



Global Year Against Pain in Women

real women, real pain

Gender and the Brain in Pain

Several reviews have demonstrated that women respond to noxious and potentially noxious stimuli with greater pain experience than men (1, 2). In particular, women tend to have reduced pain threshold compared to men - women respond with pain to lower intensity stimuli than men. In addition, there are numerous pain conditions that show a bias towards women: Berkley listed 38 clinical pain disorders as having a female prevalence but only 15 having a male prevalence and 24 having no sex prevalence. It is tempting, therefore, to suggest that women have a biological profile that predisposes them to experience pain at lower stimulus intensities and thus also suffer a disproportionate amount of clinical pain.

This general hypothesis is supported by animal studies that have shown, for example, greater opioid mediated stress induced analgesia in male rats compared with female rats (3, 4). Stress induced analgesia may be suppressed by estrogen raising the possibility that hormonal differences between men and women contribute to differences in pain perception (5). In contrast, more recent evidence, using positron emission tomography to directly assess opioid binding in vivo, has demonstrated greater opioid receptor availability and activation of endogenous opioid activation during delivery of a noxious stimulus in a high versus low estrogen state (6). The different role of various opioid mediated mechanisms under various conditions remains open for investigation.

Advances in brain imaging technology mean that further brain differences between genders can be directly assessed in human populations. There are, for example, gender related structural differences including the size and morphology of the corpus callosum, preoptic hypothalamic area, planum temporale, the percent of gray matter in the human brain, and the density of neurons. Furthermore, it is well established that men and women have different spatial and verbal skills and these differences correlate with gender differences in brain function (7). The observed behavioral and clinical differences in pain response might also relate to structural and functional differences between men and women.

In 1998, Paulson et al demonstrated greater responses in the anterior insula and thalamus in female subjects and showed prefrontal activation in the right hemisphere in the male subjects and in the left hemisphere in the female subjects using noxious heat (8). In 2002, Derbyshire reported greater activation of the perigenual and ventral cingulate cortex in the female subjects and greater activation of the parietal, secondary sensory, prefrontal and insula cortices in the male subjects using noxious laser stimuli (9). Also in 2002, Berman et al reported greater insula activity in male subjects receiving an aversive rectal distension, opposite to the greater female insula activity seen in an earlier rectal distension study by Kern et al (2001). More recently, Moulton et al (2006) demonstrated reduced activation in primary sensory, anterior cingulate and prefrontal cortices during noxious heat in females compared to males – a result that differs both from Derbyshire et al (2002) and Paulson et al (1998). These brain imaging findings are intriguing but the considerable variation across studies remains open to interpretation. Variations in activity pattern provide good reason to be cautious before speculating too far regarding the influence of gender on brain imaging differences during delivery of noxious stimuli.

One possible reason for the variability is the fact that pain is complex and a myriad of factors might influence findings in relatively small samples. Criterion effects, differences in body size, skin thickness, or systolic blood pressure, social expectations, cognitive variation, method of stimulation, and differences in psychological traits such as anxiety and depression have all been suggested to account for observed gender differences in pain response. Biological fluctuation because of the menstrual cycle has also recently begun to receive greater attention.

Brain imaging studies on the issue are escalating, with the exciting potential for cutting through these potential sources of variation to provide a clearer understanding of the mechanisms underlying pain in general, as well as how sex and gender factors contribute to these variations.

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