Sensory Neuron Hyperexcitability is Prevented by Group 2 Metabotropic Glutamate Receptors in Mouse and Human

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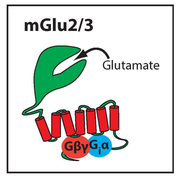
Background and Significance

1.


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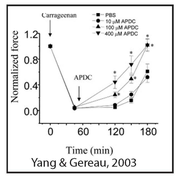

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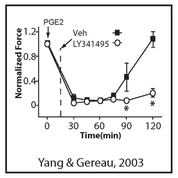
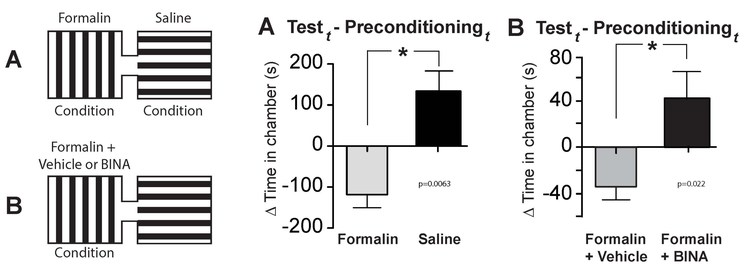


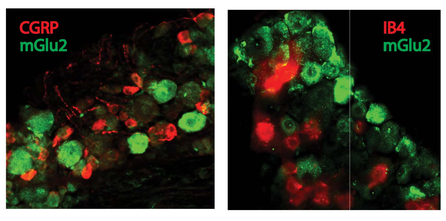
1. Group 2 mGluRs are Gi/o coupled 7 TM receptors
2. Peripheral injection of mGluR2/3 agonist during inflammation hastens recovery from hyperalgesia
3. Peripheral injection of mGluR2/3 antagonist delays recovery from hyperalgesia
4. Two ways to address the "translation problem": 1) Non-reflexive tests of ongoing pain, 2) Preclinical studies in human tissues

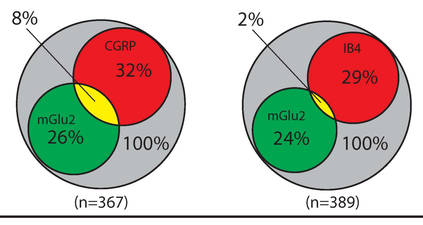
Results

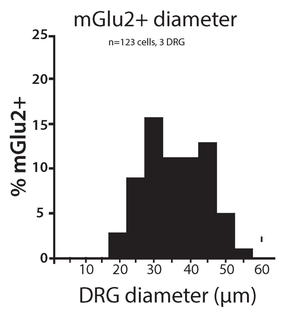
mGlu2 potentiation blocked formalin place aversion



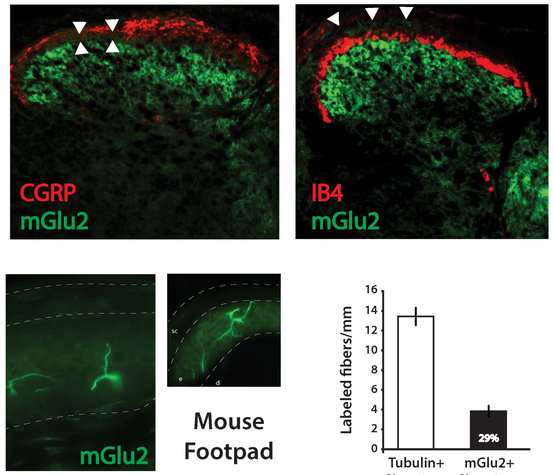
mGlu2 expression in mouse DRG



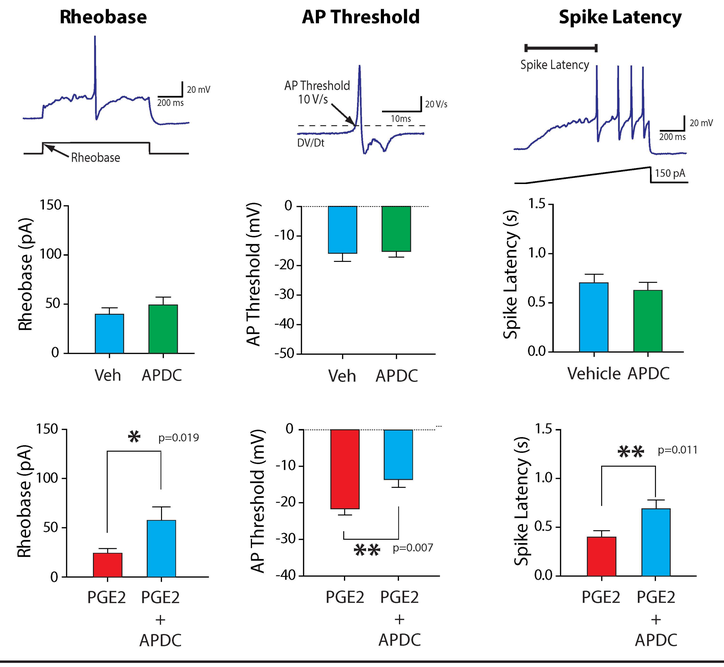




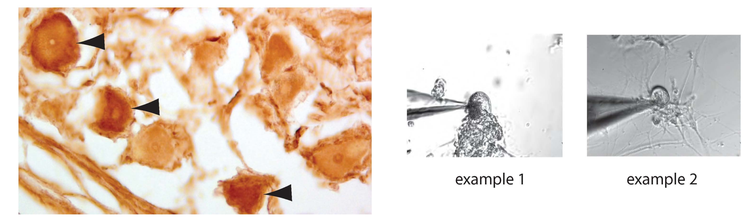
mGlu2 expression in mouse spinal cord and skin



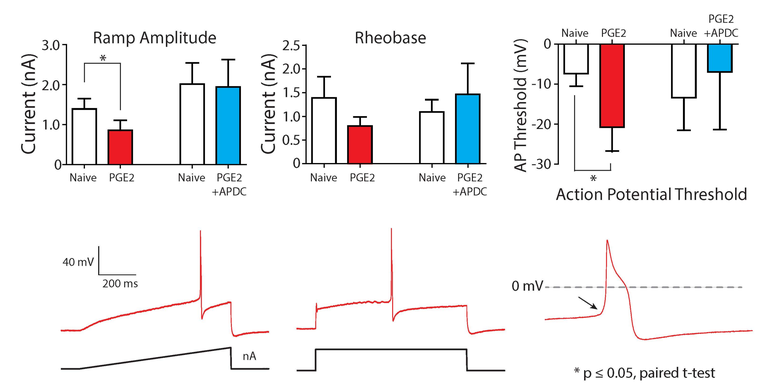
APDC blocks PGE2-induced hyperexcitability (mouse)



mGlu2 expression in human DRG and human DRG under patch-clamp conditions



APDC blocks PGE2-induced hyperexcitability (human)



Conclusions

- mGlu2 activation or potentiation of endogenous activity prevents and reverses indicators of pain.
- mGlu2 immunoreactivity is present in medium sized DRG neurons, peripheral terminals in the eipdermis and nucleus proprius of the spinal cord dorsal horn
- mGlu2 activation blocks PGE2-induced hyperexcitability in mouse and human DRG neurons.
- Non-reflexive assays of ongoing pain and preclinical human physiology are useful tools to enhance translational efficacy of potential analgesics.

Acknowledgements

NIH Grants: NRSA F32 NS076324, R01 NS042595
American Pain Society, Future Leaders Grant

National Institute of Neurological Disorders and Stroke
American Pain Society
AnaBios Corporation