HIGHLIGHTS

2023

ERWIN L. HAHN INSTITUTE FOR MAGNETIC RESONANCE IMAGING

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Erwin L. Hahn Institute for Magnetic Resonance Imaging

HIGHLIGHTS 2023

Annual Report

ERWIN L. HAHN INSTITUTE FOR MAGNETIC RESONANCE IMAGING


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Preface

Following the exchange of our 7-Tesla MRI system to the newest generation in the year 2020 and after the successful and positive evaluation of the Erwin L. Hahn Institute in 2023, our Brain & Body UHF MRI research activities at the Erwin L. Hahn Institute continued to gain pace and to attract funding.

2023 was also the year in which the Dutch 14-Tesla initiative DYNAMIC received funding from the NWO to develop and build the world's strongest MRI system in the Netherlands. Congratulations to David Norris and his colleagues of the entire Dutch UHF MRI community for this great achievement! Exciting times ahead for the worldwide UHF MRI community for the years to come. The ELH and all PIs are excited about the prospect of future collaborations in this fascinating initiative.

On October 25th, we held our annual "Erwin L. Hahn Lecture" and associated scientific workshop in the Oktogon on the grounds of Zeche Zollverein. Andrew Webb from Leiden University gave a very inspiring lecture entitled: "High field to low field to even higher fields; lessons learned often the painful way" which was very well received and lively discussed by the auditorium. The Young Scientists Award for outstanding work at the ELH was awarded to Viktor Pfaffenrot for his PhD dissertation "Laminar fMRI of long-range connections: Methods and contrast mechanisms". The 2024 ELH-Lecture will take place on November 13th again at the beautiful Oktogon with Virginie Callot form University of Marseille as our keynote speaker. Please mark your calendars!

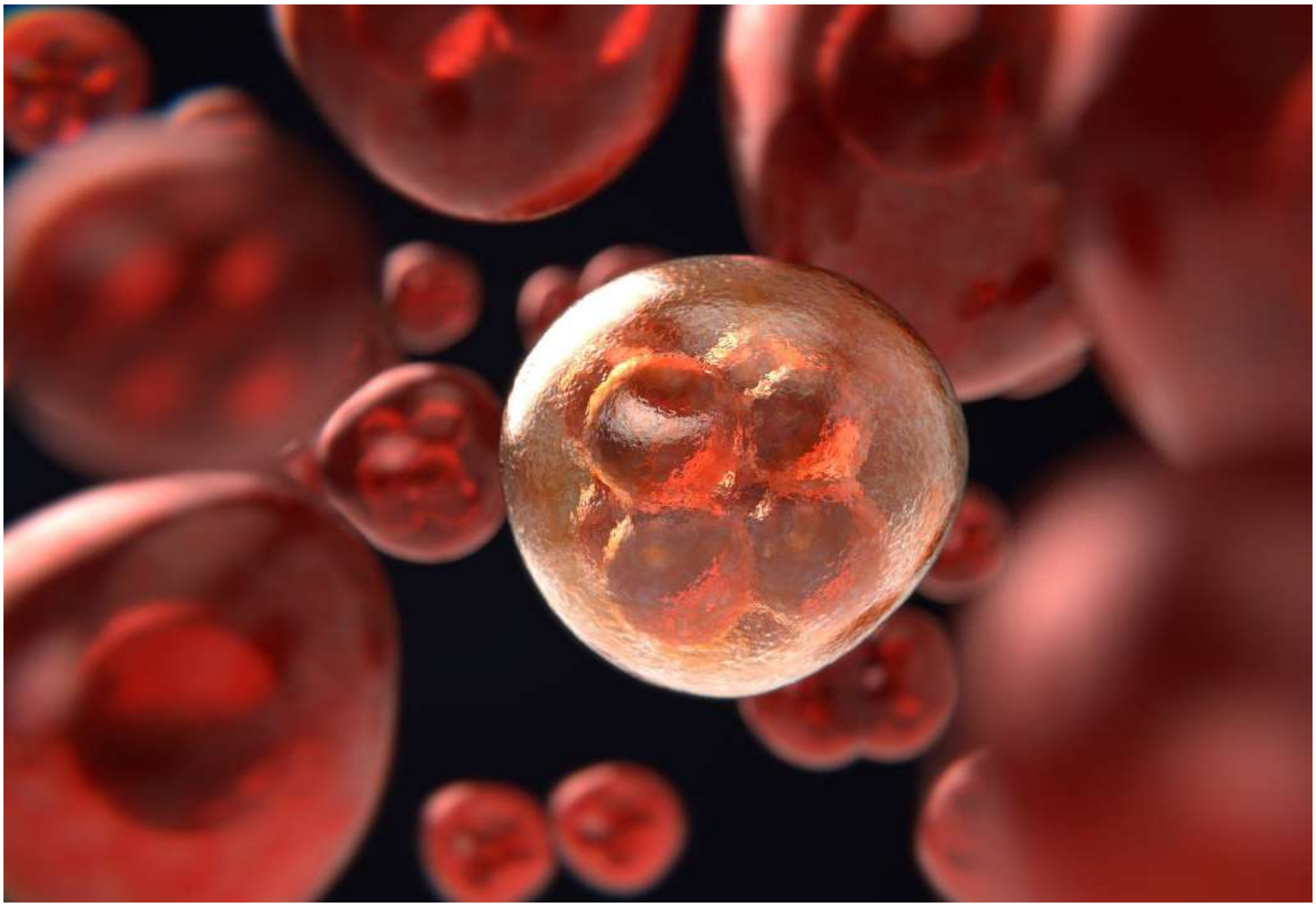
On the fun side, towards the end of the year 2023, the ELH launched its first own art contest named "ARTifact - Imaging MRI". We were thrilled how many creative and high-quality contributions were submitted and how this art contest unleashed enormous creativity among the ELH groups. Please enjoy a look at some of the artworks in this annual report and also on our homepage where you can find the high-resolution and full text versions of all contributions.

In this 2023 annual report you can find contributions and updates of our PI groups working at the ELH with UHF MRI, for example progress on the EU MITI – project on metabolic imaging, and a status update of the activities of the German 14-Tesla initiative. For the brain-related research activities allow me to provide only the following key words to raise interest: addiction, motor control, pain, and fear – all these important aspects of brain research have been investigated at the ELH during the last year.

I hope that you find the content of our Annual Report 2023 enjoyable, and look forward to another year's exciting research at the Erwin L Hahn Institute. Hope to see you all at this year's ELH Lecture!

Harald H. Quick
Essen, March 2024

Quincy van Houtum, Jennifer Schulz, Markus May,
Oliver Kraff, Thomas Meurs, Harald Quick and Tom Scheenen



EU Project MITI - Metabolic imaging for therapeutic interventions

The research group of Tom Scheenen, in collaboration with Harald Quick, focuses on the development and implementation of novel in vivo magnetic resonance imaging (MRI) and spectroscopy (MRS) methods aimed towards therapy guidance and intervention in oncology.

Radio-, chemo- or immunotherapy in the treatment of tumors all aim to destroy cancerous cells. Therapy response is assessed by evaluating morphological changes 6 to 12 weeks after starting therapy. MRS, in particular, phosphorus (^{31}P) spectroscopy, has potential to non-invasively assess a wealth of biological information in vivo on phospholipid and energy metabolism, allowing therapy response evaluation 3 weeks after the start of therapy. Cell energy metabolism can be monitored via ratios of inorganic-phosphate (Pi), phosphocreatine (PCr), and adenosine triphosphate (ATP, with α-, ß- and γ- resonances), and is mainly used to diagnose systemic and muscle diseases. Acquisition of phospholipid signals gives insight into the cell membrane precursors, the phosphomonoesters (PME), and cell membrane degradation products, the phosphodiesters (PDE). A decrease in ratios between these species during therapy is a marker of positive therapy response and can take place well before morphological changes can be observed.

The previous year, the ^{1}H imaging capabilities of the $^{31}P/^{1}H$ body array coil (BAC) from Tesla Dynamic Coils (TDC) were reported. In the EU project MITI – "Non-ionizing Metabolic Imaging for Predicting the Effect of and Guiding Therapeutic Interventions" – we, together with TDC, performed ^{31}P calibrations and additional hardware upgrades to enable near-simultaneous parallel-transmit (pTx) ^{1}H MR imaging and single transmit (sTx) ^{31}P MRS at 7T on the new Siemens MAGNETOM Terra MRI

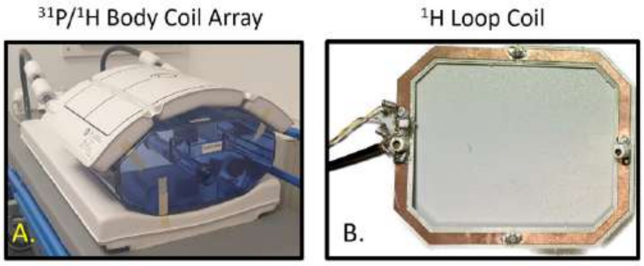


Figure 1. A) An image of the ^{31}P/^{1}H body array coil with a body-shaped phantom. **B)** The additional pTx-compatible sTx-^{1}H-loop. The coils can be connected in both pTx and sTx modes to combine parallel ^{1}H MR imaging and single transmit ^{31}P spectroscopy.

system at the ELH. This allowed us to monitor the aforementioned metabolite signals in vivo over a large field of view.

The BAC includes eight fractionated ^{1}H dipole antennas for parallel transmit (Tx) and receive (Rx) plus four RTx ^{31}P dipole antennas in combination with 24 Rx ^{31}P loops. Calibration of the ^{31}P transmit fields, to improve RF energy deposition in the center of the body, required hardware shimming, as the sTx-system does not allow in-session updating of specific transmit parameters as the pTx-system does. The additional cables which were installed to change the transmit phases of the four ^{31}P TRX antennas, resulted in a B_1^+ at the center up to 5.5 µT and 6.5 µT below the surface.

With the physical separation of the pTx-system for ^{1}H MRI from the sTx-system for X-nuclei spectroscopy, combining high-quality imaging with accurate localization of X-nuclei signals is a challenge. In sTx-mode, system calibration requires a proton signal for frequency determination and proton images to plan subsequent MRS protocols. We therefore created an additional sTx ^{1}H loop-coil, shown together with the BAC in Fig. 1. The additional coil is detuned by default, making it pTx-compatible. This means no hardware changes were necessary during a scan session and the patient/volunteer does not have to be repositioned, favouring MRS localization.

Combining the above-mentioned work allowed us to scan both legs of a volunteer. We measured ^{31}P signals in the muscles using the sTx-system for ^{31}P MR spectroscopic imaging and the pTx-system for high-resolution ^{1}H imaging for background anatomical information. Acquiring signals from both legs simultaneously is challenging as the gap between the legs distorts the main magnetic field. Implementation of novel data processing methods including principle component analysis denoising and combining all ^{31}P Rx-channels via whitened singular value decomposition increased SNR and improved data quality. Even with the gradient in signal intensity over the field of view, the SNR was sufficient to discriminate different ^{31}P species. The setup combines the strength of parallel transmit MRI and single transmit X-nuclei MRS in a single scan session. It increases high-quality anatomical and metabolic information over large FOVs without sacrificing localization accuracy or lowering patient comfort.

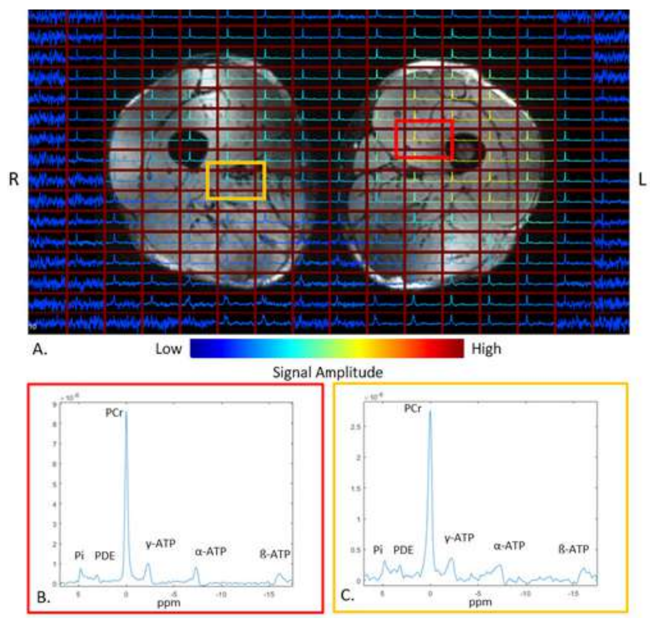


Figure 2. A) One transverse partition of a 3D ^{31}P chemical shift imaging dataset of the legs overlayed on a high-resolution multi-slice gradient echo image acquired using the TIAMO method showing the ^{31}P spectra at their appropriate location in the legs. **B** & **C)** Spectra from the voxels highlighted by the red and orange box in A respectively, with the different ^{31}P signals labeled.

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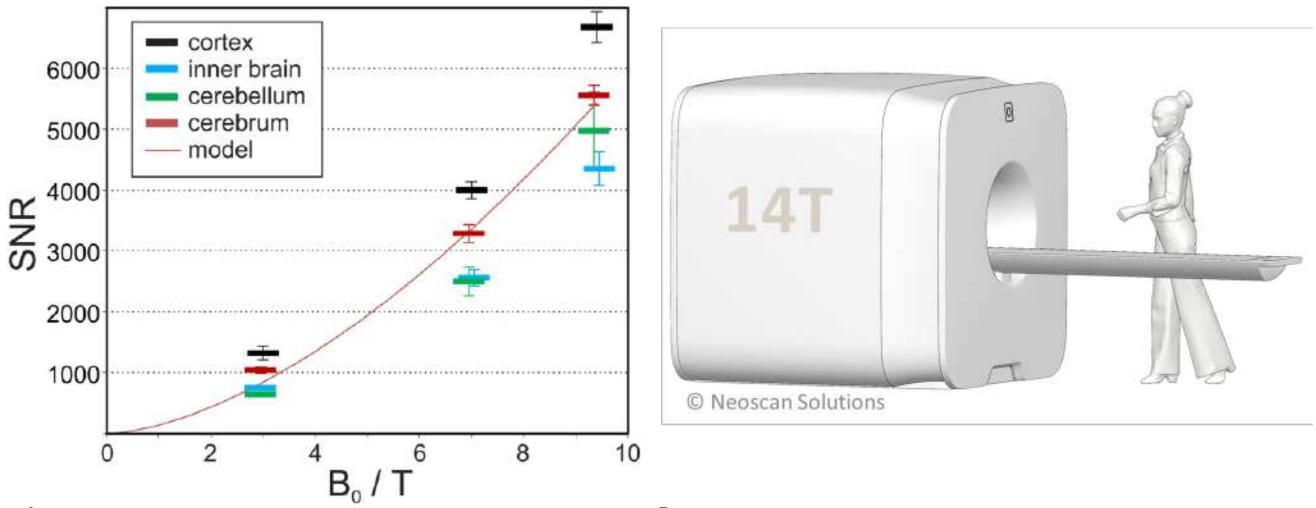
Next Stop 14 Tesla...

ELH PIs Harald Quick and Mark Ladd are both coordinators of the German Ultra Highfield Imaging (GUFI) network, which includes scientists from 12 German sites who perform human UHF MR imaging or spectroscopy at magnetic field strengths of 7 and 9.4 Tesla (https://hahn-institut.de/mr-gufi). GUFI has defined a strategic goal to establish a 14 Tesla whole-body MRI system as a national research resource in Germany as the next step in magnetic field strength for use in humans. In 2023, the network published a White Paper outlining the challenges and opportunities associated with this initiative [1].

This goal doves ideally with the work of ELH PI David Norris, who is heading a similar initiative in the Netherlands [2]. That initiative has already received funding to build and install the world's first 14 Tesla whole-body human MRI system. The initiative in the Netherlands envisions the 14 Tesla MRI as a national resource to be open to scientists focusing on cognitive neuroscience, brain disorders, and medical applications outside the brain [3].

The main limitation of MRI is its limited sensitivity due to the low thermal equilibrium magnetization. Higher static magnetic fields provide one path to address this limitation, which was the main motivation to install a 7 Tesla system at the ELH back in 2006. The sensitivity in terms of signal-to-noise ratio (SNR) has been shown in MRI simulations and experiments to scale superlinearly with the magnetic field strength provided in Tesla (Fig. 1). This context has always been the driving factor and motivation for striving to higher fields in MRI research. The enhanced sensitivity can be invested into higher spatial resolution, but also into shortening the duration of MR examinations. The latter is especially crucial for opening up completely new applications that would just last too long with today's systems, even 7 Tesla.

These applications paired with further increased soft tissue contrast at higher magnetic field strength are expected to reveal new insights into metabolism and brain function, and ultimately improve our understanding of both healthy physiology as well as disease hallmarks.



A B

Figure 1. A) The SNR of images obtained in different parts of the brain as a function of magnetic field strength using 3, 7 and 9.4 Tesla MRI [4]. **B)** Schematic representation of a 14 Tesla magnet. The magnet will be manufactured in Magdeburg by Neoscan Solutions GmbH using HTS superconductor from THEVA GmbH. Further design details can be found in the paper by Li and Roell [5]. Compared to recent UHF MRI systems for human use, the suggested 14 Tesla magnet is surprisingly compact.

The plans for implementing a 14 Tesla MRI system in Germany operated as an open research facility represent a new level of scientific cooperation between the groups focusing on UHF MR research, similar to the models followed in high-energy physics where it is customary to share resource-intensive infrastructure, and ELH researchers are committed to accomplishing this vision.

Beyond basic research, the longer-term potential is the translation of this field strength into use for clinical diagnostics, similar to the evolution of 7 Tesla from a research-only system to certification as a Medical Device in 2017.

While the planning for a 14 Tesla MRI system in Germany and the search for appropriate funding goes on, further international UHF MRI projects with high visibility in the scientific community have gained traction in recent years. Researchers of the Center for Magnetic Resonance Research (CMRR) at the University of Minnesota successfully acquired a first 10.5 Tesla MR image of a human pelvis in 2018. Since then, numerous further 10.5 Tesla projects and studies in volunteers have been successfully realized at CMRR and published. Also, the 11.7 Tesla activities at CEA in Paris-Saclay, which started already in 2004, have recently converged to achieve first 11.7 Tesla MR images of larger fruits in 2021.

Figure 2. Participants at the GUFI & Friends Meeting at the ISMRM 2023 in Toronto, Canada.

In vivo imaging of human brains commenced in 2023, and first images are expected to be published in 2024.

International German Ultrahigh Field Imaging (GUFI) Meeting at ISMRM 2023 in Toronto

At the ISMRM 2023 meeting in Toronto, Canada in June, Mark Ladd (DKFZ, Heidelberg), Harald Quick (ELH, Essen), and Oliver Speck (OVGU, Magdeburg) organized an on-site GUFI meeting with invited national and international UHF MRI partners (Fig. 2). Representatives of Siemens Healthineers also attended the event. The focus of this GUFI meeting was to provide an update on UHF MRI beyond 7 Tesla field strength. In this context, Stefan Roell from Neoscan Solutions (Magdeburg, Germany) provided an overview of design features of a 14 Tesla high-temperature superconductor (HTS) magnet design [5]. The meeting continued with a Workshop Summary from the successful GUFI Workshop on parallel transmission (pTx) in Tübingen, which was held in February 2023.

1. Ladd ME, Quick HH, Speck O, Bock M, Doerfler A, Forsting M, Hennig J, Ittermann B, Möller HE, Nagel AM, Niendorf T, Remy S, Schaeffter T, Scheffler K, Schlemmer HP, Schmitter S, Schreiber L, Shah NJ, Stöcker T, Uder M, Villringer A, Weiskopf N, Zaiss M, Zaitsev M. Germany's journey toward 14 Tesla human magnetic resonance. MAGMA. 2023;36(2):191-210. doi: 10.1007/s10334-023-01085-z.
2. DYNAMIC-Dutch National 14 Tesla Initiative in MRI and Cognition. In: NWO Large-Scale Research Infrastructure. https://www.onderzoeksfaciliteiten.nl/node/3911. Accessed 14 Jan 2024.
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4. Pohmann R, Speck O, Scheffler K. Signal-to-noise ratio and MR tissue parameters in human brain imaging at 3, 7, and 9.4 tesla using current receive coil arrays. Magn Reson Med. 2016;75(2):801-809. doi: 10.1002/mrm.25677.
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UHF MRI Sites

Kjell Büsche, Stephanie Antons and Matthias Brand

Team Brand and the Research Unit FOR2974 "on tour": Highlights from 2023

Looking back on 2023, the past year for Team Brand and the DFG-research group FOR2974 - "Affective and cognitive mechanisms of specific Internet-use disorders (ACSID)"- was characterized by our national and international collaborations, culminating in some key events that allowed us to present our work to the wider community of behavioral addiction researchers. Team Brand actively participated in various international and national conferences, presenting and discussing their ongoing research in the field. The ICBA in Incheon, South Korea, and our "Autumn School" in Frankfurt were the highlights of the year.

August 2023: International Conference on Behavioral Addictions (ICBA) in Incheon, South Korea

In August 2023, our team made a significant mark at the International Conference on Behavioral Addictions in Incheon, South Korea. Members of FOR2974 contributed a total of eleven presentations and chaired six collaborative symposia with international participants. The neuroimaging field was represented by Kjell Büsche, who gave a talk on neural correlates of behavioural addictions.

The conference also provided an excellent platform for engaging with international researchers, fostering an atmosphere of collaboration and knowledge exchange. The Gala dinner, featuring traditional musicians, added a touch of cultural richness to the event. One highlight of the ICBA was the announcements by the International Society for the Studies in Behavioral Addictions that Matthias Brand will be honoured with the "Great Achievement Award" for his work in the field of behavioral addictions. Stephanie Antons, was awarded the "Best Paper Award" for her work on "Treatments and interventions for compulsive sexual behavior disorder with a focus on problematic pornography use: A preregistered systematic review " published in the Journal of Behavioral Addictions. Both awards will be officially handed over at ICBA 2024 in Gibraltar, where Matthias Brand will also give a keynote lecture.

October 2023: FOR2974 "Autumn School" in Frankfurt

In October 2023, Team Brand and FOR2974 continued our international collaborations at our "Autumn School" in Frankfurt. The event featured insightful talks and discussions with international experts such as Marc Potenza discussing neurobiological factors and Susana Jiménez-Murcia and Fernando Fernández-Aranda talking about clinical trials in the context of behavioral addictions. Specific behavioral addictions, such as social network use disorder and gaming disorder, were explored in depth, with Silvia Casale and Zsolt Demetrovics sharing their expertise on these two disorders respectively. Recognizing the importance of mentorship, workshops were conducted for early career scientists on topics like "How to Dissertation" and "How to Speak and Give Talks".

Figure 1. Members of the Research Unit FOR2974 at the International Conference on Behavioral Addictions (ICBA) in Incheon, South Korea.

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Cerebellum: Much more than motor control

Our group studies the contributions of the cerebellum to motor and non-motor functions in humans. One of our current aims is to get a fuller understanding of how the human cerebellum supports learning and memory of fear, an important emotion for survival. Functional brain imaging studies in humans suggest involvement of the cerebellum in fear conditioning, but do not allow conclusions about the functional significance. In a recently published study we examined whether patients with cerebellar degeneration show impaired fear conditioning and whether this is accompanied by alterations in cerebellar cortical activations [1].

To this end, a two-day differential fear conditioning study was conducted in 20 cerebellar patients and 21 control subjects using a 7 Tesla (7T) MRI system. Although cerebellar patients learned to differentiate between the stimuli CS+ and CS-, acquisition and consolidation of learned fear was slowed, and extinction learning appeared to be delayed. The cerebellar fMRI signal was reduced in relation to the prediction of the aversive stimulus and altered in relation to its unexpected omission. In a parallel study performed by Melanie Mark and Johanna Pakusch at the Ruhr University Bochum (RUB), mice with cerebellar cortical degeneration (spinocerebellar ataxia type 6, SCA6) were also able to learn the fear association, but retrieval of fear memory was reduced. In sum, humans and mice with pure cerebellar cortical degeneration showed deficits in the acquisition of learned fear, but abnormalities were mild. Given that cerebellar fMRI signals predominantly reflect mossy fiber input, changes in cerebellar activations suggest that input signals related to the prediction and unexpected omission of the aversive US (unconditioned stimulus) are altered in patients with cerebellar cortical degeneration. Importantly, these differences could not be explained by cerebellar atrophy because cerebellar fMRI signal related to the presentation of the aversive stimulus (US) was not significantly different from controls (Fig. 1). Future research is warranted to study the exact nature of cerebellar input signals related to fear learning. This work was funded

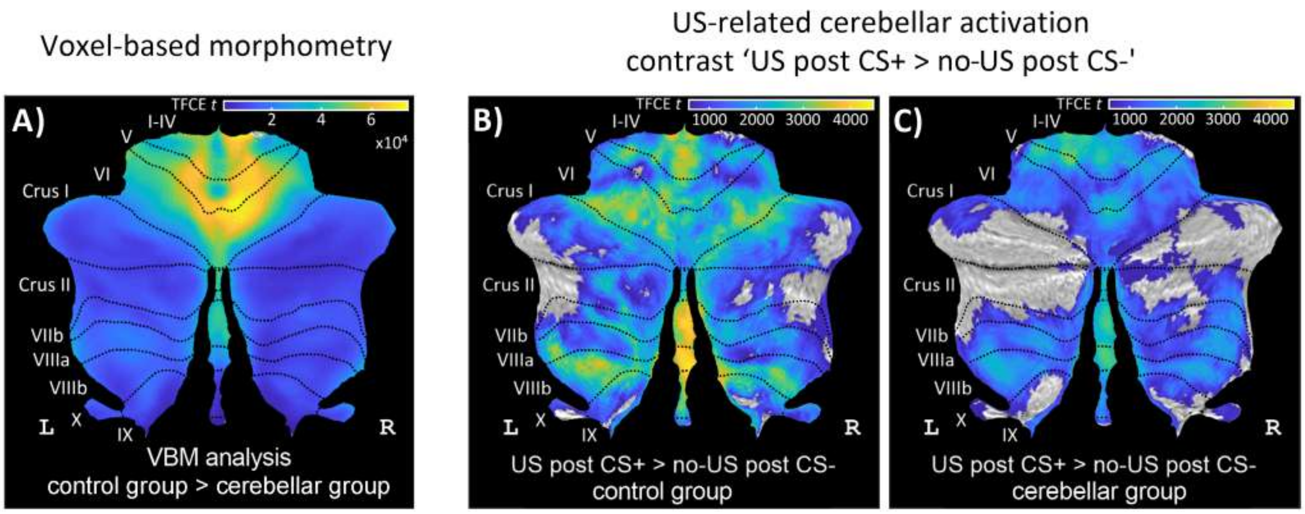

Figure 1. A) Gray matter voxel-based morphometry (VBM) [contrast 'control group › cerebellar group']. **B, C)** US-related cerebellar activation [contrast 'US post CS+ › no-US post CS- during fear acquisition training in **B)** healthy controls and **C)** cerebellar patients. CS = conditioned stimulus; US = unconditioned stimulus. [1]

by the Marie Skłodowska-Curie Innovative Training Network (ITN): Cerebellum and emotional networks (CEN) and the Collaborative Research Center (CRC) 1280 "Extinction learning" (TP A05; PIs Timmann and Quick). Dagmar Timmann is Deputy Network Coordinator of the ITN CEN, and Deputy Speaker of the CRC 1280.

In a newly funded study, we want to investigate the involvement of the human cerebellum in reinforcement learning via its connection with the ventral tegmental area (VTA). This is a joint DFG project from the ELH PIs Dagmar Timmann, Matthias Brand and Ulrike Bingel. Recent animal studies suggest that the cerebellum may process not only sensorimotor signals, but also reward signals and therewith contributes to reinforcement learning, a form of learning which is typically associated with the mesostriatal and mesocorticolimbic dopaminergic system. These observations may be key to understand the contribution of the cerebellum to non-motor control. A central structure involved in non-motor reward related behavior is the VTA. The overarching aim of our new project is to test the hypothesis that the cerebellum contributes to reinforcement learning in humans via its connection with the VTA. We will use an appetitive and aversive Pavlovian to instrumental transfer (PIT) task. High-resolution functional magnetic resonance imaging (fMRI) acquired at 7T will permit us to perform studies at the level of the cerebellar cortex, cerebellar nuclei and the VTA including their functional interactions. This study will help to elucidate how the cerebellum may contribute to non-motor function in the healthy human brain, and will give first answers to how the cerebellum may contribute to common mental disorders.

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Ulrike Bingel

The interaction between pain and cognitive processes

Our research group focuses on the interaction between pain and cognitive processes. We have a longstanding expertise in investigating the CNS mechanisms underlying nociception, pain, and pain modulation in health and disease. In our research, we use behavioural paradigms, pharmacological modulations, as well as functional and structural brain imaging. Being particularly intrigued by the reciprocal effects of pain and cognition, we have a strong focus on translational questions such as the role of expectations and prior experiences on analgesic treatment outcomes. Our interdisciplinary research group comprises neurologists, neuroscientists, psychologists, biologists, and computer scientists and is based at the Department of Neurology at the University Medicine Essen.

In 2023 our team was very glad to continue and expand our research activities after - as for many of us – the COVID-19 pandemic had slowed down experimental research activities between 2020 and 2022. Currently approaching the end of the 1st funding period of the transregional CRC 289 "Treatment Expectation" (www.treatment-expectation.de) that has been funded by the DFG since 2020, we are eagerly preparing the onsite review for the next funding period (2024-2028).

The consortium lead by Ulrike Bingel focuses on the mechanisms underlying expectations on health and treatment outcomes and explores how expectations can be systematically used to improve health care. The consortium involves many projects using brain imaging and the central scientific project Z03 co-lead by Tamas Spisak has started to develop a unique research infrastructure for harmonizing and sharing brain imaging data across sites and projects. This will provide a unique basis for pooled and meta-analytic approaches as will also benefit future collaborative engagement of the ELH. Such "mega-analyses" of several hundred datasets of the placebo imaging consortium have already fostered novel discoveries regarding the mechanisms of placebo analgesia, such as the contribution of the cerebellum, as published in Nature Communication in 2021 [1]. The cerebellum provides an ideal target to be followed up with high field neuroimaging in a joint endeavor with the group by Dagmar Timmann, a world leading expert in this field. Our team is excited to have won Dagmar Timmann as a new PI in the CRC for the new project N17. In a joint endeavor with Dagmar Timmann, there are plans for a 7T study on brainstem-thalamo-cortical pathways underlying expectation change in analgesia in project A01.

Our research group also continues the research activities in the field of learning in project A11 of the CRC 1280 "Extinction Learning", in which the mechanisms underlying pain-related learning and how this might contribute to the development and maintenance of chronic pain are investigated. To support and strengthen these lines of research, Jialin Li, a PhD from the prestigious Max Planck School of Cognition as well as Jonas Zaman as a Humboldt Fellow have joined our team.

Last but not least, together with David Norris and colleagues, we will explore the contribution of resting state activity of the spinal cord for an individual's pain sensitivity in health and chronic pain states, a project that perfectly builds upon our previous work on cerebral resting state networks and pain sensitivity in healthy volunteers.

1. Zunhammer M, Spisák T, Wager TD, Bingel U; Placebo Imaging Consortium. Meta-analysis of neural systems underlying placebo analgesia from individual participant fMRI data. Nat Commun. 2021 Mar 2;12(1):1391. doi: 10.1038/s41467-021-21179-3.

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Antoine Bouyeure, Khazar Ahmadi and Nikolai Axmacher

Mechanisms of fear generalization during fear acquisition and extinction: a 7T fMRI study

Fear conditioning is an associative learning phenomenon during which a previously neutral cue (conditioned stimulus; CS) comes to elicit an emotional fear response due to its association with an aversive event. Extinction learning, on the other hand, describes the process by which this association is progressively erased or forgotten. Past studies have suggested that impairments of fear and extinction learning are found in several psychiatric conditions such as Post-Traumatic Stress Disorder (PTSD), and could be associated to the propensity of PTSD patients to experience intrusive memories of past traumatic events. Here, we aim to shed light on the mechanisms of fear and extinction learning using a version of the trauma-film paradigm in a fear conditioning framework with sub-millimeter fMRI. We recently finished to acquire data from a group of healthy participants with a two-days design paradigm (Fig. 1). During fear acquisition (Day 1), neutral movie clips of different categories were associated with aversive (CS+) or further neutral (CS-) movie clips. The participants progressively learned the association between movie categories and their aversive or neutral outcome. During fear extinction (Day 2), all CS movies were associated with neutral movies, i.e. CS that used to be predictive of an aversive outcome were extinguished. Additionally, intrusive memories were collected in the scanner after each movie viewing session. We hypothesize that fear and extinction learning shape progressively the neural representations of neutral cues, reflecting how neural populations learn to code differentially for the features of cues as a function of their aversive or neutral outcome. We aim to leverage the precision of sub-millimeter fMRI to study neural representations in fine-grained subcortical structures (such as amygdala nuclei) as well as at the laminar level in the neocortex.

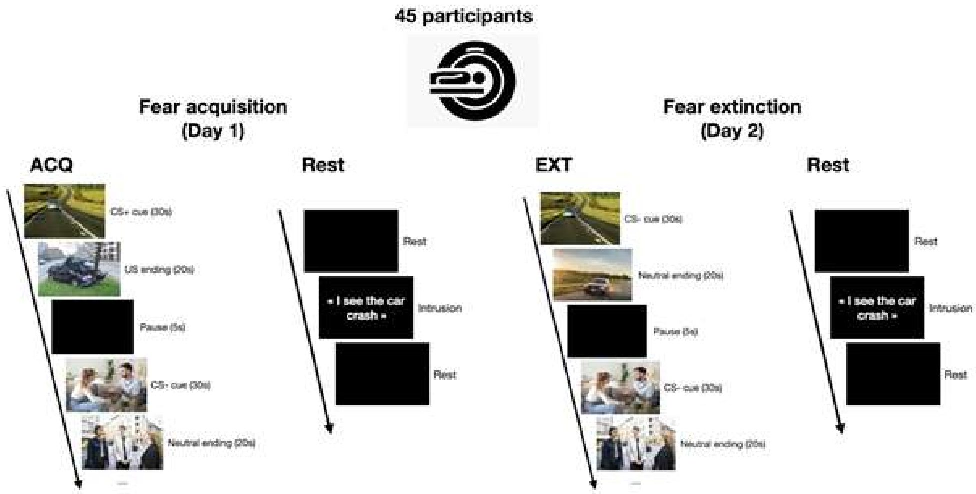

Figure 1. Overview of the paradigm.

Unlocking the laminar organization of the medial temporal lobe structures

Despite substantial progress in understanding the role of the hippocampus (HP) in memory and spatial navigation, their underlying circuit-level mechanisms remain elusive. Leveraging the 7T scanner at the ELH, we acquired functional magnetic resonance imaging data at submillimeter scale in a group of healthy volunteers to investigate the laminar organization of HP subregions during navigation and their associations with distinct navigation strategies. Participants navigated to hidden objects randomly distributed in a virtual arena. Based on their movements during the navigation phase, two navigation strategies were derived ("straightness index" and "median deviation to boundary"). Following preprocessing of the functional data, HP was segmented into subregions and three folded surfaces were subsequently generated that were then divided into depth bins, i.e. layers. We then performed linear mixed-effect models to assess the association of subregional layer-specific profiles with the aforementioned navigation strategies. Our preliminary results demonstrate the feasibility of laminar-resolution recordings in human HP and further suggest that distinct navigation strategies are differentially related to subregion-specific laminar profiles. These results will be presented at the upcoming ISMRM and OHBM conferences in 2024.

In another line of research at the ELH, we are currently acquiring submillimeter fMRI data at 7T in combination with a VR-based video game consisting of interleaved active and passive blocks to study the laminar profile of the HP and neighboring regions. During the active blocks, the participants freely explore the content of sixteen boxes that are randomly distributed across a virtual arena, whereas in the passive condition they are exposed to the movie of the free navigation of a previous participant. Specifically, we aim to i) assess weather HP subregional laminar profiles differ between active and passive learning conditions, and ii) to determine which layers in the entorhinal cortex support grid-like representations playing a key role in spatial navigation. We anticipate that the findings of this study will advance our understanding of how active learning influences mnemonic processing in the human brain.

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Viktor Pfaffenrot and David Norris

Laminar fMRI of the human hippocampus

The human hippocampus plays an important role in the context of spatial navigation, learning and memory. While its function has been studied extensively at low spatial resolutions, its functional mechanisms on a laminar level are poorly understood. Functional MRI at submillimeter resolutions allows to probe signal changes as a function of cortical depth, holding the key to study directionality of information flow non-invasively in humans. Due to its high sensitivity, the most widely used contrast for laminar fMRI is the gradient echo (GRE) blood level oxygenation-dependent (BOLD) contrast. However, this contrast is mostly sensitive to large veins draining blood away from the locus of activity, i.e. the neurons. Hence, the GRE-BOLD contrast suffers from a bias toward unspecific venous vessels, degrading its spatial specificity. In order to distinguish signal changes driven by true neuronal activity from those coming from unspecific vessels, it is imperative to have an idea of the direction the blood is drained to. However, due to the hippocampus' highly convoluted structure, the venous drainage pattern is more complicated compared to the neocortex (Fig. 1A).

In the first phase of the MERCUR grant, Norris' group investigated the directionality of venous blood flow and its associated signal change bias. Eight subjects were scanned using submillimeter veno- and angiography as well as submillimeter fMRI with multi-echo FLASH readouts during a breath-hold paradigm. The venograms were obtained by denoising and filtering 0.3 mm isotropic susceptibility weighted images (SWI) for veins (Fig. 1B). Subsequently, the filtered images were projected on a flatmap of the innermost and outermost surface of the hippocampus for each subfield using the recently published hippunfold package. Comparing the subject-averaged venous patterns between the inner and outer surface in Fig. 1C (veins and arteries in blue and red, respectively), shows an increased venous vessel density in the inner surface for the subiculum (sub, blue bar) and Cornu Ammonis 1 (CA1, orange bar). In contrast, CA2 (green bar) CA3 (red bar) and CA4 (purple bar) show a higher venous vessel density in the outer layer (Fig. 1C, bottom). Because the signal change during breath-hold is completely driven by vessel physiology, the pattern in Fig. 1C largely resembles the pattern in subject-average signal change during breath-hold as shown in Fig. 1D. These results show that the venous bias in hippocampal laminar fMRI using the GRE-BOLD contrast exhibits a subfield-dependent variation: from outer to inner surfaces in the subiculum and CA1 and in the opposite direction for CA2-CA4.

To develop methods to improve laminar fMRI of the hippocampus, a GRE-BOLD reference experiment eliciting robust single subject activation is needed. Hence, in the second phase of the grant, a benchmark laminar fMRI experiment was performed using an autobiographical memory paradigm (N = 9, all but one subject overlap with breath-hold experiment). The signals were acquired at 0.9 mm isotropic resolution with the most widely used sequence for laminar fMRI, GRE-BOLD 3D-EPI. Fig. 2A displays smoothed voxel group t-statistics showing activity of

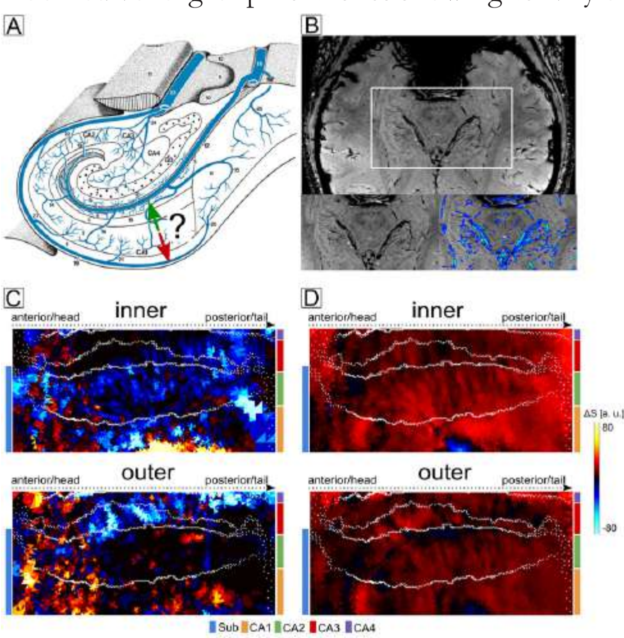

Figure 1. A) Schematic of the venous structure of the human hippocampus. For e.g. the CA1, it is unclear in which direction the venous blood is drained to the most. It could be either toward the outer surface (red arrow) or the toward the inner surface (green arrow). **B)** High-resolution (0.3 mm isotropic) denoised SWI image filtered for veins (blue). **C)** Subject-averaged (N=8) venograms (blue) and angiograms (red) projected onto unfolded maps of the hippocampus for the inner and outer surface. The white dotted lines show the boundaries between subfields. From bottom top: Sub, CA1-CA4. **D)** Subject-averaged signal change during a breath-hold task projected on the unfolded hippocampus. The patterns between (C) and (D) are to a high degree similar showing that for Sub and CA1, the signal change bias goes from outer to inner layers while for CA2-CA4, the opposite is the case.

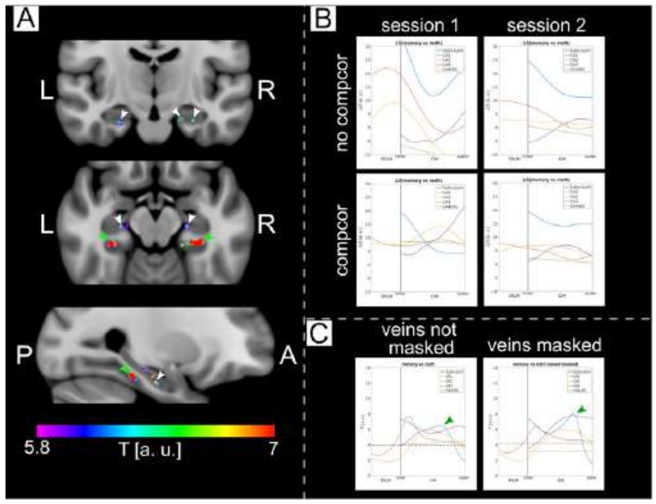

Figure 2. A) Group level t-statistics (permutation test, p<0.05, FWE-corrected) using smoothed data show expected activation patterns for the hippocampus (white arrows) and the parahippocampal gyri (green arrows) when conduction an autobiographical memory paradigm. **B)** On the laminar level, physiological noise has a detrimental effect on the interpretability of laminar profiles. With correction using compcor, the profiles' shape become more similar between sessions. **C)** Group level t-statistics on the laminar level (permutation test, black dashed line highlight p<0.05 FWE corrected, i.e. t-values above the black line are marked as significant) how distinct feature for each subfield. Masking out veins highlight peaks away from the direction of venous bias (e.g. green arrows).

the hippocampus (white arrows) and of the parahippocampal gyri (green arrows). Because GRE-BOLD is prone to physiological noise, e.g. breathing, care must be taken when investigating the hippocampus. Fig. 2B highlights the effect of physiological noise correction in an example subject scanned twice on different days. With correction (compcor), the shape of the profiles between session one and two match closer as compared to the case without physiological noise correction. Fig. 2C shows group t-statistics on the laminar level. By masking out veins as defined by the SWI venograms, peaks away from the bias direction are promoted (e.g. green arrows). The profiles in Fig. 2C show distinct laminar features for each subfield.

Contact

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Science and art don't go together? We strongly disagree! And so in 2023, the ELH launched its first ever art context, aptly named "ARTifact - Imaging MRI". Open to all members of the ELH, affiliated research groups and participating institutions, we were excited - and nervous. Would anyone send in artwork at all? What if we had been too ambitious?

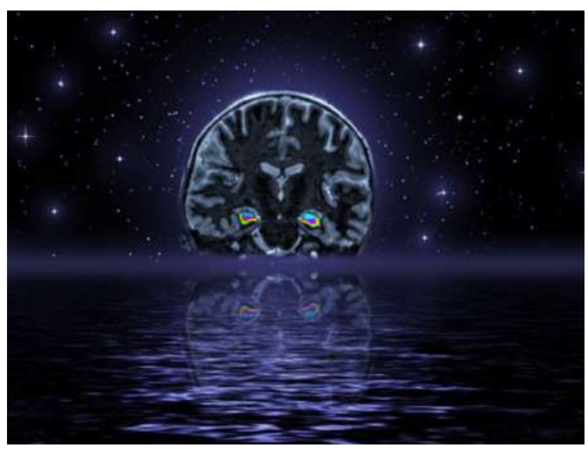
But people sent in artwork, and proved just how well science and art do, in fact, go together. We were amazed by the creativity and skill of the submitted artworks.

ART

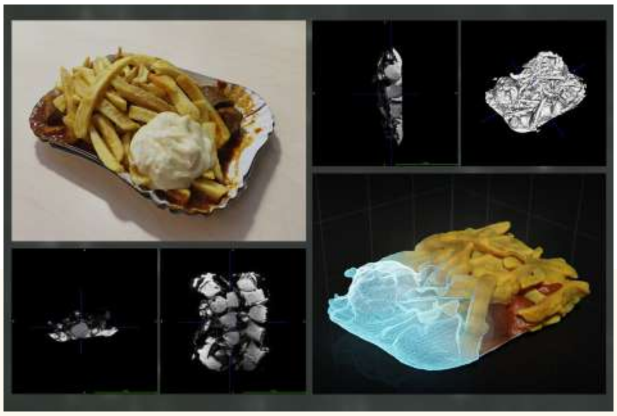
"Leaves of Thought" (Greta Wippich, Alice Doubliez and Enzo Nio)

The three winning entries.

"What Did She Feel?" (Stephanie Antons)



"Hippocampal Moon" (Khazar Ahmadi)



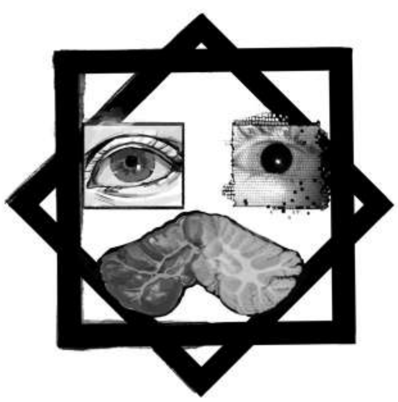
"From Cravings to Ingestion: The Brain-Body-Axis revealed through a 7-Tesla MRI Portrait of CPM" (Marcel Gratz and Harald Quick)

IFACT

IMAGING MRI

"Contrast" (Annika Verheyen)

Just some of the impressive submissions.



"Are you afraid of squares or diamonds" (Greta Wippich, Alice Doubliez and Enzo Nio)

"Beyond Boundaries: 150 Years of ELH Institute Innovation" (Marcel Gratz)

2023 IN SHORT

In March 2023, our new website launched with an updated design and some new features, like the volounteer newsletter.

First ever Erwin L. Hahn Institute art competition "ARTifact - Imaging MRI" launched

Open door event "Türen auf mit der Maus" was an overwheming success.

The ELH has acquired two state-of-the-art NVIDIA H100 Tensor-Core graphic processors which reduce running safety simulations from 14 days to just one.

On September 21st, members of the ELH participated in the "Bathrobe Challenge" to raise dementia awareness.

ISMRM Participation 2023 in Toronto, Canada

Fiedler TM, Ladd ME, Orzada S: Local and Whole-Body SAR in UHF Body Imaging: Implications for Matrix Compression. *Session: MR Safety I,* Digital Poster.

Grimm JA, Aigner CS, Dietrich S, Orzada S, Nagel AM, Ladd ME, Schmitter S: In-vivo 3D liver imaging at 7T using kT-point pTx pulses and a 32-Tx-channel whole-body RF coil. *Session: Higher Field, Higher Expectations,* Talk.

Kraff O, Theysohn JM, Theisejans J, Quick HH: 7 Tesla MRI of the knee joint after anterior cruciate ligament graft reconstruction: safety discussion and image quality study. *Session: MR Safety: Everything,* Power Pitch.

Kraff O, Schulz J, May MW, Scheenen TWJ, Meurs TB, Schmitter S, Theysohn JM, Quick HH: Application of direct signal control with variable excitation and refocusing for T2-w TSE musculoskeletal imaging at 7 Tesla. *Session: Technical Development,* Talk.

Maatman IT, Ypma S, Block KT, Maas MC, Schulz J, Scheenen TWJ: Radial Stack-of-Stars Abdominal MRI at 7 Tesla. *Session: Higher Field, Higher E*, Talk.

May MW, Kraff O, Schulz J, Scheenen TWJ, Orzada S, van Uden M, Meurs TB, Schmitter S, Quick HH: Prostate Imaging at 7 Tesla: Comparison of Two 8-channel Transmit/Receive RF Local Body Arrays. *Session: Progress & Challenge,* Digital Poster.

Pfaffenrot V, Leitão D, Verheyen A, May M, Tomi-Tricot R, Malik SJ, Norris DG: Increasing MT contrast in laminar fMRI using PUSH pTx pulses. *Session: High- & Low-Field fMRI,* Digital Poster.

Pfaffenrot V, Norris DG: Validating NORDIC denoising on high-resolution fMRI data at 7T. *Session: fMRI Acquisition,* Digital Poster.

Pham SDT, van Vliet JT, van Tuijl RJ, Biessels GJ, Costagli M, van Buchem MA, Kraff O, Villringer A, Ladd ME, de Rochefort L, Siero JCW, Zwanenburg JJM: Quantitative Flow Velocity in Cerebral Perforating Arteries with 7T MRI: the EUFIND study. *Session: Flow, Perfusion & CSF,* Talk.

Harald Quick is honoured "Senior Fellow" at the ISMRM meeting in Toronto, Cana-

Erwin L. Hahn Workshop & Lecture 2023

ELH director Harald Quick welcomes speakers and listeners to the Erwin L. Hahn Lecture & Workshop.

The Oktogon is popular among and appreciated by participants for its laid-back atmosphere.

Left to right: ELH directors Harald Quick and David Norris, key speaker Andrew Webb from Leiden University, ELH PIs Tom Scheenen, Mark Ladd and Dagmar Timmann.

Harald Quick presents the ELH Award for Young Scientists to Viktor Pfaffenrot for his outstanding PhD dissertation "Laminar fMRI of long-range connections: Methods and contrast mechanisms".

Ansje Fortuin from Radboud University talks about using 7T MRI to detect small lymph node metastases in prostate cancer.

Catching up with colleagues and friends during a coffee break.

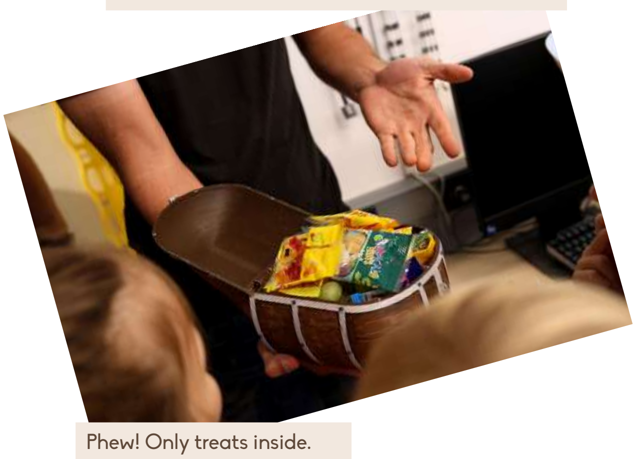
Wertvolle Schätze

Türen auf mit der Maus

2023

Oh no! A pirate had left a treasure chest at the ELH! To find it, the children had to answer MRI questions during a scavenger hunt ...

But obviously, once the chest was found, it had to be scanned to make sure there was nothing dangerous inside,



Phew! Only treats inside.

Future MRI scientists.

ELH scientist Jenni Schulz exlpains how an MRI scanner works.

The ELH's "mock scanner" was developed and built to give children an impression of what being inside an MRI feels like (without actually being exposed to magnetic field strength).

It turned out to be quite popular with the kids who all got their picture taken inside to take home!

Exhausted but happy.

From left to right: Markus May, Jenni Schulz, Stefanie Zurek, Lena Grunwald.

Not pictured: Annika Verheyen, who helped a lot in the weeks leading up to the event, and was the secret mastermind behind the scavenger hunt,

Current Grants

DFG

N. Axmacher
CRC1280 - A02. Neural mechanisms of context generalization (2021-2025)

N. Axmacher, D. Timmann, R. Kumsta
CRC 1280 - F02. Focus Group Neuroimaging and Genetics (2021-2025)

N. Axmacher, E. Genç
CRC 1280 - A03. Functional role and dynamic change of extinction network connectivity (2021-2025)

U. Bingel
CRC 128 - A11: Appetitive and aversive pain-related learning in health and chronic back pain (A11) (2021-2025)

U. Bingel
CRC/TRR 289 Treatment Expectation (2020-2024)

M. Brand
FOR 2974 - Affective and cognitive mechanisms of specific Internet-use disorders (ACSID) (2020-2024)

H.H. Quick, N. Avdievich
F. Mauconduit (co-funded by ANR)
NeuroBOOST: Novel Parallel-Transmit Nead/Neck RF Coil Arrays for Ultra-High Field MRI at 7T, 9.4T, and 11.7T (2023-2026)

D. Timmann, U. Bingel, M. Brand
DFG: **Involvement of the human cerebellum in reinforcement learning via its connection with the ventral tegmental area (VTA)** (2023-2026)

D. Timmann, H.H. Quick
DFG: **CRC 1280 - A05. The contribution of the cerebellum to extinction: intrinsic mechanisms and cerebello-cerebral interactions** (2021-2025)

EFRO/EU

D. Klomp, H.H. Quick, T. Scheenen
Non-ionizing Metabolic Imaging for predicting the effect of and guiding Therapeutic Interventions (MITI) (2022-2024)

T. Scheenen
EFRO: **MI-Robot** (2021-2023)

D. Timmann
Marie-Skłodowska-Curie Innovative Training Network: Cerebellum and emotional networks (CEN) (2021-2025)

D. Timmann
Spinocerebellar ataxias: Advanced imaging with ultra-high field MRI (SCAIFIELD) (2021-2024)

MERCUR

N. Axmacher, D. Norris
Unlocking the function of the hippocampus with laminar fMRI (2022-2024)

M. Brand
Application for continuated funding: **FOR 2974 - Affective and cognitive mechanisms of specific Internet-use disorders** (2023)

O. Güntürkün, U. Bingel, M. Brand
ReThink (2022-2026)

NWO

R. Cools, D. Norris, W. Schellekens
Unravelling dopamine's role as gatekeeper of prefrontal cortex (2022-2027)

More information about the individual grants is available at the Erwin L. Hahn Institute website. (hahn-institute.de)

Publications

Antons S, Yip SW, Lacadie CM, Dadashkarimi J, Scheinost D, Brand M, Potenza MN. Connectome-based prediction of craving in gambling disorder and cocaine use disorder. *Dialogues in Clinical Neuroscience*. DOI: 10.1080/19585969.2023.2208586

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Chen B, Dammann P, Jabbarli R, Sure U, Quick HH, Kraff O, Wrede KH. Safety and function of programmable ventriculo-peritoneal shunt valves: An in vitro 7 Tesla magnetic resonance imaging study. *PLOS One*. DOI: 10.1371/journal.pone.0292666

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Ladd ME. The Medical Device Regulation and its impact on device development and research in Germany. *Zeitschrift für Medizinische Physik*. DOI: 10.1016/j.zemedi.2023.09.002

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Orzada S, Akash S, Fiedler TM, Kratzer FJ, Ladd ME. An investigation into the dependence of virtual observation point-based specific absorption rate calculation complexity on number of channels. *Magnetic Resonance in Medicine*. DOI: 10.1002/mrm.29434

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Personnel & Organisational Structure at the ELH

Managing Director/PI
Prof. Dr. Harald H. Quick

Directors/PIs
Prof. Dr. Matthias Brand
Prof. Dr. David G. Norris

PIs
Prof. Dr. Nikolai Axmacher
Prof. Dr. Ulrike Bingel
Prof. Dr. Onur Güntürkün
Prof. Dr. Mark E. Ladd
Prof. Dr. Tom W.J. Scheenen
Prof. Dr. Dagmar Timmann

Administrative Director
Dr. Franziska Günther

Staff Scientists
Dr. Oliver Kraff
Dr. Stefan Maderwald

Technician
Kim Jotzo

Radiographer
Daniel Osenberg

Public Relations
Stefanie Zurek

Scientists

Dr. Khazar Ahmadi
Dr. Stephanie Antons
Dr. Mareike Bacha-Trams
Dr. Giorgi Batsikadze
Dr. Antoine Bouyeure
MSc. Kjell Büsche
MSc. Alice Doubliez
Dr. Friedrich Erdlenbruch
Dr. Thomas Ernst
M.Sc. Arslan Gabdulkhakov
Dr. Erhan Genc
Dr. Carlos A. Gomes
Dr. Marcel Gratz
Dr. Balint Kincses
Evgenij Knorr
Dr. Tijmen Koëter
Dr. Magnus Liebherr
Dr. Maike Lindemann
MD Qi Liu
Dr. Marnix Maas
M.Sc. Ivo Maatman
Dr. Markus May
Dr. Silke M. Müller
Dr. Justinas Narbutas
MSc. Enzo Nio
Dr. Stephan Orzada
Patrick Pais Pereira
Dr. Mykola Petrenko
Dr. Viktor Pfaffenrot
Dr. Jennifer Schulz
MSc. Daniel Sharoh
Dr. David Stawarczyk
MSc. Carlijn Tenbergen
Dr. Jan-Willem Thielen
Dr. Andreas Thieme
Dr. Quincy van Houtum

Students

Yasmin Abdelnaby
Niklas Deuermeier
Lena Grunwald
Carolin Hensel
Melina Kascha
Neil Knöbel
Aron Lichte
Denis Mai
Maya Metzger
Jakob Stührk
Jana Theisejans
Annika Verheyen
Leon Voß
Miriam Weirauch
Luca Wessing

New in 2023

Left in 2023

Yasmin Abdelnaby
Lena Grunwald
Jana Hupe
Jennifer Schulz
David Stawarczyk
Miriam Weirauch

Glimpses of 2023

Conferences, Networking, Viral Challenges ...

Hall of Fame

Dissertations/Masters & Bachelor Theses

Weirauch, Miriam. Entwicklung und Evaluation eines 8-Kanal Sende- und Empfangsarray-Gehäuses zur Optimierung der Körperbildgebung mittels 7 Tesla MRT. (Bachelor Thesis)

Awards

Stephanie Antons Norddeutscher Suchtforschungsverbund Young Scientist Award for her paper "Treatments and interventions for compulsive sexual behavior disorder with a focus on problematic pornography use: A preregistered systematic review".

Ulrike Bingel made fellow of the Max Planck School of Cognition.

Oliver Kraff MRM distinguished reviewer award 2023.

Enzo Nio Best Poster prize, Gordon Research Conference Cerebellum in Boston, USA.

Viktor Pfaffenrot ELH Young Scientist Award for his PhD dissertation "Laminar fMRI of long-range connections: Methods and contrast mechanisms".

Harald Quick honoured as Senior Fellow of the ISMRM in Toronto, Canada.

Andreas Thieme DAAD Travel Grant for participation at the 2023 SFN meeting in Washington, USA.

Dagmar Timmann made honorary member of the German Heredo-Ataxia Society e.V..

Dagmar Timmann elected to the review board of the German Research Foundation (DFG).

Invited Talks

Viktor Pfaffenrot "Principles and practices of laminar functional MRI", neurophysiological seminar, University Hospital Essen.

Picture Credits

Title Page: "Leaves of Thought" (Greta Wippich, Alice Doubliez and Enzo Nio)

Marcel Gratz/ELH
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ICBA
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Oliver Kraff/Markus May/ELH
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Dagmar Timmann
Page: 35

Elisa Wegmann
Page: 13

Stefanie Zurek/ELH
Pages: 26-29, 35

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Pages: 6, 8, 12, 14, 16, 18, 20, 24 (background)

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