Supplementary Material for

Long-Range-Projecting GABAergic Neurons Modulate Inhibition in Hippocampus and Entorhinal Cortex

Sarah Melzer, Magdalena Michael, Antonio Caputi, Marina Eliava, Elke C. Fuchs, Miles Whittington, Hannah Monyer*

*To whom correspondence should be addressed. E-mail: h.monyer@dkfz-heidelberg.de

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Materials and Methods

Generation of SOM\textsuperscript{Cre} mice

The targeting vector was the pBluescript vector containing a 10 kb BamHI fragment of the murine SOM gene, comprising the two exons of the SOM gene. The Cre recombinase cassette followed by a neomycin cassette flanked by two frt sites was introduced 30 bp upstream of the translational start codon of the SOM gene in exon 1. The targeting vector was linearized at the unique NotI site, and after electroporation of embryonic stem cells (R1), nine positive clones were identified by Southern blot analysis with a 5’-outside fragment as a probe, located directly upstream of the 5’ end of the targeting construct. One clone was injected into C57/BL6 blastocysts, and chimeric animals were crossed with C57/BL6 mice for germline transmission of the targeted allele. SOM\textsuperscript{Cre/neo} mice still containing the neomycin cassette were bred with flp-deleter mice (S1). FLP-mediated recombination results in the removal of frt-flanked fragments. The excision of the neomycin cassette was assessed by PCR and Southern blot analysis. After successful removal of the neomycin cassette, SOM\textsuperscript{Cre} mice were continuously bred with C57/BL6 to obtain a uniform genetic background with R26R reporter mice (S2). In the R26R mice, Cre-mediated recombination enables expression of \textit{lacZ}-encoded \(\beta\)-Gal.

Virus Injections

pAAV-double floxed-hChR2(H134R)-mCherry-WPRE-pA (AAV-DIO \textit{Chr2-mCherry}) and pAAV-double floxed-hChR2(H134R)-YFP-WPRE-pA (AAV-DIO \textit{ChR2-YFP}) vectors were obtained from Karl Deisseroth (S3). These vectors carry an inverted version of Channelrhodopsin2 fused to the fluorescent markers mCherry or YFP. In the presence of Cre recombinase, the cassette is inverted into the sense direction and the fused proteins are expressed from the EF1 promoter. AAV chimeric vectors (virions containing a 1:1 ratio of AAV1 and AAV2 capsid proteins with AAV2 ITRs) were generated as described (S4).

We injected 8 weeks old male SOM\textsuperscript{Cre}, GAD\textsuperscript{Cre} and PV\textsuperscript{Cre} mice. Animals were anesthetized with isoflurane, mounted in a stereotactic apparatus and kept under isoflurane anesthesia during surgery. For hippocampal injections a small craniotomy was made 2.4 mm posterior to bregma and 2.0 mm lateral to the midline. Virus was delivered through a small durotomy by a glass micropipette with a tip resistance of 2 to 4 MΩ. A volume of 0.5 µl virus (AAV DIO \textit{Chr2-mCherry}) was injected 1.6 mm below the cortical surface into the dorsal hippocampus and held in place for 7 min. The pipette was retracted 50 µm toward the surface, and held in place for another 2 min before complete retraction from the brain. For entorhinal cortex injections coordinates were 3.1 mm lateral from the midline, 0.2 mm anterior to the sinus sigmoideus and 1.7 mm below the cortical surface, and virus volume was 150 nl. The glass micropipette was lowered into the cortex with an antero-posterior angle of 9°. The scalp incision was sutured, and post-surgery analgesics were given to aid recovery (0.03 mg/kg KG Metamizol). All virus injections were performed according to the
guidelines for animal treatment (Regierungspräsidium Karlsruhe, license Az 35-9185.81 G-94/06).

**Retrograde tracer injection**

Eight weeks old wild type, GAD67EGFP \((S5)\) and SOMCre mice were injected with 0.03 µl Fluorogold 0.5% or 0.03 µl RedRetrobeads. Surgery and coordinates for FG injection were as described above. The pipette was held in place for 20 min before being retracted from the brain.

For RedRetrobeads injection into the medial septum a small craniotomy was made 1.0 mm posterior to bregma. RedRetrobeads was injected 0.6 mm lateral, 4.0 mm deep at an angle of 8°. The glass micropipette was held in place for 15 minutes. The pipette was retracted 50 µm towards the surface and held in place for another 5 minutes before complete retraction from the brain.

**Immunohistochemistry**

Mice were transcardially perfused with 4% paraformaldehyde (PFA). Coronal and sagittal sections were cut at 50 µm thickness on a vibratome and washed with phosphate buffered saline (PBS). Free-floating sections were permeabilized and blocked for 2 hrs with PBS containing 5% BSA and 0.2% Triton X-100. The incubation of the sections with primary antibodies was performed for 48 hrs at 4°C. For double-labeling experiments both primary antibodies were incubated at the same time. Sections were washed with PBS and incubated for 2 hrs with Cy3-conjugated secondary antibody (1:1000 Jackson ImmunoResearch, Newmarket, UK) or AlexaFluor488 secondary antibody (1:1000; Invitrogen Darmstadt, Germany). After repeated washing with PBS the sections were mounted on 0.1% gelatin-coated glass slides and mounted in Mowiol 40-88. Pictures were taken using a BX 51 microscope and a confocal laser-scanning microscope.

**Primary Antibodies**

Rabbit anti-somatostatin (Millipore, Temecula CA, 1:1000); anti-β-galactosidase (ICN, Costa Mesa, CA, 1:3000); rabbit anti-Ds-red (Clontech, Mountain View CA, 1:1000); mouse anti-parvalbumin (Millipore, Temecula CA, 1:3000); rabbit anti-fluorogold (Fluorochrome, LLC, Denver CO, 1:500); mouse anti-VGAT (Synaptic Systems, Goettingen, Germany, 1:1000); mouse anti-VGluT1 (Synaptic Systems, Goettingen, Germany, 1:100); rabbit anti-EGFP (Invitrogen, Darmstadt, Germany, 1:5000).

**Electronmicroscopy**

For hippocampal viral injections, two mice injected with AAV-DIO ChR2-mCherry were transcardially perfused with 4% PFA in phosphate buffer (PB) containing 0.05% glutaraldehyde (GA) at pH 7. Sections were incubated with rabbit anti-DsRed antibody and labeling was visualized using the standard avidin-biotin complex protocol and diaminobenzidine (DAB) chromogen. The DAB reaction product was silver-gold intensified (SGI-DAB), and the sections were processed according to conventional EM protocols. For entorhinal cortex viral injections,
four mice injected with AAV-DIO ChR2-YFP were analyzed. The staining followed the above protocol except that a rabbit polyclonal anti-EGFP antibody was used.

**Image analysis**
For quantification of retrogradely labeled neurons in entorhinal cortex, 50 μm thick sagittal sections were used from 10 hemispheres of 5 GAD67EGFP hippocampal FG injected mice. Cells were counted in 500 μm² areas from microscope pictures. VGAT⁺ and VGluT1⁺ varicosities were quantified in 50x50 μm optical sections in layer VI, layer III and layer I/II of the MEC as well as stratum lacunosum-moleculare of CA1 and CA3 and in stratum moleculare of the DG using 4 slices per hemisphere. Data are presented as mean ± SEM.

**Electrophysiology**
Whole-cell patch-clamp recordings were performed in 300 μm thick sections. Sagittal sections were used for most experiments performed in hippocampus-injected mice. However, for reconstructions, horizontal sections were used. Experiments in MEC-injected mice were performed mostly in horizontal slices. Morphology of target cells, however, was investigated in both sagittal and horizontal sections. Following viral injections, we waited at least 3 weeks before performing electrophysiological experiments. Mice were deeply anaesthetized with inhaled isoflurane and were subsequently transcardially perfused with ~30 ml ice-cold sucrose solution containing (in mM) 252 sucrose, 24 NaHCO₃, 1.25 NaH₂PO₄, 3 KCl, 2 MgSO₄, 10 glucose and 0.2 CaCl₂, oxygenated with carbogen gas (95% O₂/5% CO₂, pH 7.4). Sections were cut in ice-cold oxygenated sucrose solution, followed by incubation in oxygenated extracellular solution containing (in mM) 12.5 NaCl, 25 NaHCO₃, 1.5 NaH₂PO₄, 2.5 KCl, 2 CaCl₂, 1 MgCl₂ and 25 glucose. Whole-cell patch-clamp recordings were performed at 30 to 32°C using pipettes pulled from borosilicate glass capillaries with resistances of 3 to 5 MΩ. Liquid junction potentials were not corrected. Sections were continuously perfused with oxygenated extracellular solution. CNQX (10 μM), D-AP5 (50 μM) and gabazine (10 μM; SR 95531 hydrobromide) were added in some cases. Cells and mCherry fluorescence were visualized by an upright microscope equipped with infrared-differential interference contrast and standard epifluorescence. Action potentials in long-range projections were evoked by 5 ms laser pulses (473 nm) with maximal power. PSCs and reversal potentials were measured using Cs⁺-based intracellular solution containing (in mM) 126 Cs⁺-gluconate, 4 CsCl, 10 Heps, 10 phosphocreatine, 4 Mg-ATP, 0.3 GTP and 2.5 QX-314, pH 7.3 adjusted with CsOH. Firing patterns were recorded with K⁺-based, high Cl⁻ intracellular solution containing (in mM) 127.5 KCl, 11 EGTA, 10 Heps, 1 CaCl₂, 2 MgCl₂, 2 Mg-ATP and 0.3 GTP, pH 7.3 adjusted with KOH and PSCs were measured at -70 mV. Firing patterns were analyzed in current-clamp mode applying 1 s current pulses with 3 s intersweep interval, starting at -50 pA and gradually increasing the amplitude in 20 pA steps until maximal firing
frequency was reached. Firing patterns were analyzed off-line using Igor Pro and Pulse.

The effect of long-range axon activation was investigated using an intracellular solution that contained (in mM) 130 K-gluconate, 10 Na-gluconate, 10 Hepes, 10 phosphocreatine, 4 NaCl, 4 Mg-ATP, 0.3 GTP, pH 7.2 adjusted with KOH. Target cells were depolarized to sub- or suprathreshold potentials and 20 sweeps à 5 s with 8 or 40 Hz stimulation of long-range projections during the third second were recorded. All cells that were tested using the 40 Hz stimulation protocol were also tested for modification of subthreshold and/or suprathreshold activity following 8 Hz stimulation. Data were analyzed using Matlab. Spectrograms were generated averaging over 20 sweeps obtained from single cells. For power graph, 20 sweeps of every cell were filtered at 7-9 or 39-41 Hz, power was calculated and normalized to the first second of recordings.

Series resistance was continuously monitored in voltage-clamp mode during PSC recordings measuring peak currents in response to small hyperpolarising pulses. Series resistances of 37 MΩ were accepted for analyzing PSCs. Stimulus delivery and data acquisition was performed using Pulse software. Signals were filtered at 3 kHz, sampled at 10 kHz.

Data are given as mean ± SEM except for analysis of firing patterns, where standard deviations are given. P-values were calculated using the matched-pair t-test.

Biocytin filling and reconstruction
For morphological analysis of electrophysiologically identified target cells, we filled whole-cell patch-clamped neurons for up to 30 min with biocytin (1 to 4 mg/ml, dissolved in intracellular solution). Subsequently, sections were fixed overnight in 4% paraformaldehyde, washed and quenched in 1% H₂O₂ for 5 min. After renewed washing, sections were permeabilized in PBS with 1% Triton X-100 for 1 hr. Subsequently sections were incubated with avidin-biotin-horseradishperoxidase complex in PBS for 2 hrs at room temperature. Following washing in PBS, sections were developed with DAB and mounted in Mowiol. Labeled cells were reconstructed using the Neurolucida tracing program.

Extracellular recordings
Extracellular recordings were performed in acute brain slices from male GAD<sup>Cre</sup> and SOM<sup>Cre</sup> injected and C57BL/6 control mice at an age of 3-7 months at least 3 weeks after injection. Mice were anaesthetized with inhaled isoflurane, immediately followed by an intramuscular injection of ketamine (≥ 100 mg/kg) and xylazine (≥ 10 mg/kg). Mice were perfused intracardially with ~50 ml of sucrose modified artificial cerebrospinal fluid (sACSF). The brain was removed and submerged in ice-cold sACSF during the dissection procedure. Hippocampal saggital slices (450 μm) were cut in ice-cold sACSF oxygenated with carbogen gas (95% O₂/5% CO₂) using a microtome and transferred to a holding chamber at RT at the interface between oxygenated ACSF and warm, moist carbogen gas. Slices were permitted to equilibrate for at least 45 min before being transferred to the recording chamber and 15 min again after transfer before
recordings were made. During recordings, slices were maintained at 30-34°C at the interface between a continuous perfusion of ACSF (perfusion rate: ~1.5 ml/min) and humidified carbogen gas. Pipettes were pulled from borosilicate glass capillaries with resistances in the range of 2–5 MΩ. Pipettes were filled with ACSF. Extracellular recordings were performed in hippocampal CA1 area. Theta oscillations were induced by bath application of DHPG (25-200 μM) followed by NBQX (5-20 μM) as soon as gamma oscillations were established. Oscillations were recorded for 3 seconds taking 10 sweeps per slice. 5 ms laser-light pulses were applied at 8 or 40 Hz during the 2nd second of every sweep. All 8 and 40 Hz recordings were performed in the same slices. Recordings were analyzed with Matlab. Power graph was achieved filtering every trace at 3-7, 35-39 or 41-45 Hz, calculating power, normalising to the first second of recordings and averaging all sweeps of every slice. Data are given as mean ± SEM. P-values were calculated using the matched-pair t-test.

References

S1. C. I. Rodriguez et al., High-efficiency deleter mice show that FLPe is an alternative to Cre-loxP. Nat Genet 25, 139 (Jun, 2000).
S2. P. Soriano, Generalized lacZ expression with the ROSA26 Cre reporter strain. Nat Genet 21, 70 (Jan, 1999).
S5. N. Tamamaki et al., Green fluorescent protein expression and colocalization with calretinin, parvalbumin, and somatostatin in the GAD67-GFP knock-in mouse. J Comp Neurol 467, 60 (Dec 1, 2003).
**Fig. S1.** Retrogradely labeled cells in the dorsal hippocampus after FG injection into the MEC. (A) FG injection site in the MEC. Left: schematic illustration of a sagittal mouse brain section indicating the location of the injection site. Right: fluorescence image subsequent to FG injection into the MEC. Scale bar, 200 µm. (B) Fluorescence images of retrogradely labeled cells in stratum oriens of CA1. Three cell types could be detected: FG⁺/SOM⁺ (arrow), SOM⁺ (filled arrowhead) and FG⁺ neurons (triangles). Scale bar, 30 µm.
Fig. S2. Generation of mice expressing Cre recombinase in SOM* interneurons and correct fluorescent labeling following injection of AAV DIO ChR2-mCherry into the dorsal hippocampus of SOM^{Cre} mice. (A) Generation of the SOM^{Cre} mouse via knock-in approach. Schematic representation of gene segments of the wild-type (WT) SOM allele, the targeted SOM^{Cre/neo} allele and the SOM^{Cre} allele subsequent to breeding with flip-deleter mice. Grey boxes indicate exons, solid circles indicate the 5’ and 3’ end. Positions of EcoRV (E) and BamHI (B) restriction sites are indicated. The black arrowheads stand for the two frt sites flanking the neomycin selection cassette (neo). The location of PCR fragments used as probes (a, outside 5’ probe; b, neo probe) for the Southern blot analysis.
are indicated as black bars. (B) Southern blot analysis of genomic DNA obtained from WT and SOM\textsuperscript{Cre/neo} ES cells (left) with the 5' probe demonstrating the presence of a 5.8 kb fragment specific for the modified allele (the >10 kb fragment derives from the WT allele). EcoRV restricted genomic DNA from SOM\textsuperscript{Cre/neo} and SOM\textsuperscript{Cre} mice (right) hybridized with the neo probe showed a 1.2 kb fragment that indicates the presence of the neo cassette in SOM\textsuperscript{Cre/neo} mice and the absence in SOM\textsuperscript{Cre} mice. (C) Pattern of beta-galactosidase staining in a SOM\textsuperscript{Cre/R26R}\textsuperscript{neom} mouse hippocampal slice reveals Cre expression in putative SOM\textsuperscript{+} cells. Scale bar, 200 µm. (D) MCherry labeling of SOM\textsuperscript{+} cells in a sagittal section of the dorsal hippocampus. Cell bodies of labeled SOM\textsuperscript{+} cells can be detected mainly in stratum oriens of CA1 and in the hilus of the DG. Axonal arborizations of labeled SOM\textsuperscript{+} O-LM cells branch highly in stratum lacunosum-moleculare. Scale bar, 200 µm. (E) Schematic drawing showing the typical location of a CA1 SOM\textsuperscript{+} cell with cell body in stratum oriens and axonal arbor in stratum lacunosum-moleculare (red). A pyramidal cell is shown in black. Abbreviations: or, stratum oriens; pyr, stratum pyramidal; rad, stratum radiatum; lm, stratum lacunosum-moleculare; mo, stratum moleculare; gr, stratum granulare; h, hilus.
Fig. S3. Long-range projecting hippocampal SOM$^+$ neurons target the striatum. Left panel shows a lower magnification with digitally encoded mCherry$^+$ long-range projecting axons. Right panel shows a higher magnification of the area indicated by the rectangle. Scale bar, 100 µm.
Fig. S4. Distinct populations of hippocampal SOM+ cells project to the MEC and the medial septum (MS). FG injection into the MEC and RedRetrobeads (RR) injection into the medial septum (left) leads to retrograde labeling of non-overlapping populations of SOM+ cells in the dorsal hippocampus (right). Cells were analyzed in stratum oriens of CA1. Of 96 RR-labeled cells none was co-labeled with FG (n = 5 hemispheres of 4 mice). Scale bar, 5 µm.
**Fig. S5.** Target cells (red dots) of hippocampal long-range projecting GABAergic neurons are located at the transition zone between LI and LII. Schematic drawing of lateral, intermediate and medial sagittal sections (upper row) and higher magnifications of the corresponding MEC (lower row) indicating the location of detected target cells close to the indicated transition zone between LI and LII.
### Fig. S6

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<th>others (range, n=10 cells)</th>
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**Graphical Data**

- **type I neurons**
  - Interneurons
  - FS
  - Stellate cell
**Fig. S6.** Target cells of hippocampal long-range projecting GABAergic neurons comprise different types of neurons. Table lists electrophysiological properties of indicated target cells: the most frequently found cell type (type I), a fast spiking interneuron (FS) and other interneurons. Firing patterns of a type I neuron, FS neuron and two other interneurons, as well as of a stellate cell are shown below. Examples for different cell types illustrate a trace at maximal firing frequency (left), just above threshold of action potential generation (middle) and upon hyperpolarization (-50 pA) (right). An enlargement of an individual action potential (first action potential from middle trace) is shown on the far right. Scale bars, 200 ms, 20 mV (left and middle), 200 ms, 10 mV (right), 50 ms, 10 mV (far right).
Fig. S7. Long-range hippocampal GAD$^+$ neurons target the MEC as revealed by AAV DIO ChR2-mCherry injections into the dorsal hippocampus of GAD$^{Cre}$ mice. (A) Fluorescent labeling following injection into CA1 of the dorsal hippocampus. mCherry is expressed by several subtypes of interneurons e.g. O-LM cells and basket cells. The typical arborization of O-LM cell axons in stratum lacunosum-moleculare and the baskets of basket cells in pyramidal cell layer are clearly visible. Scale bar, 200 µm. (B) GABAergic long-range projections in the striatum were also observed in GAD$^{Cre}$ mice (n = 7 mice). Left: overview with digital encoding of mCherry-labeled axons (red). Right: higher magnification of the indicated area. Scale bar, 200 µm. (C) GABAergic long-range projections in the MEC of a GAD$^{Cre}$ mouse. Expression of mCherry in hippocampal GAD$^+$ cells reveals dense innervation of all MEC layers. Projections indicated by rectangles are shown as higher magnification in the right panels. Scale bar, 150 µm. (D) VGAT and VGluT1 in the MEC of hippocampal injected GAD$^{Cre}$ mice. High resolution confocal images show an optical section (50x50 µm, scale bar, 5 µm) of VGAT and VGluT1 stainings with corresponding higher magnification on the right. VGAT$^+/m$Cherry$^+$ varicosities (arrows) were counted in deep layer VI, layer III and superficial layer I/II. Bar histogram (right) represents average number of VGAT$^+/m$Cherry$^+$ varicosities ± SEM (60 optical sections from 5 hemispheres of 4 mice). Most VGAT$^+/m$Cherry$^+$ varicosities were found in layer III. Only few VGAT$^+/m$Cherry$^+$ varicosities were detected in layer VI. We did not detect VGluT1 in the viral labeled axons. (E) Inhibitory PSCs recorded in a target cell at indicated holding potentials. Scale bar, 20 ms, 50 pA. (F) Firing pattern and reconstruction of a representative postsynaptic MEC interneuron. Scale bars, 200 ms, 20 mV (left and middle traces), 200 ms, 10 mV (right trace), 50 ms, 10 mV (far right enlargement of first action potential), 100 µM (reconstruction).
Fig. S8. VGAT and VGlut1 in the hippocampus of MEC AAV DIO ChR2-mCherry injected GAD<sup>Cre</sup> mice. High resolution confocal images show an optical section (50x50 μm, scale bar, 5 μm) of VGAT and VGlut1 stainings with corresponding higher magnification on the right. VGAT+/mCherry+ varicosities (arrows) were found and counted in stratum lacunosum-moleculare of CA1 and CA3 and stratum molecule of the DG (48 optical sections from 4 hemispheres of 3 mice). Bar histogram represents average number of VGAT+/mCherry+ varicosities ± SEM. We did not detect VGlut1 in the viral labeled axons.
### Fig. S9

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**Fig. S9.** Target cells of MEC long-range projecting GABAergic neurons comprise different types of interneurons. Table lists electrophysiological properties of indicated target cells: the most frequently found cell types (type I and type II) and other interneurons. Firing patterns of a type I neuron, a type II neuron and three other interneurons are shown below. Examples for different cell types illustrate a trace at maximal firing frequency (left), just above threshold of action potential generation (middle) and upon hyperpolarization (-50 pA) (right). An enlargement of an individual action potential (first action potential from middle trace) is shown on the far right. Scale bars, 200 ms, 20 mV (left and middle), 200 ms, 10 mV (right), 50 ms, 10 mV (far right).
Fig. S10. Entorhinal PV⁺ neurons form functional synapses on hippocampal interneurons. (A) Retrograde labeling of a PV/EGFP⁺ cell in the MEC in GAD67EGFP mice after FG-injection into the hippocampus. Scale bar, 20 μm. Of note, we could not detect any retrograde labeling in calretinin⁺, calbindin⁺, 5-
HT3\textsubscript{A} serotonin receptor\textsuperscript{+}, neuronal nitric oxide synthase\textsuperscript{+} or SOM\textsuperscript{+} neurons. (B) Fluorescent labeling following injection of AAV DIO ChR2-mCherry into the MEC of PV\textsuperscript{Cre} mice (left; scale bar, 200 \textmu m) and higher magnifications of labeled axons in stratum lacunosum-moleculare of CA1 (middle), and stratum moleculare of the DG (right; scale bar, 40 \textmu m). (C) Inhibitory PSCs recorded in a target cell in stratum lacunosum-moleculare in a horizontal slice of the dorsal hippocampus at -70 mV holding potential with high chloride intracellular solution and CNQX in the extracellular solution. The inhibitory response was blocked by gabazine. Scale bar, 20 ms, 50 pA. (D) Firing pattern and reconstruction of a representative postsynaptic hippocampal interneuron. Scale bars, 200 ms, 20 mV (left and middle traces), 200 ms, 10 mV (right trace), 50 ms, 10 mV (far right enlargement of first action potential), 200 \textmu M (reconstruction). Abbreviations: pyr, stratum pyramidale; rad, stratum radiatum; lm, stratum lacunosum-moleculare.
**Fig. S11.** Activation of GABAergic long-range projections at 8 but not at 40 Hz affects rhythmic activity at the single cell and network level in target areas. (A-G) MEC target cells in hippocampal AAV DIO ChR2-mCherry injected SOM<sup>Cre</sup> mice (left) and hippocampal target cells in MEC AAV DIO ChR2-mCherry injected GAD<sup>Cre</sup> mice (right) were patched and depolarized to induce sub- or suprathreshold activity. Long-range projections were stimulated at 8 Hz (red ticks) or 40 Hz (red bar). (A) Firing rates of target neurons before (averaged over 2 seconds), during (averaged over 1 second) and after (averaged over 2 seconds) 8 Hz stimulation showed no significant changes in overall firing rate. (B) Spectrograms showing that activation of long-range projecting axons at 40 Hz did not entrain target cells to fire rhythmically at gamma range frequency. Note different scales of color codes for theta (lower panel) and gamma (upper panel) band activity. (D-G) Enhanced subthreshold oscillations in target cells upon laser stimulation. Representative unfiltered (D) and filtered (7-9 Hz) (E) traces showing subthreshold oscillations. (F) Representative spectrograms showing that activation of long-range projecting axons entrains target cell to oscillate at theta range frequency. (G) Increase in theta power (7-9 Hz) in target cells during laser stimulation. (H) Averaged power of DHPG/NBQX-induced CA1 network oscillations during 40 Hz stimulation of long-range projections, filtered at indicated frequencies and normalized to power before stimulation, showed no differences between wildtype (black) and GAD<sup>Cre</sup> injected mice (red). Scale bars (D and E), 1s, 2 mV (unfiltered traces), 0.5 mV (filtered traces).