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Dietary Analgesia: An Overview

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Disclosure statement information


The speaker has no financial interest, investment or research collaboration of any kind in a company whose interests are in the area to be discussed in this talk. No support of any kind was given by such company to the speaker

Diet as an analgesic modality

- Evidence from experimental animals
- Human data
- Future targets

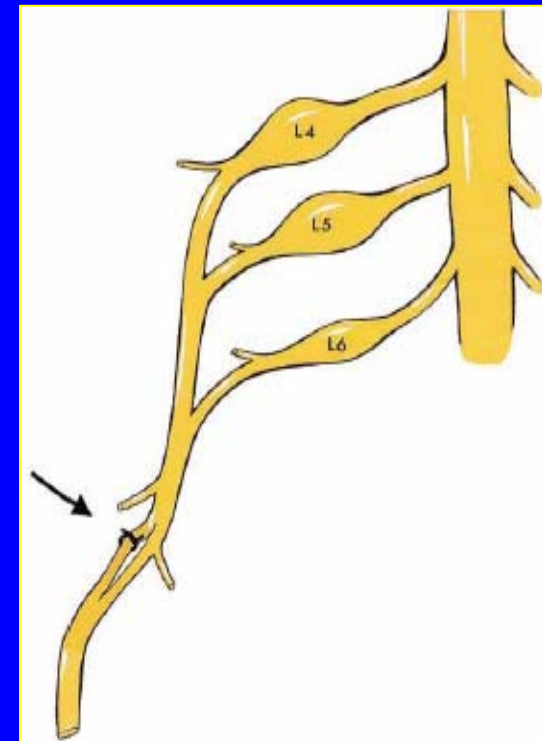
Dietary anti-nociception in rodents



An aerial photograph of a large university campus. The campus features several large, multi-story buildings with varying architectural styles, including some with prominent columns. There are numerous parking lots filled with cars, and roads winding through the campus. The surrounding area includes residential housing and green spaces. A blue text box is overlaid on the right side of the image.

Why have I started testing diets in pain models?

The Partial Sciatic nerve Ligation model (PSL)



The PSL model

- Chronic “**CRPS Type II**” like syndrome:
 - Tactile allodynia
 - Mechanical & heat hyperalgesia
 - Spread to the contra-lateral limb
 - Sympathetically dependent

This is the reason!



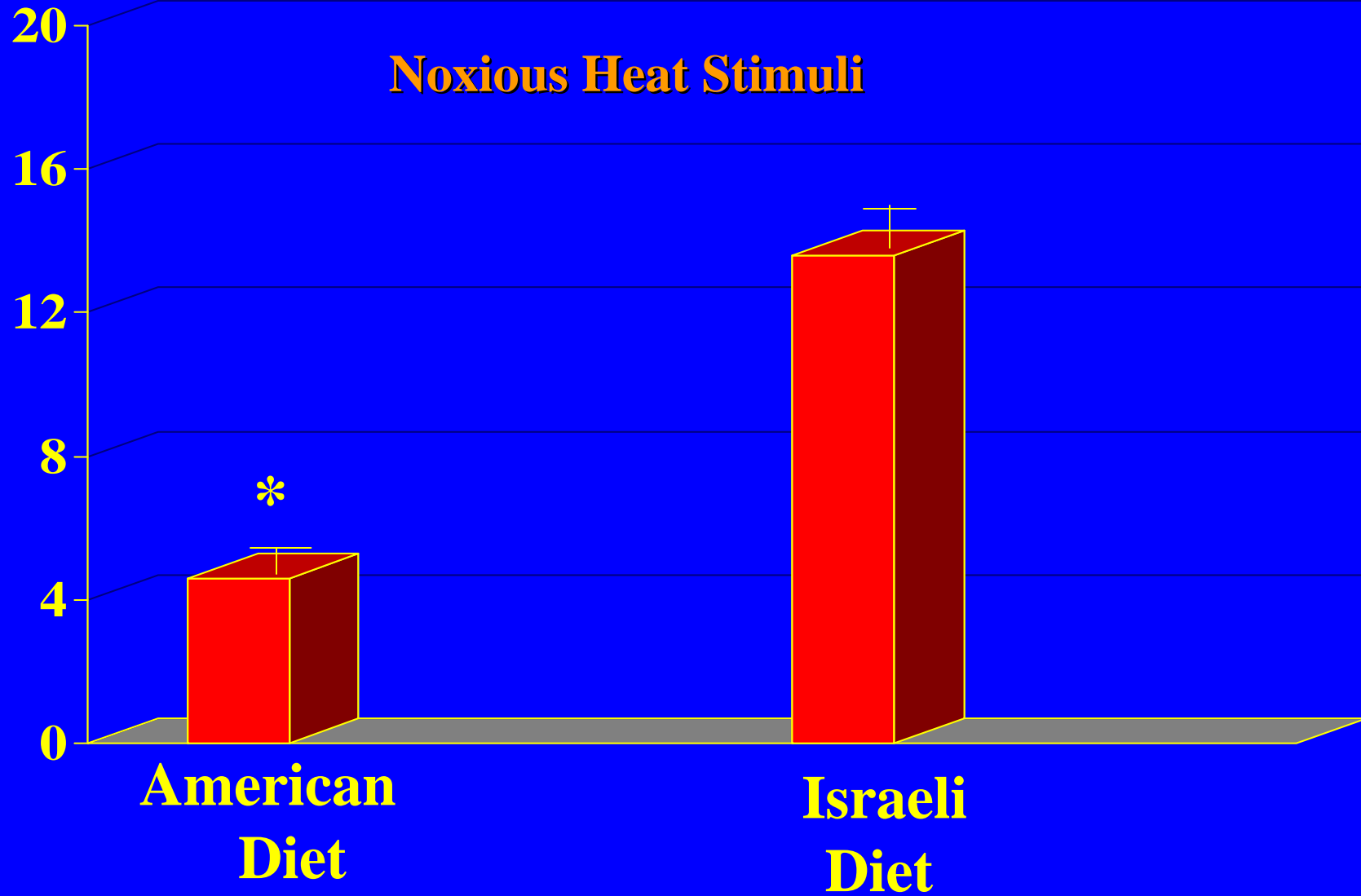
PSL pain suppression in different environment

- Modification of 12 environmental and technical variables has not revealed the source of anti-nociception
- Finally, feeding rats with “Israeli” diet reversed pain suppression¹

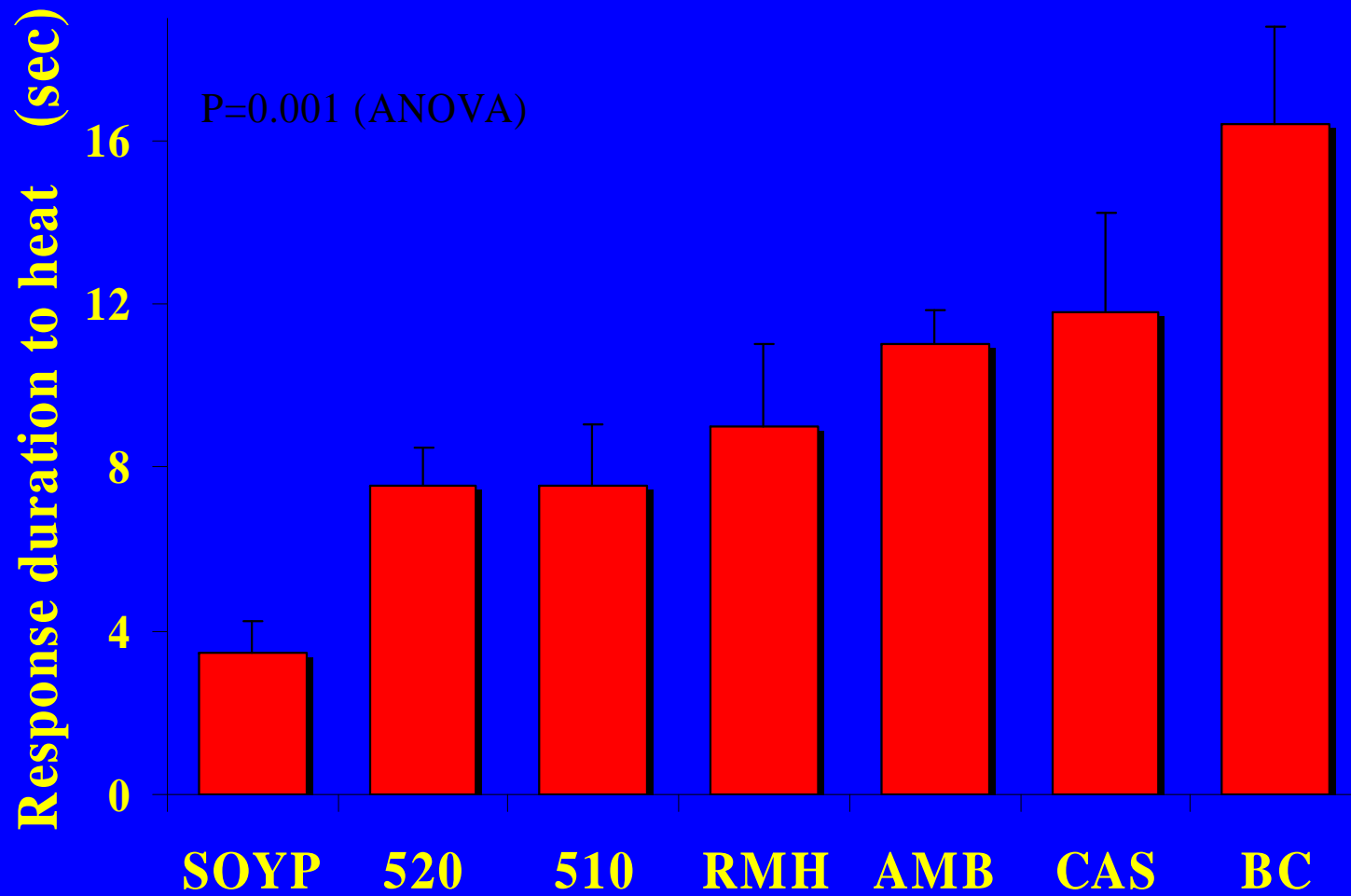
¹Shir Y, et al, Neurosci Lett 1998

Dietary origin vs. chronic pain

Response duration to heat (sec)



Dietary type *vs.* nociception following PSL



Carbohydrates *vs.* anti-nociception

- Sweet analgesia in pups & adult rats¹
- Effective through modulation of the endogenous opioid system²

¹Ren K, et al., Proc Natl Acad Sci USA 1997; ²Kanarek RB, et al., Brain Res 2001

Traditional and herbal remedies

- Ginseng root for tonic pain¹
- Tart cherry for inflammatory pain²
- Soy phytoestrogens in PSL³
- Vitamin B complex for neuropathic pain⁴

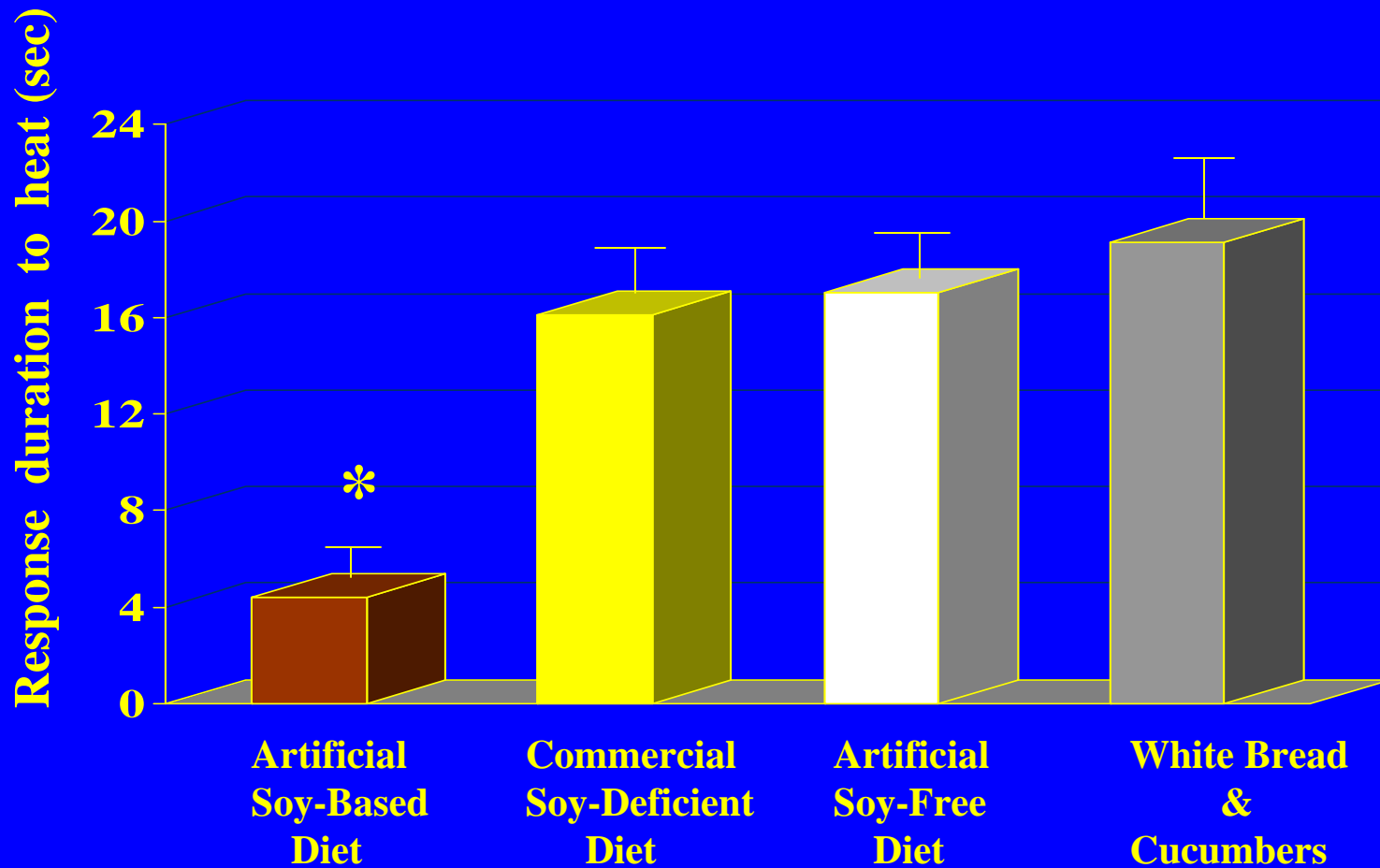
¹Mogil J, et al., Brain Res 1998; ²Tall et al., Behav Brain Res 2004; ³Shir Y, et al., Anesth Analg 2002; ⁴Wang ZB, et al, Pain 2005;

Amino acids & protein *vs.* anti-nociception

- Taurine-rich diets decreased nociception in a rat model of phantom pain¹
- Soy protein decreased nociception in the PSL model²

¹Belfer I, et al., Neuroreport 1998; ²Shir Y, et al., Anesth Analg 2001

PSL model: hyper-nociception with soy –deficient diets



Soy protein hypo-nociception

- Not associated with experimental site, testing methods, rat strain, vivarium, food vendor, caloric intake & weight gain
- Dietary soy hypo-nociception is mainly apparent when supplemented preemptively but not after nerve injury¹

¹Shir Y, et al, Anesthesiology 2001

Fatty acids *vs.* anti-nociception

- Changes in dietary fat content increase heat pain threshold in intact rats¹
- Dietary soy & corn oils are anti-nociceptive in models of chronic neuropathic pain^{2,3}

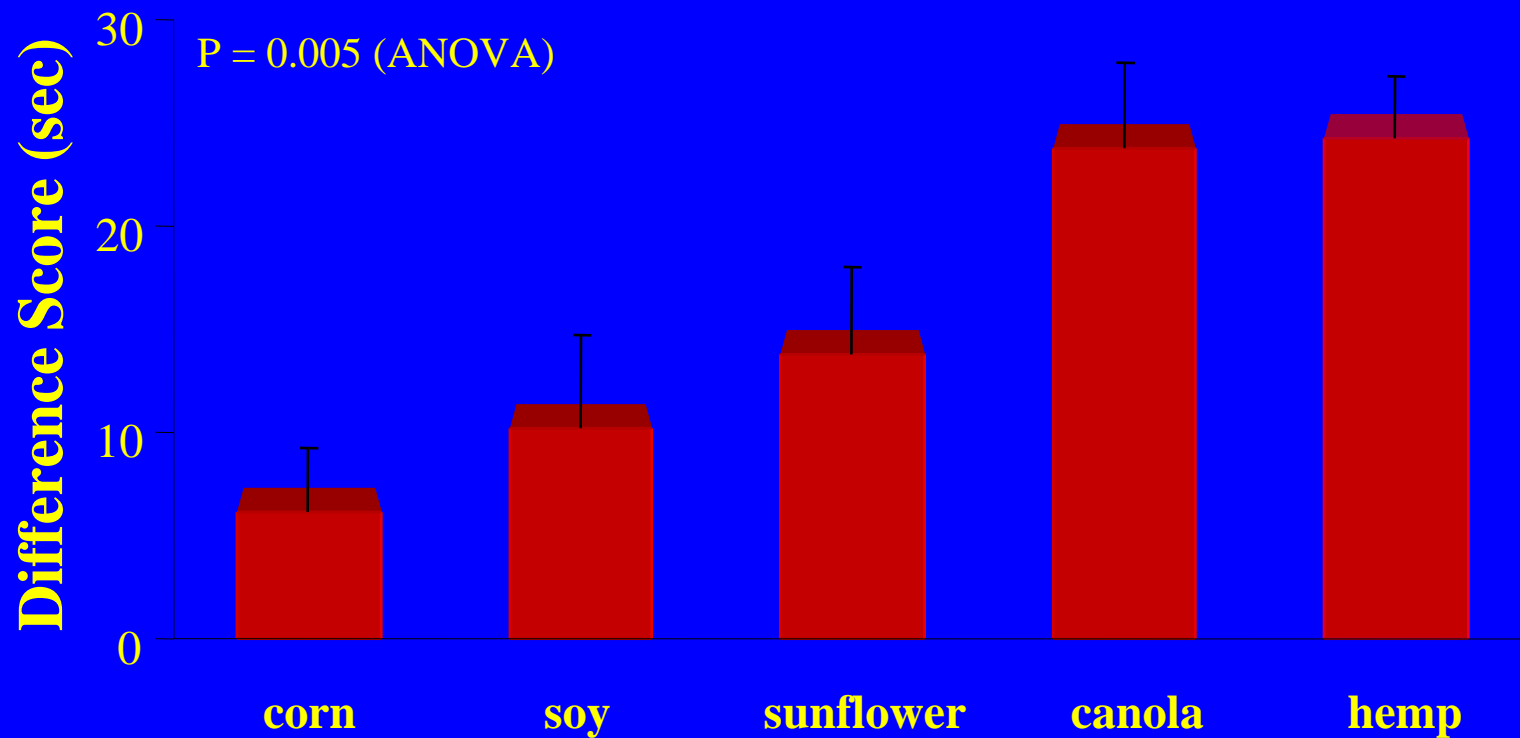
¹Yehuda S, et al., Intern J Neurosci 1987; ²Perez J, et al., Pain 2004; ³Perez J, et al., Anesth Analg 2005

Fatty acids analgesia: possible mechanism

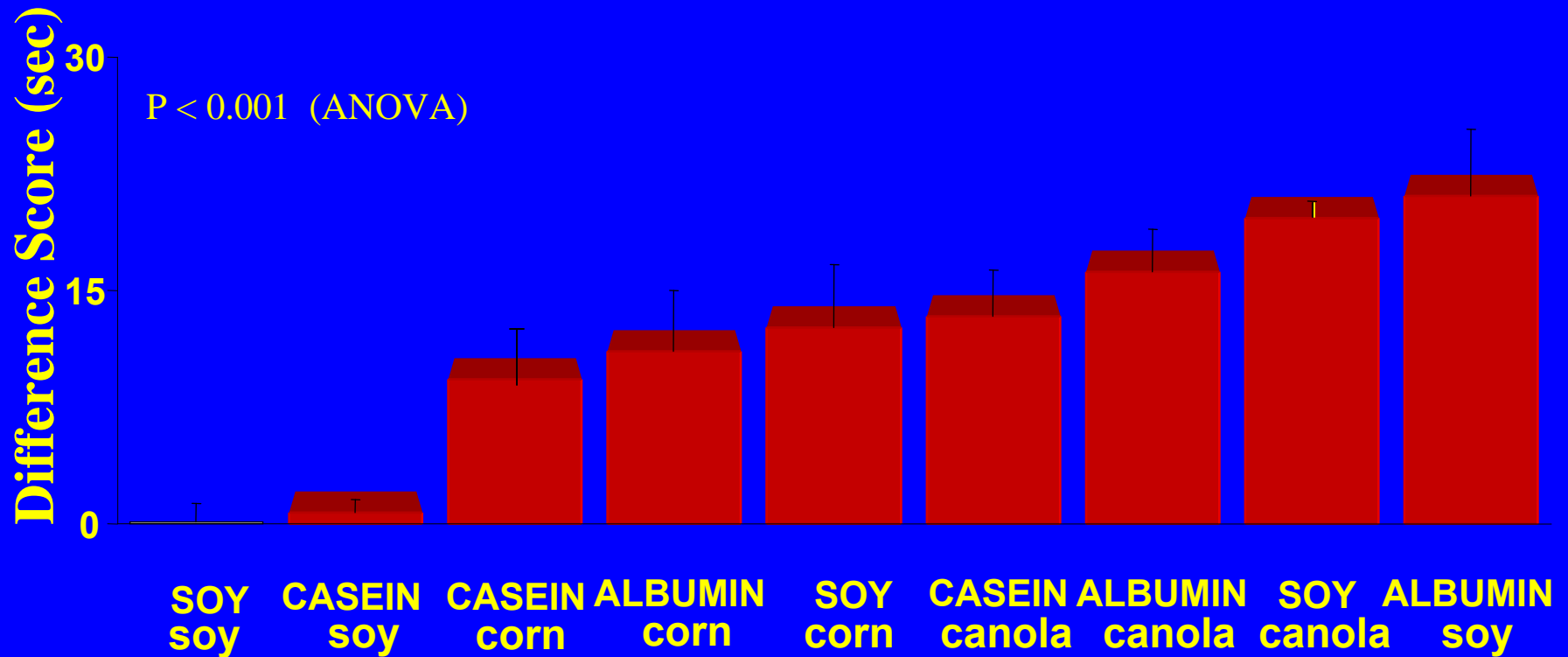
- Limit or regulate immune reactions¹
- Suppress inflammatory response²
- Crucial components of neuronal membranes³
- Modulation of Na⁺ & calcium⁺⁺ channels⁴

¹Harbige LS, Lipids 2003; ²Calder BC, et al., Br J Nutr 2002; ³Holmes PR, et al., Ann N Y Acad Sci 1983; ⁴Hong MP, et al., Brain Res 2004

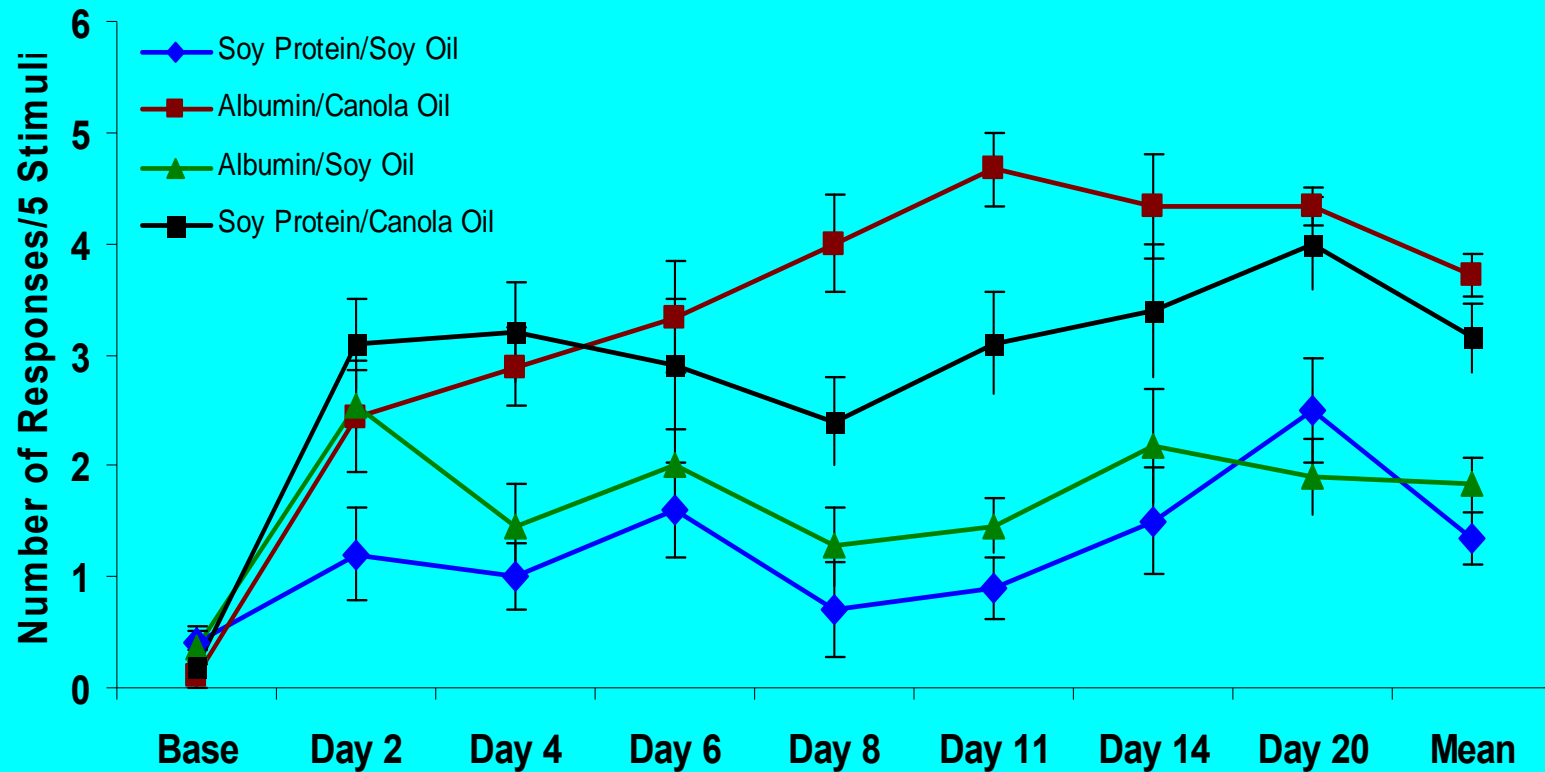
PSL-induced nociception vs. dietary fat



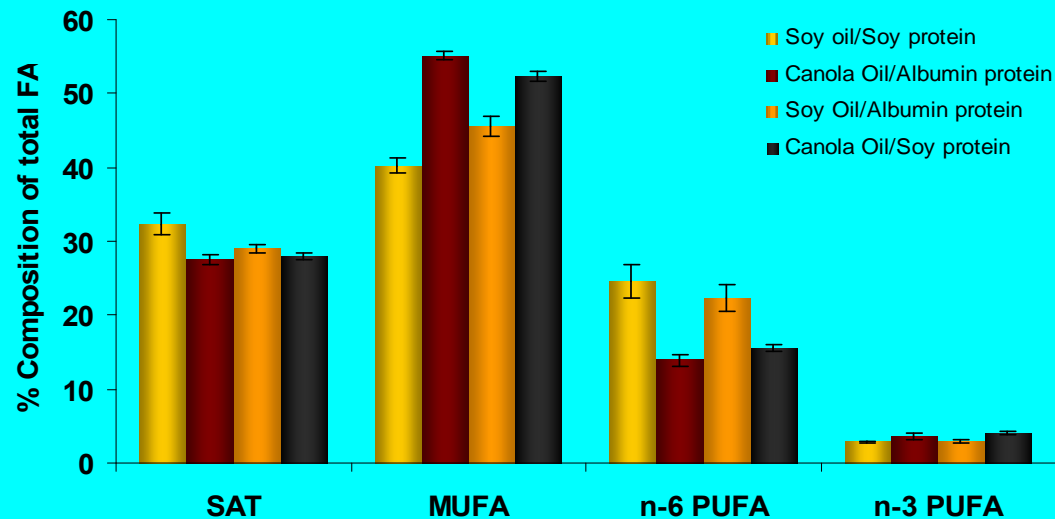
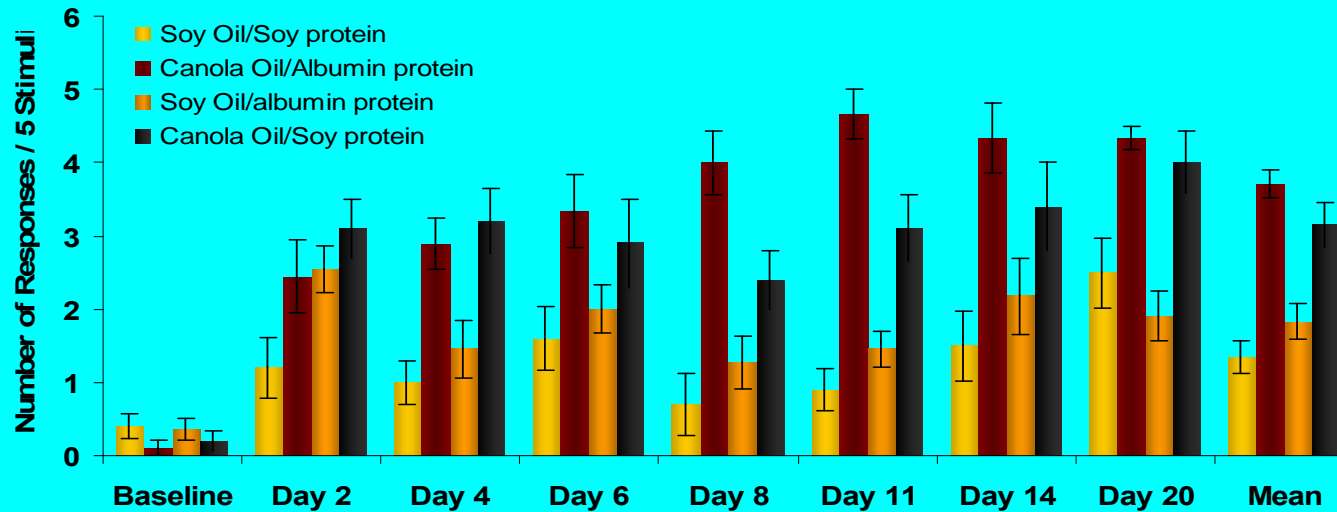
The combined effect of dietary fat and protein



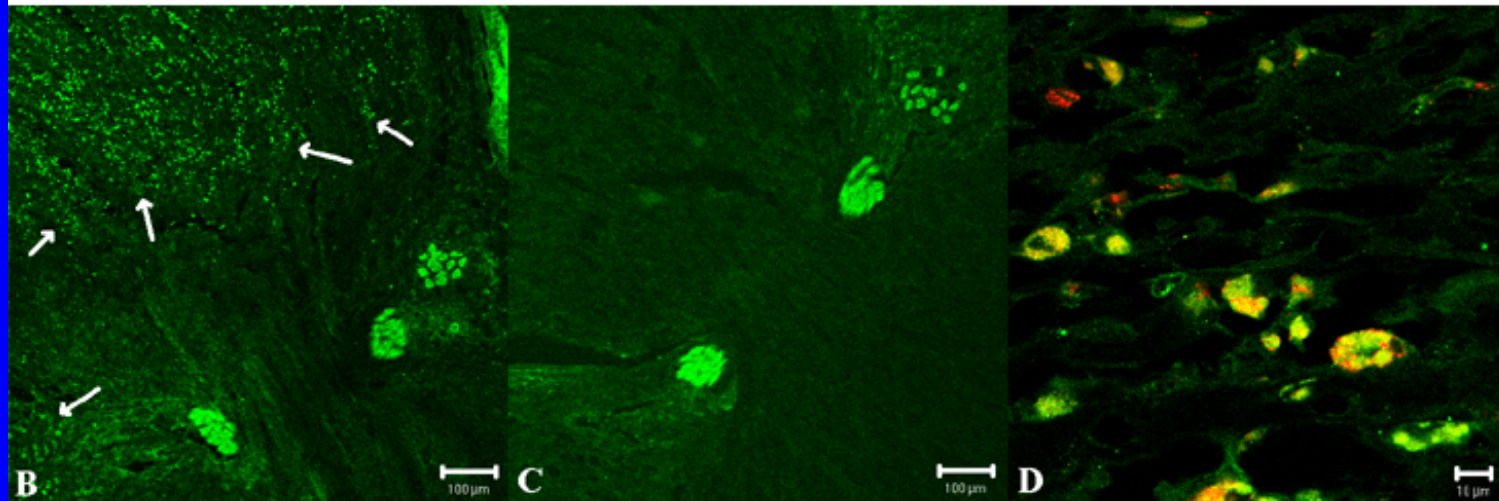
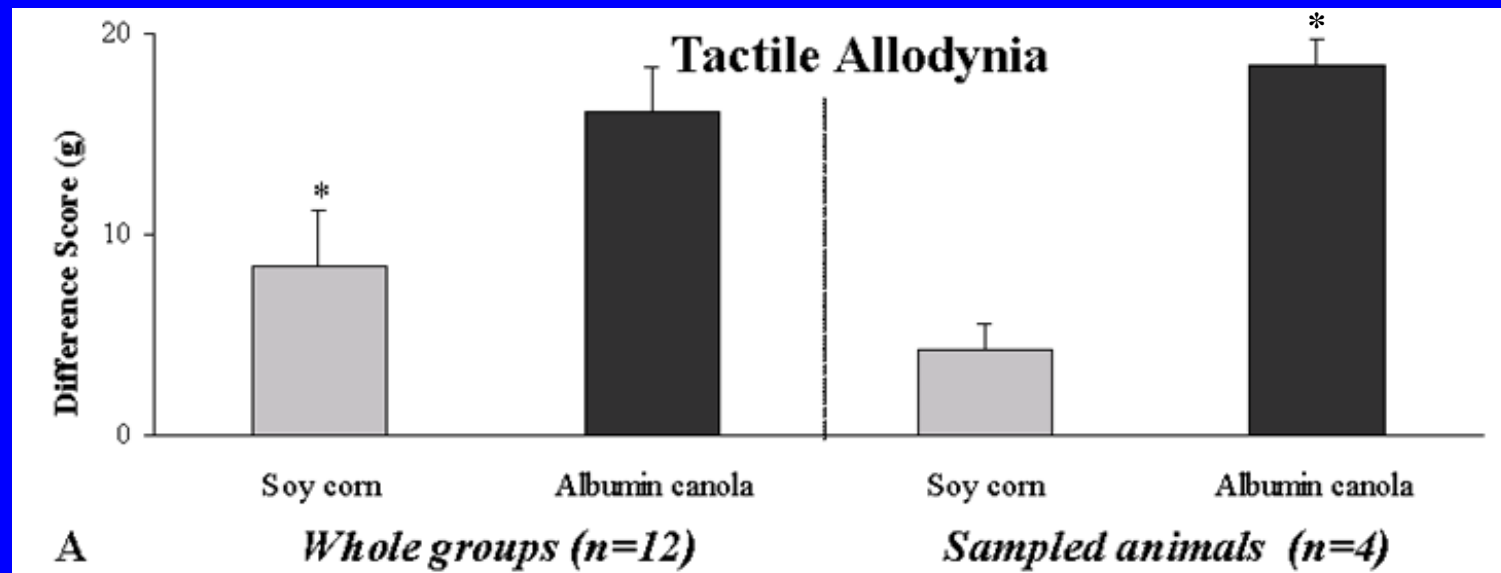
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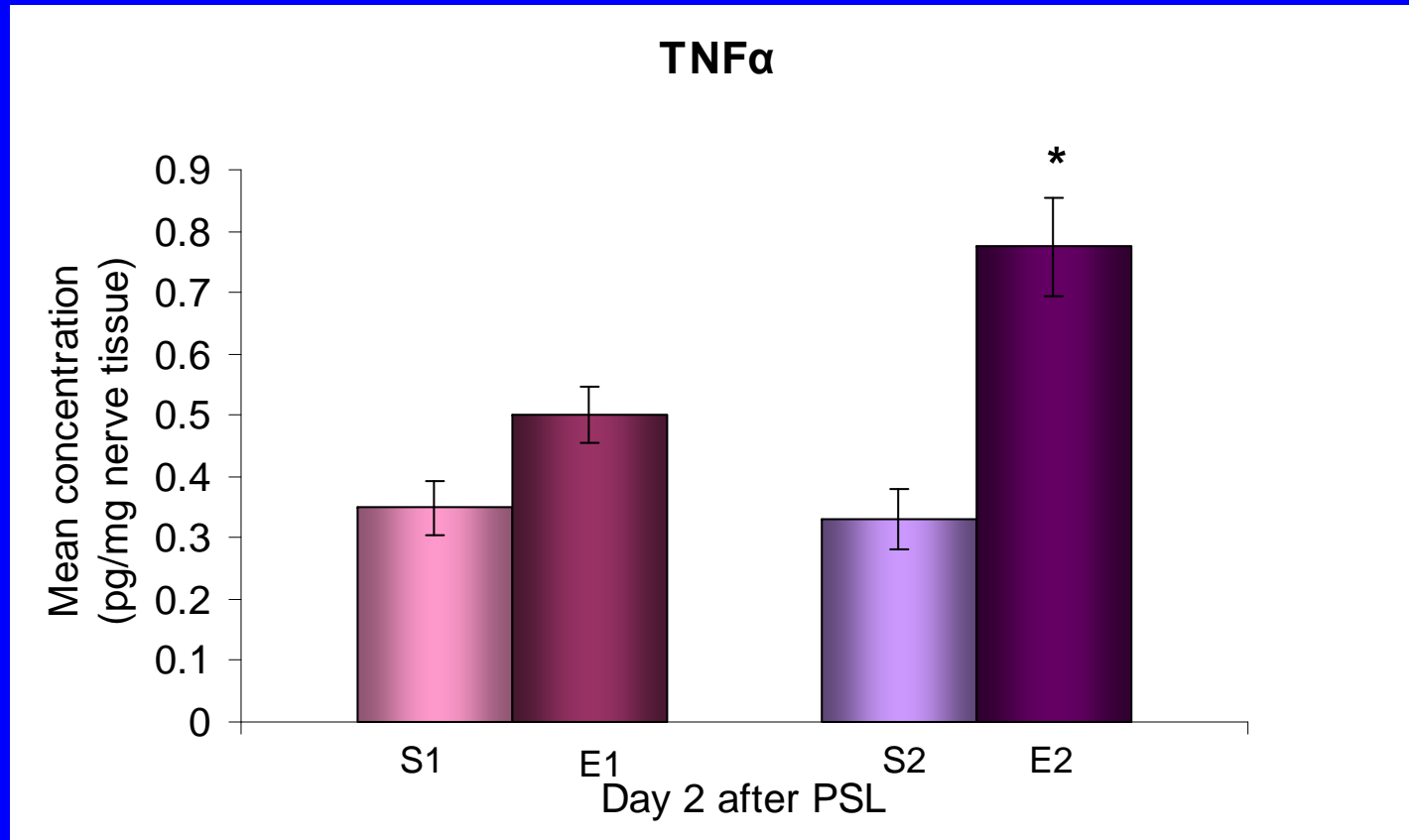
Dietary anti- nociception vs. neural fatty acid concentrations



Diet vs. TNF- α expression in injured nerve



Diet vs. TNF- α expression in injured nerves



1-Hypo-nociceptive diet (soy protein/soy oil); **2**-hyper-nociceptive diet (albumin protein/canola oil); **S**-sham surgery; **E**-PSL injured sciatic nerve; * $p < 0.05$ E2 vs. E1

Summary: Diet vs. nociception in rodents

- Rodents' diet is anti-nociceptive in acute and persistent pain models
- Rodents' diet could predict levels of nociception
- Existing data justify more trials in humans

Diet used for rodents' experiments should be standardized and reported

- Diet type & vendor should be added to the routine:
“rats were housed...soft bedding...free access to food and water...12 h day/12 h night cycle”

Diet *vs.* nociception in humans



Time Magazine, 2006

Diet *vs.* experimental pain in humans

- Pain levels decreased with:
 - High fat/low carbohydrates diet¹
 - Sweet taste²

¹Zmarzty SA, et al., *Physiol Behav* 1997; ²Lewkowski MD, et al., *Pain* 2003

Clinical dietary analgesia in humans

- Oral sucrose decreased procedural pain in infants¹
- Omega-3 PUFA decreased recurrent migraines² & inflammatory pain³
- Tryptophan was beneficial for neuropathic pain⁴
- Vitamin C prevented CRPS after wrist fractures⁵
- Higher fiber intake was associated with lower levels of menstrual pain⁶

¹Akman I, et al., J Pain 2002; ²Harel Z, et al., J Adolesc Health 2002; ³Cleland LG, et al., Drugs 2003; ⁴King RB, J Neurosurg 1980; ⁵Zollinger PE, et al, J Bone Joint Surg Am 2007; ⁶Nagata C, et al, Eur J Clin Nutr 2005

Soy analgesia in humans

- Soy protein mildly decreased cyclical breast pain in healthy women¹
- Soy decreased pain associated with osteoarthritis²
- Soy-enriched diet could decrease chronic post-traumatic neuropathic pain³

¹McFadyen IJ, et al, Breast 2000; ²Arjmandi BH, et al, Phytomedicine 2004;

³Shir Y, et al, Ann Meeting CPS, Halifax 2005 (abstract)

Future targets

- Isolating the specific analgesic ingredient in diet is not practical:
 - Soy protein alone contains hundreds of possible targets (e.g., phytoestrogens, phytates, saponins, phenolic acids)
- We should move early from the lab to the clinical setting
- We should concentrate on available, easy to test ingredients

Clinical study:

Can preoperative consumption of soy protein prevent chronic post-mastectomy pain?

- ~50% of women with breast cancer develop post mastectomy pain
- we plan to test preemptive soy supplementation in these women, based on our results in PSL rats



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