Advancing our understanding of neuronal network dynamics in neurodegenerative diseases requires the investigation and simultaneous imaging of neuronal populations and their interactions in the intact CNS. The discovery of a rapidly gated light-sensitive cation channel ChR2 suitable for noninvasive control of neuronal activity has made it possible to optically control membrane depolarization on the millisecond timescale in genetically defined neurons, using a non-metallic optical fiber for stimulation. Furthermore, the same optical fiber can be used for recordings of fluorescent calcium indicators, thereby bridging the gap between fMRI and optical imaging. Here, we proved the feasibility of rat fMRI at high field strength in combination with optical fiber based calcium imaging in vivo, directly mirroring neuronal activity. Also, transduction of mouse adult stem cells with ChR2-YFP and subsequent neuronal differentiation should demonstrate the feasibility of an all-optical physiology, combined with fMRI.

Methods
Rats were anesthetized with an intraperitoneal injection of medetomidine, followed by a continuous i.v. infusion into the tail vein (0.01 mg / h). For Calcium recordings, 2 µl of Calcium sensitive dye Oregon green 488 BAPTA-1 AM (Molecular Probes) were stereotactically injected 500 µm into the left somatosensory cortex upon craniotomy (from bregma: AP: 0 mm, ML: +/-1 mm, DV: 0.3 mm). Subsequently, an optical fiber was implanted in the exact location and fixed at the skull. A custom made recording setup was used to excite the calcium dye, the optogenetic construct ChR2 and record fluorescence emission. For electric stimulation, two needle electrodes were inserted into the left forepaw and connected to a stimulator (Digitimer DS4, Hertfordshire, England). A classical block design was established (15 s stimulation at 3 mA, 3 Hz, 300 µs pulse duration, 45 s baseline). Rat fMRI experiments were performed on a 17.6 T Bruker Avance 750 WB scanner with a rat head coil with an inner diameter of 38mm. The fMRI experiments were performed on a 17.6 T Bruker Avance 750 WB scanner with a rat head coil with an inner diameter of 38mm. The spatial resolution of all functional images was 200 x 312 µm. Functional MRI DICOM images were analyzed using statistical parametric mapping (SPM, Wellcome Department for Neuroimaging, London). Data analysis was performed using the general linear model (GLM).