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## Spinal 5-HT1A receptor plays a major role in directing serotonergic modulation toward inhibition on mechanical allodynia of carrageenan inflammation

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**Introduction:** Descending serotonergic projections may facilitate or inhibit nociceptive processing in the spinal cord depending on several factors. Unlike other pain states, spinal 5-hydroxytryptamine 3 receptors (5-HT3R) were shown to play a limited role in nociceptive transmission of carrageenan-induced inflammatory pain. Instead, a facilitatory role of 5-HT1AR and 5-HT1BR in spinal nociceptive processing was observed during early-phase of carrageenan model. Although, the maximum release of 5-HT in spinal cord reaches the maximum 2-3 hours after carrageenan injection (early-phase), its release returns to baseline 8 hours.

**Aim:** To identify the role of Spinal 5-HT1A receptor in directing serotonergic modulation toward inhibition on mechanical allodynia of carrageenan inflammation.

**Methods:** Effects of intrathecal (i.t.) nonspecific 5-HTR agonist, subtype agonist or antagonists (5-HT1AR, 5-HT1BR, 5-HT3R), and 5,7-dihydroxytryptamine (5,7-DHT, a serotonergic neurotoxin) on mechanical allodynia were tested for early- and late-phase allodynia.

**Results:** Lesioning spinal serotonergic projections with 5,7-DHT induced a significant increase in the intensity of mechanical allodynia at both early and late-phase. This increase was attenuated by i.t. 5-HT. Also, i.t. 5-HT itself produced a significant antiallodynic effect in late-phase, but not in early-phase. Similarly, i.t. 5-HT1AR agonist (8-OH-DPAT) attenuated the intensity of late-phase allodynia in a dose-dependent manner which was antagonized by 5-HT1AR antagonist (WAY-100635), but produced no effect on the early-phase allodynia. However, other agonists or antagonists of 5-HT1BR and 5-HT3R did not produce any anti or pro-allodynic effects.

**Conclusion:** Descending serotonergic modulation plays a vital role in inhibition of nociceptive processing during late-phase allodynia, which involves spinal 5-HT1A, but not 5-HT1B or 5-HT3 receptors in carrageenan-induced inflammation. However, the defined role of 5-HT1A and serotonergic inhibition during early-phase remains undetermined.

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## Pain management techniques

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In the present study, we hypothesized that listening to music would modulate the effects of allodynia, hyperalgesia and fatigue in patients with fibromyalgia (FM). Due to its emotional effect, we expected that listening to music would have a greater moderating effect on the perception of pain and fatigue than listening to non-musical sounds. To investigate this hypothesis, we carried out a study in which people with FM were given a listening device for four weeks enabling them to listen to either music or environmental sounds when they experienced pain, in either an active (while carrying out a physical activity) or passive (at rest) situation, while measuring changes in levels of pain and fatigue. The results of this study indicate that when people with FM listen to music or environmental sounds when they are at rest, their pain and fatigue decreased after 20 minutes of listening. This physical improvement persists for ten minutes after the end of the listening session. In physical active situations their pain did not decrease but it did not increase. Contrary to our expectations, music and environmental sounds produced the same effect on pain and fatigue, with no extra benefit gained by listening to music rather than environmental sounds.

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