RUHR-UNIVERSITÄT BOCHUM

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IGSN - COLLOQUIUM

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Steroid modulation of NMDA receptors

Phasic activation of N-methyl-D-aspartate receptors (NMDAR; subtype of glutamate-gated ion channels) by synaptically released glutamate plays a key role in synaptic plasticity and can be neuroprotective, but excessive tonic NMDAR activation by elevated extracellular glutamate mediates excitotoxicity. Therefore, there is much interest in pharmacological agents capable of selectively blocking tonically activated NMDARs, while leaving phasically/synaptically activated NMDARs intact.

The results indicate that naturally found steroids and their synthetic analogues have a higher potency to inhibit tonically activated than synaptically activated NMDA receptors (with up to a 10-fold difference in the IC50). Behavioral experiments indicated neuroprotective activity of synthetic steroids in the absence of psychoactive-like symptoms (that are typical for other NMDAR antagonists).

Our conclusions provide a unique opportunity for the development of new therapeutic neurosteroid-based ligands to treat diseases associated with the dysfunction of the glutamate system.

Host:

MICHAEL HOLLMANN
Receptor Biochemistry, Faculty of Chemistry and Biochemistry, Ruhr University Bochum

Guests are welcome