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Activity-dependent gating of lateral inhibition by correlated mitral cell activity in the mouse main olfactory bulb

Armen C Arevian[1,3] and Nathaniel N Urban*[1,2,3]

Address: [1]Center for Neuroscience, University of Pittsburgh, Pittsburgh, PA, USA, [2]Dept. of Biology, Carnegie Mellon University, Pittsburgh, PA, USA and [3]Center for the Neural Basis of Cognition, Pittsburgh, PA, USA

Email: Nathaniel N Urban* - nurban@cmu.edu

* Corresponding author

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Excitatory mitral and tufted cells (M/Ts) provide the primary output of the mouse main olfactory bulb (MOB). M/Ts provide excitatory input to and receive inhibitory input from GCs via the dendrodendritic synaptic connections. These circuits provide both recurrent and lateral inhibition among M/Ts. However, given the large area spanned by M/T secondary dendrites as well as the lack of evidence for a clear correlation between the proximity of M/Ts and their odor response profiles, we asked what mechanism could provide for specific and useful lateral inhibitory connectivity? To address this question we conducted whole-cell patch clamp recordings of pairs of M/Ts in the MOB. Current steps (400 ms, 0–1200 pA) were injected into one of the paired cells (Cell A). We then compared the firing rate of Cell A when it was stimulated alone vs. when it was stimulated during simultaneous activation of a second M/T (Cell B) at approximately 80 Hz. We found that activity of Cell B significantly reduced the firing rate of Cell A only when Cell A was firing at frequencies between 35 and 110 Hz (19%/17 Hz peak reduction, $n = 16$ pairs, $p < 0.05$). This effect, which we call activity-dependent lateral inhibition, is presumably due to activation of GCs correlated M/T cell activity and subsequent saturation of GC output. Furthermore, activation of larger populations of presynaptic M/Ts via extracellular stimulation in the glomerular layer produced similar activity-dependent lateral inhibition but of higher magnitude and occurring at lower frequencies (25% peak reduction between postsynaptic firing rates between 25 and 65 Hz, $n = 8$, $p < 0.05$). We then implemented this physiologically characterized mechanism in a network model with all-to-all connectivity. Results show that initially correlated patterns of activity are decorrelated in a spatially independent manner using this activity-dependent mechanism. These results suggest that the magnitude of inhibition received by M/Ts is dynamically determined based on the pattern of activity within the bulb and can be used to decorrelate similar input patterns, enhancing odor discrimination. Supported by R01 – DC005798.