Center for Lifespan Psychology

Director: *Ulman Lindenberger*

Research Project 6: Brain Imaging Methods in Lifespan Psychology

Research Scientists

Nils C. Bodammer

Ulman Lindenberger
Naftali Raz
Davide Santoro

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

The two main goals of the *Brain Imaging Methods* project are to: (a) ascertain and improve the measurement quality of standard brain imaging protocols at the Center; and (b) 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., Bender et al., 2018; Dahl et al., 2019; Keresztes et al., 2017; Kleemeyer et al., 2017; see Figure 18).

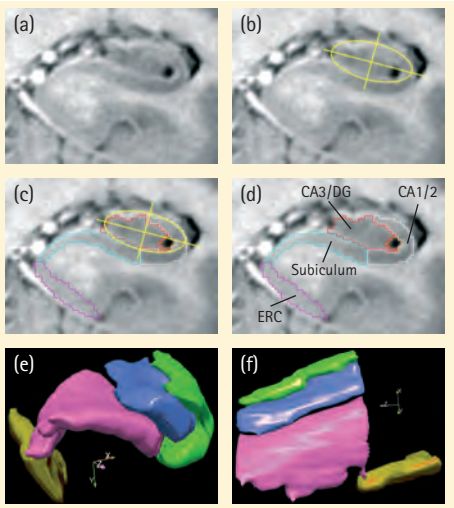

Figure 18. Illustration of the anatomic-geometric heuristic for manual morphometry. (a) A representative slice of anterior hippocampal (HC) body following the visualization of the uncal sulcus. To facilitate tracing, the T_2-weighted contrast has been inverted to mimic a T_1-weighted image. (b) Placement of the ellipse and bisecting lines (the major and minor axes of the ellipse). (c) The minor axis bisecting the ellipse marks the point from which a vertical line is dropped to create a boundary separating the subiculum from CA1/2, and CA 1/2 from CA3–4/DG, as shown in (d). Bottom: 3-D illustrations of sagittal (e) and oblique coronal (f) views of manual subfield labeling in the HC body from one participant (adapted from Bender et al., 2018).

Structural and quantitative MRI methods occupy a central place in the project. During the reporting period, the project has focused on: (a) T_1-mapping by means of an MP2RAGE acquisition protocol to obtain estimates of laminar myelination across the cortical sheet; (b) myelin water fraction (MWF) imaging, which maps the fraction of short T_2 relaxation rates quantitatively and appears to yield more valid estimates of myelin than other widely used methods; (c) advanced methods in high angular resolved diffusion imaging (HARDI), from which maps of water diffusion in brain tissue can be deduced that permit estimates of local axonal orientation and thereby enable the identification of particular fiber tracts in white matter; and (d) neuromelanin-sensitive high-resolution imaging of the brainstem to determine the individual position and extent of the loci coerulei (Dahl et al., 2019).
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: (a) functional imaging with high spatial or temporal resolution by exploiting multiband echo-planar imaging (MB-EPI) acquisition strategies; and (b) task-related, time-resolved applications of proton MRS, with a focus on glutamate. Work on MR spectroscopy and MWF imaging, on the one hand, and on T_1 mapping, on the other, has been done in collaboration with Jeffrey A. Stanley (Wayne State University, Detroit, USA) and José P. Marques (Donders Institute, Radboud University, Nijmegen, Netherlands), respectively. For more information about the Institute's MRI facility, see p. 298.

T_1 Mapping Using MP2RAGE With B_1 Map Corrections

The longitudinal relaxation time T_1 in the cortex is affected by the myelin content in the laminae. T_1 mapping offers a noninva-

Key Reference

Bender, A. R., Keresztes, A., Bodammer, N. C., Shing, Y. L., Werkle-Bergner, M., … Kühn, S., Lindenberger, U., & **Raz, N.** (2018). Optimization and validation of automated hippocampal subfield segmentation across the lifespan. *Human Brain Mapping, 39*(2), 916–931. https://doi.org/10.1002/hbm.23891

Key References

Arshad, M., Stanley, J. A., & **Raz, N.** (2017). Test-retest reliability and concurrent validity of in vivo myelin content indices: Myelin water fraction and calibrated T_1w/T_2w image ratio. *Human Brain Mapping, 38*(4), 1780–1790. https://doi.org/10.1002/hbm.23481.

Santoro, D., Rivoire, J., Meise, F., Terekhov, M., Salhi, Z., Gast, K., & Schreiber, L. M. (2011). Three-dimensional mapping of the B1 field using an optimized phase-based method: Application to hyperpolarized ^{3}He in lungs. *Magnetic Resonance in Medicine, 65*(4), 1166–1172. https://doi.org/10.1002/mrm.22683

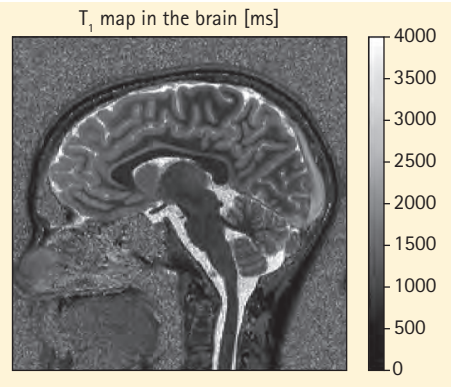

Figure 19. Typical T_1 map of a child's brain (1 slice out of a 3D volume) obtained with our protocol using MP2RAGE and B_1 map correction.

sive method to determine cortical structures and their changes over time. We have been developing a new protocol that makes use of multiple MP2RAGE sequences developed by José Marques and colleagues for the accurate estimation of high-resolution T_1 maps in the full brain. We have chosen tailored paired values for the inversion times to cover the whole range of T_1 values in the brain. The resulting T_1 map is then corrected by a B_1 map to cancel hardware imperfections and radio frequency inhomogeneities across the brain (see Figure 19). The B_1 mapping method used (Santoro et al., 2011) was optimized in-house for our studies. The full protocol for a 1 mm isotropic T_1 map of the full brain of children takes about 16 minutes, with work in progress to reduce its duration.

Myelin-Water Fraction Imaging (MWF)

Based on a time series of T_2-weighted MR images with increasing echo-times acquired by a 3D GRAdient and Spin-Echo (GRASE) sequence, MWF imaging evaluates the transversal relaxation in a multiexponential manner by applying a nonnegative least squares (NNLS) fitting algorithm. The fraction of short T_2s (< 40 ms) provides an estimate of the portion of water molecules located between myelin sheaths, presumably reflecting the degree of myelination within white matter (Arshad et al., 2017).

High Angular Resolved Diffusion Imaging (HARDI)

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 hampered less along than across fiber tracts. Hence, principal diffusion directions can be identified with the orientations of axonal tracts. Special MR protocols sensitized to the diffusion of water molecules in tissue allow to measure such diffusion orientation profiles. In his thesis, Maximilian M. Wichmann (2018), a master's student in our project, determined the precision and estimates of accuracy of the analyzed principal diffusion directions as a function of the diffusion-sensitizing gradient scheme and the model to describe diffusion profiles. The tensor model was significantly outperformed by two competing models (sticks-and-ball, constrained spherical deconvolution).