Department of Neuroscience
Laboratory of Neurophysiology

Fusao Kato, *Professor and Director*

General Summary

We are attempting to clarify the mechanisms underlying dynamic cell-to-cell signaling in the central nervous system. 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 for various types of disease, and animals with experimental manipulation of gene expression.

Research Activities

Regulation of synaptic transmission in the brain network

1. Molecular mechanism of neurotransmitter release

To clarify the roles played by specific molecules in transmitter release in brain synapses, we developed a novel method for *in-vivo* gene silencing with RNA interference against genes coding presynaptic proteins, which is followed by functional analysis of synaptic transmission with patch-clamp recording in brain slices.

2. Glia-neuron interaction at synapses

To identify the functional role of gliotransmitters in the regulation of synaptic transmission, we developed a novel method of applying ATP, a "gliotransmitter" released from astrocytes, onto synapses in a time- and space-limited manner using laser-based photolysis of caged ATP compounds in brain slice preparations. Time-limited application of ATP onto synapses in the nucleus of the solitary tract immediately facilitated glutamate release through direct activation of presynaptic P2X receptors.

3. Central mechanism of frequency-dependent decoding of afferent information

To understand how the brain analyzes sensory signals from visceral organs, we analyzed the postsynaptic responses of second-order neurons in the nucleus of the solitary tract and the dorsal motor nucleus of the vagus nerve to repeated stimulation of afferent fibers in brainstem slices. These synapses showed distinct types of short-term plasticity with distinct Ca^{2+}-dependency, which might underlie the frequency-dependent "tuning-in" of visceral information.

Central mechanisms of pain-related negative emotion

Using rat models of chronic neuropathic pain, we demonstrated that excitatory synaptic transmission in the central nucleus of the amygdala, a structure playing principal role in the expression of emotional behaviour, is markedly potentiated.

Synaptic responses to metabolic failures in motor neurons

To elucidate the mechanism underlying selective vulnerability of motor neurons in various types of diseases involving mitochondrial dysfunction, we analyzed the responses to metabolic stress of hypoglossal motor neurons in brainstem slices. Hypoxia and NaCN markedly facilitated synaptic glycine release, which in turn potentiated N-methyl-D-aspartate-receptor-mediated currents by glycine-binding site activation.

Molecular target of volatile anesthetics

We found by analyzing membrane potentials and currents in pontine slice preparations that volatile anesthetics, but not intravenous anesthetics, directly excite neurons in the locus coeruleus through a mechanism involving the opening of gap-junction channels.

Publications

Ikeda R, Takahashi, Y, Inoue K, Kato F. NMDA receptor-independent synaptic plasticity in the central amygdala in the rat model of neuropathic pain. *Pain* 2007; **127:** 161–72.

Kono Y, Shigetomi E, Inoue K, Kato F. Facilitation of spontaneous glycine release by anoxia potentiates NMDA receptor current in the hypoglossal motor neurons of the rat. *Eur J Neurosci* 2007; **25:** 1748–56.

Yamazaki K, Shigetomi E, Ikeda R, Nishida M, Kiyonaka S, Mori Y, Kato F. Blocker-resistant presynaptic voltage-dependent Ca^{2+} channels underlying glutamate release in mice nucleus tractus solitarii. *Brain Res* 2006; **1104:** 103–13.