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Research Interests

Changes in neurotransmitter concentration in the extracellular space of the brain is a cornerstone of intercellular communication that drives brain function. Uncovering the mechanisms of release and removal of transmitters, as well as spatial and temporal patterns of release under different conditions, will enable a better understanding of how neurochemistry mediates behavior and pathophysiological mechanisms. We have developed novel approaches to measuring the dynamics of neurotransmitters in vivo and used these technologies to study neurotransmitter mechanisms in addiction, learning and memory, and stress responses. In addition, we continue to explore novel technologies for neurotransmitter detection and monitoring.

For most of our in vivo experiments we use sampling probes, such as microdialysis, coupled with sophisticated analytical techniques to simultaneously monitor amino acids and dopamine at 10 s intervals in discrete locations of the brain. Our technology is the only method that enables multi-chemical measurements at such high temporal resolution. This is critical for uncovering the true dynamics of transmitters in vivo. Using this approach, we have uncovered the transmitters that underlie Pavlovian learning and memory expression, stress responses, responses to addictive substances, and spontaneous stereotypical behavior in mice (a model of obsessive-compulsive disorders).

In one project, we are studying the neurochemistry underlying the interaction of stress and addiction potential. We demonstrated that brief pulses of glutamate concentrations in the nucleus accumbens were temporally correlated with behavioral activation in rats exposed to an odor from a predator (a type of stress). Furthermore,



individual differences in behavior were accurately predicted by the magnitude of glutamate change. Because glutamate release in the accumbens may influence addiction, and responsivity to stress is an indicator of propensity to addiction, these results have led to a hypothesis that glutamate release in this brain region is the neurochemical link between stress and addiction. Future studies will be aimed at testing this hypothesis.

In another project, we have examined the chemical release that underlies emotional learning and memory using a fear conditioning experiment. In this experiment, rats learn to associate a sound or environment with a footshock. After the association, the sound or environment elicits fear behavior. While the circuits involved have been well-mapped, we have little knowledge of the chemical dynamics that underlie this learning and memory. In collaboration with Stephen Maren and Terry Robinson, we have shown that large pulses of GABA and glycine in the basal lateral amygdala accompanies the initial learning of tone-shock pairing. Furthermore, these transmitters are relatively unchanged in environmental learning, but they are released upon memory expression (i.e., expressing fear in response to the sound or environment). These results imply a role for these transmitters in learning to associate sound with painful stimuli and in remembering that association. Future studies will be aimed at uncovering the source of the released GABA and Gly and manipulating their concentration to control learning and memory.

We also have several projects aimed at uncovering mechanisms of addiction to psychostimulants. These projects include ascertaining the neurochemical effects of sex hormones on neurochemicals involved in addiction. In addition, we are investigating the effects of different routes of drug administration on neurochemistry. This project is of interest because of the differences in rates of addiction associated with different rates of administration of the same drug. These projects are in collaboration with Professors Becker and Robinson in Biopsychology.

Finally, we continue to develop novel technologies for investigating neurotransmitters. We have developed techniques for identifying and screening novel neurotransmitter candidates. We are also exploring instrumentation for analyzing release and reuptake at the single cell level.

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