# Department of Neuroscience
# Laboratory of Neurophysiology

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## General Summary

The integration and coordination of functions throughout the body are realized mainly through intercommunication via nervous systems. To understand how activities of the organs affect brain activity and, in turn, how the brain controls the activities of organs to optimize these integrative functions, it is absolutely necessary to clarify the mechanisms of dynamic cell-to-cell signaling in the central nervous system underlying various specific functions, such as autonomic regulation and pain sensation. In particular, plastic changes of the central nervous system "wiring," realized through variability of synaptic connections in response to various environmental changes, form the core mechanism for optimizing human and animal behaviors. We use approaches at the molecular, cellular, and network levels, including the patch-clamp recording of synaptic currents and the real-time imaging of the intracellular $Ca^{2+}$ concentration in living brain tissues from normal animals, animal models of various diseases, and animals with experimental manipulation of gene expression, and combine them with the behavior of these animals.

## Research Activities

*Central mechanisms of pain-related negative emotion*

Using rat models of chronic neuropathic pain, we demonstrated that structural consolidation is involved in synaptic potentiation at the excitatory synapses between afferent fibers arising from the lateral parabrachial nucleus and neurons in the central nucleus of the amygdala, an important structure in the expression of emotional behavior. We also demonstrated using neonatal capsaicin treatment that peripheral C fibers expressing the transient receptor potential vanilloid 1 channel are necessary for establishing this synaptic potentiation. This result indicates that a specific set of nociceptive afferents is essential for the pathological enforcement of the link between nociception and negative emotion.

*Synaptic mechanism underlying acquisition and extinction of fear memory*

The Pavlovian fear-conditioning paradigm depends on the association between a contiguously applied cue (e.g., tone) and an aversive signal (e.g., electrical shock). We aimed to establish transgenic mice that express specific fluorescent marker proteins in response to fear conditioning or its extinction to enable selective fluorescence-guided recording of the identified amygdala neurons in brain slices after behavioral tests. This preparation will enable analyses of specific synaptic changes in the neurons involved in these processes.

*Glia-neuron interaction at central synapses*

To clarify the role played by the transfer of lactate from astrocytes to neurons in synaptic transmission, we analyzed the effects of selective inhibitors of monocarboxylate transporters on synaptic transmission in neurons of the nucleus of the solitary tract. We found that lactate transport is essential for maintaining the postsynaptic responses in both the presence and absence of glucose supply.

*Specific mechanism underlying motor neuron vulnerability*

We have previously demonstrated in brainstem slices that anoxia and hypoxia facilitate glycine release in an action potential-independent manner in hypoglossal motor neurons but not in the dorsal nucleus of the vagus nerve. To determine whether this facilitation is a common feature in cranial motor neurons, we recorded synaptic inputs in facial and oculomotor neurons and analyzed how these inputs were affected by anoxia. We found that in oculomotor neurons, the anoxia facilitated release of GABA but not of glycine. This difference in the response to anoxia of the inhibitory transmission between distinct motor neurons might provide a basis for the distinct vulnerability of these motor neurons in the motor neuron degenerative diseases.

## Publications

***Yamamoto K, Noguchi J, Yamada C, Watabe AM, Kato F.*** Distinct target cell-dependent forms of short-term plasticity of the central visceral afferent synapses of the rat. *BMC Neurosci* 2010; **11:** 134.

***Moody TD, Watabe AM, Indersmitten T, Komiyama NH, Grant SG, O'Dell TJ.*** Beta-adrenergic receptor activation rescues theta frequency stimulation-induced LTP deficits in mice expressing C-terminally truncated NMDA receptor GluN2A subunits. *Learn Mem* 2011; **18:** 118–27.

***Ono K, Tsukamoto-Yasui M, Hara-Kimura Y, Inoue N, Nogusa Y, Okabe Y, Nagashima K, Kato F.*** Intragastric administration of capsiate, a transient receptor potential channel agonist, triggers thermogenic sympathetic responses. *J Appl Physiol* 2011; **110:** 789–98.