

Supplemental methods section:

Electrophysiology *in vitro*: The pups underwent HT-induced, or bicarbonate-induced seizures, or the HT+CO₂-treatment at P9-P10. After 5-11 d, the animals were anesthetized, decapitated and the brains removed as described previously¹. Horizontal hippocampal slices were cut at 300 µm thickness in an ice-cold solution containing (in mM) NaCl 87, sucrose 75, NaHCO₃ 26, KCl 2.5, NaH₂PO₄ 1.25, CaCl₂ 0.5, MgSO₄ 7, glucose 25, and saturated with 95% O₂/5% CO₂ and heated to 35 °C for 30 min. All recordings were done at room temperature in a physiological solution containing (in mM) NaCl 119, NaHCO₃ 26, KCl 2.5, NaH₂PO₄ 1, CaCl₂ 2.5, MgSO₄ 1.3, glucose 10 and equilibrated with 95% O₂ and 5% CO₂. The recording chamber was mounted on an Olympus microscope equipped for IR-DIC microscopy. Whole-cell recording electrodes were filled with (in mM): K-gluconate 135, Hepes 10, Mg-ATP 2, KCl 20, EGTA 0.2; pH was adjusted to 7.2 using KOH. Excitatory and inhibitory synaptic responses were blocked with 1 µM 2,3-Dioxo-6-nitro-1,2,3,4-tetrahydrobenzo[f]quinoxaline-7-sulfonamide (NBQX) and 1 µM 6-imino-3-(4-methoxyphenyl)-1(6*H*)-pyridazinebutanoic acid hydrobromide (SR 95531; Gabazine) (Tocris Cookson). After the whole-cell configuration was established, we monitored holding current and series resistance for at least 5 minutes before switching to current-clamp mode. Holding potential was -60 mV (**Fig 3a₁,b₁**) or -55mV (**Fig 3a₂,b₂**).

Western blotting. Rats were decapitated 1, 2, 3, 5, 10 and 120 days after induction of HT-seizures or the HT+CO₂ treatment, and 5 days after bicarbonate seizures or the bicarbonate+CO₂ treatment. The hippocampi were rapidly dissected out and homogenized in 200 µl lysis buffer containing 0.3 M sucrose, 10 mM HEPES, 1 mM EDTA, pH 6.8. The protein concentrations were determined using D_C Protein Assay kit (Bio-Rad). Protein samples (50 µg) were separated using 7.5 % sodium dodecyl sulphate-polyacrylamide electrophoresis gel and transferred onto Hybond ECL nitrocellulose membrane (Amersham, Pharmacia Biotech). Western blot analysis was performed in an experiment-blind manner using a rabbit antibody raised against the C terminus of the rat CB1 protein². Blots were probed with the antibody at 1:5000 dilution and developed using ECL-plus (Amersham, Pharmacia Biotech, UK) on x-ray films. Optical densities of the bands were analyzed with the AIDA imaging software (Raytest).

Reference List

1. Schmitz, D., Mellor, J., Breustedt, J., & Nicoll, R. A. Presynaptic kainate receptors impart an associative property to hippocampal mossy fiber long-term potentiation. *Nat. Neurosci.* **6**, 1058-1063 (2003).
2. Hajos, N. *et al.* Cannabinoids inhibit hippocampal GABAergic transmission and network oscillations. *Eur. J Neurosci.* **12**, 3239-3249 (2000).