

ERA-NET NEURON Joint Transnational Call 2008 'Neurodegeneration' Impact Report

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Abbreviations

AD Alzheimer's Disease

AKA Suomen Akatemia, Academy of Finland (Finnish NEURON partner)

ALS Amyotrophic Lateral Sclerosis

ANCS-MEdR Autoritatea Nationala Pentru Cercetare Stiintifica – Ministry of Education and Research

(Romanian NEURON partner)

ANR Agence Nationale de la Recherche (French NEURON partner)

AT Austria

BMBF Bundesministerium für Bildung und Forschung (German NEURON partner)

CNRS Centre de la Recherche Scientifique (French NEURON partner)

COO Coordinator

CSC Call Steering Committee

CSO-MOH Ministry of Health (Israeli NEURON partner)

DE Germany

DoW Description of Work EC European Commission

ERA-NET European Research Area Network

ES Spain

FCSAI Instituto de Salud Carlos III (Spanish NEURON partner)

FI Finland

FNR Fond National de la Recherche (Luxembourgian NEURON partner)

FR France

FWF Fonds zur Förderung der Wissenschaftlichen Forschung (Austrian NEURON partner)

HD Huntington's Disease

IL Israel

INSERM Institut National de la Santé et de la Recherche Médicale (French NEURON partner)

IT Italy

JCS Joint Call Secretariat

JTC Joint Transnational Call for research proposals

LU Luxembourg

MEC Ministry of Education and Science (Spanish NEURON partner in 2008)

MSRIT Ministry of Scientific Research and Information (Polish NEURON partner before 2008)

MOH Ministero della Salute (Italian NEURON partner)

MoU Memorandum of Understanding

MRC Medical Research Council (British NEURON partner)

NCBiR Narodowe Centrum Badan i Rozwoju (Polish NEURON)

NEURON Network of European Funding for Neuroscience Research

PI Principal Investigator
PD Parkinson's Disease

PL Poland

PRP Peer-Review Panel

PT-DLR Projektträger im Deutschen Zentrum für Luft- und Raumfahrt (German NEURON part-

ner; NEURON coordinator)

RO Romania

UK United Kingdom



<u>Abstract</u>

NEURON represents a new mode of cooperation between ministries and public funding organizations across Europe, Israel, and Canada funded by the European Commission. By initiating collaboration on international, national, or regional levels, a new European Research Area Network (ERA-NET) focused on a better understanding of brain function and diseases was shaped. In addition to creating a strategically operating group of funding organizations in Europe and beyond, Joint Transnational Calls (JTC) for research proposals are the core activity of NEURON. These annual calls address important topics in the fields of fundamental neuroscience, neurology, or psychiatry. Small-scale transnational research consortia can jointly apply.

The topic of the JTC launched in 2008 was on neurodegenerative diseases of the central nervous system. Twelve successful consortia passed the pre-proposal and the peer-review process, and their research projects were funded for three years. Monitoring the results of the projects and evaluating the outcome of those research consortia provides information on the success or shortcomings of this funding programme. After the termination of the funding period all consortia were asked to complete a questionnaire regarding the outcome of the projects. The results of that evaluation are presented in this report.

In brief, the JTC 2008 appears to have been a very successful funding measure. The degree of collaboration among the researchers was high and fruitful as indicated by the good publication record reported back to the NEURON consortium. The results underline that transnational funding support of disease-related neuroscience research provides a clear added value over purely national strategies. The strong focus on multidisciplinary research consortia and collaborative translational approaches enables outcomes accelerating the generation of knowledge that potentially leads to novel therapies and new strategies to combat neurodegenerative diseases – and eventual benefit for the afflicted patients.

Introduction

ERA-NETs are projects funded by the European Commission (EC) in various fields of research. Their goal is to create a European Research Area (ERA) in which research is funded and conducted across countries, allowing research groups to jointly investigate specific scientific questions, exchange ideas, and benefit from cross-border expertise and resources.

The Network of European Funding for Neuroscience Research (NEURON; http://www.neuroneranet.eu) was initiated in 2003 as a Specific Support Action funded by the EC. The four founding organizations of this pilot activity were BMBF (Germany, represented by PT-DLR), CSO-MOH (Israel), MSRIT (Poland), and FNR (Luxembourg). To-date, 24 ministries and funding agencies from 18 countries across Europe, Israel, and Canada have joined forces to support research on diseases of the brain and the nervous system. According to estimates by the World Health Organization, more than one billion people suffer from brain diseases. In most cases the underlying mechanisms are still not well understood and no curative treatments are available. Facing medical, societal and financial challenges, NEURON aims to support basic, clinical, and translational research directed at a better understanding of the brain, its diseases and their progression in order to pave the way for new or improved diagnostics and therapies. In 2008 NEURON was coordinated by PT-DLR (Germany) and comprised the following partners: Austria (FWF), Finland (AKA), France (ANR, INSERM, CNRS), Germany (BMBF/ PT-DLR), Israel (CSO-MOH), Italy (MOH), Luxemburg (FNR), Poland (NCBiR), Romania (ANCS-MEdR, NCPM), Spain (ISCIII, MEC), Sweden (SRC), and United Kingdom (MRC).

Objectives of NEURON

The objectives of NEURON are to create a strategically aligned operating group of relevant research funding organizations across Europe, including other non-European countries where feasible, and to



support a coordinated implementation of research programmes in the area of disease-related neuro-science. The roadmap to achieve these objectives comprises several steps:

- Exchange of information about participating organizations and their programmes, identification of common needs (benchmarking),
- Quality assurance according to the results of the benchmarking activities,
- Establishing a platform for programme managers and researchers as an interface between science and funding policy, to feed back into future national funding programmes,
- Coordination of existing funding programmes and activities,
- · Development of concepts for future joint activities,
- Mutual operating support of funding programmes through joint multilateral calls.

NEURON is based on the concept of a variable geometry in which each funding organization decides, independently of the other partners, whether or not they should participate in joint activities of the network. While allowing maximum flexibility for all funding bodies, this and the involvement of all partners in the decisions ensure that national strategies, requirements and legal aspects are met and respected. .

Joint Transnational Calls for Research Proposals

Joint Transnational Calls (JTC) for research proposals are the centerpiece of NEURON's transnational activities. On behalf of national ministries and funding organizations, NEURON coordinates an annual launch of a JTC in the field of disease-related neuroscience, addressing central issues in the wide fields of fundamental neuroscience, neurology, or psychiatry. Call topics are usually broad and cover various aspects of a research field, allowing and encouraging cross-disciplinary applications. Researchers from Europe, Israel and Canada may apply as small scale research consortia (up to five partners per consortium). Selection criteria for funding of research projects are (i) scientific excellence (innovative ideas, methodology), (ii) feasibility of the project, (iii) international competitiveness of participating groups in the field, (iv) high quality of the collaborative interaction between the groups, (v) a clear added value of the research consortium, and (vi) high impact of the expected results on clinical and other health-relevant applications. Detailed information on the selection criteria and the peerreview process are described in Annex 1. Each consortium has to be comprised of a minimum of three research groups eligible for funding, from at least 3 different countries. The total number of research groups in a consortium must not exceed five and not more than two research groups can be from the same country.

By evaluating and monitoring the results of the funded consortia, NEURON's intent is to assess the outcome against the expectations of the NEURON partners. Feedback from the research community was also attained in order to improve, where necessary, NEURON's performance during future calls. Hence, a questionnaire was sent to the coordinators of the JTC 2008 after the end of the funding period (see Annex II). The results are displayed in the present report and will be discussed below.

Joint Transnational Call for Research Proposals 2008

The first JTC of the ERA-NET NEURON was entitled 'European research projects on neurodegenerative diseases of the central nervous system' and was launched in January 2008.

This JTC was prepared in close collaboration by several partners: representatives from INSERM and CNRS (France) organised a scientific workshop on the topic of neurodegeneration in order to shape the thematic framework of the call. Subsequently, delegates from FWF (Austria) and PT-DLR (Germany) prepared the documents for the administrative official procedures (Memorandum of Understanding, Call Text, and 'Procedures Document'). Thirteen out of the 15 NEURON partners contributed to the JTC 2008 and formed the Call Steering Committee (CSC). The peer-review and funding selection of proposals was coordinated by a Joint Call Secretariat (JCS) run by the PT-DLR.



Call Preparation

The topic of the first joint call was selected during several NEURON meetings prior to the call launch. At first, all partners agreed that neurodegenerative diseases were a major global burden and that understanding the pathological mechanisms and developing novel diagnostics and therapies were very important research topics. Members of NEURON's Scientific Advisory Board and a group of renowned neuroscience experts were invited to present an overview about different research areas within the field of neurodegenerative diseases. The scientists supported the suggestion of the topic in a scientific workshop 'Neurodegeneration: State of the Art and Future Orientations' held in Paris in October 2007 (for more details see Annex III and the related NEURON newsletter available at http://www.neuroneranet.eu/ media/Neuron_newsletter 1_June_2008.pdf).

Call Procedures and Memorandum of Understanding

The Call Steering Committee composed a 'Procedures Document' which provided a detailed description of the processes related to the Joint Transnational Call. The regulations included the duties of the CSC, the eligibility criteria for applicants, the submission and evaluation procedures, the funding itself, and the reporting requirements. The process description was part of a Memorandum of Understanding (MoU) that served as a mutual statement of intention and was signed by all NEURON partners participating in the JTC 2008. All signatories agreed to make every reasonable effort to fulfil the intent expressed in the JTC as well as its implementation.

Budgetary Aspects

NEURON partners decided to use the 'virtual common pot' model to fund the multinational research consortia. In this model, funding organizations provide support for the researchers from their own country in the respective successful consortia. The earmarked budgets from all participating partners were part of the MoU. The actual final call budget provided by the funding organizations amounted to 10.3 million €.

The Peer-Review Process

A one-step procedure (full proposals only) was used for this JTC. All submitted proposals were evaluated by three external reviewers. The peer-review panel (PRP) consisted of 16 members. After intense discussion of each proposal, the reviewers agreed on a ranking list of projects recommended for funding. Based on this ranking list and availability of means, the funding organizations decided to support twelve research consortia. In September 2008, the funding decision was made public and the final list of twelve funded consortia was announced (see Fig. 1 and Table 1). The review process and results were published on the NEURON web site (http://www.neuron-eranet.eu/en/220.php).

Results of the Peer-Review Process

Overall, 20% of the proposals were funded (for call statistics and overview see Table 1 and 2).

Table 1: Submission details and success rate.

	Proposals	Funded projects
No. of proposals	59	12
Principal Investigators involved	234	45
Overall funding requested	56 million €	10.5 million €
Proposal success rate	20%	



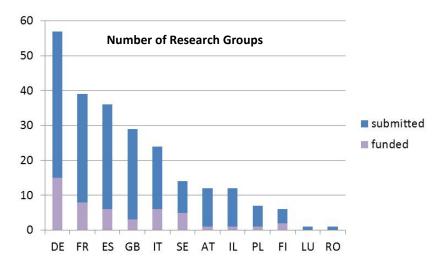


Fig. 1: Total number of research groups included in all proposals. The numbers are split into submitted and funded per country.

Table 2: Projects selected for funding in JTC 2008. The average consortium was comprised of 4 research groups.

Acronym	Project Title	Coordinators and Principal Investiga- tors	Project Keywords	Patho -logy
ADTest	Role of proteases and their inhibitors in pathophysiology and diagnosis of Alzheimer Disease	M. Glatzel (DE) H. Jahn (DE), T. Clausen (AT) I. Ferrer (ES)	Biomarkers, CSF, mass spectrometry, diagnosis, protease inhibitors/ testican, mouse models	AD
EPITHERAPY	An epigenetic approach towards the recovery of neuronal network plasticity and cognitive function in neurodegenerative disease	A. Fischer (DE) A. Barco (ES) X. Leinekugel (FR)	Histone acetylation, HDAC inhibitors, mouse models, biomarkers	HD, AD
ERMCC- NDEG	The activity-driven ER-mitochondria Calcium Cycle (ERMCC) and protein misfolding in neurodegenerative diseases: finding targets for therapy	J. Grosskreutz (DE) B. Keller (DE) J. Garcia-Sancho (ES) M. T. Carri (IT)	Mouse models, presenilin, SOD1, apoptosis, calcium imaging, Electrophysiology	AD, ALS
FamPD	Identification of new genes causing familial forms of PD	T. Gasser (DE) N. Wood (UK) A. Brice (FR)	Patients cohorts, linkage analysis, copy-number varia- tions, next-generation se- quencing, exome sequencing	PD
heteropark	Synthesis and validation of antiparkin- sonian drugs targeting GPCR heter- omers	R. Franco (ES) MT. Armentero (IT) C. E. Mueller (DE) J. L. Lanciego (ES)	Drug discovery, animal mod- els, adenosine receptors, cannabinoid receptors	PD
IpsoALS	Modelling sporadic ALS in motor neu- rons by genetic reprogramming of patient skin fibroblasts	G. Haase (FR) B. Reubinoff (IL) P. Andersen (SE) J. M. Heard (FR) T. Misgeld (DE)	Induced pluripotent stem cells, motor neurons, alsin/ALS2, Golgi, tubulin, mouse models, mitochondria	ALS
mGluRPatho	Group III metabotropic glutamate receptors (mGluRs): from new molecules to therapeutic development for the treatment of Parkinson's disease	M. Amalric (FR) F. Acher (FR) G. Fisone (SE) F. Nicoletti (IT)	In silico optimization, mouse models, FRET-based sensor, in vivo microdialysis, L-DOPA- induced dyskinesia	PD



MIPROTRAN	Transfer of misfolded protein as a pathogenetic mechanism in neuro-degenerative disease	P. Brundin (SE) R. Melki (FR) M. Jucker (DE) O. Riess (DE)	Misfolded proteins, α -synuclein, prion, mouse models, amyloidosis, brain tissue grafting, in vivo imaging	Sev- eral
nEUROsyn	Molecular mechanisms underlying synaptic dysfunction in prototypic neurodegenerative diseases related to protein misfolding	F. Tagliavini (IT) J. R. Naranjo (ES) G. Binetti (IT) JY. Li (SE)	Mouse models, NMR spectroscopy, DREAM (Downstream Regulatory Element Antagonist Modulator), CSF, HD patients lymphoblasts	Sev- eral
PARKCDNF	Development of an experimental ther- apeutic strategy using the newly identi- fied growth factor CDNF for treatment of Parkinson's disease	K. Krieglstein (DE) M. Saarma (FI) E. Fuchs (DE) R. Tuominen (FI) O. Lindvall (SE)	Non-human primates, gene therapy, nigrostriatal dopa- mine neurons, encapsulated cell biodelivery	PD
PhysioIDBS	Physiological mechanisms of Deep Brain Stimulation in Parkinson's dis- ease	J. Volkmann (DE) C. Hammond (FR) P. Winn (UK) A. Priori (IT) A. Schnitzler (DE)	Subthalamic nucleus deep brain stimulation, magne- toencephalography (MEG), bioengineering, mouse mod- els, electrophysiology	PD
ProGen	Protecting against neurodegeneration by somatic gene therapy	T. Arendt (DE) J. Uney (UK) B. Nawrot (PL)	Gene therapy, convection enhanced delivery, cell cycle	Sev- eral

Funding Details

The following table (Table 3) provides an overview of the proposals and selection process in JTC 2008:

Table 3: Proposal distribution and selection.

Country	DE	FR	ES	ES	GB	IT	SE	AT	IL	PL	FI	LU	RO	13 funding bodies, 12 countries
Total number of COOs within all proposals	19	9	10	2	2	5	1	5	2	2	2	0	0	59 COO = 59 proposals
Total number of research groups within all proposals	57	39	25	11	28	24	14	10	12	7	6	1	1	234 research groups in total
Funded COOs	7	2	1	0	0	1	1	0	0	0	0	0	0	12 COO = 12 funded consortia
Funded Re- search Groups	15	8	6	0	3	6	2	1	1	1	2	0	0	45 funded research groups within 12 consortia
Requested Funds (of all 59 proposals; m €)														69.3
Allocated Funds (m €)														10.5€

COO = research consortium coordinator



Impact of the JTC 2008

Impact Analysis and Methods

Evaluation of the funding activities should provide information and insight for short- and long-term strategic planning and for improving NEURON's performance. To achieve this aim, several indicators for monitoring the anticipated impact and the added value of NEURON JTCs were defined and used for this impact report.

Table 4 summarizes the main objectives of the NEURON funding programme, the key performance (output) indicators, and the means to evaluate them. These indicators were used to analyse the twelve funded projects. A questionnaire was created using these indicators for self-evaluated impact analysis (see Annex II). It was collected from the project coordinators after the end of the project funding period of three years.

Table 4: Relation of output indicators and way of measuring them to the objectives of the funding programme.

Objective of the	Output Indicators	Measures (i.e. questions in the questionnaire)
Funding Programme		
Enhance cooperation between European scientists working in the field of neuroscience	NEURON JTC as a catalyst for new collaborations New research groups from other countries joining the	Question 3.1 Have the partners participating in the NEURON project collaborated before applying for the NEURON JTC2008? Question 3.2 During the life-time of the project has the consortium established collaboration(s) with other teams (not already particities).
	Sustainability of the collaboration (obtaining further funding for the same consortium)	pating in the JTC 2008 project)? Question 3.3 Have the results led to new initiatives in other types of funding programmes?
	Intensity of collaboration (meetings, mobility)	Question 3.4 List of meetings, lab visits/exchange of researchers, and training within the consortium
	Level of excellence of the funded research	Question 1.2 Use of bibliometric indicators (IF, h-index, other indicators)
2. Promote multi-	Composition of the consortium	List of research groups; analysis of full proposals
disciplinary consortia and	Involvement of patients	Analysis of full proposals
encourage translational research proposals (from bench to bedside)	List of patents and other out- comes with potential impact on health	Question 2 Patents and other outcomes with potential impact on health
3. Support development of innovative or shared resources and technologies	Evaluation of the development and use of new resources	Question 4.1 and 4.2 Has the consortium created a new or further developed an existing transnational patient registry, database or biobank? Have the consortium partners exchanged bioresources (DNA, tissues, cells, animals)?
4. Support research to develop new strategies for diagnosis, therapy, and rehabilitation procedures for neurodegenerative diseases	Evaluation of the development of new strategies for diagnosis, therapy, and rehabilitation procedures for neurodegenerative diseases	Question 5.1 Have the results of the NEURON research projects allowed the development of new strategies for: diagnosis, therapy (preparation of clinical trials), rehabilitation procedures for neurodegenerative diseases, prevention or anything else?
	Major achievements	Question 5.2 Please list the major achievement of the consortium.



1. Enhanced Cooperation between European Scientists Working in Neuroscience

Indicator: NEURON JTC as a Catalyst for New Collaborations

This indicator was measured by question 3.1 in the impact questionnaire: 'Have the partners participating in the NEURON project collaborated before applying to the NEURON JTC 2008? If so, please indicate the partner numbers of teams that previously collaborated.'

One third of the funded consortia included research groups that had not collaborated before applying to the NEURON JTC 2008 (4 out of 12; these are named 'new consortia', see Fig. 2). The remaining 66% 'pre-existing' consortia consisted of two to five groups that had previously collaborated with each other. The coordinator was always included within the previously collaborating groups.

In summary, new consortia were formed in response to the JTC 2008, although the majority of projects was carried out by researchers who had known each other before the call was published. Hence, funding by NEURON served both purposes, establishing new collaborations and helping to sustain and foster collaborations that already existed.

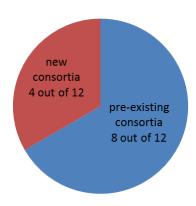


Fig. 2: Results of indicator 1.1, the NEURON JTC 2008 as a starter of new collaborations.

New consortia = consortia with partners that had not previously collaborated.

Pre-existing consortia = consortia with partners that had been or still were collaborating before applying to NEURON JTC 2008.

Indicator: New Research Groups from other Countries Joining the Consortium

This indicator was measured through question 3.2 in the impact questionnaire: 'During the lifetime of the project, has the consortium established collaboration(s) with other team(s) (not already participating in the JTC 2008 project)? If so, please name the institutions and countries.'

Overall, 53.7% of all consortia (7 out of 12) formed new additional collaborations during the lifetime of the project. Among these, most of them (6 out of 7) were pre-existing consortia that actively increased the number of collaborators. This means, in turn, that new consortia were less likely to expand their activities compared to pre-exiting consortia.

Of note, most of these newly collaborating research groups came from countries that were not already included in the respective consortium (5 out of 7). This fact adds to the transnational character of NEURON.

In summary, consortia funded through JTC 2008 were able to attract new research groups.

Indicator: Sustainability of the Collaboration

One way to measure the sustainability of NEURON-funded consortia is by counting the number of consortia that applied for further transnational funding during the lifetime of the NEURON project. This indicator was measured through question 3.3: 'Have the results led to new initiatives in other types of funding programmes?'



Overall, one third of the funded consortia (4 out of 12) had at least two Principal Investigators (PIs) applying jointly for further funding. Perhaps not surprisingly, all of these PIs were part of pre-existing consortia, i.e., they already had experience in collaborating transnationally.

The transnational funding programmes to which the PIs applied were:

- NEURON JTC 2012 on 'Novel Methods and Approaches towards the Understanding of Brain Diseases' (4 out of 4 consortia);
- FP7 programmes (3 out of 4 consortia).

In summary, one third of all consortia applied to other funding schemes or calls in their current constellation based on the successful NEURON participation. This suggests that - in some cases - NEURON may pave the way for a sustainable collaboration beyond its funding period. However, two thirds of the consortia did not apply for further funding, and the reasons remain a matter of speculation. Obviously, it was not for lack of success, as shown by their high output. More funding opportunities with a transnational focus may be necessary to increase the sustainability of high-level transnational consortia such as the NEURON-funded ones.

Indicator: Intensity of Collaboration (Meetings and Mobility)

This indicator was measured by the number of meetings including at least two research groups of each individual consortium.

All funded consortia participated in the mid-term and final symposia which were organized by NEU-RON. A total of 75% of consortia had at least three extra meetings with their respective partners. No exchange visits of students or scientists were reported.

In summary, the meetings organized by NEURON were well-attended underlining their benefit for call-steering matters, monitoring, and scientific and feedback purposes. Internal consortia meetings were also a well-used means for administrating a research consortium. The lack of mobility of students and scientists may reflect the difficulties organizing such exchange and the high costs involved such as travel and accommodation.

Indicator: Level of Excellence of Funded Research

Despite the well-known limitations of assessing publication numbers and Impact Factors, one way to measure this indicator is by analysing the lists of publications (Question 1: Please indicate the number of publications and communications in which NEURON support was acknowledged).

The NEURON-funded consortia were very productive and successful in terms of dissemination of results: in total, 182 scientific publications were reported. 41.6% of funded consortia (5 out of 12) published at least four primary research publications in a peer-review journal with an Impact Factor above 5. In addition, 50% of the consortia (6 out of 12) published at least one primary research publication in a peer-review journal with an Impact Factor above 10:

- Lancet (1),
- Science (3),
- Journal of Clinical Investigation (1),
- EMBO Molecular Medicine (2),
- PNAS (1).

In summary, the outcome of this JTC in terms of publications in high-ranking journals was very impressive. This reflects the excellent quality of the funded projects. It also shows that the transnational consortia worked very well and closely together. The exchange of knowledge, data transfer, and the collaborative approach in general were successful tools for conducting research on relatively small budgets (i.e., as compared to some national or EU schemes).



2. Multidisciplinary Consortia and Translational Research Proposals (from Bench to Bedside)

Indicator: Composition of the Consortium

The analysis of the career background of funded researchers showed that

- in 67% of the consortia (8 out of 12) the coordinator was a medical doctor;
- in 83% of the consortia (10 out of 12) at least one Principal Investigator was a medical doctor;

Furthermore, the analysis of each project showed that 66% of funded consortia (8 out of 12) undertook multidisciplinary research, e.g. combining different disciplines within or beyond biomedical research.

In summary, the collaboration of research groups from different background by means of the NEU-RON JTC 2008 truly allowed scientists to work together merging synergistically their expertise across disciplines.

Indicator: Involvement of Patients

In order to measure the translational aspect of the funded research, projects were analysed with regard to their work with patients.

- patients were involved in 50% of the projects (6 out of 12),
- pre-clinical work was performed in order to pave the way for clinical trials in 16.7% of the projects (2 out of 12),

Overall, 66% the funded projects were using a bench-to-bedside approach (8 out of 12).

In summary, NEURON's mission is to support disease-related neuroscience research that aims to accelerate the translational or "bench-to-bedside" process. The high percentage of translational research matches this aim well and gives momentum to the development of diagnostic tools or potentially novel cures through the projects funded in JTC 2008.

Indicator: Patents and Other Outcomes with Impact to Health

33% of all funded consortia (4 out of 12) submitted at least one European or international patent; other outcomes with potential impact for health are shown below (see also Fig. 3).

- Launching of a product or service:
 - PARKCDNF: in collaboration with Icosagen Ltd. biotech company the CDNF ELISA is now commercially available; http://www.icosagen.ee/products/elisa-kits/cdnf
- Creation of a platform available to a community:
 - o mGluRPatho: development of a FRET based sensor compatible with HTS, and being used for ligand characterization on the ARPEGE platform; http://www.arpege.cnrs.fr/.
 - EPITHERAPY: creation of a free web-based database search for activity dependent neuronal gene expression; http://in.umh-csic.es/NADtranscriptomics/.
- Foundation of a firm, fund-raising:
 - o MIPROTRAN: foundation of the Swedish firm Neurprotex (2010, terminated 2011)
 - PARKCDNF: Finnish global neurosciences firm HermoPharma Ltd. to take CDNF to the clinic; http://www.hermopharma.com/.

In summary, a considerable number of consortia funded through JTC 2008 registered patents and developed data banks and other products, emphasizing the fruitfulness of this transnational funding scheme and its impact for broad application.



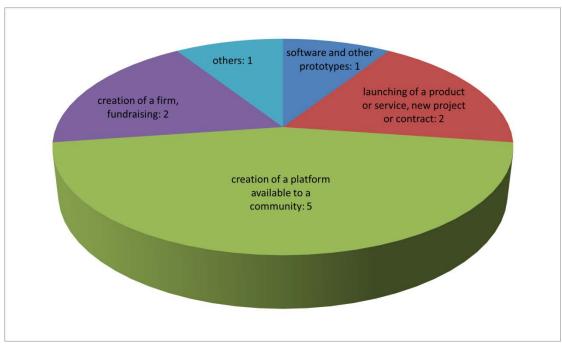


Fig. 3: Patents and other outcomes with potential impact for health.

3. Innovative or Shared Resources and Technology

Indicator: Evaluation of the Development and Use of New Resources

The indicator chosen to assess this objective was the number of consortia that effectively developed and/or shared innovative resources or technology.

Question 4.1: Has the consortium created a new or further developed an existing

patient registry?
patient database?
biobank?
8%, 1 out of 12 consortia
17%, 2 out of 12 consortia
8%, 1 out of 12 consortia

Question 4.2: Have the consortium partners exchanged any material (DNA, tissues, cells, animals or clinical data)?

• 92% of consortia (8 out of 12) had some exchange of material or data (see Fig. 4).

In summary, few consortia shared open source data. Creating large scale databases such as patient registries or databases and bio banks were beyond the scope of NEURON with limited funds and a run time of only three years. Nevertheless, the exchange of unprocessed clinical data or specimens was more or less standard within the consortia and was part of a frequent exchange among the research groups.

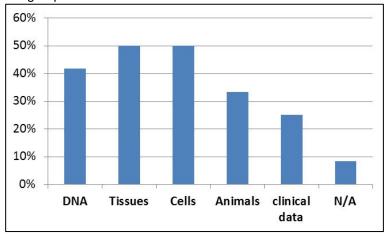


Fig. 4: Exchange (percentage of all consortia) of DNA, tissues, cells, animals or clinical data. N/A stands for other laboratory material that was exchanged.



4. New Strategies for Diagnosis, Therapy, and Rehabilitation Procedures

Indicator: Development of New Strategies for Diagnosis (Question 5.1) and Therapy, and Rehabilitation Procedures; Major Achievements of the Funded Consortia (Question 5.2)

A total of 66% of all consortia (8 out of 12) developed new strategies for novel therapies. A quarter also developed new methods for diagnosing disease. These advancements towards new therapeutic strategies included the discovery of new drug targets, the analysis of the genetic backgrounds of hereditary forms of neurodegenerative diseases in patients, the identification of neuroprotective targets (clinical phase I trials planned), and new mechanistic insights opening opportunities for new therapies. The projects funded through JTC 2008 had not proposed disease prevention or rehabilitation.

In summary, two thirds of all consortia produced data that will potentially help to develop novel therapies and improve diagnostics, underlining the translational character of their work and importance for patients.

From a list in the questionnaire the researchers could pick themes that described the type of results of their research best (see Fig. 5 and Question 5.2 in Annex II).

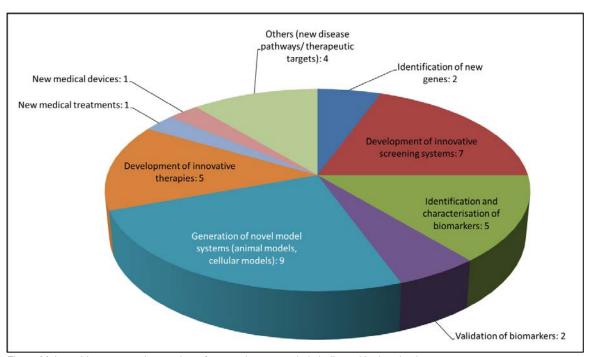


Fig. 5: Major achievements: the number of respective consortia is indicated in the pie chart.

In summary, developing novel therapies and treatments including new medical devices and drug targets were chosen by most consortia as major achievements underlining the translational character of consortia funded through JTC 2008. The generation of model systems to simulate disease or to test new substances were also frequently selected as important achievements. Hence, NEURON consortia actively participated in the quest for better pre-clinical research systems to find novel therapies. Furthermore, diagnostic tools were developed as shown by the identification of new biomarkers and screening systems that will help patients to be more accurately diagnosed and to tailor and personalize future therapies. Taken together, all these achievements will potentially result in better treatments for patients and hopefully reduce the suffering induced by neurodegenerative diseases.



Overview of all Results

Table 5: Results of the feedback questionnaire.

Objective of the	Output Indicators	Results
Funding Programme	Output muicators	Results
1. Enhance cooperation between Euro-	NEURON JTC as starter of new collaboration	→ 33% of newly formed consortia were funded.
pean scientists working in the field of neuroscience	New research groups from other countries joining the consortium	ightarrow 54% of consortia acquired new collaborations during the lifetime of the project.
	Sustainability of the collaboration (obtaining further funding for the same consortium)	\rightarrow 33% of consortia had at least 2 PIs applying jointly for further funding.
	Intensity of collaboration (meetings, mobility)	 → 100% funded consortia participated to the mid- term and final NEURON review meetings. → 75% of consortia held at least 3 meetings with all consortium partners.
	Level of excellence of the funded research	 → 42% of consortia published at least four primary research publications in a peer-review journal with an Impact Factor above 5. → 50% of consortia published at least one primary research publication in a peer-review journal with an Impact Factor above 10.
2. Promote multi- disciplinary consor- tia and to encourage translational re- search proposals (from bench to be- side)	Composition of the consortium	 → In 67% of funded consortia (8 out of 12) the coordinator was a medical doctor. → In 83% of funded consortia (10 out of 12) at least one Principal Investigator was a medical doctor. → In 83% of consortia (10 out of 12) basic research labs were associated with either clinical research labs, or hospitals.
	Involvement of patients	 → Patients were involved in 50% of the projects (6 out of 12). → Pre-clinical work was performed in order to pave the way for clinical trials in 16.7% of the projects (2 out of 12). → Overall, 66% the funded projects were using a bench-to-bedside approach (8 out of 12).
	Patents / other outcomes with impact to health	ightarrow 33% of all funded consortia (4 out of 12) submitted at least one European or international patent; other outcomes with impact for health are shown below
3. Support devel- opment of innova- tive or shared re- sources and tech- nologies	Evaluation of the development and use of new resources	 → created/developed a: patient registry: 1 consortium patient database: 2 consortia bio bank: 1 consortium → 92% of consortia (8 out of 12) exchanged bio resources (tissues: 50%, cells: 50%, DNA: 41%).



4. Support research to develop new strategies for diagnosis, therapy, and rehabilitation procedures for neurodegenerative diseases Evaluation of the development of new strategies for diagnosis, therapy, and rehabilitation procedures for neurodegenerative diseases

Major achievements

- \rightarrow 66% of consortia developed strategies for (i) new diagnosis and (ii) novel therapies.
- \rightarrow 75% of consortia generated novel model systems (cellular or animal models).
- \rightarrow 58% of consortia developed innovative screening systems.
- ightarrow 41% of consortia developed innovative therapies.

Summaries of the individual outcome reports are published on the NEURON web site (http://www.neuron-eranet.eu/en/224.php).



Annex I

Call Text JTC 2008

1. Purpose

The maintenance, improvement and restoration of human health are of fundamental importance and priority in all countries. Biomedical and health research provide an important basis for the improvement of healthy living. Among the many diseases affecting human health, disorders of the brain are major causes of morbidity, mortality and impaired quality of life. According to estimates by the World Health Organization (World Health Report 2001), more than one billion people suffer from disorders of the central nervous system. In Europe, disorders of the brain account for approximately one-third of the total burden of all diseases. With increasing average life-expectancy of the population especially in highly industrialized countries this percentage will continue to rise, as the incidence of neurodegenerative conditions increases with age. Thus, neuroscience research and its translation into diagnostic and therapeutic measures are of high priority.



Fig. 1: The call was published on the NEU-RON web site in January 2008

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

Under the umbrella of NEURON, the following funding organizations have agreed to fund the first joint transnational call for transnational research projects on neurodegenerative diseases. The call will be conducted simultaneously by the funding organizations in their respective countries and coordinated centrally by the Joint Call Secretariat (JCS).

- Austrian Science Fund (FWF), Austria
- National Research Agency (ANR), France
- · Federal Ministry of Education and Research (BMBF), Germany
- Chief Scientist Office, Israel Ministry of Health (CSO-MOH), Israel
- National Research Fund (FNR), Luxemburg
- Ministry of Science and Higher Education (MNiSW), Poland¹
- National Authority for Scientific Research Ministry of Education, Research and Youth (ANCS MECT), Romania
- Ministry of Education and Science (MEC), Spain
- Institute of Health Carlos III (ISCIII), Spain
- Swedish Research Council (SRC), Sweden
- Medical Research Council (MRC), UK

Possible partners:

- Academy of Finland (AKA), Finland²
- Ministry of Health (MOH), Italy³

¹ The implementation of the call will be conducted by the The National Centre for Research and Development (NCBiR).

² Provided the positive decision of the Academy Research Councils in February 2008.



2. Aim of the call

The aim of the call is to enable transnational, collaborative research projects that will address important questions relating to human neurodegenerative diseases of the central nervous system. Cerebrovascular diseases (e.g. stroke) are not included in the present call. The call may receive proposals within the breadth of research from understanding basic mechanisms of disease through to proof-of-concept clinical studies in man. The ERA-NET NEURON funding organizations particularly wish to promote **multi-disciplinary working** and to encourage **translational research proposals** (from bench to patient bedside) that combine basic and clinical approaches.

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

- a) Fundamental research on the pathogenesis and aetiology of neurodegenerative diseases. This may include the development of innovative or shared resources and technologies. The relevance of the research to disease must be clearly indicated.
- b) Research to develop new strategies for (early) diagnosis, therapy, and rehabilitation procedures for neurodegenerative diseases.

Projects may include, **for example**, identification, characterisation and validation of biomarkers, biological targets, development of innovative screening systems, generation of novel model systems, gene or cell therapies. Clinical studies are eligible up to the point of proof of concept.

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

3. Application

3.1 Eligibility

Joint transnational research proposals may be submitted by research groups working in universities (or other higher education institutions), non-university public research institutes, hospitals, as well as commercial companies, in particular small and medium-size enterprises. The eligibility of the afore-mentioned institutions, together with details of eligible costs (personnel, material, consumables, travel money, investments,...), are subject to the individual administrative requirements of individual funding organizations and may therefore vary. Please note particularly that commercial companies are for some funding organizations not or only under certain conditions eligible (e.g. only in partnership with academic institutions in the consortium). Clarification may be obtained from the individual funding agencies (see contact details below).

Only transnational projects will be funded. Each proposal must involve a minimum of three research groups from three different participating NEURON partner countries and a maximum of five research groups. Research groups from countries whose funding organizations are not partner of the ERA-NET NEURON may participate in projects if they are able to secure their own funding. They must state clearly in the proposal if these funds are already secured or if not, how they plan to obtain funding in advance of the start of the project.

The composition of the consortium should be appropriate for the aims of the research project and **clearly demonstrate added value by the international collaboration**. Each consortium should have the critical mass to achieve ambitious scientific goals and should clearly demonstrate added value from working together.

One project coordinator among the project partners who represents the consortium externally will be responsible for its internal management.

³ Subject to formal commitment in February 2008.



Whilst applications will be submitted jointly by groups from several countries, individual components (subprojects) will be funded by the individual NEURON funding organization(s) respective of the country from which applicants have applied. Subproject applications are therefore subject to eligibility criteria of individual funding organizations.

Therefore, applicants are strongly advised to discuss their intentions and confirm eligibility with their respective funding organizations in advance of submitting an application.

3.2 Financial and legal modalities

Funding is available for projects of a duration of three years and is subject to national regulations. Eligible costs may vary according to the corresponding national funding agency's regulations. Each group is subject to the rules and regulations of its respective national funding agency.

3.3 Submission of joint transnational proposals

One joint proposal document (in English) shall be prepared by the partners of a joint transnational proposal, and must be submitted to the Joint Call Secretariat (JCS) by one spokesperson, the coordinator, in **electronic format** by the **deadline no later than April 07, 2008**, and in a signed paper version **(1 original + 4 copies) no later than April 14, 2008**.

Proposals must include the following information, provided on the respective forms (proposal template, template for financial data, electronic application) available through the NEURON website:

- Names and full affiliations of the project coordinator
- Names and full affiliations of the subproject leaders and other personnel participating in the joint project.
- Scientific abstract (max. ½ page)
- Lay abstract (max ½ page)
- Background and present state of the art in the research field and rationale (max. 2 pages)
- Work plan highlighting the originality and novelty (aims, methodology, involvement of participants, time plan, project coordination and management; max. 8 pages)
- Financial plan for each subproject provided on the respective table available within the electronic application data sheet.
- Justification of requested budget (also specifying co-funding from other sources necessary for the project, if applicable; max. 1 page)
- Added value of the proposed collaboration (max. 1 page)
- Possible exploitation of expected project results including data management and data sharing (max. ½ page)
- Handling of intellectual property rights (IPR) (e.g. any barriers to sharing materials or results), both within and outside the research consortium (max. ½ page)
- Description of patents and ongoing projects of each participating group related to the present topic, indicating funding sources and possible overlaps with proposal (max. ½ page per subproject)
- Ethical and legal issues (e.g. informed consent, data protection, use of animals), if applicable, according
 to national regulations
- Brief CVs for each participating subproject leader with a list of up to five relevant publications within the
 last five years demonstrating the competence to carry out the project (max. 1 page each)

3.4 Further information

If you need additional information, please contact the Joint Call Secretariat, or your national funding agency representative (see Annex for contact data).



4. Evaluation and decision

4.1 Formal check of proposals

The Joint Call Secretariat (JCS) will assess proposals to ensure that they meet the call's formal criteria (date of submission; number of participating countries; inclusion of all necessary information in English). The JCS will also check the scientific eligibility of the proposal (e.g. conformity with the disease spectrum of the call).

In parallel, the JCS will forward the proposals to the national funding organizations which will perform a formal check of compliance with their respective regulations. Proposals not meeting the formal criteria will be rejected. Proposals passing both checks will be forwarded to the joint Peer Review Panel (PRP) for consideration for funding.

4.2 Peer-review of proposals

The PRP members will carry out the evaluation according to specific evaluation criteria:

- 1. Relevance to the aim(s) of the call
- 2. Scientific quality of the proposal (innovation potential, methodology)
- 3. International competitiveness of participating research groups in the field(s) of the proposal (previous work in the field, expertise of the research groups)
- 4. Feasibility of the project (adequacy of project work plan, budgetary and other resources, time schedule)
- Quality of collaborative interaction between the groups, and added value, on both levels scientific and transnational, of the research consortium
- 6. Potential of the expected results for future clinical and other health relevant applications

4.3 Decision

The international Joint Peer Review Panel will establish a ranking list of the proposals. Based on this ranking list, the Call Steering Committee will suggest the projects to be funded. Based on these recommendations, final decisions will be made by the national funding agencies and will be subject to budgetary considerations.

5. Funding procedure / Responsibilities / Reporting requirements

Projects can be funded for a period of three years. Funding is expected to start at the end of 2008 or early in 2009.

Subprojects of successful collaborative projects will be funded directly by the respective national funding organizations who will also meet the necessary administration and management costs. Funding will be administered according to the terms and conditions of the responsible national funding organizations, taking into account all other applicable national regulations and legal frameworks.

A single project coordinator, who represents the research consortium towards the ERA-NET NEURON and externally, will be responsible for its internal management. Although he or she bears the overall scientific responsibility for the project towards NEURON, each principal investigator of a subproject is fully responsible for the research outcome towards the NEURON partner organization respective of the country from which he or she has applied.



The project coordinator will be required to submit a brief annual scientific progress report on the project, on behalf of the research consortium, to the Joint Call Secretariat. It may also be necessary for subproject leaders to submit reports individually to their national funding body should it be required.

Annex

Please note that country specific requirements might apply to this call. For further information follow the links below or contact your national representative:

Country	Contact person	Links to national calls mentioning particular requirements
Austria	Dr. Herbert Mayer	Austrian Science Fund (FWF) herbert.mayer@fwf.ac.at http://www.fwf.ac.at
Finland	Dr. Mika Tirronen	Academy of Finland (AKA) mika.tirronen@aka.fi http://www.aka.fi/fi/
France	Dr. Véronique Briquet- Laugier	National Research Agency (ANR) Health & Biology Department Veronique.briquet-laugier@agencerecherche.fr www.agence-nationale-recherche.fr
Germany	Dr. Rainer Loose	PT-DLR Programme Management Health Research rainer.loose@dlr.de http://www.gesundheitsforschung-bmbf.de
Israel	Dr. Nava Levine	Chief Scientist Office - Ministry of Health (CSO-MOH) nl@013.net.il http://www.health.gov.il/
Italy	Dr. Massimo Casciello	Ministero della Salute m.casciello@sanita.it http://www.ministerosalute.it/
Luxemburg	Dr. Frank Glod	Fonds National de la Recherche (FNR) frank.glod@fnr.lu http://www.fnr.lu/
Poland	Dr. Izabela Rzepczynska	National Centre for Research and Development (NCBiR) eranet-neuron@ncbir.gov.pl http://www.ncbir.gov.pl/?lang=pl (+48)515061529
Romania	Prof. Dr. Leon Zagrean	CAROL DAVILA University of Medicine and Pharma- cy/Neuroscience lzagrean@univermed-cdgm.ro http://www.mct.ro/ancs_web/index.php
Spain I	Dr. Julio Barbas	Ministry of Education and Science (MEC) julio.barbas@mec.es http://www.mec.es/
Spain II	Dr. Rafael De Andrés Medina	Instituto de Salud Carlos III (ISCIII) Fund for Health Research (FIS) rdam@isciii.es tel: (++34) 918222508 http://www.isciii.es/htdocs/index.jsp
Sweden	Dr. Leif Järlebark	The Swedish Research Council (SRC) leif.jarlebark@vr.se http://www.vr.se/
UK	Dr. Joanna Latimer	Medical Research Council (MRC) joanna.latimer@headoffice.mrc.ac.uk http://www.mrc.ac.uk/index.htm



Annex II

Questionnaire / Impact of the Project

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

Q.1 Publications and communications

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

Q.1.1 Number of publications and communications

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

Add lines as appropriate

Q.1.2 List of publications and communications

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

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

Add lines as appropriate

Q.2 Patents and other outputs with impact to health

Q.2.1 Number of patents, licences and other outputs

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

Add lines as appropriate



Q.2.2 List of patents

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

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

Add lines as appropriate

Q.2.3 List of other outputs with impact to health

Please list below:

	Category: if applicable, please specify	Partner(s)		
	software and other prototypes:			
	launching of a product or service, new project or contract:			
	creation of a platform available to a community:			
	creation of a firm, fundraising:			
	others (please specify):			
Q.3 Consortium – collaboration and sustainability				
Please tick when applicable				
Q.3.1 Have the partners participating in the NEURON project collaborated before applying for NEURON JTC 2008? YES \(\scale \) NO \(\scale \)				
	▶If YES, please indicate the partner numbers of teams that previously collaborated:			
Q.3.2 During the lifetime of the project has the consortium established collaboration(s) with other team(s) (not already participating in the JTC 2008 project)? YES \square NO \square				

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

▶ If YES, please name the institutions and countries:

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

.....



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

A. Collaboration meetings

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

Add lines as appropriate

B Young scientists' involvement in the project, training and mobility between partners

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

Partner #	Career stage	Academic dis- sertation (year, degree)	Year of birth	Name, Gender	Exchange from / to (country)	Duration of Exchange weeks / months
					From to	

Q.4 Development of innovative or shared resources and technologies				
Q.4.1 Has the consortium created a new or further developed an existing transnational				
Patient registry ☐ Patient database ☐ Biobank ☐ N/A ☐ ?				
▶If YES, please complete (repeat this section as many times as necessary):				
Name of the registry/database/biobank:				
How was the registrydatabase/biobank created?				
Totally new set-up ☐ By compiling national sources that existed already ☐				
How were new patients recruited?				
○ Via already existing network of clinicians				
 By the establishment of contact with NEW networks of clinicians 				
 Please specify how the registry/database/biobank will be maintained/financed after the end of this projects 				
Q.4.2 Have the consortium partners exchanged bioresources (DNA, tissues, cells, animals)?				
DNA				
►If YES, please specify:				
 Were there enough samples in order to reach the goal? YES ☐ NO ☐ 				

Have the samples allowed common studies? YES \square NO \square



Q.5 Potential health impact / achievements

Q.5.1 Have the results of the NEUR	ON resea	arch projects allowed the development of new strategies for:				
 Diagnosis 						
Therapy (Preparation of cli	nical trials	(a)				
Rehabilitation procedures	degenerative diseases					
 Prevention 						
Other (please specify)						
Q.5.2 Please list the major achievements of the consortium						
Achievements		Please specify				
Identification of new genes						
Development of innovative screening systems						
Identification and characterisation of biomarkers						
Validation of biomarkers						
Generation of novel model systems (animal models, cellular models)						
Development of innovative therapies						
New medical treatments						
New medical devices						
Neurosurgical innovation						
Others						

Add lines as appropriate



Annex III

Scientific Workshop 2007:

Presentations of the scientific workshop held in Paris in October 2007 (http://www.neuron-eranet.eu/media/Neuron newsletter 1 June 2008.pdf):

- Ignacio Torres, Spain: "Loss of IGF-I input as a common cause of neurodegeneration"
- Shlomo Rotshenker, Israel: "Microglia activation in injury and disease"
- Charles Duyckaerts, France: "Alzheimer disease"
- Giovanni Frisoni, Italy: "Keeping Europe in the mainstream of the fight against ALZ-HEIMER'S:The search for disease markers"
- Thomas Gasser, Germany: "European Parkinson Research: Focus on Genetics"
- Jörg Schulz, Germany: "Parkinson and other movement disorders"
- Wolfgang Oertel, Germany: "Parkinson-Syndrome and other Movement Disorders"
- Jens Volkmann, Germany: "Deep brain stimulation for movement disorders: State of the art and future needs"