GLUTAMATE RECEPTORS PLAY A KEY ROLE IN INFORMATION PROCESSING AND SYNAPTIC PLASTICITY THROUGHOUT THE CNS. HOWEVER, WE STILL KNOW VERY LITTLE ABOUT THE EXTENT TO WHICH THESE RECEPTORS ARE ACTIVATED DURING SENSORY INPUT OR EXPERIENCE-DEPENDENT LEARNING. OUR RESEARCH AIMS TO UNDERSTAND THE ROLE OF PRE- AND POSTSYNAPTIC GLUTAMATE RECEPTORS DURING SENSORY INFORMATION PROCESSING AND MOTOR LEARNING IN THE CEREBELLUM.

GLUTAMATE RECEPTORS

The processing of sensory information is a fundamental operation of neurons within the brain. Each neuron receives hundreds of weighted synaptic inputs from other neurons, which it must process in order to evoke a functionally relevant output. The synaptic inputs to any given neuron are modifiable and activity-dependent changes in synaptic efficacy are thought to underpin network development, learning and memory, and behaviour. Although we are beginning to understand the rules that govern synaptic integration and plasticity in vitro, little is known about how neurons encode sensory information or how experience-dependent changes in synaptic efficacy relate to learning and behaviour.

Glutamate receptors (GluRs) play a pivotal role in regulating synaptic integration and plasticity throughout the mammalian CNS. Activation of GluRs depends on several factors: the source of glutamate release; the spatiotemporal dynamics of glutamate within the extracellular space; and the localisation of receptors with respect to the source of glutamate release. Upon activation, pre- and postsynaptic GluRs can act via a variety of downstream signalling pathways to alter the probability of vesicle exocytosis, postsynaptic receptor activation and overall spike output. In the cerebellum, glutamate receptor-dependent changes in synaptic efficacy have been proposed as the cellular basis for several forms of cerebellar motor learning including associative eyeblink conditioning and adaption of the vestibulo-ocular reflex.

Fig.1. In vivo whole-cell patch-clamp recording from a cerebellar granule cell during ipsilateral whisker stimulation.
While the majority of our knowledge about glutamate receptors is derived from in vitro experiments, we still know very little about the extent to which these receptors are activated during sensory stimulation or during experience-dependent learning in the intact brain. By taking advantage of recent advances in in vivo intracellular recording techniques, our research aims to decipher the molecular and cellular mechanisms involved in experience-dependent plasticity in the cerebellum and to understand how short- and long-term changes in synaptic efficacy relate to cerebellum-dependent motor learning.

**SENSORY INFORMATION PROCESSING**

To understand how sensory information is encoded in the intact brain, it is essential to determine the patterns of synaptic activity evoked during sensory experience and the integrative properties of individual neurons. Although single unit recordings in vivo have provided a basic understanding of sensory responses in single neurons, these experiments lack detailed information regarding subthreshold synaptic activity, spatial patterns of synaptic input, and the subcellular mechanisms involved in synaptic integration. We aim to understand the role of pre- and postsynaptic glutamate receptors during ongoing sensory experience by studying the cellular and molecular mechanisms involved in synaptic integration in single neurons and small inhibitory microcircuits in the cerebellum in vivo.

**EXPERIENCE-DEPENDENT PLASTICITY IN THE CEREBELLUM**

A central theory in modern neuroscience is that modifications in synaptic strength underpin learning, memory and behaviour. Activity-dependent changes in synaptic efficacy can proceed via a variety of signalling pathways that impact on the presynaptic release machinery or postsynaptic receptors mediating the response. Recent evidence suggests that both excitatory and inhibitory synaptic connections are modified during experience-dependent learning in the cerebellum. However, the rules that govern this process remain largely unknown. Our research aims to explore the cellular mechanisms involved in glutamate receptor-dependent synaptic plasticity to help understand how short- and long-term changes in synaptic efficacy contribute to motor learning in the cerebellum.

**INHIBITORY MICROCIRCUITS AND MOTOR LEARNING**

Inhibitory microcircuits play a key role in regulating neuronal excitability in the intact brain and understanding their function has been a primary goal for neuroscientists for several decades. However, little is known about the extent to which interneuron circuits are modifiable by sensory experience and the molecular mechanisms involved. This is an important question as inhibitory synaptic connections are essential for determining patterns of neuronal activity. We are studying the plasticity of inhibitory synaptic connections in the molecular layer of the cerebellum during motor learning to decipher what role ionotropic glutamate receptors play in this process.

**SELECTED REFERENCES**


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