

Permanent lack of estrogens reduces pain inhibition in the formalin model: a behavioural and immunocytochemical study in the transgenic ArKO mouse.

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Aim of Investigation: The purpose of this study is to better understand how estrogens can modulate pain.

Methods: Aromatase-knockout (ArKO) mice, which lack endogenous estrogen production, and wild-type (WT) littermates were compared in the formalin model of persistent pain. Eight mice in each group were used as controls. Sixteen animals received a formaldehyde injection in the upper lip, after which their grooming behaviour was recorded and counted during 9 min as an indicator of pain. The animals were then sacrificed. The density of descending 5HT- and of peripheral CGRP-immunoreactive terminals was assessed in the superficial laminae of trigeminal nucleus caudalis.

Results: Grooming stopped 6 minutes after formalin injection in WT, but persisted in ArKO. Furthermore, WT and ArKO mice, which exhibited similar immunoreactivities for serotonin and CGRP in normal baseline conditions (without formalin injection), showed a significantly different variation of respective fibre densities 9 min after the formalin injection. Bilateral serotonin immunoreactivity was significantly higher in WT compared to ArKO mice whereas CGRP immunoreactivity was significantly lower on the injected side in WT than in ArKO mice.

Conclusions: These findings suggest that the capacity to respond to a noxious stimulus is different between the two groups. Lack of estrogens seems to be associated with persistence of pain after the first phase in the formalin model. This is immunocytochemically correlated with a segmental decrease of descending serotonergic fibers as well as an increase in peripheral CGRP afferents and may thus be due to an imbalance between pro- and antinociceptive mechanisms.

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