Activin tunes GABAergic neurotransmission and modulates anxiety-like behavior.

Abstract:

Activin, a member of the transforming growth factor-beta superfamily, affords neuroprotection in acute brain injury, but its physiological functions in normal adult brain are largely unknown. Using transgenic (tg) mice expressing a dominant-negative activin receptor mutant under the control of the CaMKIIalpha promoter in forebrain neurons, we identified activin as a key regulator of gamma-aminobutyric acid (GABA)ergic synapses and anxiety-like behavior. In the open field, wild-type (wt) and tg mice did not differ in spontaneous locomotion and exploration behavior. However, tg mice visited inner fields significantly more often than wt mice. In the light-dark exploration test, tg mice made more exits, spent significantly more time on a well-lit elevated bar and went farther away from the dark box as compared to wt mice. In addition, the anxiolytic effect of diazepam was abrogated in tg mice. Thus the disruption of activin receptor signaling produced a low-anxiety phenotype that failed to respond to benzodiazepines. In whole-cell recordings from hippocampal pyramidal cells, enhanced spontaneous GABA release, increased GABA tonus, reduced benzodiazepine sensitivity and augmented GABA(B) receptor function emerged as likely substrates of the low-anxiety phenotype. These data provide strong evidence that activin influences pre- and postsynaptic components of GABAergic synapses.
in a highly synergistic fashion. Given the crucial role of GABAergic neurotransmission in emotional states, anxiety and depression, dysfunctions of activin receptor signaling could be involved in affective disorders: and drugs affecting this pathway might show promise for psychopharmacological treatment.

Zeitschriftentitel / Abkürzung:
Mol Psychiatry

Jahr:
2009

Band:
14

Heft / Issue:
3

Seiten:
332-46

Sprache:
eng

Pubmed:

Print-ISSN:
1359-4184

TUM Einrichtung:
r Neurowissenschaften

Occurences:
- Einrichtungen > Fakultäten > Fakultät für Medizin > Kliniken und Institute > Institut für Neurowissenschaften > 2009

entries: