Supplementary Figure 1

Miniature microdrive, spike sorting and sleep stage detection.

**a**, A movable recording probe with 8-tetrodes (32-channels). It weighs ~1g. **b**, A mouse implanted with 8 tetrodes in the MnR and 4 tetrodes in the hippocampal CA1. **c**, An example of four well-isolated units and representative spike-waveforms recorded from one tetrode. Each dot represents one spike waveform. **d**, An example of the CA1 local field potential (LFP) recorded during active-awake and immobility/sleep states. All the data analyzed for MnR activity with respect to ripples during immobility were collected when mice were in the cardboard box filled with cotton fiber material (Nestlets™), i.e., “bed”, where they exclusively slept. Typically as soon as mice became immobile in their beds, a series of ripple activity and sleep-like LFPs were detected in the CA1. Outside of the bed, the mice walked around, drank water, ate food, and displayed little immobility, accompanied by no sleep. **e**, Power spectrogram of the CA1 LFP (as shown in d). Notice strong power levels in the theta band (6–10 Hz) during awake and in the delta band (1–4 Hz) during immobility/sleep. Theta/delta ratio was calculated and smoothed with a Gaussian filter in Matlab (top panel).
Supplementary Figure 2

Identification of MnR putative serotoninergic neurons and classification of non-serotoninergic type I and II neurons.

a,b. Electrodes placements in the hippocampal CA1 (a) and the MnR (b) from the dual-site recording mice (n = 6). c. Representative spike-trains of two putative serotoninergic neurons. Note that neuron 1 displayed tonic activity only, while neuron 2 displayed both tonic and high-frequency firing (*). d. Inter-spike interval (ISI) histograms and representative spike waveforms of the neurons shown in c (5000 spikes overlapped; spike width, 1 ms). Arrows indicate the peaks of ISI that were used for neuron identification as shown in f. Seventy-nine percent (23/29) of the classified putative serotonin neurons displayed tonic activity only, while the other 21% displayed both tonic and high-frequency activity. e. Firing rate histograms of the two neurons shown in c,d upon i.p. injection of the serotonin 1A receptor agonist 8-OH-DPAT (0.2 mg/kg; arrows indicate the injection time point, and the mice were freely moving before and after injection). Effects of 8-OH-DPAT were examined on 12 putative serotonergic neurons of freely-moving mice, since serotonergic neurons are known to be inhibited by the autoreceptor agonist. The most of them (11/12) were inhibited for at least 10 min: either completely (4/12) or partially (7/12), strengthening the validity of the ISI procedure in determining serotonergic neurons. f. Log-log plot of the mean firing frequency vs. latency of ISI peak for all the MnR neurons recorded during immobility. g. Mean firing-rate changes of individual type I and type II neurons prior to ripple events (left panel). A histogram showing a distribution pattern of the type I and type II neurons based on firing-rate changes prior to ripple (right panel). Firing-rate change was calculated 1 s prior to ripple compared against a 2-s baseline activity (between 2 and 4 s prior to ripple). A ~20% or lower in frequency change was classified as type I; and the rest of the ripple-correlated neurons were classified as type II.
Supplementary Figure 3

Ripple correlated MnR neural activity during immobility and feeding

**a.** Firing rates of the 3 types of MnR neurons plotted in relation to the ripple peak during immobile state, most likely asleep (top panels) and during feeding rodent chow or rice (bottom panels).

**b.** Firing rates of individual putative serotonin (5-HT; n = 12), type I (n = 17) and type II (n = 19) neurons during immobility (top panels) and feeding (bottom panels). Neurons were recorded in consecutive sessions and are arranged in the same order for the top and bottom panels. Colour bars represent z-scored firing-frequency.
**Supplementary Figure 4**

MnR type I neuron firing properties and its relation to ripple events.

**a.** Histograms (bin = 10 ms) showing probability of inter-spike interval (ISI) of 3 representative type I neurons. ISIs varied extensively among type I neurons. Inserts: histograms with a 1-ms bin. **b.** Distribution of type I neurons based on their ISI ranges. **c.** Distribution of type I neurons based on their mean instant firing rates. **d,e.** Mean auto-correlations (solid line; s.e.m.: dashed line) of the MnR type I neurons (d) and ripple events (e). The inserts of panels d,e show respective analyses in a finer time resolution.
Supplementary Figure 5

Coordinated activity between MnR 5-HT and type I neurons during immobility.

a,b, Rate histograms (a) and cross-correlation histogram (b) of two simultaneously recorded MnR neurons. Representative tetrode-recorded spike waveforms of the 2 neurons are shown in a (inserted panels, 1000 spikes overlapped; spike width, 1 ms). c, Z-scored cross-correlations for all the simultaneously recorded 5-HT and type I neuron pairs (n = 35 pairs). Type I neurons were used as the reference for cross-correlation analyses in b and c.
Supplementary Figure 6

Ripple cluster termination coincides with high-rate and synchronous firing of MnR type I neurons.

a, Representative hippocampal CA1 LFP and the filtered ripple activity. Ripples tended to occur in clusters (#1–5), which were defined as 3 or more consecutive ripple events occurring above 1 Hz. b, During immobility, 58.1 ± 1.7% (mean ± s.e.m.; n = 19) of ripple events occurred in clusters. c, e, Mean firing rates (solid line; s.e.m.: dashed line) of type I neurons in relation to the onset (blue lines) and offset (red lines) of ripple clusters during the high-, mid-, low-rate (c), and high-, mid- low-synchrony (e) states. For definition of the above six categories of firing states, see Online Methods. Inserts: mean firing rates and s.e.m. of type I neurons shown in a finer time resolution. d, f, Mean peak frequencies and s.e.m. of the type I neurons immediately after the onset and offset of ripple clusters. Peak frequency was defined as the maximum frequency within 100 ms (bin = 10 ms) after the onset or offset of ripple clusters. P values were derived with Wilcoxon signed rank tests (n = 32 for d and n = 26 for f; Type I neurons with mean frequency above 1 Hz were used for analyses). n.s., P > 0.05; * P < 0.05; ***P ≤ 0.001.
Supplementary Figure 7

Characterization of hippocampal CA1 neurons upon MnR photostimulation.

a, A plot of the mean firing frequency vs. the action potential (AP) width for all the recorded CA1 neurons. Blue and red dots represent individual inhibited and excited CA1 neurons, respectively, upon MnR photostimulation. b, Response latencies of the inhibited (top) and excited (bottom) CA1 neurons upon MnR photostimulation. Response latency was defined as the latency of the first bin from at least 3 consecutive bins (peri-event histogram bin = 2 ms) that exceed the z-score of 1.96.
Supplementary Figure 8

Optical fiber placements for the mice used in the fear conditioning experiment.

The tips of optic fibers are shown by black rectangles, and just below, red colour-filled rectangles indicate zones (0.5 mm) most powerfully affected by photostimulation. ChR2-group mice (n = 11) and EYFP-group control mice (n = 10). One of the control mice was found at the level of bregma –3.88 mm, and its placement is not shown here.
Supplementary Figure 9

Addressing issues involving MnR photostimulation.

a, Mean ripple-event frequencies (error bars: s.e.m.) upon MnR photostimulation delivered on two different interval schedules. We conducted additional experiments to verify that the MnR photostimulation on a fixed-interval schedule of 2 s (FI2; 2-pulse train per 2 s) suppresses ripples activity. Using a group of 5 mice, we compared two schedules of photostimulation: One was the same scheduled described in Fig. 4 a–d, and the mice received photostimulation on a variable interval schedule of 10 s (VI10; ranged between 5 and 15 s). The other was essentially the same as the one used for disrupting ripple after fear conditioning; the mice received photostimulation on a FI2 for 3–4 hours. Compared to photostimulation on the VI10, FI2 photostimulation suppressed ripple activity with a shorter duration, followed by rebound activation (1–2 sec). These results confirm that MnR photostimulation on a FI2 readily suppress ripple activity with the caveat that this frequent suppression schedule triggers a compensatory process. b, Percentages of time spent on slow-wave sleep (SWS) and rapid-eye movement sleep (REM) with/without photostimulation. Sleep stages were determined by hippocampal LFPs, and the amounts of SWS and REM were compared between the session with the FI2 photostimulation and a session with no photostimulation. The photostimulation condition did not alter the amounts of SWS sleep, but slightly increased REM (unpaired t-tests; n = 5). c, Representative coronal sections of glial fibrillary acidic protein (GFAP) staining. GFAP expressions were compared between mice (n = 3) that did not receive photostimulation and mice (n = 3) that received MnR photostimulation (2 pulses with 3-ms pulse duration) on FI2 during immobility over the course of 4 hours (the same procedure as the fear conditioning mice as shown in Fig. 7a). Scale bars, 0.2 mm. d, Quantification of the GFAP fluorescence intensity. Fluorescence intensities were measured in areas below optical fiber placements as shown in the squares, and did not differ between the conditions with/without photostimulation ($2_{\text{group}} \times 3_{\text{section}}$ ANOVA: $F_{1, 4} = 0.70$, $P = 0.45$; n = 3 per group).
Supplementary Figure 10

SWS/REM cyclic sleeping pattern during MnR photostimulation session.

a. Representative power spectrogram of the CA1 LFP recorded during a 20-min sleep session in a mouse that received no photostimulation. Notice strong power levels in the theta band (6–10 Hz) during REM sleep and in the delta band (1–4 Hz) during SWS. Theta / delta ratio was calculated and smoothed with a Gaussian filter in Matlab (top panel). b. Power spectrogram of the CA1 LFP recorded from the same mouse during MnR photostimulation session (2-pulse train per 2 s; pulse width, 3 ms; 16 mW).