Symposium 11: Neural circuits of social-emotional behaviors (Fri July 30, 16:40-18:40 JST)
Chair: Hailan Hu (Zhejiang University, Hanzhou, China)

16:40-17:10 Zhihua Gao (Zhejiang Univ Sch of Brain Science and Brain Medicine, China)
The Magnocellular Neuroendocrine System-structural and functional insights

17:10-17:40 Fusao Kato (Jikei University School of Medicine, Tokyo, Japan)
The central amygdala plasticity controls widespread chronic pain

17:40-18:10 Kun Li (Tsinghua University, Beijing, China)
A Cortico-hypothalamic circuit controls estrus-dependent sociosexual behavior in females

18:10-18:40 Ja Wook Koo (Korea Brain Research Institute, Daegu, Korea)
Dopaminergic regulation of accumbal cholinergic interneurons defining susceptibility to cocaine addiction

Symposium 11 Speaker 1

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The Magnocellular Neuroendocrine System-structural and functional insights

The hypothalamo-neurohypophysial system (HNS), comprising hypothalamic magnocellular neuroendocrine cells (MNCs) and the neurohypophysis, plays a pivotal role in regulating reproduction and fluid homeostasis by releasing oxytocin and vasopressin into the bloodstream. However, its structure and contribution to the central actions of oxytocin and vasopressin remain incompletely understood. Using viral tracing and whole brain imaging, we reconstructed the three-dimensional architecture of the HNS and observed collaterals of MNCs within the brain. By dual viral tracing, we further uncovered that subsets of MNCs collaterally project to multiple extrahypothalamic regions. Selective activation of magnocellular oxytocin neurons promoted peripheral oxytocin release and facilitated central oxytocin-mediated social interactions, whereas inhibition of these neurons elicited opposing effects. Our work reveals the previously unrecognized complexity of the HNS and provides structural and functional evidence for MNCs in coordinating both peripheral and central oxytocin-mediated actions, which will shed light on the mechanistic understanding of oxytocin-related psychiatric diseases.

Symposium 11 Speaker 2

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The central amygdala plasticity controls widespread chronic pain

Pain is a sensory and emotional experience, which may occur regardless of the presence or absence of tissue damage. In particular, in several types of chronic pain, such as the "chronic primary pain" (International Classification of Diseases, 11th edition, 2019), the experience of pain is unrelated to tissue injury and the pain is localized in widespread body regions. To identify the brain mechanism underlying the widespread sensitization, we created a novel preparation that shows long-lasting (for ~2 weeks) ectopic sensitization at the bilateral hindpaw in response to acute facial inflammation. As nociceptive information from the trigeminal spinal nucleus mainly targets the central amygdala (CeA) by way of the parabrachial nucleus (PBN), we analyzed the neuronal activation in these nuclei. We found that the acute inflammation was followed by a latent increase in c-Fos expression and the robust synaptic potentiation of the PBN-CeA synapse predominantly in the right CeA. This predominance of the right CeA was similarly observed regardless of the side of inflammation, suggesting its somatotopy-independent convergent activation. This model also showed a decrease in the hierarchy rank of the dominant animal when it was inflamed among the co-housed conspecifics. This also destabilized the rank of the non-inflamed animals in the same cage, as well. Chemogenetic suppression of the right CeA neuronal activities mitigated the bilateral hindpaw sensitization after facial inflammation, and excitation of the right CeA, but not that of the left CeA, in non-inflamed animals gave rise to de novo expression of bilateral sensitization. The essential role of the right CeA in regulating tactile sensitivity in the whole-body regions in response to primary transient inflammation will be discussed.

Symposium 11 Speaker3

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A Cortico-hypothalamic circuit controls estrus-dependent sociosexual behavior in females

Gender differences in social and emotional disorders have been widely reported. We have previously showed that oxytocin receptor interneurons (OxtrINs) in the medial prefrontal cortex (mPFC) regulate sexually dimorphic anxiety-like behavior in male mice and estrus-dependent sociosexual behavior in female mice. However, the downstream molecular and circuit mechanisms by which OxtrINs regulate sociosexual behavior in females remain unknown. Here, we identify that cacna1h expressing neurons, which project to anterior hypothalamic nucleus (AHN) are innervated by OxtrINs in the mPFC. Silencing of cacna1h+ neurons or deletion of cacna1h gene in the mPFC specifically reduces female social interest toward male mice during estrus. The internal estrous cycles in females drive the temporal changes in transcriptome profile as well as synaptic plasticity of cacna1h+ neurons in the mPFC. We further show that calcium activities of cacna1h neurons dynamically encode social approach behaviors in females at estrous phase of their cycles. Our data identify the critical role of Cacna1h+ neurons for responding to estrous cycle in the mPFC and reveal the circuit mechanism that mPFC OxtrINs act directly on Cacna1h+ neurons projecting to AHN to promote sexually dimorphic estrus-linked sociosexual behavior in females.

Symposium 11 Speaker 4

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Dopaminergic regulation of accumbal cholinergic interneurons defining susceptibility to cocaine addiction

Striatal cholinergic interneurons (ChINs) play critical roles in processing value information for natural rewards and drugs of abuse, mainly by shaping the activity of medium spiny neurons of nucleus accumbens (NAc). However, their contribution to development of addiction and underlying mechanisms remain largely unknown. Using mouse models, we assessed seeking behaviors under a prolonged progressive ratio schedule of cocaine self-administration, which was followed by ChIN-specific RNA sequencing of striatal regions. ChINs, which were selectively isolated by fluorescence-activated cell sorting, were prepared for the transcriptome profiling with ChAT+ cells. Such cell-type specific transcriptome analysis revealed that dopamine D2 receptor (DrD2) are highly expressed in the NAc of mice that are more prone to cravings for cocaine. ChIN-specific DrD2 overexpression *per se* is sufficient to induce addiction-like behaviors, which could be normally evoked by repeated infusion of cocaine. We also found that *in vivo* activity of accumbal ChINs was diminished upon cocaine infusion. Collectively, our data establish a novel mechanism underlying core behavioral symptoms of drug addiction.