

ERA-NET Neuron NEWSLETTER 28



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News From NEURON Cofund

2018 Call for Proposals for Transnational Research Projects on "Mental Disorders" was launched and the deadline for sending preproposals is March 8th, 2018.

JTC 2017 on "Synaptic Dysfunction in Disorders of the Central Nervous System" - 12 projects were chosen for funding out of 93 pre-proposals. Overall funding requested: 12.4 m€

From the desk of the coordinator | February 2018



Marlies Dorlöchter

NEURON conducted its yet largest Mid-term symposium in 2017. In Riga we welcomed researchers of our two joint transnational calls 2015, "Neurodevelopmental Disorders" and "Ethical, Legal, and Social Aspects (ELSA) of Neuroscience". Moreover, the winner of the EPNA Award 2016, Dr Gabriele Deidda, presented his paper on the Down syndrome.

It is always delightful to meet the researches funded by NEURON at the Mid-term symposia and to learn about their projects' progress. This year's meeting was extraordinary: For the first time we were able to bring together both, the neuroscientific and ELSA communities. ELSA stands for ethical, legal and societal aspects. ELSA research is of high relevance as issues arising from the rapid advances in neuroscience are tackled. The symposium aimed to stimulate exchange and encourage dialogue among and between the



More information can be found on our website
<http://www.neuron-eranet.eu/index.php>
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two research communities. Judging by the animated discussions at dinner, we may have succeeded to connect our attendants: in total 75 principal investigators and early career researchers, representing the 15 funded consortia, and more than 20 representatives of international funders. Special thanks go to our four chairs who supported us in our monitoring of the projects and enriched the discussion.



Chairs NEURON: Prof Leda Dimou-Rörentrop, Prof Paul Emmelkamp.

Chairs ELSA NEURON: Prof Hervé Chneiweiss, Prof António Jácomo

Early Career Researchers

The symposium also offered a unique opportunity to support early career researchers. For one, we had the privilege of listening to the presentation of our Excellent Paper in Neuroscience Award (EPNA) awardee Dr Gabriele Deidda. With his publication entitled “Reversing excitatory GABAAR signaling restores synaptic plasticity and memory in a mouse model of Down syndrome” published in Nature Medicine he won the EPNA 2016.



Dr Gabriele Deidda (on the left) receiving the EPNA prize from Dr Marlies Dörflöcher and Dr Erkki Rauilo, Young Scientist Programme leader

Furthermore, early career researchers were invited to present their projects in a poster session. The best poster was awarded with 300 Euro. A scientific committee selected one out of 28 great posters as outstanding: Carolin Schwelger received the prize for her poster on "MCI-patients' and caregivers' expectations towards risk prediction of AD: preliminary findings from the PREDADQOL interview study".



Participants at the Mid-term Symposium

In this newsletter you can find the abstracts of all 15 projects presented at the Mid-term Symposium in Riga. We wish them all much success in the second part of their projects.

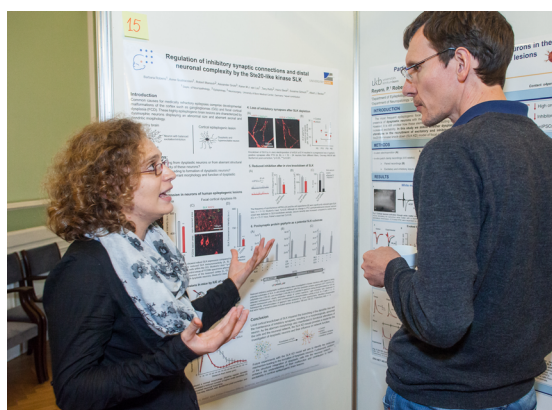
Last but not least - after an extensive reviewing process, NEURON is glad to announce that 12 new projects were chosen for funding under JTC-2017. You will hear all about them in NEURON's next newsletter.

Sincerely yours,

Marlies Dorlöchter.



Impressions from the Symposium



Mid-term Symposium - JTC NEURON 2015

“Neurodevelopmental Disorders”

Modelling syndromic autism caused by mutations in the ADNP gene [AUTISYN]



Frank Kooy



Project Coordinator: Frank Kooy, University of Antwerp, Department of Medical Genetics, Belgium

Project Partners:

Ilana Gozes, Department of Human Molecular Genetics and Biochemistry, Tel Aviv University, Israel

Pierre-Luc Germain, Dipartimento di Oncologia Sperimentale, Istituto Europeo di Oncologia (IEO), Italy

Christopher Pearson, The Hospital for Sick Children, University of Toronto, Canada

Autism is a mysterious and devastating disorder that is perhaps best characterized by having a lack of social skills. It comes in many different flavours, but in fact, we know little about the different subtypes of the disorder. Over the last years, we have discovered that genetics plays an important role in the origin of the various forms of autism. In this project, we will study a specific form of autism that is caused by mutations in a single gene called ADNP. Mutations in this gene lead to autism in almost all patients known to date. Using an established mouse model of Adnp-autism, which mimics the disorder allows us to study the disorder and to test drugs for possible later use in humans.

For instance, it is known that a specific part of the ADNP protein called NAP can replace many of the functions of the entire protein, thereby indicating that NAP can be a primary drug candidate for testing in the Adnp-autism mouse model. In addition, as we know little of the consequences of the mutation in human cells, we will produce patient brain cells generated from skin biopsies using a specialized technique called induced-pluripotent stem cells. Thus, we will be able to study the processes that are disturbed in patient brain cells.

By applying a variety of state of the art technologies, our network will detect novel pathways in cells disturbed in ADNP that is also relevant for related forms of autism. Once we have identified and characterized those pathways, we can try to modify them using novel drugs to improve the condition of the patients. Finally, since many unrelated patients share the very same ADNP mutation, we will determine the mechanism of how these mutations arise. Knowledge of the mutational mechanism may be another way of detecting or preventing the disease in the future.

Key Determinants of Synaptic Excitation/Inhibition Imbalance in Autism Spectrum Disorders - From Genetic Animal Models to Human Patients [SynPathy]



Joris de Wit

Project Coordinator: Joris de Wit, KU Leuven, Belgium

Project Partners:

Ann Marie Craig, Brain Research Centre, University of British Columbia, Canada

Nils Brose, Max Planck Institute for Experimental Medicine, Germany

Daniel Choquet, University of Bordeaux, Interdisciplinary Institute for Neuroscience, France

Thomas Bourgeron, Institut Pasteur, France



Nerve cells in the brain communicate via specialized contacts called synapses, and information processing in the brain critically depends on a proper balance between stimulatory (excitatory) and inhibitory signaling at synapses (E/I balance). Mutations in genes that determine synapse function and E/I imbalances are observed in many brain disorders, including autism spectrum disorders (ASDs) and schizophrenia, which led to the notion that they are - at least in part - disorders of synaptic connectivity or "synaptopathies". Fascinatingly, neuronal networks in the brain typically maintain an exquisite E/I balance although neural activity varies constantly, but the molecular and cellular mechanisms that allow neurons to maintain stable E/I ratios are largely unknown. Synaptic adhesion molecules, which connect neurons at synapses and regulate excitatory and inhibitory synapse formation and function, are thought to be major players in tuning E/I balance. However, their function is yet unclear.

We aim to unravel key molecular mechanisms that control E/I balance in the brain.

Specifically, we propose that the interplay between two classes of surface proteins that have opposing functions and were both shown to be involved in ASD and schizophrenia - MDGAs and NLGNs - tunes E/I balance. We propose (i) that the interaction between the synapse development-suppressing MDGA proteins and the synapse development-promoting NLGN proteins precisely controls the function of key synaptic adhesion molecules, the recruitment of synaptic neurotransmitter receptors, and the local synaptic protein synthesis machinery, and (ii) that perturbations of these processes lead to E/I imbalances and, consequently, to neurodevelopmental disorders.

To test these hypotheses, we will study novel genetic mouse models that model human disorders and patient-derived neurons. With our focus on two classes of proteins involved in ASDs and schizophrenia, combined with the use of highly sophisticated experimental models and the synergistic expertise of the partners, we expect to be able to determine key disease mechanisms and to provide important leads for diagnostic and therapeutic approaches.

Role of Serotonin in the Pathogenesis Of Neurodevelopmental Disorders [RESPOND]



Michael Bader

Project Coordinator: Michael Bader, Max-Delbrück-Center for Molecular Medicine, , Germany

Project Partners: Frank Edenhofer, Julius-Maximilians-University Würzburg, Institute of Anatomy and Cell Biology, Germany

Piotr Popik, Institute of Pharmacology, Polish Academy of Sciences, Poland

Patricia Gaspar, Judith Homberg, Radboud, University Medical Centre, Donders Institute for Brain, The Netherlands



The European Academy of Neurology represents more than 20.000 neurologists in Europe and has the purpose to promote Excellence in Neurology in Europe. The two most important goals in this context are to “support neurological research” and to “increase the availability and standards of neurological services”. In this context the development of European guidelines for the treatment of neurological diseases are of very high importance.

In order to reach the goals we need to closely collaborate with basic neuroscience in the fields of molecular biology and systems biology. The aim is to develop an intense interaction to elaborate translational therapies. In addition, the phenotyping methodologies of basic research are of particular interest for neurology. The final goal of all such research developments is to develop treatment that needs to be assessed in pilot and large-scale trials.

Patient organisations are important to improve research questions that are meaningful to the patients and to adjust clinical research protocols to the latest developments. Patient organisations are very important to lobby for research resources at the European Commission and to collaborate in convincing politicians to improve the health systems in the European countries.

It is only the three components of stakeholders, namely: basic researchers, neurologists and patients, that can significantly forward the care of neurological patients.



Angel Barco



Chromatin-related Intellectual disability syndromes: Molecular etiology and therapy [ChromISyn]

Project Coordinator: Angel Barco, Universidad Miguel Hernández de Elche,
Instituto de Neurociencias, Spain

Project Partners: Lidia Larizza, Istituto Auxologico Italiano, Italy

Kobi Rosenblum, Sagol Dept. of Neurobiology, University of Haifa, Israel

Eloisa Herrera, Agencia Estatal Consejo Superior de Investigaciones Científicas,
Instituto de Neurociencias, Spain

Intellectual development disorders represent one of the biggest medical challenges in our society. Their cause includes the mutation of genes encoding proteins involved in the regulation of gene expression through changes in the chromatin. Our proposal focuses on one of such disorders, the Rubinstein-Taybi syndrome (RSTS). This rare genetic disorder is caused by mutation in the genes that encode the proteins CBP and p300. These two proteins mediate the acetylation of the chromatin, a chemical reaction that is thought to favor transcription. Here, we propose to investigate the role of these two proteins in development of the nervous system, neuronal plasticity in the adult brain, and pathophysiology of cells derived from patients. Next, we will take advantage of recent technological advances that allow a comprehensive and fully unbiased analysis of changes in the chromatin, to identify the molecular mechanisms underlying the defects observed in the cells from patients and animal models of the disease. Finally, we will also use novel techniques that allow a precise manipulation of the chromatin to correct the detected alterations and assess whether this correction ameliorates or eliminates the observed defects. Of note, the impact of our project goes well beyond RSTS because other intellectual development disorders are likely to affect the same processes.

Deciphering hyperexcitable networks associated with neurodevelopmental lesions [DeCipher]



Albert J.
Becker



Project Coordinator: Albert J. Becker, University of Bonn Medical Center (UKB), Dept. of Neuropathology, Germany

Project Partners:

Alfonso Represa, Ist. de Neurobiologie de la Méditerranée, INSERM, Faculté des Sciences de Luminy, France

Ilan Lampl, Department of Neurobiology, Weizmann Institute of Science, Israel
Heinz Beck, Laboratory of Experimental Epileptology and Cognition Research, Life & Brain Center, Germany

Viktor Jirsa, Institute de Neurosciences des Systèmes and CNRS, Aix Marseille Université (La Timone), France

Developmental malformations of the cortex (MCDs) are associated with a significant disease burden and often devastating epilepsies that are resistant to antiepileptic drugs. Neurodevelopmental disorders comprise a large spectrum of malformations and particular tumor entities that are rare in general brain tumor series. These neoplasms, with so-called gangliogliomas as most frequent type, are composed of often “dysplastic” neuronal elements and generally slowly growing glial cells. Common features of developmental lesions and tumors are neurons that either do not reach their correct destination during cortical development or have substantially aberrant shape, particularly with respect to their size and/or structure of processes.

Therefore, “displaced” as well as “dysplastic” neurons represent the edges of the pathology spectrum of aberrant neurons in MCDs. In recent years, our understanding of pathological intracellular signaling of these disorders has substantially emerged. However, these important advances have not led to substantially improved therapies. We suggest that this is due to our poor understanding of the mechanisms underlying increased excitability of neurons in these disorders. Data obtained by this consortium so far suggest a common mechanism underlying increased excitability in rodent models of neurodevelopmental disorders: a profound imbalance between excitation and inhibition in the grey matter of the brain, which is functionally encoded by aberrant neurons and respective networks. Here, we examine this



concept in two key models of neurodevelopmental lesions associated with severe epilepsies: Firstly, a model of so-called doublecortex associated with mutations in the doublecortin (DCX) gene with the neuropathological hallmark of “displaced” neurons and secondly, a novel model of malformations harboring prominent “dysplastic” neurons.

We examine the neuronal basis of epileptic seizure generation in these models using recent methodologies that allow controlled stimulation (by so-called advanced photostimulation and optogenetic techniques) and analyses of the functional consequences (by in-vivo electrophysiology and imaging) in the brains of living experimental rodents. These approaches allow us to analyze in detail and in a highly controlled fashion aberrant function of cellular sub-domains, i.e. synapses as functional intersections between neurons, down to the scale of individual compartments of processes, i.e. dendrites as main input structures of neurons, entire neuronal cells and networks of aberrant architecture. The technical approaches particularly allow an improved understanding of failure of interaction of neurons that constitute the MCD with normal environmental brain structures, since we can manipulate and “read” individual aspects of this aberrant interaction in-vivo. These approaches will shed light on the aberrant connectivity of “displaced” and “dysplastic” neurons that underlie the emergence of seizures. The results of our joint efforts foster the implementation of a conceptually novel approach directed towards better therapies.

Understanding and reprogramming developmental visual disorders: from anophthalmia to cortical impairments, [ImprovVision]



Paola
Bovolenta

Project Coordinator: Paola Bovolenta, Centro de Biología Molecular Severo Ochoa and CIBERER, Spain

Project Partners:

Michèle Studer, Institut de Biologie Valrose, Univ. de Nice Sophia Antipolis (UNS), France

Carolina Frassoni, Unit of Epilepsy and Experimental Neurophysiology, Fondazione Istituto Neurologico Carlo Besta, Italy

Marta Nieto, Centro Nacional de Biotecnología, Madrid, Spain

Benedikt Berninger, Institute of Physiological Chemistry, University Medical Center Johannes Gutenberg University Mainz, Germany



Diseases of vision can originate in genetic defects, that affect the embryonic development of the various components of the “visual system”: the eyes, their connection to the brain by nerves, and the brain areas that process visual information and convert it into a mental image of what we see. How genes shape our visual system, and how their malfunctioning leads to neurodevelopmental diseases of vision, is very poorly understood, and is the general question addressed by our Project. Our laboratories generated mutant mouse strains, in which specific genes are mutated, that allow to study in detail the specific contribution of individual genes to visual development. We address, in particular, genes encoding transcription factors, proteins that control the activity of many genes in parallel that, altogether, give rise to the organized development of the visual system. We already know about the importance of these genes, because their mutation impairs visual system development in mice and in patients and discovered that the genes we study are functionally connected within a “gene regulatory network”. We will use cell cultures, mouse, zebrafish models and human samples to investigate the full consequences that genetic defects already known to cause Neuro Developmental Visual Disorders have on the rest of the brain, thus determining the full extent of visual abnormalities. This knowledge will be then translated to patients and further applied to evaluate if cell reprogramming at postnatal stages could improve visual function in models of neurodevelopmental diseases of vision. We are confident that, if successful, the ambitious goal of ImprovVision will lead the field of vision disease beyond the current state of the art.

Deciphering the multifaceted pathways underlying MCPH pathogenesis in the mouse and human [MicroKin]

Project Coordinator: Pierre Gressens, Inserm, Paris Diderot University, France

Project Partners: Pierre Vanderhaghen, Institute of Interdisciplinary Research Neuroscience Institute (UNI) Université Libre de Bruxelles, Belgium

Marcos Malumbres, Spanish National Cancer Research Centre, Spain

Wieland Huttner, Max Planck Institute of Molecular Cell Biology and Genetics, Germany



Pierre Gressens



The microcephalies are common disorders of development characterized by abnormally small brains, leading to a small head size, and associated with mental retardation. These small brains are the result of the inadequate production of neurons during development, a complex process involving several progenitor types. The orientation of these progenitors, their plane and mode of division, the number of divisions undergone by each as well as their precise timing are all strictly controlled during normal embryonic development, and are crucial to generate the large number and variety of neurons that populate the mature brain. Any deviation from this highly detailed blueprint results in anomalies of brain development, and consequently, behavioral and intellectual disorders in childhood and adulthood. While several different factors, both genetic and environmental, have been identified as being associated with the different types of microcephaly, little is known about the process by which these factors interfere with normal neuronal production.

The MCPH (or congenital autosomal recessive primary microcephaly) family of disorders is caused by mutations in at least 12 identified genes, which, despite their diversity, mostly appear to play very specific roles in the division of progenitor cells during development. Based on this limited knowledge, we propose to study the pathways by which defects in these genes could lead to aberrant cell divisions and/or the large-scale death of progenitors that attempt to divide under sub-optimal energetic or other conditions, leading to a shortage of adult neurons of the correct type.

We will use both mouse models of MCPH in which one or more of these genes is genetically modified to be suppressed or overproduced, as well as cell lines derived from patients with MCPH microcephaly to (i) study how alterations in the expression or function of these genes could lead to the defective cell division or premature death of progenitors and, consequently, microcephaly, (ii) identify the molecules with which they interact within progenitor cells, and in particular to determine the role of cell-cycle kinases in guiding MCPH proteins to their appropriate locations and their subsequent function, and (iii) study differences in these processes between the mouse and human brain, in order to use this knowledge to guide future investigations and eventually, design appropriate treatment strategies.

Deciphering the Neuro-Developmental Research on the Etiology of Amblyopia and its Management [Neuro-DREAM]



Jochen Triesch

Project Coordinator: Jochen Triesch, Frankfurt Institute for Advanced Studies and Goethe Universität, Germany

Project Partners:

Maria Fronius, Goethe Universität Frankfurt, Germany

Robert Hess, Department of Ophthalmology, McGill University, Canada

Concetta Morrone, Faculty of Medicine, University of Pisa, Italy

Amblyopia, also called "lazy eye", is a disorder causing impaired vision in millions of infants and young children worldwide. It occurs in around 3.5% of the population and is therefore of great clinical and societal importance. Despite its common name "lazy eye" it is not really an eye disorder but a disorder of the visual cortex, the part of the brain that processes visual information. Amblyopia leads to poor vision in one eye that appears otherwise normal. Unfortunately, the causes of this disorder are not fully understood and current treatments are ineffective in a large number of patients.

The most common treatment is to patch the unaffected or non-amblyopic eye, forcing the brain to use and train the affected eye. However, such treatment usually leads to poor coordination of the two eyes. Precise coordination of the two eyes is essential for accurate depth perception, which is strictly required for many occupations including aviation, shipping, the police, surgeons, or operators of heavy duty equipment as well as sports and leisure activities. Thus children suffering from amblyopia are severely disadvantaged in many aspects of their lives. Recent empirical and theoretical research from our team has highlighted the importance of binocular interactions in the development of normal vision and strongly suggests that different treatment methods could lead to greatly improved intervention outcomes in children and adults. To further address this issue, our project aims to improve our understanding of the basic brain mechanisms underlying amblyopia and its treatment, develop novel treatment approaches for children and adults based on this improved understanding, and directly compare the effectiveness of different treatments. Neuro-DREAM has the potential to revolutionize the way we treat amblyopia, improving vision and quality-of-life in millions of patients — truly a DREAM come true for all affected families.



Striatal development and Meis1 Action in Restless legs syndrome [SMART]



Juliane Winkelmann

Project Coordinator: Juliane Winkelmann, Institute of Neurogenomics, Helmholtz Zentrum München, BMBF, München, Germany

Project Partners:

Miguel Torres, Centro Nacional de Investigaciones Cardiovasculares (CNIC), Spain

Wojciech Krezel, Institut de Génétique et de Biologie Moléculaire et Cellulaire, France



Restless legs syndrome (RLS) is a common and debilitating neurodevelopmental disorder characterized by persistent discomfort and restlessness in the legs, with symptom severity increasing at night. This causes severe sleep disruption leading to significant secondary effects on physical, mental and social health. The cause of RLS is not well understood, and available treatments such as dopaminergic agents are thus limited in efficacy, particularly for long-term disease management.

RLS is a complex disorder with genetic and environmental factors contributing to the phenotype. The strongest known genetic risk factors for RLS are variants in the gene MEIS1. Published and preliminary data indicate that the activity of MEIS1 affects the development of the striatum, an RLS-associated brain region which integrates sensory input and movement-related output. We propose to comprehensively study the role of MEIS1 in the mechanisms underlying RLS.

We will investigate the effect of Meis1 deficiency on development of the striatum in mice. In addition, we will investigate genes and proteins targeted by MEIS1 to convey its effects on development. This approach is expected to identify other novel genes and proteins involved in RLS. We will directly test the importance of MEIS1 in the developing striatum for generating RLS by specifically deleting Meis1 in the developing striatum of mice and evaluating RLS-related behaviors. Finally, we will investigate the effects of MEIS1 genetic variants on the response to the dopaminergic class of therapeutic agents. This is expected to provide further insight into the effect of MEIS1 variants on the function of the striatum. In addition, this will enable genotype-based precision medicine for RLS patients.

Collectively, these studies are expected to characterize the developmental origin of RLS, provide significant insight into the precise causes of RLS, and define novel targets for more effective therapeutic approaches.

Stem cells and mechanisms contributing to human cortical malformations [STEM-MCD]



Fiona Francis

Project Coordinator: Fiona Francis, Institut du Fer à Moulin, Inserm, France

Project Partners:

Orly Reiner, Weizmann Institute of Science, Department of Molecular Genetics, Israel

Laurent Nguyen, GIGA-Neurosciences, Developmental Biology Unit, Belgium

Nadja Bahi-Buisson, Inserm Institut Imagine, France

Julia Ladewig, Institute of Reconstructive Neurobiology, Universitaetsklinikum Bonn, Germany



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NEURON Joint Call 2015: "European Research Projects on Ethical, Legal, and Social Aspects (ELSA) of Neuroscience"

Enhancing the Informed Consent Process: Supported decision-making and capacity assessment in clinical dementia research [Ensure]



Julia Haberstroh

Project Coordinator: Julia Haberstroh, Johann Wolfgang Goethe-Universität Frankfurt, Frankfurt Forum for Interdisciplinary Ageing Research, Germany

Project Partners: José Antonio Seoane, Universidade da Coruña, Spain
Jochen Vollmann, Ruhr-Universität Bochum, Germany

Ana Sofia Carvalho, Universidade Católica Portuguesa, Institute for Bioethics, Portugal

As a result of an ageing population, the already high number of people suffering from dementia will significantly increase in European countries and beyond in the coming decades. No treatments are currently available that can reverse or even halt the neurodegenerative process, and dementia leads to a considerable burden on patients and caregivers, as well as societies as a whole. For this reason, there is a substantial need for further medical dementia research. People with dementia have the right to decide whether or not they want to participate in clinical research and to give their free, prior and informed consent. However, as dementia progresses, they can lose their ability to give informed consent to complex medical research because of an increasing loss of cognitive functions.

At first sight, it seems ethically problematic to involve dementia patients in research, as people with impaired mental capacity must be protected against the risks of research participation, not least because of various conflicts of interests involving the researcher and the pharmaceutical industry. Furthermore, in contrast to informed consent to medical treatment, an individual benefit from participation in research largely depends on the research design and can rarely be taken for granted. However, people with dementia also have a right to benefit particularly from neuroscientific and medical research, so their categorical exclusion would appear to be ethically problematic too. From an ethico-legal point of view, high standards for the informed consent process and a thorough assessment of mental capacity are therefore regarded as important measures to protect research participants.

This project aims to provide recommendations for clinical researchers on how to a) enhance the capacity to consent of people with dementia, b) improve the assessment of decision-making capacity, c) protect those who do not have the capacity to consent, and d) ensure the inclusion of people with dementia in neuroscientific and medical research is ethically justifiable. The results of this project will contribute towards achieving an adequate balance between autonomy and protection of dementia patients in clinical research.

The integration of cross-disciplinary research in neuroscience and social science – a methodological case study on economic policies and the neuroscience of agency [INSOSCI]



Jens Harbecke



Project Coordinator: Jens Harbecke, Witten/Herdecke University, department of economics and department of psychology, Germany

Project Partners: Jaakko Kuorikoski, University of Helsinki, Department of Political and Economic Studies, Finland

Bernard Feltz, Université Catholique de Louvain, Philosophy and Neuroscience, Belgium

In recent times, many governments in the Western world have invited experts from the neurosciences, psychology and social sciences to advise them on public policies. The motivation lies in the accumulating research on failures of rational behaviour in many contexts, such as financial markets, consumption habits or addiction. The idea is to use these insights in order to “nudge” people into adopting better behaviour in their own interest.

However, these approaches suffer from many deficiencies so far, and they stay in conflict with certain basic notions of rights and individual freedom in modern societies. One difficulty lies in the lack of an integrating conceptual framework, as many scientific disciplines are involved. This is especially challenging for policy design, since the different disciplines often refer to many different levels of possible intervention points, such as neuronal or hormonal mechanisms, individual choices and information, or institutional design.

This project tackles these issues and chooses one especially salient and politically important issue domain, namely financial markets. In popular conceptions, many dysfunctional phenomena in financial markets relate to an alleged clash between emotions and rationality. For economists, notions such as that “bankers are greedy” may not fit into their theoretical design, but nevertheless psychology provides perspectives on this. Putting those different disciplines into one framework would certainly improve the quality of the scientific foundations of public policy. Achieving such a framework is a task for modern analytical and theoretical philosophy and the philosophy of science.

Therefore, in this project philosophers and experts from the different disciplines collaborate in creating such a framework and in drawing up a map of this complex field in order to identify intervention points and evaluate alternative intervention designs.

Intelligent Neuro-Technologies Restoring Functions of Action and Communication: an Evaluation Study [INTERFACES]



Ralf J. Jox

Project Coordinator: Ralf J. Jox, Ludwig-Maximilians-Universität München, Institute of Ethics, History and Theory of Medicine, Germany

Project Partners: Eric Racine, Institut de recherches cliniques de Montréal, Neuroethics Research Unit, Canada

Jan Christoph Bublitz, University of Hamburg, Department of Criminal Law and Legal Philosophy, Germany

David Rodríguez-Arias, Universidad de Granada, Departamento de Filosofía, Spain

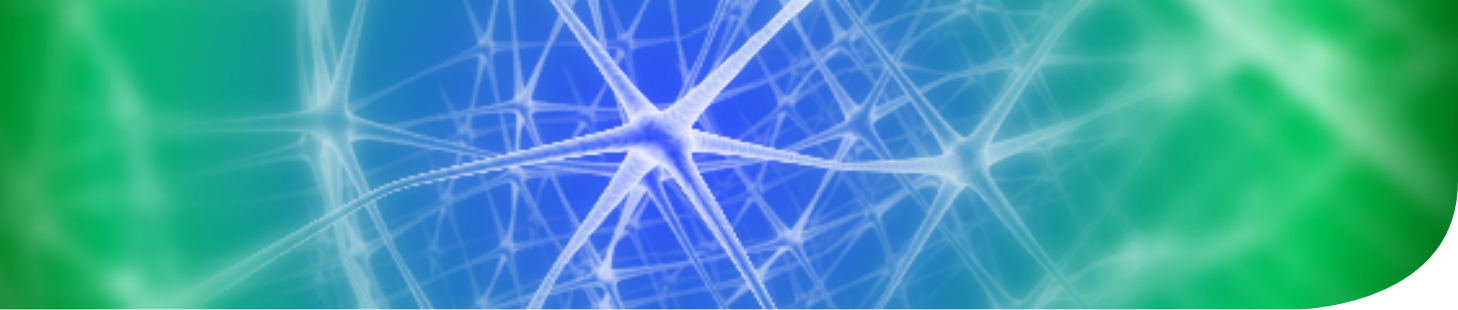


INTERFACES is an international research project on ethical, legal, and social aspects of brain-computer-interfaces (BCI). This relatively new technology connects the brain with a computer and enables one to directly control computer and other electronic devices by his/her mind.

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) analyze the fundamental theoretical, ethical and legal questions associated with BCI and (3) utilize the resulting insights to offer orientation for medicine and society.

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 organized 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.



Psychiatric Neurosurgery – Ethical, Legal, and Societal Issues, [PNS]



Project Coordinator: Sabine Müller, Charité – Universitätsmedizin Berlin, Department for psychiatry and psychotherapy, Germany

Project Partners: Tade Matthias Spranger, Rheinische Friedrich-Wilhelms-Universität Bonn, Institute of Science and Ethics (IWE), Germany

Judy Illes, University of British Columbia, National Core for Neuroethics, Vancouver, Canada

Roberto Martínez-Alvarez, Hospital Ruber Internacional, Médico-Neurocirujano, Spain

Chris Bervoets, Universitair Centrum voor obsessieve-compulsieve stoornissen, Belgium



Psychiatric neurosurgery (PNS) is defined as neurosurgery for treating psychiatric disorders, which are not directly caused by brain diseases like brain tumors or epileptogenic tissues and whose biological underpinnings are unknown. Until the 1970ies, rather crude forms of “psychosurgery” had been used in hundreds of thousands of mentally ill patients. The abuse of psychosurgery has been brought to the public consciousness by Ken Kesey’s famous novel “One flew over the cuckoo’s nest”. Due to public criticism and the development of anti-psychotic drugs, psychosurgery became nearly completely abandoned, and was forbidden in many countries. However, since 2010, there is a renaissance of psychiatric neurosurgery, albeit in a much more refined and safer form. Contemporary PNS procedures include deep brain stimulation (DBS) and ablative neuro-surgical procedures. For DBS, thin electrodes are inserted deep into the brain, which are connected with a stimulator that gives permanently current to the targeted brain area in order to activate or deactivate these areas. The ablative neurosurgical procedures comprise thermal or radiofrequency ablation procedures, and radiosurgery (Gamma Knife). These procedures create tiny lesions in brain areas, which play a crucial role in psychiatric symptoms. Radiosurgery does not require brain surgery; either by heat or radiation.

Although these modern forms of psychiatric neurosurgery have lesser adverse effects and risks, and are more precise due to neuroimaging studies, many ethical issues remain. For example, is it justified to intervene in the brain of mentally ill patients with the aim to change their personality and behavior? How is the risk-benefit-ratio for the patients? For which kinds of disorders can the use of PNS be justified – also for drug addiction or anorexia nervosa? In addition, many legal questions are open. The legislation with regard to PNS differs significantly across the countries. We will investigate these issues in a broader social context with a particular focus on economic interests, and the role of the media and social media.

Our international project will investigate ethical, legal, and societal issues of all kinds of contemporary psychiatric neurosurgery. We will publish recommendations for a responsible use of PNS.

Ethical and Legal Framework for Predictive Diagnosis of Alzheimer's Disease Quality of Life of Subjects at Risk and their Close Others [PreDADQoL]



Christiane
Woopen



Project Coordinator: Christiane Woopen, University Hospital of Cologne, Research Unit Ethics, Germany

Project Partners:

Mercè Boada, Fundacio ACE, Alzheimer Treatment and Research Center, Spain

With new bio-medical technologies, it is now possible to predict Alzheimer's Disease (AD) in elderly people with mild memory impairment. However, the prediction is not perfect; only in 80 % of the cases, the prediction is correct. Also, there is no treatment for AD available, which would delay the onset of the disease itself. Knowing in advance about a high risk to suffer from a devastating and untreatable disease can deeply impair quality of life and affects close others as well. But it can also be an important information with regard to life-decisions concerning family planning or working. On a societal level possible effects of stigmatization, discrimination and access to insurance and health care are to be considered.

In this project an ethical and legal framework will be developed for prediction of AD including a guideline on how to counsel patients and their close others before and after predictive diagnosis. It will be created on theoretical grounds and based on a study in patients, which addresses the attitudes and expectations as well as the subjectively perceived consequences of predictive testing for AD in patients and their close others. The study is performed in Germany and in Spain. A framework and guideline of this kind is urgently needed, because the worldwide usage of predictive testing in these patients is worldwide rapidly increasing.