; identifying biomarkers in canine anxiety; metabolic biomarkers identified for dogs.
- Identification of VGLUT3 and VAChT (related to substance use disorders).
- Identification of brain morphological and functional (within and between brain structures) markers of cocaine addiction-like behaviour.
- Identification of TAO2 as a possible and significant contributor to the brain size and connectivity issues in patients with 16p11.2 microdeletion.
- Identification of long-distance cortical-subcortical oscillatory coupling in OCD as a candidate biomarker.

Generation of novel model systems (animal models, cellular models):

- Novel animal model to selectively investigate the role of brain human CYP2D6 in the response to drugs that act on the central nervous system.

- Biobank of canine models of neuropsychiatric disorders, knockout mouse models.
- Identification of VGLUT3cKO, VAChTcKO, VGLUT3T8I/T8I as possible Biomarkers for substance use disorders.
- Establishment of Cdkl5 knockout mice and in vitro models for studies on better understanding the pathophysiology of CDKL5 encephalopathy.
- Establishment of a Tsc2+/- breeding colony, generation of Mid1 and Mid2 knockout mice, as well as Mid1 and Mid2 double knockout mice, generation of iPSC cells from a female with Opitz/BBB/G syndrome (OS).
- DAT-tg rat model of Tourette-Syndrome.

Development of innovative therapies:

- Combined treatment with hyperforin (TRPC6 channel activator) and NMDA receptor antagonist as a potential long-lasting effective antidepressant strategy.
- Advancement of neuromodulation for treatment of Tourette-Syndrome. Specification of brain sites and implementation of non-invasive strategies.

New medical treatments:

- Initial discussion with a local pharma to utilize the material collected in the project to try new drugs for canine separation-anxiety (project CBGC).

Others:

- One consortium established mitochondrial responses as major evolutionarily conserved and genetically controlled stress-response in mice and humans. This finding allows targeted mechanistic studies to understand how mitochondrial function may be compromised in chronic stress and anxiety disorders.
- One consortium identified dynamically regulated metabolites within panic attacks in patients with panic disorder, which are linked to CCK system and potentially indicative for therapy response.
- One consortium developed a mobile platform for animal owners with a behavioural survey as a one of the many components to recruit large canine cohorts.
- Identification of novel mother-to-child transmission pathways after maternal Early Life Stress (ELS) exposure.
- Validation of a functionally relevant genetic variation in a priori defined gene *locus* (*e.g.* OXTR rs237895);
- Identification of individuals at high risk for intergenerational transmission of ELS-associated long-term effects with implications for secondary prevention.
- Identification of molecular patterns that show that chronic stress is an important modulatory factor in tuberous sclerosis.
- Development of a novel reversal-learning paradigm incorporating metacognitive assessment.

Summary & Discussion

Overall JTC2013 contributed to the main goals of NEURON:

- ❖ Enhance excellent cooperation between scientists working in the field of neuroscience (shown by the exchanges of materials, personnel, co-authored publications, meetings, etc.).
- ❖ Promote multi-disciplinary consortia and to encourage translational research proposals (from bench to bedside).
- ❖ Support development of innovative or shared resources and technologies.
- ❖ Support research to develop new strategies for diagnosis and therapy.

and to the specific goals of this Joint Transnational Call:

- ➢ Multinational and multidisciplinary, collaborative research projects that addressed important questions related to Mental Disorders;

- Proposals addressing from understanding basic mechanisms of disease through proof-of-concept clinical studies in humans;
- Fundamental research on the pathogenesis and/or aetiology of mental disorders (may include the development of innovative or shared resources and technologies);
- Research to develop new strategies for (early) diagnosis, therapy, and rehabilitation procedures for mental disorders;
- Involvement of young scientists.

Table no 5 summarises the outcomes produced by the different consortia by categories. As it can be noticed, with the exception of project HYPZITRP, the productivities of JTC2013 funded consortia are very similar. The coordinator of HYPZITRP pointed out several issues that may justify such short results, namely, cuts in the budget of two of the partners, maternity leave of the coordinator, and problems in communication between the partners in the consortia.

A point for improvement in the future is to dedicate higher efforts in the involvement of clinicians as we observed a low participation of them in JTC2013 as only 17% of partners were from the clinical sector, even if the call was focussed in a topic with high clinical relevance.

Consortium		Project Outcomes (No)			Valorisation of results & Innovation (No)			Training & Mobility (No)		Material Exchange (No)	Total (No)
Acronym	Partners (No)	Model Systems, Therapies, New Biomarkers, etc.	Registries, Databases, Biobanks	Scietific publications	New Strategies for Diagnosis, Therapy, and Rehabilitation Procedures	Patient Involvment	Patents, Lincences, SMEs	Young Scientists	Mobility		
AnxBio	4	3	0	7	0	0	0	6	2	3	25
BrainCYP	4	1	0	4	1	0	0	8	2	1	21
CBGC	3	6	1	6	3	0	2	9	NA	1	31
COCACE	5	3	2	4	0	0	0	5	1	2	22
COCADDICT	4	1	0	6	0	1	1	4	0	0	17
HYPZITRP	3	1	0	0	0	0	0	4	0	0	8
IMFLAME-D	5	0	0	6	0	0	0	11	0	3	25
MecTranGen	5	1	0	9	1	0	0	8	3	2	29
mTOR-DIDS	4	3	0	0	1	0	0	9	1	4	22
RD_aDBS	3	2	0	8	1	0	0	9	0	2	25
TAO2	4	2	1	7	1	0	0	11	0	3	29
TYMON	3	2	0	9	0	0	0	2	0	0	16
Total	**47**	25	4	66	8	1	3	86	9	21	**270**

Table 5 – Performance of JTC2013 individual projects in most of the indicators applied.

NEURON shows possibilities to improve valorisation of results

As for every JTC launched within the scope of NEURON the real level of valorisation of results is difficult to judge, as effective valorisation often occurs at later stages than 3 to 6 months after the end of the project, for which the final reports were analysed. Nevertheless, JTC2013 funded projects achieved relevant results for new strategies for diagnosis, and therapy that may benefit patients. Although economic valorisation is not one of the key aims for JTC2013, two out of the twelve consortia have submitted patents, one of which was approved. In addition, one out of the twelve consortia indicated the creation of a SME - **Petsofi Ltd**. **As for the use of European Infrastructures and involvement of patients there is still room for improvement in the future.**

NEURON outcomes have impact on patients life

Many important outcomes were reached by the funded projects:

- The discovery of new causative genes and mutations associated to substance abuse disorders, and new genes involved in anxiety, compulsive behaviours, impulsivity.
- The discovery of new Diagnosis and Testing has a promising health impact.

- The discovery of possible Therapeutic options has a major impact on the life and quality of life of patients.
- The creation of new model systems will allow new tests, and a better understanding of the pathophysiology of various disorders.
- The discovery of new Biomarkers may facilitate early detection of disease, with a possible positive impact on the way and efficiency of patient treatment.

NEURON strengthens the ERA

The analysis of JTC2013 herein presented shows that the NEURON programme continues to contribute to the ERA:

- New countries participated in this JTC (Iceland, Latvia, Sweden) in a total of 16 participating countries, showing the growing reputation and attractiveness of NEURON.
- Many young scientists were involved (n=79), either as trainees or contracted researchers.
- The numbers concerning the valorisation of results are satisfactory and directed, showing promising possibilities for the future.
- Biobanks & Registries were created and/or coordinated, in most cases using those already existing at the national level.
- Several collaborations were initiated with the funded project, but also during the course of the projects with members outside the consortia.

In the future NEURON should carry discussions on how to improve the feedback rate from Coordinators, what actions shall be done to have projects tackling rehabilitation, make researchers aware of the advantages to publish in open access journals, and take actions to increase the number of women in the consortia.

Annex I- Call Text JTC 2013 Excerpt

Call for Proposals for

"European Research Projects on Mental Disorders"

Submission deadline for pre-proposals: March 11, 2013

weblink to
Proposal template

weblink to
Electronic proposal submission

For further information, please visit us on the web

http://www.neuron-eranet.eu

or contact

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1. Purpose

The maintenance, improvement and restoration of human health are of fundamental importance and priority in all countries. Biomedical and health research provide an important basis for the improvement of healthy living. Among the many diseases affecting human health, disorders of the brain are major causes of morbidity, mortality and impaired quality of life. According to estimates, more than one billion people suffer from disorders of the central nervous system. In Europe, disorders of the brain account for approximately one-third of the total burden of all diseases. Thus, neuroscience research and its translation into diagnostic and therapeutic measures are of high priority.

In this context, the 'Network of European Funding for Neuroscience Research' (NEURON) has been established under the ERA-Net scheme of the European Commission (http://www.neuron-eranet.eu). The goal of the ERA-Net NEURON is to coordinate the research efforts and funding programmes of European countries in the field of disease related neuroscience.

Under the umbrella of NEURON, five transnational joint calls have been launched on different topics from 2008 to 2012. The sixth joint transnational call (JTC-6) is now launched in the field of mental disorders. The following funding organisations have agreed to fund the joint call for multinational research projects in this scientific area. The call will be conducted simultaneously by the funding organisations in their respective countries and coordinated centrally by the Joint Call Secretariat.

- Austrian Science Fund (FWF), Austria
- Research Foundation – Flanders (FWO), Belgium
- Canadian Institutes of Health Research (CIHR), Canada
- Fonds de recherche du Québec-Santé (FRQS), Québec (Canada)[1]
- Academy of Finland (AKA), Finland
- French National Research Agency (ANR), France
- Federal Ministry of Education and Research (BMBF), Germany
- The Icelandic Centre for Research (RANNIS), Iceland
- Chief Scientist Office, Ministry of Health (CSO-MOH), Israel
- Ministry of Health (MOH), Italy
- Latvian Academy of Sciences (LAS), Latvia
- National Research Fund (FNR), Luxembourg
- National Centre for Research and Development (NCBiR), Poland
- Foundation for Science and Technology (FCT), Portugal
- Executive Agency for Higher Education, Research, Development & Innovation Funding (UEFISCDI), Romania
- Slovak Academy of Sciences (SAS), Slovakia – *new participant as of Feb-04, 2013*
- Swedish Research Council (SRC), Sweden

[1] Subject to availability of funds voted annually to FRQS by the National Assembly of Québec

2. Aim of the call

The aim of the call is to enable multi-national, collaborative research projects that will address important questions relating to mental disorders. The call may receive proposals within the breadth of research from understanding basic mechanisms of disease through proof-of-concept clinical studies in humans. These may include research on affective disorders, stress-related and anxiety disorders, schizophrenia and delusional disorders, substance use disorders, and other mental disorders. **Research on dementia is not included in the present call.**

The ERA-Net NEURON funding organisations particularly wish to promote **multi-disciplinary work** and to encourage **translational research proposals** that combine basic and clinical approaches.

Research proposals should cover at least one of the following areas:

a) Fundamental research on the pathogenesis and/or aetiology of mental disorders. This may include the development of innovative or shared resources and technologies. The relevance of the research to disease must be clearly indicated.

b) Research to develop new strategies for (early) diagnosis, therapy, and rehabilitation procedures for mental disorders.

One of the aims of NEURON is to provide support to young researchers, and to facilitate their integration as independent PIs into the consortia, an experience that would be a valuable step forward in their research careers.

The individual components of joint applications should be complementary and contain novel, ambitious ideas. There should be clear added value in funding the collaboration over the individual projects.

Clinical studies are eligible up to the point of proof of concept.[2]

3. Application

3.1 Eligibility

Joint transnational research proposals may be submitted by research groups working in universities (or other higher education institutions), non-university public research institutes, hospitals, as well as in commercial companies, in particular small and medium-size enterprises. The eligibility of the afore-mentioned institutions, together with details of eligible costs (e.g. personnel, material, consumables, travel money, investments), are subject to the individual administrative requirements of individual funding organisations and may therefore vary. Please

[2] Eligibility and funding requirements for clinical trials vary between the partner countries. Clarification may be obtained from the individual funding agencies.

note particularly that, for some funding organisations, commercial companies are not eligible or are only eligible under certain conditions (e.g., only in partnership with academic institutions in the consortium). Clarification may be obtained from the individual funding agencies (see contact details below).

Only transnational projects will be funded. Each consortium submitting a proposal must involve a minimum of three research groups eligible to be funded by organisations listed in this call text (see above), and these three groups must be from three different countries. The total number of research groups in a consortium must not exceed five. Therefore, the maximum number of countries involved in one consortium is five. Not more than two research groups should be from the same country.

Research groups from countries whose funding organisations are not partners in the ERA-Net NEURON may participate in projects if they are able to secure their own funding and clearly provide an added value to the consortium. They must state clearly in the proposal if these funds are already secured or, if not, how they plan to obtain funding in advance of the project start. In any case, the total number of research groups in one consortium must not exceed five.

It is obligatory that the coordinator of a consortium is eligible to be funded by one of the organisations listed in this call text.

Each consortium should have the critical mass to achieve ambitious scientific goals and **should clearly demonstrate added value** from working together. One project co-ordinator among the project partners who represents the consortium externally will be responsible for its internal scientific management.

Although applications must be submitted jointly by groups from several countries, the individual research groups will be funded by the individual NEURON funding organisation(s) of their respective countries. Eligibility criteria are the matter of individual partner funding organisations.

Therefore, applicants are strongly advised to follow the instructions contained in the country-specific eligibility tables which are published on the NEURON webpage and to contact their national/regional funding organization to confirm eligibility matters before submitting an application.

3.2 Financial and legal modalities

Projects can be funded for a period of up to three years and according to funding organisations' regulations. Eligible costs may vary according to the corresponding funding agency´s regulations. Each group is subject to the rules and regulations of its respective national/regional funding agency.

3.3 Submission of joint transnational proposals

There will be a **two-stage procedure** for joint applications: **pre-proposals** and **full proposals**. In both cases, one joint **proposal document** (in English) shall be prepared by the partners of a joint transnational proposal, and must be submitted to the Joint Call Secretariat by one spokesperson, the co-ordinator.
Pre-proposals must be submitted in electronic format no later than **March 11, 2013** (23:59:59 CET) via the **electronic submission** system.

NOTE: Full proposals will be accepted only from those applicants **explicitly invited** by the Joint Call Secretariat to submit them.

3.4 Further information

For further details, please refer to the respective submission forms available through the NEURON website. If you need additional information, please contact the Joint Call Secretariat, or your funding agency representative (see Annex for contact data).

4. Evaluation and decision

In accordance with the two-stage application procedure for joint proposals (pre-proposals and full proposals), there will also be a two-stage review procedure.

4.1 Formal check of proposals

The Joint Call Secretariat will assess proposals to ensure that they meet the call's formal criteria (date of submission; number of participating countries; inclusion of all necessary information in English). In parallel, the Joint Call Secretariat will forward the proposals to the national/regional funding organizations, which will perform a formal check of compliance with their respective regulations. Proposals not meeting the formal criteria will be rejected.

The Call Steering Committee may reject proposals if they are clearly outside the scope of the call.

Proposals passing these check points will be forwarded to the joint Peer Review Panel for evaluation.

4.2 Peer-review of proposals

The reviewers will carry out the evaluation according to specific evaluation criteria:

1. Relevance to the aim(s) of the call
2. Scientific quality of the proposal (innovation potential, methodology)

3. Feasibility of the project (adequacy of project work plan, budgetary and other resources, time schedule)
4. International competitiveness of participating research groups in the field(s) of the proposal (previous work in the field, expertise of the research groups)
5. Quality of collaborative interaction between the groups, and added value, from both scientific and transnational perspectives, of the research consortium. Consortia not meeting these criteria will be downgraded.
6. Potential of the expected results for future clinical and other health relevant applications.

4.3 Decision

4.3.1 Pre-proposals

The eligible pre-proposals will be reviewed via a written (remote) peer review process. Based on the scores in the written reviews a ranking list will be set up. By mid May 2013, the coordinators of the top proposals will be invited by the Joint Call Secretariat to submit a full proposal **no later than June 25, 2013**.

4.3.2 Full proposals

The international Joint Peer Review Panel will establish a ranking list of the fundable proposals based on scientific assessment. Based on this ranking list the Call Steering Committee will determine the projects to be funded, taking into account the national budgets available. Based on these recommendations, final decisions will be made by the funding agencies and will be subject to budgetary considerations.

5. Funding procedure / Responsibilities / Reporting requirements

5.1 Funding procedure

Projects can be funded for a period of up to three years and according to funding organisations' regulations. Funding is expected to start early in 2014.

The research groups of successful collaborative projects will be funded directly by the respective funding organisations.

Funding will be administered according to the terms and conditions of the responsible funding organisations, taking into account all other applicable regulations and legal frameworks.

5.2 Responsibilities

Each project must nominate a project coordinator, who represents the consortium externally and is responsible for its internal management (e.g., controlling, reporting, intellectual property rights issues, etc.) to the ERA-Net NEURON Joint Call Secretariat. Within a joint proposal, each group leader will be the contact person for the relevant national/regional funding organization.

The coordinators of funded projects together with the respective funding agencies shall make every effort to seek a common start date for all research groups in the consortium.

5.3 Reporting Requirements

On behalf of the research consortium, the project coordinator will be required to submit a brief annual scientific progress report on the project and one final report in the end, to the Joint Call Secretariat. Group leaders may be required to submit reports individually to their national funding organization; information regarding such reporting will be forwarded by the relevant funding organization, as applicable.

Annual reports shall be submitted within four months after the end of the respective calendar year. Annual reports do not need to be submitted if the project ends within three months of the following year (i.e., between January and March). In this case, submitting a final report suffices. However, instead of submitting the final report within the regular period of six months after the end of the project (see below), the final report has to be submitted within four months after the end of the project.

The deadline for submitting final reports is six months after the end of the project. It is the task of the coordinators to define a date on which the projects “officially” end. This step is necessary, as partners might be granted extensions of different duration. Coordinators will be informed about this procedure by the Joint Call Secretariat and will receive the report template in due time.

The coordinator will be asked to present the progress under the funded research project during one intermediate and one final status symposium. Group leaders will be asked to participate in the latter. Travel budgets should be planned and managed accordingly.

Funding recipients must ensure that all outcomes (publications, etc.) of transnational NEURON projects include a proper acknowledgement of ERA-Net NEURON and the respective funding partner organisations.

Annex

Please note that country specific requirements might apply to this call. We strongly advise you to contact your national/regional representative prior to submitting a pre-proposal:

Country (Region)	Contact person(s)	Links to national/regional calls mentioning particular requirements
Austria	Dr. Herbert Mayer	Austrian Science Fund (FWF) herbert.mayer@fwf.ac.at www.fwf.ac.at
Belgium (Flanders)	Dr. Olivier Boehme	Research Foundation – Flanders (FWO) Egmontstraat 5 1000 Brussel www.fwo.be olivier.boehme@fwo.be
Canada	Dr. Elizabeth Theriault Jeff Warren	Canadian Institutes of Health Research - Institute of Neurosciences, Mental Health and Addiction (CIHR-INMHA) Elizabeth.Theriault@ubc.ca 604 827-4744 http://www.cihr-irsc.gc.ca/e/8602.html Strategic Program Design and Analytics Research and Knowledge Translation Portfolio, CIHR Jeff.warren@cihr-irsc.gc.ca 613-948-2813
Canada (Québec)	Nicolas Hoffmann	Fonds de recherche du Québec-Santé (FRQS) nicolas.hoffmann@frq.gouv.qc.ca www.frqs.gouv.qc.ca
Finland	Dr. Hannele Lahtinen	Academy of Finland (AKA) hannele.lahtinen@aka.fi www.aka.fi
France	Dr. Natalia Martin Dr. Deborah Zyss	French National Research Agency (ANR) Health & Biology Department Deborah.ZYSS@agencerecherche.fr +33 1 78 09 80 88 natalia.martin@agencerecherche.fr +33 1 73 54 81 33 www.agence-nationale-recherche.fr
Germany	Dr. Petra Lüers	Programme Management Agency (PT-DLR) – Health Research, on behalf of the Federal Ministry of Education and Research (BMBF) petra.lueers@dlr.de +49 228 3821 1194 www.gesundheitsforschung-bmbf.de
Iceland	Dr. Katrin Valgeirsdottir	RANNIS – The Icelandic Centre for Research katrin@rannis.is +354 515 5800
Israel	Dr. Nava Levine	Chief Scientist Office - Ministry of Health (CSO-MOH) nl@013.net.il www.health.gov.il/
Italy	Dr. Gaetano Guglielmi	Ministero della Salute g.guglielmi@sanita.it www.ministerosalute.it/
Latvia	Dr. Uldis Berkis	Latvian Academy of Sciences www.lza.lv uberkis@latnet.lv

Luxembourg	Dr. Frank Glod	Fonds National de la Recherche (FNR) frank.glod@fnr.lu www.fnr.lu/
Poland	Marcin Chmielewski	National Centre for Research and Development (NCBiR) Section for Research Projects BIOMED marcin.chmielewski@ncbr.gov.pl phone: + 48 22 39 07 109 fax.: +48 22 20 13 408 www.ncbir.pl
Portugal	Dr. Anabela Isidro	Fundação para a Ciência e Tecnologia (FCT) Departamento das Relações Europeias, Bilaterais e Multilaterais Anabela.Isidro@fct.pt phone: Tel:+351 21 391 15 52 www.fct.pt
Romania	Prof. Leon Zagrean	Executive Agency for Higher Education, Research, Development & Innovation Funding (EAHERDIF) , leon.zagrean@uefiscdi.ro phone/fax +40213120880
Slovakia	Dr. Jan Barancik	Slovak Academy of Sciences (SAS) Department for International Cooperation barancik@up.upsav.sk +421 2 5751 0137 www.sav.sk
Sweden	Prof. Mats Ulfendahl	Swedish Research Council (Vetenskapsrådet) Box 1035 SE-101 38 Stockholm, Sweden mats.ulfendahl@vr.se www.vr.se

Funded by the European Commission