Abstract:

We assess the neural mechanisms of learned associations in operant-learned behaviors. These learned associations or memories involve complex sets of highly specific information that must be stored with a high degree of resolution. In contrast, most studies to date examined low resolution neural mechanisms in whole brain areas, cell types or randomly selected neurons regardless of whether they were activated and.
participated in the behavior. Instead, high resolution memories are thought to be stored by alterations induced selectively within sparsely distributed patterns of neurons, called neuronal ensembles, that are selectively activated by cues relevant to the memory. We developed the Daun02 inactivation procedure with transgenic FosLacZ rats to demonstrate that different patterns of strongly activated Fos-expressing ensembles mediate different memories. Since these ensembles encode the memory, we developed methods that use (1) FACS to discover multiple molecular alterations and (2) FosGFP transgenic rats to discover multiple electrophysiological alterations that are induced only within Fos-expressing neurons. We have since developed a Fos-Tet-Cre transgenic rat system that allows us to selectively manipulate these alterations within Fos-expressing ensembles to assess whether they play a causal role in operant learned behaviors. It is our hope that a focus on the behaviorally activated ensembles that store the memories will permit more focused novel treatments of behavioral disorders.

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