Hiroshi and Aya Irisawa Memorial Award Symposium

Hiroshi and Aya Irisawa Memorial Award for Excellent Paper in the Journal of Physiological Sciences

Multiple functions and roles of serotonin signaling

(March 18, 9:00–11:00, Room B)

3S44B-1

Electrophysiological Properties of GABAergic Cells in Mouse Dorsal Raphe Nucleus

Gocho, Yoshihiro; Saitow, Fumihito[1]; Yanagawa, Yuchio[2]; Sakai, Atsushi[1]; Suzuki, Hidenori[1]([1]*Department of Pharmacology, Nippon medical school,* [2]*Dept Genetic and Behavior Neurosci, Gunma University*)

The dorsal raphe nucleus (DRN) is the origin of the central serotonin (5-HT) system and has been thought to be composed of heterogeneous neuronal groups that differ in expression of neurotransmitters such as 5-HT, GABA and glutamate. To understand 5-HT system, characterization of the types of cells in the DRN is necessary. We performed electrophysiological recordings in acute slices of glutamate decarboxylase 67-GFP knock-in mice. We utilized this mouse to discriminate visually GABAergic (GFP(+)) cells from non-GABAergic (GFP(-)) cells. Among GFP(-) cells, serotonergic cells could be distinguished by immunoreactivity for tryptophan hydroxylase. Putatively, remaining GFP(-) cells might be glutamatergic. Therefore, at least, properties of three types of cells were explored. Compared with serotonergic cells, GFP(+) cells displayed a narrower half-height width of the action potentials. The input-output relationship curve of GFP(+) cells were steeper than that of serotonergic cells. Next, we examined postsynaptic responses mediated by activation of 5-HT receptors. Various current responses were elicited by 5-HT and specific 5-HT receptor agonists in GABAergic cells. These results suggested that multiple 5-HT receptor subtypes such as 5-HT1A, 5-HT2A/2C and 5-HT7 receptors were overlapping in GABAergic cells, and their combination might be implicated in the control of 5-HT cells. Understanding the postsynaptic 5-HT feedback mechanisms may contribute to elucidate the 5-HT system and facilitate to develop novel therapeutic approaches. No COI.

3S44B-2

The serotonin/GAD67—positive neurons in the rat dorsal raphe nucleus are transiently expressed during the weaning period and preferentially activated by the novel environment stress

Yoshida, Takayuki(*Department of Neuropharmacology, Hokkaido University Graduate School of Medicine*)

The serotonergic (5-HTergic) system arising from the dorsal raphe nucleus (DRN) is implicated in various physiological and behavioral processes, including stress responses. The DRN is comprised of several subnuclei, the lateral wing (DRL) the dorsal (DRD) or ventral (DRV) parts. Furthermore, subsets of 5-HTergic neurons are known to coexpress GABA. However, the properties, distributions, and involvement in stress of GABA-containing 5-HTergic neurons remain unknown. In this study, we characterized functional properties of GAD67-expressing 5-HTergic neurons (5-HT/GAD67 neurons) and compared their properties with those of other 5-HT or GAD67-positive neurons. We confirmed 5-HT/GAD67 neurons were selectively distributed in the DRL, but not in the DRD or DRV. Unexpectedly, They expressed plasmalemmal GABA transporter 1, but lacked vesicular inhibitory amino acid transporter. By using patch-clamp recording, the input resistance and firing frequency of 5-HT/GAD67 neurons were significantly lower than those of 5-HT neurons. As revealed by c-Fos immunohistochemistry, neurons in the DRL, particularly 5-HT/GAD67 neurons, showed higher responsiveness to exposure to an open field arena than those in the DRD and DRV. By contrast, exposure to contextual fear conditioning stress showed no such regional differences. These findings indicate that 5-HT/GAD67 neurons constitute a unique neuronal population with distinctive neurochemical and electrophysiological properties and high responsiveness to innocuous stressor. No COI.

3S44B-3

Birth regulates sensory map formation in the brain through serotonin signaling

Kawasaki, Hiroshi(*Graduate School of Medical Sciences, Kanazawa University*)

Although the mechanisms underlying the spatial pattern formation of sensory maps in the brain have been extensively investigated, those triggering sensory map formation during development are largely unknown. Here we show that the birth of pups instructively and selectively regulates the initiation of somatosensory map formation in the cerebral cortex by reducing serotonin concentration. We found that preterm birth accelerated somatosensory map formation, while it did not affect whisker lesion-induced barrel structural plasticity. We also found that serotonin was selectively reduced soon after birth, and that the reduction of serotonin was triggered by birth. The reduction of serotonin was necessary and sufficient for the effect of birth on somatosensory map formation. Interestingly, the regulatory mechanisms described here were also used in the visual system, suggesting that they are utilized in various brain regions. Our results shed light on hitherto unidentified roles of birth and serotonin in sensory map formation during development. No COI.

3S44B-4

Abnormal serotonin in a CNV mouse model for autisms

Takumi, Toru(*RIKEN BSI*)

Recent advance in neuroscience reveals that psychiatric diseases may be based on synaptic abnormality. Autism spectrum disorders (ASD) are child psychiatric illnesses that are characterized by impairments in social interactions and verbal and non-verbal communications, and pervasive stereotypic behavior. Most of their causes are unknown, whereas there are several known causes of ASD, in syndromic cases (fragile X syndrome, tuberous sclerosis, Rett syndrome, etc.), chromosomal abnormality (15q11-13 duplication, other CNVs), and rare mutations. Among CNVs and rare mutations, cell adhesion molecules that are involved in synapse formation and other related molecules to synaptic functions are particularly intriguing. The cause of ASD might be considered as abnormality in postnatal development of synapses. We generated a mouse model (patDp/+) for duplication of human chromosome 15q11-13 using a chromosome-engineering technique. The patDp/+ mice show abnormal social behavior, abnormality in serotonin signaling and levels, altered spine morphology and excitatory/inhibitory imbalance. No COI.