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Announcements from NEURON

DON'T MISS

**2024 Call for Proposals on:
"Bi-directional Brain-Body
Interactions"**

**Pre-proposal submission deadline:
8th March 2024 | 14:00 CET**

[Details](#)

HAVE A LOOK!

**Winning videos from the 'Story of
our Research' video competitions**

JTC2020: [AID](#); [IMPULSES](#)

JTC2021: [MULTIFACT](#)

From the desk of the coordinator | February 2024



Dear All,

We are excited to commence a new year of continuous efforts to fund, support and foster excellent, innovative, and collaborative research into the health and disorders of the brain.

In this issue of the ERA-Net NEURON newsletter we focus on the 20 consortia that are funded under our two Joint Transnational Calls launched in 2023 (JTC2023): 15 projects funded under the call on 'Mechanisms of Resilience and Vulnerability in Mental Health' and 5 projects funded under the call on 'Neuroethics'. Read more about the calls, their outcomes and the funded projects on [page 4](#).

Our next call for proposals, JTC2024, was recently launched on January 8th – on the topic of 'Bi-directional brain-body interactions' (more details on the call [here](#)).




More information can be found on our website

<http://www.neuron-eranet.eu/index.php>

 [EraNeuron](#)

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Procced by CSO-MOH, IL



During the past year 2023, we organized two more webinars for lay audience. This lecture series demonstrates NEURON's dedication to raise public awareness to diverse aspects and great importance of brain research. The webinar 'It takes guts to think' took place in June 2023. Pascal Derkinderen, professor of neurology at Nantes University and INSERM U913 in France, explained exciting aspects of the trendy topic of the brain-gut axis (watch a recording of the [webinar](#)). In the second webinar of the year on November 29th, Prof. Hervé Chneiweiss, a renowned neurologist and neurobiologist and chairman of INSERM's Ethics Committee, gave an overview of research into neuroethics and focused on the ethical challenges of neurotechnologies (watch a recording of the [webinar](#) on our [YouTube channel](#)).

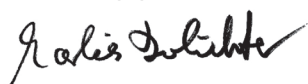
In the framework of our continuous support for early-career researchers in neuroscience, we conducted another two rounds of the 'The Story of our Research' video competition – for the young researchers of the [JTC2020 projects](#) on Sensory Disorders and the [JTC2021 projects](#) on Neurodevelopmental Disorders. The winners of these competitions are projects [AID](#) and [IMPULSES](#) from JTC2020 tied for 1st place and project [MULTIFACT](#) from JTC2021. They are invited to present their videos at the festive NEURON JTC2021 Midterm Symposium, which will take place in May at Berlin, Germany.

In addition, we are thrilled to announce that the recipient of the prestigious Excellent Paper in Neuroscience Award from ERA Net NEURON for the year 2023 is Dr. Ana Dorrego-Rivas for her paper: 'The core PCP protein Prickle2 regulates axon number and AIS maturation by binding to AnkG and modulating microtubule bundling' published in *Science Advances*, 2022. The award underscores the significance of investigating brain function and its associated disorders, serving as a means of providing support and encouragement to early-career researchers who are in the initial stages of their professional journey. The award ceremony for the "Excellent Paper in Neuroscience" will take place during a special lecture at the FENS Forum 2024 on 25-29th of June 2024, in Vienna, Austria.

We extend our invitation to keep informed with our latest updates by visiting our [website](#), following us on [X](#), and becoming a part of our [LinkedIn group](#). This will ensure you stay connected with our community and receive timely information about upcoming calls, activities, and events. Don't forget to subscribe to our [YouTube channel](#) for access to recordings of our lay lecture series and diverse videos showcasing our funded projects and more.

Wishing you a fruitful and rewarding year 2024!

Sincerely yours



OPEN SCIENCE SUPPORT FOR FUNDED PROJECTS OF JTC2023 'RESILIENCE AND VULNERABILITY IN MENTAL HEALTH' and 'ELSA'

The ERA-Net NEURON supports excellent, innovative and collaborative neuroscience research, and, thus, organizes and invites the coordinators of the JTC2023 funded projects on 'Resilience and Vulnerability in Mental Health' and Ethical, Legal and Social Aspects (ELSA) of Neuroscience for a workshop on Open Science. The two-day workshop will take place as a physical event on February 21st – 22nd, 2024 and is organized in cooperation with the BIH QUEST Center – Charité University Hospital in Berlin, Germany.

Any lack of reproducibility has a negative impact on public trust in the conclusions of science. The trustworthiness of research results is crucial for scientists and indispensable for citizens. The ERA-Net NEURON supports the selected and funded projects and researchers in their efforts to conduct the projects on the highest possible standards on design, conduct, analysis and reporting.

The four parts of the workshop center around the following topics:

- 'How to write a Data Management Plan (DMP)'. Since the submission of a project's DMP is obligatory for ERA-Net NEURON funded projects, and the number of online tools and services huge, a tutorial tour around the tools aims to support researchers for creating their own project DMPs.
- Patient and public involvement (PPI) methods and tools sessions support researchers to implement quality PPI and improve the relevance and transparency of the research and its translation into practice.
- Data sharing in brain research, a most important issue for all projects and DMPs.
- Interactive consultation sessions with experts for translational approaches in neuroscience aim to identify possible additional routes of the translation of results into innovation.

Last but not least, the workshop provides the opportunity to meet and network with other researchers funded under the call.

The ERA-Net NEURON's approach of Open Science Support for researchers is in line with many other European funding organisations and the European Commission strategies. And, in fact, to avoid useless and costly repetition is a most important item for funding organisations, as those invest taxpayers' money in research. Moreover, it is regarded unethical to sacrifice small numbers of animals several times instead on one confirming approach. The positive perception of science it is of utmost importance and should be enhanced by the implementation of open science and the FAIR data principle, a set of old and new practices aimed at enhancing the scientific process. By increasing the openness and the transparency of all steps of the research process, the likelihood increases that research & development results will be valid, and therefore, reliable and reusable.



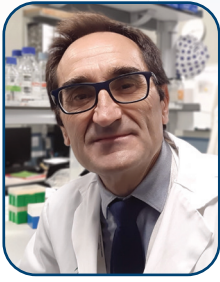
NEURON Joint Transnational Call 2023: “Mechanisms of Resilience and Vulnerability in Mental Health”

Mental disorders, in particular depression and anxiety, are the leading cause of disability worldwide. According to the OECD, one in every two people experience mental illness in their lifetime and these numbers may steadily increase as a consequence of recent global and regional crises. Furthermore, adverse environmental, lifestyle, social, and economic factors also influence the risk of developing long-lasting mental health condition, but these stresses produce different reactions among individuals who experience them, some are more resilient and others are more vulnerable and prone to develop mental health conditions. It is presently unknown how traumatic and/or stressful events and adverse environmental context become neurobiologically embedded, increasing the vulnerability to mental disorders. Similarly, how biological, social, cultural, psychological, and ecological factors manifest in neurophysiological mechanisms for the development of individual coping capabilities to enhance resilience towards adverse experiences is presently poorly understood. Therefore, it is of great importance to improve our understanding of the pathophysiological and adaptative mechanisms of our mental health with the potential to develop therapeutic and preventive approaches to preserve and improve mental health in Europe and worldwide.

Fifteen multinational research consortia were selected for funding under [JTC2023](#) on the topic of ‘Mechanisms of Resilience and Vulnerability in Mental Health’. In total, 75 research groups from 20 NEURON partner countries collaborate in these research projects, which cover diverse mechanisms of resilience and vulnerability to environmental stresses in mental health using numerous methodological approaches. The total funding volume of the call amounts to ~16.8 M€.

As part of ERA-Net NEURON’s mission to actively involve patients in the biomedical research process, proposals of the Joint Transnational Call 2023 underwent a patient review as part of the evaluation process. Nine international patient experts reviewed the full proposals from the perspective of patients and carers. Besides providing a full written evaluation to the applicants, the patients actively participated in the discussion at the review panel meeting and presented their appraisals and concerns.

We wish all the funded consortia great accomplishments and hope their outcomes help in the essential task these days of protecting our mental health and assisting in the understanding and potential prevention and therapeutics of mental health disorders.



Benedicto Crespo-Facorro



B3Phrenia

Dysfunction of the Blood-Brain Barrier in schizophrenia: molecular underpinnings of vulnerability or resilience

Project Coordinator:

Benedicto Crespo-Facorro, Institute of biomedicine-IBIS, CIBERSAM, Sevilla, Spain

Project Partners:

Matthew Campbell, Trinity College Dublin, Ireland

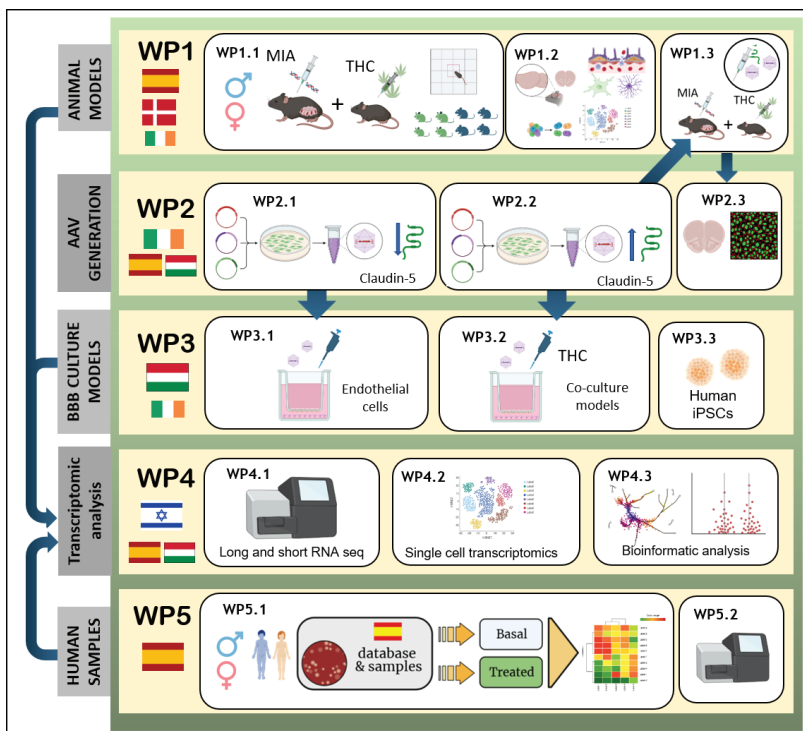
Maria A. Deli, Biological Research Centre, Szeged, Hungary

Hermona Soreq, Hebrew University of Jerusalem, Jerusalem, Israel

Konstantin Khodosevich, Biotech Research and Innovation Centre, Copenhagen, Denmark

Schizophrenia (SZ) is a sexually dimorphic neurodevelopmental disorder that involves both genetic predisposition and environmental risk factors in early and later life (i.e., maternal immune activation (MIA) by prenatal infection and cannabis use) that are associated with increased risks of SZ. However, the underlying biological mechanisms remain to be elucidated.

The aim of the B3phrenia project is to investigate the link between blood-brain barrier (BBB) tightness and the vulnerability or resilience to SZ, to explore sex-dependent molecular changes and to characterize BBB adaptation to risk factors (MIA/cannabis) to understand the neurobiological bases of SZ. Combined in vivo and in vitro analyses of molecular alterations of the integrity of BBB on animal models and iPSCs reprogrammed from patients with SZ will shed light on our understanding of the complex relationships between cannabis, sex, and the function and structure of BBB, and so enhance our knowledge about resilience and vulnerability to SZ.



The interdisciplinary team of world-class researchers will employ state-of-the-art techniques such as transcriptome and proteome profiles of peripheral blood mononuclear cells obtained from a unique clinical cohort of first-episode SZ patients to identify molecular pathways of BBB dysfunction and suitable sex-modulated targets with the aim of enhancing resilience and develop refined stratification schemes of SZ patients.



Freddy Jeanneteau

CLEVER

Rebalancing gluCOse utilization in vulnErability to chronic stress: a nOvEl strAtEgy to promote Resiliency against psychopathology

Project Coordinator:

Freddy Jeanneteau, CNRS/ Institut de genomique fonctionnelle/ University of Montpellier, Montpellier, France

Project Partners:

Chadi Touma, University of Osnabrück, Osnabrück, Germany

Stephanie Witt, Central Institute of Mental Health/ Medical Faculty Mannheim/ Heidelberg University, Mannheim, Germany

Nico Mitro, Istituto Europeo di oncologia, Milano, Italy

Mariusz Papp, Maj Institute of Pharmacology/ Polish Academy of Sciences, Kraków, Poland



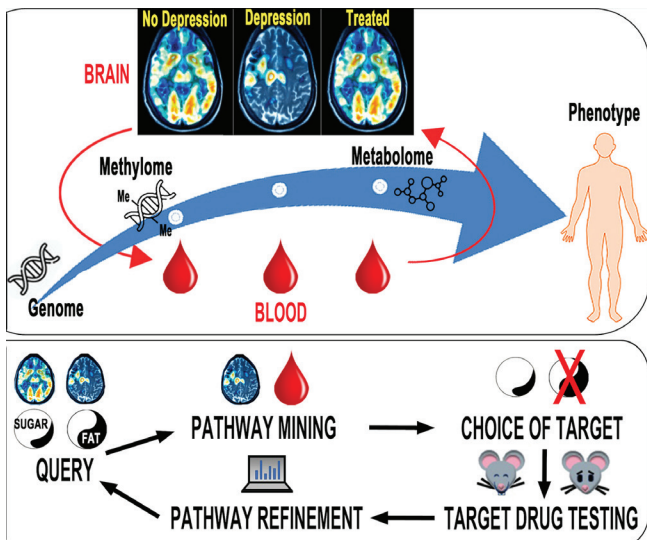
The lifetime prevalence (~20%) and economic burden (\$350 billion annually) associated with major depressive disorders (MDD) make them one of the most common and debilitating psychiatric illnesses. Currently, the diagnosis of MDD and suicidal behaviors are subjective and quantitative biomarkers for early detection and long-term assessment are lacking. Without such objective biomarkers, diagnosis, monitoring and treatment adjustments rely exclusively on suboptimal clinical examination.

We hypothesize that regional changes of brain activity linked to MDD reflect the utilization of distinct fuel sources for its metabolism. Specifically, we propose that MDD patients rely more on lipids than carbohydrates to meet energy demands, whereas successful treatment would reduce lipolysis and promote glycolysis.

The primary objective of the project is to discover genes and pathways with high relevance for individuals that are more vulnerable to MDD and insufficient treatment response. The secondary objective is to exploit the candidate genes and pathways as proof-of-concept to restore fuel utilization

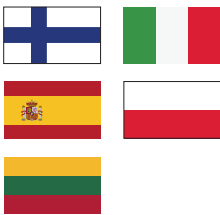
towards more carbohydrates and less lipids in the brain of preclinical animal models of MDD.

The project is designed as a reverse translation from patients to animal models and back with a proof-of-concept for intervention. The project will provide conceptual advance in normal and dysfunctional brain/body metabolism, paving the way for predictive metabolic representations of trajectories to successful treatment and prevention. It will also provide novel targets for therapeutic intervention that could significantly improve the quality of life of the affected individuals and their families.





Claus Normann



EnviroMood

Neurobiological mechanisms of the environment - plasticity - behaviour interaction

Project Coordinator:

Claus Normann, University Medical Center Freiburg, Freiburg, Germany

Project Partners:

Eero Castren, Neuroscience Center, University of Helsinki, Finland

Igor Branchi, Istituto Superiore di Sanità (Italian Institute of Health), Rome, Italy

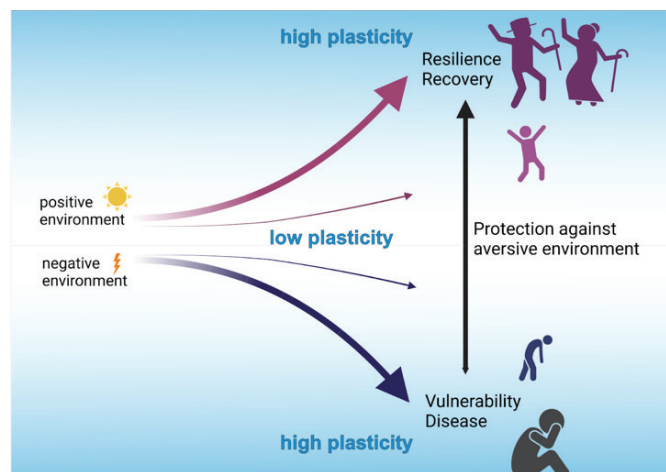
Shira Knafo, University of the Basque Country, Spain

Ewelina Knapska, Nencki Institute of Experimental Biology, Warsaw, Poland

Urtė Neniskytė, Life Sciences Center, Vilnius University, Lithuania

Depression is a serious mental health condition that affects how a person feels, thinks and behaves. People who are depressed often feel persistently sad, empty, or hopeless. Depression is very common and affects more than one in ten people during their life, females twice as often as males.

In this research project, we examine the role of brain plasticity in the development and treatment of depression. Brain plasticity means that connections between nerve cells and different areas in the brain can be strengthened, weakened or reorganized in response to experiences, learning or environmental changes. In depressed patients, brain plasticity is generally weaker than in healthy people; and antidepressants increase brain plasticity. However, this might not always be good. If people are treated with antidepressants while living in very negative conditions (e.g. are poor, have conflicts in their family or have suffered serious trauma), medication might work worse. It is therefore important to know how exactly the environment influences plasticity in the brain; and how antidepressants work to enhance brain plasticity. With this knowledge, it might be possible to predict how patients with depression should be treated. Another long-term goal of our research, based on this knowledge, is to develop new antidepressant treatments, which have fewer side effects and work better than the existing drugs. In this research project, an international group of researchers examines healthy and depressed humans, animals and nerve cells to improve the treatment of depressed patients and to prevent that depression affects so many people.





Santiago Canals

IBRAA

Inflamed Brain Response in Alcohol Addiction: Understanding the role of neuroinflammation, immunotypes and gut-brain reactivity for heterogeneity in disease course and therapy response

Project Coordinator:

Santiago Canals, Instituto de Neurociencias, Spanish National Research Council (CSIC), Universidad Miguel Hernández (UMH), San Juan de Alicante, Alicante, Spain

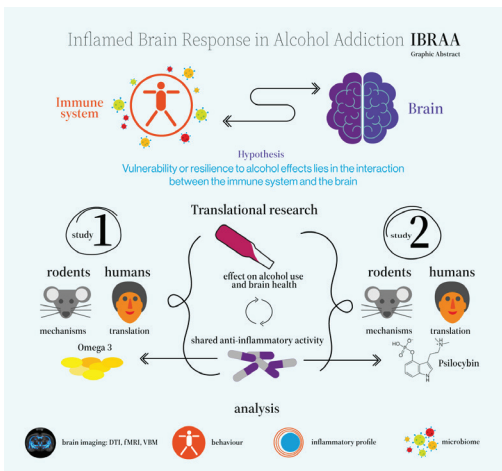
Project Partners:

Sophie Layé, NUTRINEURO UMR1286 INRAE, Univ BORDEAUX, BORDEAUX, France
Amandine Luquiens, University hospital of Nîmes (CHU de Nîmes), Addiction Dept., Nîmes, France

Wolfgang Sommer, Institute of Psychopharmacology at Central Institute for Mental Health (CIMH), Mannheim, Germany

Philippe De Timary, Institute of Neuroscience, Addiction and Mental Health Laboratory, Université catholique de Louvain, Brussels, Belgium

Raul Cristian Muresan, Asociatia Transylvanian Institute of Neuroscience, Cluj-Napoca, Romania



Alcohol addiction is a widespread mental health condition that lacks effective treatment options for many individuals. Even low to moderate levels of alcohol consumption can have detrimental effects on health, but people’s responses to alcohol vary greatly within the population. We believe that a significant portion of this variability stems from the interaction between the immune system and the brain. Our research focuses on studying vulnerability in individuals with alcohol dependence during the early stages of abstinence, which represents a critical period for relapse prevention. We hypothesize that individuals with heightened immune reactivity will experience an intensified neuroinflammatory response during early abstinence. Conversely, less reactive immunotypes may offer protection against these negative outcomes. This research seeks to define biomarkers that identify vulnerable individuals to brain damage and relapse risk and provide effective treatments. We will explore interventions that can reduce the neuroinflammation that occurs soon after alcohol withdrawal. Our main strength is a multidisciplinary team that brings together experts in the field with complementary skills to understand vulnerability and resilience factors in Alcohol Use Disorders (AUD). The team’s background ranges from medicine, neurobiology, and immunology, to physics, advanced brain imaging, and data science, and includes patient organizations for proper integration and communication. If our hypotheses are strongly supported, it will lead to modifications in clinical practice, including the use of nutritional supplements as potential treatments to enhance resilience in AUD individuals.



Beat Lutz



KetoResi

Ketogenic signaling in resilience promotion

Project Coordinator:

Beat Lutz, Leibniz Institute for Resilience Research (LIR), Mainz, Germany

Project Partners:

Alexandra Sebastian, University Medical Center of the Johannes Gutenberg University Mainz, Mainz, Germany

Francois Tronche, Neuroscience Paris-Seine (CNRS; INSERM UMR8246), Sorbonne Université, Paris, France

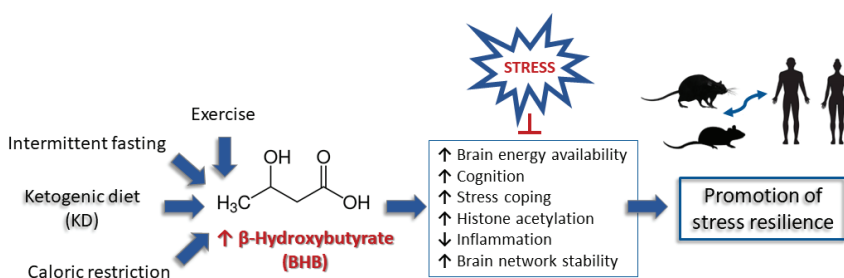
Marc Claret, Fundació de Recerca Clínic Barcelona-Institut d'Investigacions Biomèdiques August Pi i Sunyer (FRCB-IDIBAPS), Barcelona, Spain

Maria Morena, Santa Lucia Foundation, IRCCS, European Center for Brain Research (CERC), Rome, Italy

Stress-related mental disorders are often comorbid with metabolic dysregulation, e.g., hyperglycemia, insulin resistance and low-grade inflammation. Furthermore, epidemiological studies have shown that high glycemic diets can promote the occurrence of depression. Thus, stress-related and metabolic disorders appear to be highly intertwined. Individual responses are commonly observed to stressor impact, coining the term stress resilience for those subjects that stay mentally healthy despite high stressor load. In this translational study involving (i) two rodent stress resilience models and (ii) human cohorts from a longitudinal stress resilience study, we will assess the hypothesis that ketone body signaling is a promising strategy to boost stress resilience. This hypothesis is substantiated by the current knowledge on candidate stress resilience mechanisms and also on data showing that ketogenic signaling is able to positively modulate many of the potential resilience mechanisms. Here, we aim at investigating several of these underlying mechanisms and identifying potential molecular and behavioral predictors of stress resilience. In a multidisciplinary approach, this consortium will implement a broad range of state-of-the-art techniques including behavioral analyses, cell type-specific transcriptomics, chromatin analysis, cell-type viral strategies to perform chemogenetic interventions, metabolic studies, in vivo imaging in rodents (fMRI, calcium imaging, neurotransmitter sensors) and in humans (fMRI).

We explore the link between stress resilience and metabolism. The suggested interventions are easily applicable, self-determining, and affordable, and

importantly without ethical dilemmas. Thus, in the current times of high stressor load, this project will decisively contribute to improve the general health and to alleviate stress-related disorders.





Markus Reichert



MASE

The motor activity - subjective energy (MASE) project: Neurobiological and digital phenotyping towards digital mental health interventions in depression

Project Coordinator:

Markus Reichert, Dept. of eHealth and sports analytics, Faculty of Sport Science, Ruhr University Bochum, Bochum, Germany

Project Partners:

Urs Braun, Research Group Complex Systems in Psychiatry, Hector Institute for Artificial Intelligence in Psychiatry, Dept. of Psychiatry and Psychotherapy, Central Institute of Mental Health, Medical Faculty Mannheim/Heidelberg University, Mannheim, Germany

Sebastian Walther, Translational Research Center, University Hospital of Psychiatry and Psychotherapy, University of Bern, Bern, Switzerland

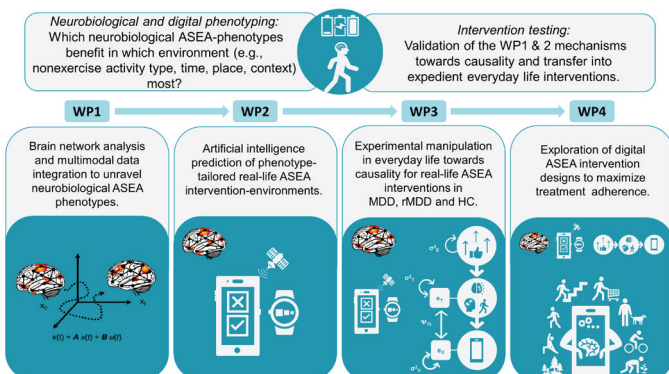
Amaia Méndez Zorrilla, eVida Research Group, Faculty of Engineering, University of Deusto, Deusto, Spain

Steriani Elavsky, Dept. of Human Movement Studies, Faculty of Education, University of Ostrava, Ostrava, Czech Republic

Major depressive disorder (MDD) is considered a worldwide leading source of disability. Behavioral activation (BA), a successful therapeutic approach for nearly 50 years, increases activation through short and rewarding experiences; e.g., taking a shower. However, BA alone is not superior to other forms of psychotherapy. Recently, researchers identified a new potential starting point for MDD treatment, ASEA: real-life physical activity-subjective energy association. It describes how people feel more energized and awake when moving. While past MDD research focused on exercise, we and others found that not sports (e.g. jogging) but nonexercise activity (e.g., walking stairs) improves energy, and we determined a specific brain region related to ASEA. From a clinical perspective, ASEA is highly relevant since activity reductions and loss of energy symptoms strongly affect patients.

Hence, short ASEA interventions are likely to improve MDD prevention and treatment. However, it is unclear who benefits most from which intervention (activity-type, timing, location, context). For example, people with a certain brain structure may profit from a short slow walk in the morning to increase energy and reduce depression, while others may benefit from fast stair-climbing in the evening. Therefore, we aim to apply brain network

analyses to identify types of brains likely to profit (WP1), use artificial intelligence to detect where and when nonexercise activity helps people with certain brain properties most (WP2), conduct an experiment to test the intervention-suggestions (WP3), and develop a smartphone-app that delivers suggestions when and where to engage in which nonexercise activity (WP4).





Ali Jawaid



MUSE ACE

Metabolic Underpinnings of Susceptibility to Adverse Childhood Experiences

Project Coordinator:

Ali Jawaid, Nencki Institute of Experimental Biology, Warsaw, Poland

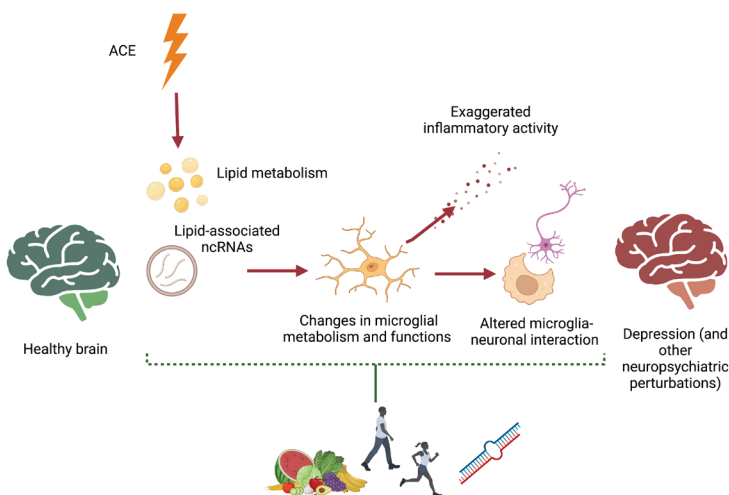
Project Partners:

Rosa Paolicelli, University of Lausanne, Lausanne, Switzerland

Anthony Hannan, The Florey Institute of Neuroscience and Mental Health, Melbourne, Australia

Exposure to adverse conditions during childhood can severely impact our mental health as adults. We now know that eating unhealthy diet or lack of physical activity can further accentuate the harmful effects of childhood adversity, whereas some other factors like exercise are protective. We believe that this is due to the fats present in our blood, which determine the vulnerability to the impact of adverse childhood experiences (ACE) on adult mental health. Our previous studies on children that were exposed to forced separation from their mothers revealed that those who developed depression after this traumatic experience had specific changes in blood fats. Our recent research indicates that such changes in blood fats have the possibility to impact the immune cells in the brain known as microglia. Thus, it is plausible that microglia serve as the bridge between changes in blood fats and the long-term psychological effects of ACE. To test this hypothesis, we plan to feed laboratory mice a fat-enriched diet after exposing them to early life stress. We will then study their microglial functions. Then to test whether microglia are related to mental disturbances after ACE, we

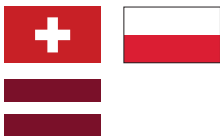
will deplete these cells in the brain of mice fed on either regular or fat-enriched diet. Furthermore, we will also stimulate lab-grown human brain tissue-like structures with the blood samples from different populations that have been exposed to ACE. Finally, we will check if improving good fats in the blood through dietary supplements will enhance resilience to the mental disturbances after ACE.



Adverse childhood experiences (ACE) lead to changes in peripheral lipids and lipid-associated ncRNAs (including specific miRNAs) that distinctly or collectively converge to alter microglial metabolism and functions. Modifications in microglial inflammatory and phagocytic properties alter microglia-neuronal interactions via induction of inflammation and/or impaired synaptic remodeling. Sustained changes in microglial functions via ACE-induced alterations of peripheral lipids manifest as neuropsychiatric disease, such as depression and associated affective disorders. Preclinical validation of this hypothesis could pave the way for new modalities to enhance resilience against the long-term behavioral sequelae to ACE via manipulation of peripheral lipids through life-style modifications and/or dietary supplements, as well as targeted miRNA therapeutics.



Raffael Kalisch



PHASR-PP

PHarmacological Augmentation of Stress Resilience - Proof of Principle

Project Coordinator:

Raffael Kalisch, Leibniz Institute for Resilience Research (LIR), Mainz, Germany

Project Partners:

Oliver Tüscher, UNIVERSITÄTSMEDIZIN DER JOHANNES GUTENBERG-UNIVERSITÄT MAINZ (UMC-Mainz), Mainz, Germany

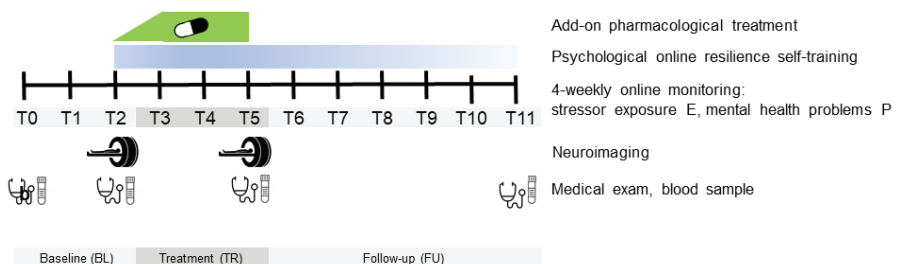
Flurin Cathomas, UNIVERSITÄT ZÜRICH (UZH), Zurich, Switzerland

Dorota Kobylińska, UNIWERSYTET WARSZAWSKI (UNIWARSAW), Warsaw, Poland

Signe Mezinska, LATVIJAS UNIVERSITATE (LU), Riga, Latvia

Stress-related mental problems and disorders often start during adolescence or early adulthood, and they have their highest levels during this life period. During the COVID-19 pandemic, children, adolescents and young adults were among the most strongly mentally affected groups. The prevalence of mental disorders in this age group is on the rise. Health care services are increasingly overburdened. This situation motivates a search for new strategies to combat stress-related mental health problems in this age group. Further, individuals who experience severe mental health problems already early in their lives are more vulnerable for the rest of their lives, having an increased risk to develop mental disorders. Therefore, emerging adulthood might be a “window of opportunity”, where to intervene in a preventive fashion might have long-lasting benefits and be a very efficient way to reduce the burden of stress-related mental disorders in society as a whole.

Based on findings from animal research, we test for the first time in a clinical trial whether a 3 months treatment of young adults at risk for mental health problems with a well-known and well-tolerated commercially available drug that is currently used in the treatment of bodily disorders will reduce the probability that these individuals will develop stress-related mental health problems. We also test the assumption that the drug will exert this effect by protecting the function of the Blood-Brain Barrier (BBB), which is a tissue surrounding blood vessels in the brain that shields the brain against damaging factors in the blood, including in states of stress and stress-related inflammation, and which can itself become dysfunctional under stress. A pharmacological method to prevent stress-related disorders would be novel and may well complement psychological approaches. Ethical and social issues potentially raised by this pharmacological approach will also be investigated.





Marianne B. Müller



PROGRESS

Disease-predisposing or resilience-promoting? Decoding the systems biology and behavioural predictors and determinants of the tipping point of stress

Project Coordinator:

Marianne B. Müller, Leibniz Institute for Resilience Research, Mainz, Germany

Project Partners:

Helena Sork, University of Tartu, Institute of Technology, Tartu, Estonia

Iiris Hovatta, University of Helsinki, SleepWell Research Program, Helsinki, Finland

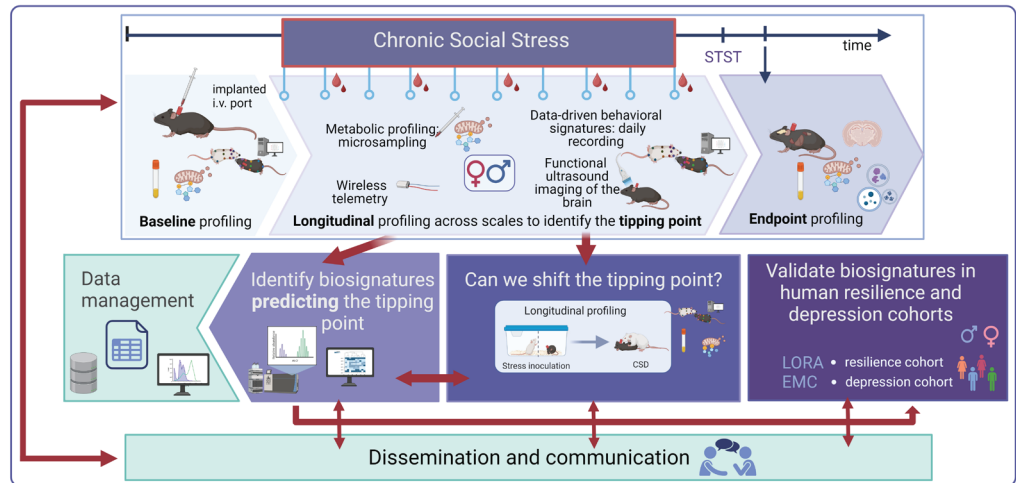
Nils Gassen, University Clinic Bonn, Dept. of Psychiatry and Psychotherapy, Bonn, Germany

Johannes Bohacek, ETH Zurich, Dep. of Health Science and Technology, Inst. for Neuroscience, Zurich, Switzerland

Igor Jurisica, Slovak Academy of Sciences, Inst. of Neuroimmunology, Bratislava, Slovakia

The concept of a tipping point can be easily visualized when we consider the climate crisis: through more and more detailed insights into climate change, we have learned that even the smallest events can ultimately throw a complex system out of balance when the dynamics approach a critical threshold, the so-called tipping point. A very similar scenario can be observed when it comes to the effects of stress on our body: moderate stress is positive and protects us against future stressful experiences, a phenomenon called stress inoculation. Prolonged exposure to severe stress, in turn, can have negative effects on the body. The precise mechanisms that decide whether the consequences of stress are positive or negative remain largely unclear, and we don't yet understand what happens at this tipping point. Chronic social stress is an important risk factor for depression, but while under chronic stress, only a minority of people develop clinical depression. The majority are able to maintain good mental health despite unfavorable conditions, a phenomenon called resilience. Resilience to stress is an active process, however, the exact biological mechanisms strengthening resilience are still poorly understood. This project takes a very unique approach to understanding what molecular, biochemical, and behavioral changes herald and signal this tipping point where stress switches from its positive to negative effects: our consortium will combine the expertise of leading European scientists in the fields of behavior, computational, molecular and physiological analyses, and neuroscience to identify "fingerprints" of stress resilience. We will also test whether stress inoculation training can increase resilience and shift the tipping point. Our goal is to identify markers which precede or signal the tipping. Our results will allow early prediction of the tipping point so that preventive measures can be taken in time to prevent full-blown depression from developing.

Finally, this knowledge will contribute to develop tailored prevention or treatment strategies to fight stress-associated depressive disorders more effectively in the future.





Ersin Yavas



REJUVENATE

Rerouting towards REsilience to JUVENile stress-induced psychopATHologiEs in Adulthood: Spotlight on behavioural profiling and lifestyle interventions

Project Coordinator:

Ersin Yavas, Bartın University, Dept. of Psychology, Experimental Psychology, Bartın, Turkey

Project Partners:

Gabrielle Girardeau, Sorbonne université, Institut du fer à moulin, Inserm U1270, Paris, France

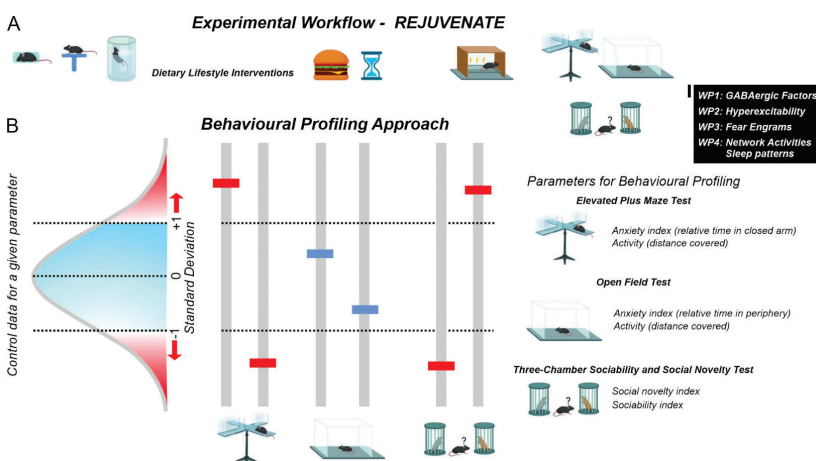
Fuat Balci, Koç University, Dept. of Psychology, Research Center for Translational Medicine, İstanbul, Turkey

Charlotte Boccara, University of Oslo, Dept. of Molecular Medicine, Institute of Basic Medical Sciences, Oslo, Norway

Gal Richter-Levin, University of Haifa, Sagol Dept. of Neurobiology, Haifa, Israel

Gürsel Çalışkan, Otto-von-Guericke University, Dept. of Genetics and Molecular Neurobiology, Institute of Biology, Magdeburg, Germany

This study investigates the enduring impact of childhood adversities, specifically Juvenile Stress (JS), on mental health. JS is linked to an increased susceptibility to mood and anxiety disorders in adulthood, but resilience varies among individuals. The primary objectives include understanding the mechanisms connecting JS to vulnerability and resilience, testing lifestyle interventions for mitigating JS's negative effects, and addressing sex-related differences in stress responses and intervention effectiveness. The study focuses on hippocampal functioning, GABAergic alterations, and aims to explore behavioral, cognitive, molecular, cellular, and network-level outcomes in resilient and susceptible individuals. Lifestyle interventions like diet patterns will be assessed, considering sex-dependent variations. Early neural and behavioral biomarkers will be examined to predict long-term outcomes and intervention effects. In this collaborative project, we will combine advanced expertise in behavioral neuroscience with systems, cellular, and molecular methodologies to thoroughly investigate the neural foundations of the impact of Juvenile Stress (JS) on vulnerability and resilience later in life. Our goal is to establish multimodal predictive and descriptive biomarkers capable of identifying the risk and resilience outcomes



associated with JS. Additionally, we will assess the effects of lifestyle interventions on behavior and related mechanisms, aiming to establish highly translational interventions as a potential approach to enhance mental health resilience following exposure to JS.

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Igor Nenadić

ResilNet

Resilience and vulnerability: from neural circuits to networks

Project Coordinator:

Igor Nenadić, Cognitive Neuropsychiatry Lab, Dept. of Psychiatry and Psychotherapy, Philipps-Universität Marburg, Marburg, Germany

Project Partners:

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Paolo Brambilla, Dept. of Neurosciences and Mental Health, Fondazione IRCCS Ca' Grande Ospedale, Milano, Italy

Rafael Romero Garcia, Instituto de Biomedicina de Sevilla, Dept. of Medical Physiology and Biophysics, University of Sevilla, Sevilla, Spain

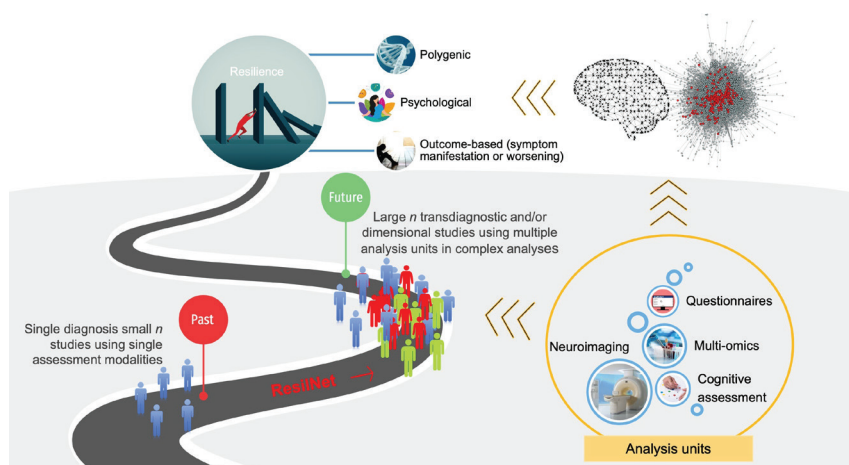
Ahmad Abu-Akel, School of Psychological Sciences, Haifa University, Haifa, Israel

Timothea Touloupoulou, Dept. of Psychology, Bilkent University, Ankara, Turkey



Throughout our lives, difficult events we encounter have a profound impact on our mental well-being. Our capacity to adapt and recover from adversity ultimately influences the health outcomes we experience. Resilient individuals are better able to cope with adversity and less likely to develop mental health problems or they experience symptoms typically less severe. So far, we do not know enough to develop effective strategies that can build resilience in those in which it is low, nor enough to properly identify less resilient individuals who are at the greatest risk of poor mental health.

ResilNet is a new research initiative, which brings together a multidisciplinary network of scientists. We aim to improve our understanding of resilience on multiple levels, including the genetic/polygenic makeup of individuals, psychological factors like thinking styles or behaviour and outcomes such as clinical symptoms developing over time. ResilNet will make use of large databases of thousands of individuals, including people with schizophrenia, bipolar disorder, depression, anxiety and autism, as well as sub-clinical (non-diagnosed) symptoms. Novel computational neuroscience approaches like machine learning and network theory will be applied to large data sets of brain scans (neuroimaging), genomic/"multi-omics", psychological/questionnaire data and cognitive/clinical assessments. This approach will be extended to people at risk of developing mental health problems because of exposure to traumatic situations or stressors, including COVID, war, or earthquakes – paving the way for a better understanding of resilience mechanisms and improvement of health interventions aimed at a wide range of mental health issues.





Muriel Koehl



ResiPreS

Neurobiological basis of resilience/vulnerability to prenatal stress in mice

Project Coordinator:

Muriel Koehl, Neurocentre Magendie, INSERM U1215, Bordeaux, France

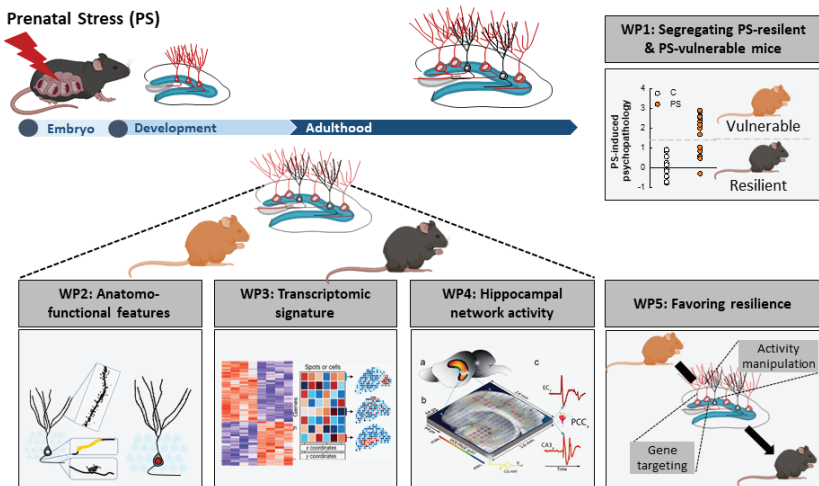
Project Partners:

Jan Rodriguez Parkitna, Dept. of Molecular Neuropharmacology, Maj Institute of Pharmacology of the Polish Academy of Sciences, Krakow, Poland

Hayder Amin, Biohybrid Neuroelectronics Group, German Center for Neurodegenerative Diseases, Dresden, Germany

When mothers experience stress during pregnancy, known as prenatal stress (PS), it may increase their offspring’s risk of developing mental health conditions like Post-Traumatic Stress Disorder (PTSD), a devastating stress-related disorder that develops in the aftermath of a traumatic life event. However, not everyone exposed to trauma develops PTSD, pointing to the existence of resilience factors that need exploration. Using a mouse model to analyze these factors, we found that PS can cause PTSD-like memory issues in some, but not all mice. This observation, which mimics the human situation suggests that it constitutes a valuable model for understanding the mechanisms underlying resilience / vulnerability to stress.

Our mechanistic target is a brain region called the dentate gyrus of the hippocampus, which is crucial for emotional memory control. It is characterized by a continuous neurogenic development, leading to the existence of temporally distinct neuronal populations. Our hypothesis is that these distinct neuronal populations may present different responsiveness to PS, thus leading to the establishment of the individual’s resilience or vulnerability to stress. In this project, our aim is to investigate these neurons’ anatomo-functional properties, their gene expression patterns, and their contribution to hippocampal network activity using cutting edge techniques. Once we have identified specific cells or genes involved, we will test their direct impact in resilience /vulnerability to stress.



Overall, by studying the mechanisms that determine why some people develop PTSD and others do not, we hope to highlight new therapeutic targets and better, more effective, treatments for PTSD and similar conditions that develop in individuals exposed to deleterious life events.



Chantal Martin Soelch



RESIST-D

Reward-stress interactions as neural substrate for resilience and vulnerability in mental health: A translational large-scale project

Project Coordinator:

Chantal Martin Soelch, Unit of Clinical and Health Psychology, Dept. of Psychology, University of Fribourg, Fribourg, Switzerland

Project Partners:

Natasa Hlavacova, Dept. of Endocrine Regulations and Psychopharmacology, Biomedical Research Center, Slovak Academy of Sciences, Bratislava, Slovakia

Thomas Hinault, U1077, Pôle des Formations et de Recherche en Santé (PFRS), Caen, France

Heike Tost, Dept. of Psychiatry and Psychotherapy, Central Institute of Mental Health (CIMH), Mannheim, Germany

Dara Cannon, Clinical Neuroimaging Laboratory, Centre Neuroimaging Cognitive Genomics, University of Galway, Galway, Ireland

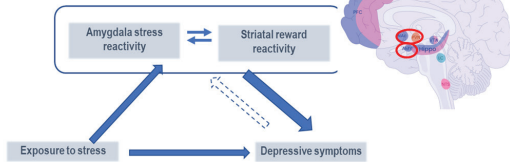
Maria-Magdolna Ercsey-Ravasz, Asociatia Transylvanian Institute of Neuroscience, Network Science Dept., Cluj-Napoca, Romania

While the association between the experience of early life stress (ELS), that is, stressful events related to different forms of child abuse or neglect, and heightened risk of mental health problems, in particular depression, is well-established, the reasons for divergent outcomes remain unclear, as does the understanding of age-related variations in the onset of depression. Depression is one of the most frequent mental health problems, yet it remains difficult to treat; and little is known about the etiology of late-life depression. We focus here on the neurobehavioral responses to rewards and to acute stress as key neurobiological mechanisms underlying the risk of developing depressive symptoms at different ages after ELS. The project is divided into five work packages, encompassing preclinical models (WP1), human studies on individuals exposed to ELS across different age groups (WP2) using functional magnetic resonance imaging (fMRI) and electroencephalogram (EEG) measures, investigations in currently depressed participants (WP3), computational analysis of brain networks (WP4), and the creation of a Fair, Accessible, Interoperable, and Reusable (FAIR) database for large-scale analyses (WP5). We aim to identify biomarkers and adopt a transdiagnostic and dimensional approach to depression. The emphasis on a developmental, lifetime perspective may significantly advance the understanding of depression at different ages, with potential implications for clinical use. The creation of a FAIR database specific for ELS available in open-access after the end of project will be an important deliverable of this project.

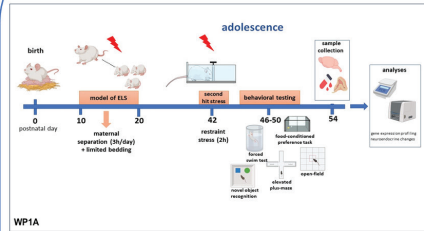
Overall, by studying the mechanisms that determine why some people develop PTSD and others do not, we hope to highlight new therapeutic targets and better, more effective, treatments for PTSD and similar conditions that develop in individuals exposed to deleterious life events.

RESIST-D: NEUROBEHAVIORAL MECHANISMS UNDERLYING THE RISK TO DEVELOP DEPRESSION AFTER EARLY LIFE STRESS (ELS)

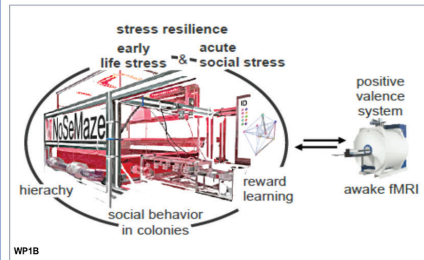
HYPOTHETICAL MODEL



WP 1: preclinical models

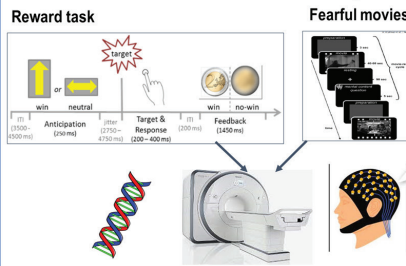


WP1A

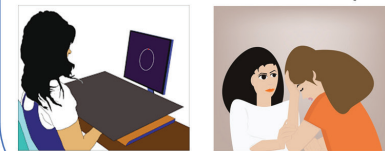


WP1B

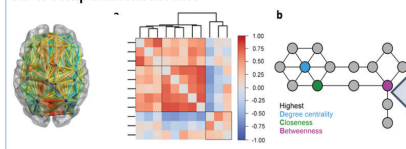
WP 2: data collection and datasets of individuals exposed to ELS



WP3: data collection in individuals with depression



WP4: computational models



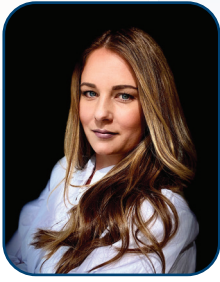
WP 5: FAIR database

RESIST-D - OVERVIEW OF DATA STRUCTURE & INTEGRATION

WP	STRESS	SAMPLE	EMA	CLINICAL & BEHAVIOR	MICROCELLULAR			BRAIN IMAGING			GENETIC
					HPA	ANS	EEG	T1	fMRI	rsfMRI	
1A		Rats									
1B		Mice									
2A		Legacy cohort data									
2B		ELS exposed young adults									
2C		ELS exposed older adults									
3		Clinical									
4		Data									

5. OVERARCHING HYPOTHESIS: TESTING & DATA INTEGRATION ACROSS PARTNERS & WP1-5

Data collection and legacy data: preclinical to clinical



Natalie Matosin



TrauMAP

Features of exposure to childhood adversity in the insular cortex in MDD and PTSD

Project Coordinator:

Natalie Matosin, University of Sydney, School of Medical Sciences, Sydney, Australia

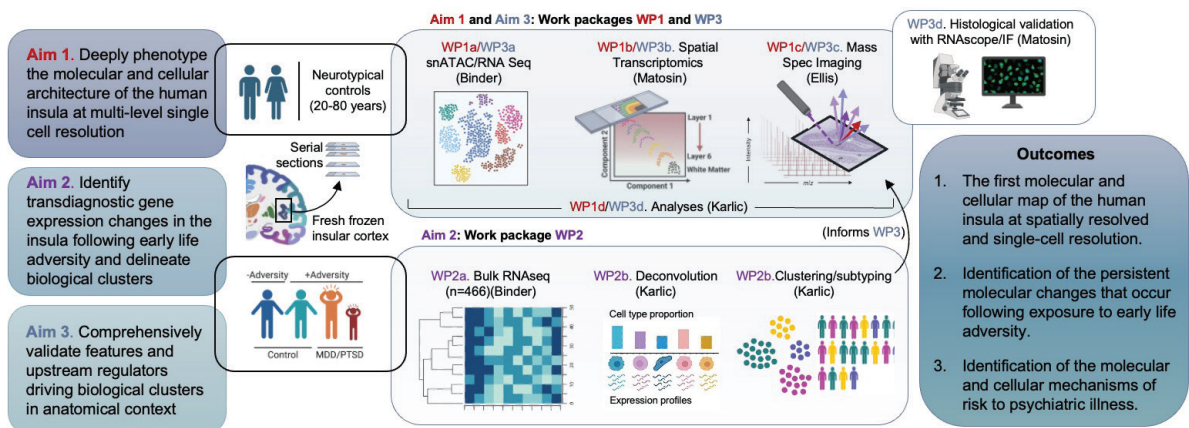
Project Partners:

Elisabeth B Binder, Max Planck Institute of Psychiatry, Institute Director, Dept. of Genes and Environment, Munich, Germany

Rosa Karlič, University of Zagreb, Faculty of Science, Dept. of Biology, Zagreb, Croatia

Shane Ellis, Molecular Horizons Institute, University of Wollongong, Mass Spectrometry Imaging Laboratory, Wollongong, Australia

Early life adversity is the strongest environmental risk factor for psychopathology and is associated with increased disorder severity, comorbidity, chronicity and treatment resistance. Determining the altered biology responsible for how early adversity raises risk of psychiatric disorders is key to develop interventions and treatments for a large portion of patients. The overall goal of this project is to identify molecular and cellular mechanisms of psychiatric risk in the insular cortex (insula) – a highly important brain area relevant to psychiatric disorders – to provide a springboard for accurate patient subtyping and personalised drug development. Firstly, we will deeply phenotype the human insula in neurotypical controls using single-cell, spatial transcriptomics and mass spectrometry imaging, and make this atlas freely available to the neuroscience community. We will then study a large sample of individuals with depression, PTSD and controls, with and without early adversity, to identify transcriptomic changes and biological clusters related to exposure and risk in the insular cortex. Lastly, we will validate the features driving the identified biological clusters using our single-cell and spatial omics approaches, providing functional insight into the genes, cell types and pathways affected. This innovative approach will contribute to the identification of new biological subtype-based treatment approaches for psychopathology, to overcome trial-and-error prescribing.





Sara Poletti

VIRAL-MI

Profiling vulnerability and resilience for mental illness following viral infections: translating epidemiology to deep-phenotyping

Project Coordinator:

Sara Poletti, Division of Neuroscience, Psychiatry and Psychobiology Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy

Project Partners:

Dana Tzur Bitan, University of Haifa, Haifa, Israel

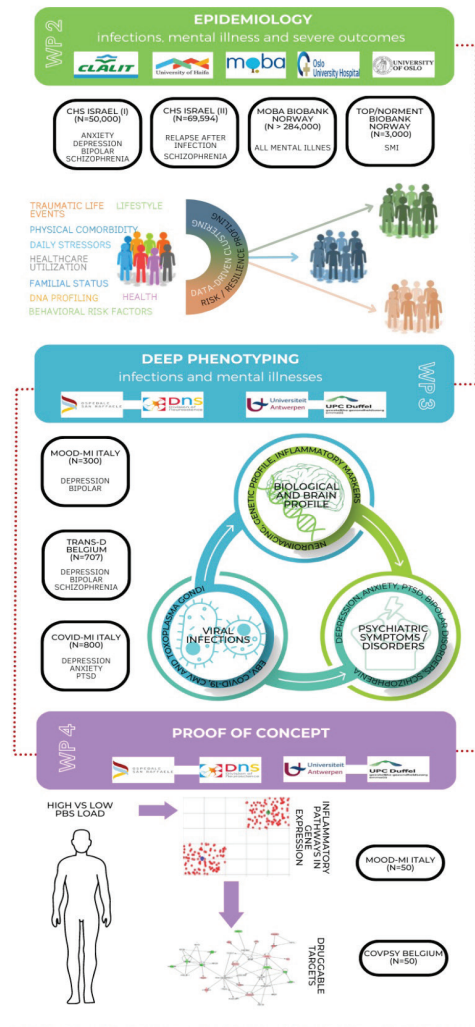
Nils Eiel Steen, University of Oslo, Oslo, Norway

Livia De Picker, University of Antwerp, Antwerpen, Belgium and University Psychiatric Hospital Duffel, Duffel, Belgium



History of infections is known to increase the risk to develop depression and other mental disorders. Individuals diagnosed with a mental disorder tend to develop a more severe course of infective illness and are also at increased risk to die from infectious disease. We aim to identify the underlying neurobiological and environmental mechanisms leading to either increased vulnerability or resilience to mental illness in case of infection, as well as the contribution of these mechanisms to severe infective outcomes in individuals

with pre-existing mental illness. We will move from exploration of large databases covering large samples of population, to specific, well-defined samples deeply characterized from a biological, psychiatric, and neuroimaging point of view, thus allowing the identification of genetic and neurobiological modulations following infections. First, we will explore the association between clinically relevant infections and subsequent development of a mental disorder, then, we will focus on biological underlying mechanisms. Social, economic and cultural factors will be used to build a predictive model which will determine what are the environmental characteristics leading to increased risk for mental disorder and severe outcome in pre-existing mental disorder. The profiles of highly vulnerable versus highly resilient individuals will be examined in the deeply characterized samples, to assess whether there are specific brain structures, genetic patterns or an immune response which further characterize them. These models will set the stage to identify potential brain or immune markers which can later be used to develop drugs, as well as to offer new therapeutic and preventive strategies.





NEURON Joint Transnational Call 2023: “Ethical, Legal and Social Aspects of Neuroscience”

Neuroscience research constantly increases our basic understanding of the structure and function of the human brain under healthy and pathological conditions. This knowledge is fundamental for the development of new preventative approaches, diagnostics and treatments for patients suffering from neurological or psychiatric disorders. At the same time, neuroscientific research has implications for the understanding, and thus potentially also the control, of human decision-making, behaviour, emotions, and social interactions. Therefore, it is of major importance to investigate the ethical, legal, and social aspects (ELSA) of the neurosciences and their recent advances. This knowledge helps to ensure that neuroscientific methods and findings are utilized in ways which are of the best possible benefit for our society.

Five multinational research consortia were selected for funding under JTC2023 on the topic of ‘Ethical, Legal and Social Aspect of Neuroscience. In total, 19 research groups from Germany, Switzerland, Spain and Taiwan collaborate in these research projects, which cover quite diverse aspects of ELSA in neuroscience. The total funding volume of the call amounts to about 3.2 M€.



Jan-Hendrik Heinrichs



BRAINTREE

Brain Age Prediction – Diagnostic method or reconceptualizing age

Project Coordinator:

Jan-Hendrik Heinrichs, Forschungszentrum Jülich, Jülich, Germany

Project Partners:

Bogdan Draganski, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland

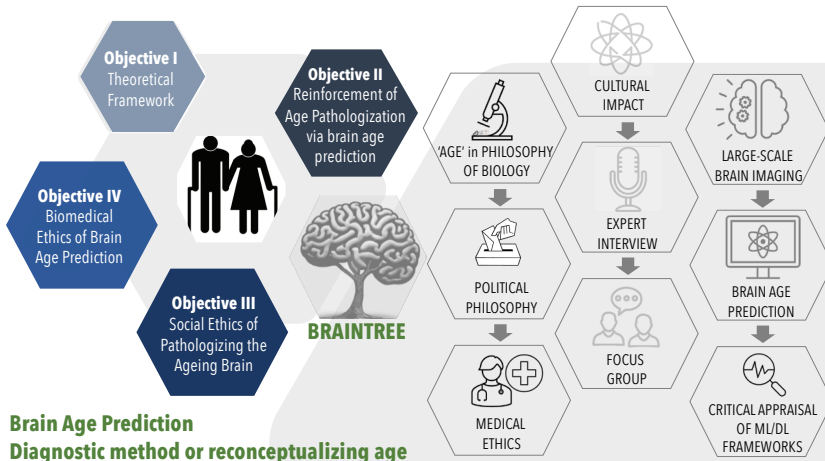
Yin-Yueh Lo, Shih Hsin University, Taipei, Taiwan

This project investigates the social and ethical aspects of machine-learning based estimation of individual’s age using brain magnetic resonance images of a normative population, coined “brain age”. Brain age prediction is a novel and powerful tool for neurology, psychiatry and beyond. Novel neuroscientific results and technologies affect established psychological and anthropological concepts. Similarly, brain age prediction is likely to affect the concept of age. The project will generate an empirically informed and comprehensive analysis of the social and ethical dimension of brain age prediction. It will comprise of three parts:

- 1) An investigation whether and how brain age prediction can differentiate normative ageing from ageing-associated disorders; how it can accommodate lifetime factors trajectories in “healthy” and “pathological” ageing; including a critical appraisal of existing machine- and deep-learning frameworks.
- 2) An Analysis of the communication and understanding of brain age prediction. A combination of quantitative and qualitative measures will shed light on the potential impact on society and individuals and generate insights into how people make sense of new technology more generally.
- 3) An ethical analysis of the medical ethics of using brain age prediction in the clinic, and of the social impact, which might arise, if brain age prediction really contributed to a pathologization and consequent stigmatization of age and the ageing.

The promises and perils of brain age prediction generalize well to several novel AI-based markers in the neurosciences and beyond. This investigation thus

generates a solid foundation for the ethical analysis of future brain-based predictive markers.





Claudia Bozzaro

COMPAIN

The Complexity of Pain and Its Normative Implications

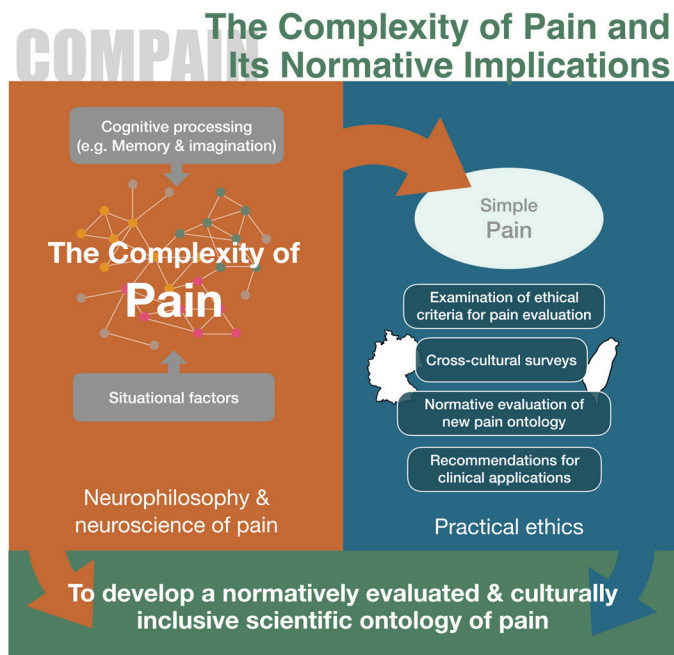
Project Coordinator:

Claudia Bozzaro, Institute for Experimental Medicine, Working Group Medical Ethics, Christian-Albrecht-University Kiel, Germany

Project Partners:

Sascha Benjamin Fink. Faculty of Human Science, Otto-von-Guericke-University Magdeburg, Germany

Ying-Tung Lin, National Yang Ming Chiao Tung University, Taipei City, Taiwan



Current developments in the neurosciences as well as in neurophilosophy have started to treat pain as a complex, heterogeneous or even modular phenomenon, which is also influenced by the environmental setting and other cognitive processes like memory or imagination. This emerging complexity is, however, not sufficiently reflected in (bio)ethics, where pain is mainly treated as something monolithic, that generally ought not to be. Based on this discrepancy, the COMPAIN consortium’s primary research aim is to examine in what way a complex and heterogeneous view of pain in the neurosciences and in neurophilosophy must influence the normative evaluation of pain in (practical) ethics. To achieve this goal, the COMPAIN consortium will, firstly, explore existing ontologies of pain in neuroscience and in philosophy and identify ethically relevant criteria for their evaluation taking into account cultural aspects; secondly, develop a joint scientific ontology of pain which will be validated by surveys with relevant stakeholders in Germany and Taiwan; and, thirdly, normatively evaluate this joint scientific ontology and develop context-sensitive and culturally inclusive recommendations for its implementation in clinical practice.



Karen Yan



PsyTrans

Psychedelic Transformations: A Taiwanese-German Comparison of Ethical and Sociocultural Aspects of New Therapies

Project Coordinator:

Karen Yan, Institute of Philosophy of Mind and Cognition, National Yang Ming Chiao Tung University, Taipei, Taiwan

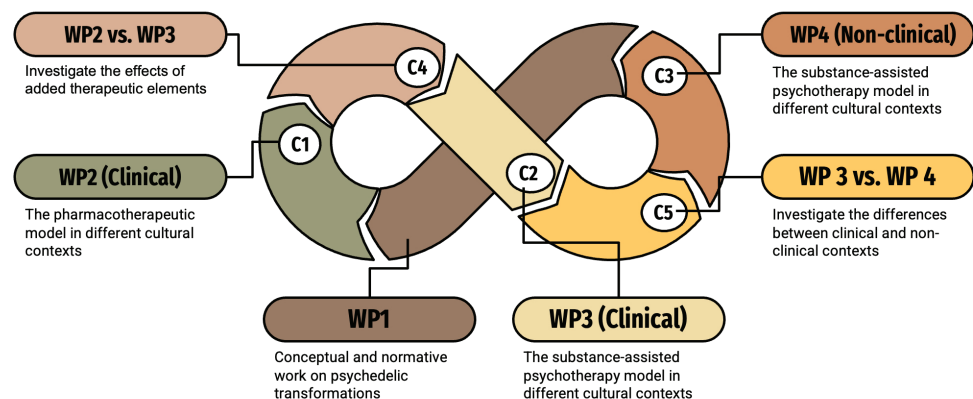
Project Partners:

Dimitris Repantis, Charité-Universitätsmedizin Berlin, Dept. of Psychiatry and Neurosciences, Campus Charité Mitte, Berlin, Germany

Sascha Benjamin Fink, Institut III: Bereich Philosophie, Fakultät für Humanwissenschaften, Otto-von-Guericke-Universität Magdeburg, Magdeburg, Germany

Psychedelic therapy is a new form of therapy used in psychiatry. It involves using psychedelics, a class of drugs that can induce changes in one’s consciousness, including one’s experience of oneself, time, space, and environment. Using them within therapy has shown promising results. Still, more research is needed to address some ethical concerns about how psychedelics can change one’s personality, attitude toward death, and other core beliefs. One important challenge is that the transformative changes caused by psychedelics are unpredictable to some degree. Thus, it is important to investigate ways of managing the transformative power of psychedelics. Well-designed clinical guidelines and assessment tools are needed to protect patients from harm while benefiting from the transformative insights obtained through psychedelic therapy to cope with their mental disorders. This project aims to assess the ethical implications of forms of personal transformations via psychedelic therapy in the German and Taiwanese contexts and compare them to investigate their similarities and differences. This project will generate policy recommendations for increasing the context and cultural sensitivity of future international and national clinical regulations and guidelines of psychedelic therapy.

The project design





Matthé Scholten



VIRTUETHIC

The Promise and Perils of Virtual Reality in Forensic Mental Health: Charting a Path Towards Ethical Guidelines

Project Coordinator:

Matthé Scholten, Institute for Medical Ethics and History of Medicine, Ruhr University Bochum, Germany

Project Partners:

Jan Christoph Bublitz, Faculty of Law, Dept. of Criminal Sciences and Criminology, University of Hamburg, Germany

Madleina Manetsch, Dept. of Forensic Psychiatry, University Psychiatric Hospitals Basel, Basel, Switzerland

Lydia Feito, Faculty of Medicine, Complutense University of Madrid, Spain

Javier Júdez, Instituto Murciano de Investigación Biosanitaria Pascual Parrilla (IMIB) and Fundación para la Formación e Investigación Sanitarias de la Región de Murcia (FFIS), Servicio Murciano de Salud, El Palmar, Murcia, Spain

Virtual Reality (VR) applications can be used in psychological or psychiatric treatment. In virtual computer-generated worlds, people can make new experiences. Although people know that they are in a simulation, they nevertheless have the feeling that they are present in that environment. Our environment influences our thinking, feeling, and behavior. This effect can be used in therapy: VR enables therapists to influence people and elicit reactions from them. The possibilities of using VR in psychiatry are currently being tested in research. One subfield is forensic psychiatry, which treats and rehabilitates persons with mental health problems who committed a crime. It seems probable that the first VR treatments to prevent aggression will soon be ripe for introduction into forensic practice. This raises numerous ethical and legal questions that need to be addressed. The interdisciplinary consortium will provide answers to these questions in close collaboration with forensic clinicians from around the globe and with people detained in forensic settings. Both groups will be interviewed several times and asked for their views on controversial matters. Combined with the findings of our conceptual, ethical, and legal analyses, this will lead to the world's first set of

ethical guidelines for using VR in forensic treatment.

