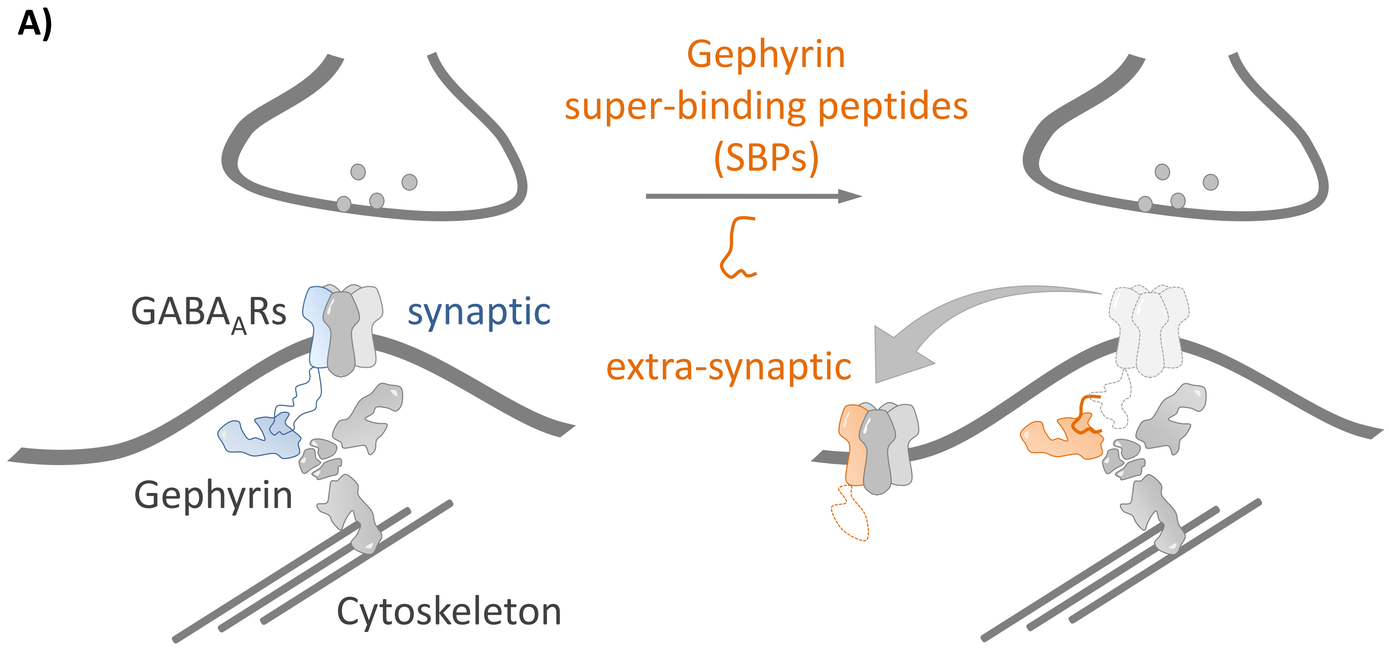
Novel Modulators of Fast Synaptic Inhibition

New peptide based compounds act on Gephyrin to modulate GABAergic Transmission

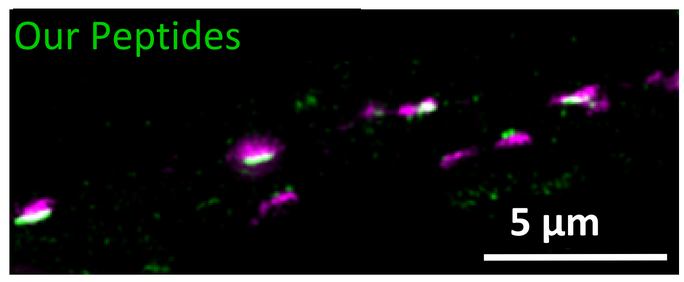
Biotech and Health Care

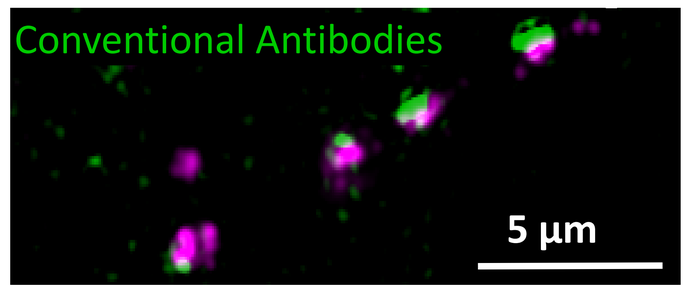
A)



A) Pharmacological action of the gephyrin super-binding peptides. The peptides exert their activity on GABAergic and glycinergic transmission through their high-affinity binding to the receptor-binding site of gephyrin, which interferes with the gephyrin-mediated recruitment of the receptors to synaptic sites.

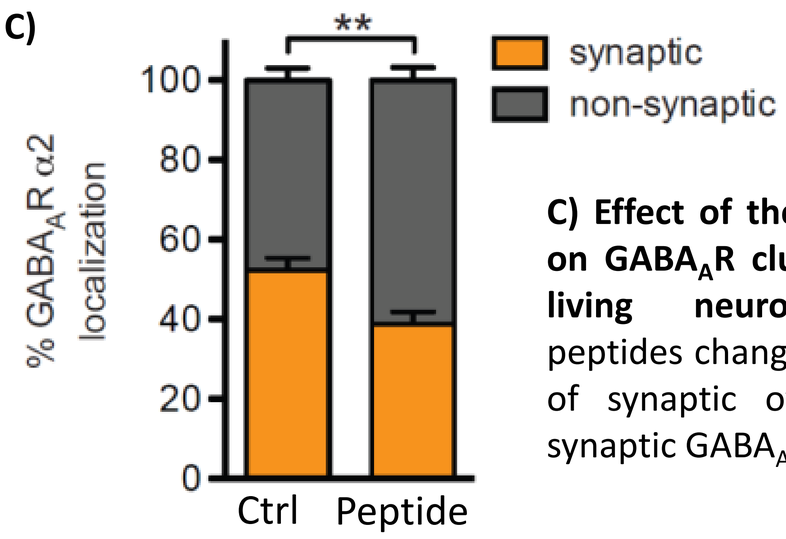
B)





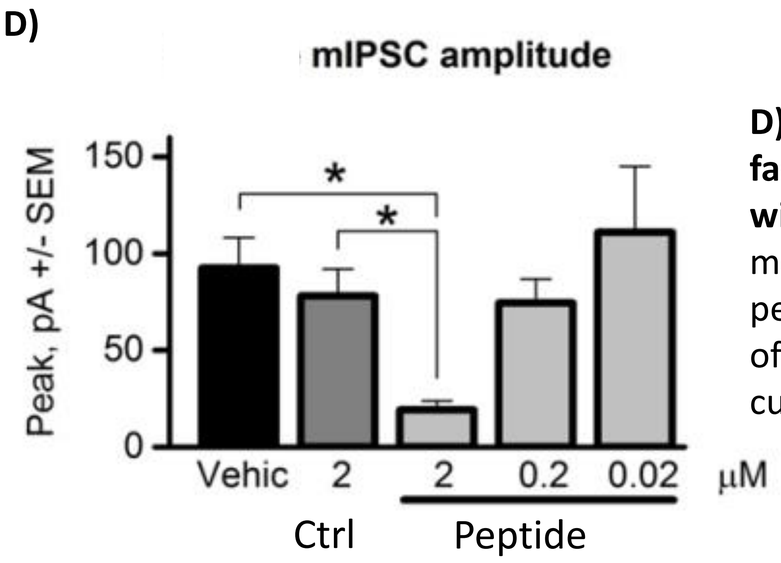
B) Visualization of the inhibitory post-synapse via SIM imaging. Note that the peptide-based labeling appears more confined than the corresponding immunogenic labeling. Peptides affect

C)



C) Effect of the peptides on GABA$_A$R clustering in living neurons. The peptides change the ratio of synaptic over extra-synaptic GABA$_A$Rs.

D)



D) Effect of the peptides on fast synaptic transmission within brain slices. At micro molar concentrations the peptides reduce the amplitude of miniature post-synaptic currents (mIPSCs).

Value proposition/USP

Potential pharmacological treatment of mental disorders by a unique and conceptually novel mode of action. Our peptides are highly subtype-specific and do not interfere with normal receptor function.

Business Opportunity/Objective/commercial perspectives

Medicines such as benzodiazepines that target GABA receptors are among the most prescribed psychoactive drugs on the marked and are useful to treat numerous mental disorders. Nonetheless, current medicines alter the normal receptor function and suffer from poor receptor subtype-specificity.

Because of its unique pharmacological action our invention is likely to be superior to current treatments. Due to their unpreceded high binding affinity and selectivity, the invention can also be used for visualization of the inhibitory synapse, superior to antibody-based approaches.

Technology description/technology Summary

The gephyrin protein controls the recruitment of GABA receptors to the synaptic sites by binding specifically to intracellular regions of receptor subunits. By binding to gephyrin, our peptides reduce GABA receptor recruitment to the synapse and thereby modulate the fast synaptic inhibition.

Development phase/current state

Our studies *in vitro* confirm the peptides' ability to modulate GABAergic transmission by binding to gephyrin. We are currently studying their effect *in vivo* in a mouse model.

The inventors

Professor Kristian Strømgaard and Asst. Prof. Hans Michael Maric from the Department of Drug Design and Pharmacology.

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Intellectual property rights

PCT patent application nr. PCT/DK2016/050369 filed on 16 November 2016. The University of Copenhagen holds all the rights to the invention.

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