



Measurement of Pain in claimants undergoing an Independent Medical Examination - A gender perspective .



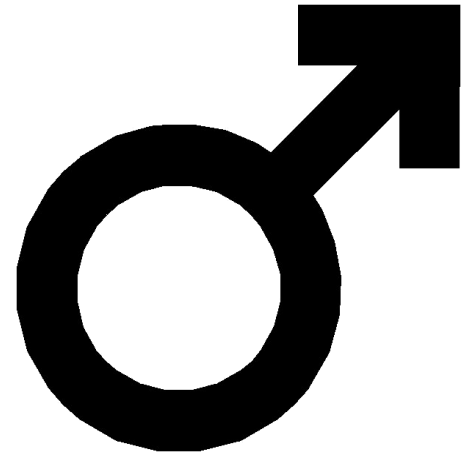
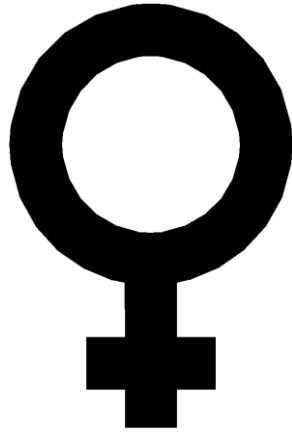
On behalf of Irene Lund



**Karolinska
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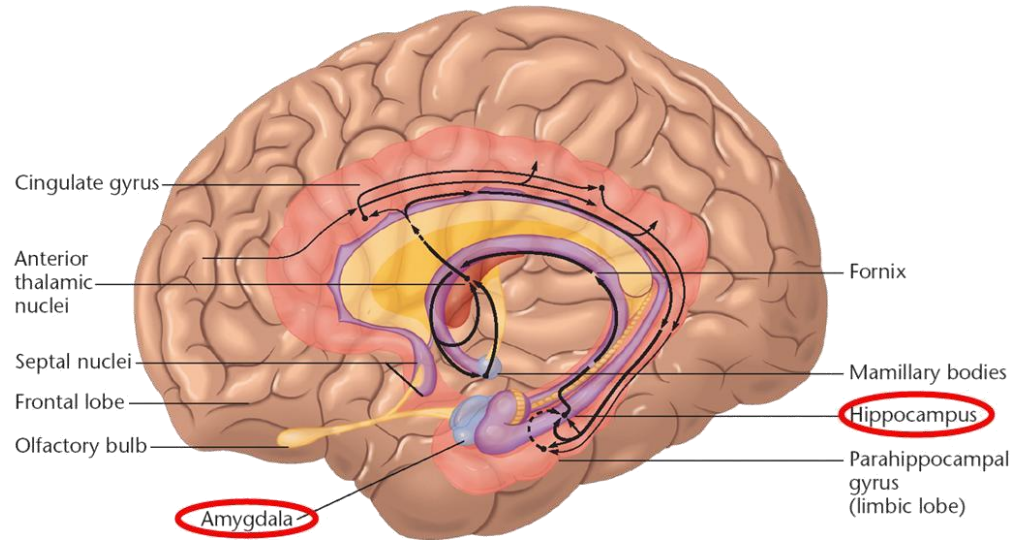
SEX
humans)

biological aspects (animals and

GENDER socio-cultural aspects (humans)



**Before 1993 – women were excluded from pharmacological studies!
The male sex has been the norm even in animal studies.**



Hippocampus -

size ♀ > ♂

affinity of glucocorticoid receptors half in women than in men

Amygdala -

size ♂ > ♀

left amygdala activated in women and right in men

Prefrontal cortex -

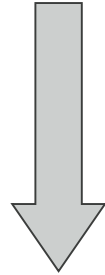
left activated in women, right in men

Cahill. Why sex matters for neuroscience. Nat Rev Neurosci 2006;may:1-8

“Specifically, men seem to have more access to an amygdale-mediated recruitment of the endogenous pain inhibitory system.”

Linman et al. Sex similarities and differences in pain-related periaqueductal gray connectivity. Pain 2012;153:444-454

Stress



♀ ↑ stroke volume, cardiac output

♂ ↑ vascular resistance (adrenergic sensitivity)

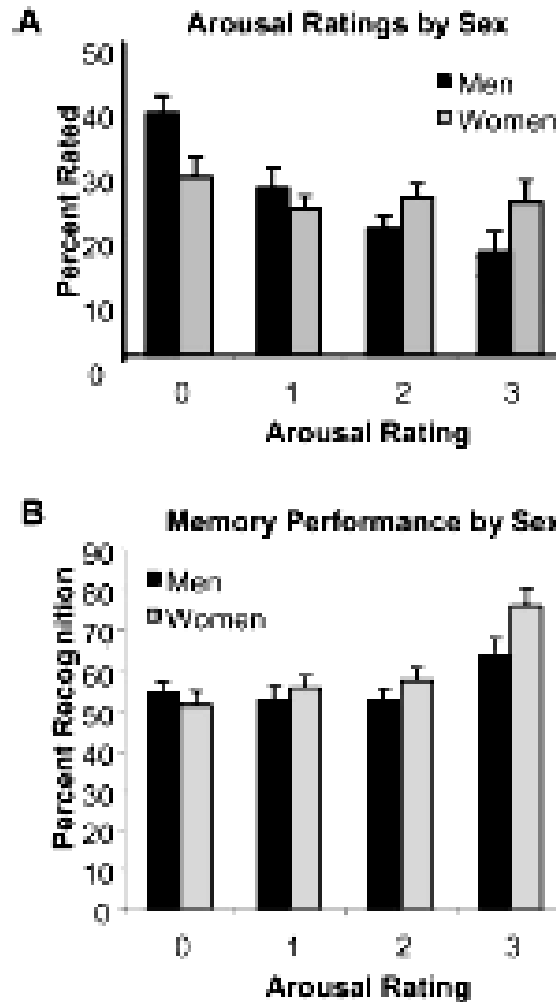
↑ release of cortisol

Girdler and Light, 1994

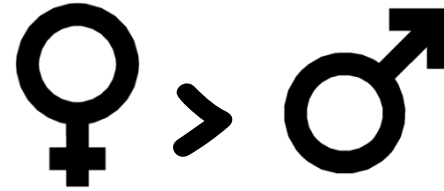
Meh and Denislic, 1994

Zimmer 2003

Different emotional memories?



Clinical pain



- Higher level of perceived pain
- Pain from more body regions
- Longer duration of pain
- Higher prevalence in painful conditions

e.g. knee-osteoarthritis pain, fibromyalgia, TMD, migraine, RA, IBS, post-traumatic stress syndrome (PTSD), depression

Filligim RB. Sex, Gender and Pain. Progress in pain research and management, vol 17. IASP press 2000

Bekker MHJ, vn Mens-Vershulst J. Anxiety disorders: Sex differences in prevalence, degree, and background but gender-neutral treatment. *Gend Med* 2007;4:S178-S193.

Kajantie E. The effects of sex and hormonal status on the physiological response to acute psychosocial stress. *Psychoneuroendocrinol* 2006;31:151-178.

Accortt et al. Women and major depressive disorder: Clinical perspectives on causal pathways. *J Womens Health* 2008;17:1583-1590.

Epidemiology

"Married women suffer from more pain than unmarried"

	-	+
Men	Over weight Unemployment Long-term sick-leave	Jogging Highly educated
Women	Over weight Anxiety about economy Half time work Long-term sick-leave	Hard work Single, divorced

Bingefors. Epidemiology, co-morbidity, and impact on health-related quality of life of self-reported headache and musculoskeletal pain--a gender perspective. Eur J Pain. 2004;8:435-450.

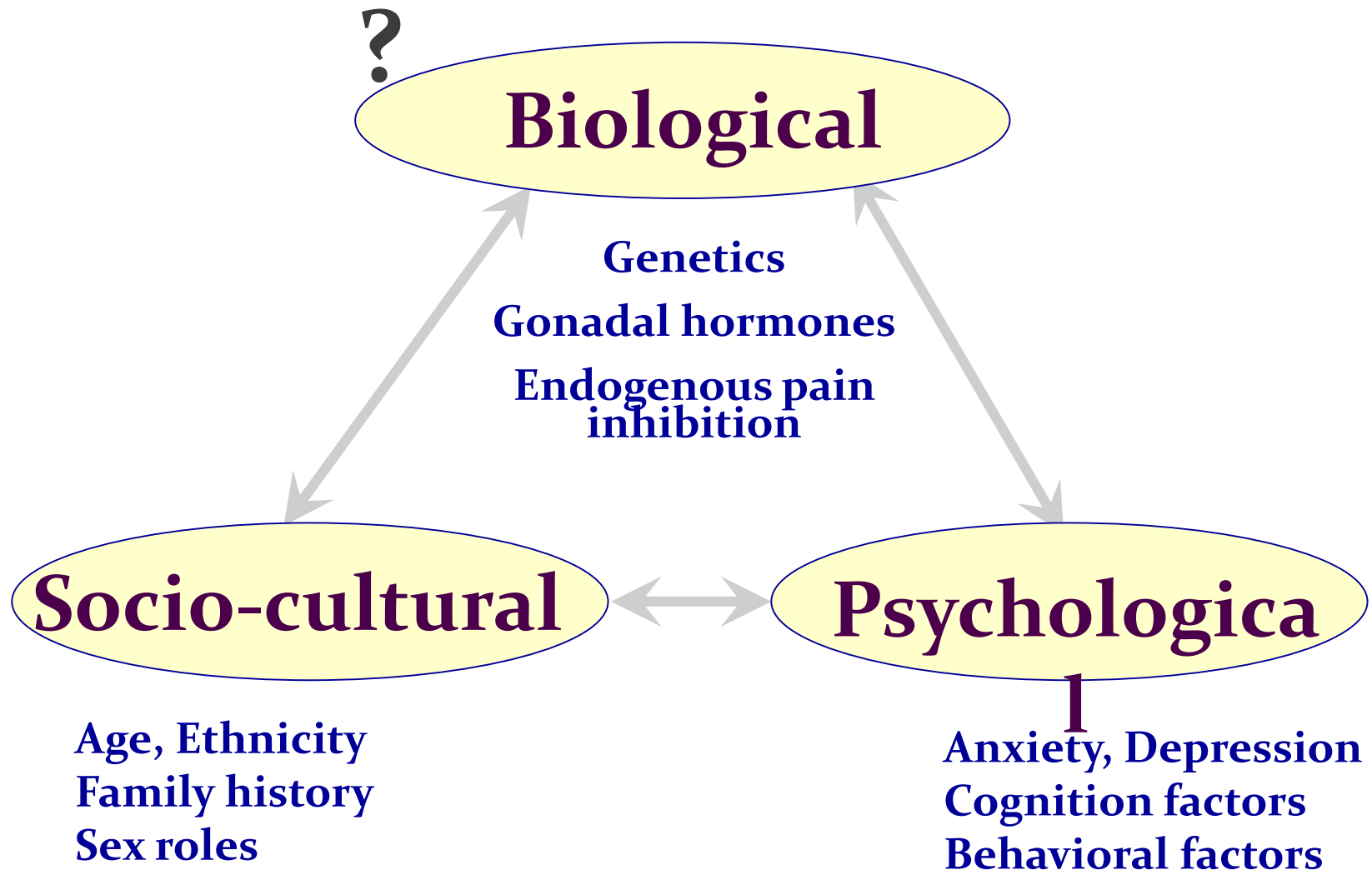
Analgesic use

Women vs Men ♀ > ♂

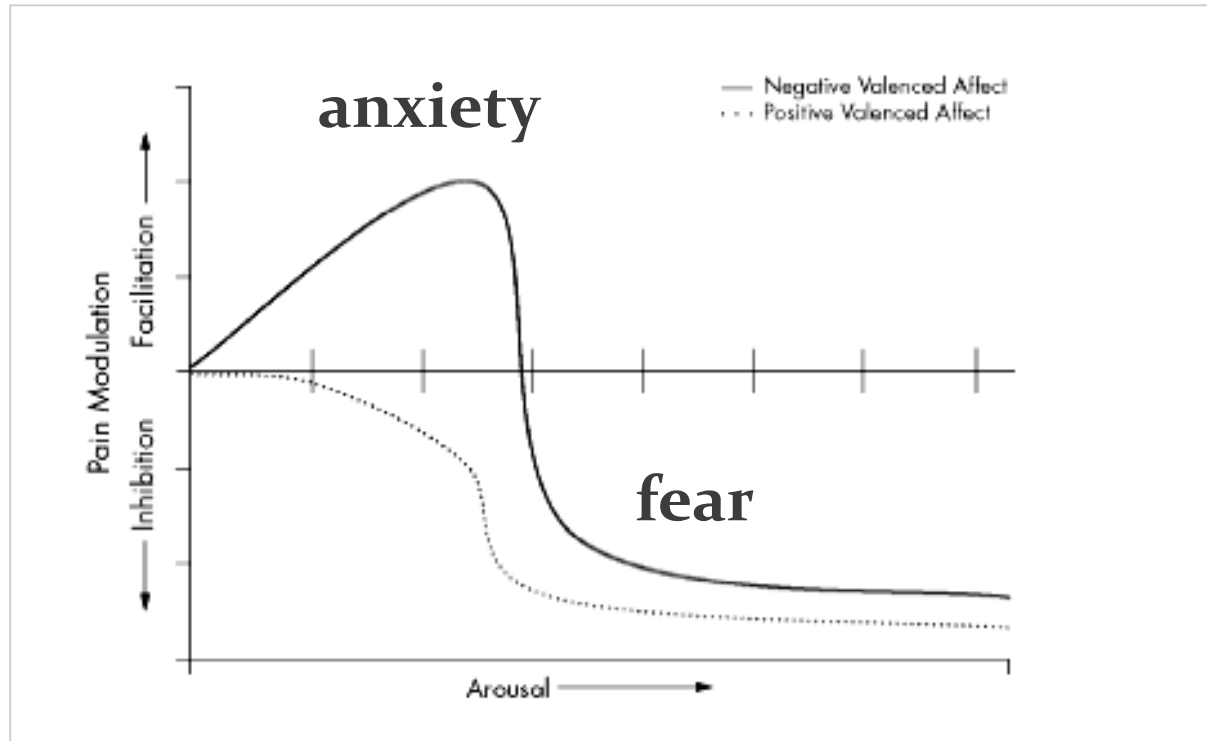
younger ♀ > older ♀

Isacson. Epidemiology of analgesic use: a gender perspective. Eur J Anaesthesiol Suppl. 2002;26:5-15.

Mechanisms



Gender differences in pain: do emotions play a role?

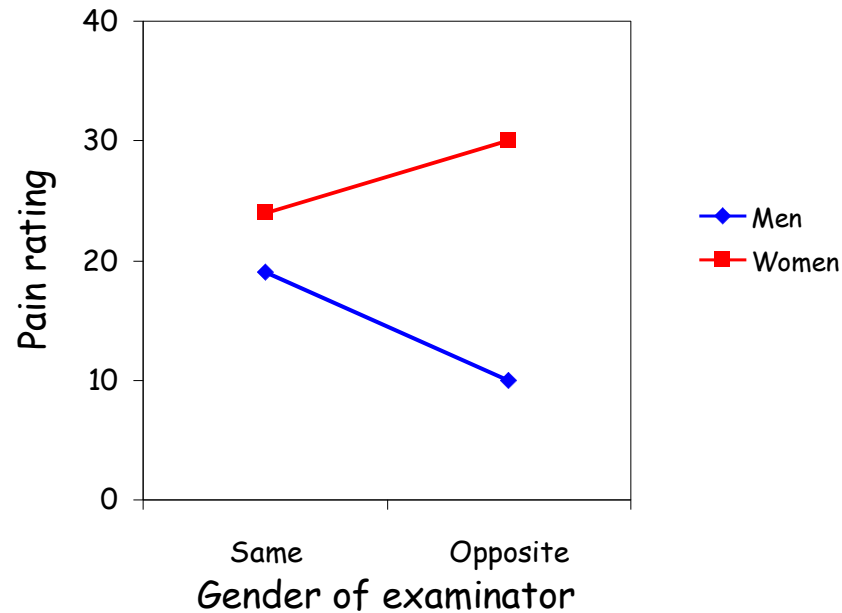
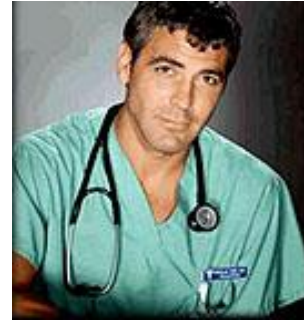


Differences in the experience and processing of emotions - differently altering pain processing

♀ more sensitive to negative stimuli (threat related)

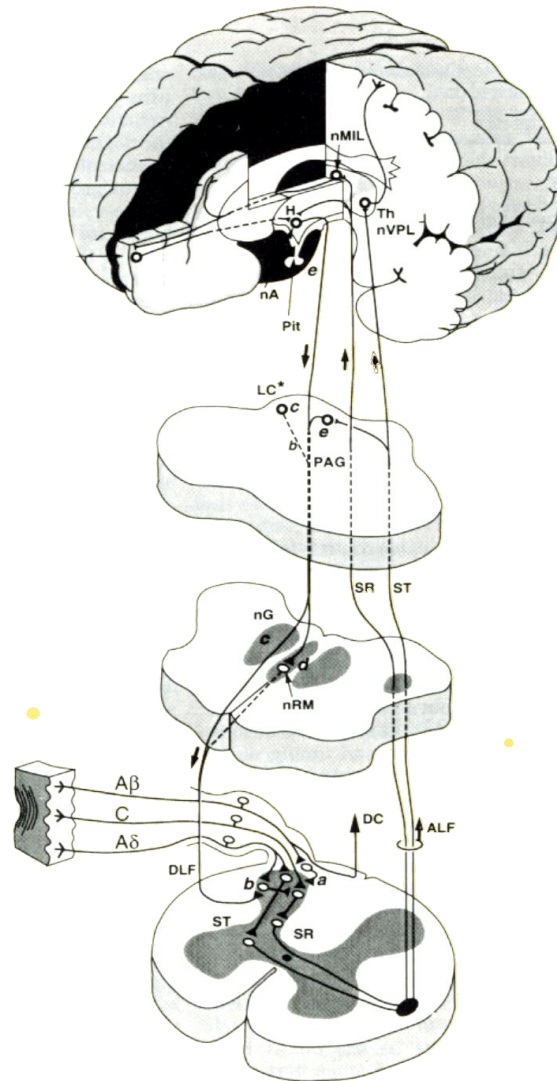
♂ more sensitive to positive stimuli (sexual/erotic)

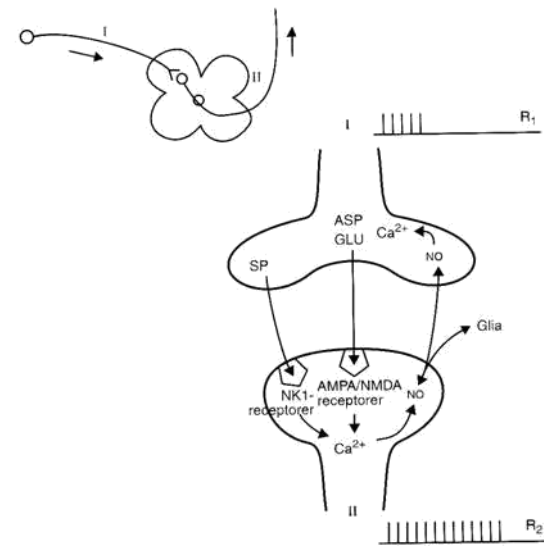
The gender of the examiner – does it matter?



Levine et al. The effects of experimenter gender on pain report in male and female subjects. *Pain* 1991;44:69-72

Endogenous pain inhibition





Nisell,
Lundeberg

Differences in pain regulating systems

Increased number of NMDA receptors in women as compared to men?

NMDA receptors activated by female gonadal hormones

Sensitized pain system due to repeated visceral pain (menses, labour)?

Wind-up present to a higher degree in women than in men (thermal skin pain)

Cairns. The influence of gender and sex steroids on craniofacial nociception. *Headache Curr* 2007 feb. 319-324

Fillingim et al. Sex differences in temporal summation but not sensory-discriminative processing of thermal pain. *Pain* 1998;75:121-127



Perceived pain, quality of life and function can be assessed by rating but is difficult/impossible to measure

---despite that, the information from what is perceived is needed to describe data on individual and group level being the basis for

- diagnosis and choice of therapy
- evaluation of the effect of different therapies

Rated experiences of pain

Ratings of pain - different aspects

- Intensity
- Unpleasantness
- Cognitions

Rated "type" and when

- Right now
- "The most common"
- "The mildest"
- "The worst"
- The last week

Rated change

- Very much worse
- Much worse
- Somewhat worse
- Unchanged
- Somewhat better
- Much better
- Very much better

Ex Patient Global Impression of Change, PGIC

Type of measurement instrument and does operationalization matter?

Verbal descriptive scale (VDS)

How much....

- none
- very mild
- mild
- moderate
- severe
- very severe

How much...?

- no pain
- moderate
- severe

Visual analogue scale (VAS)

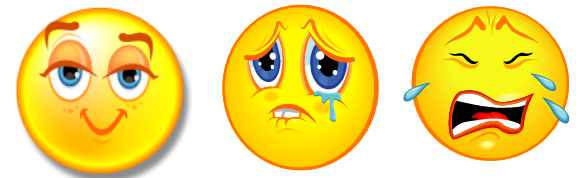
no |-----| extremely

labels: (-) (+) (++)

Numeric rating scale (NRS)

0 1 2 3 4 5

Pictogram

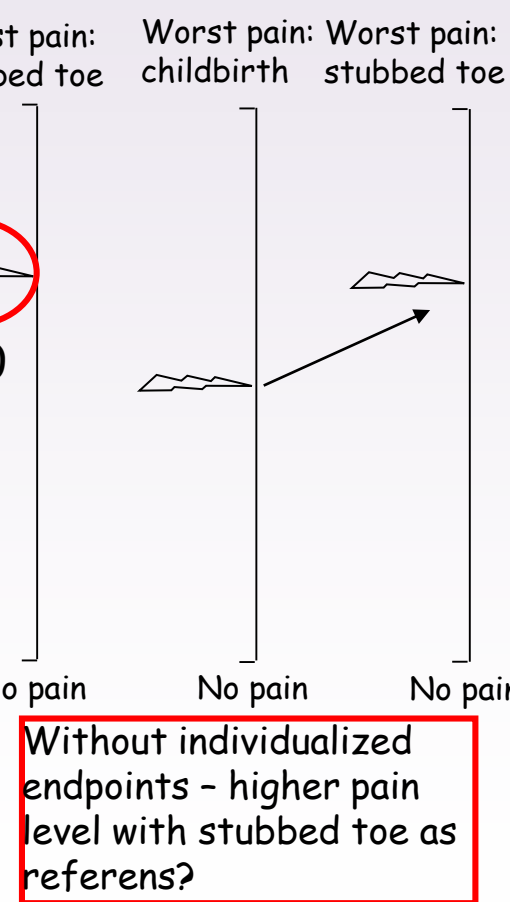
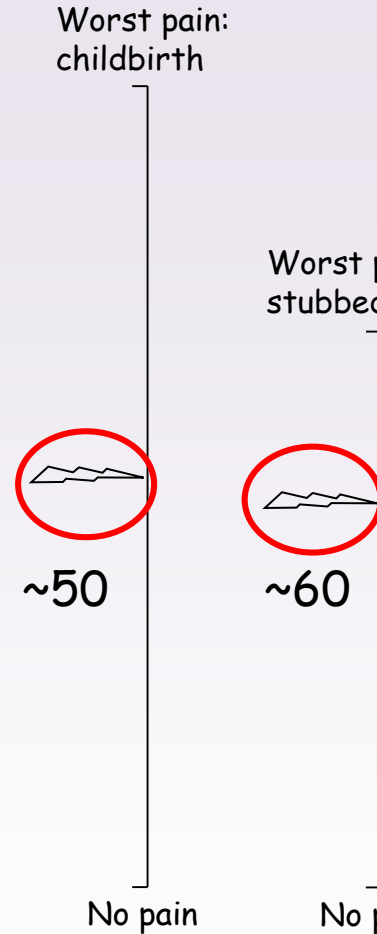
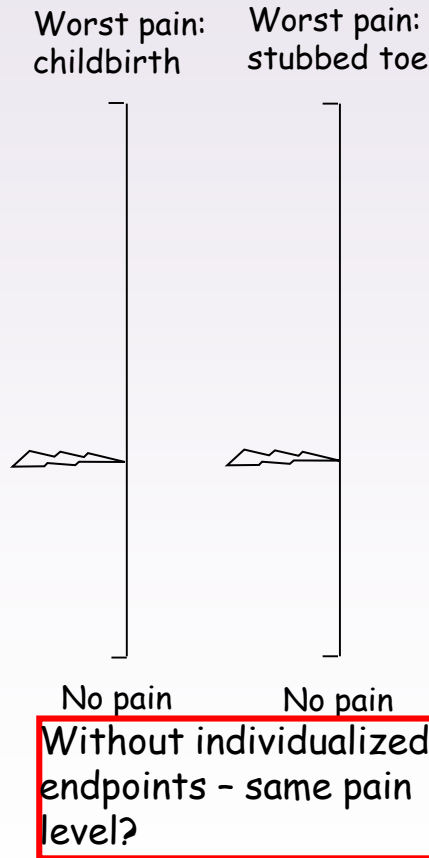
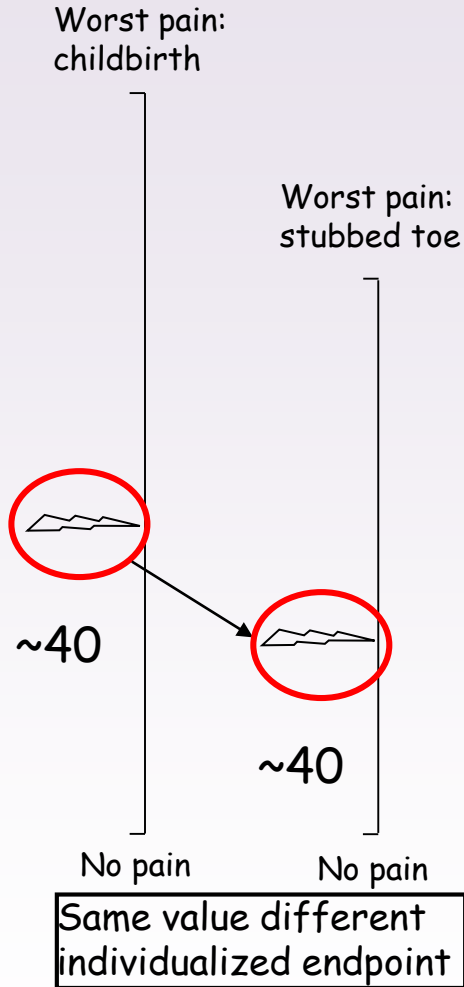


Real world

Measurement artifact

Real world

Measurement artifact



How?

Production of data from...

Objective measurements

based on physical, chemical properties

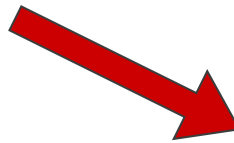
Eg. bloodanalyses, alko-testing, weight, length, amount

→ Quantitative data

Subjective assessments

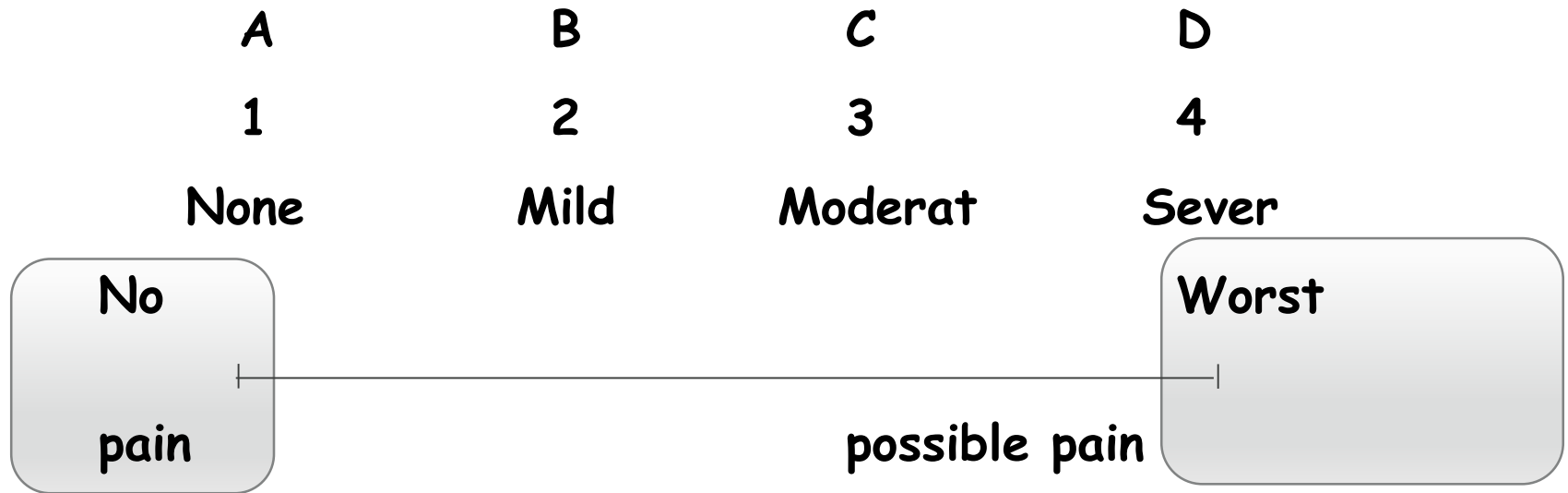
based on ratings on scales or other type of categorization according to specification

→ Category data



Categorical data

Measuring level - ORDINAL DATA

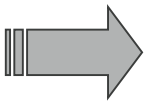


Properties of ordinal data

- Only order (1,2,3, a,b,c, +, ++, +++)
- Numbers \neq Figures - are only labels without mathematical properties
- No standardized distance between categories
- No defined size (magnitude)

The operational definition of the variable decide the level of measurement of the data

Level of measurement	Example
Dichotomus data	Hypertoni/no hypertoni, painless, not painless (+) (-)
Categorical data (nominal data)	Diagnosis Type of drug
Categorical data with order structure (ordinal data)	None, light, moderate, strong pain Low, normal, high blood pressure Completely agree, partly agree, do not agree at all Always, often, sometimes, seldom, never
Quantitative numerous data	Number of painful locations, Heart rate (beats/minute)
Continuous quantitative data (interval, quota data)	Blood pressure (mmHg), temperature, body weight (kg), S-kolesterol (mmol/l)



**ORDINAL
DATA**

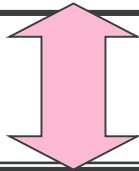
Order

**Ranges
Percentiles:
Median
Quartiles**

**Quantitative
data**

Distance and magnitude

**Sum, Differences
Quote
Distance
Mean value
Standard deviation**



Assessments (ratings) with visual analogue scale (VAS) only indicates the estimate's position on the scale and also produces ordinal data

EX: Pain intensity VAS,
Mean 25.3 (SD 22.8)



Interpretation? CHOICE AND CONSEQUENCE!!

Subvariabel pain fromn Foot and Ankle Outcome Score, FAOS

Foot and Ankle Outcome Score (FAOS), English version LK1.0

Pain

P1. How often do you experience foot/ankle pain?

Never Monthly Weekly Daily Always

What amount of foot/ankle pain have you experienced the **last week** during the following activities?

P2. Twisting/pivoting on your foot/ankle

None Mild Moderate Severe Extreme

P3. Straightening foot/ankle fully

None Mild Moderate Severe Extreme

P4. Bending foot/ankle fully

None Mild Moderate Severe Extreme

P5. Walking on flat surface

None Mild Moderate Severe Extreme

P6. Going up or down stairs

None Mild Moderate Severe Extreme

P7. At night while in bed

None Mild Moderate Severe Extreme

P8. Sitting or lying

None Mild Moderate Severe Extreme

P9. Standing upright

None Mild Moderate Severe Extreme

FAOS responsiveness has been confirmed in patients undergoing treatment for Achilles tendinosis (see below) and plantar fasciitis (work in progress).

A User's Guide to:
Foot and Ankle Outcome Score
FAOS

1. PAIN $100 - \frac{\text{Total score P1-P9} \times 100}{36} = 100 - \frac{\quad}{36} = \underline{\quad}$

2. SYMPTOMS $100 - \frac{\text{Total score S1-S7} \times 100}{28} = 100 - \frac{\quad}{28} = \underline{\quad}$

3. ADL $100 - \frac{\text{Total score A1-A17} \times 100}{68} = 100 - \frac{\quad}{68} = \underline{\quad}$

4. SPORT&REC $100 - \frac{\text{Total score SP1-SP5} \times 100}{20} = 100 - \frac{\quad}{20} = \underline{\quad}$

5. QOL $100 - \frac{\text{Total score Q1-Q4} \times 100}{16} = 100 - \frac{\quad}{16} = \underline{\quad}$

Statistical toolkit



- what analyses tool could be used?

Independent data

- Differences between groups, Mann Whitney U test

Dependent data from paired assessments

- **Association**, Spearman rank-order correlation, Svensson method
- **Change before/after (effect)**, Sign test (differences between paired proportions), Svenssons rank-based method (designed for paires of ordinal data from all types of ordered assessments; separates systematic disagreement between two assessments, group based, from individual variations, noise, in assessments)
- **Agreement, inter-/intra-assessments**, Svensson method

E. Svensson. Val och konsekvens: mätnivån avgör den statistiska verktygslådan. Läkartidningen 2005;102:1331-1337.

E. Svensson. Vad är behandlingseffekt om patienten blev bättre men ingen vet hur mycket? Läkartidningen 2205;102:-3138-3145.

Does 2 different instruments say the same?

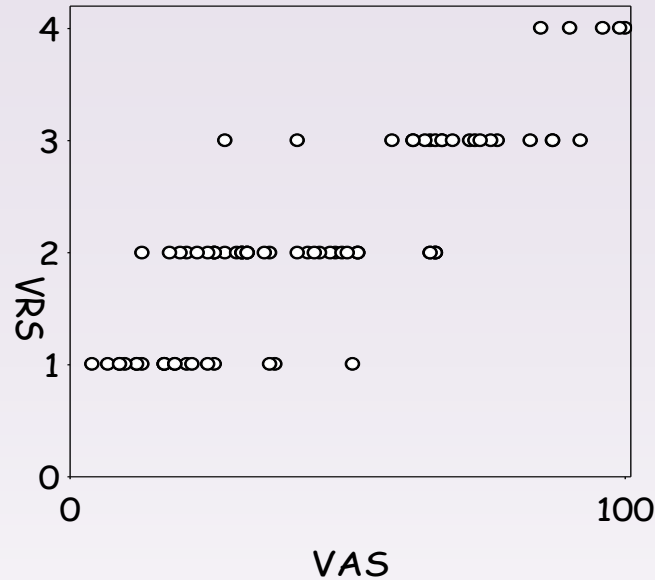
Worst possible pain

Severe pain

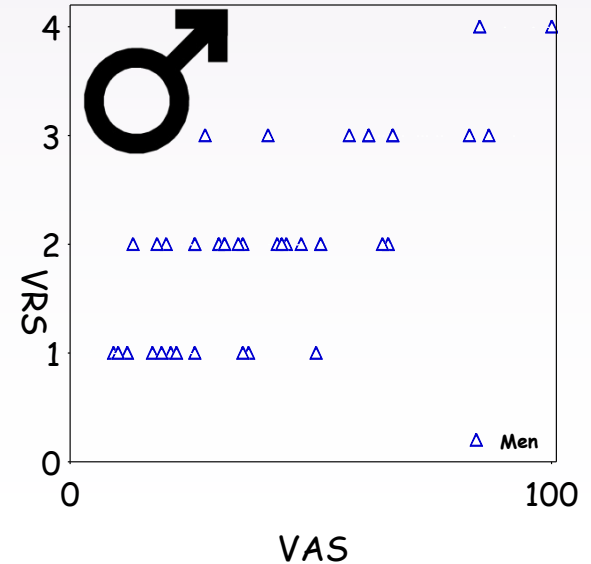
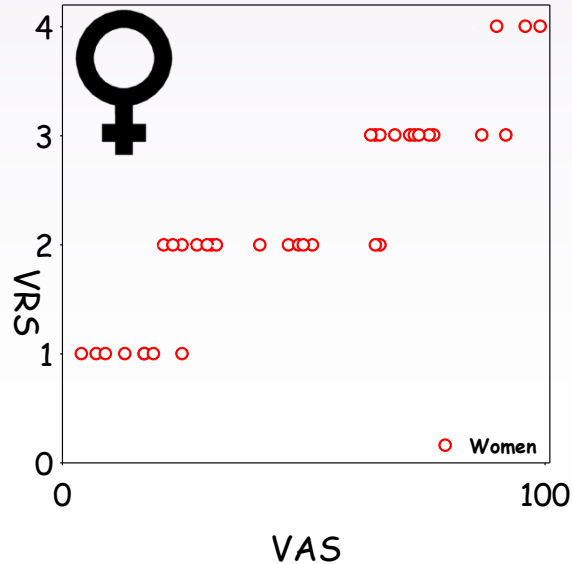
Moderate pain

Mild pain

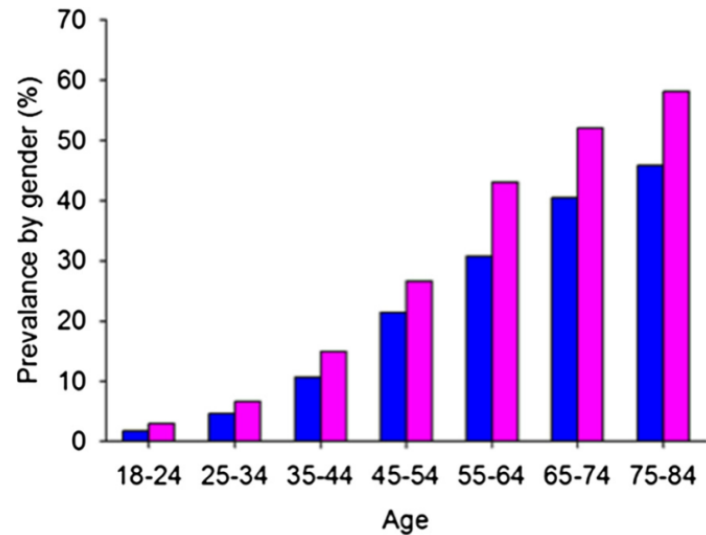
No pain



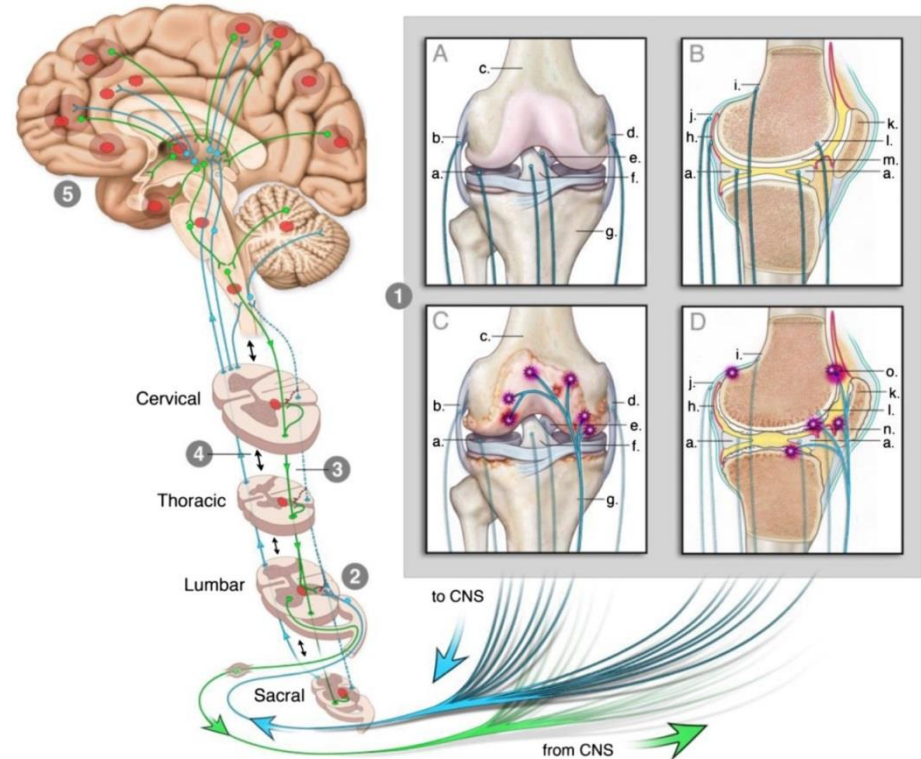
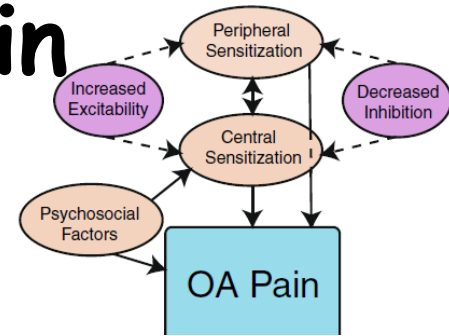
Lund I et al. BMC Med Res Methodol 2005 Oct 4;5:31



Knee-osteoarthritis pain

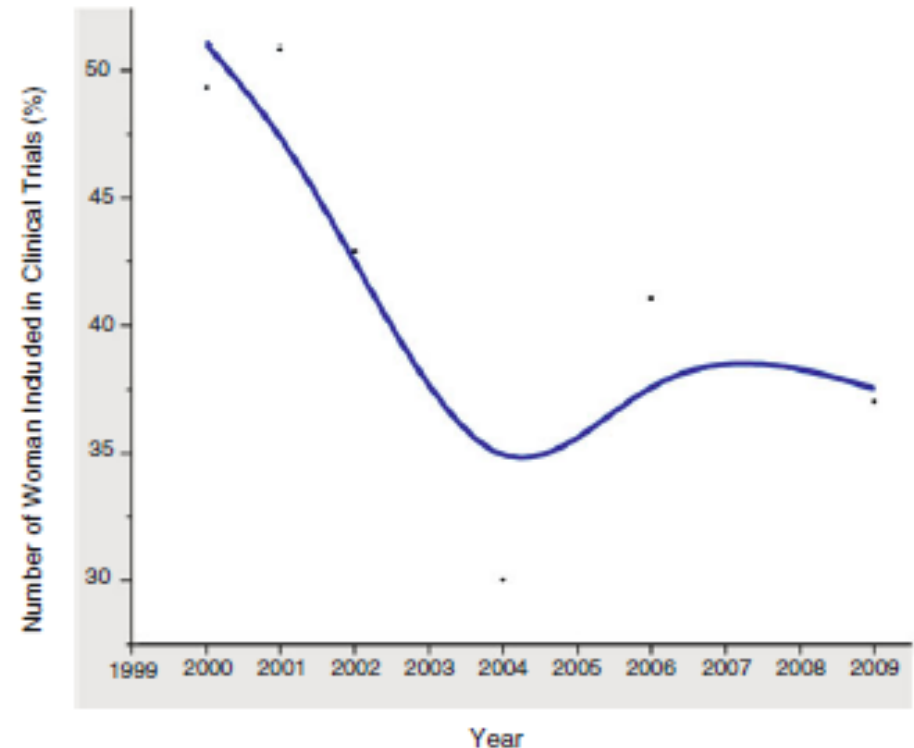
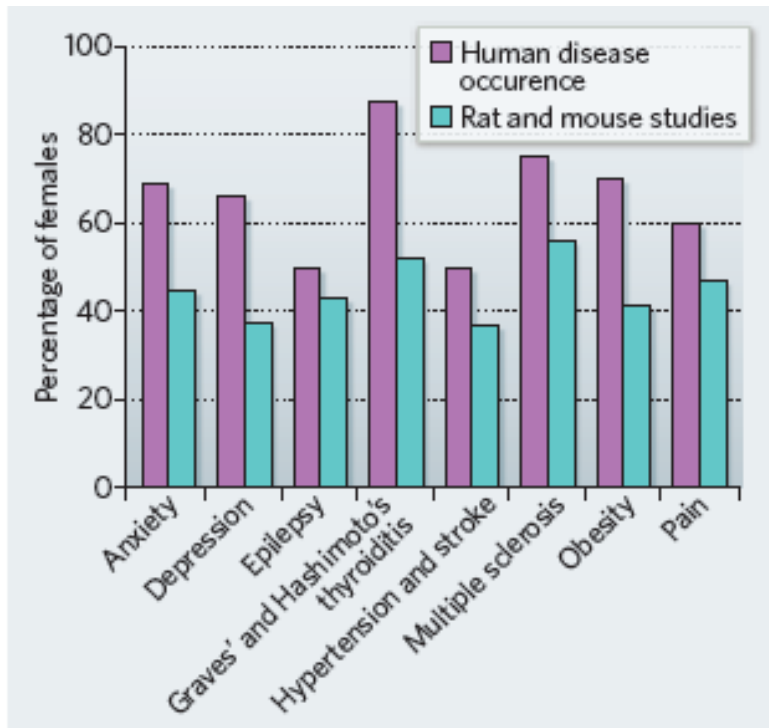


Women report more load-related pain and reduced function



Sluka et al. Neural and psychosocial contributions to sex differences in knee osteoarthritic pain. *Biology of Sex Differences* 2012, 3:26
 Boyan et al. Addressing the gaps: sex differences in osteoarthritis of the knee. *Biology of Sex Differences* 2013, 4:4
 Boyan et al. Hormonal modulation of connective tissue homeostasis and sex differences in risk for osteoarthritis of the knee *Biology of Sex Differences* 2013, 4:3
 Tonelli et al. Women with knee osteoarthritis have more pain and poorer function than men, but similar physical activity prior to total knee replacement. *Biology of Sex Differences* 2011;2:12

Sex/Gender gap - females/women are still underrepresented in animal and human studies



Berry, Zucker. Sex bias in neuroscience and biomedical research. *Neurosci Biobehav Res* 2001;35:565-572.
Zucker I, Beery AK. *Nature*. 2010 Jun 10;465(7299):690

Raz L, Miller VM. Considerations of sex and gender differences in preclinical and clinical trials. *Handb Exp Pharmacol*. 2012;(214):127-147.

CONCLUSION

- Pain appears differently in men and women - ranging from neurobiological to socio-cultural aspects
- Women are reported to suffer from pain more than men
- Observations on males/men cannot be generalized indiscriminately to females/women and vice versa.

In order to increase our knowledge

- Influence of sex/gender related effects should be considered when designing, analyzing and reporting acupuncture studies
- Sex/gender differences when only one sex is studied, could be indicated in article titles.
- More studies separating the two sexes/genders are needed
- Study of mechanisms underlying sex differences should be a high priority.