LS-BK SEMINAR

"Neural coding of cognitive control at cellular resolution"

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- **Inquiry: Prof. Joung-Hun Kim (279-2347)**
- **Abstract:**

Cognitive flexibility is a fundamental feature of high-level brain function. However, neuronal pathways that control flexibility and the mechanisms by which flexibility is encoded are unknown. Previous studies have reported that neurons in the orbitofrontal cortex (OFC) encode the value of an external environment and lesions in the OFC area in human have led to deficits in choice behavior. Depletion of serotonin in the OFC area caused impaired reversal learning (RL). However, we still do not know how flexibility is represented by individual neurons or synapses. Fundamental questions underlying cognitive flexibility would be to understand a specific brain condition where new information can be updated without losing existing memories. In order to understand these brain mechanisms, we examined neuronal changes within a specific time window of behavior and control the exact timing of serotonin and glutamate release. We specifically targeted the DRN-OFC circuits and controlled their functions in a high spatiotemporal resolution. In brief, we identified the direct long-range projection from the DRN to the OFC anatomically and functionally. Optogenetic stimulation of serotonergic inputs to the OFC facilitated the RL and the inhibition of DRN-OFC circuits slowed down the speed of RL. We also found that the membrane potential of pyramidal neurons was increased by serotonin, resulting in the enhanced spiking probability of the OFC network. Imaging through a miniscope in behaving animals revealed *in vivo* functions of serotonin in the OFC. Combined two-photon Ca^{2+} imaging and uncaging showed that serotonin boosted Ca^{2+} transients and promoted the synaptic plasticity at dendritic spines. Thus, we revealed that cognitive flexibility may not be encoded as a form of specific cell types or circuit pathways, but rather be represented via state-dependent synaptic plasticity. We believe that these findings are important early steps which will furnish new insights into general cognitive learning.