Noradrenaline Dependent Memory Formation in the Main Olfactory Bulb of the Mouse

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Many mammals discriminate individual conspecifics through detection of chemical cues using the olfactory systems. In mice and several other mammals, certain forms of social memory involve plasticity in the main olfactory bulb (MOB), the first station for olfactory processing in the brain. Social encounters are associated with elevated release of the neuromodulator noradrenaline (NA) from the brain stem nucleus 'locus coeruleus' (LC), which is believed to trigger MOB plasticity underlying memory.
In the MOB, olfactory sensory neurons (OSNs) make excitatory inputs onto mitral/tufted cells (M/T) that further project to deeper brain areas. Axons from all OSNs that express a given receptor type converge on an exclusive set of M/T in dense, round structures called glomeruli that cover the external surface of the MOB. Glomerular activity is potentially modulated by interneurons that form intra- and interglomerular connections, central feedback projections, and neuromodulatory input such as NA.
Previously, we induced social memories in anesthetized mice by pairing activation of LC with conspecific urine from unfamiliar mice. In a subsequent behavioral test, mice treated the 'paired urine' as if it were a familiar stimulus (exhibiting reduced interest) while they treated the 'unpaired urine' as if it were a novel stimulus. Remarkably, this behavior was reflected by correlated changes to the responses of individual M/T. Pairing either urine volatiles or arbitrary odors with LC stimulation led to a selective habituation of the response of M/T to the paired stimulus, and this effect was dependent on activation of NA receptors locally in the MOB. We hypothesize that this regulation of M/T cells is achieved by modulation of inhibitory neurons which may modify either the presynaptic input from the OSNs or the postsynaptic output of the M/T cells.
We are examining how NA-dependent memories are stored among populations of glomeruli, and whether the storage mechanisms involve regulation of presynaptic and/or postsynaptic activity in the glomeruli. As an initial step, we measured odor-driven activity in populations of glomeruli on the dorsal surface of the MOB by wide-field optical imaging of intrinsic signals. Intrinsic signals are correlated with activity in OSNs and likely largely reflect presynaptic input to the MOB. We presented several odors before, during and after pairing 30 presentations of one odor with a 20 s, 5Hz, 40 µA electrical stimulus train to LC. The population response (n=127 glomeruli; 9 animals) significantly shifted after LC stimulation, while sham controls (n=88 glomeruli; 4 animals) exhibited no change. Most (73.23%) glomeruli showed response suppression (n=93, median 62% suppression), however, many (21.26%) glomeruli increased the strength of their response (n=27, median 125% increment). We preliminarily conclude that the observed glomerular changes occur through presynaptic modulation of the OSN-M/T synapse. We also find that surprisingly, pairing odors with LC activation leads to a sparsening rather than uniform

suppression of the population response. We are working to confirm our findings by direct and exclusive measurement the presynaptic activity more directly using fluorescent activity markers (GCaMP2 and synaptopHluorin) expressed in OSNs. We are also investigating the stimulus-specificity of the effect.

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Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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