ture/silent state. We also identified functionally impaired *LRFN2* missense mutations in autism and schizophrenia patients.

Because further studies on the involvement of *LRFN2* in LDs and ASPD are warranted, we are now trying to establish new experimental systems in non-human primate neocortex. We will hopefully provide a means for understanding the cellular /or synaptic pathophysiological mechanism in higher cognitive function.

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P06.12

Differential expression of Cul4a and Cul4b by NMDA-evoked neuronal activity

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Cul4a and Cul4b are a core component of cullin-RING-based E3 ubiquitin ligase complex, which has multiple functions including DNA repair, chromatin remodeling and cell cycle regulation via ubiquitination of Ddb1-recruited target molecules. Although they have highly overlapped functions with high homology on their protein sequences as paralogue proteins, an irreplaceable role among them has been also proposed. Especially, Cul4b plays a critical role in neurodevelopment implicated with X-linked mental retardation unlike Cul4a. However, a specific role of CUL4A in nervous system has been veiled. In this study, we found that proteins of Cul4a and Cul4b are enriched in differential intracellular compartment of neurons. In addition, glutamate-evoked neuronal activity induces nuclear translocation of Cul4a with degradation of Cul4b. Pharmacological study shows that this process is mediated by intracellular calcium influx via NMDA receptor. Taken together, we suggest that Cul4a has an irreplaceable and differential role in nervous system compared to Cul4b.

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P06.13

CAST/ELKS regulates presynaptic morphology and calcium channel levels in a developing central synapse

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Synapses regulate neuronal circuits output through a network of presynaptic active zone proteins that regulate synaptic transmission, plasticity and morphology. The CAST/ELKS protein family are evolutionary conserved active zone molecules that regulate presynaptic calcium channel levels and the efficacy of synaptic transmission. Since the CAST and ELKS proteins are functionally redundant, how these proteins regulate presynaptic development and function during neuronal circuit development in the mammalian central nervous system remain enigmatic. Therefore, to unravel CAST/ELKS roles in glutamatergic presynaptic development we deleted both CAST/ELKS early in the developing calyx of Held, a central glutamatergic presynaptic terminal critical for encoding sound localization information, and analyzed calyx morphology prior to the onset of hearing. Here we report that combined deletion of CAST/ELKS result in a reduction in the surface area and volume of presynaptic terminal and increase in active zone size. In addition, we found a reduction in Cav2.1 numbers and reduction in presynaptic calcium currents. However, these morphological changes and changes in CaV2 currents did not impair synaptic transmission. Therefore, our data identify roles for CAST/ELKS proteins in regulation of presynaptic development and suggest there is a developmental compensation to preserve synaptic transmission.

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P06.14

The roles of $Na_V1.9$ and BK channels in rebound depolarization in cortical pyramidal neurons

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Rebound depolarization (RD) is a form of membrane depolarization triggered in some neurons following hyperpolarization. Typically, a series of action potentials are evoked during RD plateau. RD converts an inhibitory signal arriving to the neuron into an excitation signal, which is subsequently synaptically transmitted to other cells. The nature of RD in cortical neurons has been tested for several years without satisfactory explanation. The purpose of our study was to identify the ion channels involved in generation of RD in synaptically isolated layer V medial prefrontal cortex pyramidal neurons in slices obtained from adult rats. The key finding of our study is that following temporary hyperpolarization, two currents are concomitantly activated: (1) a low-threshold, persistent inward Na^+ current ($Na_V1.9$) that evokes RD; and (2) an outward K^+ current through Ca^{2+}-dependent K^+ (type BK) channels that opposes Na^+-dependent depolarization. These currents conceal each other in resting conditions, not allowing the emergence of RD. RD occurred when the outward K^+ current through BK channels was abolished by the extracellular application of paxilline, by removing Ca^{2+} from either the extra- or intracellular solution, by activation of phospholipase C or protein kinase C. On this basis, we conclude that the tetrodotoxin-resistant sodium channels $Na_V1.9$ and Ca^{2+}-dependent potassium channels type BK are involved in generation of RD in cortical pyramidal neurons.

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P06.15

Theta burst firing induces intrinsic plasticity in dentate gyrus granule cells

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Plasticity in the nervous system expresses at multiple scales to support reliable storage of information and in forming the substrate for learning. Despite the demonstration of encoding roles for dentate gyrus (DG) neurons as engram cells, surprisingly less

attention has been devoted towards intrinsic plasticity in the DG. Motivated by theta-modulated burst firing in DG granule cells observed *in vivo*, we investigated the ability of theta burst firing (TBF) to induce activity-dependent plasticity in these cells. We performed somatic whole-cell current-clamp recordings from granule cells in 6–8 weeks old male Sprague-Dawley rats. We recorded several intrinsic properties before and 40 minutes after the induction of TBF. In response to TBF ($n = 32$), we observed a significant 16% reduction in input resistance accompanied by a contrasting increase in firing rate, measured as a significant leftward shift in the f–I curve (~7 Hz increase for 250-pA current injection). The calcium-dependence for this form of intrinsic plasticity was evidenced from the blockade of plasticity by 30 mM BAPTA ($n = 13$), a fast calcium chelator. Although plasticity persisted in presence of synaptic blockers (AP5, $n = 12$; AMPA and GABAa blockers, $n = 11$), introduction of heparin blocked plasticity, pointing to $InsP_3$ receptors as a potential calcium source. Finally, as the opposing changes in sub- and supra-threshold excitability measurements pointed to changes in multiple channels, we performed TBF experiments in the presence of pharmacological agents that block HCN (ZD7288, $n = 12$) or NaP (Riluzole, $n = 10$) channels. Based on independent plasticity blockade by these pharmacological agents, and based on several sub- and supra-threshold measurement changes, we provide strong evidence to support that conjunctive changes in HCN and NaP channels mediate this form of plasticity. Our results unveil a form of activity-dependent intrinsic plasticity that could act as a candidate for achieving functional goals of learning and memory in the DG.

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P06.16

Application of polysome profiling analysis in the study of synaptic protein translation

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In the nervous system, synapses play a key role in information transfer within brain networks and are most closely correlated with brain functions such as learning and memory. Translation is an essential biological process for the formation, plasticity and function of synapses. Several studies have indicated that translational dysregulation is linked with neurodegenerative diseases such as Alzheimer's disease. Polysome profiling separates the subcellular fractions of the ribosomes using sucrose density gradient ultracentrifugation, which is an effective method for studying the translation state of proteins of interest. However, application of this technique to study translation of specific synaptic proteins is just starting to be reported. In the current study, we utilized polysome profiling to separate ribonucleoproteins, monosomes and polysomes from adult mouse hippocampus. Subsequently, we assessed the distribution of mRNAs of synaptic proteins in different fractions using qPCR. The result showed that different glutamate receptor subunits have different distribution profiles. For example, **t**he mRNAs of *Grin1*, *Grin2a* and *Grin2b* are more distributed in the polysome fraction, whereas more *Gria1* is associated with the monosomes. Further studies are ongoing regarding the change of polysome distribution of these mRNAs in response to synaptic activity.

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P06.17

RNA editing of ionotropic glutamate receptors in the suprachiasmatic nucleus

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RNA editing is responsible for posttranscriptional modifications of RNA. Editing of adenosine to inosine is essential for the formation of functional properties of ionotropic glutamate channels (iGluR) mediating the fast excitatory transmission. Previously, it was demonstrated the regulation of RNA editing upon manipulation with neural activity in vitro. Here, we present the data that describe the extent of iGluR RNA editing regulated by neural activity in vivo, in the structure of hypothalamic suprachiasmatic nuclei (SCN), which serve as a master circadian pacemaker. SCN neuronal activity depends on glutamatergic neurotransmission, in particular for signal transmission from the retina to the ventrolateral region of SCN, and SCN exhibits spontaneous 24 h rhythmical neural activity. Our results indicate changes in the extent of iGluR RNA editing and subunit expression in the SCN during the 24 h cycle. We assessed RNA posttranscriptional modifications using PCR amplification and subsequent sequencing of iGluR subunits. In parallel, using qPCR and in situ hybridization, we also determined the level of mRNA expression of GluA1 and GluA2 subunits and the editing enzyme ADAR2 in the SCN. Our results indicate that the level of RNA editing of iGluRs subunits is increased in conditions of light-induced neuronal activity. Analysis of mRNA expression of GluA1 and GluA2 subunits showed changes during the circadian cycle, which are likely to be controlled by endogenous circadian rhythm of the SCN. In summary, changes in expression of iGluRs subunits including their RNA posttranscriptional modifications serve as an additional mechanism involved in the signaling pathway of SCN synchronization with light stimuli.

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P06.18

Actions of neuropeptide Y on synaptic transmission in the lateral habenula

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Neuropeptide Y, a peptide neuromodulator, has known for its protective roles including anxiolytic and antidepressant-like effects in animal models of depression and post-traumatic stress disorder. The lateral habenula (LHb) is a brain region encoding aversive information and is closely related with mood disorders. Although LHb neurons express NPY receptors, the physiological roles of NPY in this region remain uninvestigated. Using whole cell patch clamp recording, we observed that NPY inhibited excitatory neurotransmission in a subset of LHb neurons whereas potentiating in a small population of neurons. Inhibitory transmission remained unchanged by NPY application in a subset of neurons but was reduced in the majority of LHb neurons recorded. The overall outcome of NPY application was a decrease in spontaneous firing rate of the LHb, leading to hypoactivation of the LHb. We found that protein kinase C but not protein kinase A mediates the inhibitory action of NPY on inhibitory transmission of LHb neurons. Our observations revealed that NPY has divergent effect on excitatory versus inhibitory transmission yet NPY receptor activation decreases LHb