



Global Year Against Pain in Women

real women, real pain

Sex Hormones and Pain

- Pain, and in particular chronic pain, shows important sex differences. There could be several reasons for the higher reactivity of females than males to a similar painful stimulation, from genes to hormonal and cultural influences. The difference between the two sexes is multifaceted, involving the occurrence of chronic pain, the kind of pain syndromes experienced, the characteristics of the complications that develop, etc.
- Pain perception varies according to the menstrual cycle phases in women with chronic pain (1). For example, temporomandibular pain is highest in the pre-menstrual period and during menses (2).
- Androgens and estrogens are vital for the proper development and maintenance of the male and female reproductive systems. They also play an important physiological role in the activity and well-being of males and females.

Estrogens are able to affect nociception and pain

Estrogen administration in women and in men can increase the incidence of chronic pain conditions (3, 4). These effects can be due to actions induced at peripheral as well as central levels. For instance estrogens:

1. Increase nerve growth factor (NGF) in the dorsal root ganglia (5),
2. Induce c-Fos expression (one of the first signs of neuronal plasticity) in the hippocampus (6),
3. Activate MAP-kinase (a growth factor) by a mechanism that appears not to use estrogen receptors (7).
4. Increase the numbers of dendrite spines and excitatory synapses in hippocampal neurons (8)
5. Rapidly excite neurons in the cerebral cortex, cerebellum and hippocampus by a non-genomic mechanism (9).
6. Potentiate glutamate binding to N-methyl-D-aspartate (NMDA) receptors (8, 10)
7. Increase postsynaptic potentials in the hippocampus by increasing currents mediated by kainate receptors (9).

All these effects can increase nociception and pain.

In addition to their hyperalgesic role, estrogens also seem to play an important role in inducing anti-nociception. For instance, simulation of pregnancy in ovariectomized rats, with high plasma levels of estrogens and progesterone, results in an increased pain threshold (11). These analgesic effects can be related to the fact that estrogens regulate the transcriptional control of opioid synthesis and of delta and kappa-opioid receptors in lamina II of the spinal cord (12). Administration of estrogen in women increases pain-induced mu-opioid receptor binding in the brain, suggesting that exogenous estrogen enhances functioning of the endogenous opioid system (13).

Androgens are able to affect nociception and pain

An inverse relationship was found between plasma testosterone and work-related neck and shoulder disorders in female workers (14). Low-dose transdermal testosterone therapy was found to improve angina threshold in men with chronic stable angina (15). In male rats, testosterone has a protective role in adjuvant-induced arthritis (16) and testosterone, administered to both male and female rats, change formalin-induced responses (17, 18) and analgesia (19).

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References available at www.iasp-pain.org.