Altered Representation of the Spatial Code for Odors after Olfactory Classical ConditioningMemory Trace Formation by Synaptic Recruitment

Dinghui Yu, Artem Ponomarev and Ronald L. Davis

Neuron 2004, 42:437-449

journal cover **In the olfactory bulb of vertebrates or the homologous antennal lobe of insects, odor quality is represented by stereotyped patterns of neuronal activity that are reproducible within and between individuals. Using optical imaging to monitor synaptic activity in the *Drosophila* antennal lobe, we show here that classical conditioning rapidly alters the neural code representing the learned odor by recruiting new synapses into that code. Pairing of an odor-conditioned stimulus with an electric shock-unconditioned stimulus causes new projection neuron synapses to respond to the odor along with those normally activated prior to conditioning. Different odors recruit different groups of projection neurons into the spatial code. The change in odor representation after conditioning appears to be intrinsic to projection neurons. The rapid recruitment by conditioning of new synapses into the representation of sensory information may be a general mechanism underlying many forms of short-term memory.**

Introduction

Memories are formed, stored, retrieved, and lost by a mysterious interplay between sensory cues and the functioning nervous system. The formation of memories occurs through a set of changes within neurons that encode the relevant sensory information. These changes, or cellular memory traces, can in principle be any molecular, biophysical, or cellular change induced by learning, which subsequently alters the processing and response of the nervous system to the sensory information. For instance, changes can occur in the expression or function of ion channels that cause neurons to be more or less excitable and therefore more or less capable of conducting action potentials or other electrical signals. Learning may mobilize neuronal growth processes that establish new connections or neurite retraction to remove existing connections. The changes may include cell signaling adaptations that alter the neuron's overall ability to integrate inputs from different types of cues and morphological or functional changes in synapses that

increase or decrease the neuron's ability to stimulate its synaptic partners. Together, these cellular memory traces comprise the overall behavioral memory trace, or memory engram (Dudai, 2002; Squire, 1987) , that guides behavior in response to sensory information. A major goal in neuroscience is to understand the nature of cellular memory traces, the mechanisms by which they form, their duration, the neurons in which they develop, and how the complete set of cellular memory traces within different areas of the nervous system underlies the memory engram.

Drosophila can develop a robust association between an odor, the conditioned stimulus (CS), and electric shock, the unconditioned stimulus (US), if the CS and the US are paired. Flies display their memory of this association by avoiding the odor CS during a test, after previously experiencing the pairing of the CS and the US. The number, nature, and the locations of the cellular memory traces that guide this acquired avoidance behavior are unknown, but significant evidence suggests that some cellular memory traces are formed in mushroom body neurons, higher-order neurons that form part of the olfactory nervous system (Davis, 1993; Dubnau et al., 2001; McGuire et al., 2001; Zars et al., 2000) . Furthermore, the evidence indicates that the memory traces are formed in part by the activation of the cyclic AMP signaling system (Davis, 1993; Roman et al., 2001) . However, the memory traces that underlie insect odor memory are probably formed in many different areas of the olfactory nervous system and in other areas of the brain as well.

We have used optical imaging of synaptic activity in *Drosophila* brains (Ng et al., 2002) coupled with behavioral conditioning to visualize and study a cellular memory trace. This trace is established as new synaptic activity after conditioning in the antennal lobe projection neurons of the olfactory system. A concept established from our results that may generalize to other forms of memory is that memories form by the rapid recruitment of relatively inactive synapses into the representation of the sensory information that is learned. In other words, the synaptic representation of the odor CS is changed by learning, with new synaptic activity added to the representation after learning.

Results

The anatomical organization of the *Drosophila* olfactory nervous system shares many fundamental similarities to that of vertebrates (Hildebrand and Shepherd, 1997; Laissue et al., 1999; Laurent et al., 2001; Lessing and Carlson, 1999; Mombaerts, 2001; Roman and Davis, 2001; Vosshall, 2000) , suggesting that the mechanisms for odor perception, discrimination, and learning are shared (Figure 1). Olfactory receptor neurons (ORNs), distributed near the surface of the antenna and maxillary palp on each side of the head, project axons to the antennal lobe, where they terminate in morphologically discrete and synapse-dense areas known as glomeruli (Figures 1B–1D) (Gao and Chess, 1999; Laissue et al., 1999; Scott et al., 2001; Vosshall et al., 2000) . The projection patterns

of the ORNs are stereotyped between animals; ORNs that express the same olfactory receptor gene, although distributed across the surface of the antenna and maxillary palps, project their axons to the same glomerular target in the antennal lobe (Gao et al., 2000; Scott et al., 2001; Vosshall et al., 2000) . There they are thought to form excitatory synapses with at least two classes of neurons: the local interneurons (LNs), a large fraction of which are GABAergic inhibitory neurons, and the projection neurons (PNs) (Laissue et al., 1999; Stocker, 1994) . A unique feature of the circuitry within the insect antennal lobe is the apparent existence of reciprocal dendrodendritic connections between the PNs and the LNs (Didier et al., 2001; Sun et al., 1997; Ng et al., 2002) . The presence of these unique junctions with both transmissive and receptive specializations indicates that each glomerulus processes and makes computations that may underlie odor perception, discrimination, and learning, rather than being a simple transit station for the throughput of olfactory information. Individual PNs generally extend dendrites into a single antennal lobe glomerulus (Jefferis et al., 2001; Marin et al., 2002; Wong et al., 2002) and then convey the processed olfactory information to two higher brain centers: the mushroom bodies and the lateral protocerebrum.

Go to the Full Article > >