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Presynaptic cGMP-dependent protein kinase-I mediates synaptic potentiation in spinal amplification of pain

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Background

Activity-dependent facilitation of pain is functionally linked to plasticity at synapses between peripheral sensory afferents and spinal projection neurons. However, the underlying cellular and molecular mechanisms are not well-understood [1]. We observed that long-term potentiation at these synapses involves a presynaptic mechanism comprising activity-induced decrease in synaptic failures. This process involves activation of the cGMP-dependent protein kinase-I (PKG-I) in presynaptic terminals of nociceptive afferents and potentiation of vesicular transmitter release via modulation of IP3 receptors and myosin light chains. Mice lacking PKG-I specifically in nociceptors did not develop spinal long-term potentiation and showed marked defects in pathological pain *in vivo*.

Conclusion

Our results reveal a causal link between PKG-I-dependent presynaptic modulation of transmitter release, long-term potentiation at spinal synapses and the induction of pathological pain.

References

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