



Gender Differences in the Pain Experience

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Objectives

- Present an overview of the gender/sex effects on pain
- Focus on the differences at the neurological/receptor level
- Discuss evidence of gender influence on experimental and “real” pain
- Evaluate the gender effects on medication efficacy and therapies



Case Studies: Pain Description

- 48 yr old (DG) with mass in pelvis, metastatic lesions in L3-4 and right femoral head, describes pain as “right hip, low back and deep pain”



Dangle *et al.* *World Journal of Surgical Oncology* 2008
6:103 doi:10.1186/1477-7819-6-103

- 54 yr old (FL) with mass in pelvis and metastatic lesions to T10-11, L3-4, right femoral head, describes pain as “right hip, low back and pelvic pain”

Nomenclature: Sex vs. Gender¹

- **Sex** = *anatomical* categorization of “male” and “female” (NB: anatomical may \neq genetic)
- **Gender** may coincident with anatomical categorization but may also denote “*identity*” as “masculine” or “feminine”



Sex may \neq Gender

¹ Robinson ME, Riley JL, Myers CD et al. Gender role expectations of pain: relationship to sex differences in pain. J Pain 2001;2:251-257.



Prevalence: ♀ > ♂

- **Osteoarthritis:**
 - OA of the knee, is 2x as common in ♀ as in ♂
 - OA of the hips affects ♂ & ♀ equally.
- **Heart disease**
 - < age 50 ♀ have more chest pain but less heart disease than ♂ do
 - > age 50 ♀ have more silent heart disease than ♂ do.
- **Migraine Headaches: 1 in 5 ♀ & 1 in 17 ♂ have migraines.**
- **Fibromyalgia: 9 x more ♀ than ♂**
- **Irritable bowel syndrome (IBS): ♀ > ♂**
- **Rheumatoid arthritis: 2-3x ♀ > ♂**
- **Chronic pelvic pain**
- **Temporomandibular joint disorder**
female to male ratio is 4:1

Prevalence of Painful Conditions: ♂ > ♀



- Cluster headache
- Coronary heart disease
- Gout
- Ankylosing spondylitis
- Duodenal ulcer
- Pancreatic disease

Pain Presentation: CAD



Chest pain most common symptom (women 70%) and men (71%)

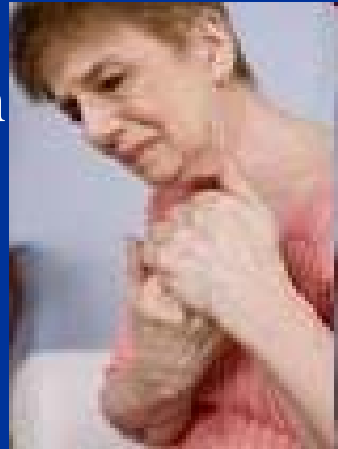
Men

- Central chest pain
- Radiating pain to neck, jaw, upper abdomen, shoulders, and arms



Women

- Midback pain
- Nausea/vomiting
- Indigestion
- Dyspnea
- Palpitations



Men (29%) and women (30%) equally likely to present without chest pain

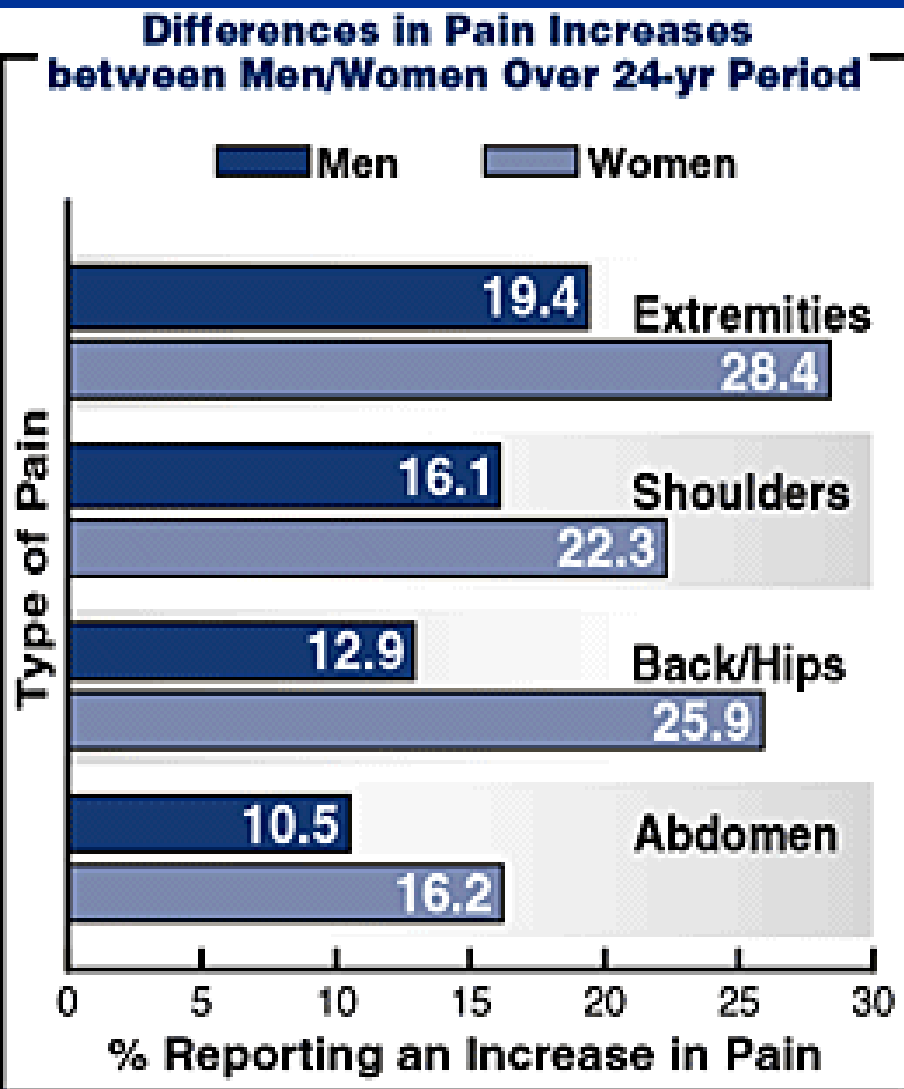


Longitudinal Changes in Chronic Pain

- **Methodology:** A 24-year study of pain patterns among 321 Swedish patients (aged 53-63 at the beginning of the study) assessed self-reported pain in the chest, abdomen and musculoskeletal system (back or hips, shoulders, elbows, legs or knees).
- **Results:**
 - Women report more pain than men
 - Statistically significantly women reported more musculoskeletal pain than men.

Brattberg G, Parker MG, Thorslund M. A longitudinal study of pain: reported pain from middle age to old age. *Clinical Journal of Pain*, 1997;13(2), pp144-49.

Longitudinal Changes in Chronic Pain



- Most notable gender difference involved **pain in the extremities**: less than one percent of the men, but 12.2% of the women reported persistent musculoskeletal pain in those areas.
- Chronic pain in elderly women is/will be a major health issue.



Gender Differences

- Women seem to show:
 - Lower pain thresholds
 - A greater ability to discriminate painful sensations
 - Higher pain ratings
 - A lower tolerance for pain

Gender-related responses to pain are not completely consistent

Dental Pain Model:

Pain Post Tooth Implantation

- **Methodology:** Followed 27 women and 21 men for 10 days after surgery to implant a replacement tooth
- **Results:**
 - The **women described** the surgery as **significantly more painful** than the men did
 - **Both sexes** rated the **pain on a pain scale as similarly intense**
 - In both sexes, pain fell by 50% within two days. In the 10 days following the surgery
 - Women tolerated low levels of pain much better than did the men.
 - Over time men were more disturbed than the women by persisting discomfort

Effect of Blood Pressure on Pain Sensitivity



- ♀ have lower blood pressures (BP) than age-matched ♂
- Animal studies have shown an association between hypertension and diminished sensitivity to noxious stimuli^{1,2}
- ↓ pain sensitivity has been found in hypertensive humans^{3,4}

1 Dworkin BR, Filewich RJ, Miller NE, Craigmyle N. Baroreceptor activation reduces reactivity to noxious stimulation: implications for hypertension. *Science* 1979; 205: 1299–301.

2 Maixner W, Touw KB, Brody MJ, Gebhart GF, Long JP. Factors influencing the altered pain perception in spontaneously hypertensive rat. *Brain Res* 1982; 237: 137–45.

3 Zamir N, Shuber E. Altered pain perception in hypertensive humans. *Brain Res* 1980; 201: 471–4

4 Ghione S, Rosa C, Mezzasalma L, Panattoni E. Arterial hypertension is associated with hypoalgesia in humans. *Hypertension* 1988; 12: 491–7.

Hypotension: Increased Pain Sensitivity¹

- Methodology



- Sensitivity to heat pain was assessed in 40 subjects with chronic hypotension (mean blood pressure 96.5/57.7mmHg) and 40 normotensive control persons (mean blood pressure 121.8/77.2mmHg).
- A contact thermode, tonic heat stimuli (45.5–47.5°C) were applied to the forearm.

- Results:



- Hypotensive individuals exhibited markedly reduced pain threshold and pain tolerance, as well as increased sensory and affective pain experience
- Suggests an inverse relationship between blood pressure and pain sensitivity across the whole blood pressure

Blood Pressure & Pain Perception

Confounding Factors: ? Race



- *African Americans rated the thermal stimuli as more unpleasant and more intense than whites*
- Resting systolic BP was related to pain ratings
- There was a trend for women to rate the thermal stimuli as more unpleasant and more intense than men
- These sex differences were explained, at least in part, by differences in resting systolic blood pressure

Gender Differences in Pain Perception across Cultures: Hong Kong Chinese

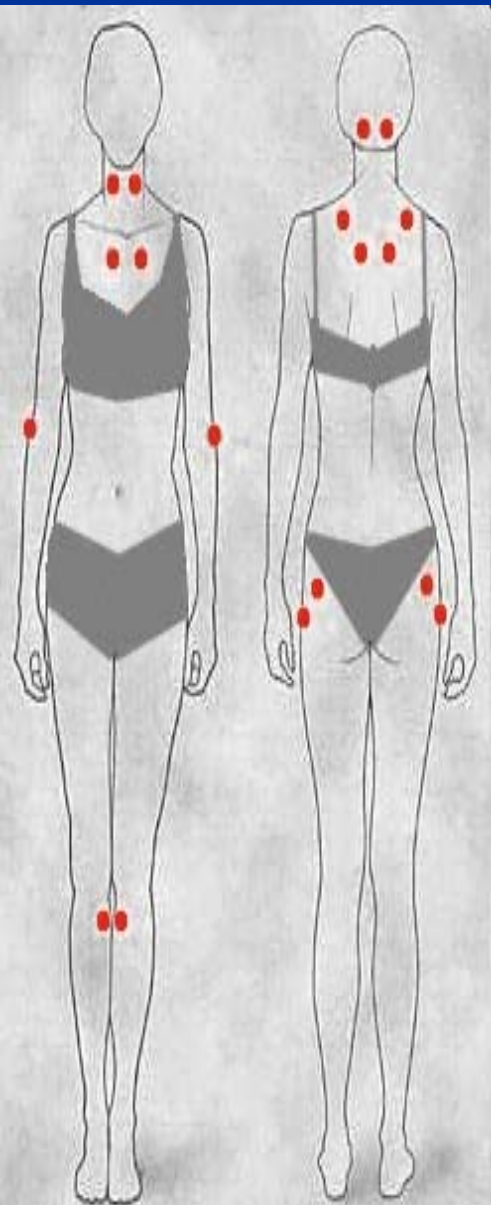
- Women had
 - Lower threshold ($p < .001$)
 - Lower tolerance ($p < .001$) for pressure pain
 - Reported more pain ($p < .01$) at the pain tolerance level.
- Higher trait anxiety scores were associated with higher pain report in men only ($r [89] = .22, p = .04$).



Results: gender differences in pain perception exist among the Chinese population in Hong Kong
(? Across cultures/races)

General Differences

- Painful experimental stimuli are generally reported to produce a greater intensity of pain in women than in men
- Clinical pain is often reported
 - With higher severity and frequency
 - Longer duration
 - *Present in a greater number of body regions in women than in men*



Fibromyalgia

Lund I, Lundeberg T, Is it all about sex? Acupuncture for the treatment of pain from a biological and gender perspective. *Acupunct Med.* 2008 Mar;26(1):33-45.

Factors Contributing to Gender Difference in Experiencing Pain

- **Stimulus specific:** type, timing & spatial aspects of the stimulus
- **Biological factors**
 - Quantitative as well as qualitative differences in the endogenous pain inhibitory systems have been implicated
 - Neural differences: differences in receptor populations or pain neuromodulators
 - Influence of gonadal hormones
- **Psychosocial factors**
 - Sex role beliefs
 - Pain coping strategies
 - Pain related expectancies
- **Exposure to repeated painful visceral events** (e.g. menses, labor) during life may contribute to an increased sensitivity to, and greater prevalence of, pain among women

Berkley KJ Sex differences in pain (Review), *Behav Brain Sci* 1997; **20**:371-80.

Lund I, Lundeberg T, Is it all about sex? Acupuncture for the treatment of pain from a biological and gender perspective. *Acupunct Med.* 2008 Mar;**26**(1):33-45.

Stimulus Variables

- **Thermal**
 - Show greatest variability
 - Rate of rise in temp determines which type of fiber is evoked
 - Slow rates of temp. rise evoke C-fiber responses, faster rates evoke A δ fibers.
 - Sex differences in heat pain are more robust when threshold is determined via the method of levels with a slow rate of rise¹
 - Sex differences in pain threshold and tolerance are more frequently observed when C fibers are evoked²
- **Pressure:** sub maximal tourniquet test (ischemia)
 - \uparrow lactate & K^+ \rightarrow peripheral nerve ending activation
 - Stimuli may also cause nerve damage \rightarrow release of neuromodulators: prostaglandins, histamine serotonin, bradykinin, leukotrienes & substance P
 - Gender affects synthesis and/or release of some of these factors (e.g. substance P³)
 - Stimulus method per se may not be as important in determining gender differences, as the stimulus-specific elicitation of neuronal/non-neuronal events, such as neurotransmitter release

¹Fillingim RB, Maddux V, Shackelford JAM. Sex differences in heat pain thresholds as a function of assessment method and rate of rise. Somatosens Mot Res 1999; 16:57-62.

²Giles BE, Walker JS: Sex differences in pain and analgesia. Pain Reviews 2000; 7:181-193.

³Binder W, Carmody J, Walker J. Effect of gender on anti-inflammatory and analgesic actions of two kappa-opioids. J Pharmacol Exp Ther 2000;292:303-309.



Sex-role Expectations...

- Sex-role expectation begin in childhood: Boys expected to be “heroic and uncomplaining”; girls encourage to show “emotions” = dissimilar environmental clues ? → ↑ ♀ willingness to report pain as adults¹

However:

- Women more susceptible to both acute and chronic pain² and suffer greater pain with the same objective pathology³

¹ Kupers R. Sex differences in pain – now for something completely different. *Behav Brain Sci* 1997;**20**:455-56.

² Berkley KJ Sex differences in pain (Review), *Behav Brain Sci* 1997; **20**:371-80.

³ Unruh AM. Gender variations in clinical pain experience. *Pain* 1996; **65**: 123-67.



Pupillary Response to Pressure Pain

- **Methodology:** 20 subjects exposed to 4 levels of tonic pressure to fingers. Pain threshold, tolerance and pupillary dilatation were measured
- No differences (male vs. female) at low pressure levels
- **Females showed at high pressure**
 - Greater pain (verbal scale)
 - ***Greater pupillary dilatation***
- **Authors conclusions:** “pain perception using an autonomic indicator – pupillary dilation- ***beyond voluntary control*** suggest that these differences reflect low-level sensory and/or affective components of pain rather than attitudinal or response-bias factors.

Ellermeier W, Westphal W: Gender differences in pain ratings and pupil reactions to painful pressure stimuli. Pain: 1995;61(3): 435-439.

Psychological Factors

- Women utilize health care service more than men: attend to pain more readily and manage pain more aggressively than men¹
- Anxiety & depression may ↑ pain severity, esp. in ♀²
- Paradox:

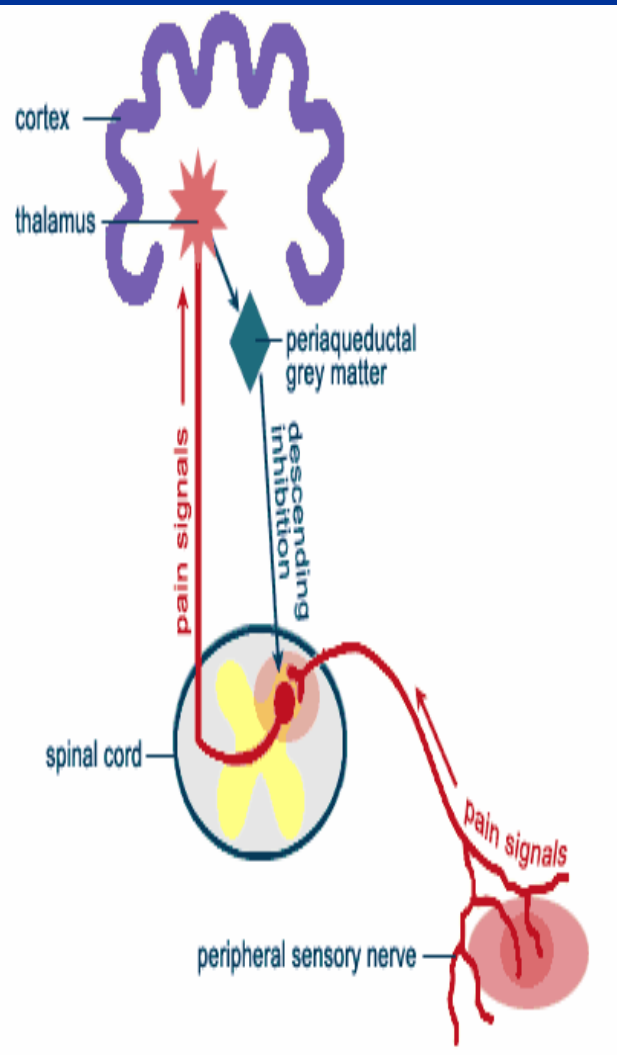


- Depression & anxiety thought to be caused by relative deficiency of 5-HT
- 5-HT is a pain producing neuromodulator
- 5-HT uptake inhibitors (antidepressants) successfully used as analgesic adjuncts in pain therapy.

¹Unruh Am. Why can't a woman be more like a man? *Behav Brain Sci* 1997; **20**: 467-68.

² Haley WE, Turner JA, Romano JM. Depression in chronic pain patients: relation to pain, activity and sex differences. *Pain* 1985; **23**: 337-43.

Neural Differences...



- **Premise:** nociceptive excitatory activity (ascending) is balanced by inhibitory activity (descending) (at both physiological and psychological levels)
- **Women suffer more painful conditions¹**
- **Postulate:** Variability in pain sensitivity may be due to sex differences in the descending inhibitory pathway

¹ Berkley KJ Sex differences in pain (Review), *Behav Brain Sci* 1997; **20**:371-80

...Neural Differences

- **Testing** via stress-induced analgesia (SIA)
Exposure to stress prior to noxious stimulation
expect → ↓ pain sensitivity ¹
- **Results:**
 - Female rodents display lower levels of SIA than males²
 - Quality of endogenous analgesia differs
 - ♂ higher level of opioid mediated analgesia than ♀²
 - In ♂ mice non-opioid mediated paradigms are mediated via NMDA receptors³
 - ♀ mice exhibit naloxone and NMDA antagonist insensitive⁴

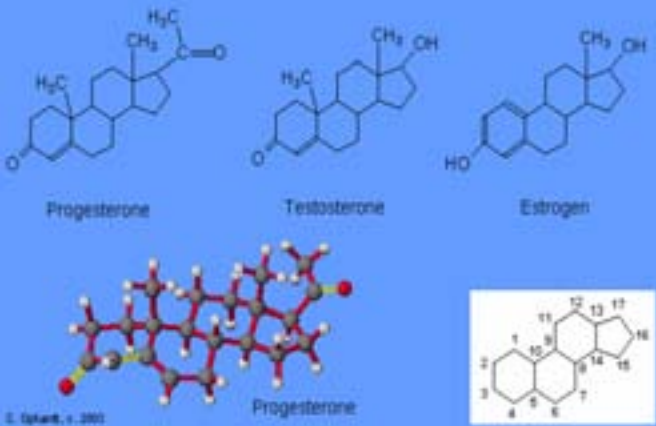
¹Aloisi AM, Ceccarelli I, Lupo C. Behavioural and hormonal effects of restraint stress and formalin test in male and female rats. *Brain Res Bull* 1998; **47**: 57-62.

²Romero MT, Bodnar RJ. Gender differences in two forms of cold water swim analgesia. *Physiol Behav* 1986; **37**: 893-97

³Mogil JS, Sternberg WF, Kest B, Marek P, Liebeskind JC. Sex differences in the antagonism of swim stress-induced analgesia: effects of gonadectomy and estrogen replacement. *Pain* 1993; **53**: 17-25.

⁴Sternberg WF, Mogil JS, Kest B et al. Neonatal testosterone exposure influences neurochemistry of nonopioid swim stress-induced analgesia in adult mice. *Pain* 1995; **63**: 321-26.

Sex Hormones



Sex Hormones

- Some pain syndromes are aggravated by exogenous hormones (TMJ)¹

- Endogenous sex hormones alter some pain syndromes
 - Fibromyalgia²
 - Rheumatoid arthritis³
 - Irritable bowel syndrome⁴

1LeResche L, Saunders K, von Korff MR, Barlow W, Dworkin SF. Use of exogenous hormones and risk of temporomandibular disorder pain. *Pain* 1997; **69**: 153-60.

2Ostensen M, Rugelsjoen A, Wigors Sh. The effect of reproductive events and alterations of sex hormone levels on the symptoms of fibromyalgia. *Scand J Rheumatol* 1997; **26**: 355-60.

3 Cardoe N, de Silva M, Glass RC, Risdall Pc. Serum concentrations of flurbiprofen in rheumatoid patients receiving flurbiprofen over long periods of time. *Crr Med Res Opin* 1977; **5**: 21-25.

4Mathias JR, Clench MH, Abell TL et al. Effect of leuprolide acetate in treatment of abdominal pain and nausea in premenopausal women with functional bowel disease: a double-blind, placebo-controlled, randomized study. *Dig Dis Sci* 1998; **43**: 1237-55.

Menstrual Cycle Variation in Pain Perception:

Meta-analysis of 16 published studies examined relationship between experimentally induced pain and menstrual cycle phase in healthy females



- During follicular phase (lowest progesterone levels) human females exhibited highest pain threshold and the greatest tolerances to pain (except electrical pain, highest in luteal phase)¹
- Contrast to rodents where injection of progesterone resulted in deep anesthesia



¹Riley JL, Robinson ME, Wise EA, Price DD. A meta-analysis review of pain perception across the menstrual cycle. *Pain* 1999; **81**: 225-35.

²Seyle H. Anesthetic effect of steroid hormones. *Proc Soc Exp Biol Med* 1941; **46**: 116-21.

Other Biological Differences

- Sex hormones influence sensitivity to noxious stimuli: pain threshold and tolerance vary with the stage of the menstrual cycle
- Imaging of the brain show differences in men/women in the spatial pattern and intensity of response to acute pain.
- Mu-receptors in the healthy female brain are activated differently than in healthy males
- Melanocortin-1 receptor gene is different in each sex and mediates response to kappa-opioids.



What Genes/Proteins have been Implicated in Sex Differences in Pain/Analgesia?

1. Estrogen Receptor
2. Mu/Kappa/Delta Opioid (MOR, KOR, DOR) Receptors
3. GABAA Receptors
4. N-methyl-D-aspartate (NMDA) Receptor
5. Melanocortin-1 Receptor (MC1R)
6. Orphanin FQ/Nociceptin (OFQ/N) Receptor
7. Protein Kinase A/C
8. G-protein coupled Inwardly Rectifying Potassium Channel (GIRK2)
9. Acid Sensing Ion Channel (ASIC)
10. Alpha-2-Adrenergic Receptor

Gender Differences in Brain Activation

PET Study of Brain Activation by Heat.

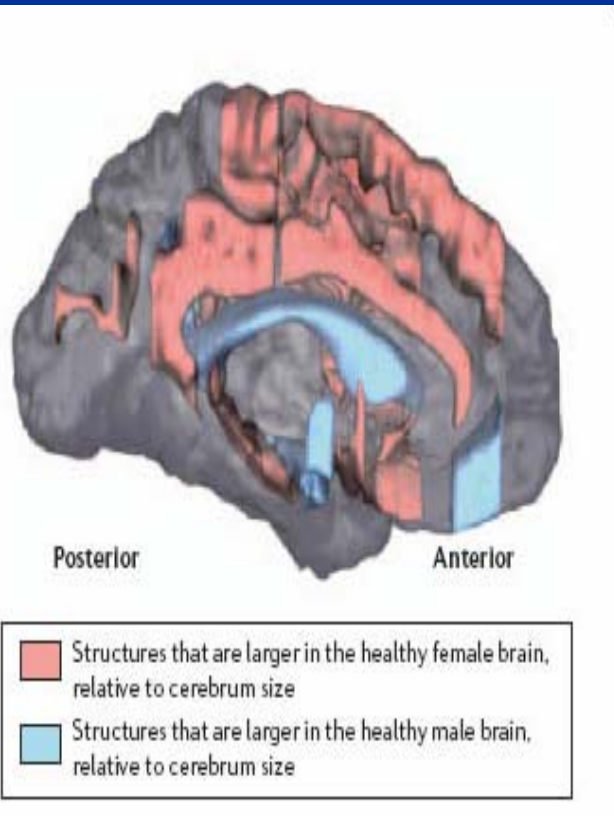
Methodology:

Normal right-handed subjects were asked to discriminate differences in the intensity of innocuous and noxious heat stimuli to the left forearm.

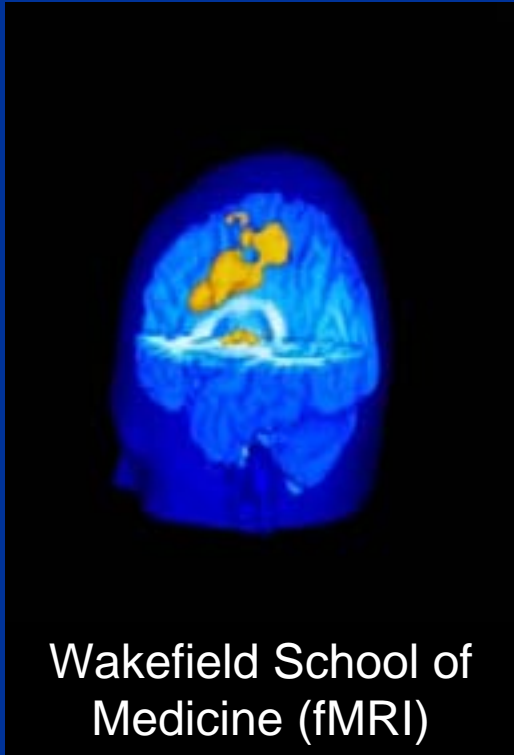
Results:

Both ♂ & ♀ rated 40° C as warm but not painful.

Both rated 50°C as painful, but ♀ rated 50°C significantly more intense than did ♂.



...PET Study of Brain Activation by Heat



- Both showed bilateral activation of premotor cortex and the posterior insula, anterior cingulate cortex and the cerebellar vermis
- Females had significantly greater activation of the contralateral prefrontal cortex and of the contralateral insula and thalamus

- Pain related differences may be due to gender, perceived pain intensity or both

Paulson PE, Minoshima S, Morrow TJ, Case KL: Gender differences in pain perception and patterns of cerebral activation during noxious heat stimulation in humans. *Pain* 76(1-2):223-9, 1998.

PET Scans in IBS

based on perceived rectal distension

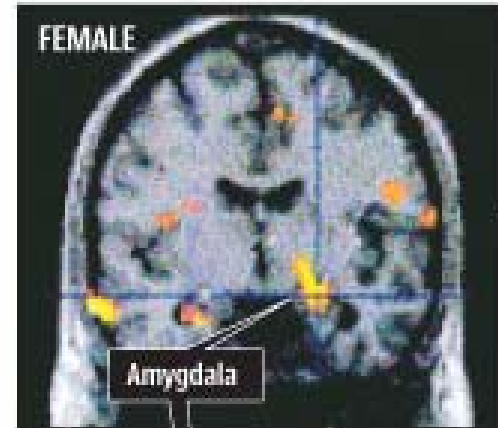
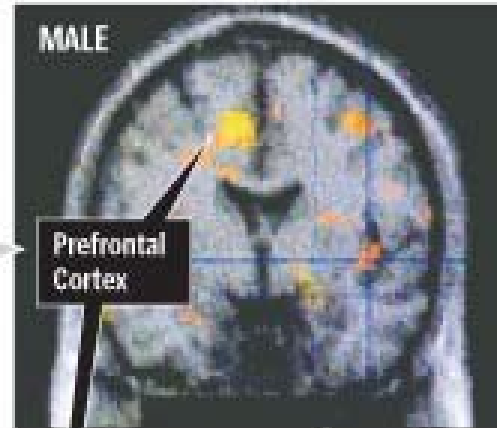
- The **female brain** showed greater activity **in limbic regions**, which are emotion-based centers. In **men**, the **cognitive regions, or analytical centers**, showed greater activity.
- Study of volunteers demonstrated
 - *Anticipation of the pain generated the same brain responses as the actual pain stimulus.*

Science Daily (Nov. 5, 2003: Gender Differences in Brain Response to Pain
Original article: Naliboff BD, Berman S, Chang L, Derbyshire SWG, Suyenobu B, Vogt BA, et al. Sex-related differences in IBS patients (central processing of visceral stimuli). *Gastroenterology*. 2003;124:1738–1747.

Some Differences in How Men and Women Experience Pain . . .

A 2003 UCLA study of people with irritable bowel syndrome shows that different parts of the brain respond to pain depending on a person's sex.

In the men, some of the cognitive regions, or analytical centers, showed greater activity. Here, the prefrontal cortex is activated, leading to the mental labeling, judging and categorizing of pain.

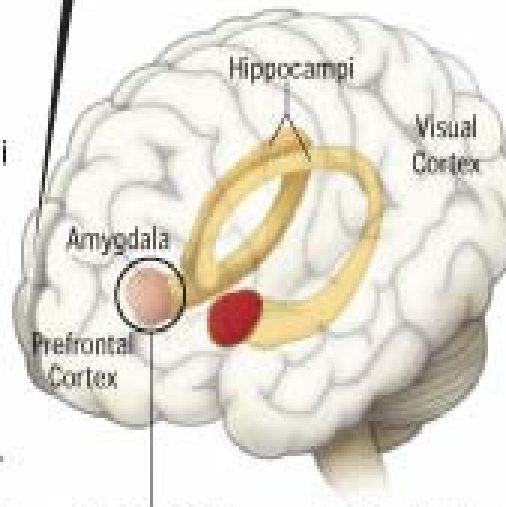


The female brain showed greater activity in limbic regions, which are emotion-based centers.

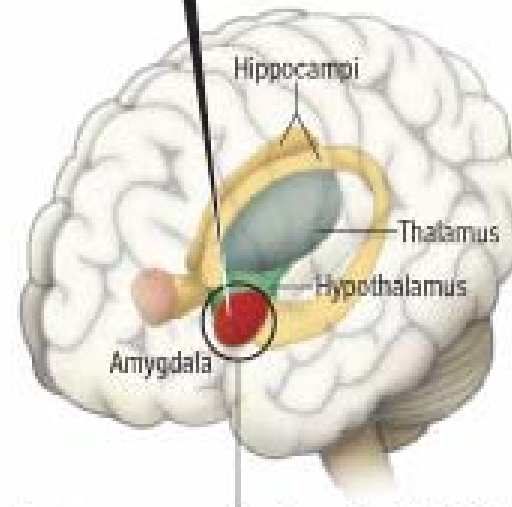
Some differences in how the brain is 'wired':

- Male and female hippocampi differ in their anatomical structure, neurochemical makeup and reactivity to stressful situations.

- The amygdala in each hemisphere functions differently in men and women.



In men experiencing pain, the right amygdala is activated. It has more connections with regions of the body involved with responding to the external environment, like the visual cortex.



In women experiencing pain, the left amygdala is activated. It has more connections to regions whose activity relates more to the internal functions of the body, such as the hypothalamus.

Gender Differences in Endogenous Mu-Opioids...

- Methodology:



Study participants were scanned as they received a pain-causing but harmless injection of salt water in their jaw muscle. (Simulates TMJ pain)

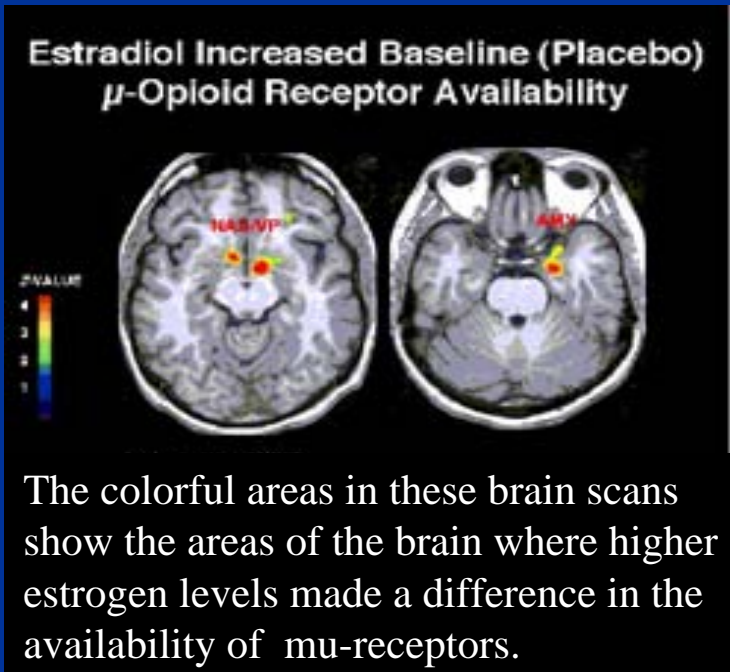
Study 1:

- 14 ♂ scanned before and during jaw pain showed increases in endorphin release in certain brain areas during the painful state
- Most of the 14 ♀ studied actually showed a reduction in endorphin release.
- The ♀ reported feeling more intense pain, and more pain-related negative emotions, than the ♂.

All the ♀ were studied at a time in their menstrual cycle when levels of estrogen and progesterone were lowest.

...Endogenous Mu-Opioids

- Study 2:
 - Women were scanned once during their early follicular phase, and again during that same phase in another month - after they had been wearing an estrogen-releasing skin patch for a week.
 - The patch made their levels of estrogen rise to levels normally seen during later parts of the menstrual cycle. (Allowed estrogen's effect to be studied without the effects of other hormones, such as progesterone, that normally increase along with it.)



Instead of the low or absent activation of the mu-opioid system seen in women during low-estrogen conditions, **the same women under high-estrogen conditions showed a marked increases in their ability to release endorphins and activate the receptors.**

Results similar to men!

Biological Differences: Rodent Studies

- Females more sensitive to noxious stimuli and have lower levels of stress-induced analgesics
- Male rodents have stronger analgesic response to mu opioids
- Transgenic mice show males a higher level of activity in the endogenous analgesic system



Wiesenfeld-Hallin Z: Sex differences in pain perception. Gend Med: 2005Sep;2(30):137-45.

Mu Opioid Analgesics

- Mu opioid agonist were more potent in one sex than another, but **SPECIES specific**.
 - Mice & rats: ♂ > ♀
 - Humans: ♀ > ♂

Species	M > F	M = F	F > M
Rat	35 (66%)	16 (30%)	2 (4%)
Mouse	7 (33%)	13 (62%)	1 (5%)
Human	0 (0%)	4 (29%)	10 (71%)

Craft RM. Sex Differences in Opioid Analgesia: "From Mouse to Man".
Clin J of Pain 2003; **19**: 175-186.

Possible Mechanisms Underlying Sex Difference in Mu Opioid Analgesia

- **Pharmacokinetics: Opioid metabolism**
 - Rodents¹: sex difference in ratio of M-3-G to morphine
 - Human²: M-3-G/Morphine = in ♂ & ♀
- **Pharmacodynamics** (opioid receptor density, in affinity of opioids for opioid receptors or in opioid receptor-mediated signal transduction)
 - Ex: PET scan showed women of reproductive age had greater mu opioid receptor binding³

1 Baker L, Ratke A. Sex-specific differences in levels of morphine, morphine-3-glucuronide, and morphine analgesia in rats. *Pain* 2002; **95**:65-74.

2 Sarton E, Olofsen E, Romberg R, et al. Sex differences in morphine analgesia. *Anesthesiology* 2000; **93**: 1245-1254.

3 Zubieta JK, Dannals RF, Frost JJ. Gender and age influences on human brain mu-opioid receptor binding measured by PET. *Am J Psychiatry* 1999; **156**:842-848.

Dental Pain Model: Tooth Extraction



- **Methodology:** Extraction of third molars by the same surgeon; evaluation of effectiveness of analgesics on post-surgical pain

- **Results:** *Kappa opioids* (pentazocine*, nalbuphine* and butorphanol*) eased pain better in women than men

* All of these agents are mixed agonist-antagonists and act at both kappa and mu-receptors

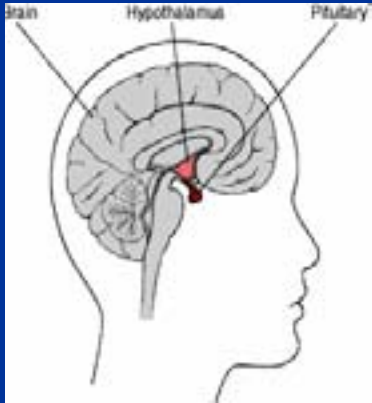
Kappa-Opioids: Why the Differences in Response

- Multiple mechanisms may explain sex differences in opioid analgesia:
 - Gonadal hormonal effects
 - Pharmacokinetics
 - Pharmacodynamics
 - Genetic influences
 - Balance of analgesic/antianalgesic processes
 - Psychological factors
- Disparity of results obtained from different pain models
 - Animals versus humans
 - Clinical pain versus experimental pain in humans
 - Suggests that the models themselves are mechanistically different

...Kappa-Opioids: Why the differences in Response?

- Disparity of results obtained from different pain models
 - Animals versus humans
 - Clinical pain versus experimental pain in humans
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Case Study: Gender Differences in Side Effects



32 yr. treated 4-5 yrs for fibromyalgia and chronic low back pain (Worker's Compensation) with multiple modal therapy including physical therapy, ultrasound, counseling, acupuncture and NSAID and opioid (ibuprophen 400mgs q8h and morphine SR 60 mgs q8h)

Presented with infertility to her family doctor. Hx of scant, sporadic periods beginning about 3 yrs ago; menstruation cessation for 4 months. Laboratory results: normal except for low HB (95), low FSH and LH and high PR.

↑ Prolactin

- ? Anterior pituitary adenoma

Sex differences in (side) effects of opioids other than analgesia may limit their therapeutic use!



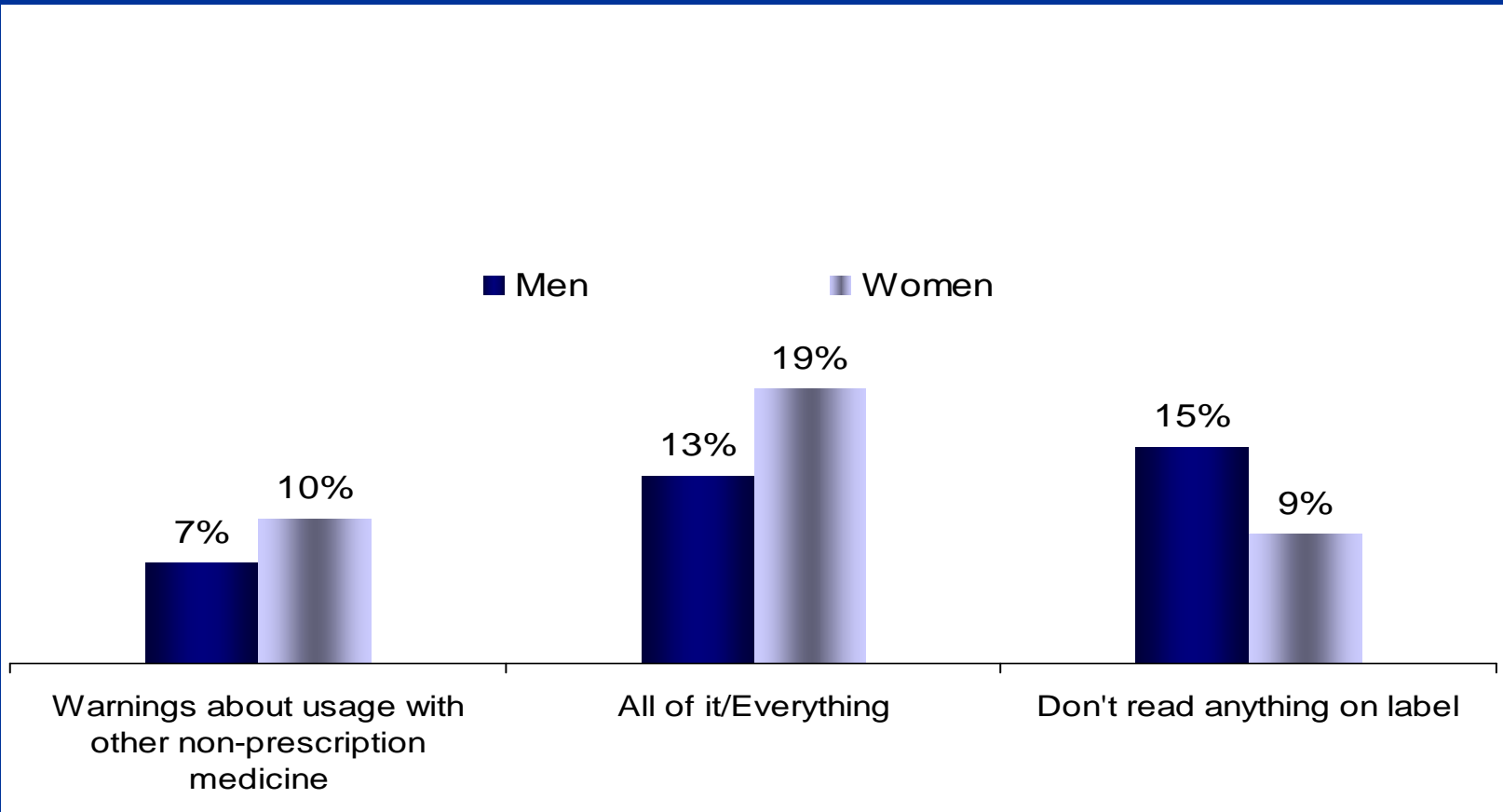
Gender Differences in Over-the-Counter Medication Usage...

- Women who take OTCs for pain are more likely than men to take these medications often
- Men are more likely than women to admit to risky attitudes or behaviors
- Men are less likely to worry about potential side effects

Humphrey Taylor: Over-The-Counter Pain Medications sponsored by the National Consumers League, Harrisinteractive market Research

Gender Differences in Over-the-Counter Medication Usage...

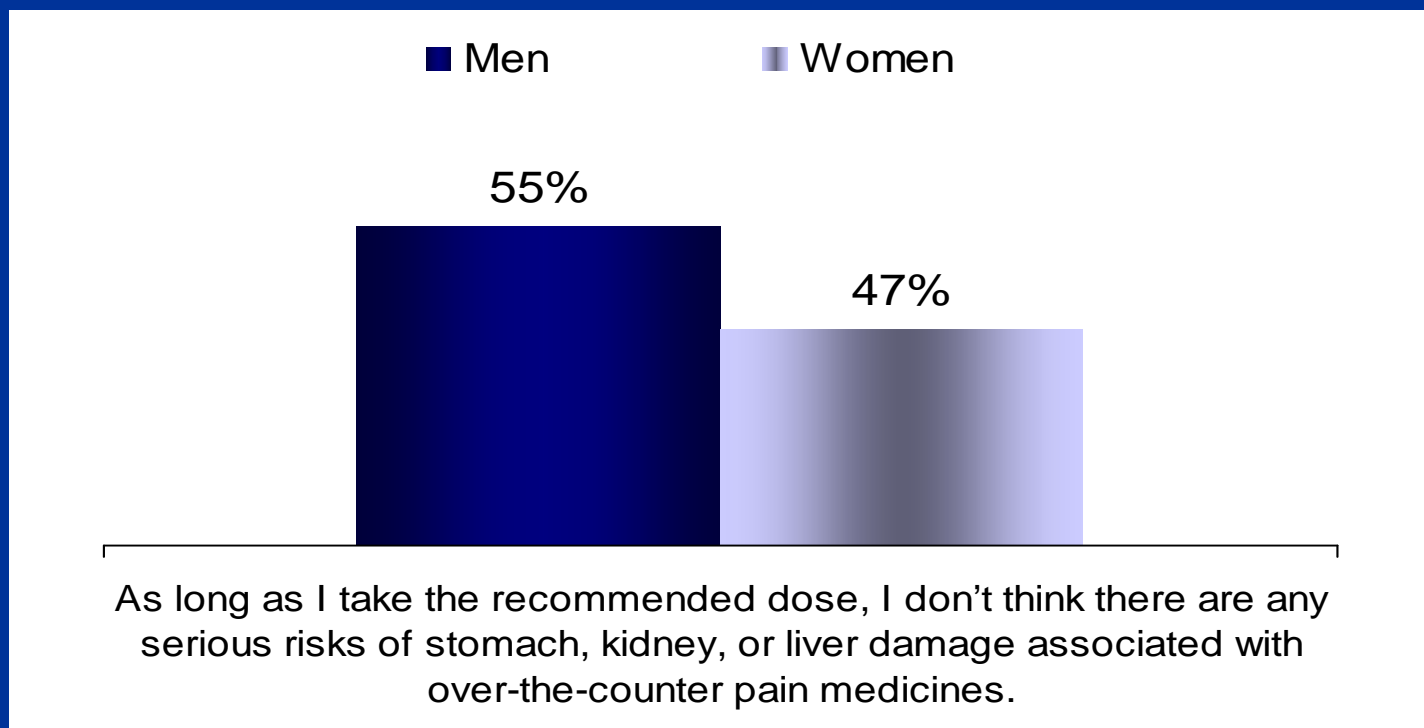
When reading the labels on their OTCs, women tend to be more thorough than men, although both genders fail to adequately read the entire label.



Humphrey Taylor: Over-The-Counter Pain Medications sponsored by the National Consumers League, Harrisinteractive market Research

Gender Differences in Over-the-Counter Medication Usage...

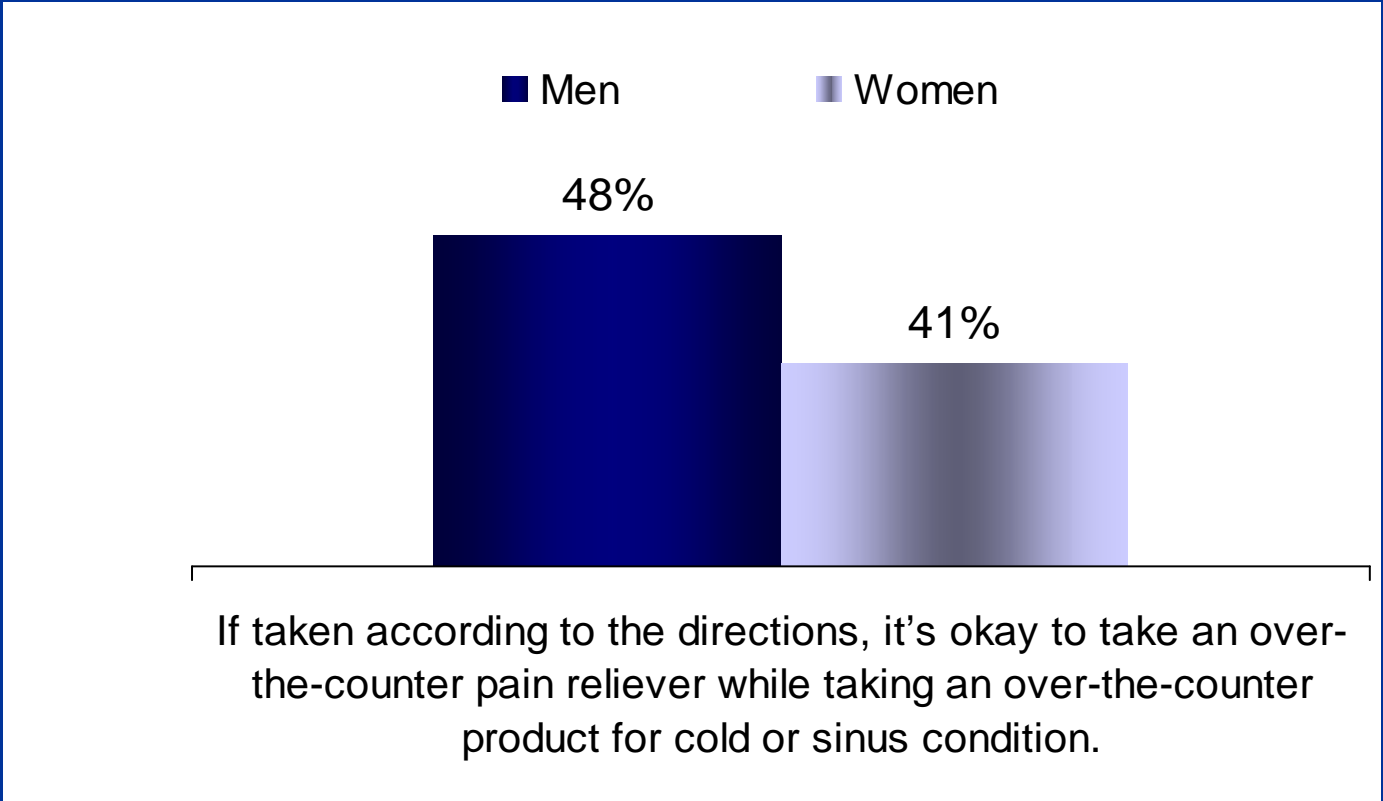
Furthermore, men are more likely than women to say that they don't have to worry about serious side effects – as long as they follow the label



Humphrey Taylor: Over-The-Counter Pain Medications sponsored by the National Consumers League, Harrisinteractive market Research

Men are more likely than women to think that it is “okay” to mix medications.

Attitudes Toward OTC Use



Base: All respondents

Psychological Factors & Pain Perception

- Influenced by personality, emotional state, and socialization factors¹

- **Chronic pain**

Patients perceive thermal stimuli normally but find these stimuli less unpleasant²

- **Emotional state:**

- **Depression** has been related to pain perception: ex.: a relationship between depressed mood and the perception of anginal pain during exercise treadmill testing³
- **Anxiety state** levels have been found to correlate with pain tolerance⁴

¹Gatchel RJ, Turk DC. Psychosocial factors in pain: critical perspectives. New York: The Guildford Press; 1999

²Gracely RH. Subjective quantification of pain perception. In: Brom B, editor. Pain measurement in man: neuropsychological correlates of pain. Amsterdam: Elsevier; 1984. p. 371–87.

³Davies RF, Linden W, Habibi H, Klinkle WP, Nadeau C, Phaneuf DC, Lepage S, Dessain P, Butters JA. Relative importance of psychologic traits and severity of ischemia in causing angina during treadmill exercise. J Am Coll Cardiol 1993; 21: 331–6.

⁴Wall PD. On, the relationship of anxiety to pain. Pain 1979; 6: 253–64.



Chronic Spinal Pain

- *Opioid use* was associated with **greater self-reported disability and poorer function** in both women and men.

- Opioid use with affective distress: The women using opioids showed lower affective distress, whereas the opioid-using men reported greater affective distress.
- *Opioid use was not associated with pain severity*, although the women reported greater pain than men.

Filligim RB, Doleys Dm, Edwards RR, Lowery D: Clinical characteristics of chronic back pain as a function of gender and oral opioid use. Spine. 2003 Jan 15;28(2):143-50.

Pain Related Health Care Use and Disability^{1,2}



- **Health Care:**
 - ♀ are more likely to seek health care for pain than ♂ are,
 - Result: a high proportion of women in many pain treatment settings.
 - Reason: The higher rate of treatment seeking among women may be due to the fact that pain is often more severe for women than for men.
- **Employment disability:**
 - It is unclear whether women or men are more likely to experience employment disability associated with pain conditions; numerous factors such as type of work and family responsibilities influence employment disability rates.
 - When disability is defined in terms of limitations in activities of daily living as well as work absence, women have higher rates of pain related disability.
- **School:** Although rates vary across populations, a median of about 20% of girls report missing school days due to dysmenorrhea

1 LeResche L. Sex, gender and clinical pain. In Flor H, Kalso E, Dostrovsky JO (Eds.), Proceedings of the 11 th World Congress on Pain. Seattle, IASP Press, 2006, pp. 543554.

2Unruh AM. Gender variations in clinical pain experience. Pain 1996; 65:123167.