receptor-derived excitatory postsynaptic potential (NMDA-R-EPSP) was used to analyze the mechanisms of these events. Taken together all the results, estradiol rapidly restored the corticosterone-induced suppression of LTP and NMDA-R-EPSP. Corticosterone receptor $\rightarrow$ phosphatase pathway is involved in these suppression effects. Restoration by estradiol is driven via estradiol receptor $\rightarrow$ MAP kinase pathway.

2P-197 多時間スケールをもつ学習モデルとその相空間構造の変化 Learning Model with Multiple timescales and Change in a Structure of Phase Space

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A novel neural-network model with multiple time scales is proposed. We first set 2 basic postulates in the learning model. 1. The learning process should not require too much information, as much as the number of neurons. 2. A model of neural system should learn input-output relationship, one by one, i.e., the system learns novel input-output pattern after one pattern has been learned. Here we introduce a biological learning model satisfying the above two postulates; Many input-out patterns are learned one by one, with just a single error information to all neurons. The synapse among neurons change under Hebbian and anti-Hebbian dynamics, with regards to the error from the output neurons and target output patterns. This model can learn the several patterns by repeating searching process with anti-Hebbian dynamics and stabilizing process with Hebbian dynamics. In the model, there are three time scales, that for neural activity change τ_{cell} , those for the changes in the feed-back synapse from the output layer τ_{FB} , and in the feed-forward synapse τ_{FF} . From extensive simulations of the model, we have shown that the model can achieve maximal capacity of memory of input-output patterns when the condition $\tau_{\text{cell}} < \tau_{\text{FB}} < \tau_{\text{FF}}$ is satisfied. With the progress of learning of successive novel patterns, the neural dynamics are shaped, so that the output neurons show the corresponding target patterns after the application of the corresponding input pattern. This learning process also alters the dynamics of spontaneous neural activities, without inputs. Indeed, the neural state itinerates over several states that correspond to the memorized target pattern, whereas there are bifurcations to fixed point attractors that give each of the target output pattern, by the application of the corresponding input.

2P-198 新規な神経スパインの解析手法とその適用 Novel methods and its applications for analysis of spines in neurons

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Dendritic spines in the brain are substrates of synaptic contacts that may be involved in neuronal computational processes. Visualization and analysis of dendritic spines is of critical importance to elucidate physiological changes of morphological plasticity, as well as effects of various hormones and pharmacological agents. Advent of laser-scanning confocal microscopy / 2-photon microscopy and fluorescent dye allowed us to collect large body of neuronal image data, namely tens of dendrites and several tens of thousands of spines residing on each dendrite of single neurons. Conventional methods using manual tracing software need time-consuming efforts by researchers and not suitable to handle large data. Therefore introduction of protocol for a new automatic analysis of neuronal structure including spines will greatly enhance progress of research in the area. Here we developed a new software, Spiso-3D, to extract spines as well as dendrites and in neuronal image based on their geometrical features. Our "geometric method" utilizes scale-free, shape-dependent analysis, making less dependent on brightness in the image. Because Spiso-3D is a Java-based program, it will readily work on a PC with a relatively limited resource. Using the Spiso, we analyzed the effect of activin, an endogenous sex hormone in the mammalian brain, on spines of hippocampal neurons. We also investigated the effect of disruption of estrogen receptors in the hippocampus using ERalpha and ERbeta KO mice.

2P-199 遺伝子改変マウスを利用した摂食調節に関するニューロンの同定

The use of gene-targeted mice to identify neurons involved in the regulation of feeding behavior

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The regulation of food intake is coordinated by neurons in two areas of the brain, known as the feeding center and the satiety center, which are both located in the hypothalamic area. This conclusion was, however, derived from rather rough studies that employed destruction experiments of hypothalamus. Recently, efforts have been made to uncover hypothalamic neuronal circuits that control feeding behavior, but are not well clarified yet. The present study aimed to identify neurons involved in the regulation of feeding behavior by use of gene-targeted mice. We developed mutant mice in which histamine H1 receptor-expressing neurons can be selectively ablated in a time- and space-specific manner. We chose H1 receptor because this receptor is profoundly involved in the regulation

of feeding behavior; H1 blocker facilitates feeding and H1 receptor-KO mice become obese. This mouse expresses immunotoxin-sensitive human IL-2 receptor in place of murine H1 receptor, and microinjection of immunotoxin will selectively eliminate H1 receptor-expressing neurons. This mouse also expresses GFP proteins in conjunction with IL-2 receptor allowing the detection of the H1 receptor-expressing neurons. If the H1 receptor-expressing neurons in the hypothalamus are involved in feeding behavior, the ablation of these neurons will affect feeding. These neurons can be identified and characterized by immunohistochemistry and then by electrophysiological methods such as slice patch clamp in which these neurons can easily be detected by their GFP fluorescence.

2P-200 瞬目反射条件付けの記憶獲得および消去に関する内在性カンナビノイドの同定

The identification of endocannabinoid ligand responsible for memory formation and extinction of classical eyeblink conditioning

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The cannabinoid receptor type 1 (CB1R) is member of the G-protein coupled receptor family, that is activated by the endocannabinoids. In mammals, a number of endogenous cannabinoids have been identified, including 2-arachidonoylglycerol (2-AG) and anandamide. Recent studies demonstrated that endocannabinoid system through the CB1 receptor plays important role for both hippocampus-dependent and cerebellum-dependent functions. The blockade of CB1R impairs extinction of hippocampus-dependent memory and facilitated hippocampal CA1 long-term potentiation. In contrast, cerebellum-dependent eyeblink conditioning and cerebellar long-term depression (LTD) are impaired by CB1R inhibition. However it still remains unclear which endogenous ligand of CB1R is responsible for these memory processes. In this study, we tested the hypothesis that elevating brain levels of endogenous cannabinoid anandamide control acquisition and/or extinction of conditioned responses during cerebellum-dependent delay and hippocampus-dependent trace conditionings. C57BL/6J mice treated with FAAH (fatty acid amide hydrolase) inhibitor URB597 (*i.p.* 1mg/kg 0.2ml) did not display any motor discoordination, but did exhibited a significant increase in the rate of delay conditioning. Extinction of delay CRs was not affected by FAAH inhibitor. On the other hand, FAAH inhibitor had no effect on both acquisition and extinction during trace conditioning. These results indicate the endogenous anandamide could participate in memory formation of cerebellum-dependent motor learning, but not in hippocampus-dependent eyeblink conditioning.

2P-201 瞬目条件反射の獲得と発現における代謝型グルタミン酸受容体 1 型(mGluR1)の役割

The functional role of mGluR1 within cerebellar Purkinje cells in acquisition and expression of conditioned eyeblink response

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Tetracycline-inducible gene expression (Tet-ON/Off) system allows reversal suppression of gene function and provides powerful tool to uncover the molecular mechanism underlying learning and memory. By using combination of cerebellar Purkinje cells (PCs)-specific promoter and the Tet system, a novel transgenic line called mGluR1 conditional KO (mGluR1c KO) mice was developed. In mGluR1c KO mice, cerebellar PCs specifically expressed the mGluR1 (metabotropic glutamate receptor-subtype 1) in a doxycycline (DOX)-dependent manner. In case of treating DOX-containing water, cerebellar PCs do not express mGluR1, whereas normal water induces mGluR1 expression within only PCs in the transgenic mice.

By utilizing the mutant mice, we first tested the role of mGluR1 within adult cerebellar PCs in acquisition of classical eyeblink conditioning. Dox-induced disappearance of mGluR1 in PCs severely impaired acquisition of conditioned responses (CRs) in the mutant mice, whereas DOX-untreated mGluR1c KO mice exhibited intact CR acquisition during the conditioning. Next, we examined the effect of switching the mGluR1 expression on eyeblink conditioning. Eyeblink CR remained severely impaired in mGluR1c KO mice conditioned with DOX even after 7-weeks DOX removal, suggesting that eyeblink memory had not been latently formed under DOX treatment. On the other hand, eyeblink CR was maintained in mGluR1c KO mice once conditioned without DOX even after 7-weeks DOX treatment, suggesting that mGluR1 is not essential for expression of acquired CR. These results clearly indicate that mGluR1 in adult cerebellar PCs is essential for memory formation but not for memory expression of eyeblink conditioning.

2P-202 ナメクジ嗅覚中枢の振動的活動における GABA 受容体を介した調節機構

GABA receptor-mediated modulation of oscillatory neuronal activity in slug olfactory center