神経病態解析学セミナー

awajiroの わがままセミナーシリーズ

本セミナーは、HBS研究部・神経病態解析学分野（准教授・笠原二郎）が不定期に主宰するセミナーシリーズで、聴衆（特に若者）への刺激とブレインストーミングを目的に、ジャンルを問わず各界の最前線でユニークな活躍をされている方々をお招きし、お話して頂きます。研究部の多くの学部生・大学院生・教職員の参加をお待ちしております。

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シリーズ第４回　演者： Prof. Maurizio Popoli

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演題：The Stressed Synapse

The Impact of Behavioral Stress and Glucocorticoids on Presynaptic Release of Glutamate

開催日時：2010年10月20日（水）17:00~18:30

開催場所：薬学部 2F 第1講義室（スタジオプラザ2F)

Popoli博士は、イタリア中枢神経薬理学界を常にリードするミラノ大学のベテラン研究者で、特に精神疾患やその治療薬とシナプス可塑性の分子機構について卓越した研究成果を挙げられています。本セミナー主宰者の笠原とは10年にわたって共同研究を続けています。藤井・大塚国際教育研究交流資金（短期招聘）により初来日されますので、この機会にセミナーをお願いしました（英語で行われます）。学内の多くの方々のご参加をお待ちしております（先端医療薬学1の講義を兼ねます）。

講演要旨

Dysfunction of glutamatergic transmission is considered a core feature of stress-related mental illnesses such as schizophrenia, mood, and anxiety disorders. However, the mechanisms whereby behavioral stress and glucocorticoids affect synaptic glutamate homeostasis are only starting to be elucidated. We have recently found that unpredictable footshock (FS)-stress induces a marked increase of depolarization-dependent glutamate release from synaptosomes of prefrontal/frontal cortex (P/FC). This change was prevented by chronic antidepressants (ADs). In addition, FS-stress caused in all stressed rats (vehicle- and AD-treated) a rapid increase of circulating corticosterone and glutamate release increase was found to be dependent on glucocorticoid receptor activation. At molecular level, FS-stress induced accumulation of SNARE complexes in presynaptic membranes. Patch-clamp recordings of P/FC pyramidal neurons confirmed that FS-stress induces an increase in glutamate release, completely prevented by AD treatment [1]. The studies in progress employ: (1) Measurement of glutamate release from synaptosomes in superfusion, comparing the effects of KCl (which, depending on the strength of the stimulus, releases neurotransmitters from the readily releasable pool [RRP] and from the recycling pool) with hypertonic sucrose (which mobilizes exclusively the RRP); (2) Analysis of the ultrastructure of asymmetric synapses and of the number of vesicles docked to presynaptic membranes with electron microscopy, in P/FC synaptosomes; (3) Evaluation of the kinetics of glutamate release with Total Internal Reflection Fluorescence Microscopy. Current preliminary results suggest that acute FS-stress increases the RRP of glutamate vesicles and changes the kinetics of release in P/FC.

Different studies on pre- and postsynaptic effects of stress suggest that different forms and durations of stress have wide ranging, but concerted effects on various components of the glutamatergic system. Together, these stress-induced effects on the glutamate synapse contribute to the processes of adaptive or maladaptive plasticity. This new understanding of stress-induced effects on the glutamate synapse provides new insight into normal brain function and the pathophysiology of stress-related neuropsychiatric disorders. Elucidating some of the physiological processes mediating the synapse's response to stress identifies several novel druggable targets that can potentially be used to develop improved interventions for the prevention and treatment of stress-related disorders.

[1] Musazzi et al., PLoS One. 2010 Jan 5;5(1):e8566.