Cholecystokinin is the Memory-writing Switch in Our Brain

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The entorhinal cortex may enable neocortical neuroplasticity through cholecystokinin (CCK)-containing neocortical projections. Here, we investigated the role of CCK in long-term potentiation (LTP) in the auditory cortex of rats and mice. Administration of a CCKB antagonist blocked high-frequency (HF) stimulation-induced LTP in the auditory cortex, whereas local infusion of CCK alone induced LTP. CCK-/- mice exhibited no neocortical LTP and deficits in learning and memory. HF stimulation of the entorhinal cortex or CCK-containing entorhino-neocortical projection neurons before the pairing of an auditory stimulus and electrical stimulation of the auditory cortex potentiated neuronal responses to the auditory stimulus. Furthermore, when electrical stimulation was pre-conditioned to a footshock, mice showed a freezing response to the auditory stimulus after the pairing of auditory and electrical stimuli, indicating that mice had formed an association. These findings demonstrate that CCK released from the entorhinal cortex enables neocortical LTP and contributes to memory formation.