CERFA Brain Awareness Week

1. Effat Salehi Far

Mapping Brain–Symptom Trajectories in Major Depressive Disorder Using Longitudinal Multimodal Data Fusion

By combining a longitudinal design with multimodal data fusion, we investigated brain–symptom dynamics in major depressive disorder (MDD). Cortical surface area (SA), cortical thickness (CT), and Symptom Checklist-90-Revised (SCL-90-R) measures were assessed at two time points in 105 participants (57 MDD, 48 healthy controls).
Previous ENIGMA studies reported cross-sectional structural differences in MDD, including cortical thinning and reduced surface area. Building on these findings, we investigated whether longitudinal components of change identified through multiset canonical correlation analysis plus joint independent component analysis (mCCA+jICA) show diagnosis-specific patterns and overlap with ENIGMA-reported regions, thereby linking cross-sectional and longitudinal perspectives on MDD.
We found diagnostically specific coupling between structural changes and symptom dimensions, with spatial patterns partially consistent with ENIGMA findings. These results reveal interpretable and clinically relevant markers of brain–symptom co-evolution, advancing efforts toward neurobiologically grounded biomarkers in affective disorders and precision psychiatry.

2. Vivian Meiritz

Functional and Pharmacological Properties of Kv7.2/7.3, Kv7.2/7.5, and Kv7.3/7.5 Heteromers in a Heterologous Expression System

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Kv7.2, 7.3, and 7.5 are the basis for the so-called M-current and are predominantly expressed in skeletal muscle and the brain, where they stabilize the resting membrane potential, contribute to neuronal afterhyperpolarization, regulate the firing frequency of tonically active neurons, and support neuroplasticity by maintaining theta resonance. Mutations in the KCNQ2, KCNQ3 or KCNQ5 genes have been linked to epilepsy [1,2,3].
We expressed Kv7.2/7.3, Kv7.2/7.5 and Kv7.3/7.5 heteromeric channels in HEK293FT cells and performed whole-cell voltage-clamp recordings. These experiments revealed significant differences in the current amplitude, potential of half maximal activation and the activation and deactivation kinetics between the different subunit compositions. Interestingly, preliminary data suggest an upregulation of the Kv7 channels by a derivative of the neurosteroid pregnenolon, implying a regulatory role in excitability and thereby supporting its role of a potential therapeutic target as previously suggested by Vallée [4].

[1] N. A. Singh et al., A novel potassium channel gene, KCNQ2, is mutated in an inherited epilepsy of newborns, Nat Genet, 1998, Volume 18, from page 25-29.
[2] C. Charlier et al., A pore mutation in a novel KQT-like potassium channel gene in an idiopathic epilepsy family, Nat Genet, 1998, Volume 18, from page 53-55.
[3] A. Lehman et al., Loss-of-Function and Gain-of-Function Mutations in KCNQ5 Cause Intellectual Disability or Epileptic Encephalopathy, Am J Hum Genet., 2017, Volume 101, from page 65-74.

[4] M. Vallée, Neurosteroids and potential therapeutics: Focus on pregnenolone, The Journal of Steroid Biochemistry and Molecular Biology, 2016, Volume 160, from page 78-87.

3. Chiara Donati

Novel Riluzole-derived compound VA942 aU'ects voltage-gated sodium and potassium currents

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Excitotoxicity has been identified as a hallmark in different neurodegenerative conditions. Excitotoxicity is targeted by Riluzole (Rilutek©), currently available for the treatment of Amyotrophic Lateral Sclerosis (ALS). Riluzole has been proven to exert a neuroprotective role by a multimodal mechanism of action, by modulating voltage-dependent sodium (NaV) and potassium channels (KV) and reducing glutamatergic neurotransmission, thereby controlling overall neuronal excitability. However, Riluzole displays a concentration-dependent mechanism of action, and its eU'icacy is often reduced in more advanced stages of the disease.
To address the pharmacological limitations of Riluzole, novel derivatives such as VA942 were synthesized by the laboratory of Prof. Anzini at the University of Siena and are we are currently analyzing the potential effect of VA942 on NaV and KV channels conductance, kinetics and voltage-dependence.
Our goal is to determine whether VA942 displays a neuroprotective profile similar to that of Riluzole, while potentially offering an improved pharmacological profile.

4. Nicole Rychlik

A novel role for kininogen in regulating neuronal excitability

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Multiple Sclerosis is a chronic inflammatory disorder of the central nervous system (CNS) characterized by neurodegeneration and altered neuronal excitability. Notably the role of the protein Kininogen in this context is unexplored. In this study we investigated that a focal injection of kininogen into the auditory cortex resulted in a significant reduction of neuronal activity. Furthermore, voltage clamp recordings revealed that Kininogen application reduces the M-current that is generated by Kv7.2 and Kv7.3 channels. These findings establish a novel link between the nonenzymatic protein and neuronal electrogenesis. This previously unrecognized modulator in neuroinflammation highlight a potential new therapeutic axis for regulating neuronal dysfunction.

5. Ciara Teague

Targeting Distinct Glial Subsets in the Drosophila Larval Brain using Split-GAL4

Glial cells are crucial components of the nervous system. Without glial-neuronal interaction, neural networks cannot unfold their full functional complexity. From metabolic support for neurons and regulation of synaptic plasticity to the guidance of axonal migration, the manifold effects of glia reflect the highly differentiated glial subsets. Despite their importance, glial subsets remain poorly understood due to the limitations of genetic drivers. Here, we utilise the Split-GAL4 system in

Drosophila melanogaster to achieve various manipulations of targeted glia cells. The extensive investigation of Split-GAL4 driver lines provide a characterization of regional and functional specialisation in glia. To gain a deeper understanding of the functional and anatomical diversity of glia at a single-cell level, we isolated distinct glial populations to provide an enhanced map of glia-mediated brain maturation in third-instar larvae. Our findings establish a necessary framework for uncovering how cell-type-specific glial signaling coordinates development of the brain.

6. Eleni Nikalexi

Neural and Behavioral Correlates of Fear Extinction during fMRI in Rats

Responding appropriately to threats is essential for survival, yet updating these responses when a previously threatening stimulus becomes safe relies on extinction learning and the formation of extinction memory. Changes in neural networks induced by fear conditioning and measured by fMRI may be used as diagnostic biomarkers of this process. For instance, the recruitment of normally inactive brain regions could serve as a tool to predict the success of extinction. To investigate this, building on a prior study of the group, animals underwent fear conditioning by pairing a flashing blue light with a foot shock, followed by extinction during fMRI scanning under light anesthesia, in which the visual stimulus was presented without reinforcement. Behavioral testing was finally conducted to correlate the results of the fMRI measurements with specific behavioral outcomes.

7. Greta Auguste Hauser

Non-invasive multiparametric fMRI to investigate epileptogenesis in a rat model of absence epilepsy

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Absence epilepsy is a non-convulsive childhood epilepsy characterized by brief seizures of impaired awareness[1]. In addition to seizures, patients are at increased risk for mood disorders, such as depression, as well as learning deficits[1]. Previous studies suggest that epileptogenesis, rather than chronic seizure activity, is crucial for the formation of a characteristic epileptic brain network[2]. Therefore, this longitudinal study focuses on animals in their first three months of life, during seizure development. It aims to characterize the brain network alterations, changes in brain metabolism and assess comorbid depressive-like behavior and learning impairments in untreated Genetic Absence Epileptic rats from Strasburg (GAERS), non-epileptic controls, as well as three groups of GAERS, which receive a chronic pharmacological treatment via their drinking water aimed to prevent epileptogenesis.

[1] G. van Luijtelaar et al, Models of Seizures and Epilepsy, 2006, 233–248
[2] L. Wachsmuth et al. Front Neurol. 2024 Mar 11;15:1355862.