

Sex-based differences in anesthetic effects

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Background knowldege

- Men and women are often treated differently in their professional, social and family lives, and sex equality is an important goal of many world bodies
- Heathcare system not different...
- More rapid and active care is provided to men admitted to hospital for acute medical conditions and also in primary care
- Both patients' preferences and systemic differences in physician decision-making have been implicated to explain variable processes and outcomes in men and women.

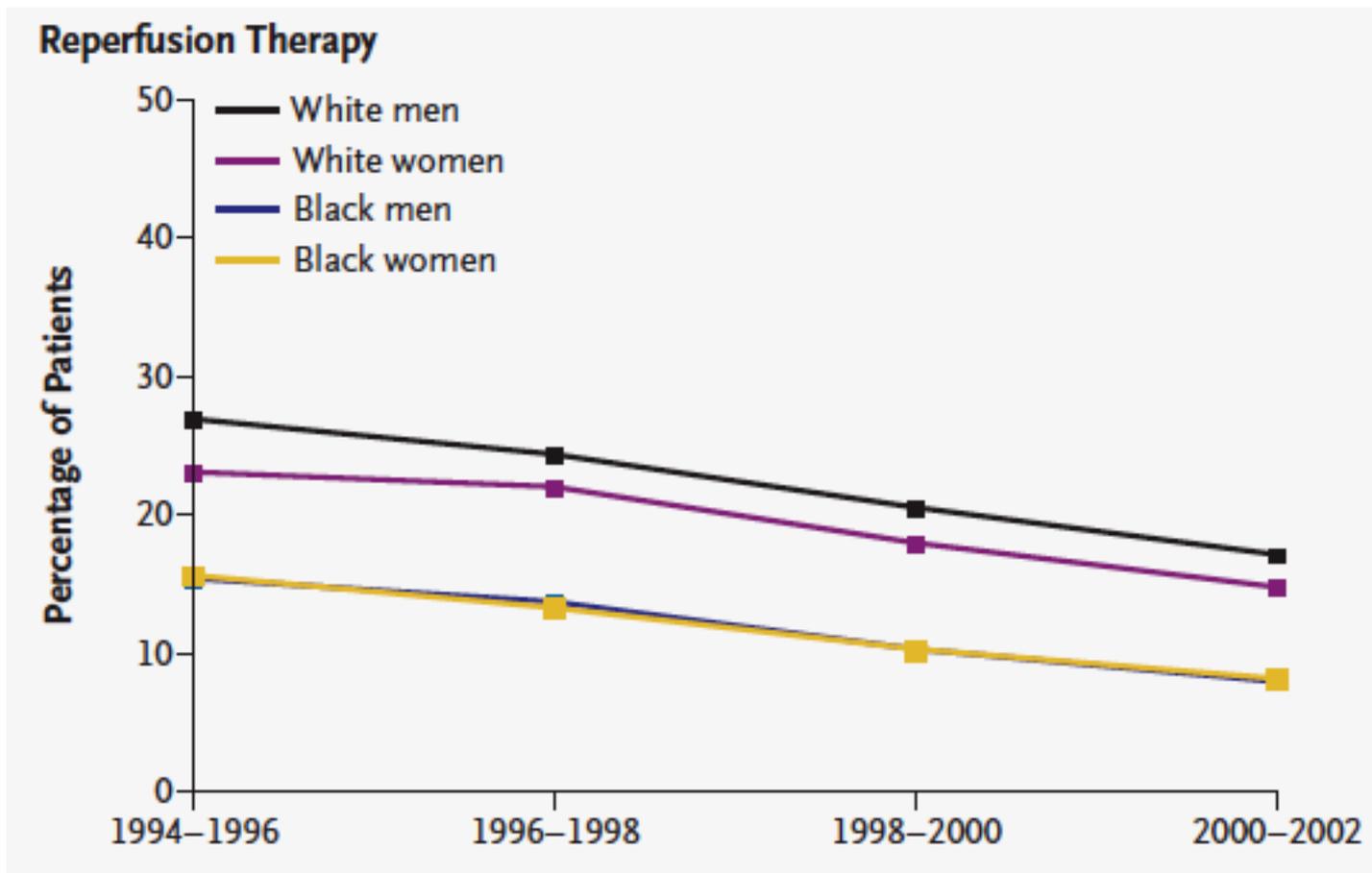
Evidence for Age and Sex Differences in the Secondary Prevention of Stroke in Scottish Primary Care

Simpson CR et al, Stroke 2005;36:1171-5

- Retrospective cross sectional study of 61 practices for 10 076 patients with stroke
- Women with any type of stroke
 - More likely to receive a thiazide drug
 - But less likely to be prescribed an ACEI
- In patients with ischemic stroke
- Women less likely to receive antiplatelet, warfarin or statin therapy than men

Sex and racial differences in the management of acute myocardial infarction, 1994 through 2002

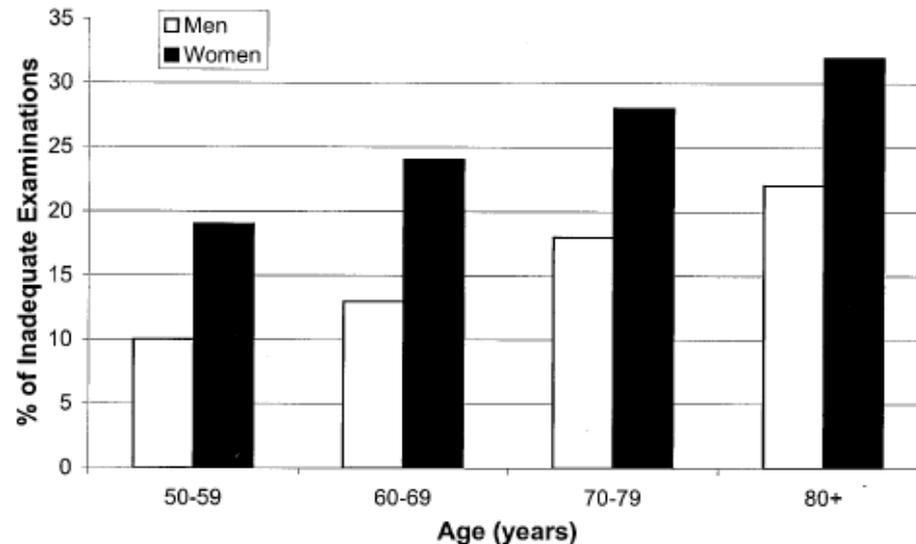
Vaccarino V et al, NEJM 2005;353:671-82



Association of older age and female sex with inadequate reach of screening flexible sigmoidoscopy

Walters LC et al, AmJ Med 2004;116:174 –178

- 15406 asymptomatic persons > 50 years
- Older age and female sex are associated with an increased likelihood of more proximal colon polyps and cancers
- Adequate depth of insertion of the sigmoidoscope if > 50 cm
- Longer colon in women (10 cm...), smaller abdominal cavity, more sensitive to pain



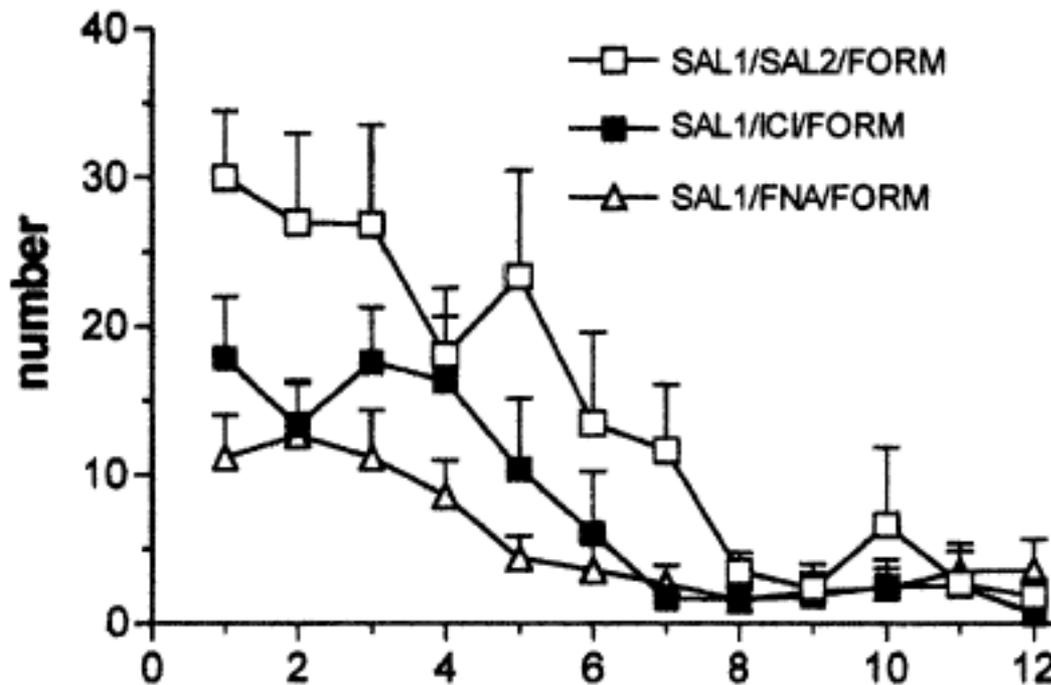
Pain and female gender

- Women, on average, reporting more intense pain, more frequent pain and pain of longer duration than men
- Women have a higher incidence of chronic pain syndromes, including irritable bowel syndrome, biliary colic, fibromyalgia, rheumatoid arthritis, migraine headache and temporo-mandibular disorders.
- Several factors have been proposed to explain sex related differences in pain perception
 - Socio-cultural and psychological factors (greater anxiety)
 - Estrogens and other gonadal hormones regulate various neuronal functions in the CNS
 - More efficient diffuse descending noxious inhibitory controls (DNIC) in males than in females

Estrogen and μ -opioid receptor antagonists counteract the 17 β -estradiol-induced licking increase....during the formalin test in male rats

Ceccarelli I et al, Pain 2004

Locomotion



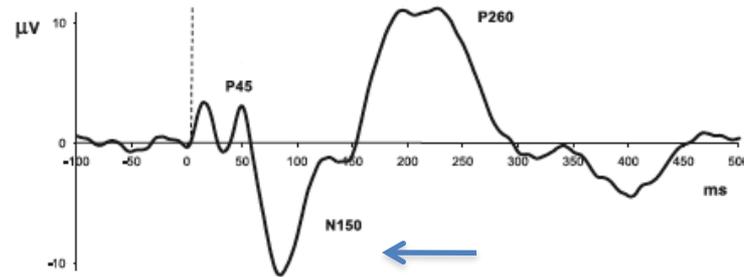
SAL: saline
FORM: formaline
ICI: estrogen inhibitor
FNA: μ opioid antagonist

Animals primed with 17 β -estradiol

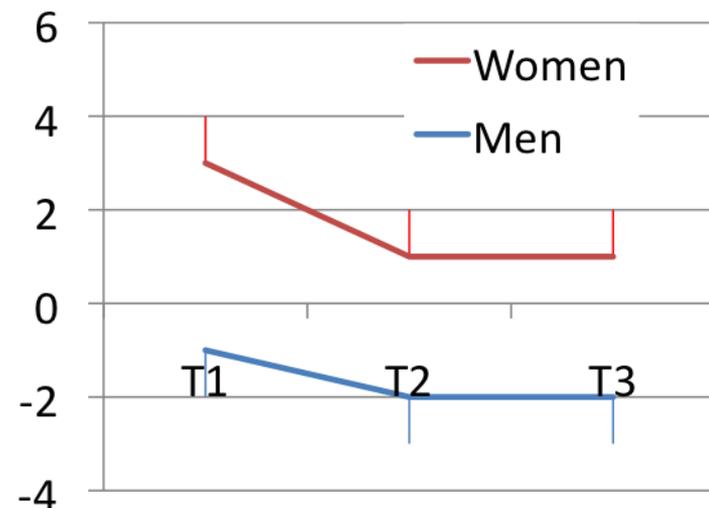
Sex differences in perceived pain are affected by an anxious brain

Goffaux P et al, Pain 2011

- Volunteers of both sexes
- No underlying pain condition
- Somatosensory evoked brain potentials after transcutaneous electrical non-painful sural stimulation
- N150 component related to anxiety



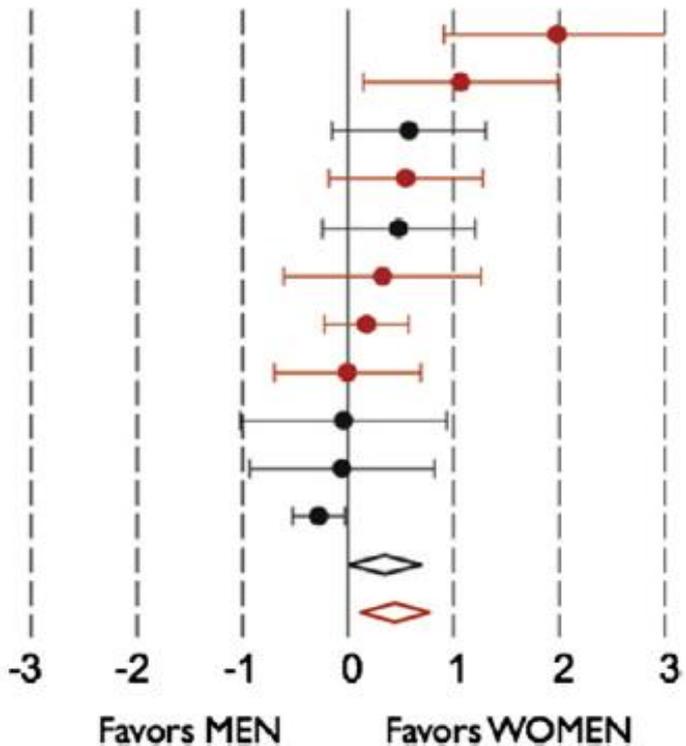
N150 amplitude



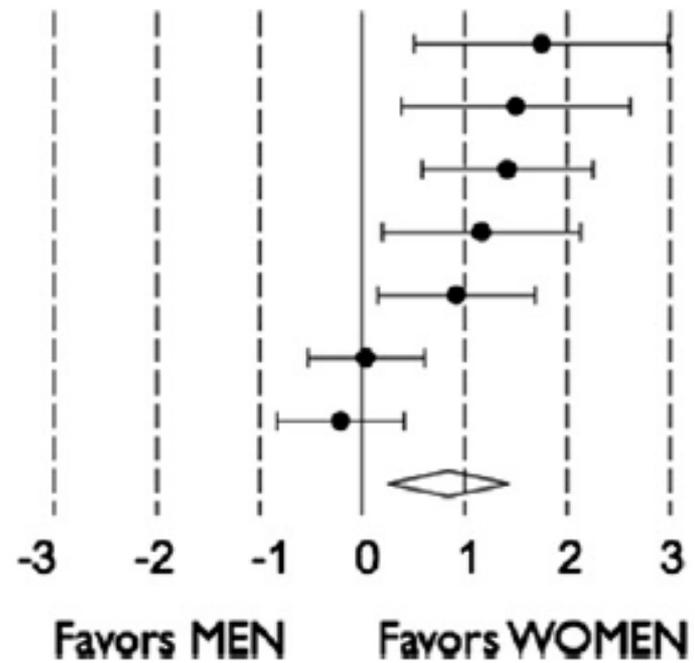
Do sex differences exist in opioid analgesia?

Niesters M et al, Pain 2010

Experimental studies with μ opioids



Clinical studies with μ opioids



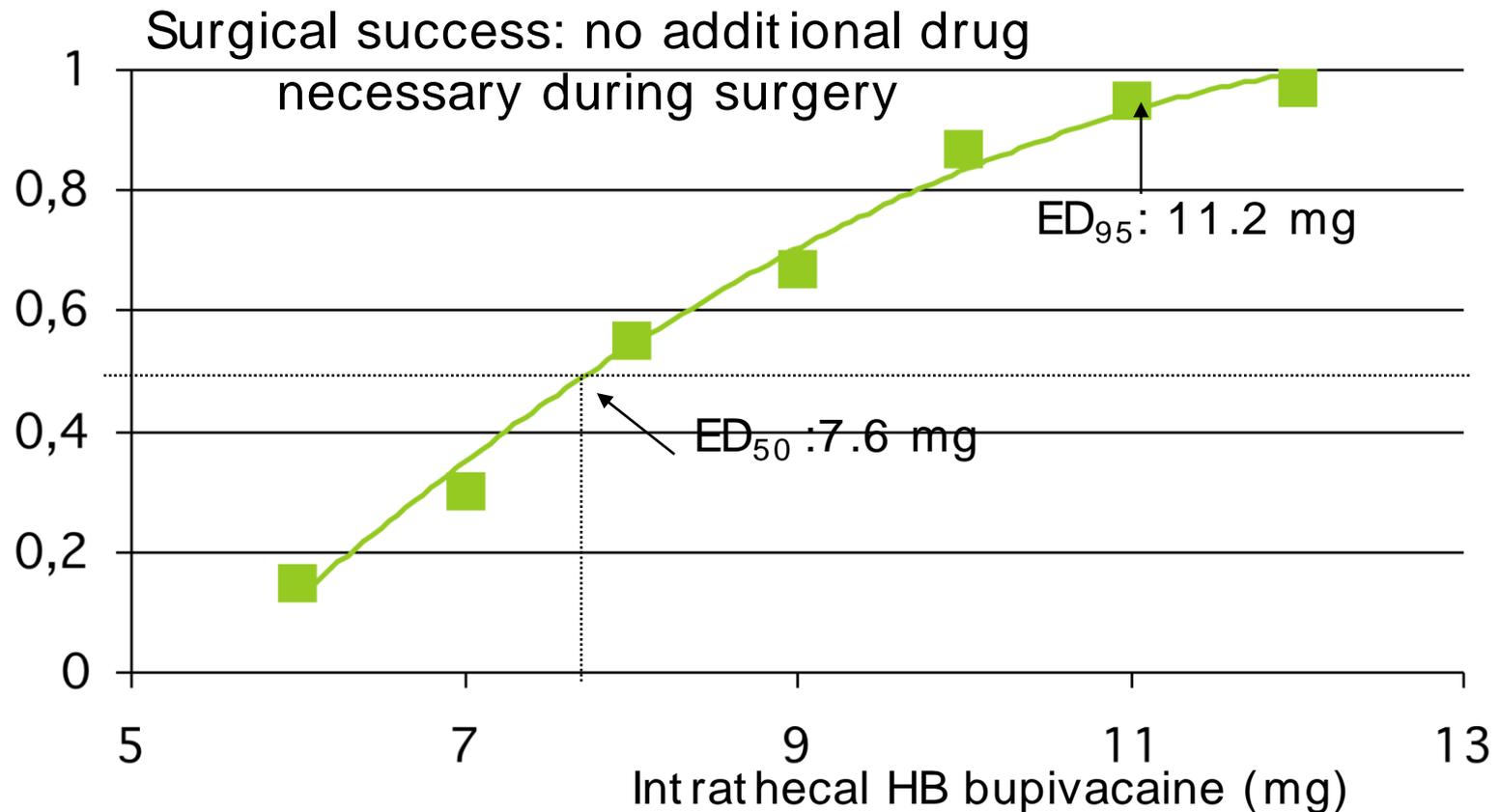
Greater morphine efficacy in women

Data on non-morphine μ and mixed μ/κ -opioids are less convincing and require further study

ED₅₀ and ED₉₅ of intrathecal hyperbaric bupivacaine coadministered with opioids for cesarean delivery

Ginosar Y et al. *Anesthesiology* 2004; 100:676–82

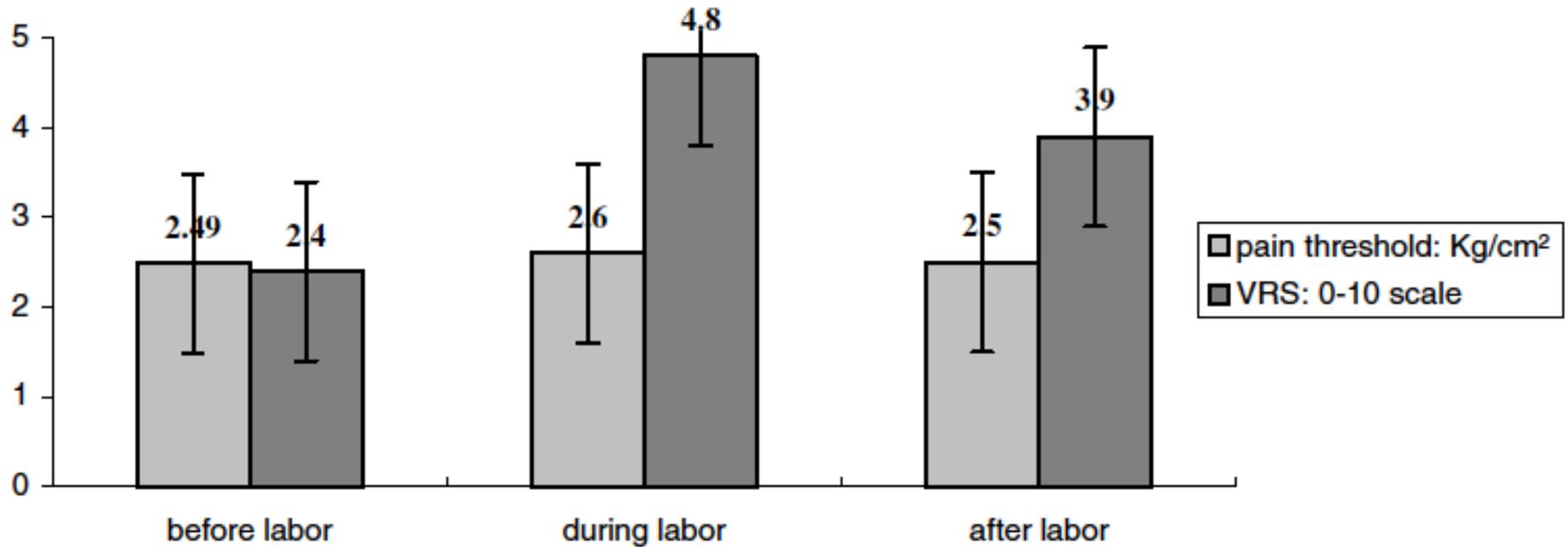
Probability of success



* fentanyl 10 µg and morphine 100 µg

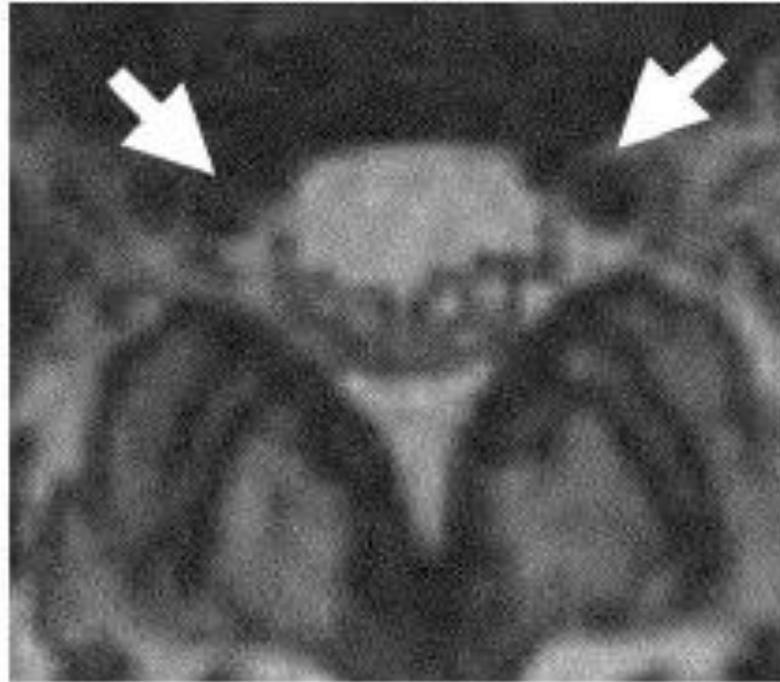
A rise in pain threshold during labor: A prospective clinical trial

Ohel I et al, Pain 2007;132:S104-S108



Compression of the Subarachnoid Space by the Engorged Epidural Venous Plexus in Pregnant Women

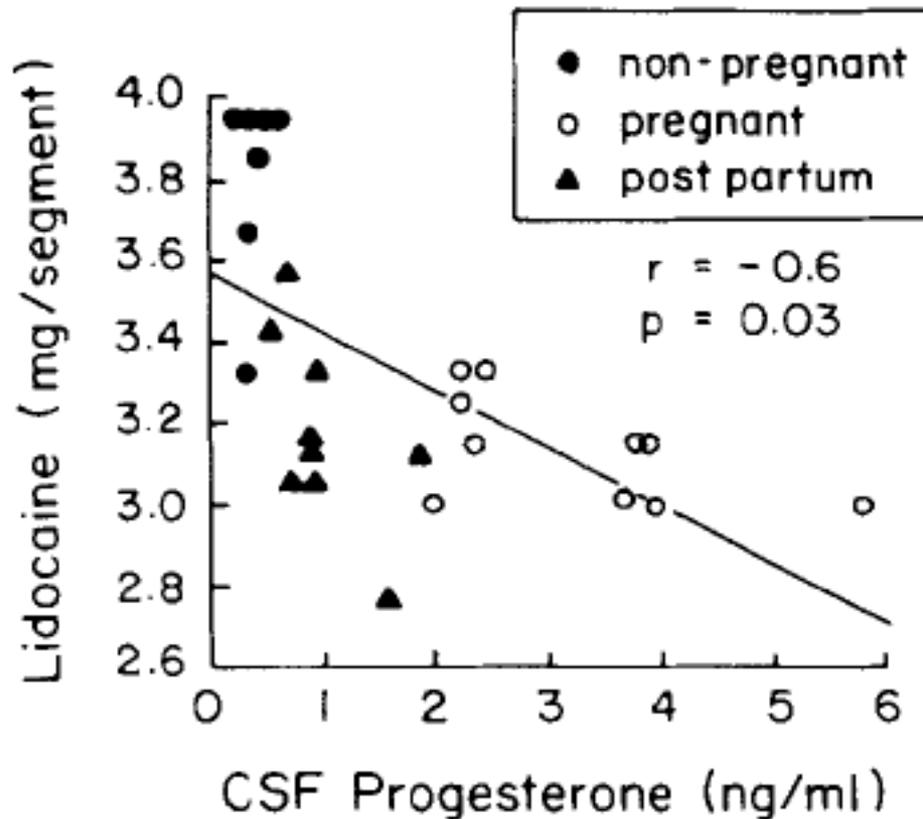
Tetsuo Takiguchi, M.D., Ph.D.,* Shigeki Yamaguchi, M.D., Ph.D.,* Masatomo Tezuka, M.D., Ph.D.,†
Naoki Furukawa, M.D., Ph.D., † Toshimitsu Kitajima, M.D., Ph.D.‡



Anesthesiology 2006; 105:848-51

Plasma and cerebrospinal fluid progesterone concentrations in pregnant and nonpregnant women

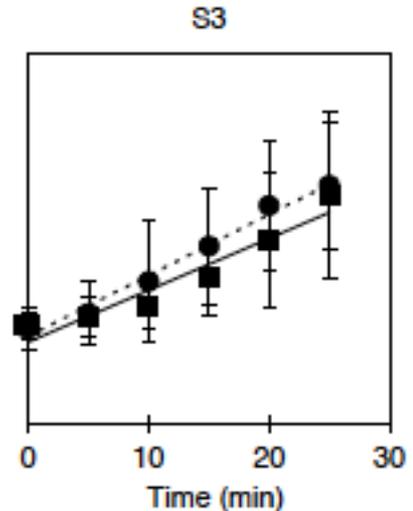
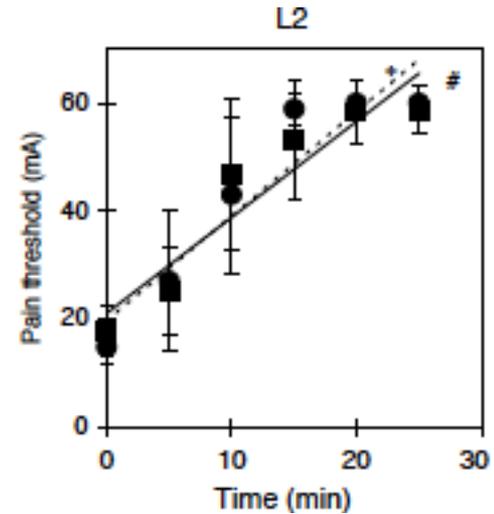
Datta S et al, Anesth Analg 1986;65:950-4



Does pregnancy increase the efficacy of lumbar epidural anesthesia?

Arakawa M. IJOA 2004;13:86-90

- 14 pregnant and non-pregnant women
- Epidural anesthesia with 17 mL of 2% lidocaine-epinephrine
- Pain threshold at L2, S1 and S3
- Spread of epidural and characteristics of the block



■ Pregnant group ● Non-pregnant group

Does pregnancy increase the efficacy of lumbar epidural anesthesia?

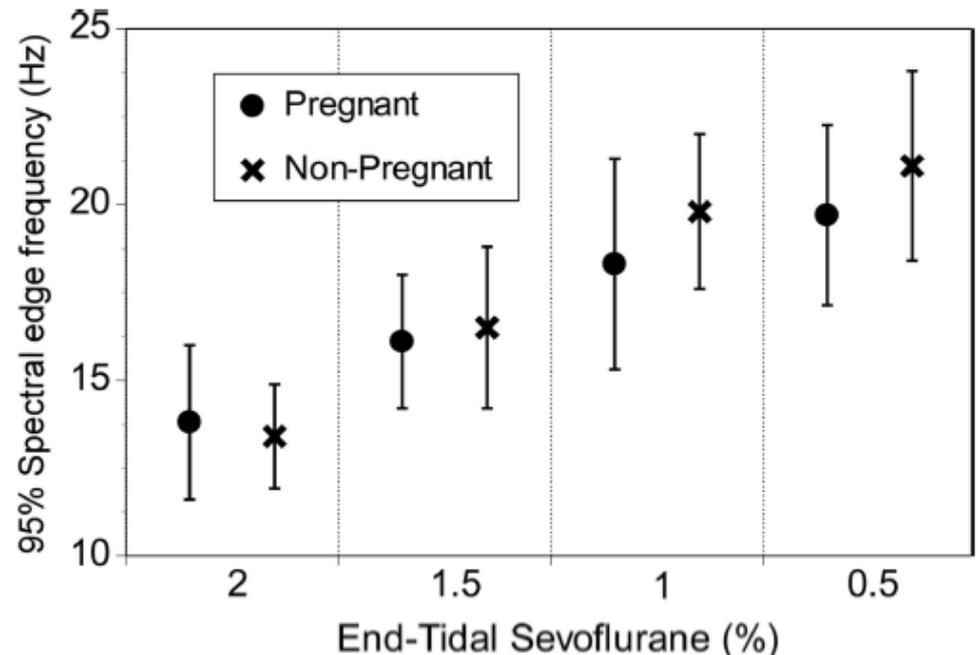
Arakawa M. IJOA 2004;13:86-90

Characteristics of the block	Pregnant	Non pregnant
Max upper sensory level	T4	T7 *
Time to L2	11	11 (NS)
Time to S3	20	18 (NS)
Bromage score (0-4) at 25 min	2	2 (NS)
Lowest blood pressure	75	78 (NS)

Pregnancy does not enhance volatile anesthetic sensitivity on the brain

Ueyama H et al, Anesthesiology 2010;113:577-84

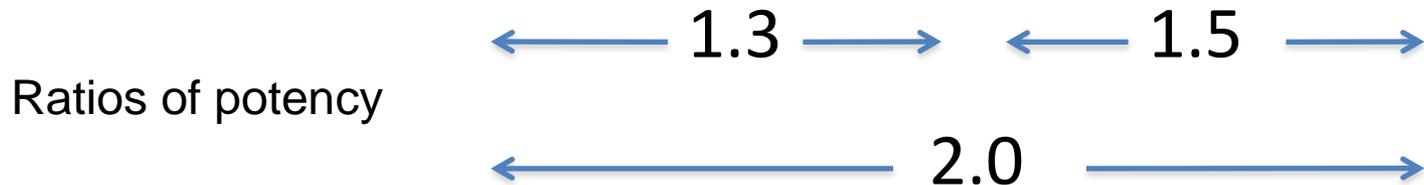
- Cesarean delivery (n =15) and elective gynecologic surgery (n = 15)
- Anesthesia induced with thiopental, fentanyl, suxamethonium
- Steady-state end tidal sevoflurane concentration at 1, 1.5 and 2 %



Effects of gender and pregnancy on potency of intrathecal bupivacaine assessed as ED50 motor block

Camorcia M et al. Eur J Anaesthesiol 2010

n = 30 x 3	Male	Female	Pregnant
ED50 motor block (mg)	6.9	5.2	3.4



Straight Leg Raise Test: 0 (no block) – 4 (complete block)

Effective motor block: score > 0

Conclusion

- The effect of gender on pain perception is well demonstrated and women report more intense and more frequent pain than men
- The effect of morphine (μ opioids) is more pronounced in women
- Pregnancy is associated with an increased « resistance » to pain, even more during labor
- Hormonal mechanisms represent the most likely mechanism although anatomic changes are probably involved
- Local anesthetic-induced sensory effects:
 - overall more marked in pregnant women than in non-pregnant women but data are conflicting
 - No data regarding comparison between non-pregnant women and men
- Local anesthetic-induced motor block effects:
 - more marked in pregnant than in non-pregnant women
 - More marked in women than in men