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General Summary

The integration and coordination of functions throughout the body is realized mainly through intercommunication via the nervous systems. To understand how the activities of organs affect brain activity and, in turn, how the brain controls the activities of organs to optimise these integrative functions, we must clarify the mechanisms underlying the dynamic cell-to-cell signaling in the central nervous system (CNS) underlying various specific functions, such as autonomic regulation and pain sensation. In particular, plastic changes of the CNS "wiring" realized through the 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, the real-time imaging of the intracellular Ca^{2+} concentration, and optogenetic approaches to activate a specific set of neurons by light, in living brain tissues from normal animals, animal models of various types of disease, and animals subjected to experimental manipulation of gene expression and combine them with the behavior of these animals.

Research Activities

Central mechanisms of pain-related negative emotion

Using a rat model of chronic neuropathic pain, we demonstrated that synaptic potentiation at the excitatory synapses between afferent fibers arising from the lateral parabrachial nucleus and neurons in the central nucleus of the amygdala, a structure playing the principal role in expression of emotional behaviors, involves structural consolidation. We also demonstrated that in the streptozocin-induced model of painful diabetes neuropathy, the synaptic potentiation in the amygdala is established selectively in the parabrachial-capsular synapses, unlike in other models. This finding further confirms the notion that the mechanism of synaptic potentiation in the central amygdala, which underlies the enhanced link between nociception and negative emotions, depends largely on the modality and duration of chronic pain.

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., electric 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 both in the presence and the absence of glucose supply.

Specific mechanism underlying motor neuron vulnerability

We have already demonstrated that, in the hypoglossal motor neurons, anoxia and hypoxia facilitate glycine release in an action potential–independent manner. We found that this facilitation of glycine release also occurs in facial motor neurons but not in oculomotor neurons, in which anoxia facilitates GABA release. This difference in the anoxia responses of the inhibitory transmission between distinct motor neurons might provide a basis for the distinct vulnerability of these motor neurons in motor neuron degenerative diseases.

Publications

Aoyama R, Okada Y, Yokota S, Yasui Y, Fukuda K, Shinozaki Y, Yoshida H, Nakamura M, Chiba K, Yasui Y, Kato F, Toyama Y. Spatiotemporal and anatomical analyses of P2X receptor-mediated neuronal and glial processing of sensory signals in the rat dorsal horn. *Pain.* 2011; **152:** 2085–9.

Yasui Y, Masaki E, Kato F. Esmolol modulates inhibitory neurotransmission in the substantia gelatinosa of the spinal trigeminal nucleus of the rat. *BMC Anesthesiol.* 2011; **11:** 15.

Arima-Yoshida F, Watabe AM, Manabe T. The mechanisms of the strong inhibitory modulation of long-term potentiation in the rat dentate gyrus. *Eur J Neurosci.* 2011; **33:** 1637–46.

Nomoto M*[1]*, Takeda Y*[1]*, Uchida S*[1]*, Mitsuda K*[1]*, Enomoto H*[1]*, Saito K*[1]*, Choi T*[1]*, Watabe AM, Kobayashi S*[2]*, Masushige S*[1]*, Manabe T*[2]*, Kida S*[1] *(*[1]Tokyo Univ Agriculture,*** [2]***Univ Tokyo).*** Dysfunction of the RAR/RXR signaling pathway in the forebrain impairs hippocampal memory and synaptic plasticity. *Mol Brain.* 2012; **5:** 8.

Reviews and Books

Kato F, Shigetomi E. Synaptic regulation by astrocytes (in Japanese). *Nihon Yakurigaku Zasshi.* 2011; **138:** 161–5.

Kato F, Takahashi Y. Nociception, pain and negative emotion (in Japanese). *Pain Clinic.* 2012; **33:** 387–94.

Kato F, Takahashi Y. What makes the pain painful? : a consideration from amygdala plasticity in chronic pain (in Japanese). *Journal of Neurosciences for Pain Research.* 2012; **13:** 1–7.