

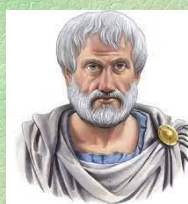
## «Θερμορύθμιση και Άσκηση: σημεία καμψής και διχογνωμίες»

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Τομέας Αθλητιατρικής και Βιολογίας της Άσκησης,  
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Εθνικό και Καποδιστριακό Πανεπιστήμιο Αθηνών



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### Turning point 1



- Born in 384 BC
- Died in 322 BC
- 20+12 years in Athens
- Spiritus rector of Alexander the Great for 7 yrs

ΚΑΚΤΟΣ 226 ΟΙ ΕΛΛΗΝΕΣ  
ΑΡΙΣΤΟΤΕΛΗΣ  
37 ΑΠΑΝΤΑ 37  
ΠΡΟΒΛΗΜΑΤΑ 1

Aristotle poses numerous questions concerning sweating, cold sensation, exercise, wellness, health and disease.

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## Theoretical context and methodology

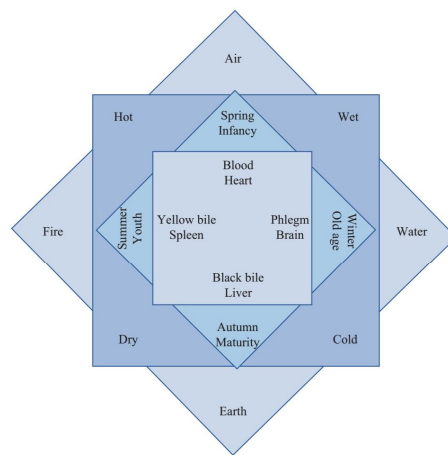


Fig. 2.1 The humoral theory. The relationship between the four qualities, elements, and humors, according to Hippocrates (460–357 BC). (Copyright Grodzinsky, E & Sund Levander, M)

- Observation
- Inductivism
- Teleology

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## Aristotle's questions

*“Why intermittent type of work induces higher sweating than continuous exercise?” “Should sweating be accumulating while resting? In addition, a bout of exercise following a break is forcefully excreting sweating. On the contrary, continuous exercising dries sweating, as sun does.” (Aristotle)*



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## Turning point 2

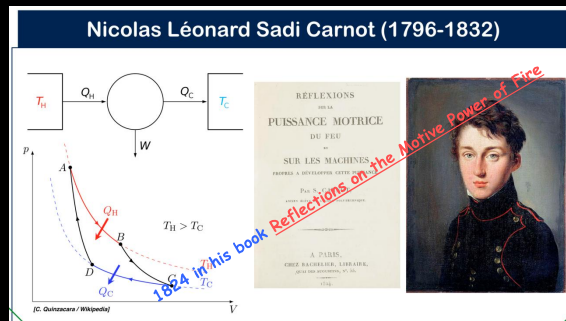
### Evolution of inductivism

- *Observational factual knowledge can be augmented by active experimentation (Roger Bacon 1214 - 1292)*
- *Introduction of Euclid's principle of falsification by Robert Grossetest (1168 - 1253) in order to supplement scientific hypotheses*
- *Teleological explanation is totally excluded (Galileo Galilei 1561- 1626)*
- *Francis Bacon criticizes (1561 - 1626) haphazard data collection, hasty generalization, overuse of enumerative inductions*
- *Creative imagination, interpretations contingent to revision (Isaac Newton, 1642 - 1727)*

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## Turning point 3

### Nicolas Léonard Sadi Carnot (1796-1832)



- James Currie (1767-1805) grasped the link between evaporation and cooling, but could not explain what actually happened .
- The first law of thermodynamics states that, when energy passes into or out of a system (as work, heat, or matter), the system's internal energy changes in accordance with the law of conservation of energy.
- The second law of thermodynamics states that in a natural thermodynamic process, the sum of the entropies of the interacting thermodynamic systems never decreases. A common corollary of the statement is that heat does not spontaneously pass from a colder body to a warmer body.

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## Turning point 4



- ❖ 1600: Thermoscope detecting human body sensible heat (open thermometer, Galileo)
- ❖ 1654: Scaled tubes (thermometer) filled with alcohol (Ferdinand II de' Medici, Grand Duke of Toscani)
- ❖ Mid 1700: Fahrenheit (German) and Celsius (Swedish) scales were agreed
- ❖ 1821: Thermocouples were invented (Thomas Seebeck, Esthonia)
- ❖ 1869, 1900: Axillary, Rectal - Oral temperatures recorded
- ❖ 1964: Tympanic membrane radiometer (Theodor Benzinger, USA)

Understanding fever and body temperature, Edited by Grodzinsky E., and Levander MS, 2020

Measuring Heat

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## Turning point 5



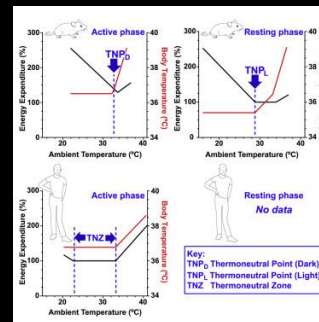
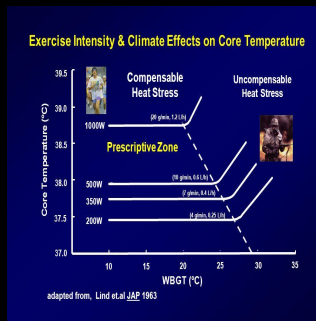
- ❖ 1849: Regulation of the internal environment (Claude Bernard)
- ❖ 1926: The term of homeostasis was introduced (Walter Cannon)
- ❖ 1932: higher brain function is required for a most stable internal environment (Barcroft)



Cannon, W.B., (1932). *The Wisdom of the Body*. New York: W. W. Norton. pp. 177-201.

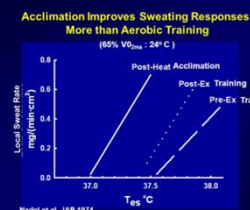
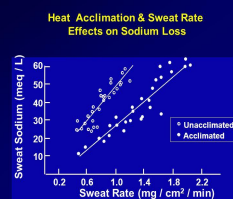
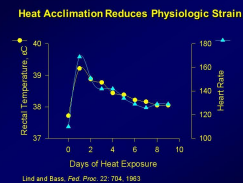
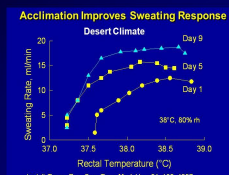
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## Thermoneutral zone, rest & environment



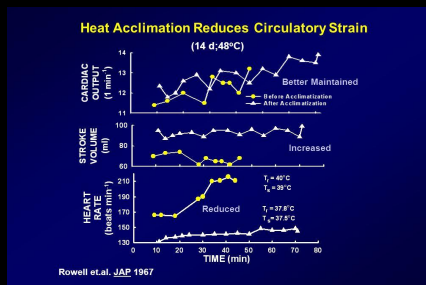
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## Exercise and temperature regulation



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## The role of cardiovascular system



Acta physiol. scand. 1962. 56. 120—129

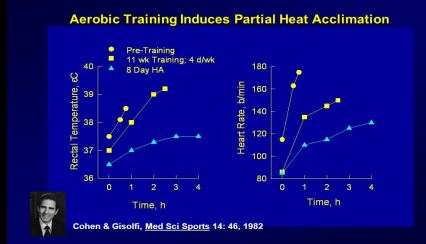
From the Zoophysiological Laboratory A, University of Copenhagen, Denmark

### Body Temperature During Work at Different Environmental Temperatures

By

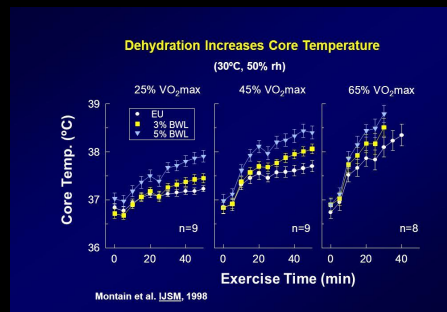
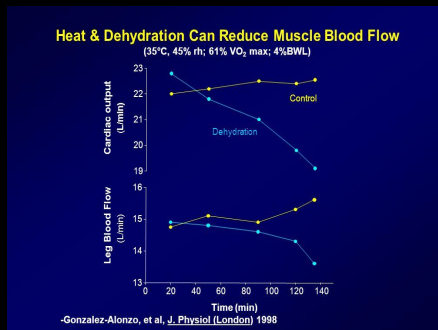
BODIL NIELSEN and MARIUS NIELSEN

Received 22 February 1962



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## The role of dyhydration



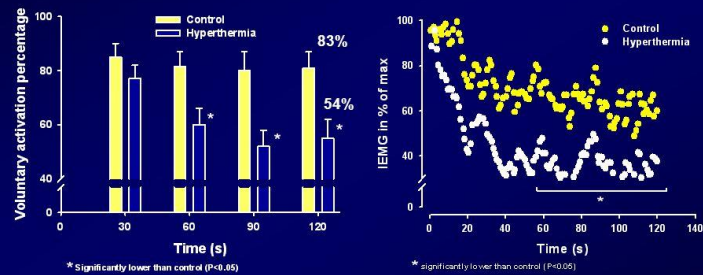
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## The role of CNS

### Hyperthermia Reduces Voluntary Muscle Force Activation

Exercise to exhaustion (60%VO<sub>2max</sub>) in hot or temperate;  
sustained MVC knee, voluntary activation by electrical stimulation to nervus femoris  
(Control T<sub>c</sub> = 38°C; Hyperthermia T<sub>c</sub> = 40°C)

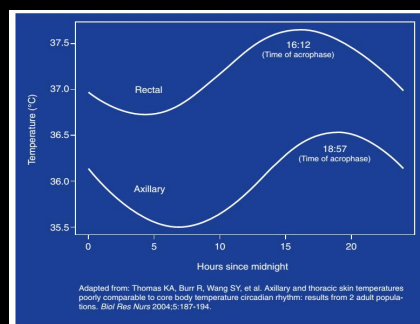


Nybo & Nielson JAP 2001

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## Disunity 1 - Πρώτη Διχογνωμία

- ❖ Where is the right place to measure core temperature ??
- ❖ Which temperature is more crucial?



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## Selective brain cooling?

- “Why people sweat more in the face? (Aristotle)”
- “Should it be that head is rich in fluids, pores, veins, and vessels .” (Aristotle) **or**
- “Should it be that selective brain cooling does exist in humans as Cabanac (1978) heretically alleges .”
- During the last 25 years 102 articles have been published investigating the question: “Is tympanic temperature representative index of regulated brain temperature? ” 59% of these articles provide positive answer whereas the resting 41% give an emphatic no.

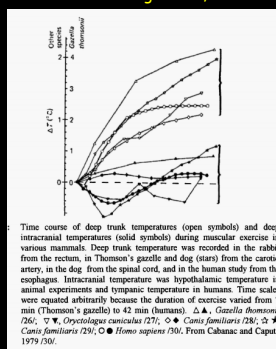
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### SELECTIVE BRAIN COOLING AND THERMOREGULATORY SET-POINT

Michel Cabanac

Département de Physiologie, Faculté de Médecine, Université Laval  
Quebec QC, Canada G1K 7P4

Freund Publishing House, 1998



*J. Physiol.* (1979), 286, pp. 255–264  
With 4 text-figures  
Printed in Great Britain

#### NATURAL SELECTIVE COOLING OF THE HUMAN BRAIN: EVIDENCE OF ITS OCCURRENCE AND MAGNITUDE

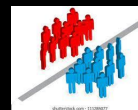
By M. CABANAC AND M. CAPUTA\*

From the Université Claude Bernard, Faculté de Médecine Lyon Sud,  
Laboratoire de Psychophysiologie (L.A. C.N.R.S. No. 181),  
B.P. 12, 69600 Oullins, France

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## Disunity 2 - Δεύτερη Διχογνωμία The mystery of active vasodilation



TEMPERATURE  
2017, VOL. 4, NO. 1, 41–59  
<http://dx.doi.org/10.1080/23328940.2016.1200203>

COMPREHENSIVE REVIEW

### Current concepts of active vasodilation in human skin

Brett J. Wong and Casey G. Hollowed

Department of Kinesiology & Health, Georgia State University, Atlanta, GA

hypothesized to operate through a co-transmission mechanism. To date, mechanisms of cutaneous active vasodilation remain equivocal despite many years of research by several productive laboratory groups. The purpose of this review is to highlight recent advancements in the field of active vasodilation.

dilation is the co-transmission theory.<sup>1</sup> The original proposition for this theory suggested that acetylcholine and an unknown co-transmitter are released from sympathetic nerve terminals, where acetylcholine mediates sudomotor activity (sweating) and the unknown neurotransmitter mediates cutaneous vasodilation. While the general notion of acetylcholine mediating a large portion of sudomotor activity is fairly well established, identification of the unknown co-transmitter responsible for cutaneous vasodilation has proven to be elusive.

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## The mystery of active vasodilation



- Increased blood flow during heating is of reflex origin and is mainly directed to the Skin
- The reflex is of sympathetic nature
- Cutaneous vasodilation (active vasodilation) and sweating appear to occur simultaneously
- Both increases may be mediated by cholinergic mechanisms

What is the nature of the vasodilator (s)?????

NO??

Histamine??

Prostaglandins???

Neurokinin - ???

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## Disunity 3 - Τρίτη Διχογνωμία

### Does thermoregulation drives sleeping or vice versa?



#### "Why people sweat more while sleeping?"

"Should it be attributed to antiperistasis, a phenomenon where heat is compressed from the surrounding cold. Indeed, internally accumulated heat extracts (body) fluids." (Aristotle)

"It has found that onset of sleep is characterized by a wave of sweating which however fades away when body temperature drops (Henane et al. (1977)). Sleep is associated with consolidated inactivity, which results in decreased heat production and thus human body has the opportunity to dissipate heat during wakefulness" (Heller et al., 1996).

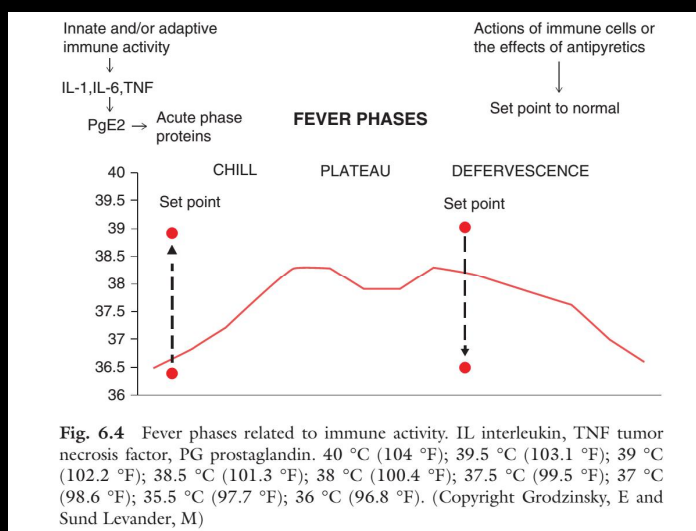


Thus, it appears that this ~~of~~ deployed scientists for

The humoral theory understood sweating as a means of excreting an excess or surplus from the body in order to restore balance. As fevered individuals began to recover, feel cooler, and indeed seem cooler to the observer's hand when they sweated, it was believed that the offending humors were leaving them in the sweat. Hence, according to the humoral

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## Set point: Is it a winning or an elusive point?



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## What is regulated during exercise?

- ❖ Why core temperature is always elevated even in cold environment
- ❖ Why fatigue coincides with a individual core temperature
- ❖ Why activation of heat dissipating mechanisms fall behind the activation of heat generating mechanisms

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**Invited Review**

*J Appl Physiol* 100: 1332–1337, 2006; doi:10.1152/jappphysiol.01068.2005.

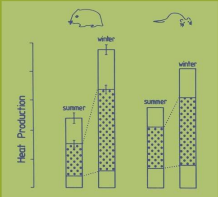
**HIGHLIGHTED TOPIC | A Physiological Systems Approach to Human and Mammalian Thermoregulation**

A theoretical consideration of the means whereby the mammalian core temperature is defended at a null zone

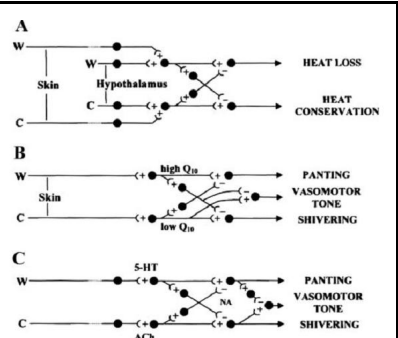
**John Bligh**  
Little Gault, High Street, Harston, Cambridge, United Kingdom

J. Bligh K. Voigt (Eds.)

## Thermoreception and Temperature Regulation



Springer-Verlag



**Fig. 2.** Three propositions of the relationships between thermosensor and thermocorrecting effectors that were derived quite independently from quite different considerations. *A*: the interpretation by Wyndham and Atkins (21) of studies of homeothermy in humans [as reexpressed by Bligh (2)]. *B*: a neuronal model by Hammel (9, 10) based largely on unit activity studies. *C*: the neuronal model of Bligh et al. (4) and Bligh (2) based on the central effects of putative transmitter substances on the homeothermy of sheep. 5-HT, 5-hydroxytryptamine; NA, norepinephrine; ACh, acetylcholine.

*J Appl Physiol* • VOL 100 •

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## Is there any inhibition?

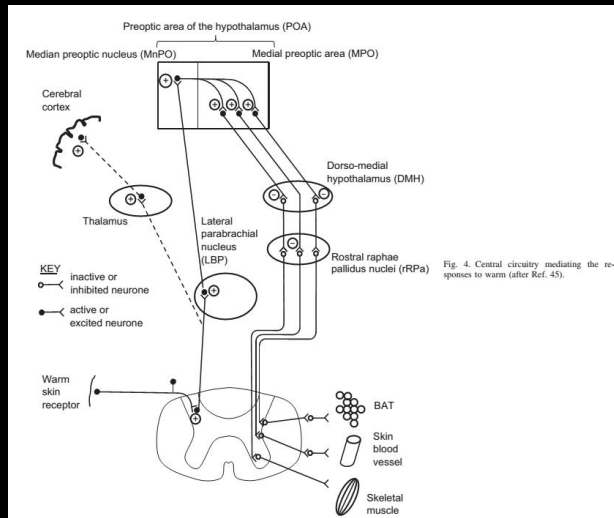


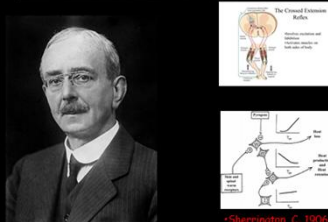
Fig. 4. Central circuitry mediating the response to warm (after Ref. 45).

Charkoudian N. Skin blood flow in adult human thermoregulation: how it works, when it does not, and why. *Mayo Clin Proc* 78: 603–612, 2003.

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## Cross inhibition

Professor Charles Scott Sherrington



Sherrington C, 1906

### Is there any experimental evidence?

- The possible central role of GABA in thermoregulation in the sheep
- Injections of GABA and its agonist muscimol into a lateral cerebral ventricle of sheep depressed both evaporative heat loss (40 and 55% respectively) at 41°C ambient temperature ( $T_{\text{a}}$ ) and metabolic heat production (27 and 32% respectively) at 3°C  $T_{\text{a}}$ . The intracerebroventricular (ICV) injection of the GABA antagonist, bicuculline (BIC), prior to an ICV injection of either pentobarbitone (5-HI) or carbonyl choline (CCh) prevented the inhibitory effects of an ICV injection of 5-HI at 3°C or CCh at 41°C on heat production and heat loss respectively (Sigh et al., *J. Physiol. Lond.* 212, 377–392 (1971)).
- Simultaneously the inhibitory effects of hot and cold ambient temperatures on heat production and heat loss, respectively, were blocked and both the heat production and heat loss pathways were activated concurrently. These results suggest that GABA may be a terminal transmitter of reciprocal inhibition between the two major thermoreceptor to thermoregulatory effector pathways in the sheep.

MS Roman

Smith DM, Bigh J., *J of Thermal Biology*, 1993

Review by Bigh J., *Humanae Therapeutics: An Integrative Thesis*, *J. Thermal Biology*, 1998.

Is this accepted?



Reciprocal Cross Inhibition or 'Cross - Talk'

Is there any evidence in humans? No  
How do we study this?

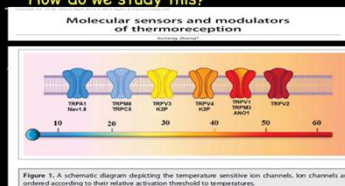


Figure 1. A schematic diagram depicting the temperature sensitive ion channels, ion channels are ordered according to their relative activation threshold to temperatures.

Molecular sensors and modulators of thermoreception

Molecular sensors and modulators by Xinyi Zhang, 2018

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# Exercise and cross inhibition

The effect of menthol application to the skin on sweating rate and the reciprocal cross inhibition theory

Exercise —→  $\uparrow$ Core rise —→  $\uparrow$ Sweat increase

Skin Cold  
TPRM8,  
menthol application —→  $\uparrow$ VO<sub>2</sub> rise  
 $\uparrow$ CV tone rise

Hypothesis: Exercise and menthol application

VO<sub>2</sub> rise, Cutaneous Vascular (CV) tone enhanced and limited Sweat Rate

(Simpfendorfer et al. 1986, Smith et al. 2000)

The effect of menthol application to the skin on sweating rate and the reciprocal cross inhibition theory

Table 1 Age, anthropometric values and maximal oxygen uptake (VO<sub>2max</sub>) for the physical education students (CON, n = 8) and the swimmers (SW, n = 8)

	CON	SW
Age (years)	27.7 (3.4)	21.3 (2.1)
Stature (cm)	182.4 (6.9)	181.8 (7.0)
Body mass (kg)	73.9 (5.6)	76.6 (5.2)
Body fat (%)	8.4 (2.1)	11.8 (2.7) <sup>#</sup>
VO <sub>2max</sub> (mL kg <sup>-1</sup> min <sup>-1</sup> )	42.1 (3.1)	46.7 (4.2) <sup>#</sup>

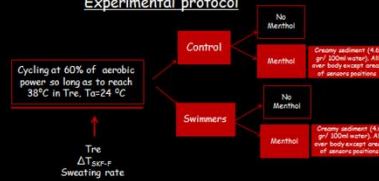
Values are means (SD)

<sup>#</sup> Significant differences between groups,  $p < 0.05$ ;  $\# p = 0.07$

Source: J. J. Botanis, D. K. Katsoulis, D. K. Katsoulis, The effect of menthol application to the skin on sweating rate, during exercise, in humans and animals, 2018

## Methods

### Experimental protocol



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# Exercise and cross inhibition

The effect of menthol application to the skin on sweating rate and the reciprocal cross inhibition theory

Results:

Table 2 Cardiovascular and thermoregulatory variables during cycling for the physical education students (CON, n = 8) and the swimmers (SW, n = 8), with (M) and without (N) menthol application

	CON	SW	CON	SW
VO <sub>2</sub> (ml min <sup>-1</sup> )	1778 (156)	1887 (158)	1842 (166)	1982 (166)
VO <sub>2</sub> (ml kg <sup>-1</sup> min <sup>-1</sup> )	24.0 (2.1)	24.5 (2.1)	25.5 (2.2)	26.0 (2.2)
HR (beats min <sup>-1</sup> )	157 (16)	158 (15)	158 (15)	159 (15)
HR (beats kg <sup>-1</sup> min <sup>-1</sup> )	201 (16.5)	201 (16.5)	201 (16.5)	201 (16.5)
Threshold for the increase (ml)	6.3 (1.0)	4.3 (1.3) <sup>#</sup>	5.5 (2.2)	2.2 (1.3) <sup>#</sup>
Time to reach 38°C (min)	22.0 (3.7)	18.0 (3.7) <sup>#</sup>	18.0 (3.7)	18.0 (3.7) <sup>#</sup>
Time to reach 38°C (min)	22.0 (3.7)	18.0 (3.7) <sup>#</sup>	18.0 (3.7)	18.0 (3.7) <sup>#</sup>
Threshold for sweating (ml)	12.0 (1.5)	7.5 (2.2) <sup>#</sup>	11.5 (2.2)	7.5 (2.2) <sup>#</sup>
Time to reach 38°C (min)	22.0 (3.7)	18.0 (3.7) <sup>#</sup>	18.0 (3.7)	18.0 (3.7) <sup>#</sup>
Threshold for sweating (ml)	12.0 (1.5)	7.5 (2.2) <sup>#</sup>	11.5 (2.2)	7.5 (2.2) <sup>#</sup>
Peak sweating rate (ml min <sup>-1</sup> kg <sup>-1</sup> )	0.47 (0.04)	0.35 (0.04) <sup>#</sup>	0.41 (0.04) <sup>#</sup>	0.35 (0.04) <sup>#</sup>
Peak sweating rate (ml min <sup>-1</sup> kg <sup>-1</sup> )	0.47 (0.04)	0.35 (0.04) <sup>#</sup>	0.41 (0.04) <sup>#</sup>	0.35 (0.04) <sup>#</sup>

Values are means (SD)

<sup>#</sup> Significant difference from CON,  $p < 0.05$ ; <sup>#</sup> Significant difference from SW,  $p < 0.05$

The effect of menthol application to the skin on sweating rate and the reciprocal cross inhibition theory

Exercise —→  $\uparrow$ Core rise —→  $\uparrow$ Sweat increase but decrease

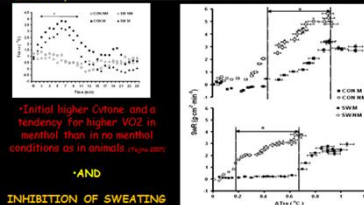
Skin Cold  
TPRM8,  
menthol application —→  $\uparrow$ VO<sub>2</sub> rise  
 $\uparrow$ CV tone rise

Hypothesis: Exercise and menthol application

VO<sub>2</sub> rise, Cutaneous Vascular (CV) tone enhanced and limited Sweat Rate

(Simpfendorfer et al. 1986, Smith et al. 2000)

The effect of menthol application to the skin on sweating rate and the reciprocal cross inhibition theory



Initial higher CV tone and a tendency for higher VO<sub>2</sub> in menthol than in no menthol conditions as in animals (Katsoulis et al. 2018)

AND

INHIBITION OF SWEATING (rate and threshold) in the menthol conditions

The effect of capsaicin application to the skin at rest and the reciprocal cross inhibition theory



Effects of capsaicin application to the skin during resting exposure to hypobaric and warm conditions  
Botanis P., Miliotis P., Kounalakis S., Koskolou G., Gelados N., Scan J Med & Sc. in Sports, 2018

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## Is there any significance?



### Non-steroidal anti-inflammatory drugs on core body temperature during exercise: A systematic review

Dawn M. Emerson <sup>a,\*</sup>, Stephen CL. Chen <sup>b</sup>, Melani R. Kelly <sup>a</sup>, Bryant Parnell <sup>c,1</sup>, Toni M. Torres-McGehee <sup>c</sup>

<sup>a</sup> Department of Health, Sport, and Exercise Sciences, University of Kansas, KS, 66045, USA

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#### ABSTRACT

**Background/Objective:** Because of their anti-pyretic effects, some individuals prophylactically use non-steroidal anti-inflammatory drugs (NSAIDs) to blunt core temperature (T<sub>c</sub>) increases during exercise, thus, potentially improving performance by preventing hyperthermia and/or exertional heat illness. However, NSAIDs induce gastrointestinal damage, alter renal function, and decrease cardiovascular function, which could compromise thermoregulation and increase T<sub>c</sub>. The aim of this systematic review was to evaluate the effects of NSAIDs on T<sub>c</sub> in exercising, adult humans.

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## Data which are not entailed in a theory are apples on the ground of an orange field

*Am I right or, as David Hume suggested, reaching at a final causal relation is an impossible task?*

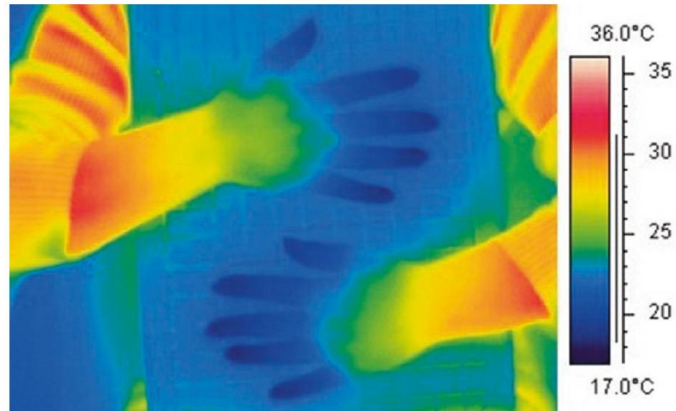
Eternity of Science



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## ΕΥΧΑΡΙΣΤΩ



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