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Gamma oscillations
Historical reference data

September 20, 2018

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INTRODUCTION

- Brain rhythms are periodically fluctuating waves of neuronal activity. Such rhythms reflect the synchronized activity of large numbers of neurons because synchronous currents sum together to generate large-amplitude fluctuations.

- Different types of brain rhythms are observed in humans, primates, as well as rodents and occur in many cortical and subcortical regions. Each type of rhythm is observed during particular behaviors, generated by specific mechanisms, associated with characteristic neuronal firing properties and are thought to perform distinct functions.

- The most ubiquitous rhythms are gamma oscillations. This rhythms represent a relevant parameter to investigate in CNS drug discovery as it is involved in cognition process and often impaired in disorders [implying cognitive deficits] such as schizophrenia, Alzheimer's disease, and depression.

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MATERIAL AND METHODS

- Preparation of acute rat hippocampal slices

Experiments are carried out with 3-4 week-old Sprague Dawley rats or 4-12 week-old mice. Transversal hippocampal slices are cut in the horizontal plane (450 µm and 400 µm thickness respectively for rats and mice) with a Leica VT1200S vibratome in an ice-cold oxygenated sucrose solution (sucrose 250, glucose 11, $NaHCO_3$ 26, KCl 2, NaH_2PO_4 1.2, $MgCl_2$ 7 and $CaCl_2$ 0.5 in mM).

The slices are incubated 1.5 hour at 32°C in aCSF of the following composition: glucose 11, $NaHCO_3$ 25, NaCl 126, KCl 3.5, NaH_2PO_4 1.2, $MgCl_2$ 1.3, $CaCl_2$ 2 in mM.

- Slice perfusion and temperature control

During experiments, the slices are continuously perfused with the aCSF (bubbled with 95% O_2–5% CO_2) at the rate of 6 mL/min with a peristaltic pump (MEA chamber volume: ~1 mL). Complete solution exchange in the MEA chamber is achieved 10 s after the switch of solutions.

The perfusion liquid is continuously pre-heated at 32°C just before reaching the MEA chamber with a heated-perfusion cannula (PH01, MultiChannel Systems, Reutlingen, Germany). The temperature of the MEA chamber is maintained at 32 °C with a heating element located in the MEA amplifier headstage.

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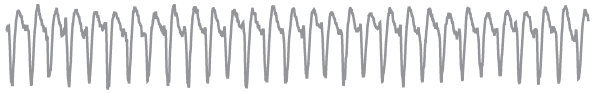
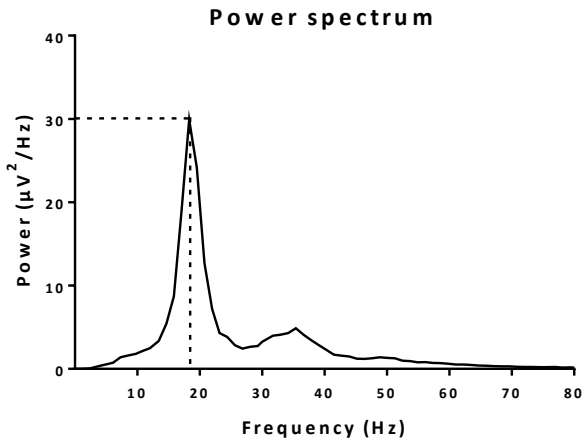
MATERIAL AND METHODS

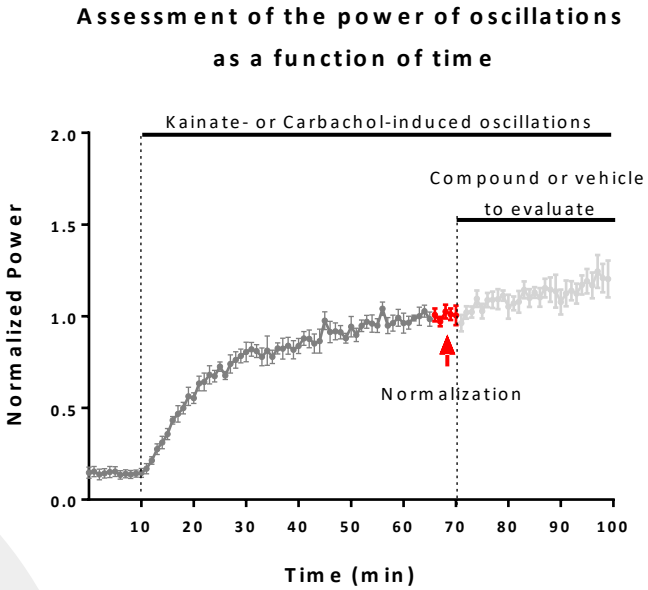
- Analysis

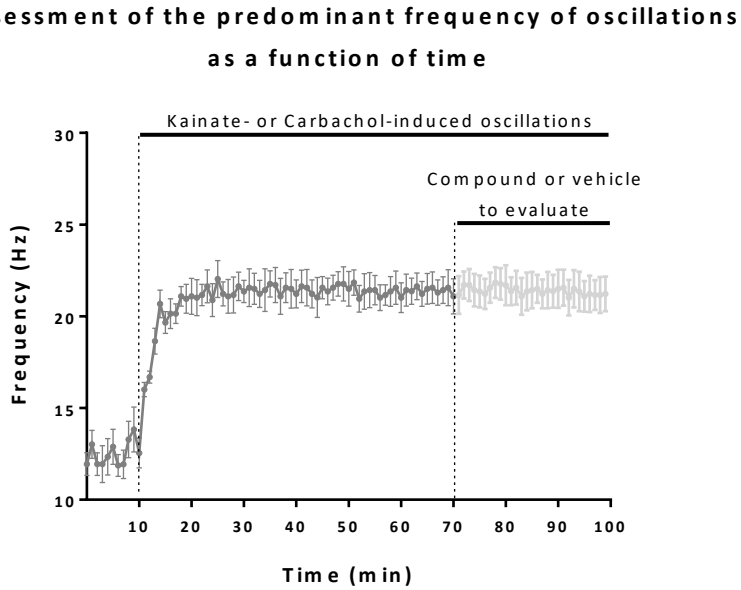


Extracellular recording of local field potential

Fast Fourier Transform
(performed at every minute time segment)







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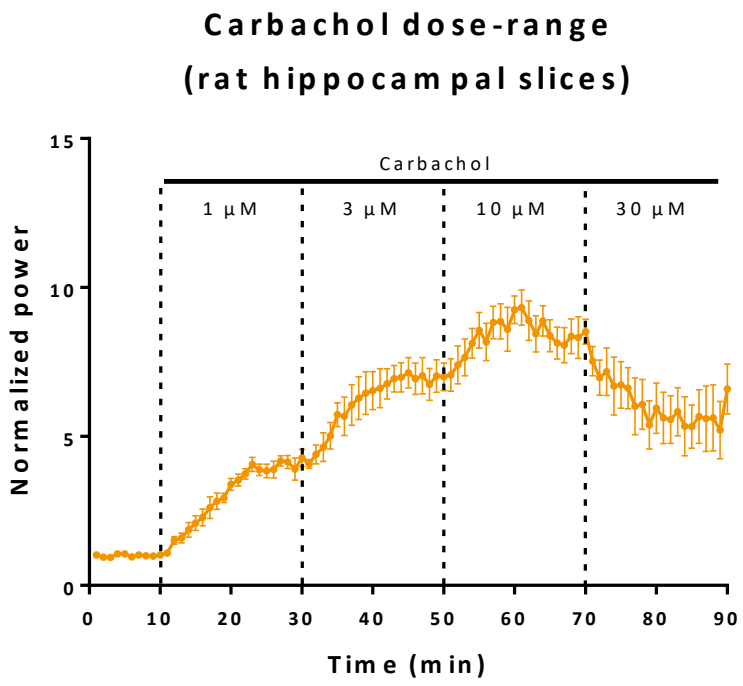
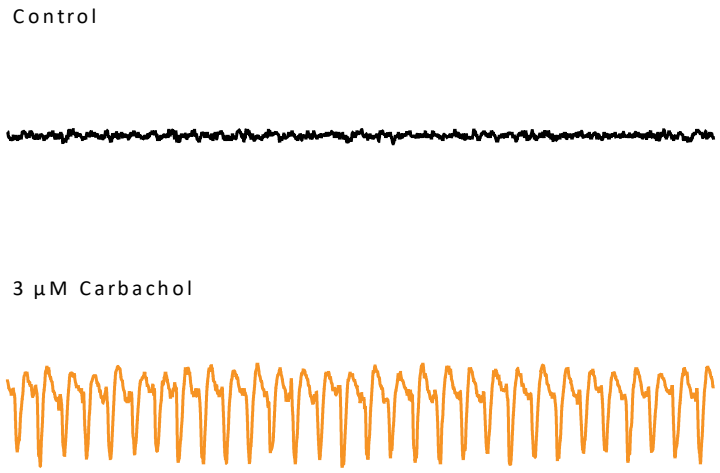
RESULTS

CARBACHOL INDUCES GAMMA OSCILLATIONS





Carbachol induced oscillations by mimicking cholinergic input to the hippocampus via the septum during exploratory behavior *in vivo*.
Oscillations are generated by alterning cycles of AMPA receptor mediated recurrent excitation followed by feedback inhibition from perisomatic-targeting interneurons. (Traub et al., 2000, Mann et al., 2005)

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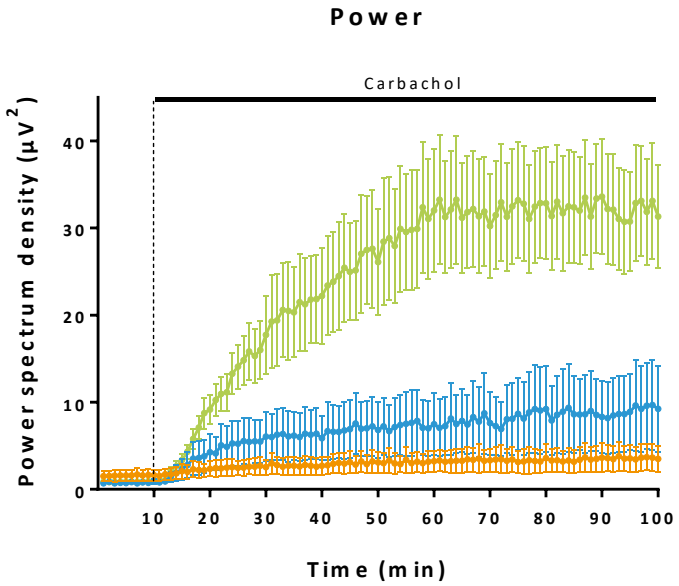
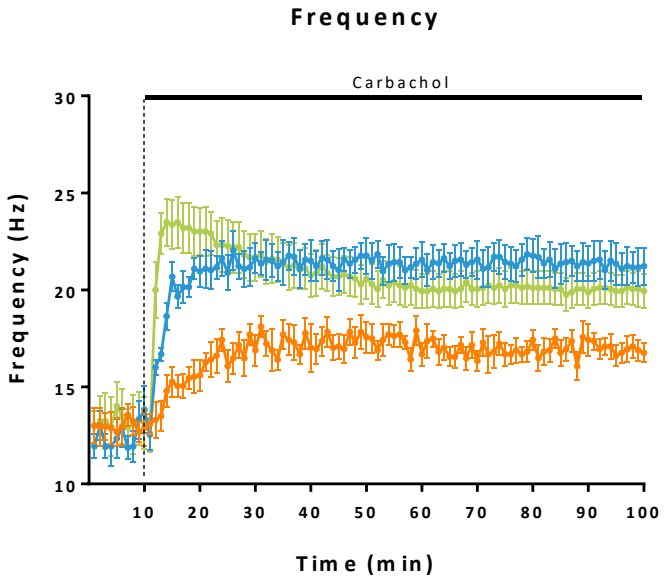
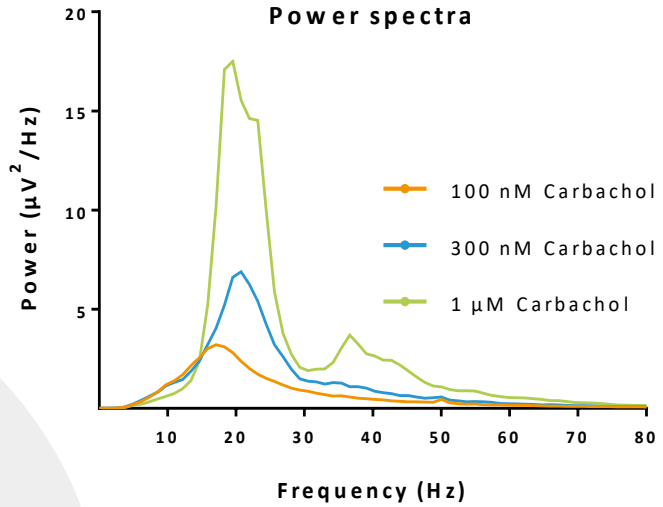
CARBACHOL INDUCES GAMMA OSCILLATIONS







100 nM carbachol triggers a weak oscillatory activity. The power of the oscillations increases as a function of carbachol concentration.

In the presence of 300 nM carbachol, the frequency of oscillatory activity was clearly higher than in 100 nM carbachol, but in the same range as in 1 µM carbachol.

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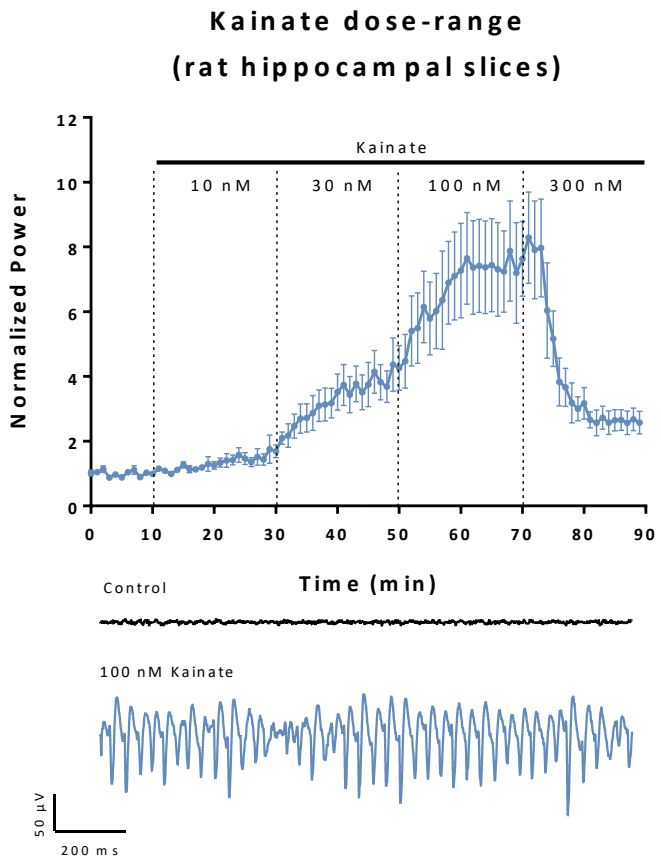
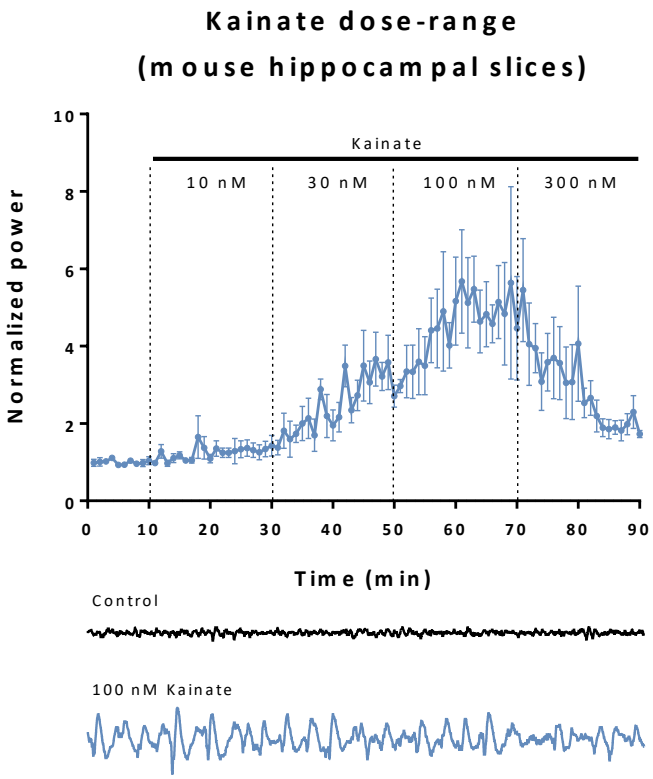
RESULTS

KAINATE INDUCES GAMMA OSCILLATIONS





Kainate induces oscillations by providing tonic excitation via ionotropic glutamate receptors activation to both excitatory and inhibitory neurons in the hippocampus (Clarke *et al.*, 1997; Fisahn *et al.*, 2004).

Network oscillations are induced in both rat and mouse hippocampal slices with maximal effect reached at 100 nM concentration.

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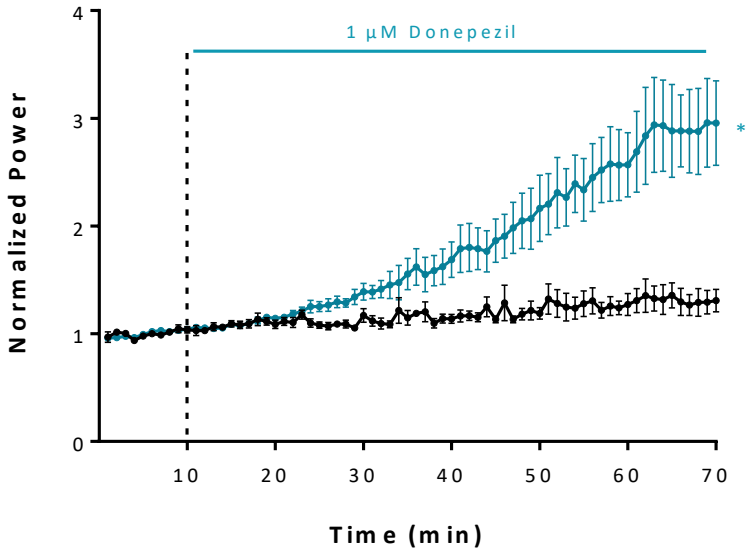
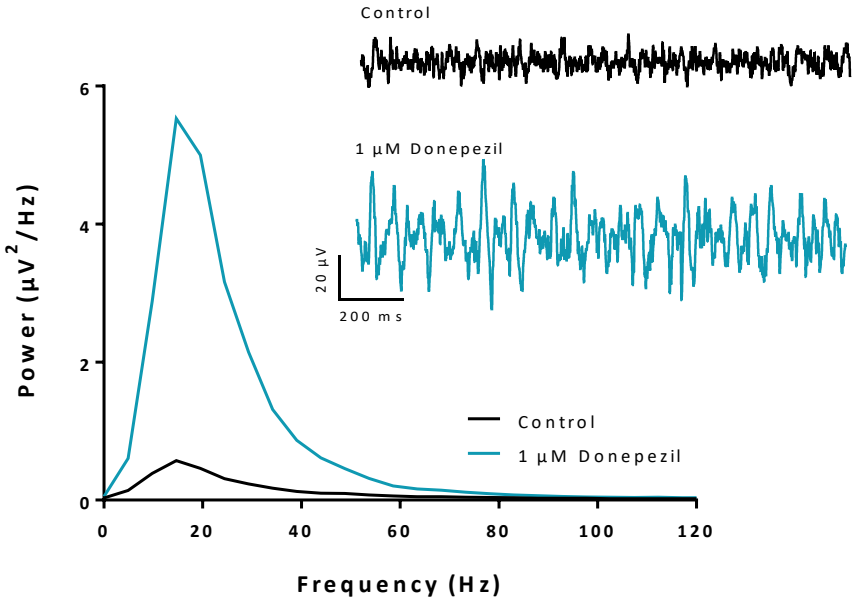
ACETYLCHOLINESTERASE INHIBITOR INDUCES GAMMA OSCILLATIONS





Donepezil – an acetylcholinesterase inhibitor approved for symptomatic treatment of patients with mild-moderate AD – is capable of inducing network oscillations.

The power of donepezil-induced oscillations continuously increased and did not reach stability after one hour of 1 µM donepezil exposure.

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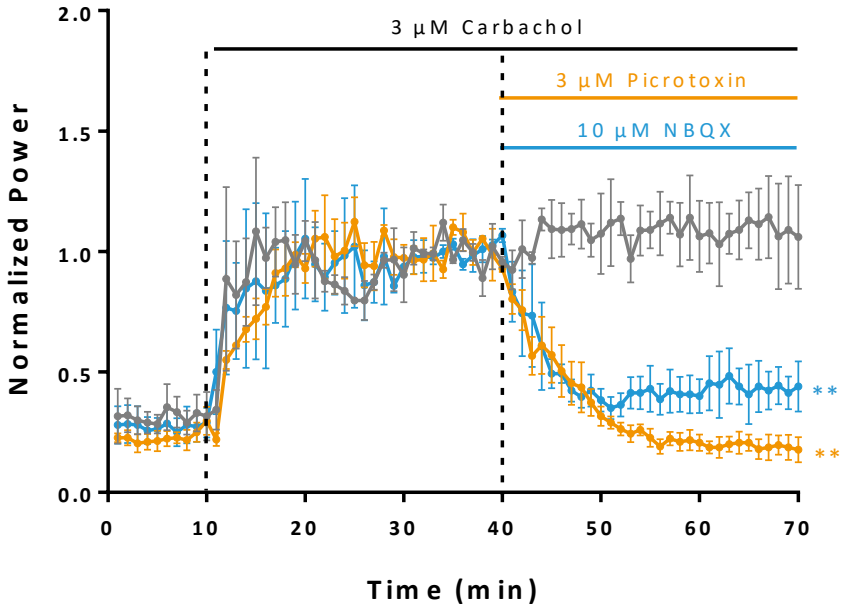
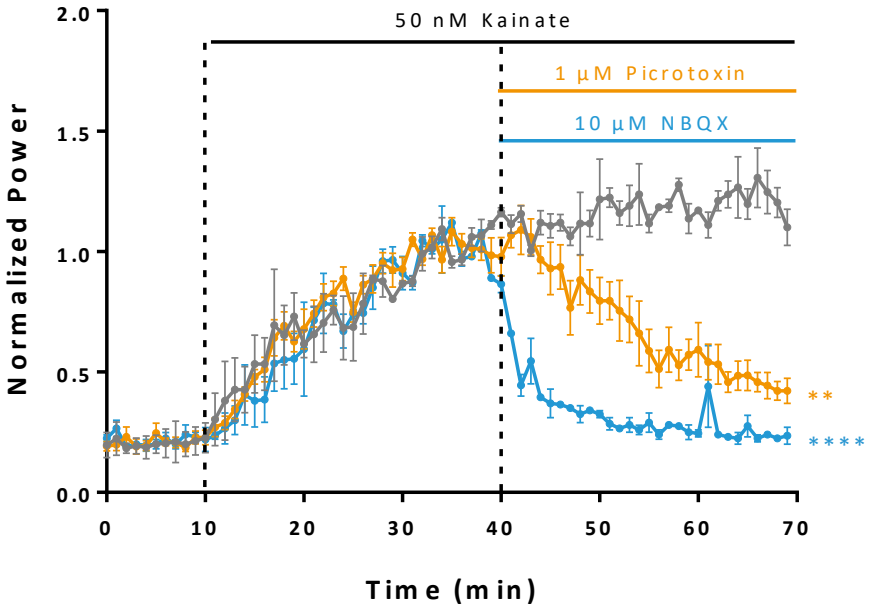
AMPA/KAINATE AND $GABA_A$ PATHWAYS PLAY A KEY ROLE TO GENERATE GAMMA OSCILLATIONS





Picrotoxin strongly inhibits both carbachol- and kainate-induced oscillations indicating a requirement of $GABA_A$-mediated inhibition within the neuronal network.

NBQX strongly inhibits both carbachol- and kainate-induced oscillations indicating an importance of AMPA/Kainate pathways.

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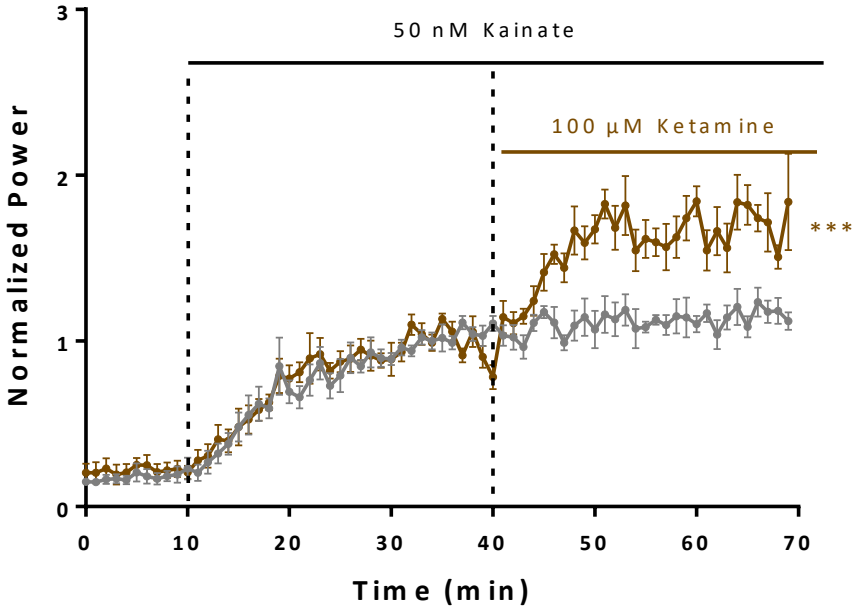
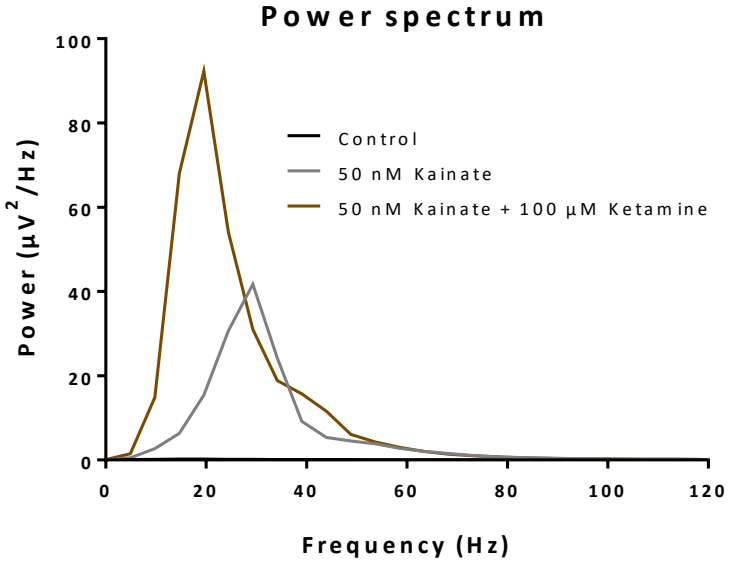
RESULTS

NMDA RECEPTOR MODULATES GAMMA OSCILLATIONS





Ketamine – a NMDA receptor antagonist – applied at 100 µM concentration increases the power of oscillations and decrease the frequency of oscillations.

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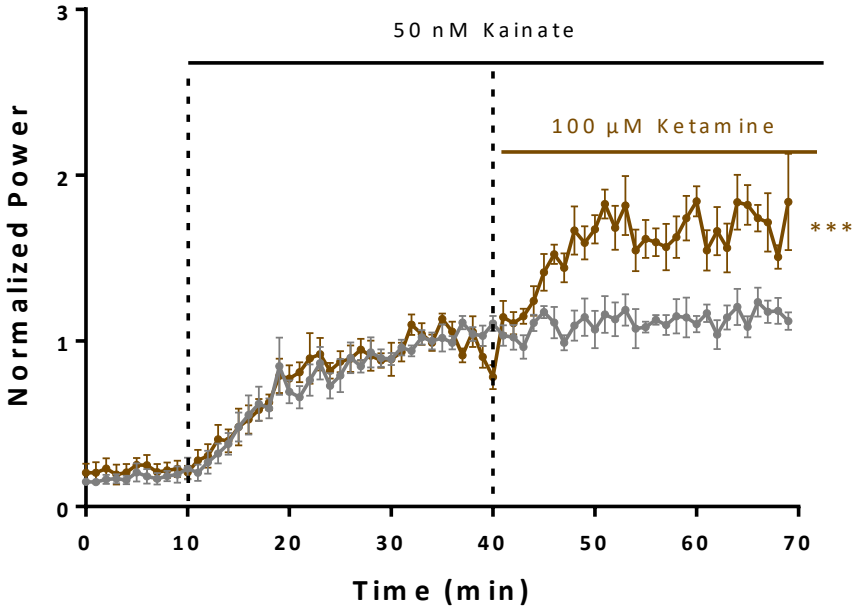
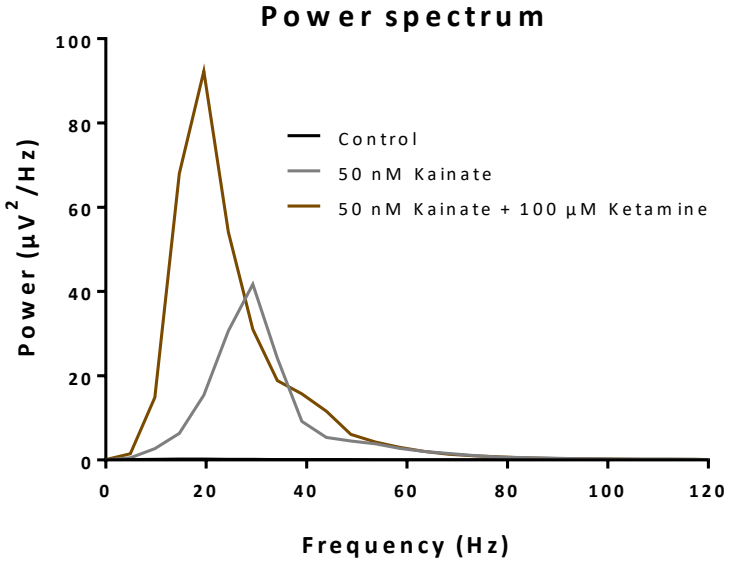
RESULTS

NMDA RECEPTOR MODULATES GAMMA OSCILLATIONS





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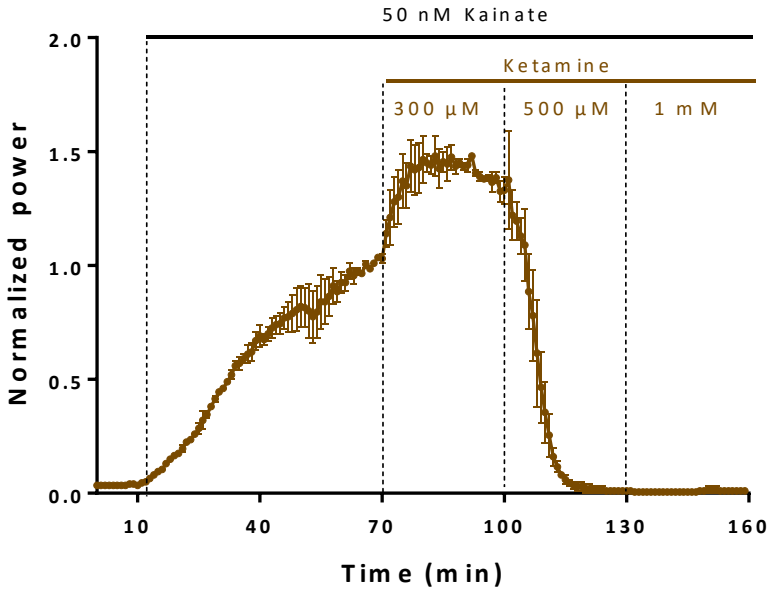

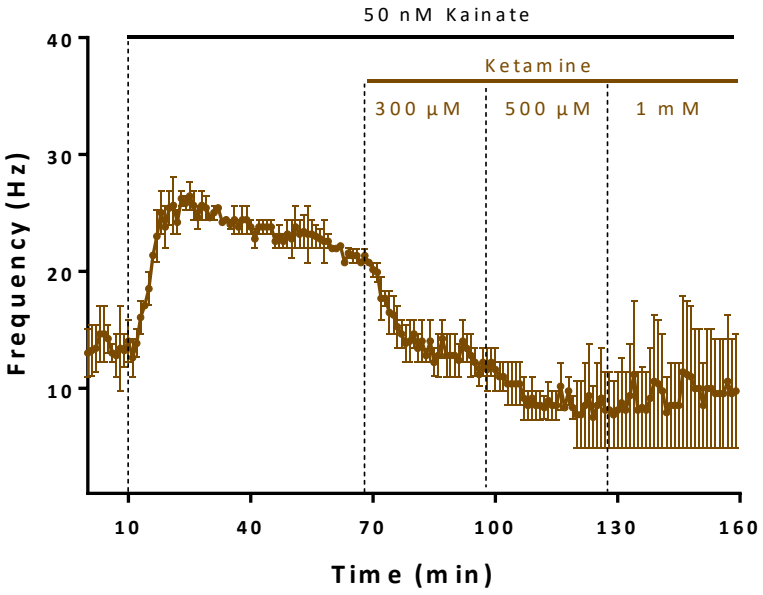

Applied at 300 µM concentration, Ketamine still increases the power of oscillations and decreases the frequency of oscillations, however, from 500 µM concentration, ketamine abolishes gamma oscillations.

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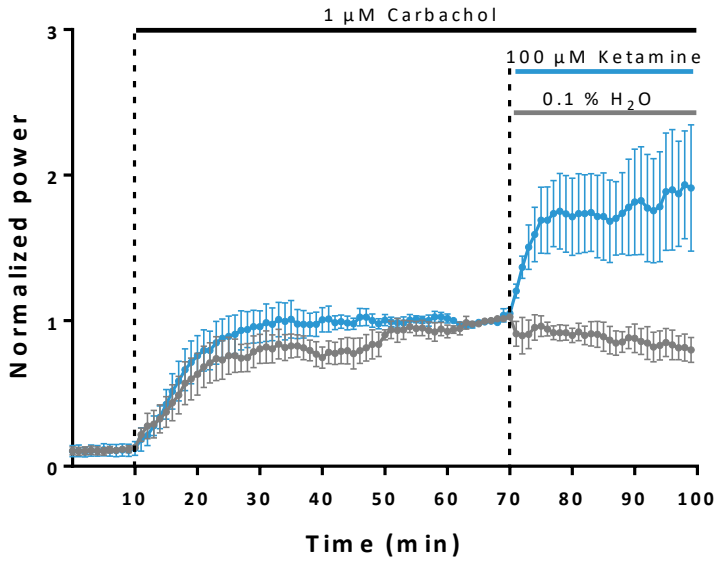
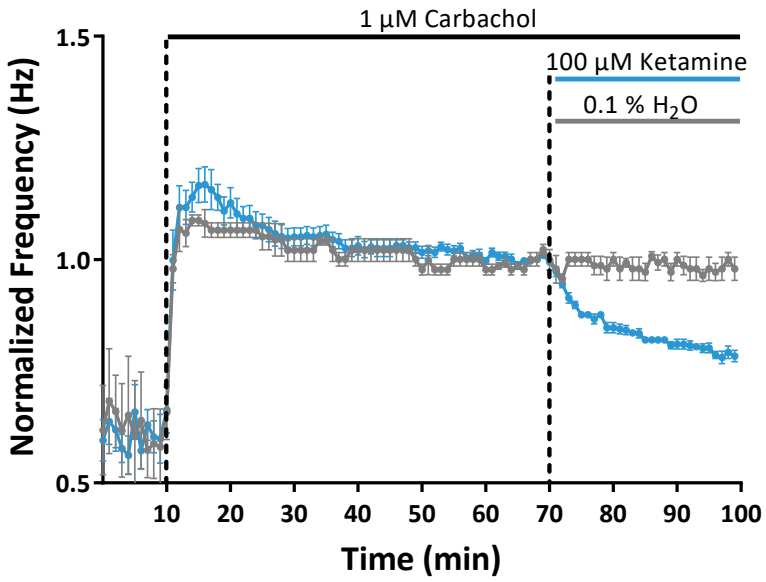
NMDA RECEPTOR MODULATES GAMMA OSCILLATIONS





As observed on Kainate-induced oscillations, 100 µM Ketamine, applied for 30 minutes, strongly increased the strength of carbachol-induced network oscillations.

The predominant frequency of oscillations also strongly decreased over the 30-minute exposure to 100 µM Ketamine.

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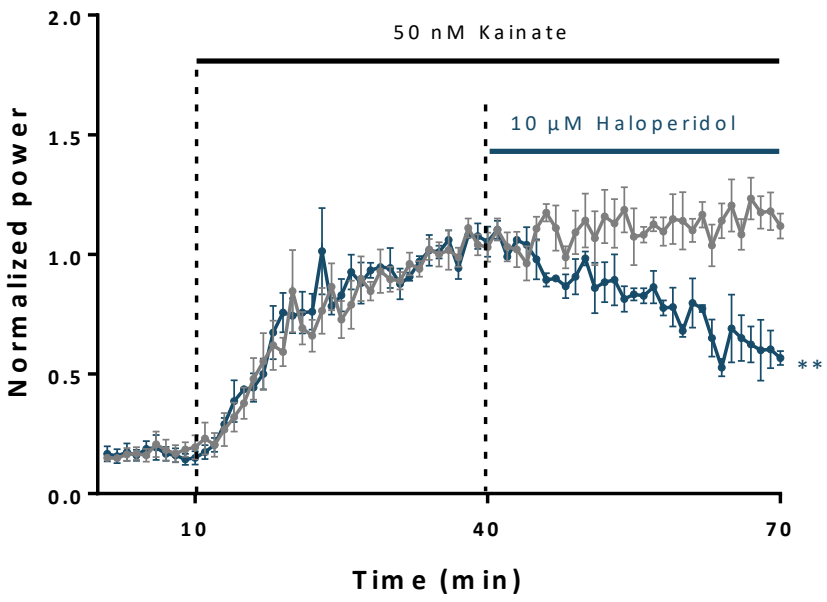
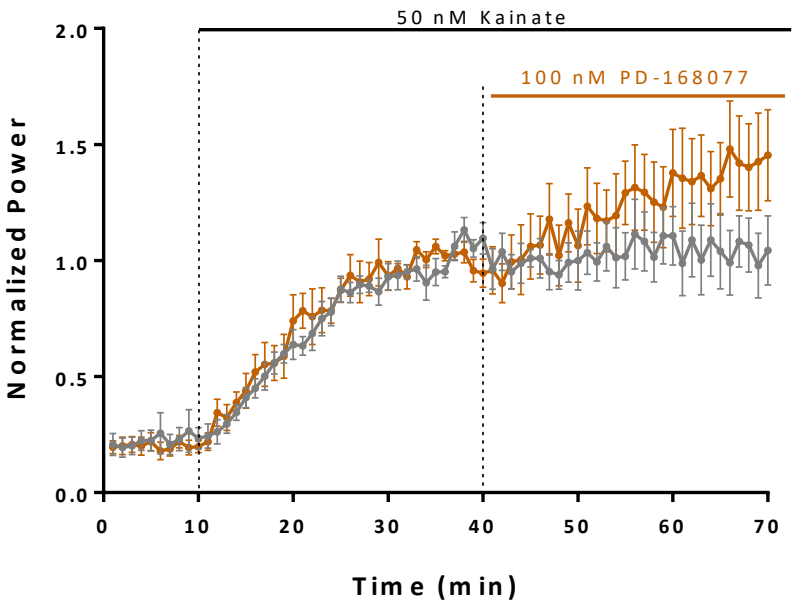
DOPAMINERGIC RECEPTOR MODULATES GAMMA OSCILLATIONS





Haloperidol – a dopaminergic receptor antagonist – applied at 10 µM concentration decreases the power of oscillations. PD-168077 – a dopaminergic D4 receptor agonist – applied at 100 nM concentration increases the power of oscillations.

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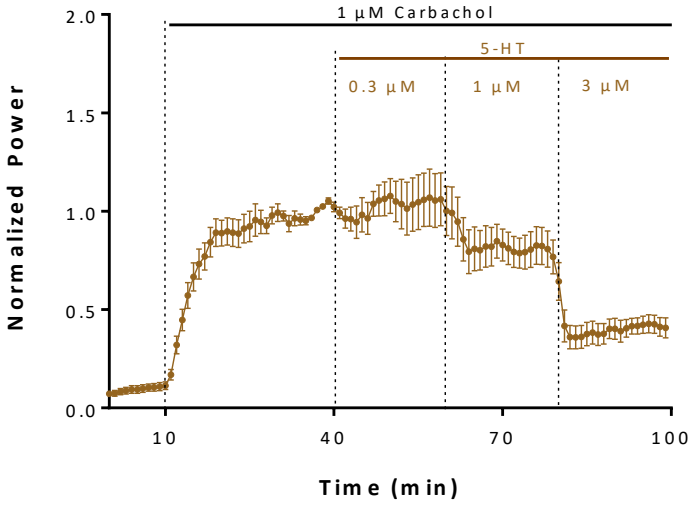
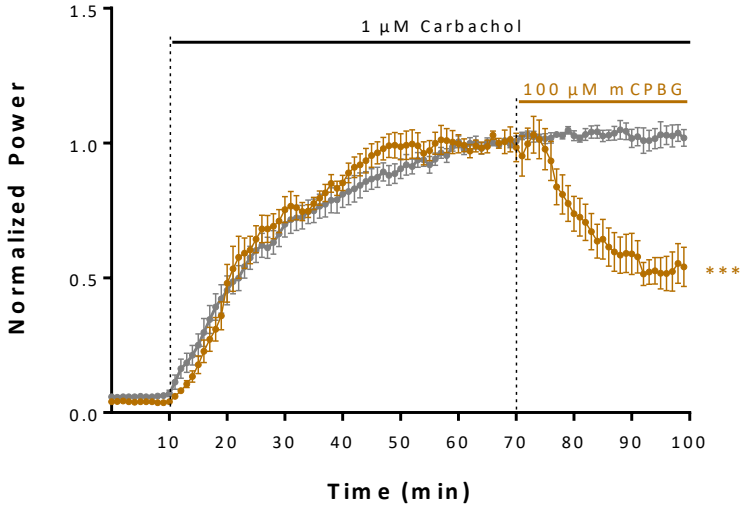
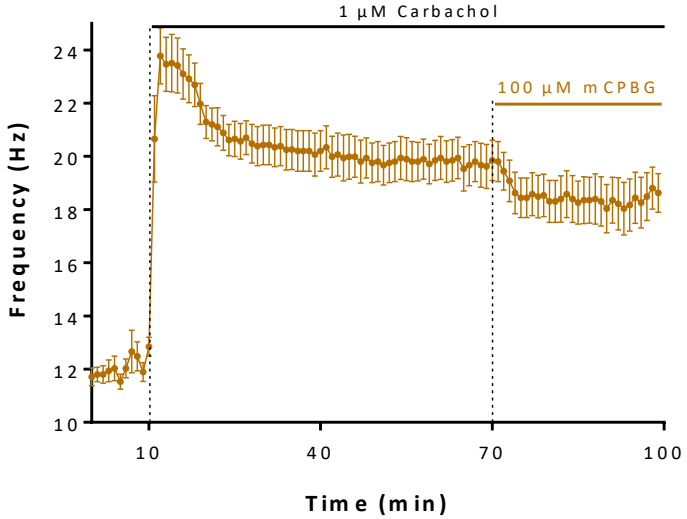
SEROTONINERGIC RECEPTOR MODULATES GAMMA OSCILLATIONS





5-HT dose dependently decrease the power of network oscillations. Similarly, mCPBG – a 5-HT_3 agonist – applied at 100 µM concentration decreases the power and the frequency of oscillations.



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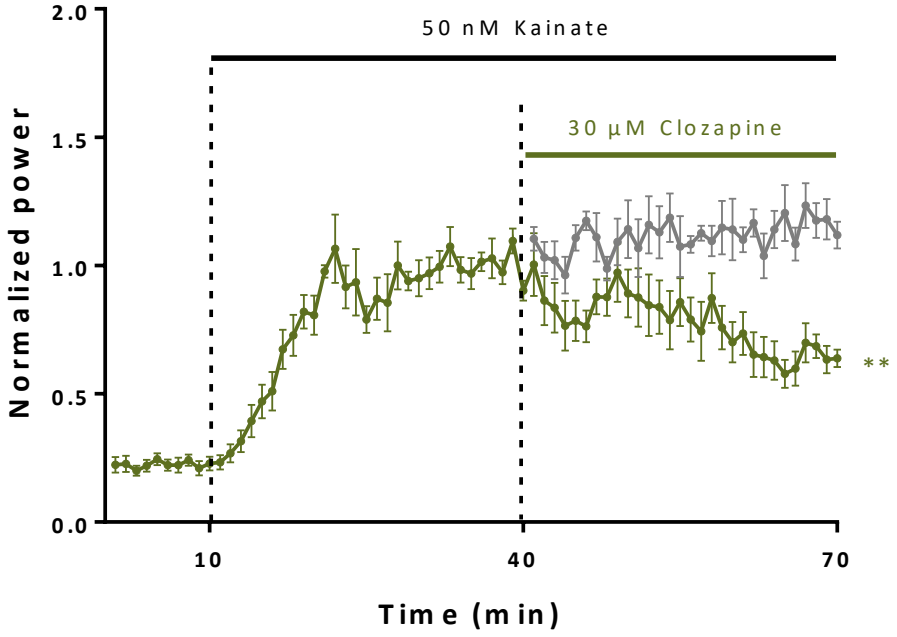
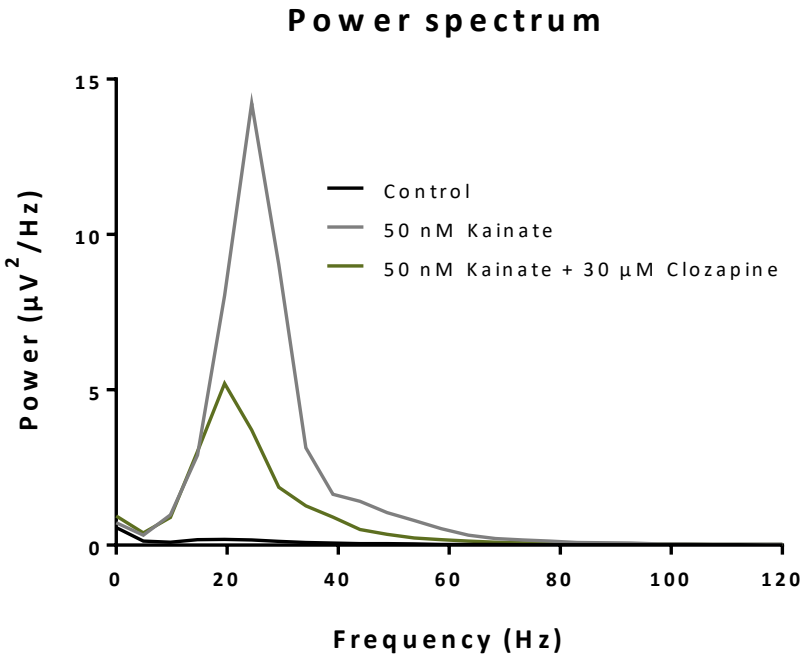
THE EFFECT OF ANTIPSYCHOTIC ON GAMMA OSCILLATIONS





Clozapine – a serotonin and dopamine receptors antagonist used as antipsychotic agent – applied at 30 µM concentration decreases the power of oscillations.

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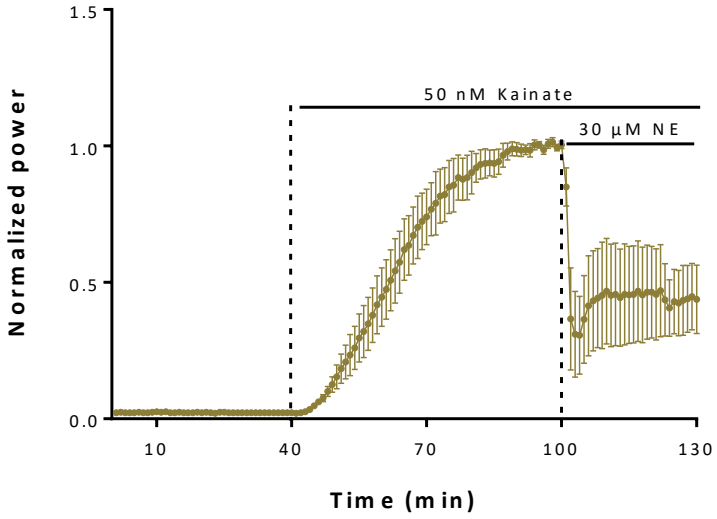
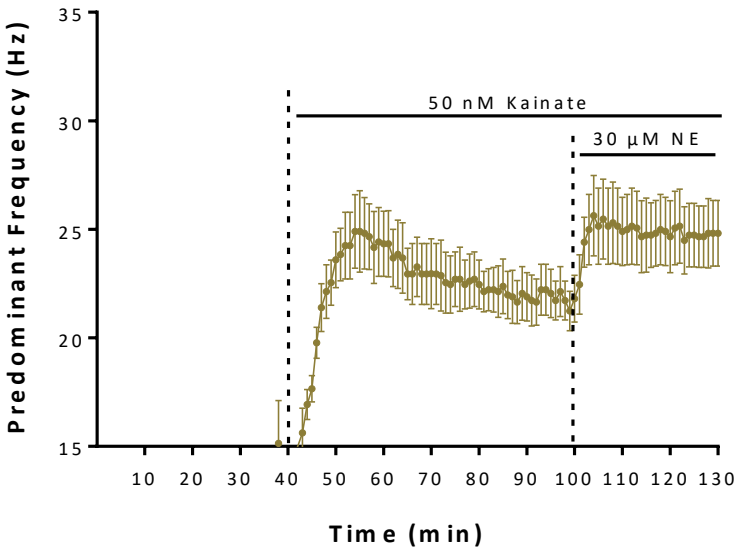
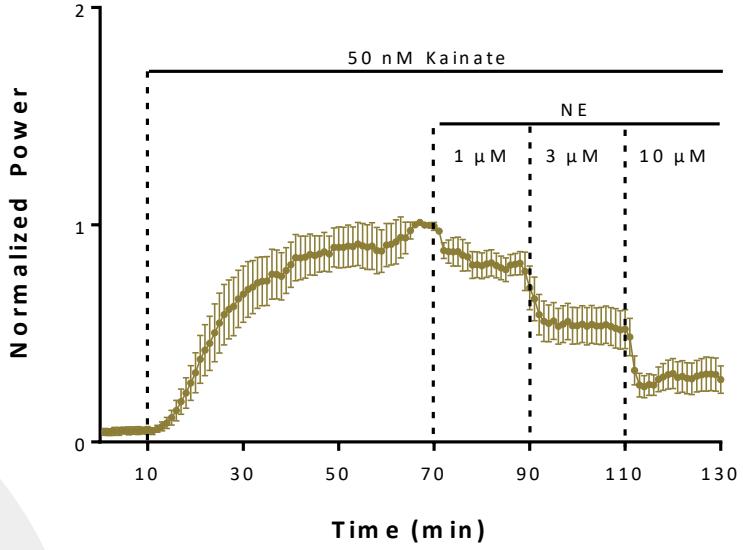
ADRENERGIC RECEPTOR MODULATES GAMMA OSCILLATIONS







Norepinephrin modulates kainate-induced network oscillations in rat hippocampal slices by decreasing their power and increasing their frequency.

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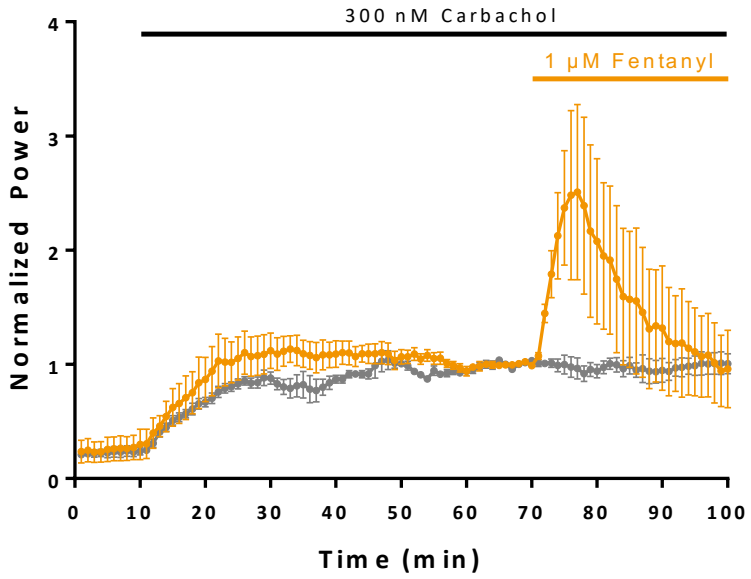
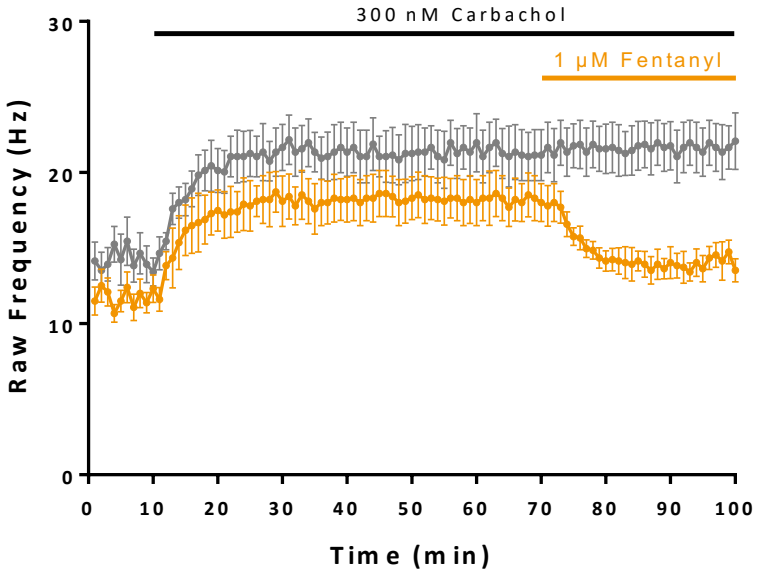
OPIOID RECEPTOR MODULATES GAMMA OSCILLATIONS





Fentanyl – a μ-opioid agonist – applied at 1 μM modulated carbachol-induced network oscillations in rat hippocampal slices by transiently increasing their power and decreasing their frequency.

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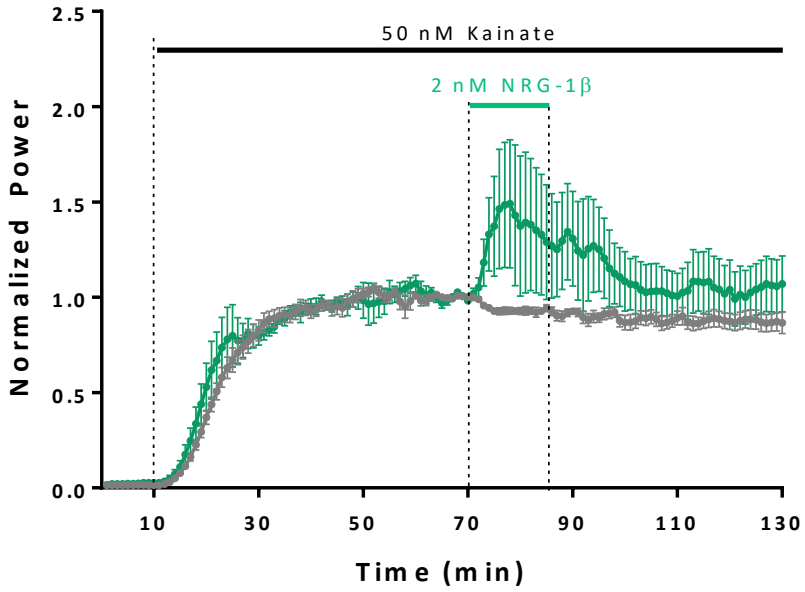
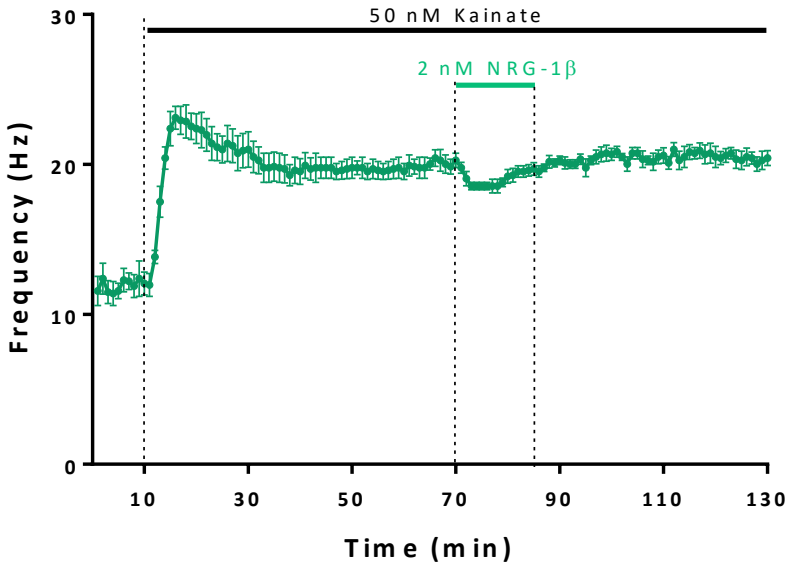
RESULTS

NEUREGULIN-ERBB4 PATHWAY MODULATES GAMMA OSCILLATIONS





NRG-1β increased the strength of network oscillations over a 15-minute period of exposure. This effect partially reversed over the first 15 minutes of the washout.

In addition, NRG-1β transiently decreased the frequency of network oscillations (by about 8% after a 5 minute exposure).

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