Supplementary Figure 1

Neuronal populations in the Tbx21-Cre (Tbet-Cre) mouse and 5-HT receptors in the OB

a) Tbet Cre mouse olfactory bulb injected with AAV 2.9 flex Gcamp6s virus showing sparse labelling of principal neurons of the OB.

b) 5-HT receptor 2a antibody (green, 1/1000 dilution, abcam ab66049) stains heavily in the external plexiform layer (EPL) and on MC bodies. Labeling performed in Tbet-Cre x Flex tdTomato mouse, so all principal cells are red.

c) Inhibitory 5-HT receptor 1a (red, 1/1000 dilution, abcam ab101914) stains non-GABAergic cells both in the EPL and MC layer (c1) and the glomerular layer (GL, c2). Staining performed in the GAD67-GFP mouse, so inhibitory cells are green.

d) Inhibitory 5-HT receptor 1b (red, 1/1000 dilution, abcam ab102700) stains non-GABAergic cells in the OB. Staining performed in the GAD67-GFP mouse (green). Granule Cell Layer (GCL).
Supplementary Figure 2

Names and structures of odorants used in study
Supplementary Figure 3

Sensitization of TC odor responses by raphe stimulation

a) Scatter plot showing sensitization in TC odor responses in 6 animals. Y axis is the observed response to paired odor and raphe stimulation minus raphe only stimulation response and x axis is odor only response.

b) Bar plot showing mean change in TC responses across animals. Mean response is calculated as the difference between paired odor plus raphe responses and (odor only + raphe only) responses.

c) Scatter plot showing the predicted response (linear model, R² = 0.7611) vs observed response for 6 animals (1087 odor cell pairs).

d) Scatter plot showing the predicted response (linear model, R² = 0.8638) vs observed response (1087 odor cell pairs).
Supplementary Figure 4

Odor inputs to the OB are not affected by brief raphe stimulation

a) Resting fluorescence image of glomeruli from an OMP-GCaMP3 mouse.
b) Example traces of odor responses from a single OMP-GCaMP3 glomerulus. Odor duration denoted by green bar at bottom.
c) Odor responses of olfactory sensory neurons measured from multiple glomeruli (left), in an OMP-GCaMP3 mouse, were not altered when the same odor was paired with raphe activation (right).
d) Scatter plot of all glomeruli odor pairs comparing average odor responses (dF/F) with and without raphe activation. Dashes are the unity line (p>0.3, Wilcoxon signed-rank, 2 mice, 26 glomeruli).
Supplementary Figure 5

Raphe projections to the main olfactory bulb

a) Anti-GFP antibody (green, 1/500 dilution; Aves GFP-1010) and anti-serotonin antibody (red, 1/1000 dilution; Sigma S5545) in a TPH2-ChR2 animal stains heavily in the glomerular layer and granule cell layer.

b) Zoomed in version of images shown in a, depicting the heterogeneity of raphe projections in different layers of the olfactory bulb.

c) Bar plots summarizing the density of raphe projections in the olfactory bulb as the mean pixel intensity in the different layers of the olfactory bulb (glomerular layer: 1.0, external plexiform layer: 0.26, mitral cell layer: 0.35, granule cell layer: 0.48, n=4). Data normalized to glomerular layer.
Supplementary Figure 6

Modulation of odor-evoked activity of principal neurons in the olfactory bulb by raphe stimulation in an awake animal

a) Time course of fluorescence changes in 36 TCs in an awake animal in response to ethyl valerate with (right) and without (left) raphe stimulation.

b) Similar plot showing time course responses of 23 MCs in an awake animal in response to ethyl valerate with (right) and without (left) raphe stimulation.

c) Scatter plot showing sensitization of odor responses in TCs with raphe stimulation in awake animals (468 cell-odor pairs, n=2). Mean change in odor response 23.71 ± 1 % (median change of 19.79 %).

d) Scatter plot showing bidirectional modulation of odor responses with raphe stimulation in awake animals (282 cell-odor pairs, n=2). Mean change in odor response 1.94 ± 0.9 % (median change of 1.79 %).