“A spoonful of sugar helps the medicine go down”

Mary Poppins

Canadian Pain Society
Pain Across the Ages
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Robin B. Kanarek
Tufts University

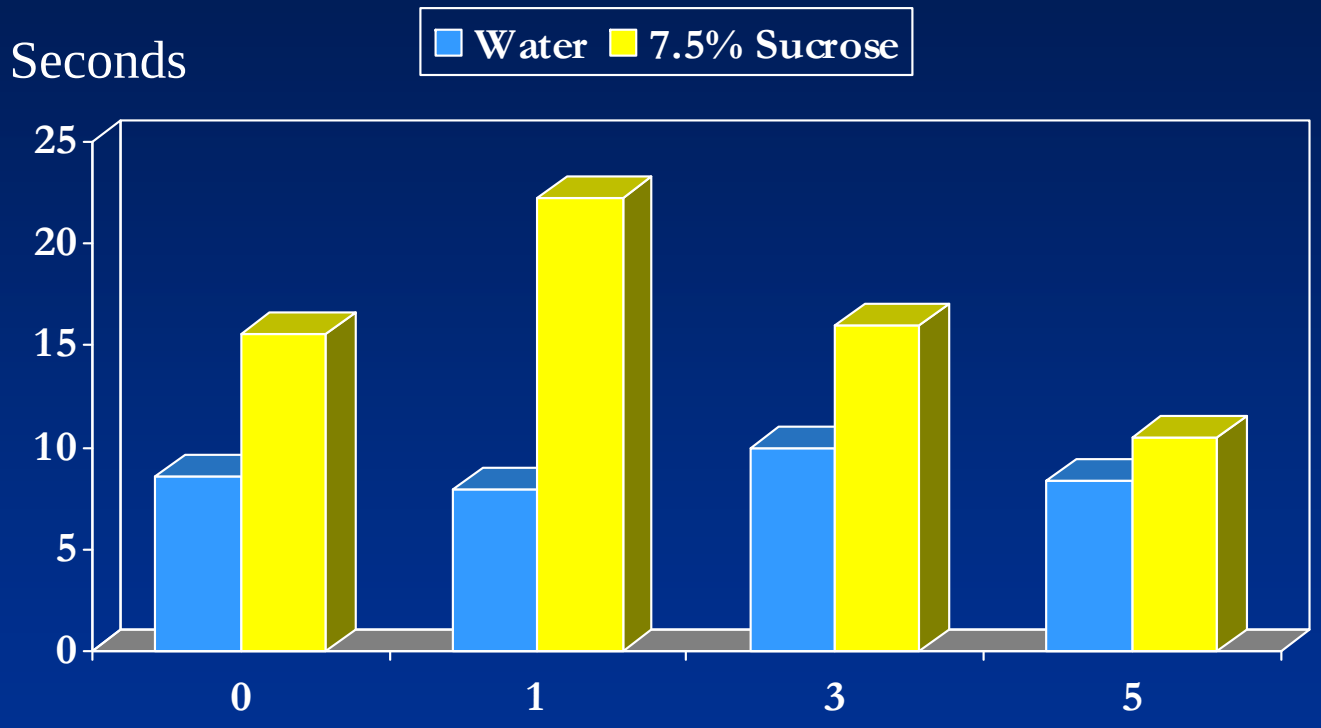
Sugar and Analgesia

Since biblical times, sweet-tasting foods and fluids have been advocated for pain relief. To lessen the pain of circumcision, in the Jewish tradition, sweet wine is placed in the mouth of newborn babies, while in the Muslin religion pieces of dates are rubbed inside the infants mouth.

Overview

- Empirical evidence that acute intake of sweet-tasting carbohydrates can have pain-relieving actions in infants, children and adults
- Intake of sweet-tasting carbohydrates can alter the pain relieving actions of opiate drugs
- Suggestions for future research

Effects of a Sucrose Infusion on Pain Sensitivity in 10-day Old Rats

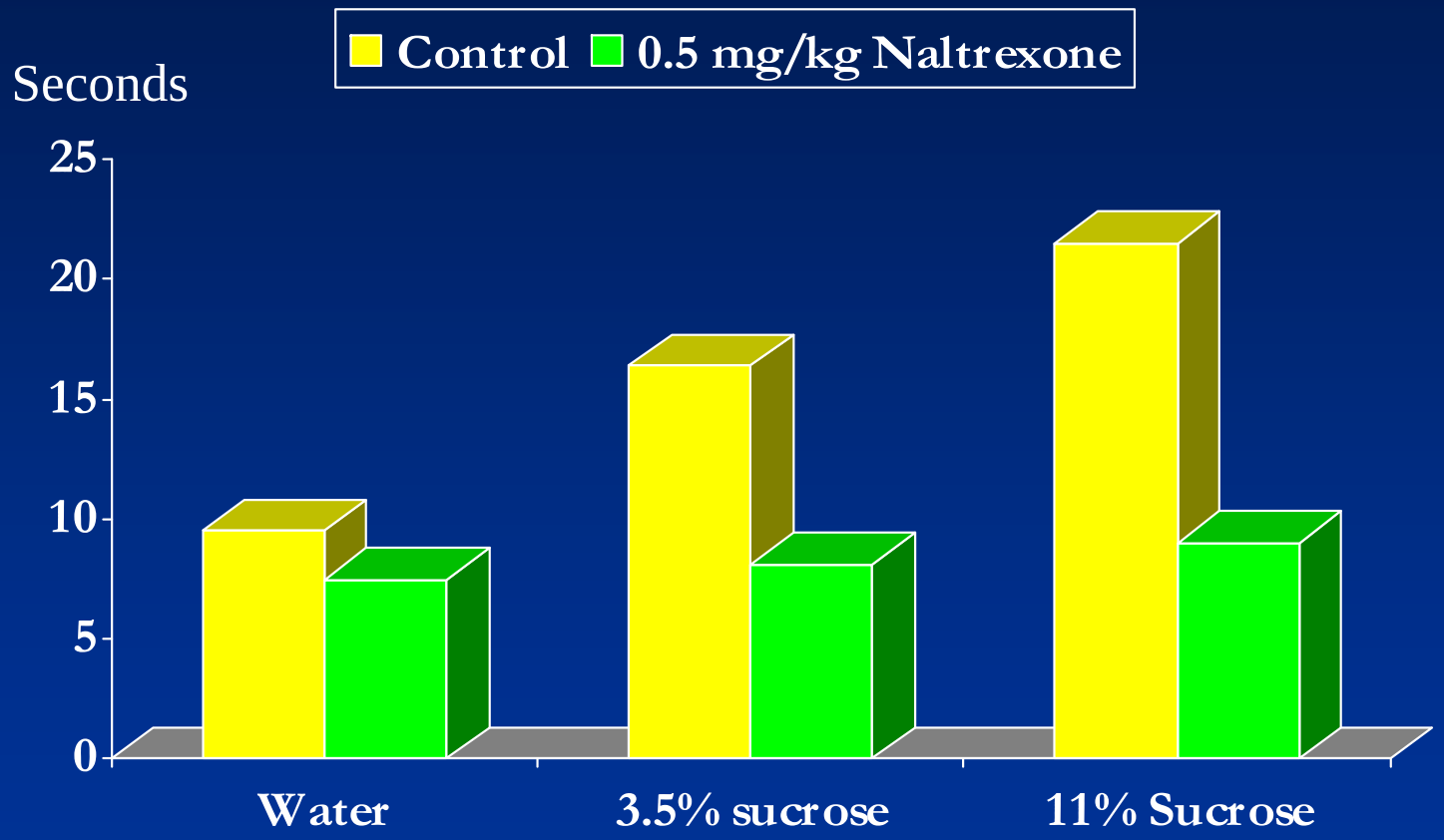


Rats orally infused with a 7.5% sucrose solution or water.

Measured time to lift paw from a hot surface (49^0 C).

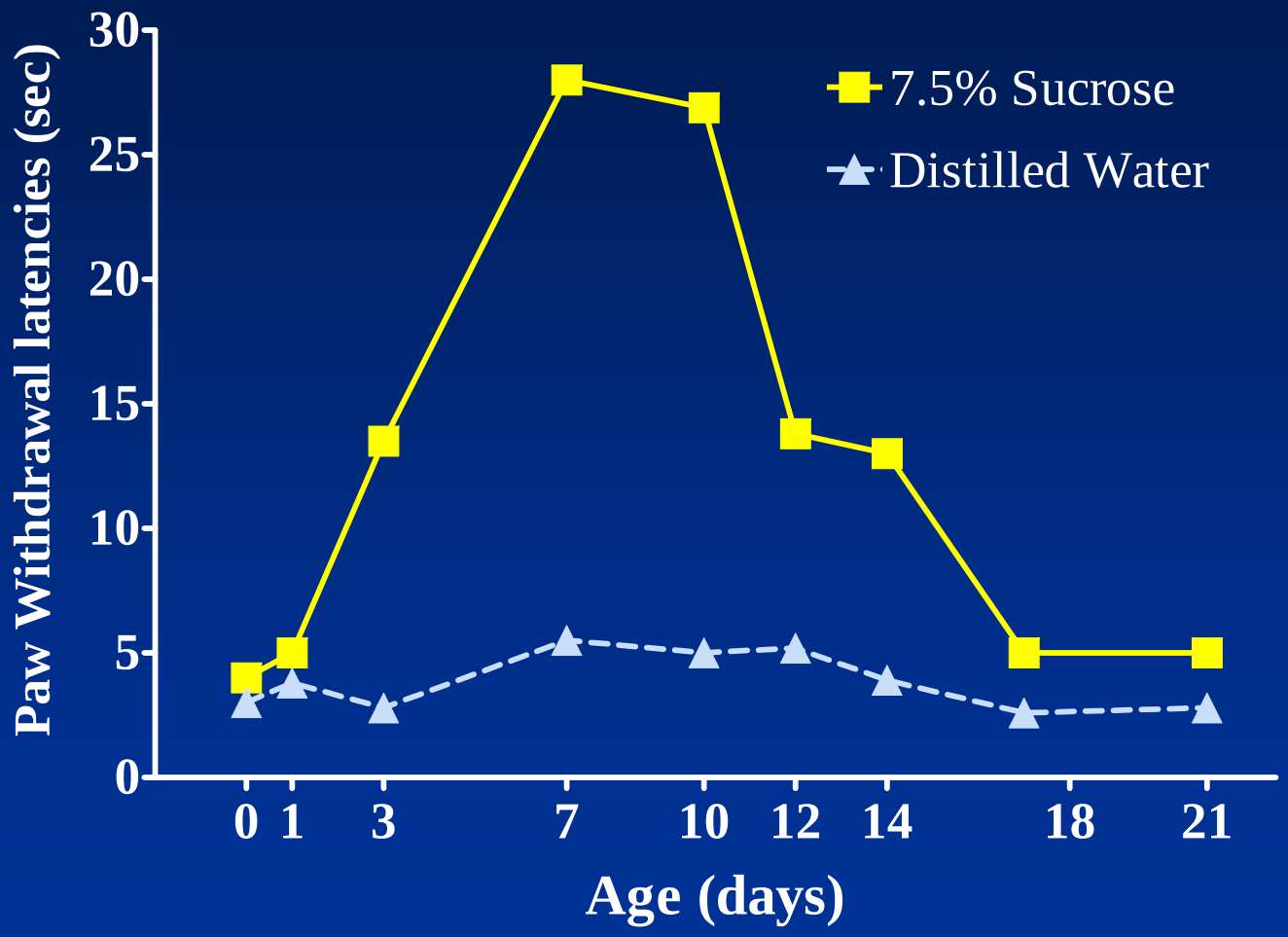
Adapted from: Blass, E., Fitzgerald, E. and Kehoe, P. Pharmacology Biochemistry and Behavior 26: 483-489, 1987.

Effects of Naltrexone on Sucrose-Induced Analgesia in 10-day Old Rats



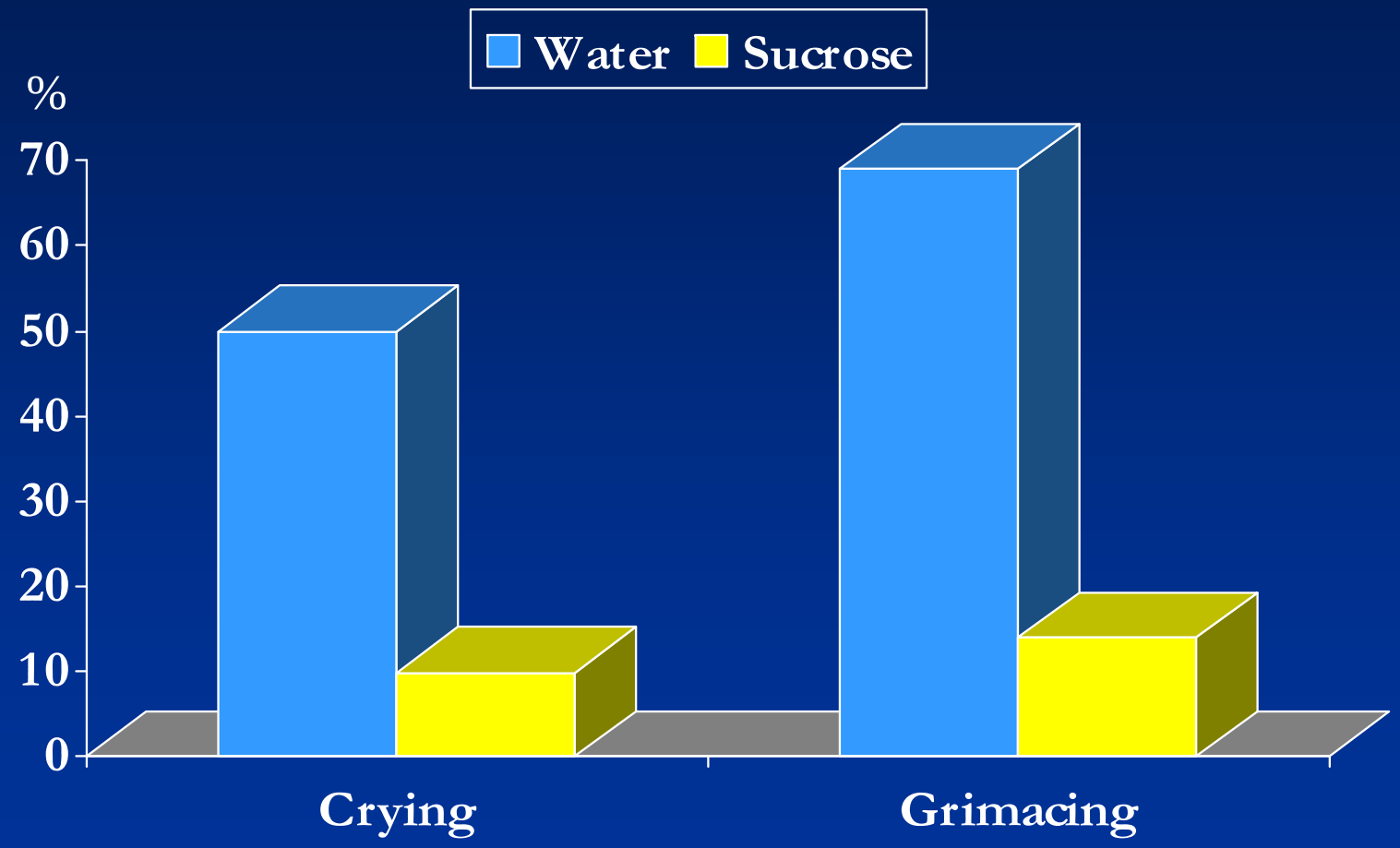
Adapted from: Blass, E., Fitzgerald, E. and Kehoe, P. Pharmacology Biochemistry and Behavior 26: 483-489, 1987.

Infusions of a 7.5% Sucrose Solution Significantly Increased Paw Withdrawal Latencies from Day 3-14 of Life in Rats



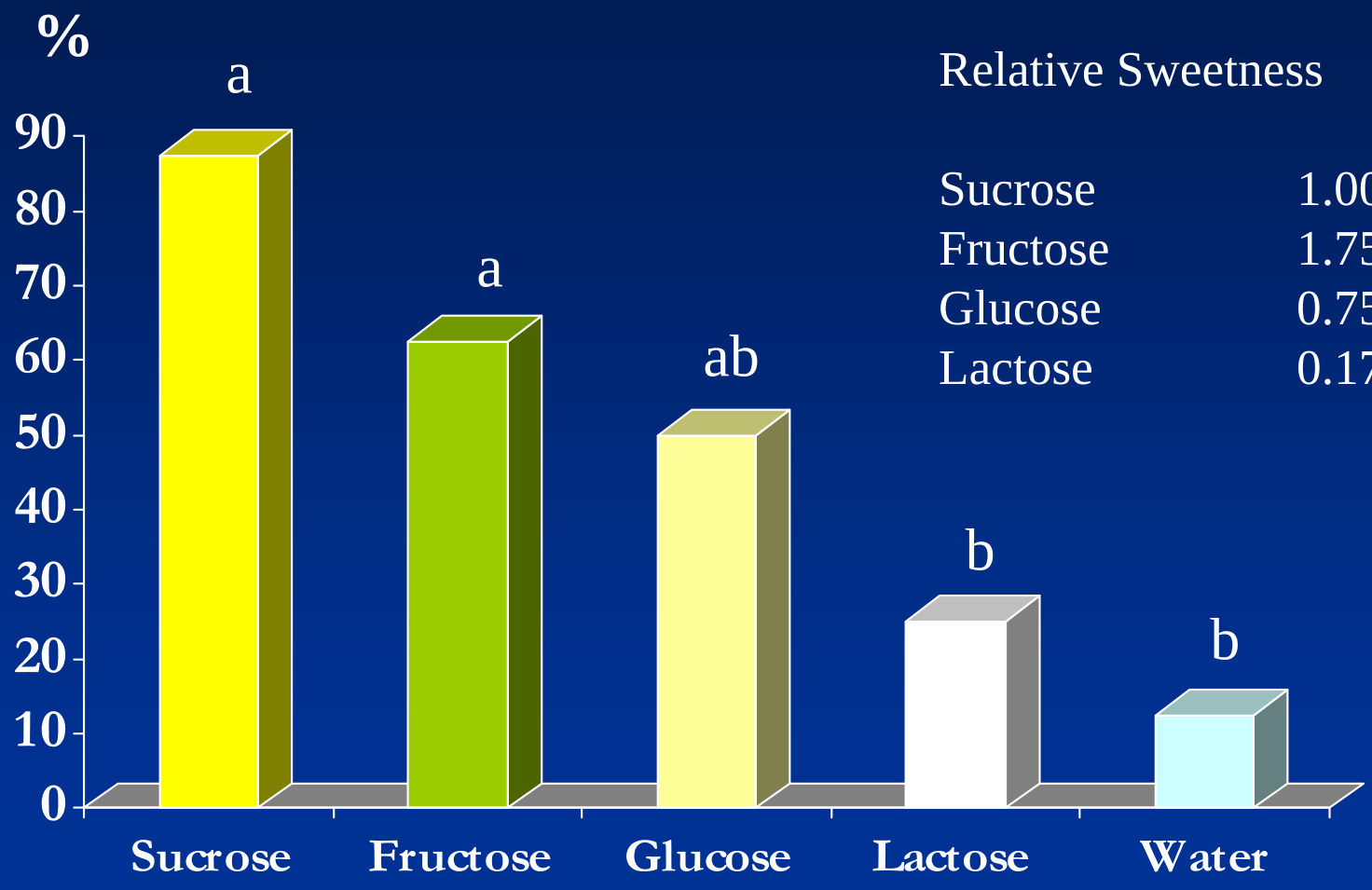
Adapted from: Anseloni et al., Pain 97: 93-103, 2002.

Percentage Time Crying and Grimacing for Infants Receiving Water or a Sucrose Solution Preceding a Blood Draw



Adapted from: Blass, E. M. and Watt, L. B. Pain: 611-623, 1999

Percent of Infants Decreasing Crying Following Oral Intake of Sugar Solutions

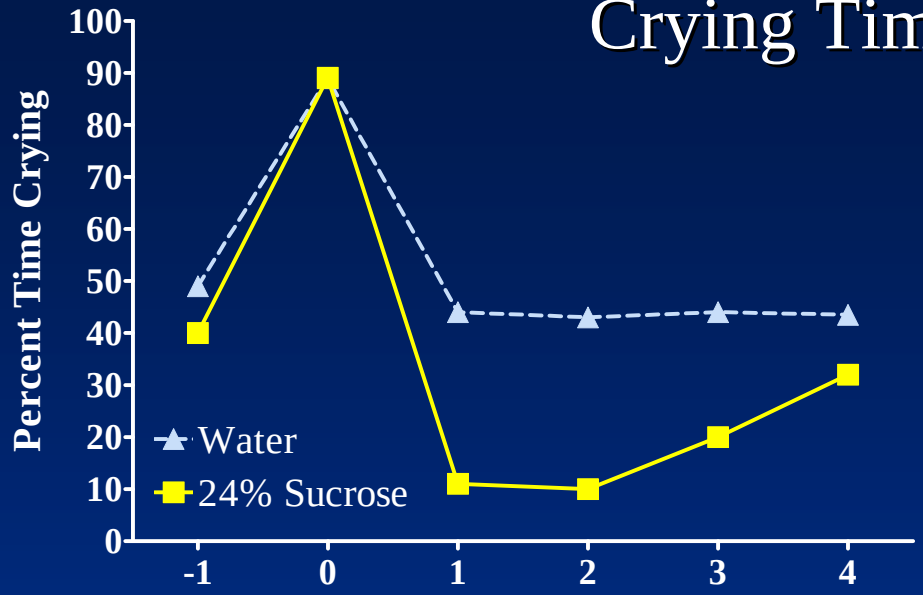


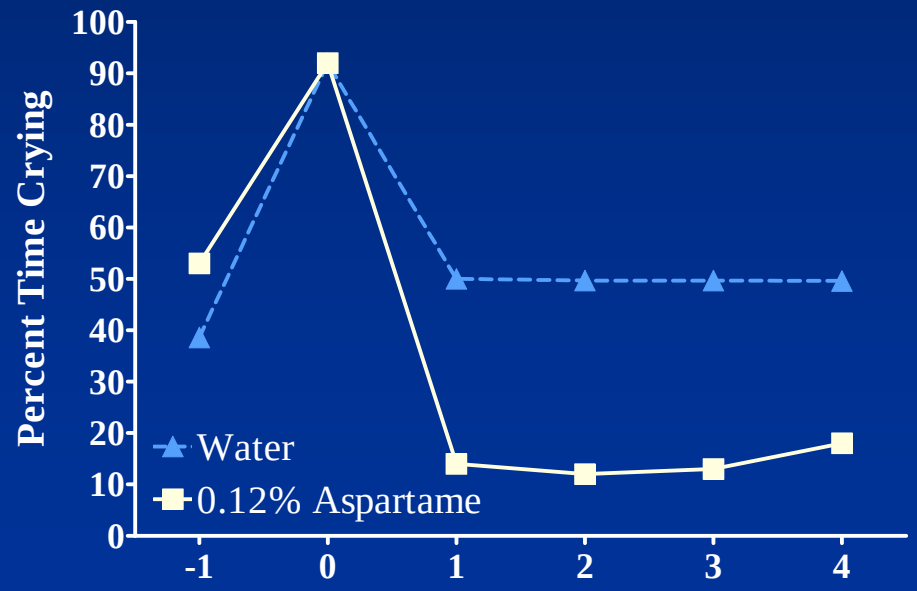
Relative Sweetness

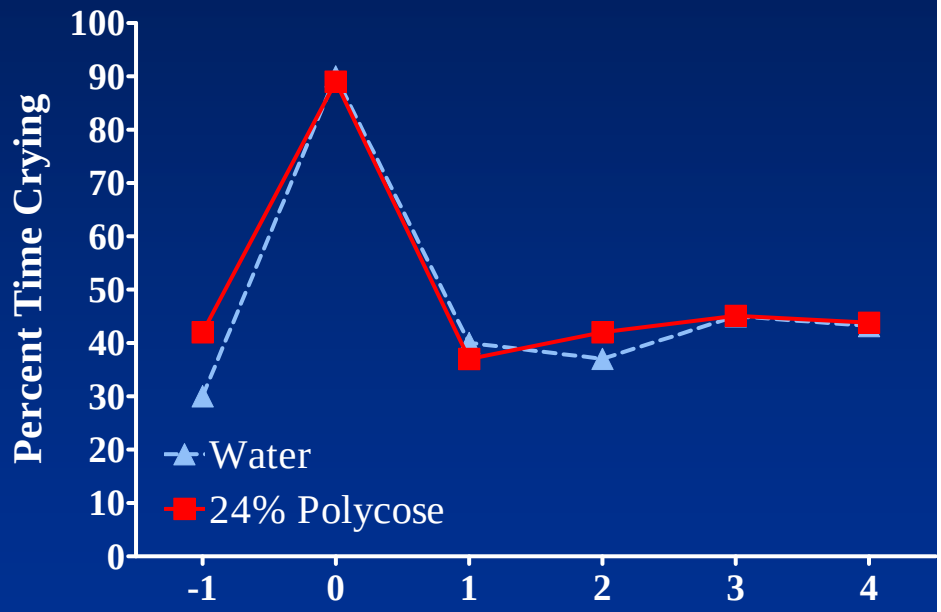
Sucrose	1.00
Fructose	1.75
Glucose	0.75
Lactose	0.17

Adapted from: Blass, E. M. and Smith, B. A. Developmental Psychology 28: 804-810, 1992

Sucrose and Aspartame, but not Polycose Decrease Crying Time in Infants







Adapted from Barr et al., Physiology and Behavior 66: 409-417, 1999

Sucrose-Induced Analgesia in Infants

- Effective dose of sucrose: 0.012 g to 0.5 g
- Effective concentration of sucrose solution: 12% to 24%
- Maximal analgesic effect: 2 minutes after sucrose administration
- Analgesic effect of sucrose begins approximately 30 seconds after exposure and lasts for at least 4 minutes

Adapted from: Stevens, B., Yamada, J. & Ohlsson, A. The Cochrane Collaboration, 2008 and Lefrak, et al., Pediatrics 118: S197-S202, 2006.

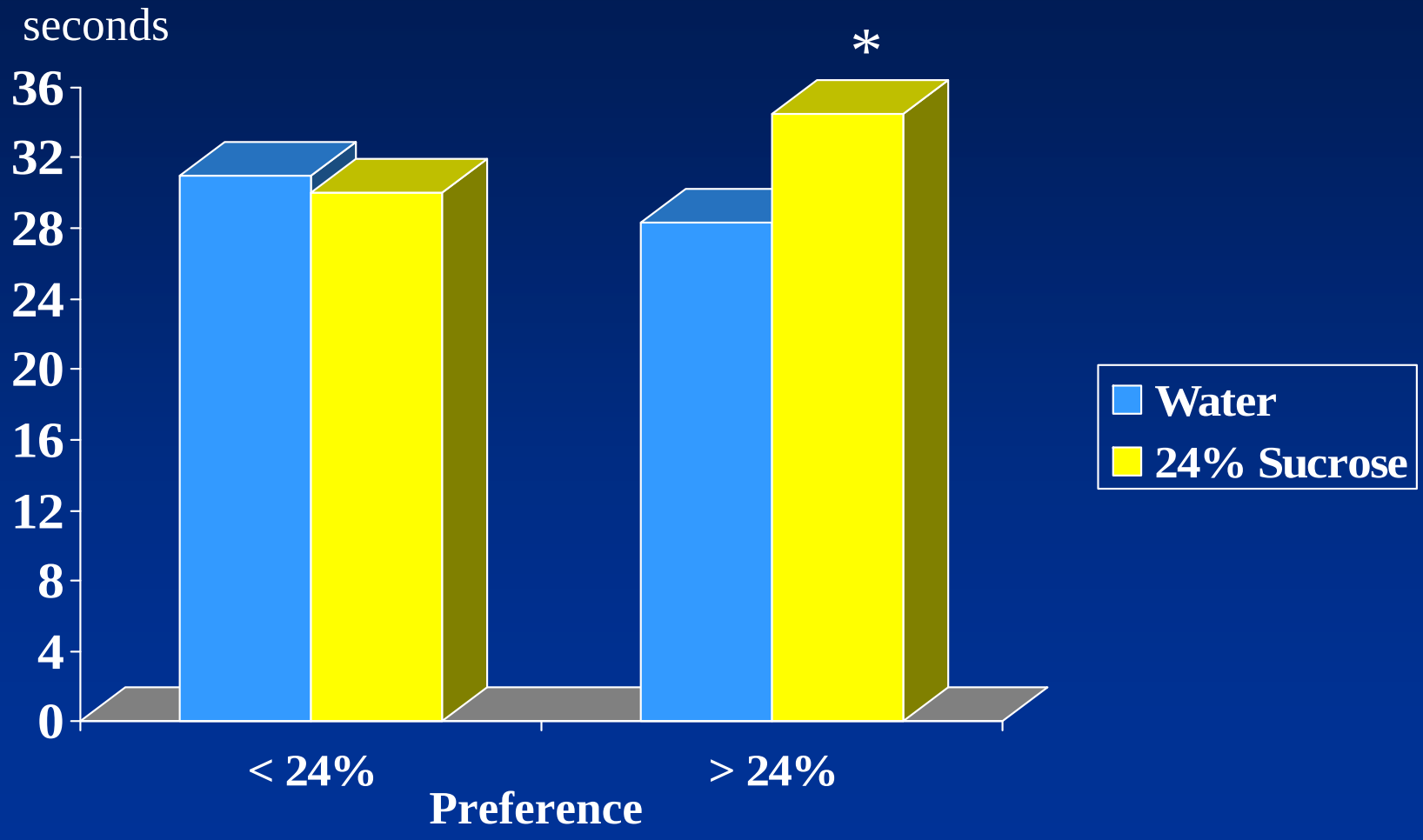
"Use of a combination of oral sucrose/glucose and other nonpharmacological pain-reduction methods (nonnutritive suckling, kangaroo care, facilitated tuck, swaddling, developmental care) should be used for minor routine procedures."

American Academy of Pediatrics and the Canadian Paediatric Society, Prevention and management of pain in the neonate: an update. Pediatrics 118: 2231-2277. 2006.

Question

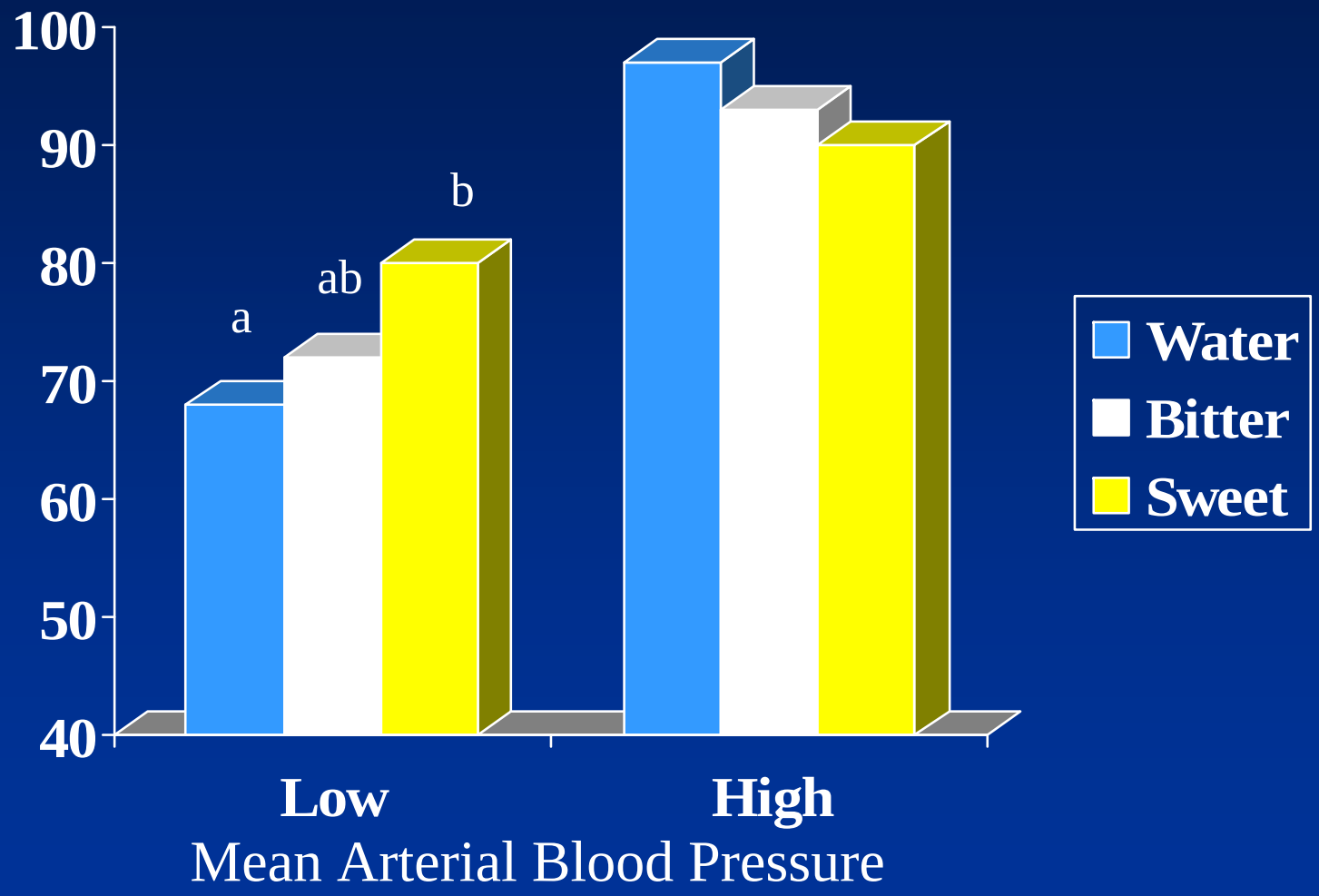
- Can acute intake of sweet tasting foods and fluids decrease pain sensitivity in older individuals?

Pain Tolerance on a Cold Pressor Test in Children Given Sucrose or Water as a Function of Preference for Sucrose



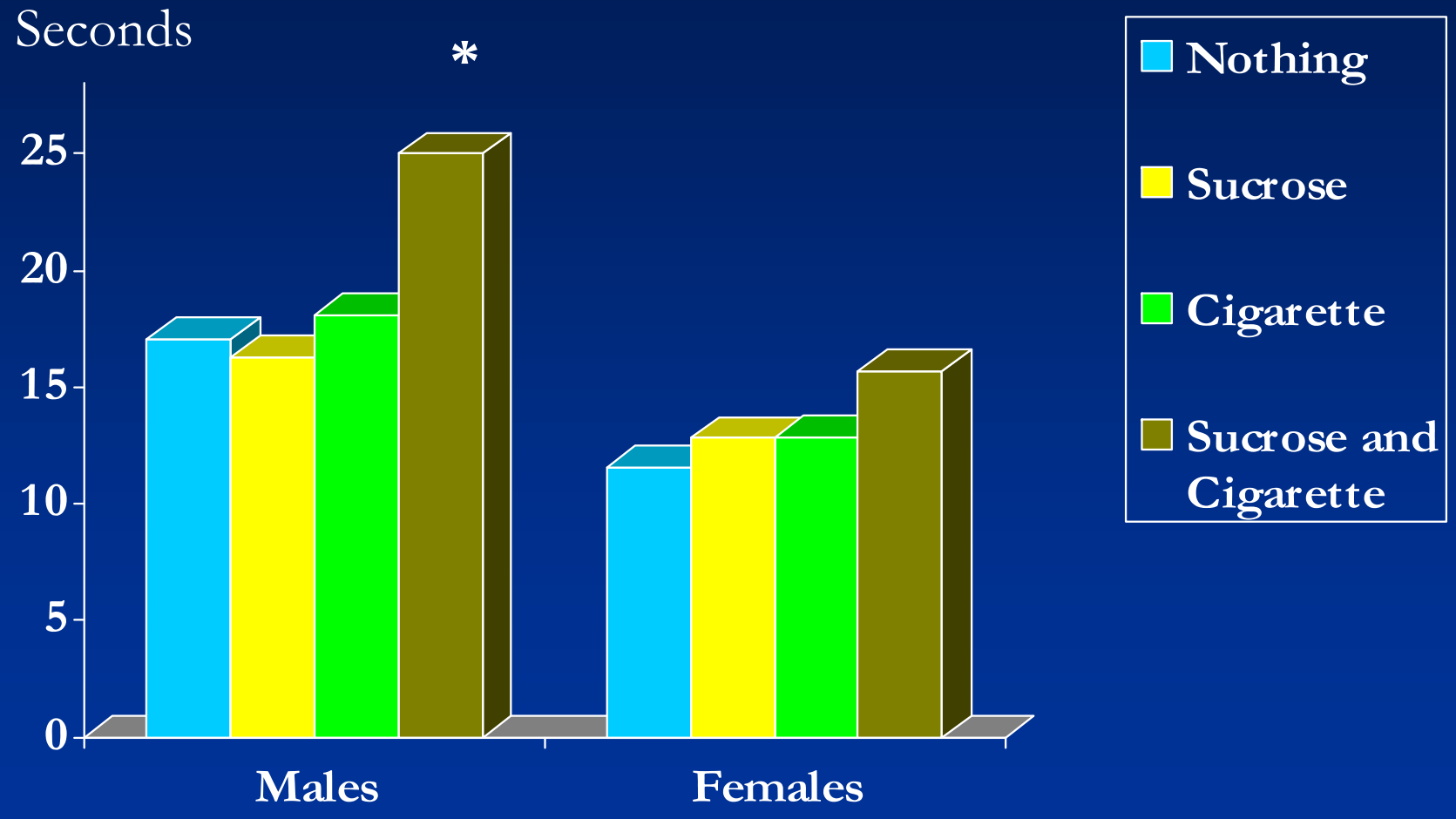
Adapted from: Pepino, M. Y. and Mennella, J. A. Pain 119: 210-218, 2005.

Pain Tolerance on a Cold Pressor Test as a Function of Fluid Intake and Blood Pressure in Young Adults



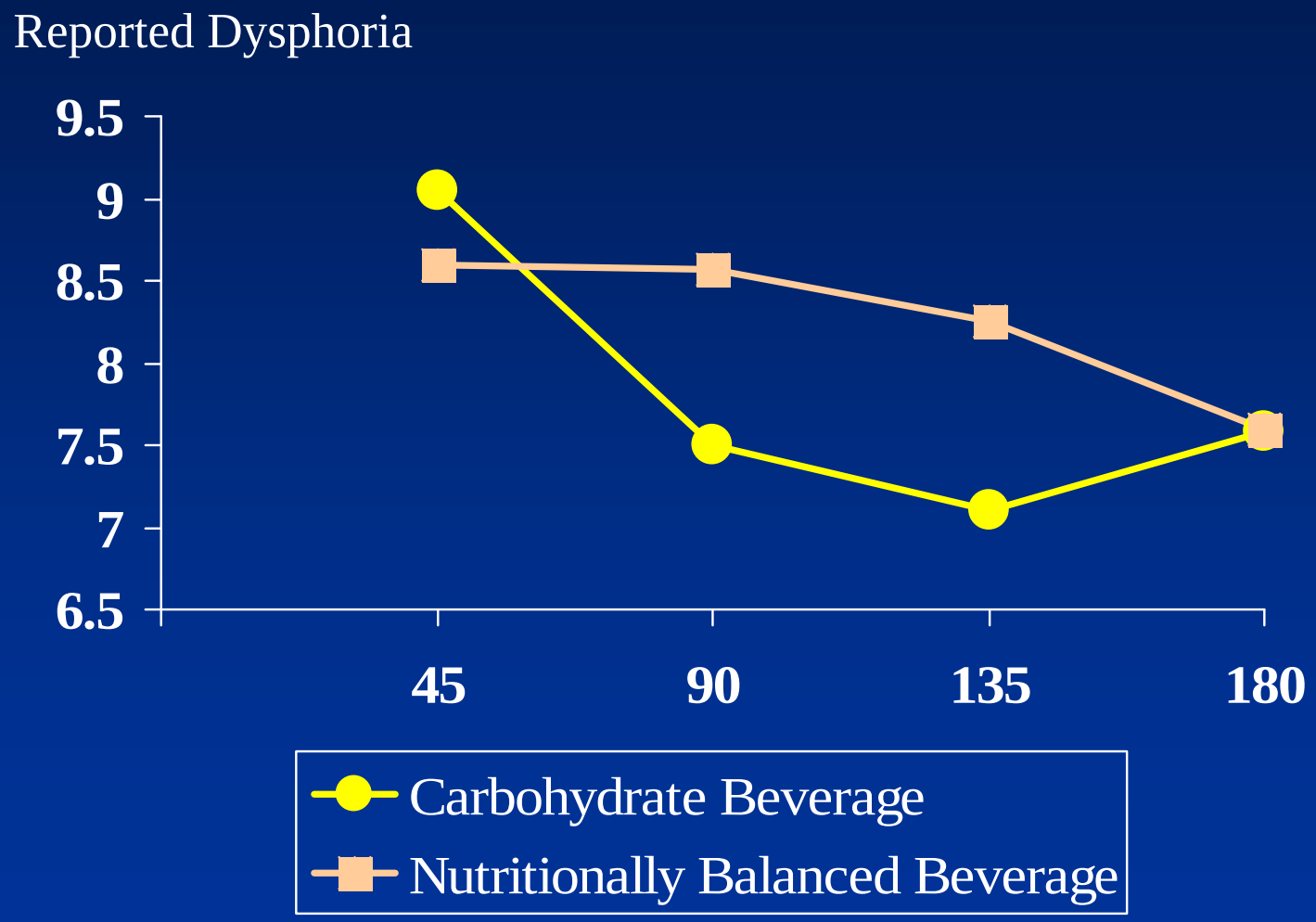
Adapted from: Lewkowski et al., Pain, 106: 181-186, 2003

Pain Thresholds on the Cold Pressor Test in Young Males and Females as a Function of Sucrose Intake and Smoking



From: Kanarek, R. B. and Carrington, C. Psychopharmacology 173: 57-63, 2004.

Intake of a Carbohydrate-Rich Beverage Decreases Dysphoria in Carbohydrate-Craving Women



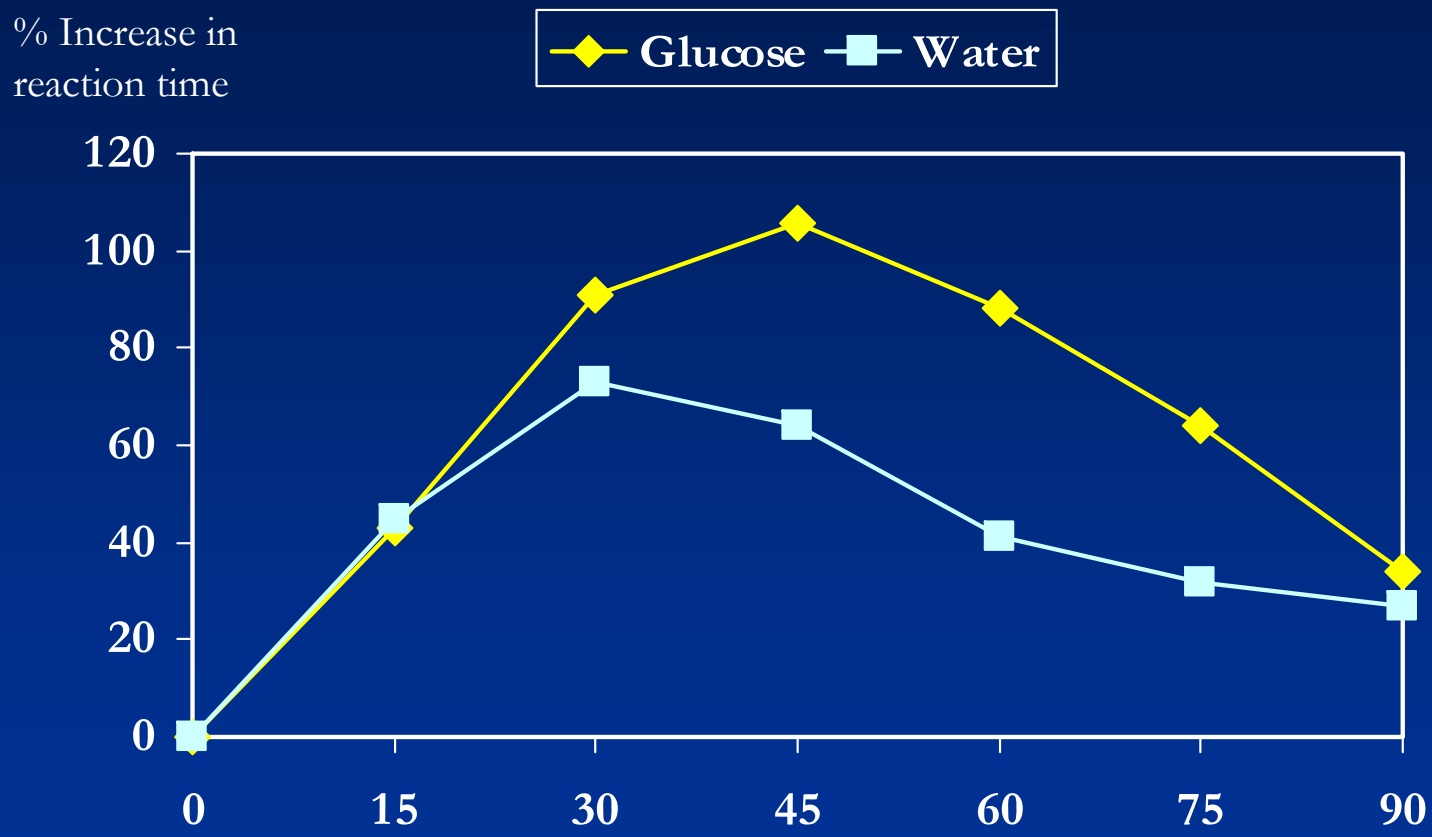
Adapted from: Spring et al., Psychopharmacology 197: 637-647, 2008.

Summary

- Sucrose can have pain relieving actions in children and adults
- However, a number of variables including gender, blood pressure, preference for sweets, and the presence of other analgesic agents may moderate sucrose-induced analgesia in older individuals

Does Intake of Sugar Modulate Opioid-Induced Analgesia?

Glucose Intake Increased the Pain Relieving Properties of Morphine in Rats



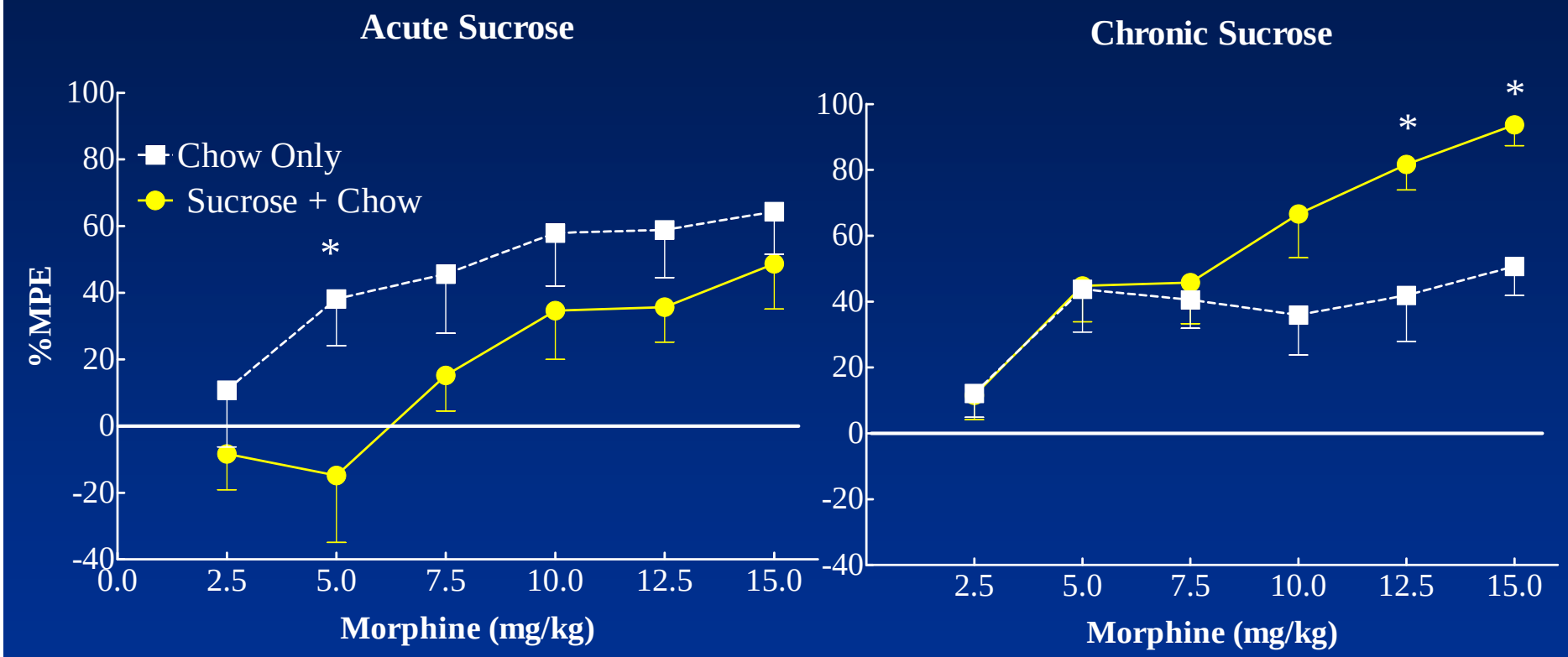
Adapted from: Davis et al., Journal of the American Pharmacological Association 45: 60-62, 1956

Factors Influencing the Effects of Palatable Fluids on Drug-induced Antinociception

- Duration of Intake
  - Acute: less than 24 hours
  - Chronic: more than 2 weeks

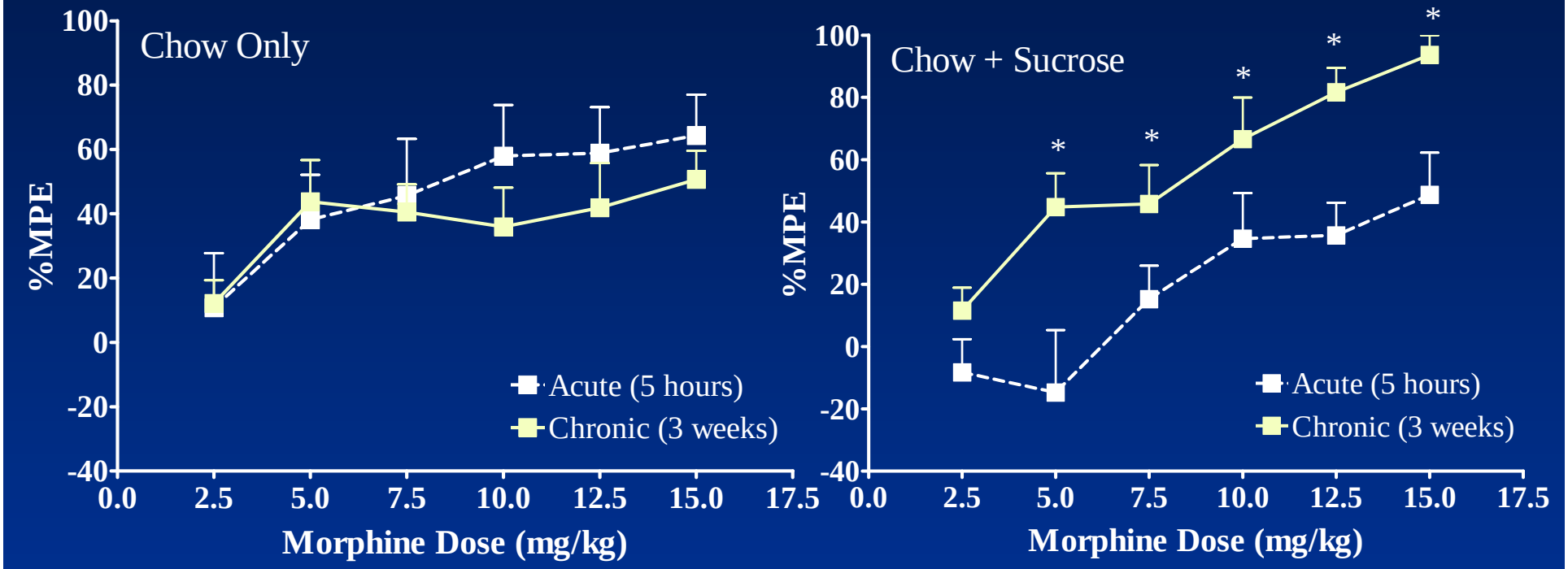
- Nutritive Value of Palatable Fluid
  - Nutritive : Sucrose
  - Non-nutritive: Saccharin

Effects of Acute and Chronic Sucrose Intake on Morphine Induced Analgesia



D'Anci et al., Pharmacology Biochemistry and Behavior, 54: 693-697, 1995

Effects of Acute and Chronic Sucrose Intake on Morphine Induced Analgesia



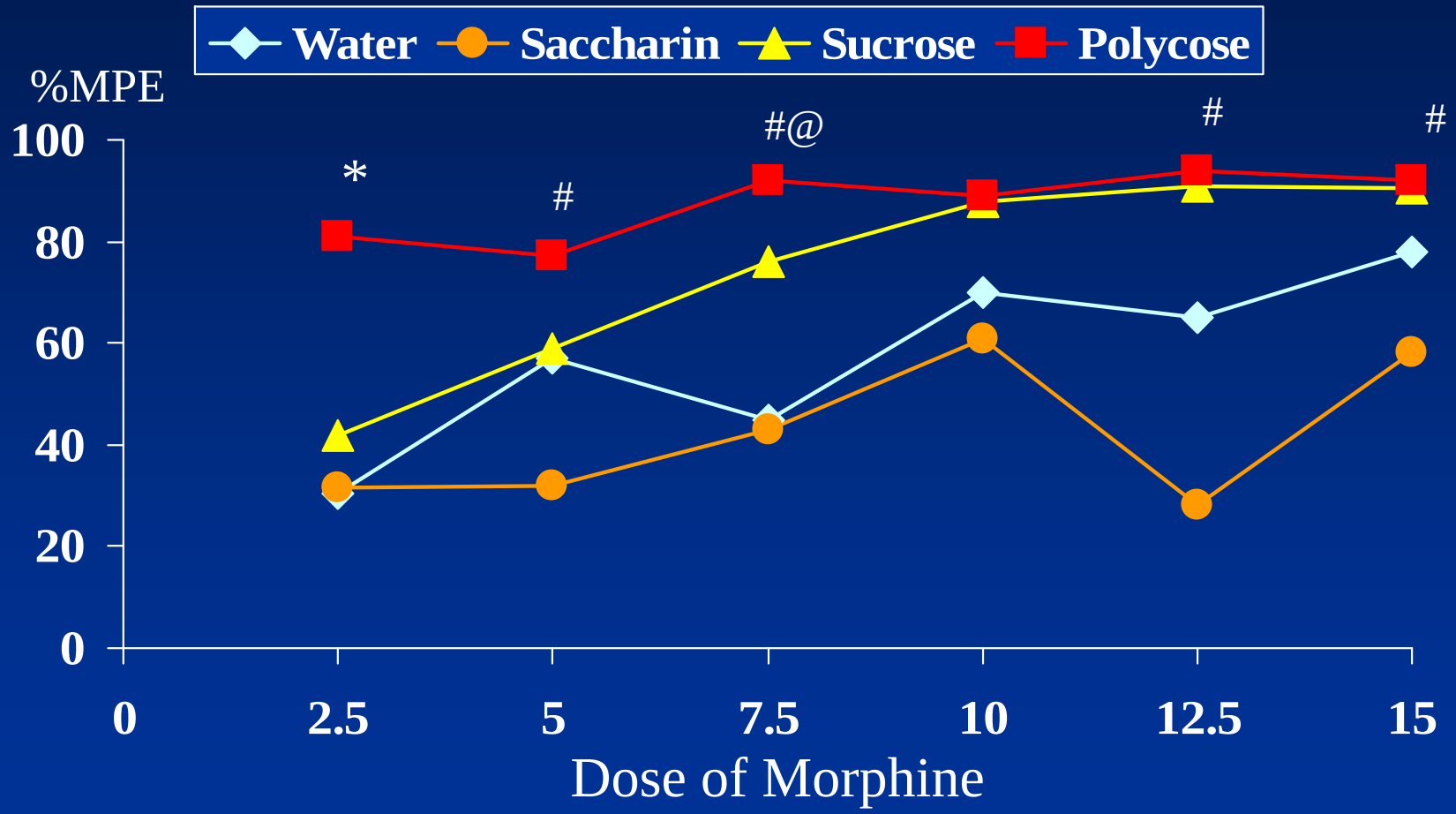
D'Anci et al., Pharmacology Biochemistry and Behavior, 54: 693-697, 1995

Question:

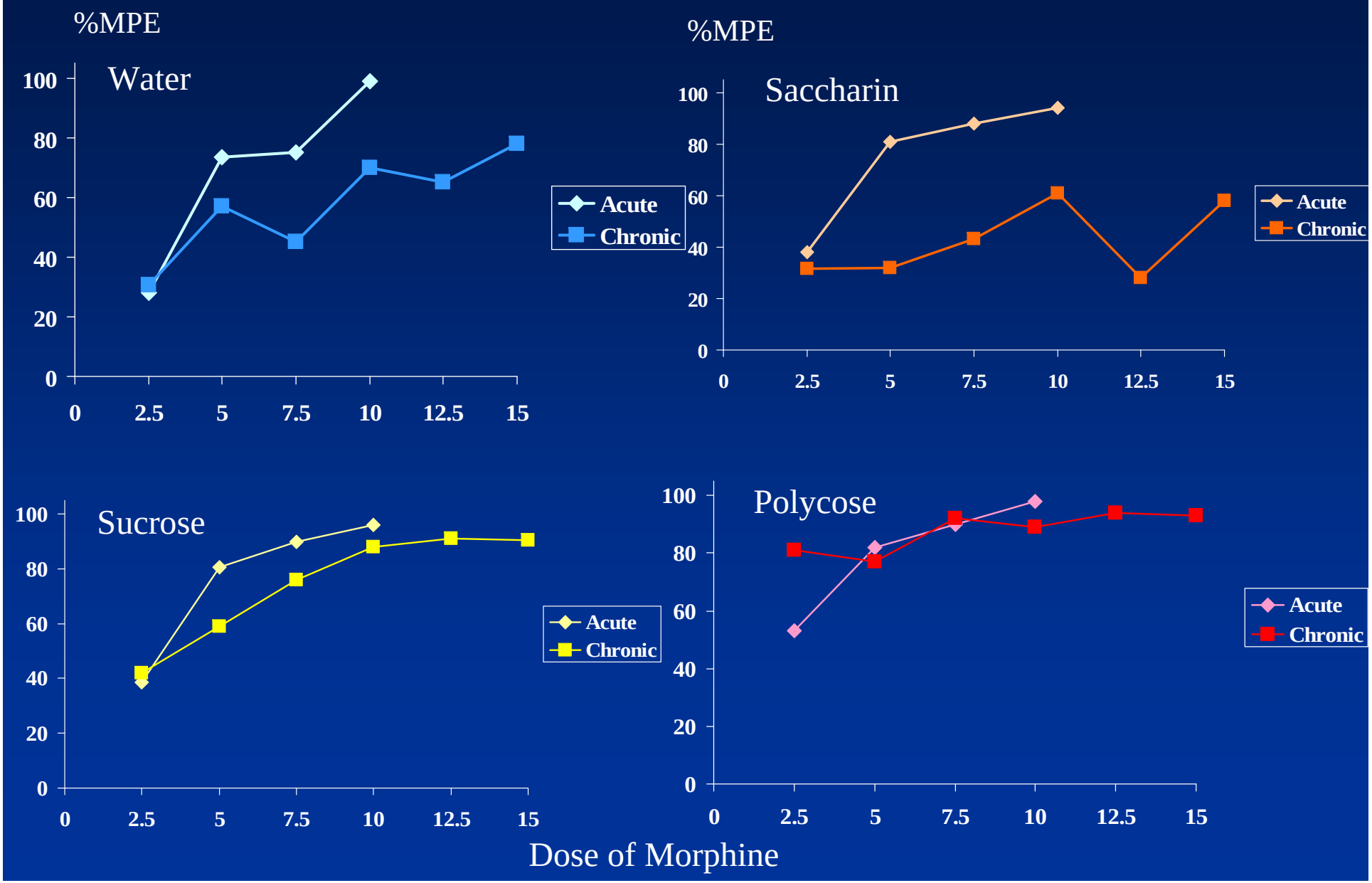
- Is the increase in morphine-induced analgesia in sucrose-fed rats a consequence of the palatable and/or nutritive value of the sugar?

  - Chow and water
  - Chow, water and a 32% sucrose solution
  - Chow, water and a 0.15% saccharin solution
  - Chow, water and a 32% Polycose solution

Chronic Intake of Sucrose and Polycose, But Not Saccharin Enhances Morphine-Induced Analgesia



Analgesia in Rats Following Acute and Chronic Intake of Sucrose, Polycose, Saccharin or Water Alone

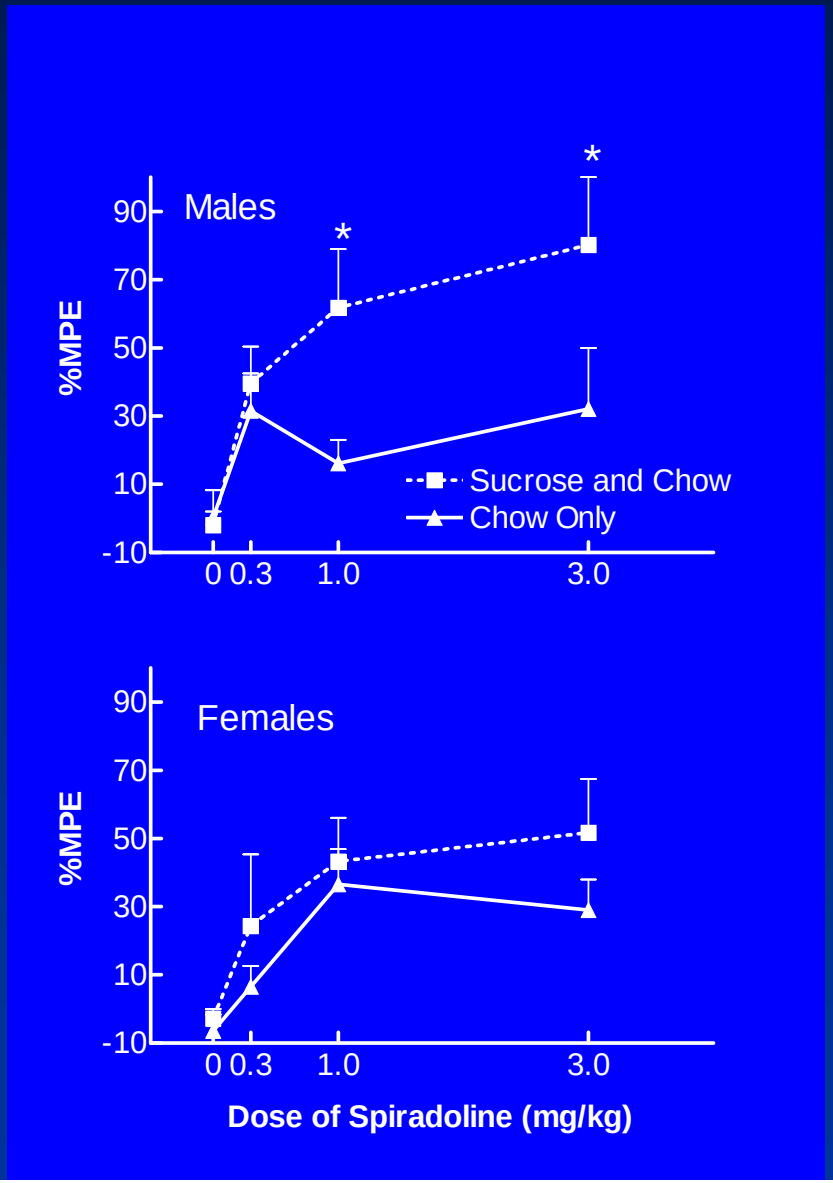


IED-50s Values (mg/kg) as a Function of Intake of Palatable Solutions

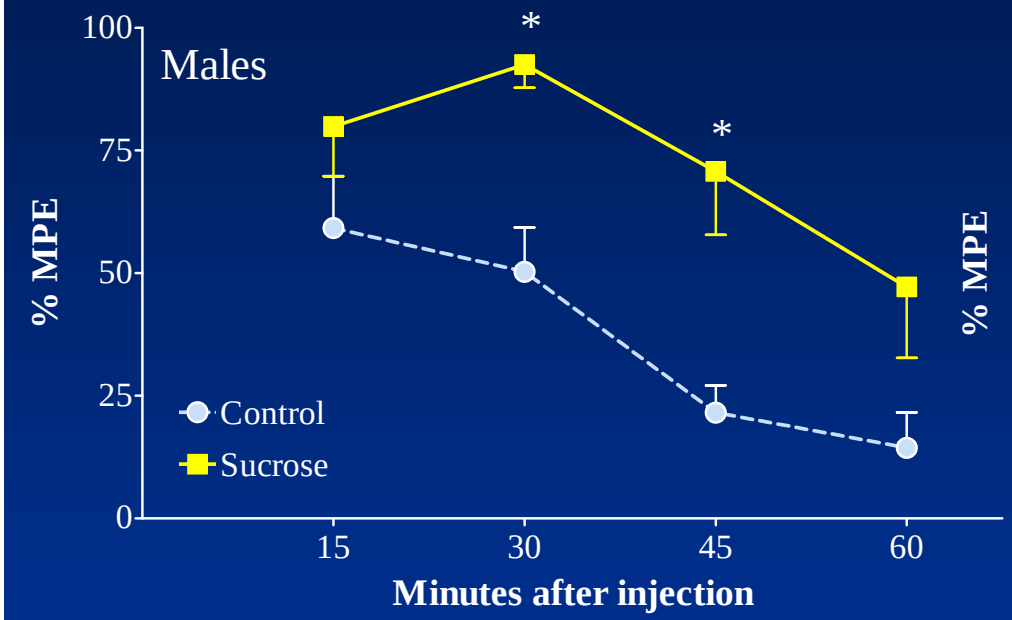
	Water	Saccharin	Sucrose	Polycose
Week 1	6.61[a**]	6.63[a**]	4.29	4.58
Week 2	7.02[a*]	6.28[a]	5.47	5.42
Week 3	11.12[b]	12.80[b*]	8.58	8.08

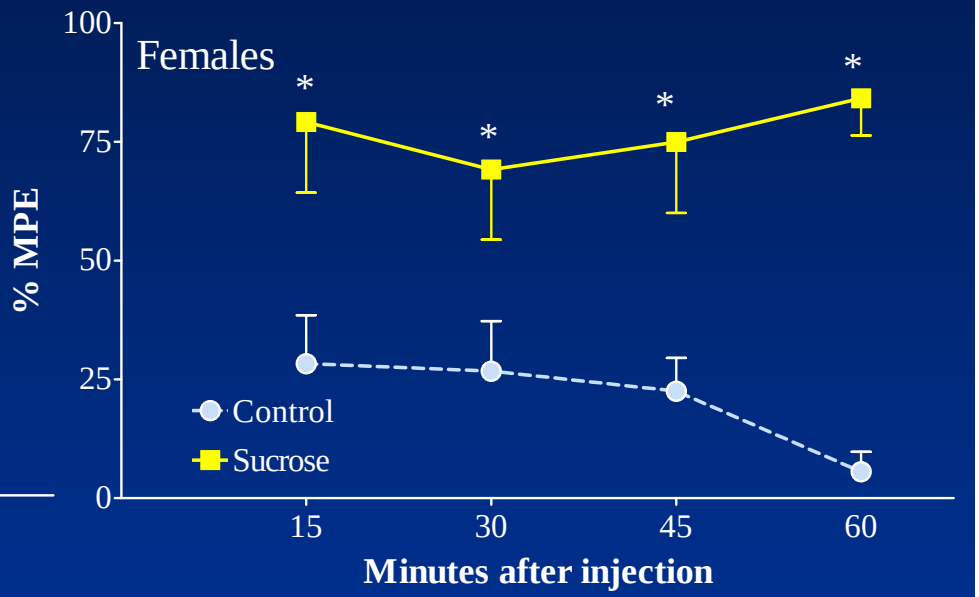
ED-50s were significantly greater for rats consuming water or saccharin than for rats consuming sucrose or Polycose. ED-50s increased significantly as a function of time for rats consuming water and saccharin, but not for rats consuming sucrose or Polycose.

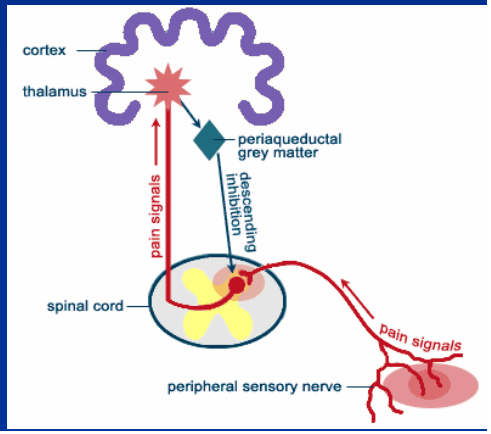
Sucrose enhances the pain relieving actions of spiradoline, a kappa opioid receptor agonist in males, but not females



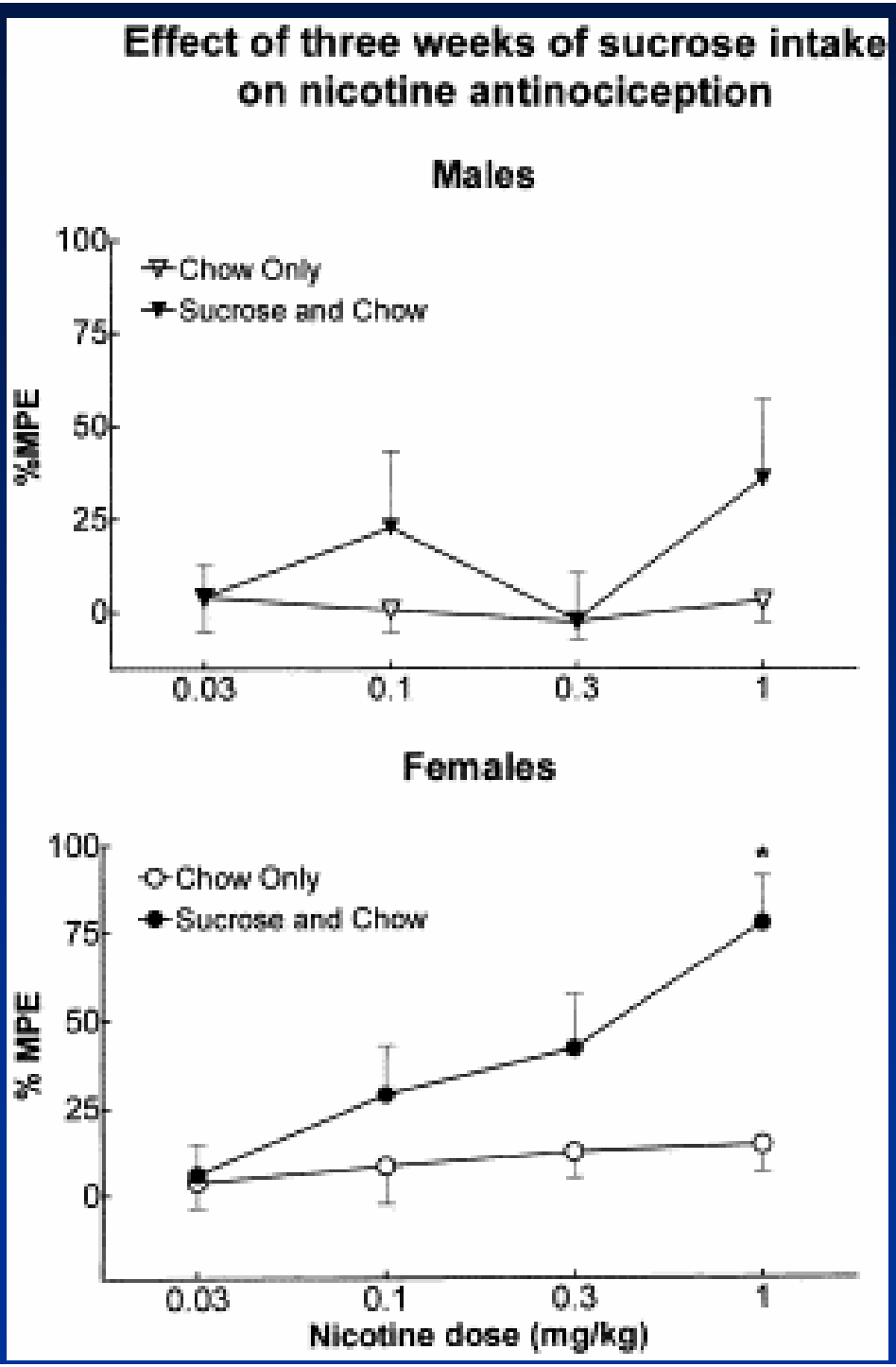
Sucrose Enhancement of Antinociception After Injections of Morphine into the Periaqueductal Grey







From: Kanarek, R. B., Mandillo, S. and Wiatr, C
Brain Research 920: 97-105, 2001


Effect of three weeks of sucrose intake on nicotine antinociception
Males
100
75
50
25
0
%MPE
Chow Only
Sucrose and Chow
0.03
0.1
0.3
1
Females
100
75
50
25
0
% MPE
Chow Only
Sucrose and Chow
*
0.03
0.1
0.3
1
Nicotine dose (mg/kg)

Summary

- Acute intake of nutritive, sweet-tasting carbohydrates decreases the pain-relieving actions of opiate drugs
- Chronic intake of nutritive, but not non-nutritive, carbohydrates increases the pain-relieving actions and delays the development of tolerance to opiate drugs
- These effects are believed to be mediated, at least in part, by the endogenous opioid system

Future Research Questions

- What are the mechanisms for carbohydrate-induced alterations in pain sensitivity and opioid analgesia?
- Can intake of palatable sweet-tasting carbohydrates moderate different types of pain?
- How do gender, age, stress, and environmental variables interact with sucrose in moderating responses to opiate drugs?
- Are the effects of carbohydrates limited to opiates, or do they extend to other analgesic modalities?
- Can data gathered from animals be used to help reduce pain in clinical situations?

Contributors

- Kristen D'Anci
- Wendy Foulds Mathes
- Silvia Mandillo
- Rinah Yamamoto
- R. Todd Coy
- Robin Marks-Kaufman
- Cheryl Frye
- Jeanne Przypek
- Mark Vitale
- Debra Chen
- Cladia Wiatr
- Brent Homoleski
- Eric White
- Matthew Biegen
- Catherine Carrington

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