N-ACETYL-CYSTEINE INHIBITS NOCICEPTIVE PATHWAY FUNCTION. A COMBINED ANIMAL AND HUMAN STUDY

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Introduction
Emerging research seeking novel analgesic drugs now focuses on agents targeting group-II metabotropic glutamate receptors (mGlu2 and mGlu3). A drug that enhances endogenous mGlu2/3 receptor activation, by activating the glial glutamate:cystine membrane exchanger is N-acetyl-cysteine (NAC). In this study, we tested whether NAC inhibits nociceptive responses induced by noxious heat stimulation in humans and animals.

Methods
In 10 healthy humans we measured changes induced by oral NAC (1.2 gr) on thermal-pain thresholds, as assessed with quantitative sensory testing (QST), and laser evoked potentials (LEP), according to a crossover, double-blind, placebo-controlled design. We also investigated changes induced by intraperitoneally-injected NAC (100 mg/kg) in the tail-flick response evoked by radiant heat stimulation in six mice.

Results
In healthy subjects, NAC treatment left thermal-pain thresholds unchanged, but significantly reduced pain ratings to laser stimuli and LEP amplitudes. NAC induced significantly greater changes in these measures than placebo. In the tail-flick test, NAC strongly reduced the nocifensive reflex response to radiant heat, and the preferential mGlu2/3 receptor antagonist, LY341495 (1 mg/kg, i.p.) abolished its action.

Conclusions
Our findings providing new evidence that NAC inhibits nociceptive transmission in humans, probably by increasing mGlu2/3 receptor activation, lay the groundwork for investigating the drug’s therapeutic potential in patients with chronic pain.

References: