First Annual Meeting Organization for the Study of Sex Differences

May 9–12, 2007
Washington, DC

The inaugural meeting of a new scientific society, the Organization for the Study of Sex Differences (OSSD), took place recently in Washington, DC. The mission of OSSD is to enhance the knowledge of sex/gender differences by facilitating interdisciplinary communication and collaboration among scientists and clinicians of diverse backgrounds. The annual meeting provides a forum for scientists and clinicians to explore aspects of sex differences research at the genetic, molecular, cellular, organ, and system levels in various model systems and to examine how these basic biologic sex differences affect human physiologic and pathologic processes throughout the lifespan. More than 150 scientists and clinicians from the United States and Canada, and a handful from other countries, attended this first meeting. Attendees represented a wide range of disciplines, with a fairly large contingent from neuroscience.

The oral sessions included opening and closing plenary speeches as well as a series of panels addressing sex differences in various diseases and conditions, such as autoimmunity, obesity and metabolic disease, lung cancer, and psychiatric disorders. There were also 2 poster sessions. One of the panels and several of the posters dealt with sex differences in pain or analgesia. The pain panel, organized by Dr Arthur Arnold, University of California, Los Angeles, had 3 main speakers—Dr Jeffrey Mogil, McGill University; Dr Roger Fillingim, University of Florida; and me (Dr Linda LeResche, University of Washington). I reviewed age and sex differences in the prevalence of a range of chronic pain conditions and discussed the evidence that these differences are influenced by sex differences in nociceptive systems, perception, pain appraisal, pain-related behavior, and social roles. I also presented an overview of findings concerning hormonal influences on pain associated with temporomandibular joint and muscle disorders in women.

Dr Mogil discussed the interaction of sex differences with genetic background in determining pain response in mice. He pointed out that sex differences are found only in certain strains of mice, and that the direction of sex differences (eg, whether males or females are more sensitive to painful stimuli) depends on genetic background. In addition to quantitative differences (eg, in pain thresholds), evidence is emerging that there may be qualitative differences between the sexes in the neural processing of pain. That is, different neural circuits, transmitters, receptors, and genes seem to be relevant to pain modulation in males and females. Dr Mogil also presented very interesting recent data suggesting that some of the social factors thought to influence sex-specific pain behavior in humans are also present in mice, at least for the strains tested to date. For example, male mice, like male humans, show higher pain thresholds in the presence of others than when alone.

Dr Fillingim summarized human laboratory studies that have investigated gender differences in pain and analgesic responses. The bulk of the findings from these studies involve quantitative sex differences, that is, sex differences in the magnitude of pain and analgesia. Human research consistently demonstrates more robust perceptual responses to experimentally induced pain among women compared to men. Although sex differences have been reported in response to analgesics—especially opioid analgesics—the direction and magnitude of these differences vary substantially across studies. In terms of qualitative differences, there are sex-related genetic associations with pain and analgesia in humans, and recent experimental research in women suggests that low levels of estradiol are pronociceptive (ie, that they decrease endogenous pain modulation, increasing pain) whereas high levels are antinociceptive. In addition, specific psychologic factors appear to be more strongly associated with pain in 1 sex versus the other (eg, anxiety has

a stronger effect on experimental pain response in males than in females).

To conclude the panel, Dr Arnold briefly reported on research from his laboratory employing a new mouse model that allows investigators to separate the effects of hormones and the effects of chromosomes on sex-related differences. These mice have all combinations of chromosomal and hormonal sex, ie, there are XY individuals with testes (normal males), XX individuals with ovaries (normal females), XY individuals with ovaries, and XX individuals with testes. Studies using this model to test responses to heat pain suggest that chromosome complement as well as gonadal sex contribute to sex differences in pain and in morphine analgesia.

Two posters were especially pertinent to possible mechanisms of orofacial pain. Dr R. Ambalavnaner (University of Maryland) and colleagues presented results of immunocytochemical studies of neuropeptide expression in trigeminal muscle afferent neurons in rats. The findings suggest that calcitonin gene–related peptide (CGRP) expression in trigeminal ganglion muscle afferents is higher in males than in females and that ovariectomy increases the expression of CGRP in females. A poster presented by Dr Nancy Berman, University of Kansas Medical Center, reported results of experiments involving injection of complete Freund's adjuvant into the masseter muscle of rats to study the effect of estradiol on secondary allodynia and hyperalgesia, as measured by withdrawal response to stimulation of the whisker pad by von Frey filaments. Addition of estradiol increased pain sensitivity and activation of extracellular-signal related kinase (ERK) in this model.

Finally, a poster by Drs Raimi Quiton and Joel Greenspan, University of Maryland, examined sex differences in distraction-evoked endogenous analgesia in humans. This study evaluated the effect on heat pain response of trancutaneous electrical stimuli designed to be distracting, stressful (but not painful), or strongly painful. Both the distraction and pain conditions reduced reported heat pain intensity and unpleasantness in both sexes (compared to a mild, nonpainful stimulus control condition); however, the effect was larger in men than in women. Men who reported higher perceived stress during the pain condition had higher levels of analgesia to the heat pain, whereas women who reported higher perceived stress had lower magnitudes of endogenous analgesia. Thus, the effects were qualitatively different for the 2 sexes, suggesting that different neural systems may be involved in endogenous analgesia in men and women.

This small initial meeting allowed for a great deal of interaction among investigators from a variety of disciplines, making for many stimulating discussions. Orofacial pain researchers who study sex differences may be interested in attending the second annual meeting of OSSD, which will take place June 4–7, 2008, in New Orleans, Louisiana.

Linda LeResche
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