Abstract

Differential effects of endogenous cysteine analogs on peripheral thermal nociception in intact rats.

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BACKGROUND: Previous in vivo studies indicate that locally injected redox-modulating agents can sensitize polymodal peripheral skin nociceptors resulting in acute changes in pain perception.

OBJECTIVE AND METHODS: Since endogenous thiol-modifying redox agents are normally present in the interstitial tissue, and could be found in higher concentration in certain conditions (e.g., tissue injury, inflammation, and ischemia), we designed this study to evaluate the peripheral nociceptive effects of locally injected endogenous-reducing cysteine analogs, L-cysteine, D-cysteine and D,L-homocysteine and endogenous-oxidizing cysteine analogs, L-cystine, D-cystine and D,L-homocystine using the acute model of thermal peripheral nociception in intact rats.

RESULTS: We found that the reducing cysteine analogs induced potent dose- and time-dependent hyperalgesia and conversely the oxidizing cysteine analogs induced potent dose- and time-dependent analgesia. In the presence of 3betaOH, a novel neuroactive steroid and potent voltage-dependent blocker of T-type Ca2+ channels, the hyperalgesic effects of the reducing agents were diminished, whereas the analgesic effects of the oxidizing agents were enhanced strongly suggesting that the observed nociceptive effects were, at least in part, mediated via the peripheral T channels.

CONCLUSION: Our findings imply that changes in the redox states of the peripheral nociceptors (favoring either reduced or oxidized forms of cysteine molecules) may function as a local intrinsic mechanism in controlling peripheral pain perception.

PMID: 16782275