

Call for applications

Students with a keen interest in mental health and neuroscience are invited to apply for one of 8 vacant doctoral studentships within the newly established PhD programme

Mental Health and Neuroscience: Disease mechanisms – Diagnostics and Therapy – Clinical Neuroscience.

The PhD programme, which is run by the Karl Landsteiner University of Health Sciences, follows international recommendations to support the integration of global mental health and neuroscience into research on psychiatric diagnosis, pathogenesis, nervous system disorders and their treatment. Students accepted into the program will receive a specialized training in:

- I. neurobiological and neurophysiological basics of brain diseases (Disease mechanisms),
- II. examination, diagnostics and therapy of mental health (Diagnostics and Therapy),
- III. clinical and applied neuroscience (Clinical Neuroscience).

For the general admission requirements please refer to

<https://www.kl.ac.at/de/studium-und-weiterbildung/doctoral-school/selection-procedures-and-admission-phd-degree>

Excellent command of English is indispensable.

For the enrolment in a PhD programme at the Karl Landsteiner University of Health Sciences the tuition fee is € 3.500,- per semester for a total of 6 semesters. Depending on the employment status of the

PhD student (e.g., university or third-party funding, clinical specialist in training) a partial tuition fee waiver can be granted.

Applications must be received by **September 15th, 2024!** The top candidates will be interviewed in Krems in September/October 2024. Research will start in October 2024 at the earliest.

Overview of research projects

- [Project 1](#): Neurosciences and Mental Health in Adult Psychiatry and Transitional Psychiatry (Supervisor Prim. Assoc. Prof. PD Dr. Martin Aigner)
- [Project 2](#): Neuronal metabolism and its role in epileptogenesis (Supervisor Ing. Matej Hotka PhD)
- [Project 3](#): Morphological changes of the CNS after particle therapy and correlation with clinical parameters (Supervisor Univ.-Prof. Dr.-Ing. Sascha Klee)
- [Project 4](#): In vitro reconstitution of $\alpha_2\delta$ protein disease mutations in hippocampal neurons (Supervisor Univ.-Prof. Mag. Dr. Gerald Obermair)
- [Project 5](#): Digital Mental Health and Health Inequalities (Supervisor Univ.-Prof. Dr. Giovanni Rubeis)
- [Project 6](#): Analysis of the radiological dynamics of primary lymphomas of the central nervous system under the influence of corticosteroid therapy (Supervisor Prim. Assoc. Prof. PD Dr. Camillo Sherif)
- [Project 7](#): CO₂ and adolescents' cognitive and motor performance (Supervisor Univ.-Prof. PD Mag. Dr. Stefan Stieger)
- [Project 8](#): Modulation of the autonomic nervous system in acute neurological diseases (Supervisor Prim. Assoc. Prof. PD Dr. Walter Struhal MSc FEAN)

Detailed project descriptions can be found on the following pages.

Project 1:

Translational research in psychiatry and transitional psychiatry, from neuroscience and mental health to clinical implementation

Supervisor: Prim. Assoc. Prof. PD Dr. Martin Aigner

Interdisciplinary collaboration between child and adolescent psychiatry and adult psychiatry can make a significant contribution to overcoming existing challenges and improving care and treatment outcomes for patients of all ages. The optimal solution could be a combination of both approaches: the establishment of specialized transition psychiatry teams within an interdisciplinary framework. Transferring the success of adult psychiatry to child and adolescent psychiatry requires careful adaptation and further development of existing approaches. By combining preventive measures, individualized therapies, interdisciplinary collaboration and the use of modern technologies, the effectiveness and accessibility of treatment for children and adolescents can be significantly improved. A holistic approach that takes into account the specific developmental needs of this age group is crucial. The same applies to the second transition from adulthood to Palliative medicine.

Methods: Interdisciplinary collaboration research to bridge the gap between basic science and clinical implementation, between subjective and objective knowledge, including validated questionnaires, advanced statistical analysis, implementation of new therapy modules, public and patient involvement.

References:

- Fischer-Grote L, Fössing V, Aigner M, Fehrmann E, Boeckle M. Effectiveness of Online and Remote Interventions for Mental Health in Children, Adolescents, and Young Adults After the Onset of the COVID-19 Pandemic: Systematic Review and Meta-Analysis. *JMIR Ment Health*. 2024;11:e46637.
- Himmerich H, Lewis YD, Conti C, Mutwalli H, Karwautz A, Sjögren JM, Uribe Isaza MM, Tyszkiewicz-Nwafor M, Aigner M, McElroy SL, Treasure J, Kasper S; WFSBP Task Force on Eating Disorders. World Federation of Societies of Biological Psychiatry (WFSBP) guidelines update 2023 on the pharmacological treatment of eating disorders. *World J Biol Psychiatry*. 2023;24:1-64.
- Fellingner M, Knasmüller P, Kocsis-Bogar K, Wippel A, Fragner L, Mairhofer D, Hochgatterer P, Aigner M. Adverse childhood experiences as risk factors for recurrent admissions in young psychiatric inpatients. *Front Psychiatry*. 2022;13:988695

Project 2:

Neuronal metabolism and its role in epileptogenesis

Supervisor: Ing. Matej Hotka PhD

Acquired epilepsy develops after injury to the brain which is followed by a phase of epileptogenesis during which neuronal processes occur leading to a seizure-prone brain. There is currently no strategy to prevent the development of epilepsy. Interictal spikes (IS), detectable by EEG in the epilepsy patients, are a hallmark of ongoing epileptogenesis. IS are caused by synchronous electrical firing of a large group of neurons, which is called paroxysmal depolarization shifts (PDS).

In this project, we will investigate the effects of PDS on neuronal metabolism. Our data suggest that PDS induce a metabolic switch making mitochondria to utilize less glucose and more glutamine. This metabolic switch protects neurons from the deleterious effects of neuronal hyperexcitability. Understanding of the details of PDS-induced metabolic switch can lead to a neuroprotective strategy and possibly shed light on the mechanism of epileptogenesis. We will map neuronal metabolism and activity using live-cell microscopy and patch-clamp.

Methods: Live-cell metabolic imaging, patch clamp electrophysiology, metabolomics

References:

- Hotka M, Kubista H (2018) The paroxysmal depolarization shift in epilepsy research, *Int J Biochem Cell Biol*. doi: 10.1016/j.biocel.2018.12.006 PMID: 30557621
- Dhoundiyal, A et al. (2022) Glycerol-3-Phosphate Shuttle Is a Backup System Securing Metabolic Flexibility in Neurons. *J Neurosci* doi: 10.1523/JNEUROSCI.0193-22.2022 PMID: 35999055
- Hotka, M et al. (2020) L-type Ca²⁺ channel-mediated Ca²⁺ influx adjusts neuronal mitochondrial function to physiological and pathophysiological conditions. DOI: 10.1126/scisignal.aaw6923 PMID: 32047116

Project 3:

Morphological changes of the CNS after particle therapy and correlation with clinical parameters

Supervisor: Univ.-Prof. Dr.-Ing. Sascha Klee

Ion beam therapy enables individualized, highly precise, localized cancer treatment. These properties are particularly utilized in the treatment of carcinomas in the brain. However, treatment in this highly sensitive area also changes the morphological and structural properties of the central nervous system. The work will systematically investigate this, model possible effects and link them to other clinical parameters.

Methods: Image processing and image analyses in MR data sets, processing and analyzing big data, development and application of automatic, intelligent segmentation algorithms, multi-level models for linking clinical parameters, development of methods for optimizing treatment plans and their quality management

References:

- Lütgendorf-Caucig MC, Pelak M, Hug E, Flechl MIB, Surböck MB, Marosi MC, Klee S, et al. Prospective analysis of radiation-induced contrast enhancement (RICE) and health-related quality of life following proton therapy for CNS and skull base tumors. *International Journal of Radiation Oncology* Biology* Physics*. 2024.

Project 4:

In vitro reconstitution of $\alpha_2\delta$ protein disease mutations in hippocampal neurons

Supervisor: Univ.-Prof. Mag. Dr. Gerald Obermair

$\alpha_2\delta$ proteins are abundantly expressed in the brain. They serve as auxiliary subunits of voltage-gated calcium channels and as such modulate calcium currents. Beyond this role they have emerged as regulators of synaptic functions, such as the formation and differentiation of excitatory synapses as well as the trans-synaptic wiring of inhibitory synapses. Considering these important functions, it is not surprising that mutations of the genes encoding for $\alpha_2\delta$ proteins are associated with neurodevelopmental disorders including epilepsy, autism, and schizophrenia. This project aims to study the underlying pathophysiological mechanisms in an in vitro model system, namely cultured primary hippocampal neurons. To this end, knockout cultures will be reconstituted with mutated $\alpha_2\delta$ proteins and the consequences on general cellular and specific synaptic functions will be analyzed. This project will provide novel insights into both, channel-dependent as well as synaptic functions of $\alpha_2\delta$ proteins and their consequential pathophysiological mechanisms.

Methods: primary neuronal cell culture, high- and super-resolution immunofluorescence microscopy, molecular biology, patch-clamp electrophysiology, live cell calcium imaging, protein biochemistry

References:

- Geisler S, Schöpf CL, Stanika R, Kalb M, Campiglio M, Repetto D, Traxler L, Missler M, Obermair GJ. Presynaptic $\alpha_2\delta$ -2 Calcium Channel Subunits Regulate Postsynaptic GABA_A Receptor Abundance and Axonal Wiring. *J Neurosci*. 2019 Apr 3;39(14):2581-2605. doi: 10.1523/JNEUROSCI.2234-18.2019. Epub 2019 Jan 25. PMID: 30683685; PMCID: PMC6445987.
- Ablinger C, Geisler SM, Stanika RI, Klein CT, Obermair GJ. Neuronal $\alpha_2\delta$ proteins and brain disorders. *Pflugers Arch*. 2020 Jul;472(7):845-863. doi: 10.1007/s00424-020-02420-2. Epub 2020 Jun 30. PMID: 32607809; PMCID: PMC7351808.
- Schöpf CL, Ablinger C, Geisler SM, Stanika RI, Campiglio M, Kaufmann WA, Nimmervoll B, Schlick B, Brockhaus J, Missler M, Shigemoto R, Obermair GJ. Presynaptic $\alpha_2\delta$ subunits are key organizers of glutamatergic synapses. *Proc Natl Acad Sci U S A*. 2021 Apr 6;118(14):e1920827118. doi: 10.1073/pnas.1920827118. PMID: 33782113; PMCID: PMC8040823.

- Ablinger C, Eibl C, Geisler SM, Campiglio M, Stephens GJ, Missler M, Obermair GJ. $\alpha_2\delta$ -4 and Cachd1 Proteins Are Regulators of Presynaptic Functions. *Int J Mol Sci*. 2022 Aug 31;23(17):9885. doi: 10.3390/ijms23179885. PMID: 36077281; PMCID: PMC9456004.
- Hessenberger M, Haddad S, Obermair GJ. Pathophysiological Roles of Auxiliary Calcium Channel $\alpha_2\delta$ Subunits. *Handb Exp Pharmacol*. 2023;279:289-316. doi: 10.1007/164_2022_630. PMID: 36598609.
- Stanika R, Obermair GJ. An ex vivo Model of Paired Cultured Hippocampal Neurons for Bi-directionally Studying Synaptic Transmission and Plasticity. *Bio Protoc*. 2023 Jul 20;13(14):e4761. doi: 10.21769/BioProtoc.4761. PMID: 37497454; PMCID: PMC10366995.

Project 5:

Digital Mental Health and Health Inequalities

Supervisor: Univ.-Prof. Dr. Giovanni Rubeis

Health inequalities have a complex relationship with digital innovation. While there is a promise of alleviating health inequalities through digitalization, there is also a risk of expanding these inequalities due to the digital divide. The aim of this interdisciplinary project is to explore this relationship with a focus on mental health. Drawing on expertise in medicine and public health and guided by supervision in digital health ethics and public health ethics, the study will investigate ethical implications and equity in digital mental health interventions. The research will quantitatively analyze mHealth apps for accessibility and effectiveness and review the literature on ethical issues in digital mental health. This research is expected to uncover barriers and facilitators to equitable digital mental health care, while providing actionable recommendations to enhance inclusivity and ethical standards in digital mental health strategies. The findings will contribute to the fields of digital mental health and public health ethics.

Methods: experimental methodologies in coding and data collection, screening and evaluating mental health mobile applications, natural language processing and latent Dirichlet allocation of Kaggle datasets, advanced statistical techniques, comprehensive literature reviews

References:

- Dubbala K, Prizak R, Metzler I, Rubeis G (2024) Towards Comprehensive mHealth App Analysis: Metadata Analysis of Heart Disease Apps in India. *Journal of Medical Internet Research* [in press]
- Rubeis G (2024) Ethics of Medical AI. *The International Library of Ethics, Law and Technology* 24. Springer Nature, Cham. doi: 10.1007/978-3-031-55744-6
- Rubeis G, Dubbala K, Metzler I (2022) 'Democratizing' Artificial intelligence in medicine and healthcare: Mapping the uses of an elusive term. *Frontiers in Genetics* 3:902542. doi: 10.3389/fgene.2022.902542
- Rubeis G (2022) iHealth: The ethics of Artificial Intelligence and Big Data in mental healthcare. *Internet Interventions*, doi: 10.1016/j.invent.2022.100518
- Rubeis G (2020) E-mental health applications for depression. An evidence-based ethical analysis. *European Archives of Psychiatry and Clinical Neuroscience*, doi: 10.1007/s00406-019-01093-y

Project 6:

Analysis of the radiological dynamics of primary lymphomas of the central nervous system under the influence of corticosteroid therapy

Supervisor: Prim. Assoc. Prof. PD Dr. Camillo Sherif

Primary CNS lymphomas (PCNSL) account for approx. 2-3 % of all brain tumors. The primary goal of surgery is to obtain tissue for histologic diagnosis. However, PCNSL cells are potentially very sensitive to corticosteroid therapy (CST) and can react with a temporary shrinkage of the tumor mass. This can make histologic diagnosis difficult or even impossible. Therefore, preoperative CST should be avoided in patients with suspected PCNSL if clinically feasible. To date, there are no high-quality data on the possible changes in imaging prior to definitive treatment of PCNSL with high-dose systemic methotrexate. We therefore aim to quantify the extent and frequency of radiologic response of PCNSL to CST in the setting of standard therapy. We will perform volumetric analysis of tumor mass before and approximately 5-10 days after biopsy when CST is routinely administered and relate these results to lesion size, CST dosing, and molecular pathology results. These results may help to better understand the interaction between PCNSL and CST.

Methods: prospective multicenter cohort study, imaging and volumetric analysis of tumor biopsies, clinical imaging and analysis techniques to investigate lesion size and pathology outcome.

References:

- Scheichel F, Popadic B, Pinggera D, Jaskolski DJ, Lubrano V, Foroglou N, et al. European survey on neurosurgical management of primary central nervous system lymphomas and preoperative corticosteroid therapy. *Brain and Spine* 2023;3:101791. <https://doi.org/10.1016/j.bas.2023.101791>. PMID: 38020980
- Scheichel F, Pinggera D, Popadic B, Sherif C, Marhold F, Freyschlag CF. An Update on Neurosurgical Management of Primary CNS Lymphoma in Immunocompetent Patients. *Front Oncol* 2022;12:884724. <https://doi.org/10.3389/fonc.2022.884724>. PMID: 35515113
- Scheichel F, Marhold F, Pinggera D, Kiesel B, Rossmann T, Popadic B, et al. Influence of preoperative corticosteroid treatment on rate of diagnostic surgeries in primary central nervous system lymphoma: a multicenter retrospective study. *BMC Cancer* 2021;21:754. <https://doi.org/10.1186/s12885-021-08515-y>. PMID: 34187419

Project 7:

CO₂ and adolescents' cognitive and motor performance

Supervisor: Univ.-Prof. PD Mag. Dr. Stefan Stieger

The increasing CO₂ concentration in our atmosphere is a hot topic in health, media, politics, and science. People often discuss the indirect impacts of increasing CO₂ on humans, such as global warming and rising sea levels, but they only rarely discuss how CO₂ directly affects our psychological functioning. A number of studies have in fact suggested that elevated CO₂ levels can affect our cognitive performance (e.g., the ability to concentrate, or make decisions). So far, however, the specific level at which CO₂ becomes detrimental is not yet clear. Moreover, there is a lack of evidence about the effects of CO₂ on vulnerable populations, different kinds of performance (e.g., reaction speed, motor control), and the role of other air contaminants such as volatile organic compounds (VOC). We therefore investigate the effects of natural indoor CO₂ and VOC concentrations (including possible interactions) in a very large sample of adolescents (N ~ 15,000 to 18,000). The adolescents in our study take a series of tests that measure, for example, their intelligence, spatial orientation, reaction time, and their arm, hand, and finger dexterity. While they are taking the tests, we measure the CO₂, VOC, temperature, and humidity. To reliably measure the room environment, we use several miniature computers and gas sensors per room. We analyze whether the CO₂ level in the room is related to how participants score on the tests. We also analyze whether certain environmental or personal characteristics make the effects of CO₂ stronger or weaker. Our results have the potential to expand discussions about the impact of rising CO₂ levels for humanity.

Methods: advanced statistics; technical understanding of gas sensor measurements

References:

- Stieger, S., & Wunderl, S. (2022). Associations between social media use and cognitive abilities: Results from a large-scale study of adolescents. *Computers in Human Behavior*, 135, 107358. <https://doi.org/10.1016/j.chb.2022.107358>

Project 8:

Modulation of the autonomic nervous system in acute neurological diseases

Supervisor: Prim. Assoc. Prof. PD Dr. Walter Struhal MSc FEAN

The autonomic nervous system innervates all inner organs and orchestrates important functions like heart rate, blood pressure, breathing, digestion, urogenital function, sexuality and others.

Peripheral autonomic activity is controlled by the central autonomic network. While there is convincing literature on acute central nervous system diseases influencing the autonomic nervous system with a possible increase of the frequency complication, very little is known on time courses on these influences. Especially in severe central nervous system disorders, including stroke, intracranial hemorrhage, infections, trauma, there is lack in knowledge in a) when the patients may be of highest risk of autonomic complications, and b) whether any differences of autonomic innervation may prove to be a valuable biomarker for diagnostic and prognostic purposes.

This research project investigates autonomic nervous system parameters from admission during the course of monitoring.

Methods: Heart rate variability, beat to beat blood pressure, breathing, ECG patterns and quality assurance, EEG patterns

Autonomic evaluation time domain/frequency domain

Algorithm development for oligoparametric/nonparametric biosignal screening

References:

- Struhal W, Hain B. A new light on an old condition. *Eur Heart J Case Rep.* 2021 Dec 14;5(12):ytab499. doi: 10.1093/ehjcr/ytab499. PMID: 34993411
- Fanciulli A, Skorić MK, Leys F, Carneiro DR, Campese N, Calandra-Buonaura G, Camaradou J, Chiaro G, Cortelli P, Falup-Pecurariu C, Granata R, Guaraldi P, Helbok R, Hilz MJ, Iodice V, Jordan J, Kaal ECA, Kamondi A, Le Traon AP, Rocha I, Sellner J, Senard JM, Terkelsen A, Wenning GK, Moro E, Berger T, Thijs RD, Struhal W, Habek M; Collaborators of European Network of Neurological Autonomic Laboratories. EFAS/EAN survey on the influence of the COVID-19 pandemic on European clinical autonomic education and research. *Clin Auton Res.* 2023 Dec;33(6):777-790. doi: 10.1007/s10286-023-00985-3. Epub 2023 Oct 4. PMID: 37792127
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Neurological ANS laboratories. Impact of the COVID-19 pandemic on clinical autonomic practice in Europe A survey of the European Academy of Neurology (EAN) and the European Federation of Autonomic Societies (EFAS). *Eur J Neurol*. 2023 Mar 15. doi: 10.1111/ene.15787. Epub ahead of print. PMID: 36920252.

- Reis Carneiro D, Rocha I, Habek M, Helbok R, Sellner J, Struhal W, Wenning G, Fanciulli A. Clinical presentation and management strategies of cardiovascular autonomic dysfunction following a COVID-19 infection - A systematic review. *Eur J Neurol*. 2023 May;30(5):1528-1539. doi: 10.1111/ene.15714. Epub 2023 Feb 8. PMID: 36694382
- van Dijk JG, Thijs RD; European Federation of Autonomic Societies (EFAS) Task Force on Tilt Table Testing. Rethinking neurological attitudes towards vasovagal syncope: The European Federation of Autonomic Societies (EFAS) recommendations regarding tilt table testing. *Eur J Neurol*. 2021 Sep;28(9):e69-e70. doi: 10.1111/ene.14963. Epub 2021 Jul 1. PMID: 34117676

General information and application

PhD candidates need to fill out the application online in “Open Campus” and upload the associated attachment to the application.

Applications must be received by **September 15th, 2024!**

We are looking forward to your application!