ERA-NET NEURON

European Research Projects on 'Novel Methods and Approaches towards the Understanding of Brain Diseases'

Joint Transnational Call 2012

Impact Report

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December 2018

Funded by the European Commission

ABBREVIATIONS

• Austrian Science Fund (FWF)	Austria
• Research Foundation – Flanders (FWO)	Belgium
• Fonds de recherche du Québec-Santé (FRQS)	Canada
• Academy of Finland (AKA)	Finland
• National Funding Agency for Research (ANR)	France
• Federal Ministry of Education and Research (BMBF)	Germany
• Chief Scientist Office, Ministry of Health (CSO-MOH)	Israel
• Ministry of Health (MOH)	Italy
• 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 and Innovation Funding (UEFISCDI)	Romania
• Ministry of Science and Innovation (MICINN)	Spain
• Institute of Health Carlos III (ISCIII)	Spain

INTRODUCTION

ERA-NET NEURON

Maintenance, improvement and restoration of human health are of fundamental importance and worldwide priority. In Europe, one out of every four citizens experiences a neurological or psychiatric condition, leading to a serious economic and social burden due to long-term disability and mortality. Neuroscience research and its translation into diagnostic and therapeutic outcomes are of fundamental importance to improve health in our society.

Most European countries invest considerably resources into research, leading to major advancements in science. Still, many important questions remain unanswered and major societal challenges need to be solved which cannot be confronted on a national level alone. In order to pool resources effectively in a concerted effort to address these issues, the European Commission has initiated European Research Area Networks (ERA-NETs) in various fields of research. The aim of the ERA-NETs is the coordination of research programmes to reduce fragmentation and duplication of efforts, thereby promoting European competitiveness in research. ERA-NETs support research that is conducted across countries, allowing research groups to jointly work on specific scientific questions, exchange ideas, and benefit from transnational expertise and resources.

The Network of European Funding for Neuroscience Research (NEURON; www.neuron-era-net.eu) was initiated in 2003 as a pilot Specific Support Action. It was developed into an ERA-NET in 2007 and has been funded by the European Commission in three phases: NEURON I (2007 – 2011), NEURON II (2012 – 2015) and NEURON Cofund (2016-2020). To this day, NEURON is the result of 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.

In the framework of NEURON I and NEURON II eight JTCs were implemented covering a diversity of topics, as detailed in table 1.

Year	Topic	Impact report
2008	Neurodegeneration	Published in 2014
2009	Method and Technology Development	Published in 2015
2010	Mental disorders	Published in 2017
2011	Cerebrovascular diseases	Published in 2017
2012	Method and Technology Development II	Ongoing
2013	Mental Disorders	Funded projects not finished yet
2014	Neuroinflammation	Funded projects not finished yet
2015	Neurodevelopmental Disorders & Neuroethics	Funded projects not finished yet
2016	External Insults to the Nervous System	Funded projects not finished yet
2017	Synaptic Dysfunction	Funded projects not finished yet
2018	Mental disorders	Funded projects not finished yet

Table 1: JTCs implemented within NEURON I & II and Cofund

Joint Transnational Call in 2012 "European Research Projects on Novel Methods and Approaches towards the Understanding of Brain Diseases"

ERA-NET NEURON partners launch annual joint calls to address the main gaps in knowledge and most urgent needs in the field of disease related neuroscience since 2008. To fulfil this aim, the ERA-Net NEURON funding organisations particularly promote integrated methodologies and approaches, multidisciplinary work and encourage translational research proposals that combine basic and clinical approaches.

NEURON recognised that important advances in the knowledge of brain function in the last decades were possible due to an impressive development of new techniques allowing a deep study and understanding of the nervous system. The 2012 call for research projects was launched to develop **Novel Methods and Approaches towards the Understanding of Brain Diseases**. The call was designed based on the strategic scientific workshop 'Future developments in Neuroscience', organised in Berlin in 2010 by ERA-NET NEURON. The call focused on projects aiming to develop or repurpose approaches and/or methodologies to be applied to the study of brain diseases, excluding the technological development of infrastructure funding *per se*. The JTC 2012 joined 14 research funding organisations from 13 countries (table 2), and a total of 12.7 M€ of committed funds (see table 2).

Country	Organisation (acronym)
Austria	Austrian Science Fund (FWF)
Belgium	Research Foundation – Flanders (FWO)
Canada	Fonds de recherche du Québec-Santé (FRQS)
Finland	Academy of Finland (AKA)
France	National Funding Agency for Research (ANR)
Germany	Federal Ministry of Education and Research (BMBF)
Israel	Chief Scientist Office, Ministry of Health (CSO-MOH)
Italy	Ministry of Health (MOH)
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 and Innovation Funding (UEFISCDI)
Spain	Ministry of Science and Innovation (MICINN), Institute of Health Carlos III (ISCIII).

Table 2: Funding organisations participating to JTC2012

The research projects submitted to this call were evaluated in two steps. One hundred and eighty four preproposals were submitted by consortia composed by more than seven hundred

research groups eligible for the participating funding bodies (the highest number received in NEURON until 2018). The submitted pre-proposals were very diverse in terms of proposed methodology and aim, in agreement with the lack of precise boundaries imposed to the call. Thirty-four consortia were invited to submit full proposals. The evaluation was performed by 83 multinational experts. Each proposal was evaluated by at least 2 but most proposals by 3 reviewers. The full proposals and their evaluations were further discussed in a peer review panel meeting.

Finally, eleven projects implicating forty-seven funded researchers in ten countries were selected and completed between January 2013 and March 2018. The funded proposals tackle a large variety of brain diseases and methodological approaches (listed below). Brain diseases: Anxiety, depression, epilepsy, eating disorders, neuropathic pain, neurodegenerative diseases, stroke and traumatic brain injury. Methodological approaches: Molecular approaches advanced, imaging and electrophysiological techniques, gene therapy, epigenetics, optogenetics, pharmacology, stem cells in different combinations (table 3).

Acronym	Title	Coordinator (in bold) and Partners	Pathology
AbetaID	Preparation of amyloid-beta aggregate species from synthetic and patient-derived material to define disease-causing mechanisms	**Erich Wanker (DE)** Bart De Strooper (BE) Luc Buée (FR) Giuseppe Lembo (IT)	Alzheimer's disease
CIPRESS	Cell stress inducible protein expression system for recovery from seizures	**Jochen Meier (DE)** Kai Kaila (FI) Richard Miles (FR) Carola Haas (DE)	Epilepsy
F4T	FOODforTHOUGHT: The epigenomics of eating disorders	**Andreas Ladurner (DE)** Rui Costa (PT) Mara Dierssen (ES) Giuseppe Testa (IT) Bartosz Wilczynski (PL)	Eating Disorders
LIGHTPAIN	Deciphering the role of peripheral and central nervous system metabotropic glutamate receptors in neurophatic pain with photoactivable ligands	**Amadeu Llebaria (ES)** Jesús Giraldo (ES) Francisco Ciruela (ES) Ferdinando Nicoletti (IT) Jean-Philippe Pin (FR)	Neuropathic Pain
MICRODEG	Neuronal Networks in microfluidic chips for the study of propagative neuronal disorders	**Jean Michel Peyrin (FR)** Jean-Louis Viovy (FR) Andreas Offenhausser (DE) Joaqín Castilla (ES) Anselme Pierrier (FR)	Neurodegenerative diseases
nEUAPPs	Role of the amyloid precursor protein APP for brain physiology and therapeutic potential for Alzheimer's disease	**Ulrike C. Müller (DE)** Fred Van Leuven (BE) Nathalie Cartier (FR) Christian Buchholz (DE)	Alzheimer's disease
RENEW IT	Restoring function in stroke via GPR17, a new receptor involved in adult brain self-repair	**Elena Tremoli (IT)** Leda Dimou (DE) José Maria Delgado-García (ES) Federico Calegari (DE)	Stroke
SEMAINE	Simultaneous MEG or fMRI And INtracranial EEG	**Jean-Philippe Lachaux (FR)** Sarang Dalal (DE) Gustavo Deco (ES)	Epilepsy
TargetECM	Superresolution imaging and therapeutic targeting of extracellular matrix-mediated signalling in brain diseases	**Alexander Dityatev (DE)** Evgeni Ponimaskin (DE) Valentin Nägerl (FR) Masha Niv (IL)	Alzheimer's disease Epileptogenesis
TBI Epilepsy	Proteolytic remodeling of the extracellular matrix in aberrant synaptic plasticity underlying epilepsy evoked by traumatic brain injury	**Leszek Kaczmarek (PL)** Asla Pitkanen (FI) Olli Tenovuo (FI) Stefanie Dedeurwaerdere (BE)	Epilepsy
WM2NA	White matter imaging, microstructure, and negative affetcs: thanslational study in humans and mice	**Jea-Luc (FR)** Naguib Mechawar (CA) Eleni Tzavara (FR) Juergen Hennig (DE) Charbel Massaad (FR)	Anxiety and Depression

Table 3: JTC 2012 funded consortia

Monitoring of the projects progress and results is of primary importance for ERA-NET NEURON, in order to improve the funding activities to better accomplish of its principal aim: to pave the way for translation of research results for the benefit of patients and those around them. The present document summarizes and analyses the outcomes of projects funded in the joint translational call in 2012.

Impact Analysis of the Joint Translational Call in 2012

In 2013 ERA-NET 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 4, and was transformed in a list of questions sent to the coordinators of funded consortia together with the final report template (see Annex I and II). 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 ERA-NET NEURON's funding activities.

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 4: Key performance indicators in relation to the objectives of the funding programme. (The number of the respective question in the questionnaire is given in brackets)

In the following section, the analysis shows the outcomes of the funded projects in the context of 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 summarizing 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 ERA-NET 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, dissertations, books, scientific meetings and other publications. A summary of the total number of such communications reported at the end of the project is depicted in table 5.

Type of publication	No. (total)	consortia (no.)
Peer reviewed articles (including reviews)	189	11
Articles under review /prep	26	9
Books/book's chapters	6	4
Reviews	18	7
Articles dedicated to general public	13	2
Communications in scientific meetings	150	9
PhD Dissertations	16	6

Table 5: Total publications resulting from projects funded through JTC 2012

As depicted in table 5 a total of 189 peer-reviewed articles were published by the funded consortia at the time when the final reports were written. The publication rate is quite variable amongst the consortia and ranges between 4 and 33 peer reviewed articles. Seventy five percent of the original articles –not considering reviews- were published in journals with impact factors between 1 and 10. Fourteen percent were published in journals with impact factors between 10 to 20 and 5 percent in journals with very high impact factor above 20 (Figure 1A). All consortia published articles at the end of the project, and all of them declared to be still preparing further publications.

Publications including at least two partners (i.e. multi-partner publications) were considered to partially account for the intensity of cooperation within the consortium. Around nineteen percent of published original articles –not considering reviews- (33 articles) implicated more than one consortium partner. Seven consortia reported at least one multi-partner article and four

consortia only reported single-partner articles in the final report (Figure 1B). All the four consortia reporting no multi-partner publications were contacted and three of them reported at least one multi partner publication released after the final report. As expected considering the number of publications in preparation reported in the final reports, this analysis underestimates the publication production and represents a fixed figure immediately after the completion of the project.

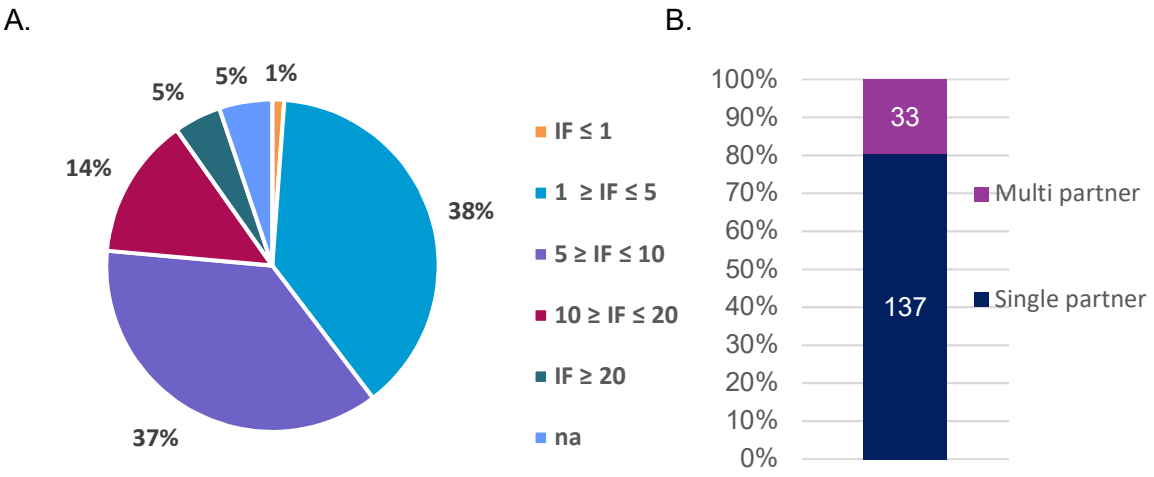

Figure 1: Peer reviewed publications. A. Distribution of peer reviewed publications by impact factor (IF). B. Proportion of multi and single-partner peer reviewed articles published by the 11 funded consortia

Indicator: The NEURON JTC as a Starter of New Collaboration

This indicator was measured in the impact questionnaire (Q3.1).

This indicator analyses the previous history of collaboration between the members of a consortium before applying to ERA-NET NEURON JTC 2012. The objective is to be able to understand to which extent ERA-NET NEURON encourages the collaboration in neuroscience research.

As shown in Figure 2, ERA-NET NEURON funding enables the establishment of new collaborations mainly through the enlargement of pre-existing consortia (i.e. members having worked together before the project in JTC 2012 adding new partners in the framework of JTC 2012)

but also through the establishment of fully new consortia. Only one consortium did not add new collaborators.

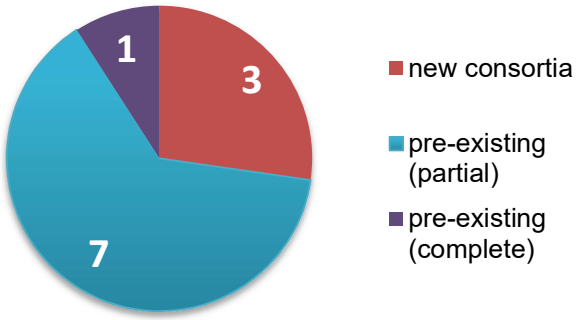

Figure 2: New collaborations between NEURON partners

Indicator: New Research Groups from other Countries Joining the Consortium

This indicator was measured in the impact questionnaire (Q3.2).

During the lifetime of the project, the majority of the consortia – eight out of eleven - established collaborations with additional teams in Germany, France, Italy, Austria, Israel, Belgium, Canada, USA, Spain, UK and one group became a member of the HBP Flagship (a large ten-year scientific research project that aims to advance knowledge in the fields of neuroscience, computing, and brain-related medicine, funded by the EC). The new collaborations doubled the number of research teams working together; forty-seven collaborations were established with research groups not funded by the call during the development of the projects.

Indicator: Sustainability of the Collaboration

This indicator was measured in the impact questionnaire (Q3.3).

Nine consortia declared that the results from the project funded by ERA-NET NEURON led them to submit new proposals in either national (14 grant submissions) or international (7 grant submission: 2 ERA-NETs and 5 H2020 or European Research Council) calls. The large majority of the applications were approved (Figure 3).

It is thus likely that the projects initiated in the framework of JTC 2012 will be further developed. The new funding will sustain the international collaborations for a period outlasting JTC 2012.

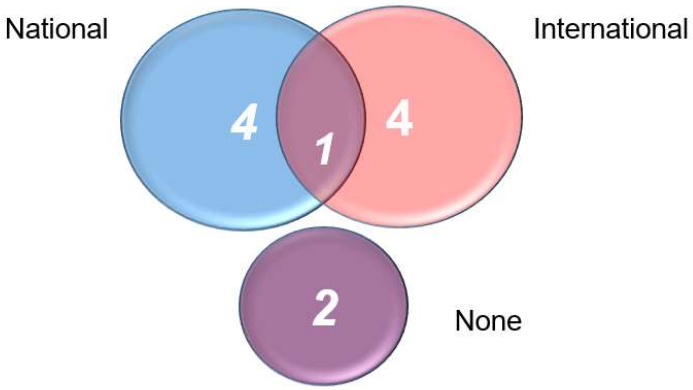

Figure 3: ERA-NET NEURON Consortia submission to other funding initiatives

Indicator: Intensity of Collaboration (Meeting, Mobility)

This indicator was measured in the impact questionnaire (Q1.1 and Q3.4).

Personnel interactions among partner members within a consortium are very relevant for the accomplishment of the project. During the lifetime of the projects, each consortium organised between 4 and 14 meetings; 3 meetings in average. Most of the groups 10 out 11- organised at least one full consortium meeting.

A total of 52 students, 36 postdocs and 5 engineers/technicians were involved in the projects funded in JTC 2012. Within the majority of the consortia 8 out of 11 students (9) or postdocs (7) visited another partner's laboratory (Figure 4).

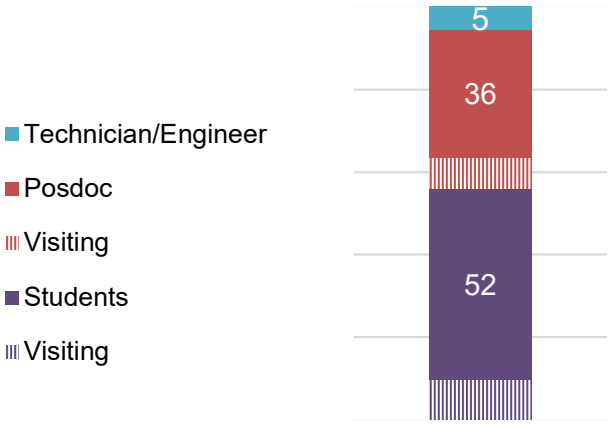

Figure 4: Intensity of collaborations. Academic staff participating in the funded projects by category. The proportion of students and postdocs visiting partner laboratories within the consortium are depicted.

In summary, even if the majority of projects were carried out by researchers with a history of having worked together before this call, NEURON funding served to establish new collaborations mainly through the inclusion of new partners to pre-existing consortia as well as through the numerous interactions established with researchers not funded by ERA-NET NEURON JTC 2012. The funded consortia are likely to continue working together since several new grants were submitted based on the outcomes of NEURON funded projects.

ERA-NET NEURON funding enables mobility and interaction between research partners in different countries. Overall, the 11 funded projects in JTC 2012 mobilise more than 180 persons including researchers, students and technicians working in 13 different countries.

The research outcomes of NEURON projects produced several co-authored high impact scientific publications, dissertations, chapters in books, communications in meetings and other outcomes. At the formal end of the project all the consortia were preparing further publications and therefore the outcomes concerning the above mentioned indicators will surely be higher.

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

ERA-NET NEURON aims to contribute to fill the gap for the translation of scientific research results into useful outcomes for the treatment of brain diseases. In order to evaluate the contribution of JTC 2012 projects to this aspect we analysed first the interaction between clinicians and basic researchers as well as the involvement of patients in the projects and second the outcomes with impact to health. These aspects are expected to vary according to the scope of the specific calls.

Indicator: Composition of the Consortium

The JTC 2012 consortia were mainly composed by academic researchers even though at least 7 out of 11 projects included between one or two medical doctors as partners; total of 11 medical doctors within the 47 partners implicated in the funded projects. In JTC 2012, only one of the projects was coordinated by a partner holding an MD/PhD –WN2NA. The number of medical doctors and projects coordinated by clinicians is substantially lower in this call compared to the previous two: JTC 2010 on Mental Disorders and JTC 2011 on Cerebrovascular diseases in which only 1 project did not include any medical doctor while 15 out of 21 projects were coordinated by clinicians Such a geometry was expected due to the nature of the call topic “Method and Technology development” and the goals associated with it, which were to “promote small transnational research consortia developing novel methods and approaches in the field of disease-related brain disorders. Research projects must be hypothesis-driven and have to combine cutting edge technological developments with a clear, substantial research question in the field of brain diseases.“

Indicator: Involvement of Patients

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 involving patients.

In the JTC 2012 call only 27% (2 out of 11) of the consortia involved directly patients in their research projects. Within those that did not involved patients in their projects 4 other consortia

used patient-derived tissue or human biological samples. This observation is again most likely related to the specificity of the call under analysis.

Indicator: Patents and Other Outcomes with Impact to Health

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

Other than the publications, the projects funded in JTC 2012 produced a series of outcomes with potential translational value. The focus of this call was on the development of methods and approaches to understand the diseased nervous system. As expected, the projects produced numerous protocols and devices as detailed below (Figure 5).

Patents and licenses. A total of five patents and one exploitation licence –listed below- were either registered or submitted to national (1) or international (5) organisms. One of them proposed a new therapeutic treatment meanwhile the others proposed new protocols or devices.

- A method for the detection of secreted Tau in biological fluids
- Glutamate receptor photomodulators
- Microfluidic devices for controlling the geometry of living bodies
- Methods and pharmaceutical composition for the treatment of Alzheimer's disease
- Device for animals immobilization
- Device for cell culture

Moreover, four projects produced and released software or prototypes as follows:

- Software for protein structure design
- Analysis software (2)
- Software to handle databases

Four other groups launched platforms for the community, such as

- Drug screen/characterisation platforms (2)
- Comparative platform for chromatin characterisation
- Graphical interphase

Finally, the outcome of one project informed a national law project on teenager's protection, and a new biotech company 'MICROBRAIN BIOTECH' was created by another project.

In summary, the outcome confirms the impact of this transnational funding scheme beyond scientific utilization of the results, as already observed in the assessments of previous calls. The approach to encourage multidisciplinary work and translational research and the topic focused on "Method and Technology Development" revealed fruitful in providing new patents, software or prototypes, platforms and even a Start-up. These achievements will surely have positive impacts on health in the future.

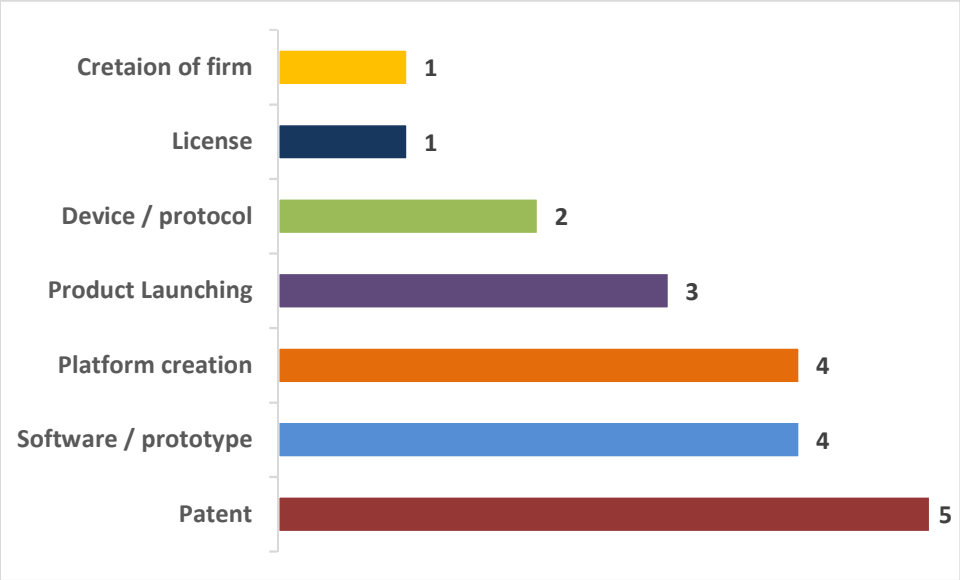

Figure 5: Outcomes with potential impact to health

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 item shows the level of biomaterial exchange as well as newly generated research resources.

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

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

A variety of biomaterials was exchanged between the partners as detailed in Figure 6.

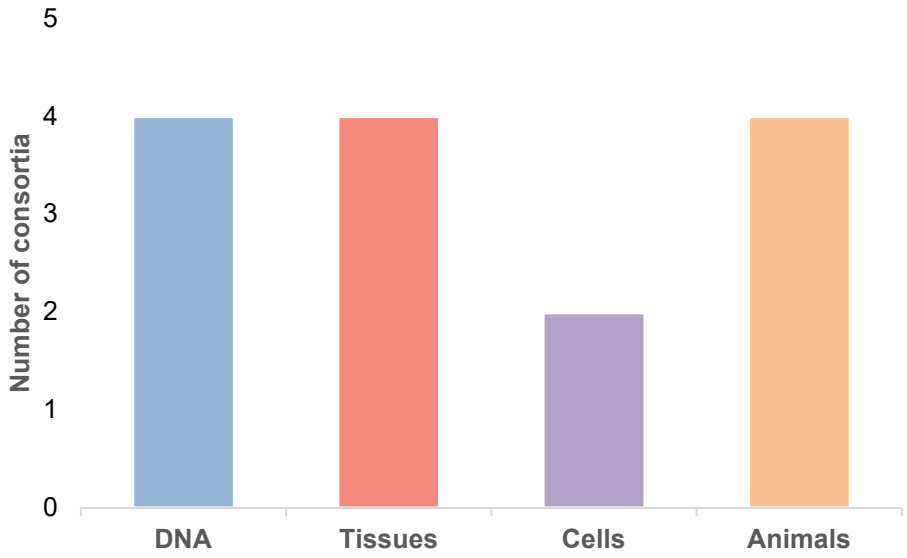

Figure 6: Exchange of biomaterials

Moreover, 4 consortia established patient databases or registries.

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

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

Indicator: Major Achievements of the Funded Consortia

These indicators were measured in the impact questionnaire (Q 5.1 and 5.2).

In agreement with the main objectives of the JTC 2012 ten out of 11 consortia declared having released new strategies of potential use for the diagnosis, therapeutics, rehabilitation or prevention of Alzheimer disease, Parkinson disease, epilepsy, stroke, dementia, eating disorders and neuropathic pain. These take the form of new screening systems, development or validation of biomarkers, development of new animal or cell models, molecular tools or the discovery of new genes associated to a disease, as detailed below:

- Diagnosis/biomarkers. Imaging biomarkers for depression outcome prediction; detection of disease relevant proteins for AD.
- Therapeutic strategies: Potential repurposing of the already marketed *montelukast* drug to reduce brain ischemia; potential modulation of 5-HT receptors for dementia treatment; assay system for the discovery of a new class of therapeutics directed at the Aβ target; development of AAV system to overexpress amyloid precursor proteins for Alzheimer disease treatment.
- Prevention strategies: Potential value in potentiating endogenous self-repair and potential value for the identification of patients at risk for posttraumatic epilepsy; use of early biomarkers for depression outcome in teenagers
- Tools/models/protocols: Antibody tools for characterization of drug effects on Aβ conformers; light operated molecular tools for the control of neuropathic pain; disease modelling for potential treatment against Alzheimer disease; reprogramming of fibroblasts; chips to reconstitute neuronal pathways to be used for screening, mouse lines to study oligodendrocytes; methods for organotypic human slice cultures; diverse tools for chromatin regulation; animal models for depression in young adults.

In summary, ERA-NET NEURON encourages multidisciplinary work and translational research. Specifically the projects funded in JTC 2012 resulted in several new avenues with potential to contribute to the improvement of diagnosis, prevention and therapeutic strategies for brain diseases. Moreover, newly-shared research resources were created and they are likely to be used in new collaborations.

Overall, ERA-NET NEURON contributes to the integration of research resources and potential beyond national border limits and helps the consortia to think forward on the translation of results from bench to bedside.

Objective of the Funding Programme	Key performance indicators	Results (percent of funded consortia, if not specified).
1. Enhance cooperation between European scientists working in the field of neuroscience	NEURON JTC as starter of new collaboration	→ 27% were newly formed consortia → 64% pre-existing consortia (part of PIs collaborated before) → 9% pre-existing consortia (all PIs collaborated before)
	New research groups from other countries joining the consortium	→ 45% acquired new collaborations during the lifetime of the project.
	Sustainability of the collaboration (obtaining further funding for the same consortium)	→ 36% had at least 2 PIs applying jointly for further funding
	Intensity of collaboration (meetings, mobility, joint publications)	→ 100% attended the mid-term symposium → On average each consortium held six meetings; 45% of the meetings were attended by all partners →17% of the articles (of all publications) were published jointly in peer-reviewed journals
	Level of excellence of the funded research	→ 82% published at least one primary research publication in a peer-reviewed journal with an Impact Factor above 10 (in total 34 articles)
2. Promote multidisciplinary consortia and to encourage translational research proposals (from bench to beside)	Composition of the consortium	→ In 9% the coordinator was a medical doctor. → In 18% at least one PI was a medical doctor. → PIs worked in basic (83% of PIs) and clinical (14% of PIs) research labs none in hospitals (0% of PIs)
	Involvement of patients	→ Patients were involved in 27% of the projects.
	Patents and other outcomes with impact to health	→ 45% submitted at least one European or international patent; other outcomes with impact to health comprise development of software and prototypes, the launch of services and platforms
3. Support develop ment of innovative or shared resources and technologies	Development and the use of new resources	→ exchanged biomaterials and data (DNA: 36%, tissues: 45%, cells: 18%, animals 36%, clinical data: 45%)
4. Support research to develop new strategies for diagnosis, therapy, and rehabilitation procedures	Development of new strategies	→ 27% developed new strategies for prevention → 9% developed new strategies for diagnosis → 27% developed new strategies for therapy → 0% developed new strategies for rehabilitation
	Major achievements	→ The major achievements that were most frequently reported include: novel model systems (45%), biomarkers (18%), and development of innovative therapies (36%)

Table 6: Summary of consortia performance against Key performance indicators

MID-TERM SYMPOSIUM

In 2014, ERA-NET NEURON organised a mid-term symposium in Malaga, Spain, in which all the 11 projects funded in JTC 2012 were presented and discussed. Two members of the evaluation panel originally involved in the funded projects selection were present to evaluate the progress of the projects. A summary of the evaluations was fed back to the coordinators. With this ERA-NET NEURON aims at supporting the funded consortia on the development of the projects.

The general evaluation of the symposium was very good with a particular high level of cross-disciplinary collaboration and evident interactions between partners highlighted for most of

the consortia. The impact of the results was considered already outstanding by the evaluators even before the end of the projects.

Indicator/Measure	ABETA	Cipress	Lightpain	MICRODEG	NEUAAPS	RENEW	TARGET ECM	TBI EPILEPSY	WN2NA	SEMAINE	F4T
New consortium	NO	NO	NO	NO	YES	NO	NO	YES	NO	NO	YES
Addition of research group	YES	YES	YES	YES	NO	YES	NO	NO	YES	YES	YES
Subsequent applications	YES	YES	YES	YES	NO	YES	NO	YES	YES	YES	YES
Intensity of collaboration											
number of meetings	14	6	10	4	5	4	6	4	8	4	5
meetings with all partners	8	0	3	1	5	4	3	2	2	1	2
Excellence											
total number of peer reviewed publications	15	27	33	29	7	4	15	17	22	7	13
number of joint publications	2	3	12	5	3	1	1	1	4	0	1
number of journals IF > 10	4	6	3	4	4	1	0	2	7	0	3
Composition of consortia											
- COO is a medical doctor	NO	NO	NO	NO	NO	NO	NO	NO	YES	NO	NO
- number medical doctors	2	0	1	0	1	1	0	2	2	0	2
- basic research labs involved	4	4	5	4	2	3	4	3	3	3	4
- clinical research labs involved	0	0	0	1	1	1	0	1	2	0	1
- hospitals involved	0	0	0	0	0	0	0	0	0	0	0
Involvement of patients or patient derived material	YES	YES	NO	YES	NO	NO	NO	YES	YES	YES	NO
Number of patents (submitted or obtained)	YES	NO	YES	YES	YES	NO	NO	YES	NO	NO	NO
Number of databases/registries/biobanks	0	1	0	0	0	0	0	0	1	1	0
Exchange of:											
- DNA	NO	YES	YES	YES	NO	NO	YES	NO	NO	NO	NO
- tissues	YES	NO	NO	YES	YES	NO	NO	YES	YES	NO	NO
- cells	NO	NO	YES	YES	NO	NO	NO	NO	NO	NO	NO
- animals	YES	YES	NO	NO	YES	YES	NO	NO	NO	NO	NO
- clinical data	NO	YES	YES	YES	YES	NO	NO	NO	YES	NO	NO
Novel strategies for:											
- diagnosis	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
- therapy	YES	NO	NO	NO	NO	YES	YES	NO	NO	NO	NO
- rehabilitation	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
- prevention	NO	NO	NO	NO	NO	YES	NO	YES	YES	NO	NO
others	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
Major achievements:											NO
- identification of new genes	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO
- screening systems	YES	NO	NO	YES	NO	NO	YES	NO	NO	NO	YES
- identification of biomarkers	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	YES
- validation of biomarkers	YES	NO	NO	NO	NO	NO	NO	NO	YES	NO	NO
- novel model systems	YES	YES	NO	YES	NO	YES	NO	NO	YES	NO	NO
- innovative therapies	NO	NO	YES	NO	YES	YES	YES	NO	NO	NO	NO
- new medical treatments	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
- new medical devices	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
- neurosurgical innovation	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
- Others		YES (molecualr tools)				YES (software)					

Table 7: Summary of outputs per project

REMARKABLE PROJECTS

Even if the majority of the projects performed adequately and produced the expected deliverables, a handful of projects were particularly remarkable in terms of their production. This section dedicates a brief paragraph describing the main outcomes of those projects beyond the publication metrics.

Lightpain. ES, IT, FR. The light pain project was aimed at developing photoactivatable ligands targeting selective metabotropic glutamate (mGlu) receptors, which represent promising drug targets for pain control. The partners produced subtype-selective positive and negative allosteric modulators for mGlu; that can be photochemically triggered by light.

The project partners produced not only the original caged compounds proposed but also photo switchable compounds capable of switching glutamate receptors on and off with light. The partners filled a patent with the produced compounds.

The new pharmacological tools were used to study the physiology of pain, and more than one of them showed analgesic effects when released in localised regions of the brain in animal *in vivo* models.

The new compounds were the base of new collaborations on brain research outside the pain field.

This project had been already highlighted as an ERANET NEURON success story in Lancet Neurology (https://doi.org/10.1016/S1474-4422(16)00026-0).

Microdeg. FR, DE, ES. The partners developed new methods to reconstruct controlled brain networks *in vitro* and used them to study Prion propagation of synuclein-related proteins.

The developed methods allowed a fine control of cell positions and axonal growth in rodent and human tissue and resulted in 2 publications and 1 patent submission. A biotech company was created to exploit the fulfilled patent.

The use of the developed technology allowed them to observe and report that synucleopathies can spread in human tissue resulting in the generation of biosafety decontamination associated to the manipulation of this material and the preparation of a publication on this relevant observation.

WM2NA. FR, CA, DE. The project conducted cross species imaging studies to identify white matter changes that correlate with anxiety and depression in adolescents.

The results of the consortium indicate a relationship between a history of stress and child abuse with impairment of myelinisation and white matter development. The results were communicated and resulted in adoption of prevention measures to this target group on national policy.

Annex I- Call Text JTC 2012 Excerpt

Call for Proposals for

"Novel Methods and Approaches towards the Understanding of Brain Diseases"

Submission deadline for pre-proposals: March 09, 2012

For further information, please visit us on the web

http://www.neuron-eranet.eu

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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, four transnational joint calls have been launched on different topics from 2008 to 2011. The fifth joint call has been focused on innovative methods and approaches towards the understanding of brain diseases. 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 (JCS).

- Austrian Science Fund (FWF), Austria
- Research Foundation – Flanders (FWO), Belgium
- Fonds de recherche du Québec-Santé (FRQS), Canada (Québec)
- Academy of Finland (AKA), Finland
- National Funding Agency for Research (ANR), France
- Federal Ministry of Education and Research (BMBF), Germany
- Chief Scientist Office, Ministry of Health (CSO-MOH), Israel
- Ministry of Health (MOH), Italy
- 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 and Innovation Funding (UEFISCDI), Romania
- Ministry of Science and Innovation (MICINN), Spain
- Institute of Health Carlos III (ISCIII) , Spain

2. Aim of the call

The aim of the call is to enable multinational collaborative research projects that address the developments and advances in methods and approaches to understand the brain and its diseases. The scope of this call is not the funding of technology development per se, and it does not lie within the funding of infrastructure. Research projects must be hypothesis-driven and combine cutting-edge technological developments with a clear, substantial research question. There is no sharp restriction concerning the specific methodologies or approaches used in the applications, although a clear justification is required that clearly shows why the approach/methodology is novel or that existing methodology will be applied to a new research area. These may include (without excluding others): Imaging techniques (including optical, MR and PET techniques), molecular, (epi)genetic and “omics” approaches, stem cells and neural differentiation in relation to cell therapy, gene targeting in the brain, molecular modelling techniques, electrical and magnetic brain stimulation, and behavioural and epidemiological methodology.

The ERA-Net NEURON funding organisations particularly wish to promote integrated methodologies and approaches and multidisciplinary work and to encourage translational research proposals that combine basic and clinical approaches.

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.

In any case 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 poi

Annex II- Questionnaire / Impact of the Project

Results of this questionnaire may be published in an anonymised way to give an overview of each call's general output.

Q.1 Publications and communications

*Please indicate the number of publications and communications in which NEURON support was **acknowledged**. Please do not mention publications anterior to the start of the project.*

Q.1.1 Number of publications and communications

Type of publication	Total N°
Peer reviewed articles	
Books or book's chapters	
Reviews	
Articles dedicated to general public	
Communications in scientific congresses	
Dissertations	
Others	

Add lines as appropriate

Q.1.2 List of publications and communications

Please list the publications that result from the funded project. Please group them according to the categories presented in the table above. In column 1, please underline the name of the NEURON-funded partners. In column 2, please point out the project partners involved by using the numbering applied in section I General information (e.g. partner 1 or P1).

Publication (authors, title, journal, year, issue, pp.)	**Partner(s)**	**Impact factor**

Add lines as appropriate

Q.2 Patents and other outputs with impact to health

Q.2.1 Number of patents, licences and other outputs

Type of patent or licence	N° Submitted	N° Obtained
International patents		
EU patents		
National patents		
Licences (of exploitation/cession)		
Creation of firm (enterprise)		
Other (specify)		

Add lines as appropriate

Q.2.2 List of patents

If details regarding patents need to be treated confidentially, please indicate as such.
In column 2, please point out the project partners involved by using the numbering applied in section I General information (e.g. partner 1 or P1)

Patent description	Partner(s) involved	Main partner (moderator)

Add lines as appropriate

Q.2.3 List of other outputs with impact to health

Please list below:

	Category: if applicable, please specify	Partner(s)
☐	software and other prototypes:	
☐	launching of a product or service, new project or contract:	
☐	creation of a platform available to a community:	
☐	creation of a firm, fundraising:	
☐	others (please specify):	

Q.3 Consortium – collaboration and sustainability

Please tick when applicable

Q.3.1 Have the partners participating in the NEURON project collaborated before applying for NEURON JTC 2011?
YES ☐ NO ☐

►**If YES**, please indicate the partner numbers of teams that previously collaborated:

……

Q.3.2 During the lifetime of the project has the consortium established collaboration(s) with other team(s) (not already participating in the JTC 2011 project)? YES ☐ NO ☐

►**If YES**, please name the institutions and countries:

…..

Q.3.3 Have the results led to new initiatives in other types of funding programmes (e.g. grants, grant applications) ? YES ☐ NO ☐

►**If YES,** please specify the partners who applied (partner numbers) and the corresponding programme (FP7, etc.) :

……

Q.3.4 Intensity of collaboration: Meetings, human mobility and training within the consortium

A. Collaboration meetings

Meetings involving at least two partners of the project (e.g. consortium meetings, WP meetings, workshops, or others)	**Partners involved**

Add lines as appropriate

B Young scientists' involvement in the project, training and mobility between partners
1. Please list academic staff involved in the project. Please also list postdocs, PhD students, master students, undergrad students…
2. Furthermore, please indicate if lab visits or longer-term exchanges between partners happened based on NEURON funding.

Partner #	**Career stage**	**Academic dissertation** (year, degree)	**Year of birth**	**Name, Gender**	**Exchange from / to** (country)	**Duration of Exchange** weeks / months
					From … to ...	

Q.4 Development of innovative or shared resources and technologies

Q.4.1 Has the consortium created a new or further developed an existing transnational…

Patient registry ☐ Patient database ☐ Biobank ☐ N/A ☐ ?

►**If YES, please complete** (repeat this section as many times as necessary):

- Name of the registry/database/biobank: ……
- How was the registrydatabase/biobank created?

  Totally new set-up ☐ By compiling national sources that existed already ☐

- How were new patients recruited?
  - Via already existing network of clinicians ☐
  - By the establishment of contact with NEW networks of clinicians ☐
- Please specify how the registry/database/biobank will be maintained/financed after the end of this projects ……..

Q.4.2 Have the consortium partners exchanged bioresources (DNA, tissues, cells, animals)?

DNA ☐ tissues ☐ cells ☐ animals ☐ clinical data ☐ N/A ☐

►**If YES, please specify:**

- Were there enough samples in order to reach the goal? YES ☐ NO ☐

- Have the samples allowed common studies? YES ☐ NO ☐

Q.5 Potential health impact / achievements

Q.5.1 Have the results of the NEURON research projects allowed the development of new strategies for:

- Diagnosis ☐
- Therapy (Preparation of clinical trials) ☐
- Rehabilitation procedures for neurodegenerative diseases ☐
- Prevention ☐
- Other (please specify) ……. ☐

Q.5.2 Please list the major achievements of the consortium

Achievements		Please specify
Identification of new genes	☐	
Development of innovative screening systems	☐	
Identification and characterisation of biomarkers	☐	
Validation of biomarkers		
Generation of novel model systems (animal models, cellular models)	☐	
Development of innovative therapies	☐	
New medical treatments	☐	
New medical devices	☐	
Neurosurgical innovation	☐	
Others	☐	

Add lines as appropriate