



**Karolinska
Institutet**

Institutionen för Neurobiologi, Vårdvetenskap och Samhälle

Aminergic Regulation of Neuronal Synchrony in the Hippocampus

AKADEMISK AVHANDLING

som för avläggande av medicine doktorsexamen vid Karolinska
Institutet offentlig försvaras i Birkeaulan, F-huset plan 5,
Blickagången, Karolinska Universitetssjukhuset Huddinge

Fredagen den 26:e oktober, 2012, 13.00

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Stockholm 2012

Abstract

Background

Gamma oscillations (25-80 Hz) are physiological electric activity patterns, prevalent in the brain, which are associated with attention, working memory, sensory perception, long-term memory encoding and recall. Importantly, in mental illnesses featuring cognitive disturbances (such as Schizophrenia or Alzheimer's disease) there are concomitant disturbances of gamma oscillations. All aspects of cognitive function are regulated by the aminergic systems of the brain, which are also associated with mental disorders. Yet little research has been done to understand how aminergic molecules modulate or control gamma oscillations.

Aims

We aimed to investigate whether gamma oscillations are modulated by aminergic G-protein-coupled receptors. We also wanted to determine which types of neurons and circuitry mechanisms are responsible for any aminergic effects uncovered.

Methods

We used an in vitro preparation of the rodent hippocampus in which stable gamma oscillations were elicited by the application of kainic acid. Combined extracellular local field potential and intracellular patch clamp recordings were used to reveal which network, synaptic and cellular parameters changed in response to various pharmacological challenges.

Results & Conclusions

We found that it is possible to bi-directionally regulate gamma oscillations in the hippocampus, without affecting the overall firing-rate of action potentials. Rather, it is the phase-synchronization of pyramidal cell and fast-spiking interneuron activity that is affected by histamine H3 and dopamine D4 receptors, respectively. This is a potential physiological mechanism by which the gain of signal transmission to downstream targets can be regulated. Targeting this mechanism may have a potential use in future antipsychotic or pro-cognitive pharmaceutical therapy.

ISBN 978-91-7457-884-3