Abstract
Most virgin male mice show aggressive behavior when they face pups. However, they show parental care after being fathers through mating and co-housing with the partner. Castrated virgin male mice show parental behavior as fathers do, and we confirmed this behavioral change were suppressed by the treatment of testosterone. This result reveals that testosterone interfere with the parental behavior. However, the neural mechanism of testosterone-induced behavioral change is still poorly understood. Thus, we examined the effects of dihydrotestosterone and estradiol, testosterone’s metabolites, on parental behavior. We embedded the silastic tubes filled with hormones in the castrated male mice subcutaneously and assessed behavioral pattern toward pups. As a result, the ratio of subjects showing the infanticide was significantly increased by the treatment of the silastic tube filled with estradiol, but not with dihydrotestosterone.

Then, we focused on the medial amygdala (MeA) which express aromatase. Aromatase is known as the enzyme that converts testosterone to estradiol. Moreover, it is previously reported that the numbers of c-Fos positive neurons in the MeA in the virgin male mice are significantly increased after pup exposure. We injected the N-methyl-D-aspartic acid, known as an excitatory neurotoxin, into the MeA and observed the behavioral pattern. The lesion of the MeA resulted in the decreased ratio of the infanticide, whereas all subjects of the control group showed the infanticide. These studies set up the hypothesis that brain testosterone are converted to estradiol in the MeA and lead to the infanticide.

PT716
Treatment with the Chemotherapeutic Drug Methotrexate Impairs Long-Term Potentiation in the Hippocampus
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Abstract
Post-chemotherapy cognitive impairment is an important problem in cancer survivors. After chemotherapy some patients suffer from memory lapses, have trouble concentrating and remembering details and have problems multitasking. Methotrexate (MTX) is used to treat various forms of cancer as well as rheumatoid arthritis, psoriasis, lupos erythematousus, Crohn’s disease and graft –versus–host disease. MTX inhibits adult hippocampal neurogenesis and produces cognitive impairment in rodents. Long-term potentiation (LTP) of synaptic transmission is one of the major cellular mechanisms underlying memory and learning. The objective of the present study was to determine whether MTX treatment impairs hippocampal LTP. Seven week-old, female C57/BL6 mice were given injections once a week for 3 weeks with either saline or MTX (30 mg/kg/i.p). One week after the last injection, hippocampal slices were prepared for electrophysiological recording in field CA1. After 2h of incubation, field EPSPs elicited by stimulation of the Schaffer collateral pathway were recorded in CA1 stratum radiatum. LTP was induced by theta burst stimulation (TBS; 10 bursts of 4 pulses at 100 Hz delivered at 5 Hz). EPSP slope values were normalized to the average slope of responses recorded during the 10min baseline, and responses were recorded for at least 30min after LTP induction. Paired-pulse facilitation, which is widely considered to reflect changes in the probability of transmitter release, was significantly impaired at most interstimulus intervals in slices from MTX-treated mice. LTP was completely absent 30min after TBS and even the short-term potentiation observed between 0 to 5min after TBS was markedly reduced in slices from MTX-treated mice. The present study is the first to report that MTX impairs LTP in the hippocampus. These results could account for some of the cognitive impairment reported in patients treated with MTX for a wide variety of clinical conditions.
hydrophobic monoamines can potentiate or inhibit acid-sensing ion channels (ASICs) depending on subunit composition. With help of short screening of endogenous monoamines, based on previous structure-activity analysis, we found that histamine selectively potentiates ASIC1a channels. The experiments were performed on the recombinant homomeric receptors ASIC1a, ASIC1b, ASIC2a and ASIC3 expressed in CHO cells using “whole-cell” patch clamp technique. Except ASIC1 homomers, ASICs were not affected by 1 mM of histamine. Potentiating activity of histamine on ASIC1a demonstrated strong dependence on activating pH. Thus, 1 mM of histamine caused 190 ± 30% (n=6) potentiation at pH=7.0 and only 14 ± 10% (n=5) at pH=5.0. Important to note that reliable potentiating effect was observed even for physiologically relevant concentrations of histamine (50 mM), during low acidification (pH=7.0). Possible mechanism of histamine action on ASIC1a is in increase of protons affinity to receptor due to allosteric modulation of proton-binding site. This hypothesis need to be verified in future studies. Our results shed light on one of the possible physiological mechanisms, underlying ASICs normal functioning in the brain.

**PT719**

Asymmetrical electroencephalographic change of human brain during sleep onset period

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Abstract

Objective: The human cerebral hemispheres are known to function asymmetrically with daytime left hemisphere superiority in most right-handed persons. It may have relevance to localization of specific function of the brain. This study attempted to reveal whether or not the functional cerebral asymmetry of wakeful state holds in the sleep onset period.

Methods: Thirty channel EEG was recorded in 61 healthy subjects (male: female = 34:27, age = 27.2 ± 3.0 years). EEG power spectra in seven frequency bands (delta, theta, alpha-1, alpha-2, beta-1, beta-2 and beta-3) were compared between two kinds of 30 second states such as wakeful stage (WS) and late sleep stage 1 (LSS1). These two stages were selected by the distribution of the alpha and the theta in O1 and O2 electrodes. WS was determined as the first 30 seconds having 100 % of alpha pattern. LSS1 was defined as the last 30 seconds of sleep stage 1. In paired recordings, synaptic potentials evoked by the theta in O1 and O2 electrodes was compared between WS and LSS1 stages.

Results: The asymmetry indices of LSS1 at some frontocentral leads were decreased in delta, theta, alpha2 and all beta bands. On the contrary, at parts of parietooccipital leads showed increased indices in theta, alphas, beta1 and beta2 bands. Any frontocentral leads did not show the increase of the index, neither did any parietooccipital leads the decrease of it.

Conclusions: During sleep onset period, power spectral asymmetry of the hemispheres showed a different pattern compared to wakeful stage. This asymmetrical pattern of EEG powers may suggest the reversal of left hemispheric dominance during sleep.

**Key words:** cerebral asymmetry, sleep onset period, EEG spectra, LORFETA (low resolution electromagnetic tomography)

**PT720**

Distinct properties of a subgroup of layer 2 neurons in mouse temporal cortex

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Abstract

The neocortex is the core structure for our mental function. The function of the neocortex should depend at least in part on the diversity of its neuron types. Recent evidence suggests that excitatory neurons in layer 2/3 can have different properties. It is unknown, however, to what extent neurons in these layers are diverse. Here we focused on layer 2 neurons located at the border between layer 1 and layer 2, referred to as layer 2 roof neurons (L2RNs), and compared the morphology, physiology, and pharmacology of these neurons to other layer 2/3 neurons in mouse temporal cortex. Combining multiple whole-cell patch clamp recording and drug application, we found that L2RNs were excitatory neurons with homogeneous intrinsic membrane properties. All L2RNs showed regular firing pattern with moderate adaptation. Compared with other layer 2/3 regular spiking neurons, they showed higher firing rate, less adaptation, more depolarized resting membrane potential, and higher input resistance. In paired recordings, synaptic potentials evoked by L2RNs could be completely blocked by DNQX, suggesting a glutamatergic nature of the synapse. Although the synaptic potentials showed no difference between L2RNs and other layer 2/3 regular spiking neurons, synaptic depression in L2RNs exhibited dependence on postsynaptic neurons. Taken together, our findings suggest that L2RNs are a subtype of excitatory neurons in layer 2/3, with distinct properties from other regular spiking neurons in these layers. The unique property of synaptic depression in L2RNs suggests their role in the dynamic aspect of brain function.

**Key words:** cortex; neuronal diversity; neuronal connections; intrinsic properties

**Background:** Recently, methamphetamine (METH) use in adolescent has increased persistently and their exposure to METH at earlier ages compared to adults can cause more severe damage in the brain. It is necessary to evaluate the cellular and molecular mechanisms associated with brain damage induced by METH depending on the age. The present study was aimed to investigate the differentially expressed genes (DEGs) and their functions in the hippocampus of cynomolgus macaques, Macaca fascicularis, according to age after the administration of METH.