Nutrition and Chronic Pain

Neda Dolatkhah MD.Ph.D
Assistant Professor
Physical Medicine and Rehabilitation Departments
Tabriz University of Medical Sciences

- **2003 WHO report**
  - Global change in diet resulting from industrialization, urbanization, and market globalization
  - Nutrition as a "major modifiable determinant of chronic disease."
- **CNS has specific nutritional requirements**
  - Essential fatty acids
  - Tryptophan
- **Micronutrients**
  - Vitamin B12 deficiency
  - Folate deficiency
  - Vitamin D deficiency
  - Scurvy
  - Other contributing factors

Nutritional strategies

- Optimizing the diet to ensure adequate intake of vitamins and essential amino acids
- Increasing intake of foodstuffs that reduce pain
- Restricting foodstuffs that may facilitate pain or reduce the effectiveness of oral analgesics

Obesity and chronic pain

- Growing evidence suggests that there is a precise relationship between obesity and chronic pain; they coexist and adversely impact each other (reciprocal negative effects).
- Obesity and pain serve to further reduce functional capacity and QoL, causing patients to become less physically active and more depressed, with consequences for sleep, stress, lifestyle, and chronic inflammation status.
- Accordingly, a reduction from high to normal BMI may improve QoL.

- The effect of obesity in chronic pain conditions has been studied in fibromyalgia, osteoarthritis, rheumatoid arthritis, and low back pain.
- Thus, the management of obesity as well as chronic pain should be considered synergistic.
- Adipose tissue is not only an energy store but also an active endocrine organ involved, among other functions, in the regulation of inflammation.
- Obese individuals suffer more chronic pain than normal weight subjects; therefore, changes in lifestyle can help improve both obesity and chronic pain conditions.

DIET AND INFLAMMATION

- "Western" dietary pattern
  - refined grains
  - high-fat foods,
  - processed meats, and sweetened
  - beverages/desserts
- Mediterranean diet
  - unrefined carbohydrates
  - nuts
  - fish
  - olive oil

Getting the right balance: the omega-3/omega-6 ratio

- Considerable change in the quantity and quality of fat consumed
- Considerably higher ratio of omega-6/omega-3 in food globally – so that the presumed "ideal" ratio of 1:1 is now 10-15:1
- The dietary omega-3/omega-6 ratio may have significance for inflammatory pain.

- The recommended intake of long-chain omega-3 PUFAs is 500 mg per day, but the actual intake in Western countries is much lower

- Omega-3 supplementation
  - Decrease overall production of PGE2 and LtB4, and increase production of PGI3 and LtB5

- reduces
  - patient-reported joint-pain intensity,
  - minutes of morning stiffness,
  - number of painful joints, and
  - NSAIDs consumption in patients

SATURATED FATS

- Saturated fats are known to have poor health outcomes associated with their intake, such as an increase in inflammatory cytokine gene expression.
- Dietary intake of SFAs has a direct stimulatory effect on the immune system via TLR4 that leads to induction of proinflammatory cytokines.
- This activation can prime the immune system in the event of future challenge and lead to hyperactive responses to damage or invasion potentially leading to chronic pain or hypersensitivity.
- This is a serious consideration for those consuming large quantities of SFAs in their diet.

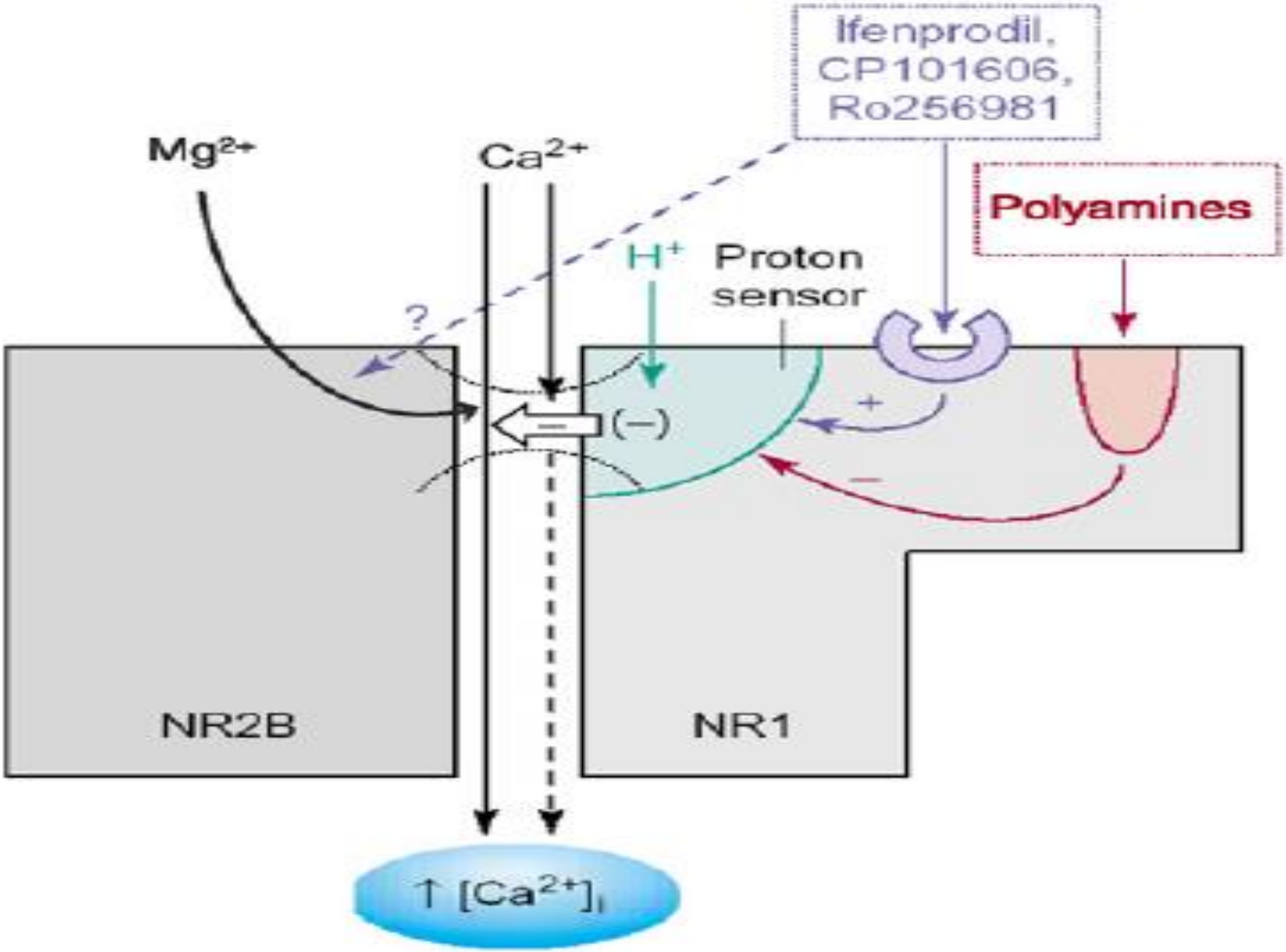
The N-methyl-D-aspartate receptor: dietary polyamines and magnesium

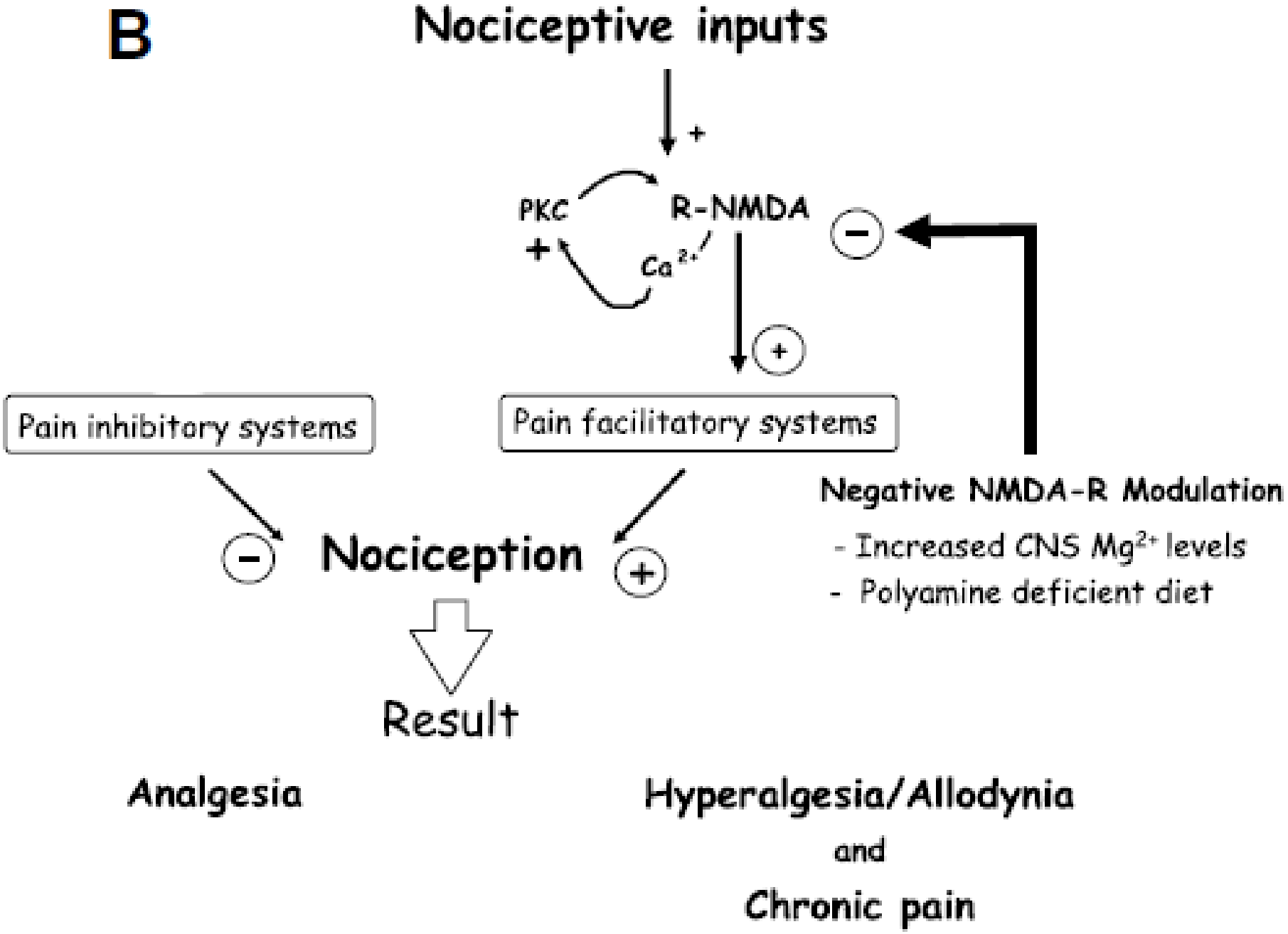
- Numerous studies indicate that overactivation of excitatory glutamate/N-methyl-D-aspartate receptor (NMDA-R) systems, particularly the NR2B subtype, plays a critical role in the activit-dependent central sensitization process
- The use of NMDA-R antagonists is limited due to unacceptable adverse effects
- To avoid the deleterious effects associated with NMDA-R antagonist use, One way of doing this is to reduce dietary polyamine intake.

- Polyamines (spermine, spermidine, and putrescine) are organic polycations at physiological pH, which positively modulate NMDAR function by shielding the NR1-located H+-sensor from protons, thus attenuating the inhibition of the NR1-NR2B channel functioning by protons.

- By positively modulating the NR1 polyamine sites, polyamines facilitate pain sensitization.

- Since polyamines mainly originate from dietary intake and gut bacterial metabolism , a polyamine-deficient diet (PD diet) could be a nutritional strategy to counteract the deleterious effect of upregulated NMDA activity and subsequent pain sensitization.


Ifenprodil,
CP101606,
Ro256981
Mg2+
Ca2+
Polyamines
H+
Proton
sensor
?
(–)
+
–
NR2B
NR1
↑ [Ca2+]i


B
Nociceptive inputs
+
PKC
+
R-NMDA
Ca 2+
−
+
Pain inhibitory systems
Pain facilitatory systems
Negative NMDA-R Modulation
- Increased CNS Mg2+ levels
- Polyamine deficient diet
−
Nociception
+
Result
Analgesia
Hyperalgesia/Allodynia
and
Chronic pain

- Polyamine and Mg2+ interactions at the N-methyl-D-aspartate (NMDA) receptor level leading to hyperalgesia

- Pain sensation level results from an equilibrium between inhibitory and facilitatory pain systems.
-
- Polyamines and Mg2+ act, respectively, as positive and negative modulators in pain facilitatory systems.

- Decreasing intake of polyamines and maintaining adequate Mg2+ levels at the NMDA receptor level act to oppose overactivation of NMDA receptors leading to hyperalgesia.

Top 12 food sources of polyamines (mg/portion) in the Dietist XP

Polyamine/food item	Portions in grams	Polyamines mg/portion
Putrescine		
Grapefruit juice, fresh	200	19.6
Orange juice	200	17.0
Sauerkraut	80	14.6
Orange	110	14.0
Crab, conserved	75	9.2
Maize	100	5.1
Peas, green	100	4.6
Pear	100	3.0
Soybean, cooked	190	1.70
Potato, cooked	150	1.68
Paprika, green	30	1.64
Soy sauce	18	1.60

Food Nutr Res

Spermidine		
Soybean, cooked	190	9.7
Peas, green	140	9.1
Pear	125	6.6
Lentil soup	250	5.5
Mushroom	50	4.4
Red beans	190	3.7
Broccoli	100	3.6
Cauliflower	100	3.0
Chicken, steak	125	2.2
Popcorn	50	2.1
Cheese	20	2.0
Potato, cooked	150	1.8

Spermine		
Liver (cow)	125	19.7
Green peas	140	7.3
Pork, ham	125	6.3
Chicken	125	5.6
Soybean, cooked	190	4.0
Beef steak	125	3.9
Pork	125	3.8
Pear	125	3.5
Cheeses	100	3.0
Tuna fish	125	2.7
Chicken breast	125	2.3
Lentil soup	250	1.85

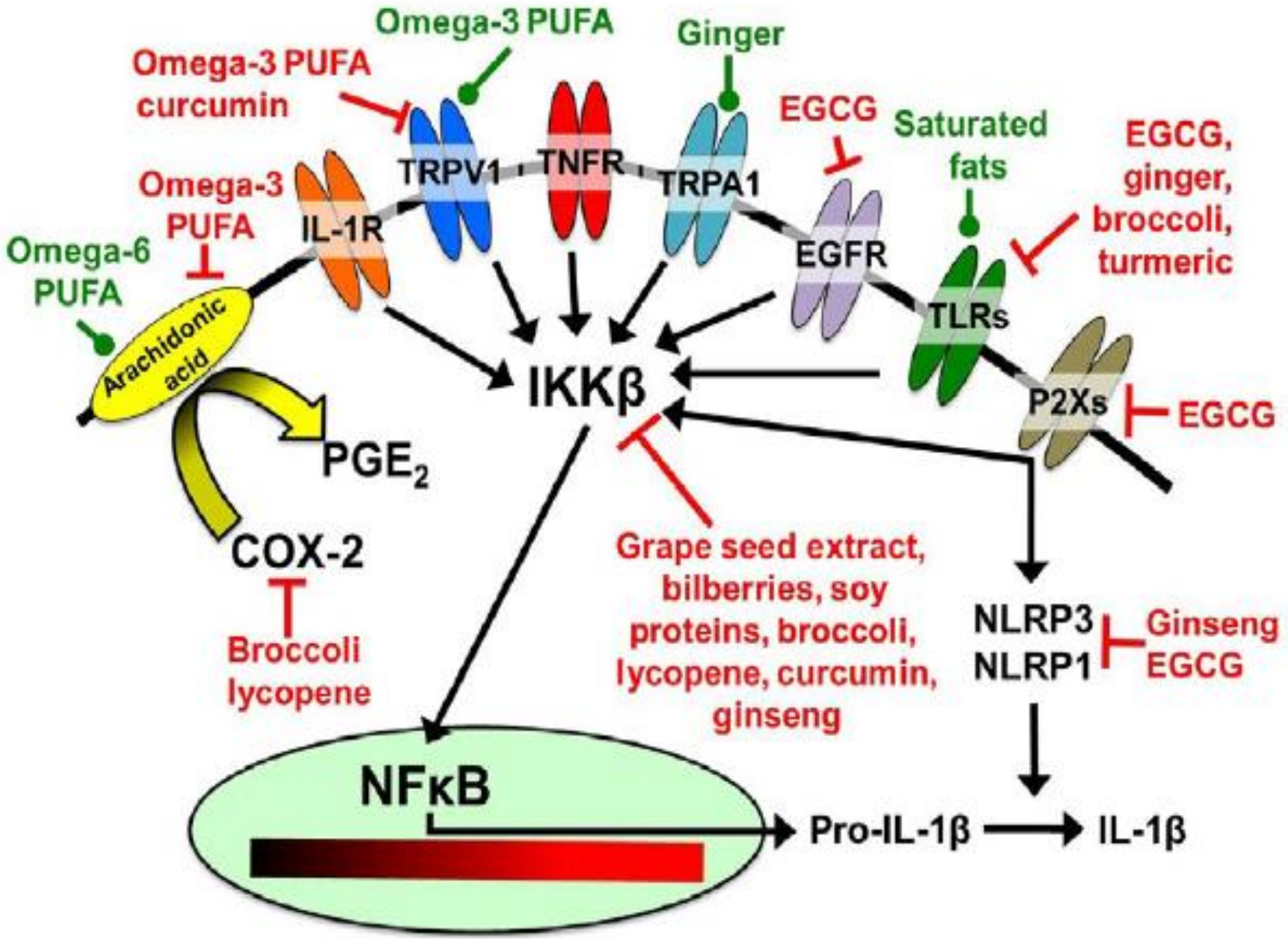
Antihyperalgesic effects of dietary constituents

- GRAPE SEED EXTRACT
  - High in anthocyanidins have a clear anti-inflammatory effect likely through inhibition of NFκB.
- GREEN TEA EXTRACT
  - potent anti-inflammatory effects of EGCG on immune cell receptors and pathways
- SOY PRODUCTS
  - soy-based diets have anti-inflammatory effects through activation of PPAR-γ and subsequent suppression of proinflammatory cytokine genes

- BROCCOLI
  - It is likely that cruciferous vegetables with high levels of sulforaphane, broccoli in particular, could reduce inflammation and subsequent pain if incorporated into the diet in sufficient amounts.
- CAROTENOIDS
  - Reduce a number of proinflammatory pathways
  - These foods are generally a large part of any dietary intervention (i.e., Mediterranean diet) and, at realistic consumable levels, should have a direct impact on pain transmission.

- GINGER
  - Recent researches support the long-held belief that ginger is a potent analgesic with clear antiinflammatory effects mediated through the immune cells.
- Turmeric
  - Similar to ginger, turmeric seems to work as an anti-inflammatory agent through multiple pathways and should be considered as an addition to the diet of patients suffering from chronic pain.

- GINSENG
  - Clear effect of ginseng on the pain pathway and a need for future clinical studies examining the efficacy of ginseng as a natural antiinflammatory.
- CAFFEINE
  - Blockade of adenosine receptors by caffeine would have a proinflammatory effect, thus, it appears that caffeine would have a negative effect on pain, but this is often not the case.
  - The positive effects in tension headaches maybe come from the established ability of caffeine to constrict cerebral blood flow (linked to the headache experienced in caffeine withdrawal)


Omega-3 PUFA
Omega-3 PUFA
curcumin
Ginger
EGCG
Saturated
fats
EGCG,
ginger,
broccoli,
turmeric
TRPV1
TNFR
TRPA1
Omega-3
PUFA
IL-1R
EGFR
Omega-6
PUFA
TLRs
Arachidonic
acid
IKKβ
P2Xs
EGCG
PGE2
COX-2
Grape seed extract,
bilberries, soy
proteins, broccoli,
lycopene, curcumin,
ginseng
NLRP3
NLRP1
Ginseng
EGCG
Broccoli
lycopene
NFκB
Pro-IL-1β
IL-1β

Influence of pro-algesic foods on chronic pain conditions

- It is known that some foods can trigger pain or aggravate existing pain conditions.
  - Consumption of gluten by individuals with gluten sensitivity can lead to gastrointestinal tract pain.
  - Migraine headache is known to be triggered in some sufferers by specific foods like chocolate or wine.

- less is known about the potential interaction between intake of specific dietary components and chronic pain conditions.

Monosodium Glutamate (MSG)

- Ingestion of large quantities of MSG is theorized to have a negative effect on pain in chronic pain patients
- Glutamate-rich foods include condensed soup, Parmesan cheese and packaged sauces, particularly tomato sauce, and seasonings
- The median daily consumption of glutamate in the Western diet from all sources is around 12 g.
- This is somewhere between 170 -250 mg/kg/day of glutamate.

- Ingestion of a single dose of 150 mg/kg of MSG increases serum glutamate levels by up to 8 times normal and can result in reports of flushing, diffuse muscle aches, and headaches.

- MSG sensitizes nociceptive nerve fibers and induces vasodilation of cranial blood vessels through activation of peripheral N-methyl-D-aspartate receptors.

- Elevated glutamate levels have been found in temporomandibular disorders and migraine headache, and reduction of dietary glutamate intake may reduce muscle pain symptoms in fibromyalgia.

Aspartame and Pain

- Aspartame (l-aspartate-l-phenylalanine-methyl ester) is an artificial sweetener ~200 times sweeter than sugar.
- One of the most common complaints related to the ingestion of aspartame is the development of headache
- Aspartame is metabolized to aspartic acid, phenylalanine and methanol, with the aspartic acid usually considered the component most likely to potentially exacerbate pain
- Daily consumption of aspartame is about 5 mg/kg, and at this level of intake, no association with pain conditions has been identified.

Pharmacokinetic food-drug interactions

- Fatty food decreases the motility of the gastrointestinal tract and can decrease drug absorption.
- Minerals bind several drugs in the gastrointestinal tract, reducing their absorption.
- Both Fe and Zn form insoluble complexes with several antibiotics, for example, ciprofloxacin

- Fruit juices can interfere with the metabolism and excretion of several drugs through different mechanisms.
- CYP3A4/5 contributes to the metabolism of an estimated 50% of all drugs
- Grapefruit juice inhibits CYP3A4/5-mediated first-pass metabolism and can increase the oral bioavailability of drugs 3-fold
- Fruit juices can also interfere with drug metabolism by inhibiting drug transporters.
- Grapefruit juice is a relatively potent inhibitor of P-glycoprotein, an efflux transporter

- The major flavonoid in grapefruit, naringin, has been shown to inhibit P-glycoprotein activity by 50% in vitro.
- On the other hand, orange juice and its major flavonoid hesperidin have been shown to be potent in vitro inhibitors of the uptake transporter OATP1A2 at relatively low concentrations
- Other juices (apple, pomelo) have been shown to interfere with drug metabolism

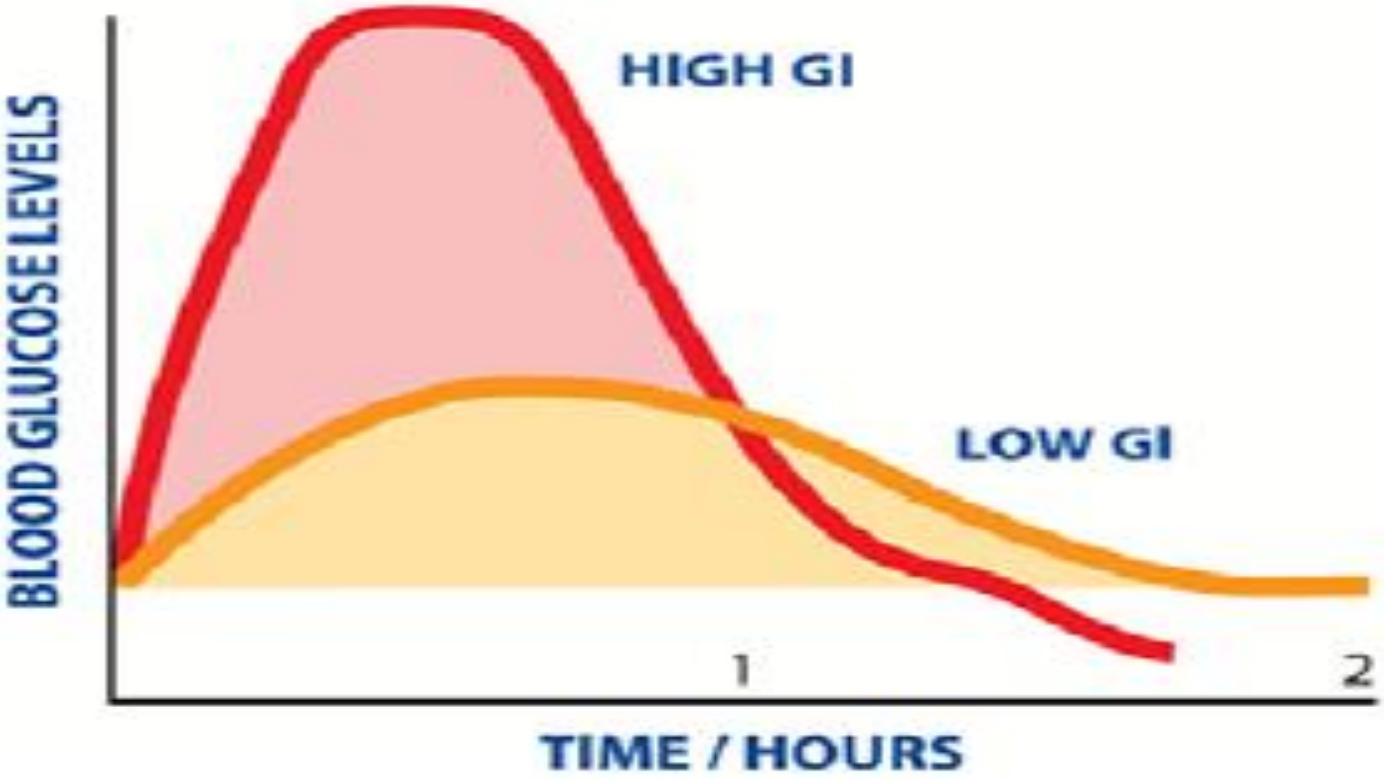
Anti Inflammatory Foods	Pro-inflammatory Foods
• All leafy green vegetables	• Sugar
• Avocados	• Bread
• Yams	• Pastries
• Berries	• Processed cereals
• Nuts and seeds	• White rice
• Lentils and beans	• White potatoes
• Quinoa	• Deep fried foods
• Buckwheat	• Red meat
• Whole grains	

TRANS FATS

- A study conducted at Harvard University, which appeared in The Journal of Nutrition, set out to find out whether trans fat simply increases cholesterol, or whether it is also pro-inflammatory.
- They found the more trans fats someone ate, the more inflammation was happening in their body. This association was independent of other possible causes of inflammation (e.g. saturated fat intake or obesity).

- Source: Lopez-Garcia E. Consumption of trans fatty acids is related to plasma biomarkers of inflammation and endothelial dysfunction. J Nutr. 2005 Mar;135(3):562-6

High Glycemic Index Foods



High Glycemic Index Foods

- Low GI diets have been shown to lower the risk of many chronic diseases that have an inflammatory cause (i.e. obesity, diabetes, back pain and heart disease).
- When you eat a high GI food, you get a "spike" in blood sugar. In response, your body has to release a ton of insulin to get your blood glucose under control. Insulin is a hormone that your body makes to get glucose out of your blood and into your cells where they belong. If a spike in insulin happens occasionally, your body has no problem adapting.
- However, if this occurs again and again, your body has a tougher time keeping up. Your body's response to this is increasing inflammation.

High Glycemic Index Foods

- Another study conducted at Harvard University, that appeared in the journal The American Journal of Clinical Nutrition showed a diet of high GI foods increases inflammation.
- They found that the higher the CRP (inflammation), the higher GI the diet tended to be. "Dietary glycemic index is significantly and positively associated with plasma CRP."

Source: Liu S. Relation between a diet with a high glycemic load and plasma concentrations of high-sensitivity C-reactive protein in middle-aged women. Am J Clin Nutr. 2002 Mar;75(3):492-8

Glycemic Index

Foods High In GI

- • Sugary (i.e. candy)
- • Processed (i.e. white bread)
- • Low in Fiber (i.e.. white rice)
- • Low in Protein (i.e.. rice cakes)

Foods Low in GI

- • Produce (i.e. most fruits and vegetables)
- • Minimally Processed (i.e. whole wheat bread)
- • High in Fiber (i.e. beans)

VITAMIN D

- *For decades, we've been talking about the importance of Calcium in the diet. The time has come to get the word out about vitamin D and its contribution to good musculoskeletal health.*
- Vitamin D has the unique property of being made in your skin with the help of sunlight. This is why it is commonly referred to as the "Sunshine vitamin".
- *"Vitamin D deficiency is an unrecognized epidemic in both children and adults throughout the world."*

Vitamin D Influences

- Cell Growth
- Insulin Resistance (Diabetes)
- Immunity
- Muscle Function
- Nervous System
- Cardiovascular System
- Blood Pressure
- Inflammation
- Low Back Pain

How Can vitamin D Improve Pain?

- *Inflammation Reduction*
- *Improve Nerve Function*
- *Increased Muscle Strength*
- *Helps Pain Medication Work Better*

The muscles that support your spine are dependent on Vitamin D

VITAMIN D

- There are a lot of different recommendations as to the amount of Vitamin D to take.
- The literature and scientists recommend 2,000-4,000 IU daily
- Also get a “sensible exposure” to sunlight.
- “Screening for vitamin D deficiency should be performed for all patients with chronic pain”
- The only way to be sure that you are getting enough vitamin D is by getting a blood test called a 25OHD test.
- Supplements are a safe, effective, and inexpensive way to get vitamin D.

THANK YOU AND ANY QUESTION?