

NEURON PARTNERS

Austria (FWF), Belgium (Flanders, FWO, Wallonia, FNRS), Canada (CIHR, Québec, FRQS), Finland (AKA), France (ANR, INSERM, CNRS), Germany (PT-DLR/BMBF), Iceland (RANNIS), Israel (CSO-MOH), Italy (MOH), Latvia (LAS), Luxemburg (FNR), Poland (NCBR), Portugal (FCT), Romania (ANCS-MEdR, UEFISCDI), Slovakia (SAS), Spain (ISCIII, MINECO), Sweden (SRC), United Kingdom (MRC).

ERA-NET NEURON

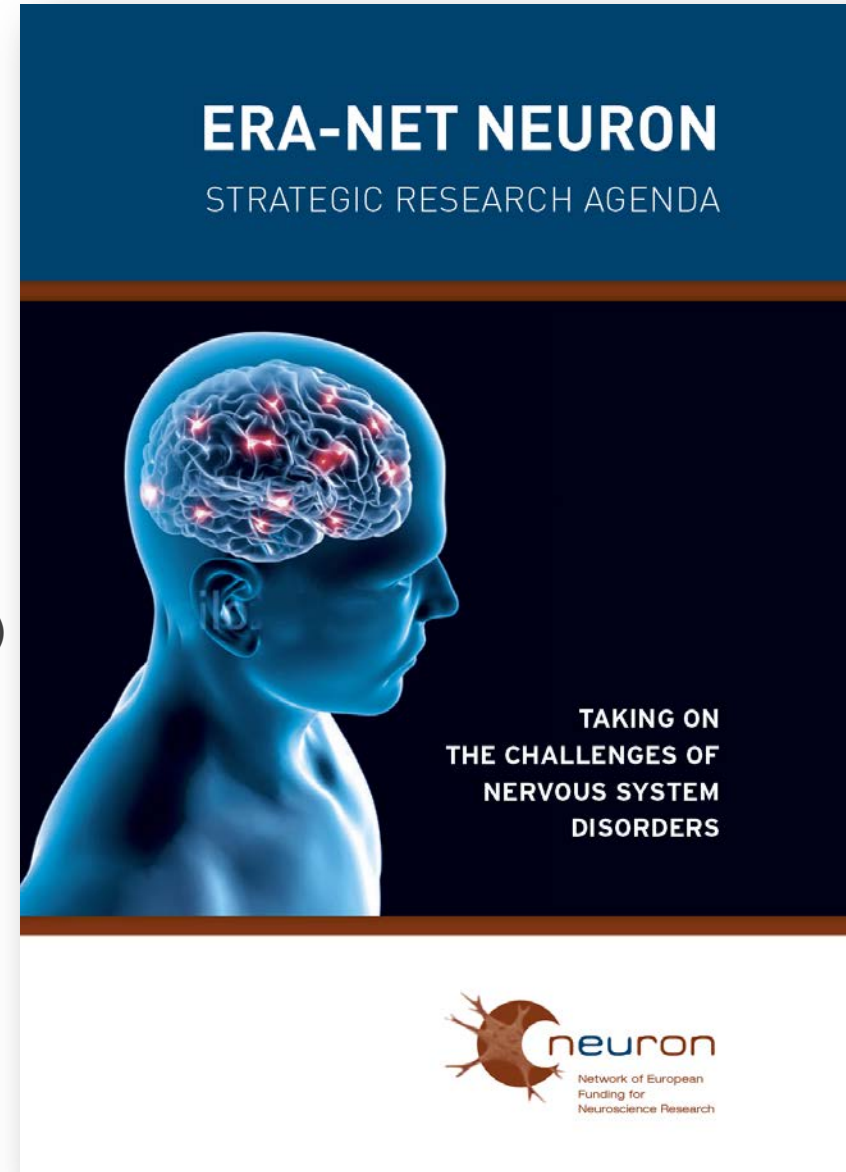
STRATEGIC RESEARCH AGENDA



Scientific Experts:

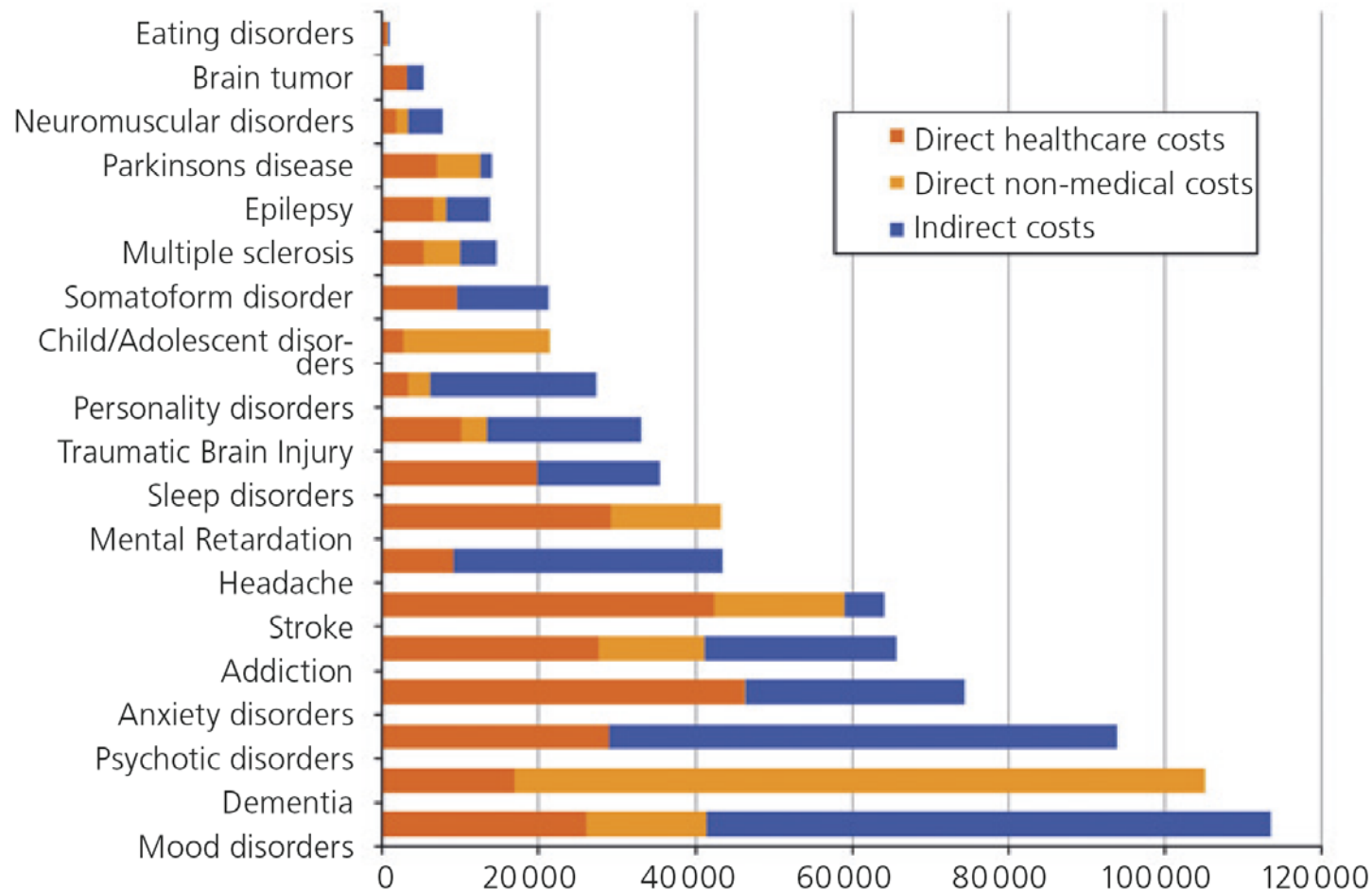
Robin Ali (London, UK),
Celso Arango (Madrid, Spain)
Vania Broccoli (Milan, Italy)
Francois Berger (Grenoble, France)
Eero Castren (Helsinki, Finland)
Joab Chapman (Tel Aviv, Israel)
Monica Di Luca (Milan, Italy)
Martin Dichgans (Munich, Germany)
Isabel Farinas (Valencia, Spain)
Christophe Mulle (Magendie, France)
Andreas Meyer-Lindenberg (Mannheim, Germany)
Alain Prochiantz (College de France, France)
Fabrizio Tagliavini (Milan Italy)
Wolfgang Wick (Heidelberg, Germany)
Moussa Youdim (Haifa, Israel)
Ana-Maria Zagrean (Bucharest, Romania)

Etienne Hirsch, Sarah Joaquim &
Marie-Louise Kemel (INSERM)
Bernard Poulain and Francois Bourre (CNRS)
Marlies Dorlöchter, Alexander Klein, &
Hella Lichtenberg (PT-DLR, Germany)



Background and Purpose

- Neurological, psychiatric, and sensory organ diseases
- 380 Mio people in the EU
- costs ~ 800 billion € p.a.

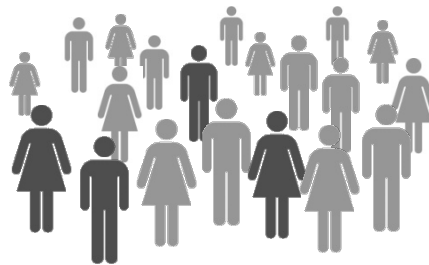


Development of SRA

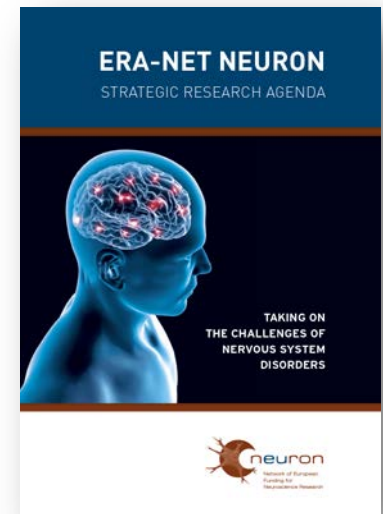
- Foundation for future joint activities
- Authored by the SAB with input from additional experts
- Conceptual framework built in 2 steps

structured questionnaire:

- major challenges of research,
- major scientific bottlenecks
- technological limits
- relevance of linking preclinical and clinical topics in the NEURON agenda



draft report
circulate
revise



mailed questionnaire

workshop
Bonn

feed-back > consent >
published on internet

3/2014

5/2014

1/2015.....

Scientific Priorities

Subject/Topic	Priorities	Outcomes
Understanding Disease Mechanisms	<ul style="list-style-type: none"> ■ develop, improve, and validate pre-clinical models for use in experimental studies ■ understand the biological basis of nervous system disorders ■ uncover mechanisms of resilience and compensation ■ understand the role of aging and comorbidity ■ identify key mechanisms underlying multifactorial disease ■ identify properties unique to the nervous system that could be exploited for novel therapeutic approaches ■ leverage novel technologies for tackling disease mechanisms including, for example, the following: optogenetics, -omics based approaches, neuronal circuits, neuronal networks, induced pluripotent stem cells, molecular and ultra-high-field MRI, ■ make use of “smart” data as well as “big” data (e.g. derived from -omics approaches) ■ foster systems approaches to disease including modeling of diseases ■ pave the ground for approaches to personalized medicine 	Identify: <ul style="list-style-type: none"> ■ Causes of disease, ■ Non-modifiable & modifiable risk factors, ■ Factors involved in resilience, ■ Triggering events, ■ Novel targets for interventions.
Understanding Disease Progression	<ul style="list-style-type: none"> ■ improve and develop biologically-driven disease classifications ■ identify markers for disease prediction, early diagnosis, and progression ■ identify markers predicting therapeutic response ■ understand diseases from a lifespan perspective ■ leverage novel methods for prognostic modeling 	Enable: <ul style="list-style-type: none"> ■ Risk prediction, ■ Early diagnosis, ■ Prognostic modeling, ■ Early treatment, ■ Predicting therapeutic response.
Promoting Interventions	<ul style="list-style-type: none"> ■ validate already existing disease models (cell-based and model organisms) for interventions ■ optimize or develop disease models for use in drug development and toxicity testing ■ optimize selection and stratification of patients for clinical studies: could be based on endo-phenotypes, biomarkers, genetic or environmental risk profiles and/or clinical endpoints thus providing a greater chance of showing efficacy. ■ identify the optimal time window to assess treatment efficacy, an issue that may have contributed to the low success rate of previous early-phase clinical trials. ■ strengthen investigation of compensatory mechanisms, including neuronal plasticity, as a basis for novel treatment approaches ■ promote the development of preventive strategies ■ make use of drug repurposing 	Facilitate: <ul style="list-style-type: none"> ■ Novel preventive strategies, ■ Innovative therapeutic approaches, ■ Novel delivery systems for pharmacological and non-pharmacological approaches, ■ Optimized use of already available drugs.

Scientific Priorities

Understanding Disease Mechanisms

Priorities

- develop, improve, and validate pre-clinical models for use in experimental studies
- understand the biological basis of nervous system disorders
- uncover mechanisms of resilience and compensation
- understand the role of aging and comorbidity
- identify key mechanisms underlying multifactorial disease
- identify properties unique to the nervous system that could be exploited for novel therapeutic approaches
- leverage novel technologies for tackling disease mechanisms including, for example, the following: optogenetics, -omics based approaches, neuronal circuits, neuronal networks, induced pluripotent stem cells, molecular and ultra-high-field MRI,
- make use of “smart” data as well as “big” data (e.g. derived from -omics approaches)
- foster systems approaches to disease including modeling of diseases
- pave the ground for approaches to personalized medicine

Outcomes

Identify:

- Causes of disease,
- Non-modifiable & modifiable risk factors,
- Factors involved in resilience,
- Triggering events,
- Novel targets for interventions.

Scientific Priorities

Understanding Disease Progression

Priorities

- improve and develop biologically-driven disease classifications
- identify markers for disease prediction, early diagnosis, and progression
- identify markers predicting therapeutic response
- understand diseases from a lifespan perspective
- leverage novel methods for prognostic modeling

Outcomes

Enable:

- Risk prediction,
- Early diagnosis,
- Prognostic modeling,
- Early treatment,
- Predicting therapeutic response.

Scientific Priorities

Promoting Interventions

Priorities

- validate already existing disease models (cell-based and model organisms) for interventions
- optimize or develop disease models for use in drug development and toxicity testing
- optimize selection and stratification of patients for clinical studies: could be based on endo-phenotypes, biomarkers, genetic or environmental risk profiles and/or clinical endpoints thus providing a greater chance of showing efficacy.
- identify the optimal time window to assess treatment efficacy, an issue that may have contributed to the low success rate of previous early-phase clinical trials.
- strengthen investigation of compensatory mechanisms, including neuronal plasticity, as a basis for novel treatment approaches
- promote the development of preventive strategies
- make use of drug repurposing

Outcomes

Facilitate:

- Novel preventive strategies,
- Innovative therapeutic approaches,
- Novel delivery systems for pharmacological and non-pharmacological approaches,
- Optimized use of already available drugs.

Specific Priorities and Challenges

...there are specific challenges to individual diseases and disease categories. The expert panel identified the following specific challenges realizing that this list is by no means exhaustive:

- **Neurological Disease**
- **Psychiatric Disorders**
- **Sensory Organ Diseases & Peripheral Nervous System Disorders**

Specific Priorities and Challenges

Nervous System Diseases

- Comorbidities
- Systems Approach
- Genetics
- Neuroimmunology
- Biology of Brain Vasculature
- Translational aspects of Neuroprotection
- Brain Circuits
- Deep Brain Stimulation
- Neuronal / glial repair | Cell reprogramming & renewal
- Spinal cord injury
- ...

Specific Priorities and Challenges

Psychiatric Disorders

- Classification of disease
- Replacement by circuit-based account
- Personalized treatment
- Role of aberrant brain development
- Genetics > Functional follow-up
- Advanced neuroimaging
- Combination with genetics
- Computational neuroscience
- Preclinical models
- Optogenetics
- ...

Specific Priorities and Challenges

Sensory Organ Diseases and Peripheral Nervous System

Eye | Ear | Skin

- Retina > „window into the brain“
- Restorative approaches & Prosthetics
- Gene- and Cell-based approaches
- Identifying the „critical period“
- Synaptic connectivity and neuronal circuits
- Biology of pain
- Autonomic nervous system
- Optogenetics
- ...

Options for Future Joint Activities

The following research areas and questions in the field of neurological, psychiatric, and sensory organ diseases can be putative topics for further exploration in focused workshops:

- Understanding the role of aging, comorbidity, and multifactorial aspects of disorders;
- Developing novel technologies for tackling disease mechanisms including data analysis, disease modelling *in vivo*, *in vitro*, and *in silico*;
- Identifying properties unique to the nervous system that could be exploited for novel therapeutic approaches;
- Uncovering mechanisms of resilience and compensation;
- Identifying biomarkers for diagnosis, prognosis, treatment response, side effects of treatment for stratification of disorders and personalized medicine;
- Understanding diseases from a lifespan perspective;
- Unravelling the mechanisms of mental disorders;
- Identifying disease-crossing mechanisms in stroke and dementia;
- Building knowledge about sensory organ disorders.

Options for Future Joint NEURON Activities

The following research areas and questions in the field of neurological, psychiatric, and sensory organ diseases can be putative topics for further exploration in focused workshops:

- Understanding the role of aging, comorbidity, and multifactorial aspects of disorders;
- Developing novel technologies for tackling disease mechanisms including data analysis, disease modelling *in vivo*, *in vitro*, and *in silico*;
- Identifying properties unique to the nervous system that could be exploited for novel therapeutic approaches;
- Uncovering mechanisms of resilience and compensation;

- Identifying biomarkers for diagnosis, progression, treatment response, side effects of treatment for stratification of disorders and personalized medicine;
- Understanding diseases from a lifespan perspective;
- Unravelling the mechanisms of mental disorders;
- Identifying disease-crossing mechanisms in stroke and dementia;
- Building knowledge about sensory organ disorders.

THE FOLLOWING DISEASES ARE INCLUDED IN THE RESEARCH AGENDA

- Diseases of the central nervous system,
- Diseases of the peripheral nervous system,
- Diseases of the neuromuscular junction,
- Diseases of the autonomic nervous system.

THE FOLLOWING DISEASES ARE EXCLUDED FROM THE RESEARCH AGENDA

- Diseases not involving the nervous system,
- Diseases primarily affecting other organs or systems.

Neurodegenerative Diseases (ND) are not excluded from the research agenda. However, it should be recognized that these diseases are covered by the 'Joint Programme – Neurodegenerative Disease Research' (JPND) with its specific Research Strategy published in 2012 (<http://www.neurodegenerationresearch.eu/>)



THE FOLLOWING DISEASES ARE INCLUDED IN THE RESEARCH AGENDA

- Diseases of the central nervous system,
- Diseases of the peripheral nervous system,
- Diseases of the neuromuscular junction,
- Diseases of the autonomic nervous system.

THE FOLLOWING DISEASES ARE EXCLUDED FROM THE RESEARCH AGENDA

- Diseases not involving the nervous system,
- Diseases primarily affecting other organs or systems.

Neurodegenerative Diseases (ND) are not excluded from the research agenda. However, it should be recognized that these diseases are covered by the 'Joint Programme – Neurodegenerative Disease Research' (JPND) with its specific Research Strategy published in 2012

Funding Measures

NEURON Funding Measures: Research Consortia and Joint Transnational Calls for Proposals

The NEURON joint funding programme is targeted to support small scale transnational consortia of up to five research groups from at least three participating countries. Consortia are encouraged to include basic scientists and clinicians across disciplines, in order to reinforce translational multidisciplinary research. They share methodology, infrastructure, materials, skills and expertise. Inclusion of studies in humans is not a requirement but strongly encouraged.

Phase III clinical trials as well as large scale omics studies requiring large budgets are usually outside the range of activities supported by the ERA-NET NEURON.

Enabling Activities

- Early Career Scientists
- Data Sharing, Material and Infrastructure
- Partnership with Industry
- Multidisciplinary Research Collaboration
- Capacity Building
- Interaction with European Initiatives

ERA-NET NEURON

STRATEGIC RESEARCH AGENDA



Scientific Experts:

Robin Ali (London, UK),
Celso Arango (Madrid, Spain)
Vania Broccoli (Milan, Italy)
Francois Berger (Grenoble, France)
Eero Castren (Helsinki, Finland)
Joab Chapman (Tel Aviv, Israel)
Monica Di Luca (Milan, Italy)
Martin Dichgans (Munich, Germany)
Isabel Farinas (Valencia, Spain)
Christophe Mulle (Magendie, France)
Andreas Meyer-Lindenberg (Mannheim, Germany)
Alain Prochiantz (College de France, France)
Fabrizio Tagliavini (Milan Italy)
Wolfgang Wick (Heidelberg, Germany)
Moussa Youdim (Haifa, Israel)
Ana-Maria Zagrean (Bucharest, Romania)

Etienne Hirsch, Sarah Joaquim &
Marie-Louise Kemel (INSERM)
Bernard Poulain and Francois Bourre (CNRS)
Marlies Dorlöchter, Alexander Klein, &
Hella Lichtenberg (PT-DLR, Germany)

