PD-26. NK1, NMDA, AND GABAB RECEPTOR ANTAGONISTS EFFECT A-DELTA OR C-FIBER HYPERALGESIA

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Low rates of skin heating activate C-fiber nociceptors while high rates of skin heating activate A-delta nociceptors. Topical capsaicin selectively activates and sensitizes C-fibers whereas DMSO selectively activates and sensitizes A-deltas. These experiments examined whether tonic C fiber activity sensitizes C and A-delta input partly by NK1 and NMDA receptor activation and whether tonic A-delta activity decreases C-fiber input by a GABAb receptor activation.

Baseline response latencies were measured in rats in response to high or low rate skin heating. Approximately 10 min. after application of 10mM capcaicin or 100 % DMSO to the dorsolateral hindpaw skin (sciatic innervated), and at 5 min. intervals thereafter, foot withdrawal latencies were remeasured on the dorsomedial surface (saphenous innervated) to determine the central effects of tonic activation of sciatic C or A-delta nociceptors on A-delta or C-fiber nociception.

Capsaicin application produced a profound transegmental potentiation of response for both A-delta and C nociception. This was blocked by intrathecal (IT) NK1 (GR82334), or NMDA(AP5) antagonists. Sciatic skin DMSO profoundly attenuated responses to saphenous skin C fiber activation, an effect blocked by IT GABAb antagonist (Saclofen).

The results indicate that tonic C fiber activity sensitizes C and A-delta input at least partly by activation of NK1 and NMDA receptors whereas tonic A-delta activity decreases C fiber input at least partly by activation of GABAb.

(1) DC Yeomans, Pain 1996, 68:133-140.
(2) DC Yeomans, IASP Press, 2000, 16:335-341
(3) J Sandluhler, Prog. Brain Res. 2000, 129:81-100