

Medial Temporal Lobe Switches Memory Encoding in Neocortex through Cholecystokinin

Jufang He

Laboratory of Applied Neuroscience, Department of Rehabilitation Sciences, The Hong Kong Polytechnic University, Hong Kong

Damage to the medial temporal lobe impairs the encoding of new memories and the retrieval of memories acquired immediately before the damage in human. In this study, we demonstrated that artificial visuo-auditory memory traces can be established in the rat auditory cortex and that their encoding depends on the entorhinal cortex of the medial temporal lobe in the rat. We trained rats to associate a visual stimulus with electrical stimulation of the auditory cortex using a classical conditioning protocol. After conditioning, we examined the associative memory traces electrophysiologically (i.e., visual stimulus-evoked responses of auditory cortical neurons) and behaviorally (i.e., visual stimulus-induced freezing and visual stimulus-guided reward retrieval). The establishment of a visuo-auditory memory trace in the auditory cortex, which was detectable by electrophysiological recordings, was achieved over 20-30 conditioning trials and was blocked by unilateral, temporary inactivation of the entorhinal cortex. We further found that cortical projection neurons in the perirhinal and entorhinal cortices, which are the gateway from the hippocampus to the neocortex, were mostly immunopositive for cholecystokinin (CCK). Local infusion of CCK in the auditory cortex of anesthetized rats induced plastic changes that enabled cortical neurons to start responding to an auditory stimulus that was paired with a tone that robustly triggered action potentials. CCK infusion also enabled auditory neurons to start responding to a light stimulus that was paired with a noise burst. *In vivo* intracellular recordings in the auditory cortex showed that synaptic strength was potentiated after two pairings of presynaptic and postsynaptic activity in the presence of CCK. Finally, infusion of a CCK receptor antagonist in the auditory cortex prevented the formation of a visuo-auditory associative memory in behaving rats. Together, these findings suggest that the entorhinal cortex of the medial temporal lobe is necessary for the encoding of artificial visuo-auditory memory in the auditory cortex and influences cortical plasticity through CCK. Thus, CCK switches memory writing in the neocortex.