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## THE MU-OPIOID AGONIST DAMGO SELECTIVELY ATTENUATES NEUROTRANSMITTER RELEASE FOLLOWING C-FIBER ACTIVATION

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**Introduction:** Previous work has shown that C fiber activation evokes the spinal release of the excitatory amino acids (EAA) aspartate (Asp) and glutamate (Glu). Selective A-delta activation releases Glu but not Asp. C nociceptors have mu-opioid receptors on their presynaptic terminals, whereas A-delta receptors do not. This anatomic configuration allows for the presynaptic opioid inhibition of C but not of A-delta mediated thermonociception. In this study, differential effects of the spinal application of DAMGO on the spinal release of Asp and Glu as evoked by selective activation of A-delta or C fibers are examined.

**Method:** Rats were anesthetized with urethane and a lumbar laminectomy performed. A specially constructed push-pull microperfusion cannula was inserted into the superficial layers of the dorsal spinal dorsal cord. Artificial cerebrospinal fluid (aCSF) was perfused through the cannula and the perfusate collected for amino acid assay by HPLC. Rat feet were repeatedly exposed to high rate (6.5 °C/sec) or low rate (0.9 °C/sec) thermal stimuli that have previously been demonstrated to selectively activate either A-delta or C fiber thermonociceptors, respectively. After collecting baseline samples, DAMGO was added to the aCSF perfusate.

**Results:** Rats exposed to C fiber stimulation demonstrated an increase of both Asp and Glu; those exposed to A-delta stimulation demonstrated an increase in Glu but not Asp. Addition of the mu-opioid receptor agonist significantly attenuated Asp and Glu release with C stimulation, but did not affect Glu release after A-delta stimulation. Discussion: Glu and Asp, released by A-delta or C fibers, may act at different EAA receptors in the spinal cord to mediate nociception. Both Glu and Asp can bind to all three of the main classes of EAA receptors: NMDA, kainate, and AMPA. While latencies of C-fiber mediated foot withdrawal responses were increased by NMDA, kainate/AMPA, and kainate antagonists, A-delta response latencies only were increased by kainate/AMPA and kainate antagonists. Spinal dorsal horn release EAA in response to selective A-delta or C fiber thermoactivation. Glu and Asp are both released from C fiber spinal terminals upon activation. Whereas A-delta activation evokes the release of Glu but not Asp. This in turn suggests that both A-delta and C fiber nociceptors may involve the release of EAA's, acting partly at kainate and or AMPA receptors. Only C fiber mediated responses involve NMDA receptors. Asp release may be used as marker for C fiber activation since the C nociceptors have mu-opioid receptors on their presynaptic terminals, whereas A-deltas do not. Spinal application of DAMGO selectively attenuates the spinal release of Asp and Glu as evoked by selective activation of C fiber but not A-delta. Responses mediated by mu-opioid agonist presynaptically attenuate primary afferent neurotransmitter release.

**References** (1) Y Lu, Society for Neuroscience Abstract, 2000, Vol 26, p2183. (2) Y Lu, V Pirec, DC Yeomans, British Journal of Pharmacology 1997, 21:1210-1216. (3) DC Yeomans, Pain 1994, 59:85-94