Karolinska Institutet

Department of Neurobiology, Care Sciences and Society

MODULATION OF HIPPOCAMPAL GAMMA OSCILLATIONS BY DOPAMINE AND SEROTONIN RECEPTOR SUBTYPES

AKADEMISK AVHANDLING
Som för avläggande av medicine doktorsexamen vid Karolinska Institutet offentligen försvaras i Inghesalen, Tomtebodavägen 18A

Fredagen den 13 juni, 2014, kl 9:00

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Stockholm 2014

ABSTRACT

Normal brain function is dependent on the efficient and effective communication between the multitudes of microcircuits that it encompasses. The brain employs neuronal-network oscillations for large-scale communication in the cortex. Fast oscillations in the gamma range (20-80 Hz) arise in the cortex and the hippocampus and are thought to be involved in important cognitive functions such as sensory perception, attention, learning, and working memory. These oscillations are often impaired in disorders that have significant cognitive-deficit symptoms, such as schizophrenia, Alzheimer's disease, and depression. Recent research has shown that hippocampal oscillations are modulated by several neurotransmitters, yet contributions of specific receptor-subtypes, their cellular localization and mechanism of action are still understudied.

Local field potential (LFP) oscillations were recorded before and after application of specific agonists and antagonists to determine specific effects. Additionally, pyramidal cells and inhibitory interneurons were recorded alone or in parallel with the LFP to test how activation of a certain receptor subtype affects the electrical properties of that cell type and what mechanisms are used.

For the studies in this thesis, the effects of activation of dopamine and serotonin receptors on gamma oscillations were investigated. D4 activation was found to augment gamma oscillations and interact with the growth factor neuregulin during activation (study I). The mechanism responsible for this increase is mediated by interneurons firing more precisely (study II). In study III, activation of serotonin receptor type 1A expressed on pyramidal cells leads to a strong reduction of gamma oscillations, which is caused by activation of an inward-rectifying potassium channel. The preliminary results also point to a deficit in inhibitory transmission in rodents exposed to the serotonin reuptake inhibitor, fluoxetine.

Understanding these mechanisms is important for the development of strategies for treating disorders that may result from imbalances in neurotransmission, and may cause cognitive decline in a number of disorders in which abnormal gamma oscillations are a hallmark.

ISBN 978-91-7549-602-3