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Injection of low-dose endothelin-1 into the rat temporomandibular joint induces nociception

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Temporomandibular disorders involving the temporomandibular joint (TMJ) are frequently secondary to inflammation and associated to hyperalgesia, allodynia or referred pain. Based on previous studies showing the participation of endothelin (ET) peptides in some nociception models, we decided to investigate the role of ET-1 in the carrageenan (CGN)-induced inflammation of the TMJ in rats.

Under inhalatory halothane anesthesia (3% v/v in O_2), male adult Wistar rats (body weight: 180-200 g) received intra-articular injections (volume: 10 µl/joint) of CGN (500 µg/joint), ET-1 or the ET_B agonist BQ3020 (both at 0.3-30 pmol/joint) into the left TMJ cavity using sterile 0.9% saline solution as vehicle. After 4 h, hyperalgesia was analysed, using an electronic analgesimeter (based on the von Frey filament method), by measuring the force threshold at which head withdrawal ocurred. The animals were then anesthetised and killed by cervical dislocation, and the TMJ cavities were washed with saline solution in order to determine total and differential leukocyte numbers. Selective antagonists of ET_A (BQ123) and ET_B (BQ788) receptors were also co-injected with CGN (10 pmol/joint) or ET-1 (1 pmol). The experimental protocol was approved by the local Ethics Committee for Animal Use (CEUA; process N° 46 of 10 June 2010).

Both ET-1 and BQ3020 (in the range 0.3-10 pmol/joint) evoked hyperalgesia (i.e., significant decrease of force treshold; $P<0.01$), and CGN-induced hyperalgesia was unaffected by any of the ET antagonists injected separately. However, the nociceptive response to CGN was abolished when both antagonists were co-injected ($P<0.001$). Similarly, each of the ET antagonists failed to completely abolish ET-1–induced nociception but were able to atenuate it (BQ123: $P<0.05$; BQ788: $P<0.01$). At all the working doses, ET agonists did not stimulate leukocyte migration to the TMJ cavity and none of the ET_1 antagonists altered CGN-induced cell migration.

Based on these results, we can conclude that ET-1 not only evokes mechanical allodynia at low doses (up to 10 pmol/cavity), but is also involved in the CGN-induced nociception through both ET_A and ET_B receptors with no apparent effects on leukocyte migration.

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