# ERA-NET NEURON

## PAN-EUROPEAN NEUROSCIENCE RESEARCH

neuron

Network of European
Funding for
Neuroscience Research

# EDITORIAL

*Marlies Dorlöchter, NEURON coordinator*

Late in 2003 five people, representing ministries and funding agencies from four countries, came together in a lovely restaurant in Luxembourg to debate over the chances and challenges of jointly promoting research into brain disorders. They had not met before but had one trait in common. They strongly believed that investigating the brain is the challenge of our society – a problem which requires international collaboration.

quired to address this task. The scientific questions need to span a wide range, from understanding the molecular mechanisms of a disease in cells or animal models up to developing diagnostic tools or clinical therapies in human studies. It became clear that it would take the best international scientists available to tackle the challenge.

And so, NEURON was born. The Network of European Funding for Neuroscience Research began with funding bodies from Luxembourg, Poland, Israel and Germany. The network was supported by 'glue money' from the European Commission, and kicked off in 2003. It took some time for the founding partners to set up the infrastructure and plan the details of their endeavor. From 2007 a fully fledged ERA-NET with 12 funding organisations was ready to begin their joint funding programmes

*»It is important to explain the importance of brain research, not only for understanding the basic principles of how our astounding brain operates, but also, and as important, for understanding the many devastating diseases of the brain (along with those working in the fields of psychiatry and neurology).«*

*Sten Grillner, Kavli Price Laureate, IBRO Secretary-General 2013–2016*

Disorders of the brain have become so commonplace now that almost everybody will know someone who suffers from one. Most of them cannot be cured. They considerably lower the quality of life of the affected individuals and impose a tremendous burden on society in terms of cost. But how can one develop therapies for diseases of an organ that is so poorly understood even when functioning normally? The challenges of unpicking the body's most powerful organ are huge.

Over dinner in Luxembourg it became clear rather quickly that the collaboration of researchers from many different biomedical disciplines is required and start unpicking the complexities and the wonders contained in the human brain.

Today, NEURON has grown even larger and has become a reliable source of research funding not just for Europe, but beyond. This issue comprises views and opinions by the NEURON partners, the foresight, and reviewing processes, the activities for Early Career Scientists (ECS) and details on the key elements, the Joint Transnational Calls. Something difficult to measure as success indicator but developed value is the trust among partners that persists to smoothen internationally different procedures and to make hard work much enjoyable for us.

# CONTENT

# 1 Development of the Network

In the Lisbon European Council in 2000 a concept of a European Research Area (ERA) was developed. It was the European Commission that suggested the creation of networks to coordinate the work of funding bodies and thus better contribute to the development of a European Research Area (ERA). This led to a clear shift in the evolution of the ERA-NETs in various scientific and societal fields as a new instrument funded by the European Commission (EU) to establish new types of co-operation between ministries and funding agencies. This was the dawn of the ERA-NETs.

One of the key objectives of ERA-NETs was and is the exchange of information as the initial step of a mutual learning process that will eventually lead to improvement of standards throughout partner countries and – as history and success proved - the highest level of cooperation and alignment among funding bodies: Joint Transnational Calls for proposals (JTCs).

Specific Support Action NEURON, **2003-2004**
- 4 funding organisations
- 4 countries

ERA-Net NEURON, **2007-2011**
- 18 funding organisations
- 13 countries

ERA-Net NEURON II, **2012-2015**
- 24 funding organisations
- 18 countries

ERA-Net NEURON Cofund, **2016-2020**
- 27 funding organisations
- 19 countries

In 2003, when the first ERA-NETs were started, the daily work of funding agencies and ministries was quite different from now. While for researchers in the life sciences, global collaboration has traditionally been a matter of fact, public funding programmes in many European countries were not linked across borders. The scientific officers responsible for these programmes often did not know their international counterparts e.g. for brain diseases in the other countries. This led to isolated programmes, fragmentation and duplication in research efforts.

## WHY NEURON?

Understanding the brain and its diseases is among the most exciting research areas of the 21st century. The brain is the most critical and mysterious organ, and is what makes us human. Brain disorders are a result of a complex interplay of genetic and environmental factors with often long-term burdens to patients, their relatives and society. Due to the demographic development in coming years the topic is highly important and relevant for health, and consequently funding is among the priorities in many European countries. Research is the key to unravelling the complexity of the brain and nervous system and the only hope for finding therapies and cures. Research into disease-related neurosciences gains enormously from an interdisciplinary approach, and it is nowadays unimaginable that important questions of brain functioning or progress on preventive, diagnostic and therapeutic measures could be achieved without the combination of methodology, skills and expertise from different scientific areas. The successful translation of research results into clinical application or the development of drugs and other therapeutic or diagnostic products needs to be tackled in multidisciplinary collaborations ranging from basic

*»We have been able to experience the efficiency, the high involvement with the NEURON goal and the intense, fruitful and pleasant meetings. Together we (Brain Foundation, ZonMw and NWO) believe that NEURON provides good opportunities to address important 'Research & Development' (R&D) issues in the field of neurological and psychiatric disorders at supranational level.«*

*Rob P. W. Heinsbroek, NWO, The Netherlands*

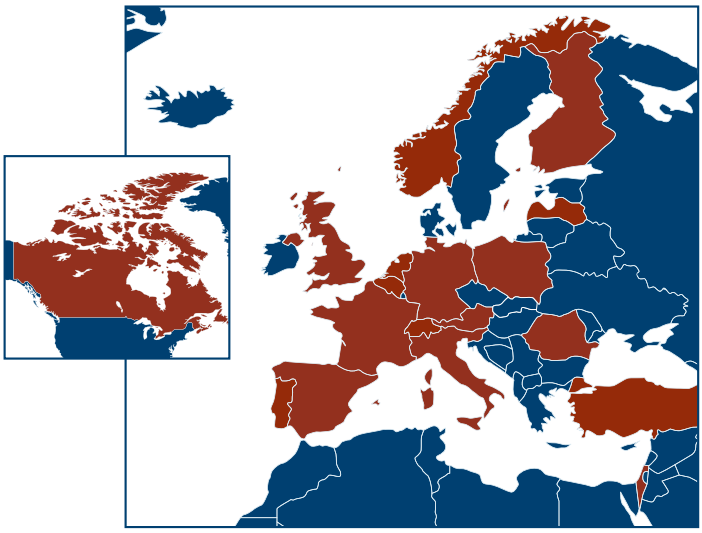
science to preclinical, and clinical research often involving high-end data generation, protection, evaluation, and storage and thus the request for (secure) information technology.

## A GROWING FUNDERS NETWORK

NEURON was launched in Luxemburg on October 9th, 2003 as a Coordination Action within the 6th EU FP on Research, Technological Development and Demonstration. It was during a small meeting with Luxembourg, Israel, Poland and Germany as the founding members. Fifteen years, twelve Joint Transnational Calls (JTCs), and about 500 funded research groups later NEURON has proven to be an extremely valuable tool for making the ends of innovative neuroscience and research funding meet.

Already four years later 18 funding organisations from 13 countries joined forces in ERA-NET NEURON. The development comprised several steps among which the spirit of common and mutual trust was not the least. In the August 2007 workshop on 'Cooperation Models' in Helsinki, cornerstones of a first joint call were discussed. Necessary documents like a 'Memorandum of Understanding, MoU' between funding agencies, and a 'Procedures'-text, detailing the application, reviewing and evaluation modalities of a joint call were consented. When NEURON aimed towards such ambitious goals, the preparations comprised exchange of knowledge about similarities and the variabilities among the partners of the consortium with regard to e.g. funding policies and philosophies, funding regulations, and best practices concerning review processes and program management. Funding of selected international projects should follow the virtual common pot model (see box, page 9). An in depth literature survey enabled the consortium to develop the joint concept for the

**12 JTCs since 2008:**
- 136 million € dedicated for funding
- 125 transnational research consortia funded
- 550 research groups (PIs) involved



first NEURON joint call for 'Proposals in basic and translational research into neurodegenerative diseases' in 2008, in which 12 countries participated. The topic of this first JTC 2008 was broad in order to address a considerable section of the neuroscience community.

Since 2012 the number of NEURON's partner funding organisations gradually increased to 27 from 19 countries, including Canada, which participated already since 2009 in the JTCs as non-NEURON partner. The main reason that European funding organisations - usually involved in national funding activities - consistently and in increasing number committed to NEURON, and thus making it one of the most successful networks of the ERA-NET scheme, is because of the key instrument of the NEURON, the JTCs. Under the umbrella of NEURON the last twelve JTCs addressed hot and cutting-edge scientific topics from mental disorders to method development and neurodevelopmental disorders. And the more funding organisations from different countries participate in a call the bandwidth of researchers that can apply in these JTCs increases.

*»Health issues are usually not limited to a single country, and often have an international character. NEURON takes international collaboration seriously.«*

*Ahmi Ben-Yehudah, Chief Scientist Office, Ministry of Health, Israel*

*August 2007, Neuroethic Symposium in Jerusalem, Israel*

What was set out in 2003 as a new manifestation of a cooperation spirit among funding bodies in the fields of disease-related neuroscience has been put forward as an almost fixed point in the European funding measure map. 125 international research consortia were or are currently funded, comprising 550 different research groups.

'Variable geometry' and 'virtual common pot' schemes: Some funding bodies focus on basic research while others prefer clinical research. Thus, together with foresight activities for relevant thematic specification of planned JTCs the research types must be individually considered. This is why, as in many other ERA-NETs, NEURON follows the **'variable geometry'** and **'virtual common pot'** schemes. Variable geometry means that for each planned call every partner may decide whether to participate or not. Taking into account national policies and – recently more sparse – available resources, there is no obligation to contribute to any JTC. 'Virtual common pot' reflects for an actual JTC the financial contribution a funding organisation can commit. Both parameters are for every planned call newly negotiated among the partners. Following a 'peer-review' scientific assessment procedure, each NEURON partner/country provides the necessary funds for the successful researchers from their own country resp. its own approved sub-projects, and there is no allocation of resources to a common pot.

## NEURON'S ACTIVITIES - MAKING ENDS MEET

Joint Transnational Call (JTC) management, detailed in Chapter 5, is the core activity of NEURON. These demanding tasks are carried out by a Call Secretariat, a rotating task that also serves as focal point for all relevant communication.

Monitoring is essential to evaluate the impact of NEURON investments in transnational research on brain-related diseases. The progress and outputs of the granted projects are monitored and summarized in so far four 'impact reports' that cover the JTCs 2008 to 2011. The results of the funded projects in terms of exchange, training, and publications bear witness for the supremacy of the scientific excellence criterion for the selection of proposals for funding. And monitoring and early career researcher support intentions match within the annual mid-term symposia. There the researchers of the funded research consortia meet the funders and present their ongoing work. Early career researchers of the participating research groups are invited by NEURON to attend and present their work with posters, and a poster prize is awarded. These MidTerm Symposia have proven indeed fruitful to further enhance exchange, cooperation and networking.

A continued dialogue between programme managers and a dedicated scientific advisory board (see Chapter 9) is necessary to keep track of the burning research questions and challenges in the field. In 2015 the Strategic Research Agenda (SRA) was developed by a group of international researchers who covered a broad range of expertise in fundamental neuroscience, neurology, psychiatry, and sensory organs. Annual scientific foresight symposia (see Chapter 10) address specific items of the SRA to identify future scientific research areas of high impact as possible call topics. Particularly the well-attended symposia make ends of science and funding policies meet to the greater benefit of research value. 15 publications on such foresight activities have already been released covering broad areas from new technologies in neurosciences to neurodevelopment and related disorders. It is important to identify priority topics that link the partners' national strategies to priorities and international strategies in the field of disease-related neuroscience research.

*Bonn, May 2014, Speakers and NEURON partners at the Foresight Symposium 'Synaptopathies'*

Outreach is one of the main activities of NEURON. Digital and print publications, video clips, an informative website, and, not at least, regular newsletters serve to make the outcome of NEURON's activities available to the broad public.

**28** newsletters have been published since 2008, and eight **(8)** educational video clips.

*Bucharest, May 2015, talk at the Foresight Symposium 'External Insults to the Nervous System'*

Since 2015 a special initiative broadens ERA-NET NEURONs activities, and that are JTCs on Ethical, Legal, and Social Aspects (ELSA) of Neuroscience (Chapter 11). Since the progress of neuroscientific research also impacts the understanding, and thus potentially also the control of human decision-making, behaviour, emotions, and social interactions, related research efforts to integrate the ethical, legal and social aspects are indispensable.

Early career scientist support is also a key element of ERA-NET NEURON's activities. The Excellent Paper in Neuroscience Award (EPNA) is an annual early career scientist award for the best paper in neuroscience. Usually the call is launched every May, and the awardee(s) is/are invited to present their work during a special lecture at a conference in the following year. In 2012, 2014 and 2016 the

Since 2009 nine **(9)** annual calls for the Excellent Paper in Neuroscience Award were launched for early career scientists, and since 2012 the awardee(s) are invited for a talk at the FENS FORUM of Neuroscience.

award ceremonies were organised as a specific session during the biannual FENS FORUMs of Neuroscience, attracting over 200 attendees. For the early career scientists this offers thus a great opportunity to address a large audience besides the honor of the actual award. Not surprisingly, the EPNA calls has become a prestigious award. Networking activities for early career scientists at the FENS conferences, and since 2017 the contribution to the highly reputated Cajal trainee courses add up to such dedicated activities.

*Early career scientists at the NEURON networking event. 10th FENS FORUM, Copenhagen, Denmark, July 2016.*


*Copenhagen, July 2016, ERA-NET NEURON's coordinator Marlies Dorlöchter opening the early career scientists networking event at the 10th FENS FORUM*

To make ends meet, the up-to-date 46 well-attended ERA-NET NEURON meetings since 2007 – including symposia and workshops - contributed a great deal to NEURON's success. The impact and success of the ERA-NET NEURON can certainly be accounted to the long standing partner's personal engage- and involvement. Not least, such history also witnesses the mutual and common trust that evolved during the years among the NEURON partners.

*Riga, September 2017, Joint Mid-Term Symposium of JTCs 2015: 'Neurodevelopmental Disorders' & 'Ethical, Legal, and Social Aspects (ELSA) of Neuroscience'*

# 2 NEURON partners: Key questions answered

**The Research Foundation – Flanders (FWO)** is an independent agency, founded in 1928, that supports fundamental research in all disciplines in Flanders. The FWO provides the necessary funding on the basis of an interuniversity selection with scientific excellence as the only criterion.

**The Centre National de la Recherche Scientifique (National Center for Scientific Research)** is a government-funded research organisation, under the administrative authority of France's Ministry of Research.

**INSERM** is the only French public organisation entirely dedicated to biological, medical and public health research.

**The Netherlands Organisation for Scientific Research (NWO)** is one of the most important science-funding bodies in the Netherlands and ensures quality and innovation in science.

**The Brain Foundation Netherlands** is doing everything it can to keep brains healthy, heal brain disorders, and improve patient care. To achieve this, it commissions research, provide educational information, and carry out innovative projects.

**The Medical Research Council (MRC)** is a publicly-funded organisation dedicated to improving human health. MRC supports research across the entire spectrum of medical sciences, in universities and hospitals, in their own units and institutes in the UK, and in our units in Africa.

The ERA-NET NEURON comprises 27 funding organisations from 19 countries, within or associated to the EU and also Canada as global partners. The motivations to join a funders's network, and the expectations on the outcome for the national science community in terms of interdisciplinary and translational research were the subjects of a discussion.

Participants were the following funding organisations: The Research Foundation Flanders (FWO, Belgium), the French National Centre for Scientific Research (CNRS, France), the National Institute for Health and Medical Research (INSERM, France), the Netherlands Organisation for Scientific Research (NWO, The Netherlands), and the Medical Research Council (MRC, United Kingdom). Representatives from the funding organisations were: Oliver Boehme and Toon Monbaliu from FWO, Bernard Poulain from CNRS, Etienne Hirsch from INSERM, Rob Heinsbroek from NWO, and Talisia Quallo from MRC.

**NEURON:** *What was your organisation's motivation to join NEURON?*

**INSERM and CNRS:** After World-War II, internationalization of research in neurosciences was initiated by International Brain Research Organisation (IBRO) with the aim at bridging western and eastern researchers. When the EU started its building up, our elders were organising the birth of the national societies and later their federation in Europe. For our entirely Post-World-War II generation, EU building up is our great challenge. The brain research challenges are so huge that not any single country can solve the problems, individually. The birth of the ERA-NET NEURON coincides with a new age of maturity for Europe of Research, which hallmarks are 'sharing and coordination': sharing ideas (has already done in the frame of

the European associations), coordinated lobby (European Brain Council, EBC) and identification of priorities, and, last but not least, sharing the individual funding from member states via their funding agencies partners of the ERA-NET. Joining NEURON is our modest contribution to organisation of European brain research and sharing the resources and expertise.

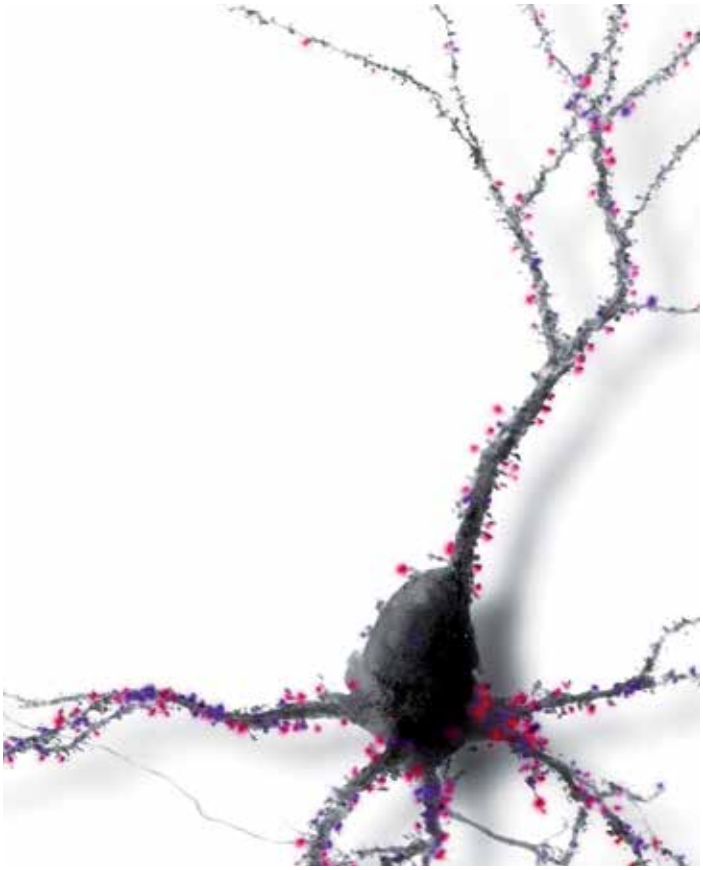
**FWO:** The Research Foundation Flanders decided to join the NEURON after performing a consultation round amongst its national/regional stakeholders. This process identified a significant interest in the research community for this particular thematic field. The possibility for our national/regional researchers to coordinate their research with both European and international experts in the field, by collaborating with them on an extensive basis are an important incentive and lead to cross-pollination and mutually beneficial outcomes for all parties involved.

**MRC:** The goals of NEURON, to understand, prevent and treat disorders of the nervous system, align with those of the Neurosciences and Mental Health Board of the UK's Medical Research Council (MRC).

*»NEURON provides excellent opportunities for European researchers to engage in crossborder research projects that address important neuroscience research questions.«* *Talisia Quallo, MRC, UK*

**NWO:** Ever since initiation of NEURON (I) the Dutch organisations ZonMw and NWO were aware of its existence. Not merely on account of the NEURON website and other forms of NEURON messages, but primarily because neuroscientific and clinical researcher knocked on our doors requesting to start joining the ERA-NET NEURON. Our research community clearly appreciated the NEURON work and calls as very relevant. When NEURON Cofund was applied for, this clearly felt a good opportunity to step in. Very helpful was also the possibility to team up with the Dutch Brain Foundation: from NEURON Cofund onwards ZonMw, The Dutch Brain Foundation and NWO collaborate in NEURON.

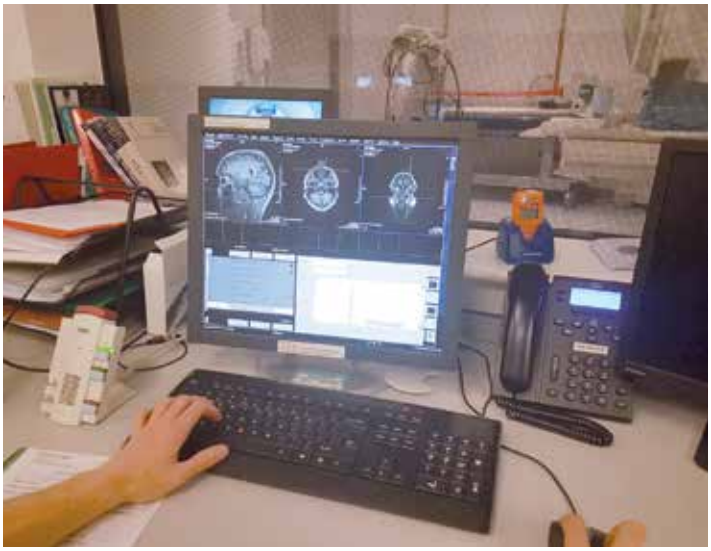
We have been able to experience the efficiency, the high involvement with the NEURON goal and the intense, fruitful and pleasant meetings.



*A labelled neuron*

Together we (Brain Foundation, ZonMw and NWO) believe that NEURON provides good opportunities to address important Research & Development issues in the field of neurological and psychiatric disorders at supranational level. Some of these are: bridging preclinical and clinical work; involving patients; addressing the manifold of brain disturbances of which by and large we have as of yet limited understanding; elevating the quality and reproducibility of research findings; lobby for more attention for brain disorders.

*MRT scanning preparation*



*MRT scanning observations*

**NEURON:** *How do you see the work of NEURON progressing in the future?*

**FWO:** We hope to see the NEURON-network continue its work, as efficiently and straightforward as it has been working for the past fifteen years, under the European 'Research and Innovation' umbrella. We encourage further internationalization of the network, without losing the primordial European dimension out of sight.

**INSERM and CNRS:** NEURON Cofund is more and more inclusive. Working with the professional and lay organisations is a major asset of the new program. It is closer to citizen demand and need; it will give us more legitimacy and help the funding organisation to spend their money where it is really needed.

**MRC:** The MRC hopes that NEURON will continue to address questions in neuroscience areas where there is an unmet international need for research, bringing together knowledge, skills and resources from across national borders.

**NWO:** NEURON is firmly established and has clear plans for fulfilling its promises and perhaps even more as new points of possible improvement are also picked up along the way. We hope the strengths of NEURON could be continued in a NEURON variant beyond 2020. Strengths are its high level of procedural organisation, its openness to new ways to improve, the trust in each other and in the collaboration, and its potential to organise funds, and transforming these to high quality research. It would be of interest to see how these strengths could be turned on potential new areas of interest. We could for instance discuss a focus on mental disorders and acknowledge that translation work and mental disorders have their very specific characteristics. NEURON could start already with joining up with the many but scattered parties trying to improve attention for this much underrated issue. If this could lead to new funds in for instance the next Framework Programme, the NEURON (follower) could start to evolve to be the

preferred party to execute the related calls. Along this line of lobby and development NEURON could also be the starting point for a new Joint Programming Initiative on mental disorders.

**NEURON:** *There is a large consortium behind the NEURON - what are the benefits or challenges of having so many members as part of the consortium?*

**INSERM and CNRS:** The next challenge of NEURON is to grow to include more European countries in the future but on the other hand to have scientists from all countries participating in the research consortia. We believe that NEURON will encompass all Europe. Including more countries if they are well integrated will make NEURON stronger *vis a vis* of the EU decision makers. On a longer term, NEURON foresight workshops may be the right place to think about what will be in the future the right size (if any!) of collaborative projects.

*Labelled hippocampus*

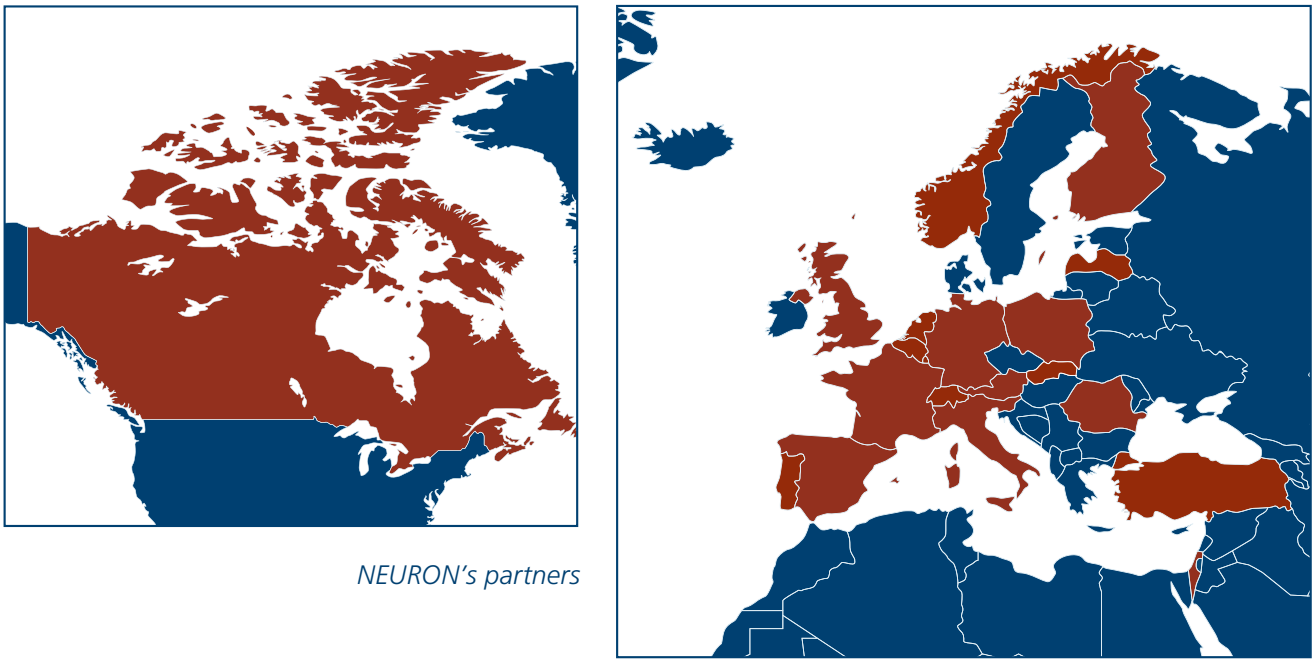
*»Another clear advantage is the broad and variable experience that is available through the many partners and partner countries that participate.«*

*Rob P. W. Heinsbroek, NWO, The Netherlands*

**MRC:** The benefits of working in a large consortium are that it brings together the knowledge and expertise of national research communities and harmonises national research efforts.

**NWO:** Benefits are many, see already what is mentioned under the above two sections. Another clear advantage is the broad and variable experience that is available through the many partners and partner countries that participate. This presents a rich source of do's and don'ts for all. Similarly, when NEURON decides to pick up a new point of possible improvement, one or two more experienced countries are more likely to be found, making efficient progress for the whole feasible. Concerning challenges, collaboration is always also that. In NEURON we experience that a high number of participant *per se* need not be more complicated.

# 3 The global perspective: NEURON's Canadian partners



*NEURON's partners*

The ERA-NET NEURON aims to create a 'European Research Area' (ERA) in which research is conducted and funded across countries, allowing research groups to jointly work on specific problems, exchange ideas, and benefit from cross border expertise.

Canada is one of the closest and longest-standing partners of the European Union. Already in 1976 the European Union's (then the European Economic Community) formal cooperation with Canada concluded a Framework Commercial and Economic Agreement with Canada and opened its overseas diplomatic mission in Ottawa, which at the time was its third worldwide. And since 1996 a Scientific and Technological Cooperation Agreement existed between Canada and the EU. Cooperation under the agreement is strong and focuses mainly on marine research in the Atlantic and the Arctic, health research, aeronautics and ICT research, agri-food and biotechnology as well as cooperation on research infrastructure and researcher mobility. Both Canada and the European Union favour multilateral solutions to international problems.

Canada joined NEURON by participation of two funding organisations – the CIHR and the FRQS – in the Joint Transnational Call 2010. Due to the variable geometry strategy and virtual common pot scheme such participation was rather simple and could not have begun at a better time. Science was already in a period of growth beyond the European geographical boundaries and researchers on both sides of the Atlantic benefit from the possibility of common research consortia. Especially the high numbers of participating research teams from Canada and their success in JTC 2010 (on 'Mental disorders') proved the importance of transnational collaboration with excellent researchers even beyond the ERA to meet the global challenge of combating diseases of the brain and nervous system.

**The Fonds de la recherche en santé du Québec (FRQS)** is the funding agency for health research in the Province of Québec and reports to the Minister of Economic Development, Innovation and Export Trade. Its mandate is to promote and provide funding for research, to disseminate knowledge, to train researchers, and to establish the partnerships required for developing Québec's research and innovation system and the international reach of Québec research.

**FRQS** is part of NEURON since 2010. The main motivation to join NEURON was our interest in working with the best research teams in Europe and to strengthen links between Quebec and Europe. It also gave us the opportunity to have a role and an impact in setting an international research agenda in neurosciences.

*»The impacts of being a member are numerous in terms of improved networking with Europe, facilitated involvement in international partnerships, greater opportunities for our students for example.«*

*Anne-Cécile Desfaits, FRQS, Canada*

In the future, we see NEURON as the catalyst of long term international collaborations for the scientific community at large and more precisely for the trainees. Being part of a network with so many members is quite challenging but we learned a lot about different cultures and approaches and it is surprisingly easy to always come up with a consensus.

The **CIHR**, through the Institute of Neurosciences, Mental Health and Addiction (INMHA), has been a partner on ERA-NET NEURON since the 2010 joint transnational call.

*»ERA-NET NEURON is significant Canada-Europe collaboration for CIHR, and was the first ERA-NET that CIHR engaged with as a funding partner.«* *Eric Marcotte, INMHA , CIHR, Canada*

The benefits to the Canadian neuroscience research community through this funding collaboration are considerable. ERA-NET NEURON provides a means to help directly support Canadian researchers and their European colleagues, with joint recognition from all supporting funding agencies. In addition to strengthening international research collaborations, participation on ERA-NET NEURON also provides exposure to broader research environments. This includes opportunities for Canadian researchers to serve as peer reviewers on other European calls, as well as international workshop participants.

CIHR-INMHA serves a very broad research community, across diverse mandate areas. Given the breadth and scope of this community – and our limited strategic (targeted) funds – we focus largely

**Canadian Institutes of Health Research (CIHR)** is the Government of Canada's agency for health research. CIHR's mission is to create new scientific knowledge and to enable its translation into improved health, more effective health services and products, and a strengthened Canadian health-care system. The Institute of Neurosciences, Mental Health and Addiction (INMHA) supports research that enhances knowledge of the brain, mental health, neurological health, vision, hearing and cognitive functioning.

on areas of research strength or needed capacity development in our domestic programs. The diverse nature of topics across ERA-NET NEURON funding calls allows us to be responsive to different segments of our research community over successive calls – that may not be well served domestically.

*»In summary, being part of NEURON helped us to move forward with more far-reaching programs.«*

*Anne-Cécile Desfaits, FRQS, Canada*

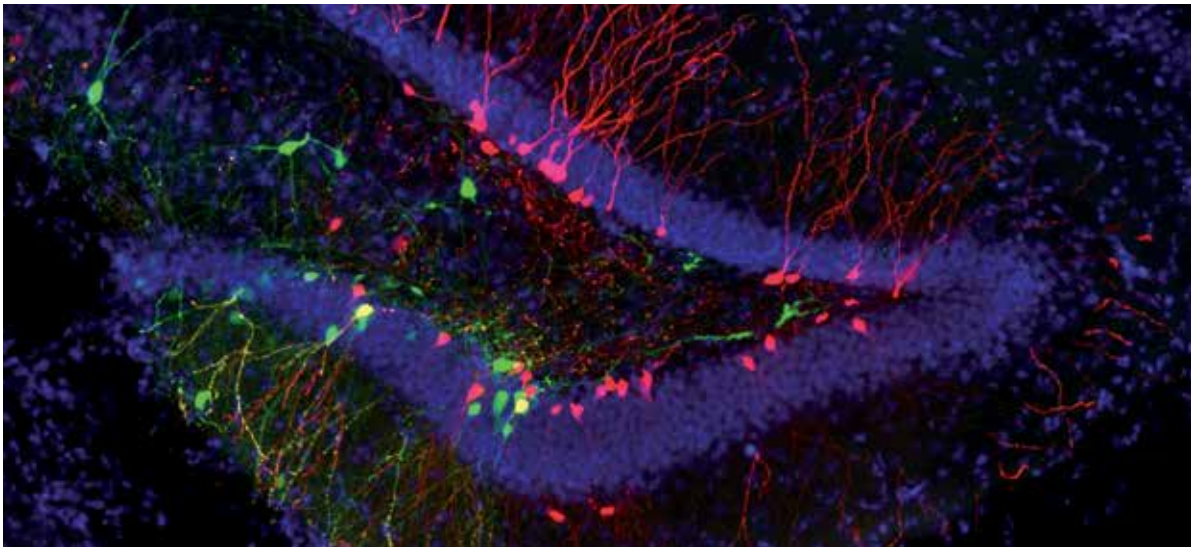
The sharing of best practices between agencies for program design, delivery and evaluation is also of great value. We all value our close working relationship with our ERA-NET colleagues.

In the Joint Transnational Call 2016 on 'External Insults to the Nervous System' also the Ontario Neurotrauma Foundation (ONF) participated due to their interest in projects on spinal cord injury.

**The Ontario Neurotrauma Foundation (ONF)** is the non-profit organisation funded by the Ontario government that works to prevent neurotrauma, and to ensure Ontarians with neurotrauma lead full, productive lives. ONF is the leader in moving research to evidence-informed practices and connects health care practitioners, researchers, stakeholders and policymakers to the information they need about neurotrauma prevention and health practices through regional, provincial, national and international collaborations and partnerships.

*»The close interaction with colleagues in European funding agencies has also facilitated the rise of direct bilateral and multilateral funding calls between CIHR and other funding agencies, on topics of joint interest.«*

*Eric Marcotte, INMHA, CIHR, Canada*



*Labelled hippocampus*

# 4 EU associated NEURON partners

As EU associated countries Israel, Norway, Turkey and Switzerland participate in ERA-NET NEURON. Whereby Israel, or rather the Chief Scientist at the Israeli Ministry of Health (CSO-MOH) was one of the founding members of NEURON, Norway by its Research Council of Norway (RCN) and Turkey via the Scientific and Technological Research Council of Turkey (TUBITAK) have joined the network in 2016 as partners. The Swiss National Science Foundation (SNSF) joins individual Joint Transnational Calls through the variable geometry scheme wherever the chosen topic of the JTC matches to the national roadmap.

The motivations for funding organisations to join the ERA-NET NEURON may be manifold. Certainly, the solid background of an established network serves as reputation, as in the words of R. Emrah Cevik (TUBITAK):

*»The NEURON project has been ongoing since 2004. This was a positive indication for our organisation that NEURON is very well established and experienced in both funding procedures and in promoting Neuroscience.«*

But the major motivation for countries and their funding organisations to join NEURON is the added value in terms of collaborations internationalization of the national communities and the enhancement of the ability to conduct cross-border high level neuroscience research.

As Ahmi Ben-Yehudah put it:

*»The CSO-MOH is one of most important funding organisations in Israel in the field of Bio-Medical translational research. CSO-MOH strives to fund all fields of research and maximize the little funds it has to promote the better understanding of disease etiology, preventive medicine, the development of better diagnosis and treatment as well as the development of rehabilitation programs, all to enhance the health of the Israeli citizens as well as all humans.«*

TUBITAK mainly

*» … aims at our national researchers' collaboration with other researchers within the ERA and Canada in order to support Neuroscience in the country and to enlarge its network.«*

*Recep Emrah Cevik (TUBITAK)*

In this regard is it indeed very positively perceived that NEURON consists of more than twenty partners from different countries.

The **Chief Scientist** is appointed by the **Israelian Minister of Health** to counsel the Minister on matters concerning medical research. Hence the Office of the Chief Scientist (CSO) is an important junction point for all issues concerning medical research in Israel and its advancement.

*»This gives the opportunity to our researchers to collaborate with many different research groups.«* *R. Emrah Cevik (TUBITAK)*

*»Joining NEURON allows the Israeli researchers to utilize their knowledge and develop collaborations with scientists in Europe and beyond.«* *Ahmi Ben-Yehudah, (CSO-MOH)*

*Vice versa,* scientists of all partner countries are involved in the development of the Strategic Research Agenda (SRA) thereby providing input to the roadmap of the future most important aspects of Neuroscience. Thus,

*»... In addition to enhancing the ability of Israeli researchers to conduct research in the field of Neuronal research, CSO-MOH joined NEURON to better coordinate research programs in Europe. Understanding where the field of Neuroscience is heading enables us, on the national level, to lead national programs in the field.«* *Ahmi Ben-Yehudah, (CSO-MOH)*

And not least,

*»CSO-MOH sees an important of its mission to promote science to our lay constituents. Hence, we have also taken ourselves the role of disseminating the achievements of NEURON, through newsletter, short videos and more.«*

*Ahmi Ben-Yehudah, (CSO-MOH)*

**The Research Council of Norway (RCN)** is a national strategic and funding agency for research activities, and a chief source of advice on and input into research policy for the Norwegian Government, the central government administration and the overall research community. It is the task of RCN to identify Norway's research needs and recommend national priorities.

The **Swiss National Science Foundation (SNSF)** has mandated the SNSF to fund research and promote young scientists in Switzerland. The SNSF's strategy and objectives are geared to fulfilling this task and strengthening Swiss research as a whole.

**The Scientific and Technological Research Council of Turkey (TÜBITAK)** is the leading agency for management, funding and conduct of research in Turkey. It's mission is to develop scientific and technological policies and in cooperation with all sectors and contribute to establishment of infrastructure and instruments to implement said policies.

NEURON partners see the importance of a network such as NEURON in the promotion of neuroscience and the enhancement of the ability to conduct high level research. Common sense is the understanding that:

*»We see the enhancement of promoting cross-border high level neuroscience research one of the most important goals of NEURON, and therefore, see ourselves as part of the network in the future.«*

*Ahmi Ben-Yehudah, (CSO-MOH)*

# 5 NEURON's advanced Origami of Joint Transnational Calls

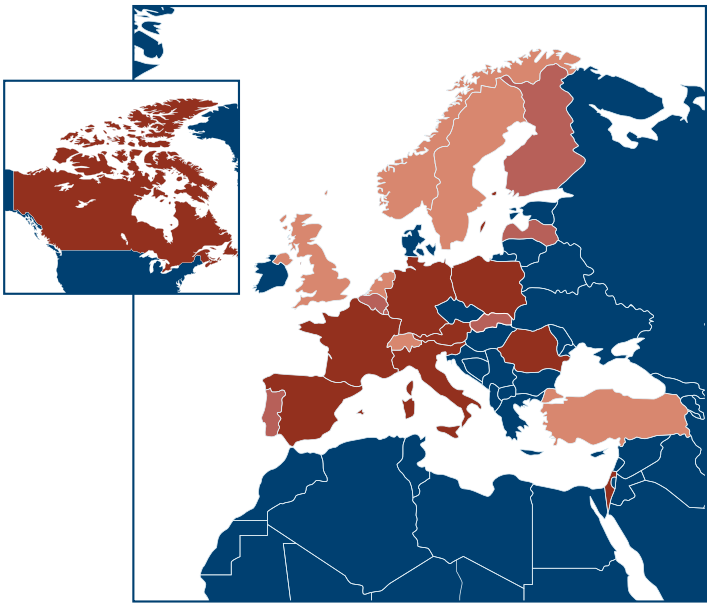
## NEURON'S ADVANCED ORIGAMI OF JOINT TRANSNATIONAL CALLS

The planning and execution of joint transnational calls for proposals is like high level Origami. Starting from a single piece of paper two-dimensional or three-dimensional objects can be created with every fold in its perfect position. When NEURON created in 2003 a strategically operating group of research funding organisations in Europe and beyond advanced Origami was begun to implement research funding programmes in the area of brain diseases.

**NWO,** The Netherlands: "NEURON provides good opportunities to address important research issues in the field of neurological and psychiatric disorders at a supranational level. Some of these are: bridging preclinical and clinical work; involving patients; addressing the various brain disturbances which we have until now limited understanding of; elevating the quality and reproducibility of research findings; lobbying for more attention for brain disorders."

When asked about the reasons for engaging in NEURON's joint transnational calls (JTCs) Sheyla Mejia (French National Research Agency, ANR) put it this way: 'Brain research challenges are so huge that no one single country can solve the problems individually.[…] Joining NEURON is our modest contribution to the organisation of European brain research and the sharing of resources and expertise.'

The French contribution, like so many other countries and research foundations has remained substantial and consistent. Over the past 15 years many EU member states, EU-associated countries as well as some countries outside Europe, have been involved in NEURON's JTCs, 21 countries in total. Together, these NEURON partners have reliably contributed substantial efforts and money to support top-notch research projects (Fig Countries). They have committed about 135 m€ of their national budgets to the NEURON programme. Due to the complex funding scheme, not the entire allocated budget can be spent in any single JTC, and to-date, the total budget distributed in grants amounts to more than 112 million Euros. The European Commission contributed part of the budget of the so called co-funded call of 2016.



*Countries involved in NEURON. The color code depicts the frequency of a country participating in joint calls. Light red up to 4 times, medium red 5-7 times, red 8-10 times.*

| JTC | Topics | # Projects | # PIs |
|---|---|---|---|
| 2008 | Neurodegeneration | 12 | 45 |
| 2009 | Development and advancement in methods and technologies | 10 | 43 |
| 2010 | Mental Disorders | 11 | 47 |
| 2011 | Cerebrovascular Disorders | 10 | 42 |
| 2012 | Novel Methods and Approaches | 11 | 47 |
| 2013 | Mental Disorders | 12 | 46 |
| 2014 | Neuroinflammation | 10 | 43 |
| 2015 | Neurodevelopmental Disorders | 10 | 42 |
| 2015 | ELSA of Neurosciences | 5 | 17 |
| 2016 | External Insults to the Nervous System, Neurotrauma | 19 | 92 |
| 2017 | Synaptic Dysfunction in Disorders of the Central Nervous System | 12 | 59 |
| 2017 | ELSA of Neurosciences | 3 | 11 |

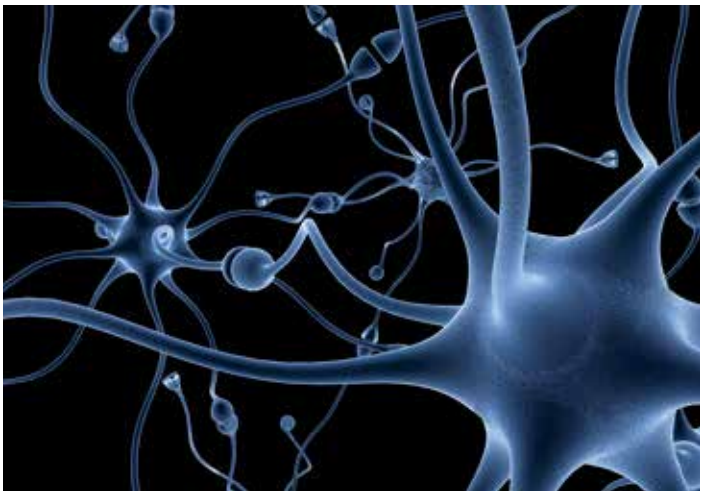
*NEURON's annual joint calls. Number of funded transnational projects and principal investigators (PIs) in each call. Funding period is color coded in blue: NEURON I: 2008-2011, NEURON II 20912-2015, NEURON Cofund starting 2016.*

## DEFINING CALL TOPICS - WHAT ARE THE PERTINENT RESEARCH QUESTIONS?

The annual JTCs form a key element of the ERA-NET NEURON and essentially provide its backbone. To foster an ever growing and improving scientific community, such regular funding opportunities are crucial. Each year a different area of disease-related neuroscience is addressed to meet current research demands.

Setting the relevant call topics is essential to make ends of science, patients and funders alike meet. To achieve this, 'hot topics' from different research communities as well as national agendas and international strategies in the field of disease-oriented neuroscience research need to be considered and aligned (see Chapters 9 and 10). Topics of continuous high priority have been repeated over the years - such as Mental Disorders (JTC 2010, JTC2013). Again another special interest – Neuroethics - even formed a new branch of funding. Rapid progress in biomedical research has an important impact on society and raises a number of legal and ethical questions. Hence, NEURON implemented two calls dedicated to Ethical, Legal, and Social Aspects (ELSA) of Neuroscience complementing NEURON's biomedical calls (see the ELSA chapter 11).

The road mapping of current and emerging hot topics in disease-related neuroscience was carried out in 2015. A strategic research agenda (SRA) was created by NEURON's Scientific Advisory Board in collaboration with a group of additional experts. This SRA sets the framework for the future NEURON activities. Encouragingly, patient organisations and professional societies expressed their positive opinion about NEURON's SRA (see 'Feedback from Professional and Patient Organisations' - SRA II) motivating NEURON to further develop its policy in this spirit (see Chapter 9).



## JOINING FORCES INTERNATIONALLY - WHO IS PARTICIPATING THIS YEAR?

NEURON brings together funding organisations across Europe and beyond (see map p. 21). The joint forces of NEURON partners make it possible to unite research groups in transnational consortia in order to strengthen the exchange of knowledge and resources.

Each year, the constellation of participating partners will vary slightly. Each funder decides on the participation in the JTCs based on national policies and available resources. This flexibility of commitment is referred to as 'variable geometry' (chapter 1). The openness of the variable geometry facilitates the involvement of a large number of partners in various JTCs.

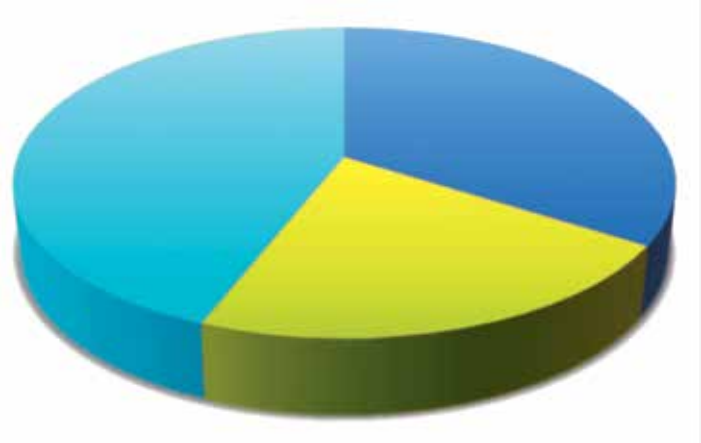
Once partners commit to partake in a call, the individual national budgets are negotiated among the partners to establish the 'virtual common pot'. This means that grants for the successful applicants are provided by the researcher's own country.

*»The ERA-NET NEURON funding format was acknowledged by all participant researchers as an excellent and unique measure to allow transnational collaborations without the high level of administration and management that is usually required by EU projects. With the help of the ERA-NET funding, we were able, for the first time, to engage in an intensive exchange of ideas, plan common research projects and keep each other updated in a timely manner on current findings and results. This fostered a transparent and effective collaboration.«* *Julia Stingl, JTC2013 consortium BrainCYP*

## THE MIX AND MATCH OF EXPERTISE - INTERDISCIPLINARITY IS CRUCIAL TO EFFECTIVELY EXECUTE HOT TOPICS IN NEUROSCIENCES

In the NEURON funding scheme, scientists have the opportunity to find optimal collaborators in order to tackle their specific research questions across borders. Required expertise and resources be it of a specific discipline or a particular method can be added from a significant number of countries. Naturally, many consortia are based on already established and known collaborations. Nevertheless, new collaborators are often incorporated. In fact, this mixed constellation of old and new collaborations is the prevalent form. But even completely new consortia may assemble with a shared vision and be successful: More than a third of the funded consortia in NEURON I were newly built!

- 34% newly formed consortia
- 22% pre-existing consortia (all PIs)
- 44% partial pre-existing consortia



*Initiation of new collaboration. 14 consortia in NEURON I were composed of partners who had not collaborated before (34% new consortia). Often, partners had previously collaborated (pre-existing). Either some or all partners were involved in previous collaborations in 44% and 22% of consortia, respectively, albeit in different subsets and in no case in a single consortium.*

Building a functioning consortium takes a lot of effort and requires good communication and organisation. Overly large structures may hamper the collaborative effort. Hence, NEURON focuses on small to medium sized consortia, comprising between three and six partners from at least three different countries.

An impact analysis of the first four NEURON JTCs shows that the funded collaborations are sustainable: Overall, almost half of the consortia reported that at least a subset of the research partners jointly applied for further funding, and also acquired new researchers during the lifetime of their project.

*»NEURON allowed us to set an excellent consortium that included not only scientists from Europe, but an excellent researcher from Canada. […] Importantly, we had a combination of basic researchers and M[edical] D[octors]-investigators in our consortium. This is especially important for future translational work.«* *Ari Waisman, JTC 2014 consortium MELTRA-BBB*

## MID-TERM SYMPOSIA - BRINGING TOGETHER RESEARCHERS AND THEIR FUNDERS

Once a project starts, it may come across obstacles along the way. The national funders and the joint call secretariat support the PIs where possible, on a case-by-case basis. Yet, it is important for the secretariat to keep an eye on the bigger picture when monitoring the projects' progress. Researchers in different consortia might be dealing with

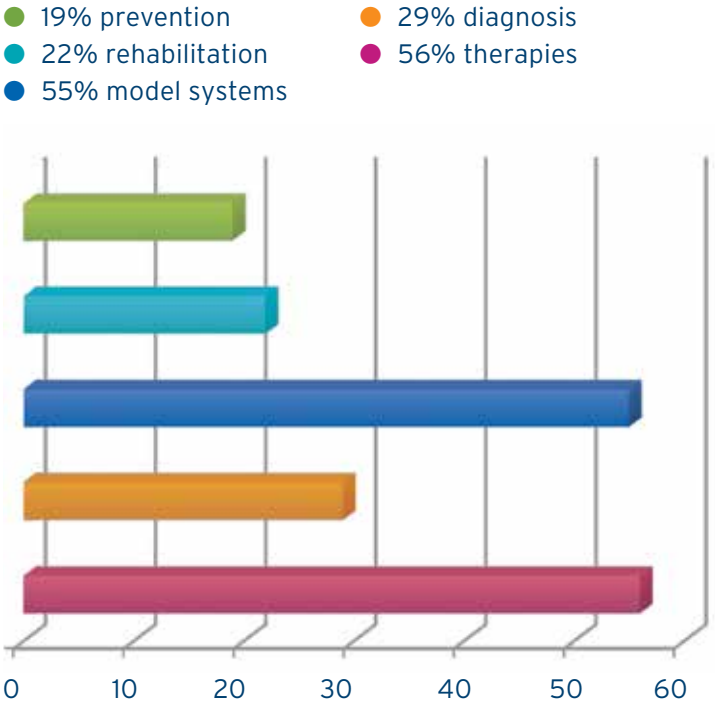
similar challenges and can often learn from one another. To this end, after about one and a half years after project start, all PIs of the funded projects in a given year and the funders gather in a large symposium. They discuss the progress and achievements of the projects as well as obstacles encountered during the first half of the project run time. To help funders assess the projects' developments, members of the original review panel are invited to attend the symposium.

*»I very much welcome the idea of bringing together research projects from the neurosciences and from the ELSA of neuroscience [at a Mid-term symposium of the JTCs 2015]. I hope that this meeting has approached the two and allowed for interesting cross-disciplinary learning and contact. Future meetings of this sort would be even more productive if structured parallel sessions would specifically address topics of cross-disciplinary work, e.g. training of young scholars, joint publication, or knowledge translation.«* *Ralf Jox, JTC2015, consortium INTERFACES*

The doctoral students and postdocs working in the funded projects participate in the symposium and network with peers and senior researchers alike. They present their work in a dedicated poster session, highlighted with a poster prize. This is an event that is greatly enjoyed by the early career scientists as a 'great opportunity to meet the people from the other consortia'.

## DRIVING INNOVATION - ACHIEVEMENTS AND IMPACT OF NEURON FUNDING

The path from bed to bedside is a long and stony one. Research results rarely translate into an immediate cure or a new powerful treatment. They can, however, make important contributions to progress in this endeavor. Hence, collaboration of biomedical researchers with clinicians, on molecules, animal models and patients is essential – this is a hallmark of so many projects funded under the umbrella of NEURON. In the long run, the results from these projects help patients, their carers and families whose quality of life is so heavily impaired by disorders of the brain. Some exemplary accomplishments already made.




*Development of new strategies in therapies, diagnosis, rehabilitation and prevention, and new model systems in the first four NEURON calls (NEURON I). Results obtained by the consortia are promising to lead to new approaches and medical application.*

NEURON provides a basis for innovative approaches building stepping stones on the way to clinical application:

*»We have shown a proof-of-concept of analgesic molecules that are adjustable to a time and specific localization to show new ways to treat pain. This can be a new and radical view of drug therapeutics. Patients can benefit by a precise personalized dose adjustment and a reduction of side-effects.«*

*Amadeu Llebaria, JTC2012 consortium LIGHTPAIN*

NEURON's calls for proposals receive a wide response from the scientific community and hence are highly competitive. This requires an elaborate selection process (See chapter 8) and results in the funding of only the most promising and excellent projects.

In the first 4 NEURON JTCs, more than 750 articles were published in relevant scientific journals including high impact journals like Nature and Science, and more than 20 patents were issued.

In the long run, funding of excellent research projects by NEURON will help the patients and their carers and families whose quality of life is often heavily impaired by the many disorders of the brain. Research is crucial and international collaborations between research teams through direct support to transnational projects are facilitated by NEURON JTCs. For each call the NEURON partners do not follow a beaten path but set out for a new round of advanced Origami.

To date, within the NEURON calls 125 research consortia have been funded, comprising more than 550 research groups. NEURON is confident that from further calls exciting projects and results will arise.

*Microscopic analysis of a brain section*

*»The translational significance of our project may be located at the complex interface between drug safety and drug side effects and models of mental health in clinical practice. A deeper knowledge on the local brain metabolism of drugs will help to avoid side effects of drugs acting in the brain. [..]«* *Julia Stingl, JTC2013 consortium BrainCYP*

# 6 Cross border research collaboration and networks

*Uldis Berkis*

## EU-13: THE LATVIAN PERSPECTIVE

In general, EU-13 countries have had long-standing, some more than 20 years, bilateral and trilateral international scientific programmes. These programmes have been highly successful measured by the outcome indicators, and are well known to the scientific communities in the EU-13. On becoming associated with the EU and later Member States, the EU-13 also became part of EU Framework programmes (of the European Commission). Since they are exposed to competition from other eastern European countries with different rules and research fields and strategies, the 'marketplace' idea of Framework Programmes is clearly not just a scientific, but also a kind of socio-cultural challenge for the new entrants – be they scientific administrations or individual researchers. The research communities in eastern EU countries are used to a system that is not so 'market-dependent', but rather has a system of scientific schools and long-term programmes supported by substantial public funds. It is not obvious to us that this strategy is inferior to the market ideology in science.

Latvia has been an active participant in the ERA-NET scheme, along with the other EU-13 countries. The country's participation has always been viewed as important because these member-state-based initiatives are transparent, and funding bodies are involved in the processes. Once Latvia gained a better understanding of the modus operandi and took an active involvement in strategic planning it found they became better integrated in the European Research Area. The ERA-NETs provided some (still limited) budgets and tools to build the research communities. Latvia first joined NEURON in 2007, but was not able to join the NEURON-II consortium because of the economic crisis. After the normalization of the situation in Latvia, the country participated in NEURON-II as an associated partner.

Many EU-13 countries have a comparatively small neuroscience community without large European or international networks. That is why supportive measures for better integration are vital, and we feel that NEURON has worked effective to actively implement a 'widening scheme' with specific measures.

**The State Education Development Agency** (VIAA) is an institution which is subordinated to the Ministry of Education and Science of Latvia.

One of the main problems of the ERA-NET network can be a lack of dynamism in some research communities and research ecosystems. Sometimes, our experience has been that scientific excellence can encourage monopolistic structures in science. From our active participation in NEURON we are expecting to improve collaborative ties between research teams, and to promote joint projects, even beyond the ERA-NET scheme.

*»We would clearly like to continue in an ERA-NET format such as NEURON. Latvia has a sound basis for participation in ERA-NETs based on its governmental agency acting as the funding body; this means that it is able to fund all projects recommended for funding based on substantial budget flexibility. The ERA-NET format is simple, understandable, and also inclusive.«* *Uldis Berkis, VIAA, Latvia*

What could be improved is the networking between researchers involving newer teams and young investigators, putting some funds aside for brokerages and an on-line platform for partnering. It is not obvious that in the present EU situation the Framework Programmes will continue to grow in size. Therefore member-state initiatives will gain importance.

Another benefit of NEURON is that the funded projects tend to deal with biomedical basic research which fits with the training activities for PhDs and postdocs, at the same time as being research projects in their own right. The EU-13 are extremely dependent on structural funds for their research funding, but structural funds are often oriented towards research and innovation strategies for smart specialization (RIS3), and are for funding of applied research or purely human resource development activities. The NEURON research projects are thus able to cover the gap in the funding landscape across the EU-13.

*By Uldis Berkis, representative of VIAA in the ERA-NET NEURON*

## PARTICIPATION OF SAS IN NEURON - THE SLOVAKIAN PERSPECTIVE

The Slovak Academy of Sciences (SAS) was motivated to join the ERA-NET NEURON because it provided an excellent chance for allowing Slovak researchers to cooperate with their counterparts in Europe on a variety of brain research topics. Based on the latest activities and achieved results, we greatly appreciate the work of the NEURON consortium.

**The Slovak Academy of Sciences** (SAS), a governmental research organisation, is the recognized leading research and scientific institution in Slovakia. The SAS as a funding body supports those scientific disciplines which have attained international level and which are deemed necessary for the advancement of Slovakia.

SAS officially became a member of the NEURON 'family' in January 2014. Research into the human brain and its diseases is one of the priorities of its 9 scientific institutes. Between 2014 and 2018 the SAS was involved in five 'Joint Transnational Calls' (JTC) for research proposals. With the Slovak team leader Dr. Adela Penesová from the Institute of Experimental Endocrinology BMC SAS, the Academy recorded its first success with NEURON JTC2014 (Neuroinflammation). A Slovak team became a member of the project consortium under the acronym 'MELTRA - BBB' as result of the NEURON 'widening' strategy: The proposal coordinators were invited to include in their full proposals researchers from EU-13 countries in order to increase the participation of previously underrepresented countries in the NEURON research consortia. This strategy successfully led to the participation of Slovak teams in NEURON, and increased support to the small scientific community working in the field of brain research in Slovakia.

In the words of Slovakian scientist Dr. Peter Filipčík from the JTC 2016 project RepImpact:

*»We expect that our participation in NEURON will lead to deep insight into the early phases of pathogenesis of non-treatable human diseases studied in real human material. We have many reasons to expect that we will significantly participate in providing an understanding and a more accurate picture of the unknown molecular mechanisms in the early phases of brain disease. This is possible due to the combined potential of every single partner in the consortium.«*

In the future the main objective of SAS is to support the participation of young Slovakian scientists in international teams. We support NEURON to develop the capacity to fund advanced project schemes that enable our groups to continue their research activities initiated under the joint calls, particularly when they can demonstrate that they have already produced promising data in the initial three-year period of time of the NEURON funding scheme.

*By Jan Barancik, representative of SAS in the ERA-NET NEURON*

# 7 EU13 participation in international neuroscience - NEURON's widening scheme

## EU13 PARTICIPATION IN INTERNATIONAL NEUROSCIENCE - NEURON'S WIDENING SCHEME

One of NEURON's main aims is to encourage and foster transnational collaboration. In general, each consortium is free to add significant expertise from up to five international partners from at least three different countries to tackle their research question. But to every rule there is a legitimate exception: Some countries - comprising, but not 100% matching to the EU13 list - have been underrepresented in NEURON calls. This may be due to the fact that their scientific community in specific fields / topics was not well developed, or merely not well connected suggesting they are not as extensively linked in international research as the EU15 countries.

**Underrepresented countries:**
The ERA-NET NEURON strives to strengthen the European Research Area by including as many partner countries as possible in its funding scheme. 'Underrepresented countries' may be identified for each call and consented with the particular candidate funding agency.

The identification is based on
a) Experience from last calls
b) High national oversubscription after the pre-proposal/ full proposal stage

Participating countries in the widening scheme to date had been Turkey and the EU-13 countries Romania, Slovakia, Latvia, Poland.

NEURON started to improve research collaboration with EU13 Member States and Turkey by the application of a 'widening' process since 2014. To that end, in a grant proposal a larger consortium of up to 6 partners is allowed if at least one partner originates from an underrepresented country (see Box for definition). Other than that the consortia receive no special treatment or bonus. In a review process the qualification and composition of the consortium are important criteria. Every group should prove an asset and add scientific value to the collaboration and common work plan.

## INCLUSION STEPS - OPTIONS TO TAKE

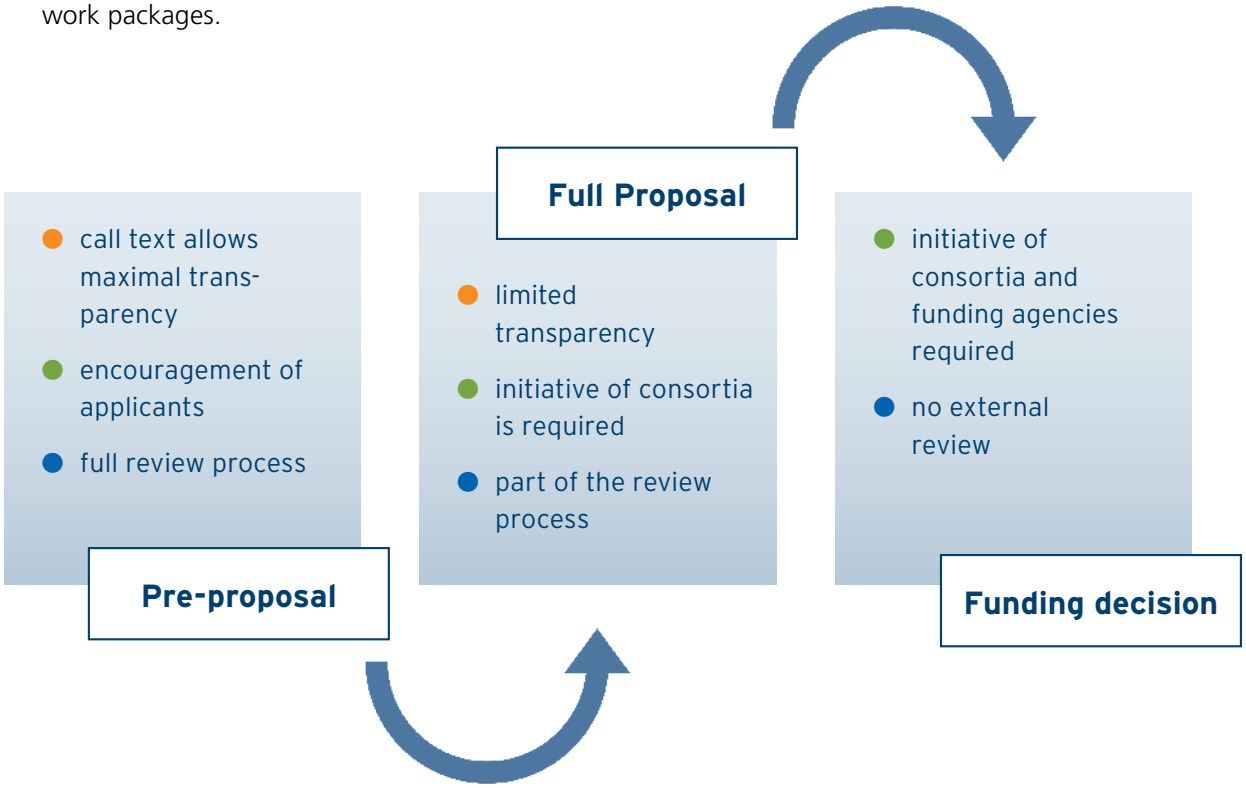
Widening can be implemented in three different stages (see Figure) in the grant application process. Each option has its incentives and consequences.

1) From the start: The inclusion of an additional group in the pre-proposal stage from a defined set of countries, as defined in the call text. This procedure allows for maximal transparency, longest preparation time for the applicants, and best evaluation practice.

2) Between pre-proposal and full-proposal stages: Sometimes only after the first review stage it is apparent which countries are indeed underrepresented. In this case, successful applicants are invited to include an additional partner - from a set list of underrepresented countries - in their full proposal. This procedure gives only limited time to add a suitable collaborator. Yet, this way the consortium enters the full proposal review process in its final composition.

3) After the funding decision: In case that some countries/funders have no candidates among the final selection for funding, 'Widening' may be applied at this last stage. Applicants are given permission to add a partner from specific underrepresented countries. Scientists/research groups from these countries are invited by the respective funding organisation to apply for one of funded consortia. In this case, only limited time is given to find suitable collaborators. The consortia evaluate and decide about the added value of candidates. They may not change their original work plan, but may add work packages.

The three steps have been implemented individually or in combination in NEURON – dependent on the actualities of the particular call. While NEURON strives for maximal transparency, the main aims are to promote multi-disciplinary approaches and to strengthen the European Research Area by including as many partner countries as possible in its funding scheme – and not least by optimizing the flux of available budget into brain research.



# 8 Scientific recruitment and selection policy is essential for funding of high quality research

## THE REVIEW PROCESS AND PROCEDURES

Each year NEURON's joint transnational calls are answered by a multitude of research proposals and the issue is of how to select the best proposals for funding. Consequently, a rigorous peer review process is the backbone of maintaining the highest scientific standards.

## CREDIT TO THE REVIEWERS

Peer review is essential for the scientific evaluation of proposals for funding with NEURON. In a selective process renowned scientists are invited as peer reviewers. NEURON is very grateful to so many high-level researchers who commit themselves to NEURON's review process, despite tight schedules and many other obligations. Without this commitment, fair and solid reviews would be impossible. NEURON attempts to keep the workload low, not least because acting as a reviewer is an honorary position.

**Peer Review Panel:** Members are chosen by the respective joint call secretariat and are approved by the call steering committee. Experts are selected from suggestions of NEURON partners, identified by online research, from previous review committees, or previous funded projects. The composition of experts on the panel is carefully chosen to cover the wide range of scientific expertise across required disciplines and methods.

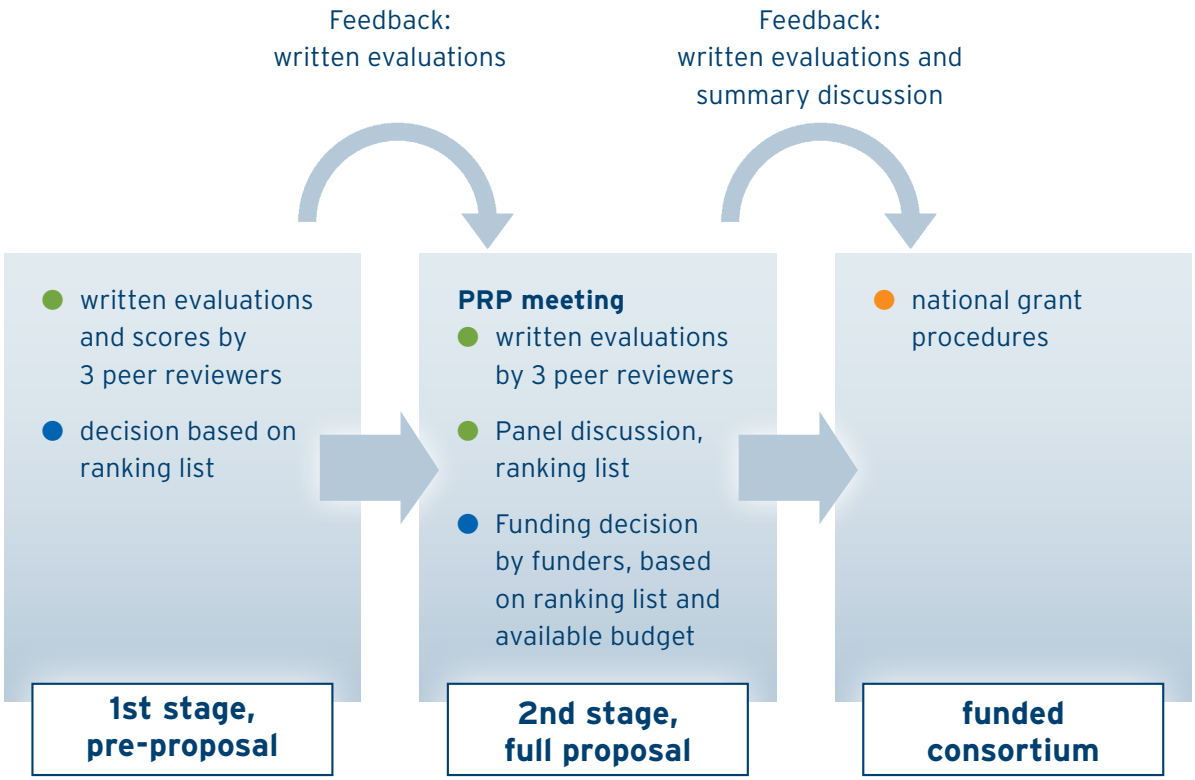
## KEEP IT SIMPLE

NEURON spends around 10 million Euros per annual call to fund cutting edge research. Still, the available budget cannot accommodate the academic demand and the calls are highly competitive. Submitted proposals can number anywhere between 60-180 per call, and out of these, only 10-12 projects will usually be funded at the end of the process. In light of these numbers, NEURON strives to keep the processes simple for both, applicants and reviewers. Therefore, a two-step application and review process is applied. Proposal submission and review process are managed via a web-based system. This ensures a standardized and secure submission for the applicants. The reviewers have easy access to the proposals, additional documents and guidance. Moreover, the reviewers can conveniently prepare their short written evaluations online.

*»What we liked especially about [the selection process] was that it was easy to apply for and the rules were easy to understand …«* *Ari Waisman, JTC 2014 consortium MELTRA-BBB*

## TWO STEPS TO SUCCESS

In the first step, only a short pre-proposal outlining the general research idea and structure of the project is requested. A peer review panel (PRP) specifically recruited for each call assesses the pre-proposals remotely.




The reviewers' scores define the ranking of the pre-proposals. Usually, the top 30% of the pre-proposals are admitted to the second step.

*»There are several aspects that are beneficial in the NEURON measure, such as the ease of the staged application process with a pre-proposal and full-proposal [and] the possibility to reply to the reviewer's comments to the proposal …«* *Joris de Wit, JTC 2015 consortium SynPathy*

In the second step applicants are invited to prepare more detailed full proposals. This way, the work load for applicants is reduced, and room is left for adjustments: The applicants have the opportunity to respond to the reviewers' suggestions. Assisted by written evaluations prepared by the PRP prior to the meeting, the PRP engages in an in-depth discussion of the scientific quality of each proposal. The outcome of the PRP meeting provides a final ranking, which is the basis for the funding decision.

## TRANSPARENCY POLICY

How is my proposal evaluated? Is the evaluation fair? These are important questions that may be asked by the applicants. Yet, from the applicants'

An outline of the review procedure is provided in the call text. The call text also specifies the evaluation criteria of the particular call (see box Evaluation Criteria). After either evaluation step, the applicants receive all reviewers' written evaluations, as well as a summary of the PRP discussion of their full proposal. Thus, the applicants can better understand the perceived strengths and weaknesses of their proposal.

point of view, the review happens behind closed doors. To build trust in the review procedures transparency is pivotal.

*»The ERA-NET NEURON funding format was acknowledged by all participant researchers as an excellent and unique measure to allow transnational collaborations without the high level of administration and management that is usually required by EU projects …«* *Julia Stingl, JTC 2013 consortium BrainCYP*

The applicants receive as much information as possible at all stages of the application and review process, without compromising confidentiality. Some information, for instance who reviewed which proposal, will not be disclosed to ensure an unbiased evaluation.

The names of the reviewers are released on the NEURON website together with the final funding decision after the process is entirely finished, and if the experts agree.

## ASSEMBLING THE PEER REVIEW PANEL

At the center of the review process is the scientific Peer Review Panel (PRP). Only the valued support of peer expert scientists can ensure an adequate assessment of each proposal. NEURON uses ad hoc PRPs that are freshly set up every year, according to the thematic focus of the specific call. For the evaluation of the pre-proposals about 40 renowned experts are invited. For the subsequent full proposal step, a subset of the initial PRP matching the full proposal topics is re-invited. The core of the full proposal evaluation is a face-to-face meeting of the PRP. NEURON always tries to achieve parity in terms of gender and nationality within the PRP.

The joint call secretariat identifies potential reviewers with the help of international research platforms (e.g. Research Gate), suggestions by NEURON partners and NEURON's Scientific Advisory Board. Valuable tools to seek out experts in relevant fields are also databases like PubMed and Scopus as well as conference programmes that are available online. For each proposal usually three reviewers covering all thematic and methodological aspects of the proposal are asked to provide written evaluations.

## REVIEW CRITERIA

Detailed evaluation criteria are published in the respective call text. The main criteria are: excellence, impact and quality of the implementation. Additional (sub-)criteria may be implemented according to the specific call topic.

**Evaluation criteria**

- **Excellence –** The quality of the scientific approach, methods and research competence of the applicants are a main criterion.
- **Impact –** The potential impact of the expected results on health.
- **Quality of the implementation –** The feasibility of the project, added value of the collaboration and appropriateness of the work plan.

## THE FINAL SAY

The PRP's funding recommendation builds the scientific basis for the funding decision taken by the funding organisations. NEURON always tries to fund as many projects as possible, starting with the top ranked projects and strictly following the PRP's recommendation. The number of projects that can be funded is limited by the available national budgets (see Box variable geometry page 9).

In the ERA-NET funding scheme, funding organisations as a rule support the Principal Investigators (PI) from their own countries. This invariably leads to the situation that at some point along the ranking list the first consortium appears, in which one PI cannot be funded for lack of further funds for this country. This situation is called a 'funding gap' and accumulates the lower in the ranking list a project is. The funding organisations make every effort to overcome funding gaps: Whenever possible, the funding organisations increase their budgets to meet the requests. If additional budget is not available, other options are explored. Supporting the exchange of personnel between countries, for example, can alleviate the situation in some cases. If no other option remains, the funding organisations negotiate reductions in the requested budgets with the applicants. Often just small reductions can make it possible to maximize the number of funded projects.

Funding gaps can also be alleviated if the EU Commission enters the game with its co-funding scheme. Co-funding contributions from Brussels can be used for any country, fill the gaps and thus allow funding of more projects down the ranking list.

And what is the outcome of all those efforts: To-date, NEURON has selected almost 125 excellent research projects through 12 joint transnational calls. The feedback of applicants and reviewers helps NEURON to maintain high quality standards and to optimize its review process for future calls.

# 9 NEURON's Scientific Advisory Board

*Martin Dichgans*

NEURON's Scientific Advisory Board (SAB) is appointed by the Network Steering Committee (NSC) to support in the planning of strategic research issues. The SAB was set up by NEURON in 2007 and has served, since then, to bring together leading neuroscientists in an effort to influence and shape orientations at the interdisciplinary level to advance strategic orientation in the field of disease-related neuroscience. Through this decision, NEURON committed to the fact that decision-making processes must be informed by scientific evidence and knowledge, and that international and transdisciplinary scientific collaboration is a prerequisite to reach sustainability. With this in mind, the SAB comprises researchers with clinical as well as non-clinical backgrounds, and neurologists as well as psychiatrists.

## SUPPORT AND REVIEW

Since 2012 I have had the privilege of chairing NEURON's SAB of twelve members, with some of them already members of the predecessor NEURON I (2003–2007). Our tasks are to support the NSC with regard to the selection of topics for Joint Transnational Calls (JTCs) for proposals, selection of *ad hoc* expert groups and making suggestions of reviewers and evaluation of scientific aspects of NEURON work.

Aside from regular information via brief reports, email and personal exchanges the SAB participates annually in one of the network meetings, and the foresight workshops. The input from the focused foresight workshops, the research communities and other stakeholders is used by the SAB to consult NEURON on the selection of priority topics for the JTCs.

*»By bringing together the collective capacity of a broad range of scientific fields the Board endeavors to strengthen the interface between science, policy, funding organisations and society.«*

*Discussion with the Scientific Advisory Board at a NEURON foresight workshop*

## LOOKING TO THE FUTURE

In 2014 the SAB, the scientific community, scientific societies and other stakeholders contributed to generate a long term Scientific Research Agenda (SRA) in the field of disease-related neuroscience. This agenda, extending beyond the four year NEURON II (2012–2015) project, was developed to create a framework for sustained research through a shared strategic vision of the funding agencies.

The establishment of new scientific and medical European collaborations is commonly associated with sustainability and due regard to the (bio) medical, social and ethical aspects of sustainable research.

## RESULTS

The finalized Strategic Research Agenda 'Taking on the Challenges of Nervous System Disorders' was published online in December 2014. In early 2015 NEURON launched a survey to seek feedback about the SRA from the scientific community. A questionnaire asked professional societies and patient organisations originating from all NEURON partner countries about their satisfaction with the SRA topics and priorities. As a result, the SRA Part II 'Feedback from professional and patient organisations' was published in May 2015.

*»Looking back over the last five years I found working for NEURON with the Scientific Advisory Board and the entire NEURON network an enormously fruitful, effective, and enjoyable experience.«*

The content was developed by the SAB and additional external experts covering a broad range of expertise in fundamental neuroscience, neurology, psychiatry, and sensory organs. This was intended to guarantee coverage of a wide spectrum of neuroscience while also balancing clinical and basic research. A key element in this process was a workshop on May 13th, 2014, in Bonn that resulted in a draft document by the chairman of the SAB. To validate the result published in the SRA, and to collect additional suggestions and topics an online survey was conducted with a broad research community. All Principal Investigators (PIS) of funded projects, all reviewers from the previous six NEURON calls, and the general research community were invited to the online survey that was published on the NEURON website.

Within the strategic orientation, specific tasks of the Scientific Advisory Board are to support NEURON in monitoring JTCs in a way that meets the needs of funders, policy makers, and eventually people living across Europe. Consequently, a set of indicators for monitoring was developed in collaboration of NEURON partners and SAB members to achieve consens between the scientific and the funders perspectives. The chosen indicators are still taken into account when designing the call documents and progress report templates for the future NEURON calls to allow for efficient follow-up of current and future funded projects.

*By Martin Dichgans, Chair of NEURON's Scientific Advisory Board, Director, Institute for Stroke and Dementia Research (ISD), Clinical Centre at Munich University*

# 10 NEURON's annual foresight symposia

*Etienne C. Hirsch*

Understanding how our brain works and what are the underlying mechanisms is one of the greatest challenges in science. Brain differs by far from any other organ by its complexity. It is comprised of at least 100 billion of neurons and as many glial cells. It is wired by several hundred thousand kilometers of axons making a little less than a billion of contacts, or synapses. It is permeated and supplied by kilometers of capillary and blood vessels.

Without nervous system there is no life. Without brain, no perception, no mental representation of external world, no language, no decision, no thought, no dreams, none of the social interactions that make human species so unique.

- In Europe, one third of citizens are living with a brain disorder (including anxiety, mood disorders, or migraine/tension headache).
- In a decade, the total annual cost has jumped from 385 billion euros in 2004 to ~800 billion euros in 2014.
- Psychiatric disorders (including mood and anxiety disorders, addiction) account for 62% of the total cost, while neurological diseases (including dementia) caused the remaining 38%[1].

Thus, the understanding of the organisation and functioning of the brain, at all its different levels of complexity and at all the ages of life, remains and will remain for a long time a forefront defy of science (viz the Obama plan in the US, Human Brain Project in Europe). To this challenge add many other related fundamental questions.

*»For instance, how variability in expression of a limited number of genes confers to each of us a unique personality? Why brain is at the same time so robust and plastic (e.g. one can remove a large portion of it without nasty consequence) and so vulnerable (e.g. exposure to a single stress may affect individual for the whole life)?«*

Sometimes, unfortunately, our brain does not work properly generating a wide range of neurological or mental health disorders.

Altogether, brain diseases are responsible for 35% of Europe's total disease, before cardiovascular disorders and cancer. The burden of brain diseases rapidly grows with population aging. Without discovery of new therapeutic solutions, themselves conditioned by research progress, this may destabilize our European society.

Given the broadness of the topics related to normal brain function and dysfunction ERA-NET NEURON has set a Strategic Research Agenda (SRA) for five years aimed at focusing on some key

[1] DiLuca and Olesen, 2014; http://dx.doi.org/10.1016/j.NEURON.2014.05.044

priorities, complementary to other Joint Programs such as the JPND. These priorities include Novel Biomarkers, Mental disorders, Neuro-Sensory organ disorders … As science is evolving rapidly, ERA-NET NEURON aims at addressing only forefront aspects within these very broad fields.

Based on the priorities of the SRA, annual foresight workshops are set with the aim to tackle these challenges: by identifying the most provocative questions in the field, identifying the still unmet needs for the patients, and collecting the feedback of key opinion leaders within a given field. INSERM and CNRS are as ERA-NET NEURON partners in charge of organising annual foresight workshops before each every NEURON JTC text is written, to guide the funding agencies in shaping the calls.

INSERM and CNRS are two French national research agencies, associated with nearly all French science and medical universities. Overall, basic and clinically oriented research in neurosciences, neurology and psychiatry represent about 20% of life-science and medical research in France. This nation-wide scientific expertise places our two organisations in a strong position to organise the workshops and select the best European speakers to cover the topics chosen by the management board.

H2020 promotes citizen science; therefore, research scientists of course but also patients and health professionals should be able expressing their opinions. Accordingly, the way the annual foresight workshops are set has evolved.

Lay organisation and patient representatives are now invited to the workshops to help the funding organisations to select the most important unmet therapeutic needs in brain diseases. Their experience is invaluable not only to select the right topics

*»A major challenge is patient's involvement in research; this is a foremost development axis for ERA-NET NEURON.«*

but also in posing new scientific challenges to try to understand the pathophysiology of what they express in term of symptoms. Patients are among our strongest supporters! They are aware, more than any others that research needs time before resulting in new therapeutic solutions. To make sure that the opinion which is expressed is the voice of a whole community and not just an addition of multiple individual requests we now invite the heads of European associations such as Global Alliance of Mental Illness Advocacy Networks-Europe. The way we obtain the feedback from the scientific or health professional communities has also evolved. Here also to avoid individual contributions or lobbies of sub-disciplines, representatives of the professional organisation are invited (Federation of European Neuroscience Societies, European Academy of Neurology, European Psychiatric association …) to the foresight workshops.

We believe that the annual foresight workshops are useful to shape ERA-NET NEURON calls because so far the numbers of applications are well adapted to the available funding of each call. High caliber scientists were generous enough to offer their time to brainstorm with the funding agencies and the SAB members of ERA-NET NEURON. These workshops were also attractive for the scientific and medical press as the Chief Editors of Lancet Neurology and Lancet Psychiatry attended some of them and commented on the meetings in their editorials.

*By Etienne C. Hirsch, Director of the ITMO Institute (neurosciences, cognitive sciences, neurology and psychiatry), representative of INSERM, and Bernard Poulain, Director of the European Neuroscience Institute at Strasbourg, representative of CNRS at ERA-NET NEURON*

# 11 The ELSA initiative

The acronym 'ELSA' or also often 'ELSI' refers to a multi-faceted research area that deals with the **Ethical, Legal and Social Aspects/Implications** of advances in science – neurosciences in the case of NEURON. ELSA goes beyond the confines of ethics, as many specialist disciplines collaborate and complement each other.

The goal of ELSA research in NEURON is to investigate the opportunities and risks for people and society that arise from the constant progress of neuroscientific knowledge.

Relevant research questions in this context range from deeply philosophical questions to practical matters that need to be considered in clinical practice.

*Brain image*

For example:

- How does the neuroscientific knowledge about the structure and function of the human brain influence the human self-understanding and consciousness?
- Psychiatric symptoms can be viewed at as biochemical imbalances in the brain. What consequences do related neuroscientific findings have in legal contexts, if i.e. a determination of accountability and 'free will' is needed?
- What consequences does the use of brain-computer-interfaces have for the 'users'?
- Can drugs achieve 'neuroenhancement', i.e. an improvement of cognitive abilities? Where can we draw a line between therapy and 'enhancement' in this context?
- How can the informed consent process for people suffering from dementia be improved in an ethical way, taking the interests of patients, relatives and society into account?

Funded projects shall serve as a basis for societal discourse, research and development, medical practice and decisions taken by politicians and legislators. Close cooperation between stakeholders in the humanities, social sciences, life sciences and in public life is a prerequisite for ELSA research. This kind of interdisciplinary research benefits very much from being carried out on an international level. Different cultural backgrounds help to find ways on how a society can cope with challenges, and specifically, societal issues should be addressed overarching national borders. NEURON's transnational collaboration aims to provide not only an intercultural perspective, but also allows access to expertise and experience across national borders.

# 12 Spotlight on ethical issues in the (neuro)sciences of the mind

'INTERFACES' is an international research project on ethical, legal, and social aspects of brain-computer-interfaces (BCI).

This a relatively new technology that connects the brain with a computer in such a way that people can directly control the computer and other electronic devices by their mind. The BCI technology has recently made huge progress and is ready to be used for various purposes: BCIs can assist handicapped people in moving their limbs or robotic limbs; they may offer a computer-aided way of communication for some people who cannot speak; they can be used for rehabilitation of stroke patients or treatment of some psychiatric disorders; and they may be of use to enhance the performance of healthy people in aviation, military, or other areas of society.

Our project aims to (1) investigate the neglected perspectives of patients, their families, health care professionals, and the public, (2) analyse the fundamental theoretical, ethical and legal questions associated with BCI and (3) utilise the resulting insights to offer orientation for medicine and society.

It aims to gain new knowledge and bring it to those in society that need this knowledge. Interview studies with neurological patients and their families who have experience with BCI studies, an international survey of health care professionals and citizens will be used to collect needed empirical data. These findings will help to find orientation in difficult value questions, e.g. whether people are responsible for the actions they produce by BCI technology or how patients' autonomy and privacy can be safeguarded. Such questions will also be discussed in a workshop of international experts organised by the project. In a final phase, the research results serve to construct video and audio podcasts informing the public about the ethics of BCI and to write recommendations for policy makers how to regulate BCI.

*Ralf Jox*

*Professor Jox, you are a physician and a philosopher by training, and pursued both interests hand in hand ever since. What is your particular interest in ELSA research?*

Health care is constantly being revolutionised by novel technologies, not only from the pharmaceutical industry, but also from engineering and information technology. As a physician, my aim is to offer to patients and their families the most up-to-date, but also the safest, most beneficial, sustainable and affordable treatments. In order to reach this aim, however, we have to be highly critical and not succumb to the temptation to blindly follow the latest fashion. ELSA research scrutinises new technology using rigorous scientific methods and philosophical inquiry. It is the only way to influence a responsible technology development for the benefit of patients and society at large.

*You chose a very timely topic of the emerging Brain-Computer-Interface technologies. What is your particular aim from a perspective ELSA research?*

Brain-Computer-Interface (BCI) technology couples the human brain with computers and external electrical devices. Its original aim was to enable

paralysed patients to move, act and communicate with the sheer force of their thoughts, without having to move any of their limbs. This objective is already remarkably well attained and BCI devices are about to move from bench to bedside and enter clinical application. Yet, BCI technology has also diversified over the last few years, and new areas of application are on the horizon.

*»BCIs may be used in rehabilitation, psychiatric treatment, and even in non-medical areas such as entertainment, economy or the military. My aim is to accompany this fast-paced development by critical reflection and pave the way for responsible use of the technology.«*

*Who do you collaborate with in this endeavour?*

In our research consortium called INTERFACES, researchers from Canada, Germany and Spain, representing the disciplines of philosophy, ethics, medicine, social sciences and law collaborate with each other in a highly interactive way. We also set up an International Advisory Board of BCI experts many of whom come from neuroscience, engineering, and information technology.

*So you can keep track of the real-life developments and innovations?*

Yes, in the beginning of our project, we organised four different visits to BCI laboratories where the INTERFACES researchers observed and actually tested BCI technology themselves. They talked to BCI scientists to fully understand the technology, anticipate future developments and get acquainted with the scientists' perspective.

*You are part of the 'first generation' of the 'ELSA of Neuroscience' within the ERA-NET NEURON. Is this your first international project?*

This is in fact the second large international research consortium that I coordinate. The first one was a consortium on the ELSA of chronic disorders of consciousness funded by a similar group of national funding agencies of various European countries and Canada.

*Why did this ERA-NET call appeal to you?*

***»The ERA-NET call appealed to me because of its close international collaborative character and the focus on neuro-technology, while at the same time being open to diverse forms of neuro-technology and neuroscience implications.«***

In addition, I was particularly content to see that after having funded neuroscience research for quite some time, this was the first call on the ELSA of neuroscience.

*How have you experienced the process of applying for this funding? What are the differences of an ERA-NET and other international funding programmes?*

Tying together an international group and launching an international, English-language application was really fun. The pleasure and success of this application was largely owed to the fantastic bilateral collaboration that I have been pursuing for almost ten years with Eric Racine, an enthusiastic, brilliant and amazingly productive neuroethicist from Montreal, Canada. The main problems, however, should also be mentioned: Extremely low funding budgets of some European countries (such as Spain and Belgium) made it extremely difficult to get good and motivated partners from these countries. I would recommend having less countries participating in the call, but instead countries who offer a substantial budget for ELSA research. International consortia are most productive when there is a certain balance between the international partners.

*As coordinator of an international consortium, what are your challenges? For example, how do you ensure the communication flow?*

Coordination of such an international consortium is indeed a demanding task. It requires experience, proven bilateral relations with the different partners and motivated people who organise the day-to-day coordination between the partners. We set up bi-monthly consortium newsletters, several teleconferences annually, a joint website, a common database and yearly workshops. Yet, the best infrastructure can only help if the partners are willing and motivated to use it frequently and to involve each other in research. It is particularly challenging to write joint papers on conceptual or philosophical issues, because the customs of working and publishing in this area are still based on the one-author principle.

*What is the specific benefit of this international format for your particular research?*

ELSA research on BCI technology has to be as international as the BCI research and development itself. In today's globalised world, ethical and legal regulations need to be transnational or at least based on a wide transnational perspective. Moreover, as researchers we can generate a far higher impact and make our results more widely known to the international scientific community if we collaborate transnationally.

*Interview with Ralf Jox, coordinator of the JTC2015 consortium INTERFACES; Institute of Ethics, History and Theory of Medicine, LMU Munich*

# 13 Project discoveries

Neuroscience targets the brain, an extremely complex network of more than 100 billion interconnected neuron (nerve) cells. These extraordinary cells build a dynamic organ specialised in information processing and transmission by simultaneous and interrelated electrochemical signalling. This complexity poses a challenge to understanding the brain at both a molecular and physiological level. Moreover, in diseased states the current therapeutic approaches do not match this huge dynamic complexity. Compared to the brain itself with its perfectly orchestrated processes any therapeutics still lack refinement and perfection. To fill this gap, NEURON strives to fund and support truly innovative advancements in brain diseases which could have the potential to radically transform future treatments and increase their therapeutic efficiency.

A few examples shed a light on the multitude of NEURON's yet funded projects and their exciting results.

From the JTC 2012 'Novel Methods and Approaches towards the Understanding of Brain Diseases' the project **LIGHTPAIN** set out to decipher the role of specific proteins in the brain involved in the development of pain.

*Amadeu Llebaria, coordinator of LIGHTPAIN*

In contrast to acute pain, which serves as a warning signal, chronic pain must be considered as a disease *per se*. Chronic pain bears a sensory and psychological dimension at the origin of mood and cognitive disorders. Being largely refractory to current pharmacotherapies, the identification of endogenous systems involved in persistent and chronic pain is crucial for the development of new therapies.

As most important result the project established light-inducible molecular actuators that enable the optical control of drug activity in living animals[1]. The researchers could demonstrate that painkilling (analgesic) molecules are adjustable not only to a time but to a specific localisation. This, so called photopharmacology approach can provide new ways of treating pain because it offers new and radical approaches to drug therapeutics. Patients may, in the future, be able to benefit from precise personalised painkilling dose adjustment and therefore a reduction of potential side-effects.

From the JTC2013 'Mental Disorders' the project **BrainCYP** investigated genetically caused modifications in drug metabolising proteins in the brain for mood disorders.

*Julia Stingl, coordinator of BrainCYP*

[1] Izquierdo-Serra et al. 2016, Nat Commun.7:12221

Understanding local drug metabolism in the brain is related to understanding the deeper and challenging issues of pharmacological effects and biological phenotypes of psychiatric diseases. A deeper knowledge on the local brain metabolism of drugs is necessary to avoid side effects of drugs acting in the brain and to prevent toxic actions of metabolites created within the brain, by local protein systems. Such increased understanding will help to increase drug safety in public health.

A distinctive success of the project is the confirmation of common biological principles of the physiological function of brain metabolism in animals and in humans[2]. The findings on genetic modifications in human brain proteins correlated with those generated in specific animal models. That is insofar very relevant, as for brain and psychiatric diseases the careful use of animal models is still the only option to tackle the most sensitive organ of human physiology. Hence, the translational significance of this result is located at the complex interface between drug safety and drug side effects and models of mental health in clinical practice. In addition, the result contributed to the present challenge of understanding the biological mechanisms of psychiatric diseases.

From JTC 2014 'Neuroinflammation' the project **CnsAflame** analysed inflammatory mechanisms following traumatic brain injury (TBI), a disorder caused by external force to the head typically during a traffic or sport accident, or a fall. While many lives have been saved in recent years due to improved emergency and hospital care, it has become evident that surviving patients often suffer from various chronic brain disorders. The initial insult to the brain involves ionic, molecular, and cellular alterations resulting in brain edema formation that, if untreated, can lead to devastating damage of the remaining tissue.

As most important result the project demonstrated that the inhibition of certain receptor proteins in the brain can improve the outcome after experimentally induced TBI when given within a clinically relevant time window[3]. Therefore, these proteins can represent a therapeutic target with clinical potential.

From JTC 2015 'Neurodevelopmental Disorders' the project **SynPathy** analysed key determinants of synaptic stimulation/inhibition imbalance in Autism Spectrum Disorders. Nerve cells in the brain communicate *via* specialised contacts called synapses, and information processing in the brain critically depends on a proper balance between stimulatory (excitatory) and inhibitory signalling at synapses. Mutations in genes that determine synapse function are observed in many brain disorders including autism spectrum disorders.

*Nikolaus Plesnila, coordinator of CnsAflame*

*Joris de Wit, coordinator of SynPathy*

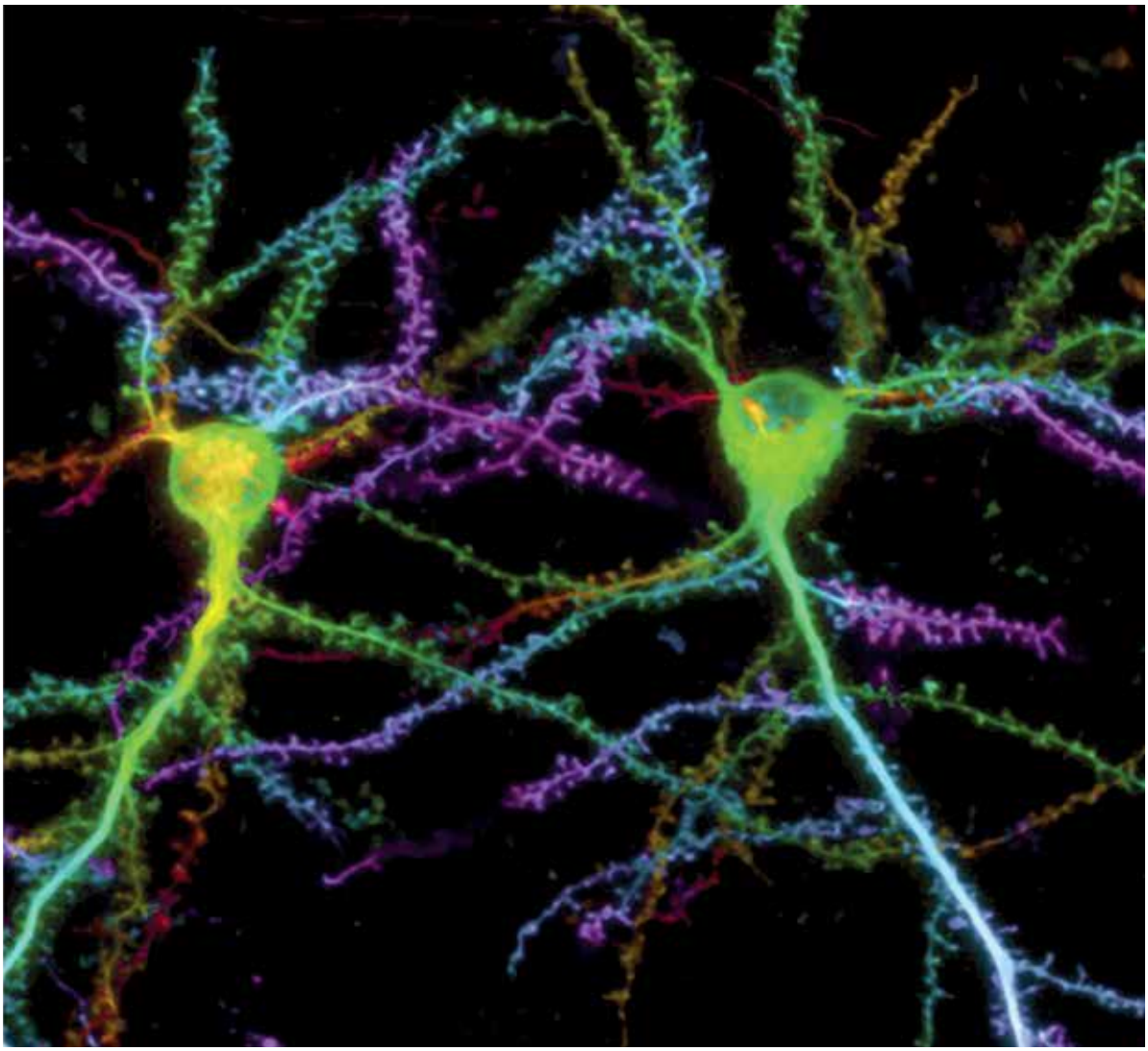
[2] Jukić et al., 2017 Molecular Psychiatry 22(8):1155-63

[3] Hopp et al., 2017 J Neuroinflammation, 14:39:1-10

For a deeper understanding of the molecular mechanisms that regulate a healthy balance between the excitement and inhibition centers of the brain, the ongoing project reported already an important interim result. Specified synaptic proteins and a mechanism were shown to modulate signalling. Their precise interaction controls the function of key molecules, and a series of further steps whose perturbations lead to imbalances and, consequently, to neurodevelopmental disorders[4].

The provision of a regular cross-linked funding opportunity to the science community working on developmental, neurological and psychiatric alterations of the nervous system has revealed an amazing number of positive results. Since 2008 ERA-NET NEURON JTCs for proposals attracted increasingly high numbers of applications. Only the most excellent proposals are funded, as is demonstrated by the funding rate of between 10% and 20%. More than 750 research publications arose from the funded projects (analysis of the first four JTCs), many of them in highest impact peer-reviewed journals, and 22 filed patents. There is, therefore, a large need for cutting-edge translational projects not limited by national borders.

[4] Elegheert et al., 2017, Neuron 95(4):896-913



*Neurons labelled with different fluorescent probes*

# 14 Public involvement in research

The latest challenge to face European research funding organisations and the European Commission itself is the issue of public involvement. A number of scientific and societal challenges can be more efficiently addressed by public engagement and participation. The topic is hot because not only the complexities of brain diseases may require new paradigms of interactions to tackle the most pressing research questions. Families, carers, clinicians and researchers already face the challenges of the demographic change (e.g. aging population, chronic diseases) in the area of brain diseases: 'fewer to care for more'.

*The question is however, when, where and how to best involve the public.*

For research funders the term 'public' should be defined, as to include patients, potential patients, care givers and people who use health and social care services, as well as people from umbrella organisations that represent service-users. Such precise definitions are necessary for funding initiatives because there is an important distinction to be made between the perspectives of the public, the perspectives of people with a professional role in health and social care services, and not least, research.

'Public' involvement thus can address several different levels and roles. The most common and direct way is when people participate in a research study. 'People' in this case refers to patients or healthy volunteers, who are being recruited to take part in a clinical trial or other research study. Those volunteers support science by contributung valuable data to address research questions. Here there is no doubt that patient organisations can and do play a valuable role in advising on the recruitment of patients as participants and on ways of engaging with the public. The latter can be cooperation with researchers by helping to disseminate information to members of the public and explaining the findings of a study.

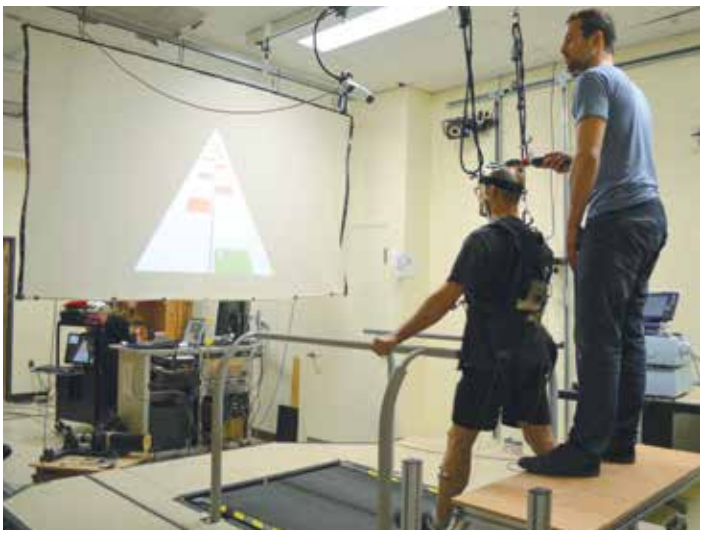
## ESTABLISHING LINKS

In January 2016, NEURON hosted a symposium with funders and renowned scientists, clinicians and representatives from patient advocacy networks to look for new areas of public involvement in the field of brain disease. Can members of the public be actively involved - besides direct participation - in research projects and in research management? As one possible way the Netherlands Organisation for Health Research and Development (ZonMW) and the Epilepsy Foundation presented a successful collaboration between funding agencies, researchers, clinicians and patient organisations by installment of a 'user' panel within the grant assessment process. Such panel involves members of patient organisations as consultants to the review of grant applications.

As e.g. members of a project advisory or steering group, patient organisations can help to design better methods of obtaining informed consent from patients and/or carers, ensure that information sheets, questionnaires and interview schedules are patient-friendly, speed recruitment by providing researchers with better access to the patient community, and, not least help to disseminate results through patient-led advocacy, relating research findings to patients' own experience and presenting them in a user-friendly manner.

Because of the role of the brain in our lives, questions over whether or not to intervene when function is damaged, makes public involvement all the more fundamental. Ensuring public confidence in treatment options such as e.g. novel neuro-technologies is crucial. This requires collaborative public engagement activities involving both researchers and clinicians, coupled with strong governance procedures and effective regulation.

A notable example of engagement activities between researchers and the public is provided by the Global Alliance of Mental Illness Advocacy Networks (GAMIAN Europe) in the area of psychiatric disorders. Besides advocacy on behalf of psychiatric patients, this patient-driven pan-European organisation provides information, education and training for patients with psychiatric illnesses and the general public; they work on anti-stigma and anti-discrimination campaigns, and cooperate and make partnerships with professional associations, pharmaceutical companies and decision making bodies.



*Rehabilitation training*

## SHIFTING POSITIONS

Reinforcement of the links between the professional communities in approaches 'from bench to bedside' should comprise several levels for fostering the interactions between scientists, clinicians and society:

- the presence of brain/mental health research related publications in mass media and social networks,
- joint statements regarding ‚hot' topics like e.g. refugee mental health,
- joint positions against stigmatisation and discrimination of people with brain/mental disorders,
- the participation of representatives of lay organisations and policy makers in guideline development committees like e.g. the European Guidance project of the European parliament,
- the participation of lay organisations in scientific congresses, and
- not least, the joint development of policy recommendations.

In conclusion, the multitude of these different activities – involvement, engagement and participation – is often linked and, although they are distinct, can complement each other. It is obvious that all sides – funders, researchers, clinicians, practitioners, carers and the actual and potential patients – will benefit from enhanced public involvement; so the next major step is to identify individually for each area and each funding initiative at which stage, and in which role, public involvement will most effectively help benefit the research being carried out.

# 15 Future perspectives

*»ERA-NET NEURON's birth coincides with a new age of maturity in European research.«* *Etienne Hirsch, INSERM and Bernard Poulain, CNRS, both France*

In the past 15 years, since that birth, NEURON has grown and became a reliable source of funding for the neuroscience community, not just in Europe but beyond. So, as we celebrate our 15th birthday, what are NEURON's objectives for the future?

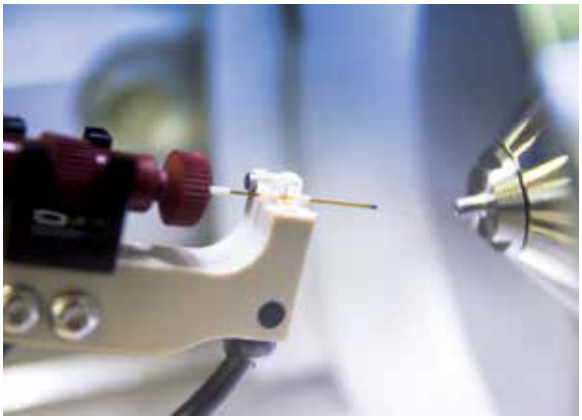
In the words of NEURON partner FWO (Belgium):

*»We hope to see the NEURON-network continue its work, as efficiently and straightforwardly as it has been doing for the past fifteen years, under the European 'Research and Innovation' umbrella. We encourage further internationalisation of the network, without losing the primordial European dimension from sight.«*

The roadmap for the future is delineated by NEURON's Scientific Research Agenda (SRA). To translate the aims defined there into topics and actions, the NEURON network developed a structured implementation plan. Bringing together the know-how and experiences of all NEURON partners, the network will continue to pursue its efforts to improve biomedical research in neuroscience in to the future.

*Researcher's instrumental fine tuning*

The first steps were taken with the start of NEURON's third phase entitled NEURON Cofund. It kicked off in January 2016 with a call 'External Insults to the Nervous System'. January 2016 marked the start of a series of annual calls to continue NEURON's core activity: funding of excellent research projects.



*Miniaturisation of research devices*

Our Latvian (VIAA) participants found that:

*»The ERA-NET format is simple, understandable, and also inclusive. […] ERA-NET research projects cover the gap well in the funding landscape for EU-13 countries.«* *Uldis Berkis, VIAA, Latvia*

Indeed, one of NEURON's main aims has always been to reach out to stakeholders and society. The foundation for future developments in that vein was laid with a symposium on how to reinforce the interactions between scientists, clinicians and society in the field of brain research.

*Medium scale sample processing*

*Data-recording*

*»… Working with professional and patient organisations is a major asset of [NEURON Cofund]. [Because it allows the funders to get] closer to citizen demand and need. It will give us more legitimacy and help the funding organisations spend their money where it really is needed.«* *Etienne Hirsch, INSERM, and Bernard Poulain, CNRS, both France*

To develop a common understanding of the needs and challenges in neuroscience research and funding, NEURON will continue to address important issues in workshops and symposia. These included hitherto patient involvement, reproducibility of research results, open access and data sharing. The exchange between NEURON partners, scientists and other relevant societal groups will help to shape NEURON's future actions and to advance a strategic alignment of funding policies across Europe and beyond.

Ahmi Ben-Yehudah at Israel's Ministry of Health (CSO-MOH) underlined how important cross border cooperation was on a national and supranational level:

*»We see the enhancement of promoting cross-border high level neuroscience research as one of the most important goals of NEURON, and therefore, see ourselves as part of the network in the future. […]Understanding where the field of Neuroscience is headed, enables us, on the national level, to lead [state wide] programs in the field.«*

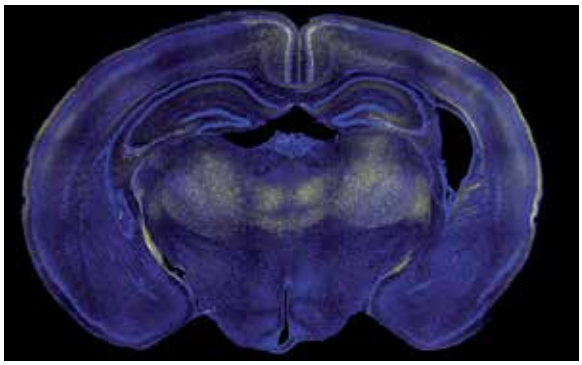
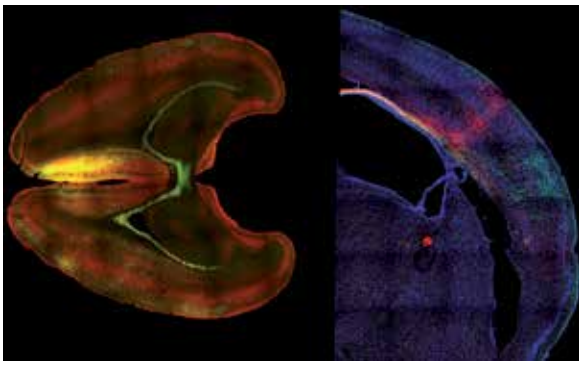


*Image of a fluorescent labelled brain section*



*Brain sections, labelled for analysis with different fluorescent probes*

We can't look at the future without making sure that the network works to value young scientists, many of whom have participated already in our funding programmes. Indeed, what would the future be without young scientists? Society needs bright minds with new ideas to tackle future challenges. To help develop the next generation of excellent neuroscientists, NEURON will continue to further progress its support of early career scientists.

Having the next generation in mind, our Dutch group wrote:

*»We hope the strengths of NEURON could be continued in a NEURON follower.«* *Rob P. W. Heinsbroek, NWO, The Netherlands*

Many of our partners expressed interest in being part of those future phases, like the UK group:

*»The MRC hopes that NEURON will continue to address questions in neuroscience areas where there is an unmet international need for research, bringing together knowledge, skills and resources from across national borders.«* *Talisia Quallo, MRC, UK*

Indeed, NEURON is already working on the next generation, building on its firmly established network of research funders in Europe and beyond.

*»NEURON's strengths are its high level of procedural organisation, its openness to new ways [of improving], trust[ing] in each other and in [collaboration], potential to organise funds and transform [all this into] high-quality research.«* *Rob P. W. Heinsbroek, NWO, The Netherlands*

NEURON partners will work together to sustain the network beyond the end of NEURON Cofund and will continue under Horizon 2020 to carry on its spirit in a subsequent phase. To this end, NEURON will also look for funding opportunities in the European Commission's next Framework Programme and hope that the excellent research undertaken to date will serve as building blocks for the network's future and cement its standing in the scientific research community across Europe and worldwide.

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Internet: http://www.neuron-eranet.eu/index.php
E-Mail: info@neuron-eranet.net

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**Layout**
sku:l communication
Michaela Richter
51674 Wiehl
www.sku-l.de

**Journalistic support**
Emma Wallis
Freelance Journalist
53424 Remagen

**Edited by**
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