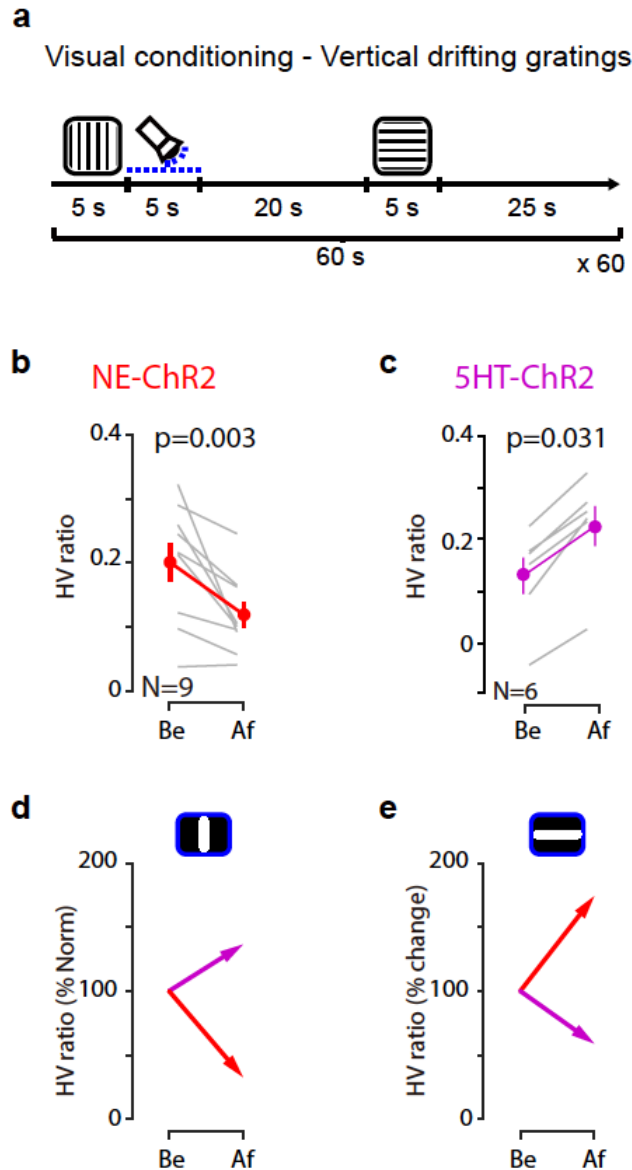
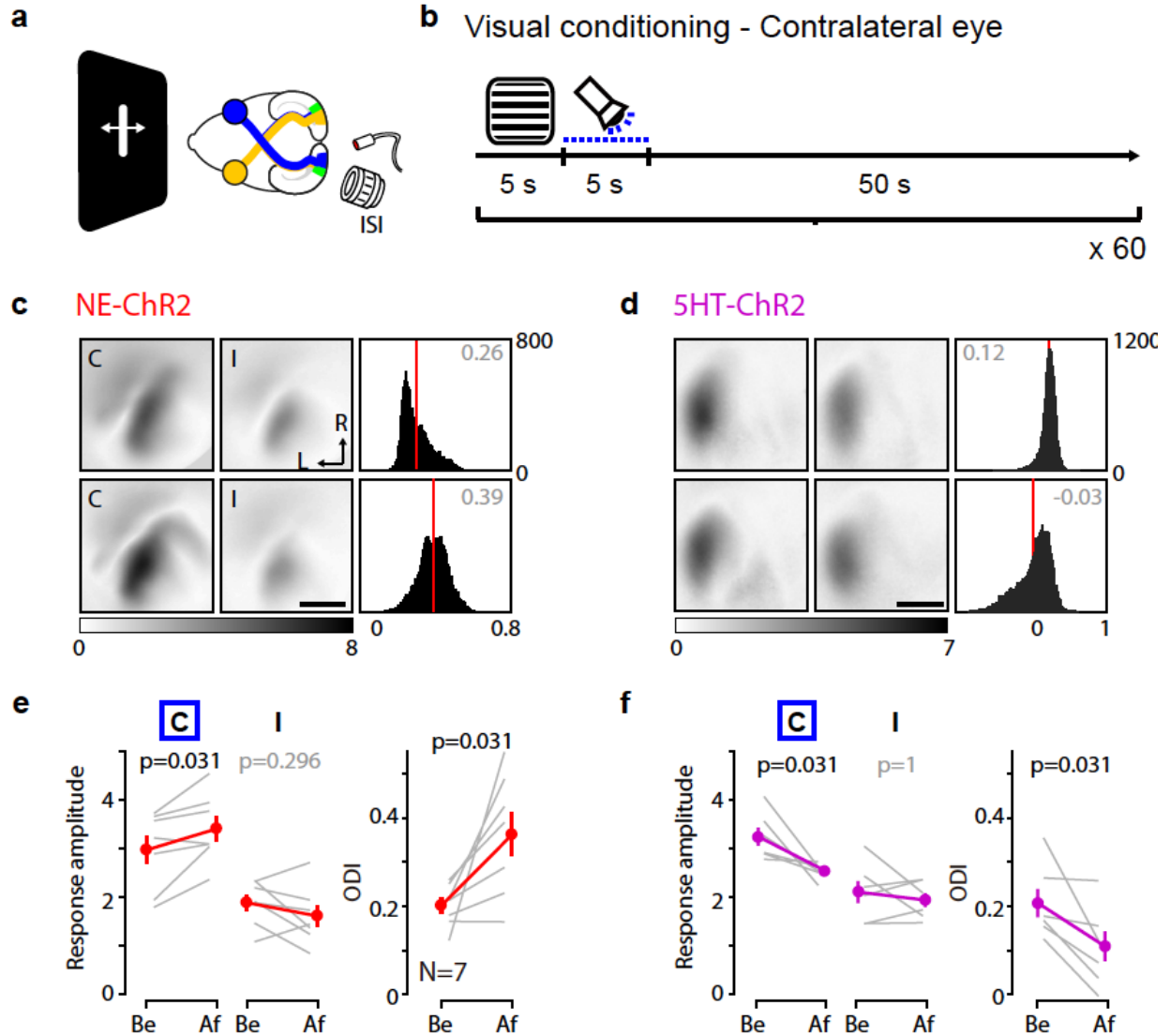


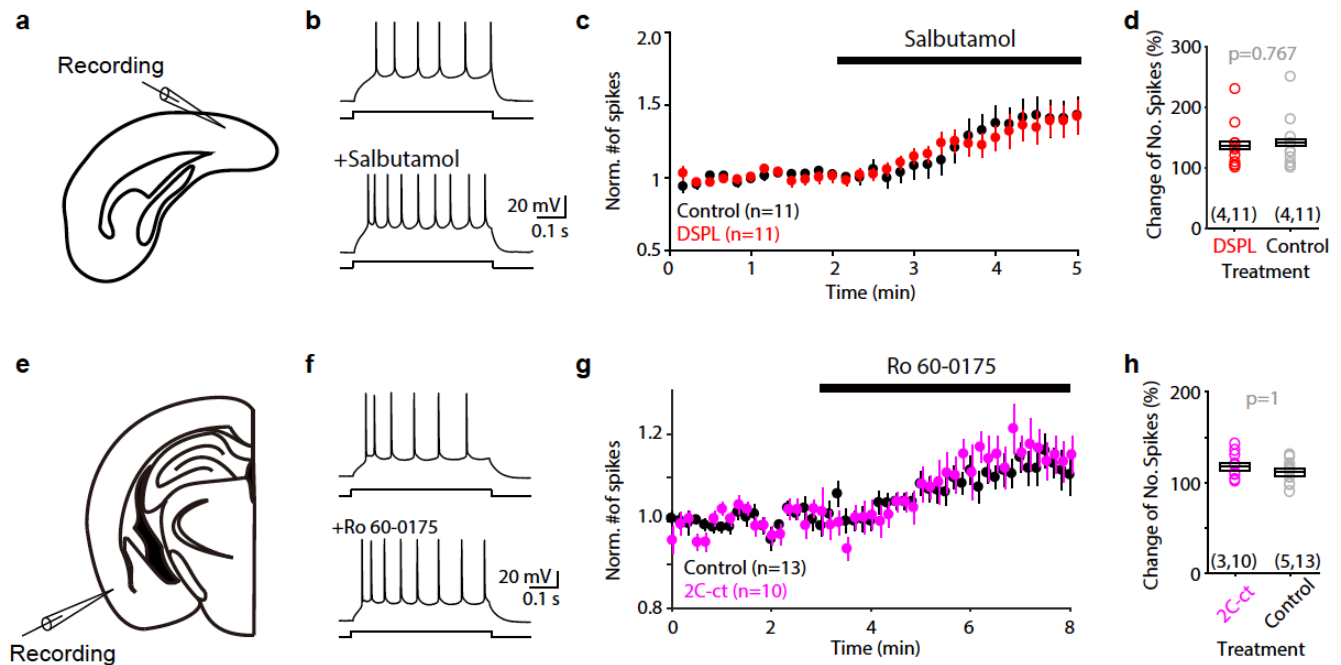


Supplementary Figure 1. Optogenetical reinforcement of V1 responses to vertical drifting gratings.

a Schematics of the conditioning protocol. Imaging of visual cortical responses to vertical and (V) horizontal (H) drifting gratings was performed as in figure 1, but with optogenetical stimulation paired to the vertical drifting gratings. **b-c**, Changes in the relative H and V responses to H (HV ratio) recorded before (Be) and after (Af) vertical conditioning in NE-ChR2 mice (**b**) and in 5HT-ChR2 mice (**c**). Thin grey lines: individual mice; thick color lines and symbols: average $\pm$ s.e.m. **d-e**, Summary of bidirectional changes in the H/V ratio optogenetical reinforcement of V1 responses to drifting gratings of vertical (**d**) or horizontal (**e**) orientation. In each panel the arrows indicate the average H/V changes (normalized to initial (Be) values) in NE-ChR2 mice (red) and 5HT-ChR2 mice (magenta).

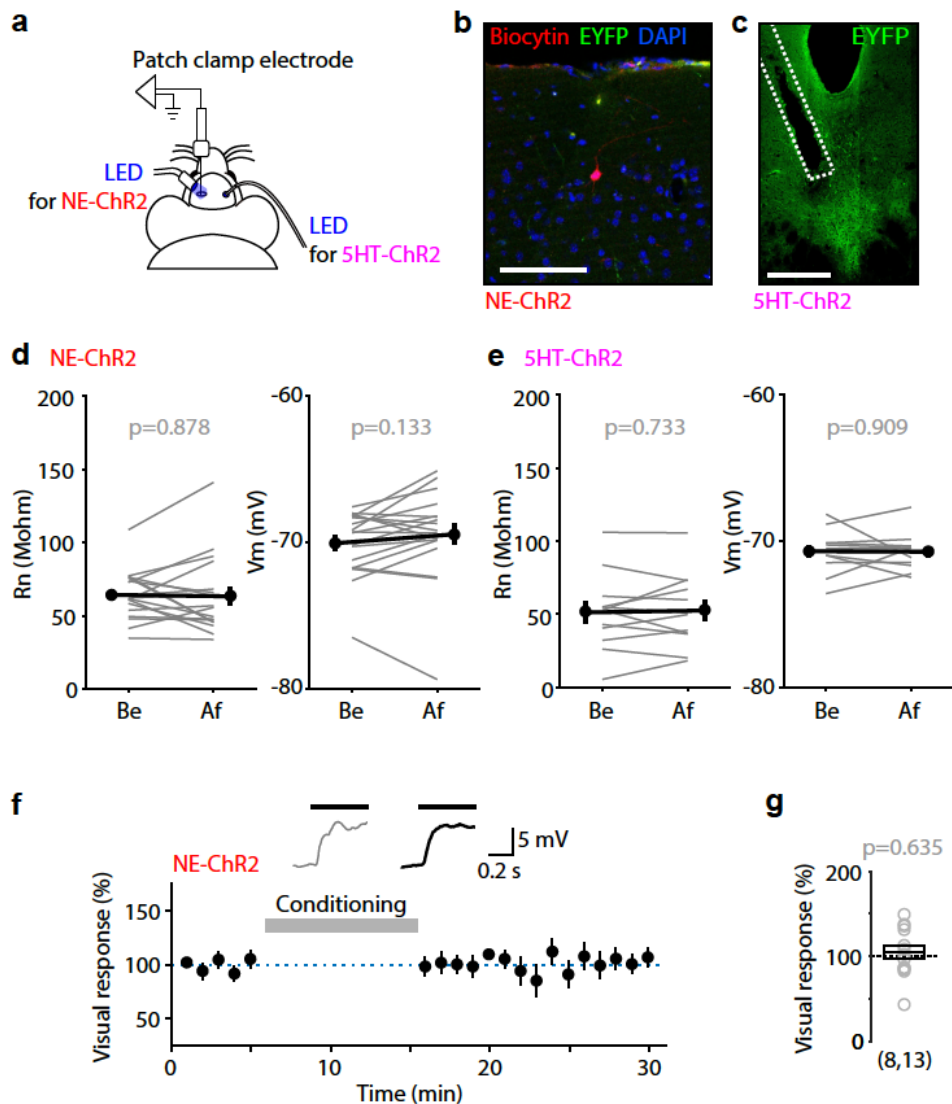


Supplementary Figure 2. Test of input specificity: conditioning one eye does not affect responses of the non-conditioned eye. **a,b** Experimental schematics. **a**, visual responses were imaged in the binocular region (green) of the V1. **b**, Conditioning protocol: the right eye was stimulated 60 times (1 per minute) with horizontal drifting gratings followed by the photoactivation to induce the release of norepinephrine. **c,d**, Example experiments in NE-ChR2 (**c**) and in 5HT-ChR2 mice (**d**). Left: visual cortical responses evoked by the eye contralateral [C] or ipsilateral [I] to the recorded hemisphere. Right: histogram of the ocular dominance index (ODI) illustrated in the number of pixels (x-axis: ODI, y-axis: number of pixels). **e,f**, Summary of the changes induced in NE-ChR2 (**e**) and in 5HT-ChR2 mice (**f**). The panels show the changes in response amplitude evoked by the contralateral (C, left) and ipsilateral (I, middle) eye as well as the change of ODI (right) before (Be) and after (Af) the conditioning. Gray scale at bottom of **c,d** represents the fractional change of reflection $\times 10^4$. Arrows in **c,d**: L, lateral, R, rostral. Scale bar in **c,d**: 1mm. Thin lines in **e,f**: individual experiments; thick lines and symbols: average $\pm$ s.e.m.



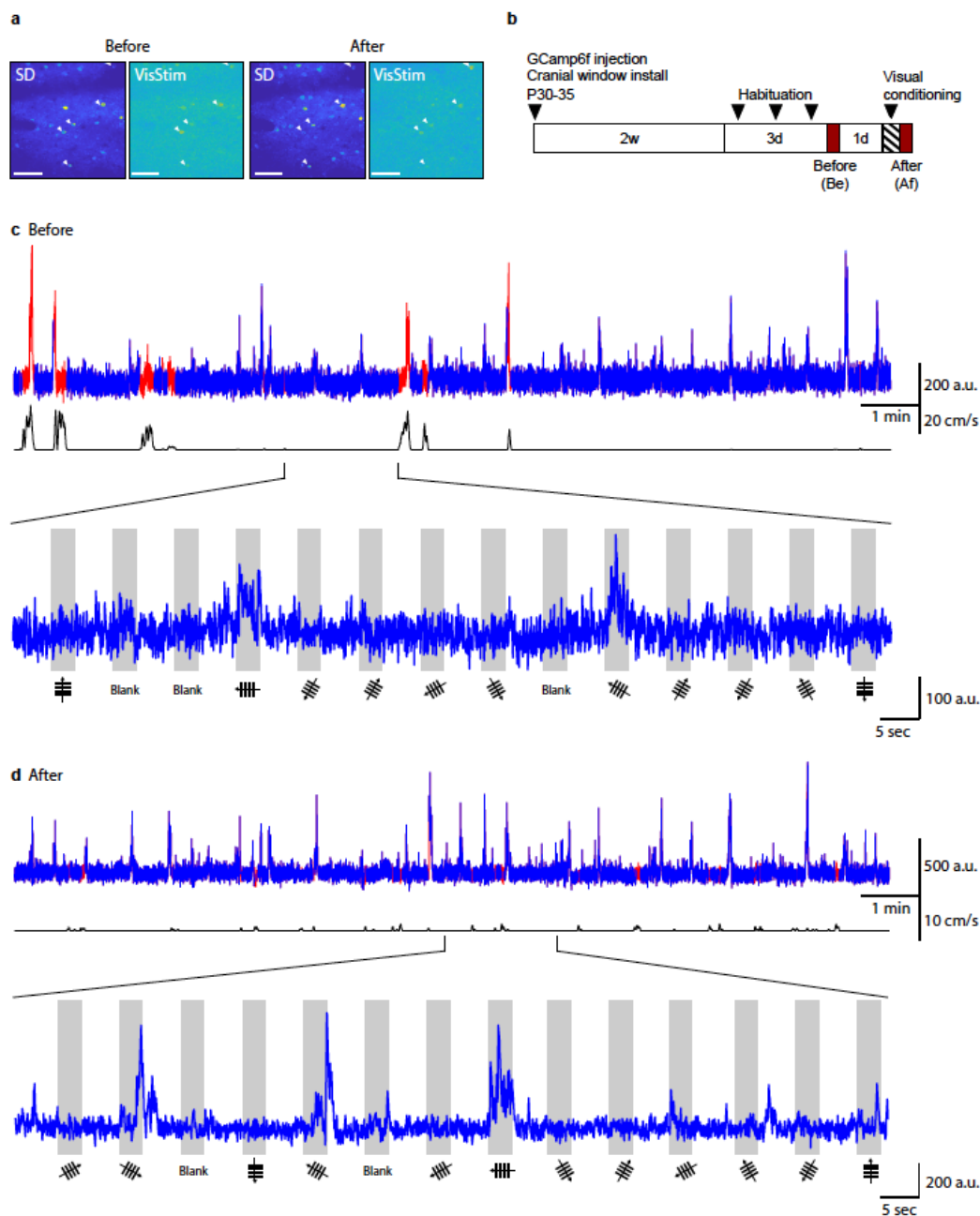
Supplementary Figure 3. The DSPL and 2C-ct peptides do not affect the β 2AR and 5HT2cR effects on intrinsic cellular excitability.

a, Experiment diagram to test the excitability change by the β 2AR agonist, salbutamol. The spike response of the layer 2/3 neurons in the V1 were recorded. **b**, Example spike response evoked by current step (bottom of the spike trace, 500 ms) before and after the administration of salbutamol. The current step amplitude was adjusted to evoke 5-6 spikes at the beginning of the recording and then maintained throughout the recording. **c-d**, Summary of the changes of the number of spikes evoked by the current step. The numbers of spikes are normalized by the average number of spikes during the baseline period (0-2 min). Slices were pre-incubated in the ACSF at least 20 min in the absence (black, Control) or presence (red) of DSPL. **e**, Experiment diagram to test the excitability change by the 5HT2cR agonist, Ro 60-0175. V1 neurons did not show excitability change by Ro 60-0175. Therefore, we tested the layer 2/3 neurons in the posterior piriform cortex, where the expression of the 5HT2cR is abundant (Clemett et. al., Neuropharmacology: 39, 123). **f**, Same in (b), but with Ro 60-0175. **g-h**, Same with (c,d), but with 2C-ct. The numbers of spikes are normalized by the average number of spikes during the baseline period (0-3 min). Box plot: average $\pm$ s.e.m.



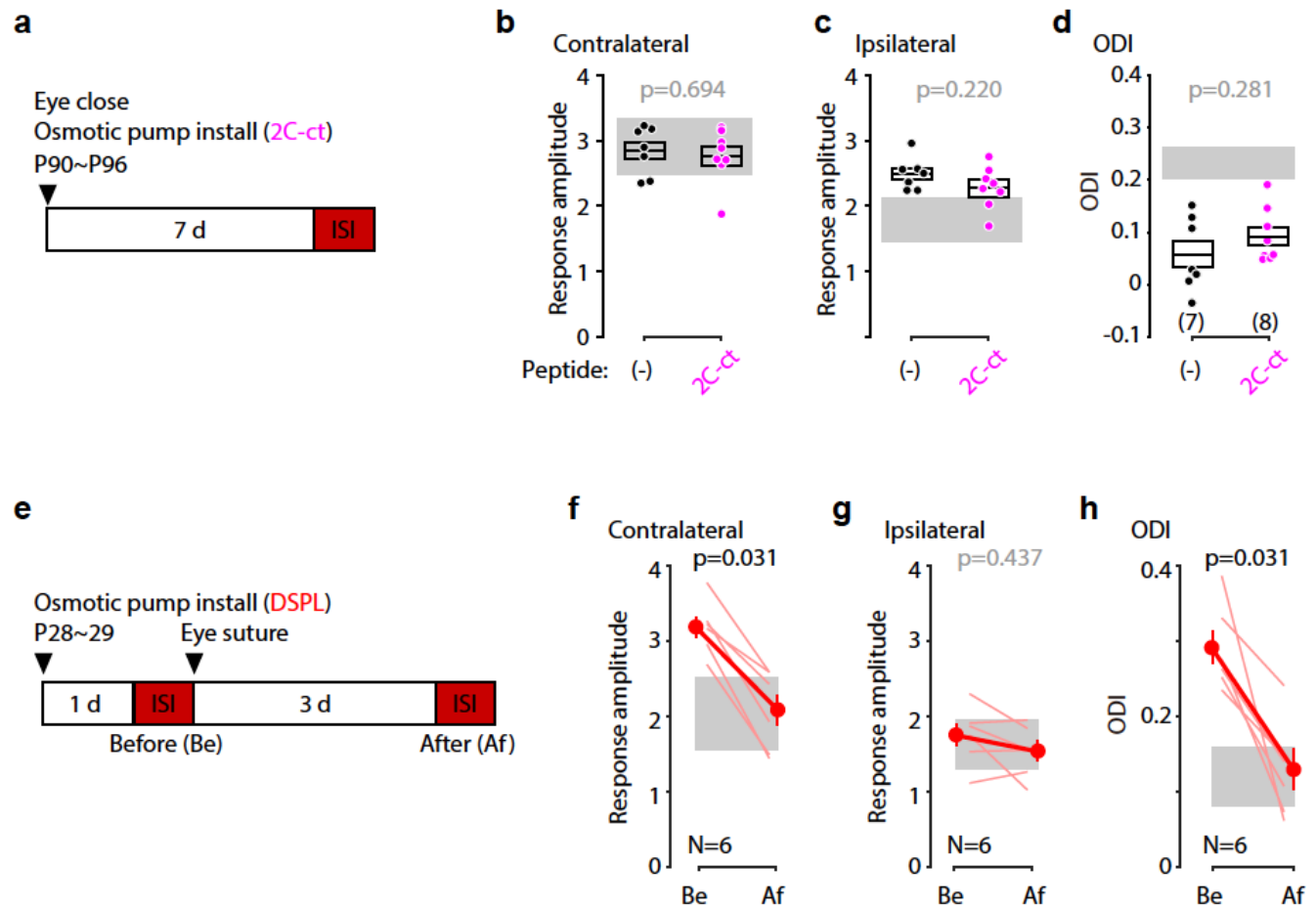
Supplementary Figure 4. In vivo whole cell recording of VEPSPs.

a, Experimental schematics of optogenetic pairing in vivo whole cell recording of VEPSPs. Norepinephrine release was induced by photoactivation of adrenergic neuron terminal ChR2 of the NE-ChR2 mice at the V1 (left). Serotonin release was induced by photoactivation of the virally expressed ChR2 in serotonergic neurons via optic fiber implanted into the dorsal raphe nucleus (DRN) of the 5HT-ChR2 mice (right). **b**, An example fluorescence image from a NE-ChR2 mouse brain slice demonstrating the adrenergic neuronal projections expressing ChR2 (EYFP, green) and the recorded neuron (Biocytin, red). Nuclei are also visualized (DAPI, blue). Scale bar: 100 μ m. **c**, An example fluorescence image from a 5HT-ChR2 mouse brain slice demonstrating the ChR2 expression (EYFP, green) in the serotonergic neurons at the DRN. White dotted line indicates the artifact by the implanted optic fiber. Scale bar: 100 μ m. **d-e**, Input resistance (R_n) and base membrane potential (V_m) before and after the visual conditioning. **f-g**, Normalized change of NC-VEPSPs amplitude of the NE-ChR2 mice by the visual conditioning without pairing of the postsynaptic spikes (**d**) and the summary of change (**e**). Inset traces on top show the VEPSPs of a representative neuron averaged initial (gray) or last (black) 5 minutes of the recording. Box plot: average $\pm$ s.e.m.



Supplementary Figure 5. Two-photon calcium imaging of superficial layer excitatory neurons.

a, Example two-photon imaging field of view visualized by fluorescence standard deviation (SD) or fluorescence correlation with the visual stimulus (VisStim) before and after the visual conditioning (see Methods). White arrows indicate the stable visually responsive neurons involved in the analysis. Scale bar: 100 μm . **b**, Experiment timeline. **c-d**, Top, fluorescence signal of the representative neuron across the recording time before (c) and after (d) the visual conditioning. Fluorescence signal during the stationary (blue) or during the locomotion (red) is illustrated based on the treadmill speed (black line). Bottom, a part of the fluorescence signal to 14 consecutive visual stimuli is demonstrated. Gray indicate the time the visual stimuli presented. The direction and the orientation of the visual stimuli are shown at the bottom.



Supplementary Figure 6. Specificity of the disrupting peptides in the interruption of the LTP or LTD trace transformation.

a-d, Interruption of LTD trace transformation does not impair the potentiation of the open eye by the MD of young adult mice. **a**, Experiment timeline to test the specificity of the 2C-ct. **b-d**, Summary of the changes of the response amplitude evoked by the contralateral (b) and ipsilateral (c) eye as well as the ODI (d) of each experimental group. The data of 7d MD group were previously shown in Fig. 6. Gray region indicates 95% confidential interval values of normal reared mice. Box plot: average $\pm$ s.e.m. **e-h**, Interruption of LTP trace transformation does not impair the depression of the closed eye by the MD of juvenile mice. **e**, Experiment timeline to test the specificity of DSPL. **f-h**, Summary of the changes in response amplitude evoked by the contralateral (f) and ipsilateral (g) eye as well as the change of ODI (h) before (Be) and after (Af) the conditioning. Thin line: individual animal; thick line and symbols: average $\pm$ s.e.m. Gray areas describe the 95% confidence interval of the mice deprived for 3 days without the disrupting peptide.