Center for Lifespan Psychology

Director: *Ulman Lindenberger*

Research Project 7: Brain Imaging Methods in Lifespan Psychology

Research on human development seeks to delineate the variable and invariant properties of age-graded changes in the organization of brain–behavior–environment systems. Magnetic resonance imaging (MRI) and magnetic resonance spectroscopy (MRS) have become indispensable tools in this context, as they allow noninvasive assessment of brain function, anatomy, microstructure, and metabolism.

The two main goals of the *Brain Imaging Methods* project are: (i) to ascertain and improve the measurement quality of standard brain imaging protocols at the Center; (ii) to complement the standard imaging repertoire by advanced sequences with enhanced interpretability that hold promise in elucidating structural changes and physiological mechanisms related to maturation, learning, and senescence. In pursuing these goals, the project serves as a resource to other projects interested in imaging (e.g., Kleemeyer et al., 2016; Wenger et al., 2017).

Structural and quantitative MRI methods occupy a central place in the project. During the reporting period, the project has focused on (i) high-resolution T_1-weighted imaging to obtain estimates of volume or thickness of specific substructures of the brain; (ii) diffusion imaging and multiparametric mapping (MPM) to obtain brain maps that permit quantitative estimates of histological parameters; (iii) susceptibility-weighted imaging to obtain maps of mineralization, especially for the brain's deep gray matter structures; and (iv) myelin water fraction (MWF) imaging by mapping the fraction of shortest T_2 relaxation rates quantitatively. The latter method provides an estimate of the portion of water molecules located between myelin sheaths, presumably reflecting the degree of myelination within white matter. Work on MPM profits from collaboration with Nikolaus Weiskopf (MPI for Human Cognitive and Brain Sciences, Leipzig, Germany).

Functional MRI and MRS are used to provide maps and spectra of brain activity during task performance or at rest. The project takes special interest in: (i) high-resolution functional imaging of the hippocampus; (ii) task-related, time-resolved applications of proton MRS, with a focus on glutamate and GABA; and (iii) phosphorus MRI to capture individual differences in brain metabolism. Work in this area involves collaborations with Mara Mather (University of Southern California, Los Angeles, USA), Florian Schubert (Physikalisch-Technische Bundesanstalt, Berlin, Germany), and Jeff Stanley (Wayne State University, Detroit, USA).

In the following, we provide additional details on three of the methods that have been the focus of our attention during the reporting period.

Diffusion Imaging

Diffusion imaging captures the movement of water molecules, termed diffusion. Diffusion in tissue is hindered by cell membranes. Therefore, the orientation-dependent diffusion profiles provide information about tissue microstructure. For instance, when water molecules are observed in myelinated neuronal fibers, their diffusion is less hampered along than across fiber tracts. Diffusion within a voxel (a three-dimensional data point) is often captured by a tensor (ellipsoid) model. However, by permitting only one directional description per voxel, diffusion tensor imaging provides an impoverished, and at times inaccurate, picture of histological reality; for instance, the crossing of fibers may go unnoticed. To enhance the microstructural veridicality of diffusion imaging, the project is working on multishell diffusion imaging acquisition schemes to improve the precision of orientational information. Diffusion models under scrutiny are the sticks-and-ball model (used by FMRIB Software Library, FSL), constrained spherical deconvolution (implemented in MRtrix), and physiologically motivated multicompartment models (e.g., neurite orientation dispersion and density imaging, NODDI). We plan to use multishell diffusion imaging in combination with nontensor diffusion modeling to move toward a more

Researchers

Nils C. Bodammer
Ulman Lindenberger
Naftali Raz
(as of 04/2016)

Davide Santoro
(as of 09/2016)

Paul Enggruber
(until 01/2015)
Felix Kreis
(until 08/2015)

Key References

Bodammer, N. C., Kaufmann, J., Kanowski, M., & Tempelmann, C. (2009). Monte Carlo-based diffusion tensor tractography with a geometrically corrected voxel-centre connecting method. *Physics in Medicine and Biology, 54,* 1009–1033. doi:10.1088/0031-9155/54/4/013

Enggruber, P., & **Kreis, F.** (2015). *Development of three-dimensional spectrally selective phosphorous magnetic-resonance imaging for analysing metabolism in the human brain.* Master's thesis, Technische Universität Berlin.

precise picture of age- and training-related changes in the brain's structural connectivity.

Quantitative Multi-Parameter Mapping (MPM)

Normal aging is accompanied by characteristic changes in the brain's morphology and microstructure. Quantitative MRI can help in characterizing the brain's microanatomy by using the physical properties of water that govern the MRI contrast as surrogate parameters to describe tissue properties. Nikolaus Weiskopf, Gunther Helms, and colleagues have developed a comprehensive quantitative multiparameter mapping approach, which provides high-resolution maps of the longitudinal relaxation rate ($R_1 = 1/T_1$), effective proton density (PD*), magnetization transfer (MT), and effective transverse relaxation rate ($R_2^* = 1/T_2^*$) (see Figure 22 showing exemplary maps for one subject examined in our project). In collaboration with the *Plasticity* project (pp. 153–156), we are currently investigating the reproducibility of MPM parameters within and across measurement occasions. For instance, we have acquired data from 15 volunteers, each measured four times on two consecutive days, either with or without repositioning, to tease apart various factors affecting reproducibility.

Phosphorus MRI

The mitochondria are organelles in eukaryotic cells that provide energy for the cell's metabolism through glycolysis (i.e., the releasing of energy stored in glucose). Adenosine triphosphate (ATP) is generated during glycolysis for high-energy short-time storage. ATP concentration levels are stabilized by the creatine kinase (CK) reaction, which buffers ATP. Phosphocreatine (PCr) markedly varies with energy metabolism. Mapping changes in PCr concentration in brain tissue can thus be used to calculate an index of the brain's energy metabolism in response to short-term peaks in energy demand. During the report-

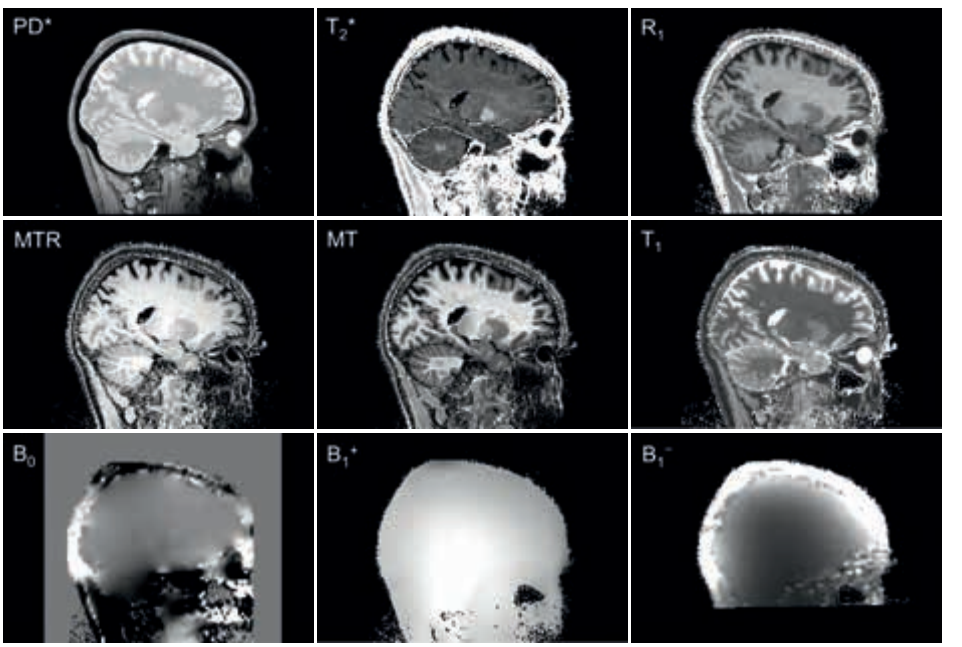

Figure 22. Sagittal slices through maps of PD* and T_2^*, R_1, MTR, MT, and T_1. Additionally, sagittal slices through the determined inhomogeneities of the static magnetic field (B_0), the high-frequency transmit field (B_1^+), and the coil-specific receive profile (B_1^-) are presented. The information about B_0, B_1^+, and B_1^- is used for further improvement of the accuracy of the quantitative magnetic property maps depicted above, which can be seen as being dependent on a set of tissue properties on a cellular level (e.g., the degree of myelination, axonal density, and mean water content) and thus permit assessment of gray and white matter microstructure (unpublished project data).

ing period, the project has developed two different variants of a spectrally selective 3D turbo spin echo (TSE) imaging sequences that selectively excites PCr (Enggruber & Kreis, 2015). One sequence version allows for the functional (i.e., temporally resolved) task-related acquisition of the PCr concentration, whereas the other is designed to generate maps of the kinetic rate of the CK reaction by using selective saturation of the gamma ATP peak (see Dissertation Julian Q. Kosciessa in Lifespan Neural Dynamics Group, p. 199). In collaboration with Jeff Stanley, the project is working on establishing phosphorus MRI as a technique that may allow researchers at the Center to study individual differences in cerebral energy consumption as a function of age and other person characteristics.

The Magnetic Resonance Imaging Laboratory

The Institute operates a Siemens TIM Trio tomograph, which has a field strength of 3 Tesla. The MR system is equipped for proton (^{1}H) MRI and MRS with 12-channel and 32-channel head radio frequency coils, and a circularly polarized birdcage headcoil. Instrumentation for phosphorus (^{31}P) MRS, that is, a dual-tuned circularly polarized head coil, a dual-tuned surface coil, and an additional high-frequency amplifier working at the resonance frequency of phosphorus, is also available. Additional components include a transcranial magnetic stimulation system with an MR-suited stimulation coil; an MR-suited EEG system; an audio/video stimulus presentation system using headphones and goggles; a visual presentation system based on video projection, mirrors, and a screen; an MR-compatible eye-tracking system; and a variety of hand-held response boxes for children and adults. The laboratory also houses a mock (i.e., fake) scanner that looks and sounds just like the real scanner. The mock scanner is used to familiarize research participants, in general, and children, in particular, to the scanning environment. As of March 2017, the core MR team consists of Sonali Beckmann (head of the MRI Measurement Facility), Nils C. Bodammer (physicist), Thomas Feg (technician), Davide Santoro (physicist), Sebastian Schröder (technician), and Nadine Taube (technical assistant). The team provides scientific and technical support for all MR imaging activities at the Institute.