THE BRAIN DOESN’T LIKE IT HOT

by Brigitte Delange

An adequate body temperature is essential for our survival. Strict control mechanisms make sure the temperature stays within a limited range. When the temperature within the body gets too high or too low normal biochemical processes are no longer possible and death follows. Minor changes can have a positive effect. A slightly higher brain temperature heightens cognition. Cooling of the brain seems to help prevent damage following a stroke. There might even exist a link between brain temperature and emotion.

The body constantly produces heat and exchanges it with the environment. Apart from basal metabolic heat production, thermogenesis occurs via food and physical activity and heat is produced through metabolism modulated by hormones, emotions, and medication. Most body heat is generated in deep organs like brain, liver, and heart and due to the contraction of skeletal muscles. Heat exchange in humans occurs through convection and radiation via the skin blood flow and through evaporation in the form of sweating. Thermoregulation is one of the pillars of homeostasis, the process of maintaining the normal body state. The normal body temperature of humans has a set point of about 37ºC. It fluctuates over the day, reaching its lowest point around 4 AM and its highest between 4 and 6 PM. The difference is about half a degree Celsius

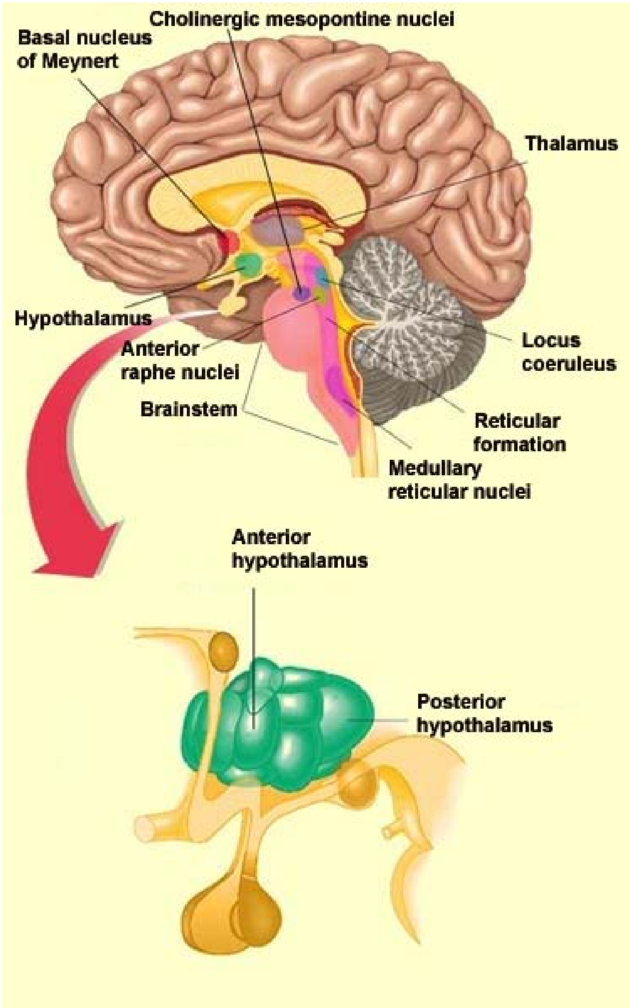
Regulation of body temperature involves integration of autonomic, endocrine, and skeletomotor responses. Information about the prevalent temperature comes from peripheral temperature receptors in skin, spinal cord, and viscera and from central receptors in the brain, mainly in the hypothalamus. The firing of neurons in the hypothalamus is highly dependent on the local temperature, which is affected by the temperature of the flowing blood. Warm-sensitive neurons and cold-sensitive neurons integrate thermal information from peripheral and central receptors.

The hypothalamus operates in two ways: directly on the internal environment and indirectly by providing information about the internal environment to higher neural systems.

The anterior hypothalamus mediates decreases in the body temperature. Measures include dilation of blood vessels in the skin, panting, and sweating. The posterior hypothalamus mediates increases in the body temperature and prompts responses that generate or conserve heat, like constriction of blood vessels and shivering.

The hypothalamus also controls endocrine responses to temperature challenges. Long-term exposure to cold for instance enhances the release of thyroxin, which increases body heat by increasing tissue metabolism.

Serotonergic pathways play important regulatory roles in hypothalamic thermoregulatory control. Serotonergic neurons in the raphe nuclei located along the midline of the brainstem help regulate body temperature.



A thermo genic region in the dorsomedial and paraventricular nuclei of the hypothalamus sends excitatory inputs to cell groups in the brainstem that increase body temperature. When the hypothalamus is warmed, the thermo genic system is turned off and the body temperature falls.

Sleep also appears to have thermoregulatory functions. Body and brain temperatures are reduced during sleep. Heating the hypothalamus in animals induces sleep. This may point to a cooling function of sleep. But sleep may also be necessary for heat retention. The body temperature of sleep-deprived rats falls dramatically and they die, even when they are allowed to sleep again.

Yawning may be linked to temperature regulation as well. It possibly serves to send cooler air to the brain to help it stay alert.

Breathing through the nose contributes to the brain's cooling system too. Cooling of the mucous membranes by nose breathing influences the blood temperature in the cavernous sinus.

The internal carotid arteries, which run from the neck to the brain, are important in heat exchange. The temperature of blood in these arteries is about 1.5ºC lower compared to rectal or brain tissue temperatures. They play a role in losing heat in the blood to nearby airways and jugular veins to help cool the brain.

Malfunctioning of this cooling system may be a cause of sudden infant death syndrome, when a baby is sleeping face down. But a chemical imbalance has also been named in the cause of cot deaths. Low levels of serotonin appear to trigger changes in heart rate and body temperature.

Hyperthermia and hypothermia

Humans have the ability to adapt to a great diversity of climates. Effective thermoregulation is reduced though in hot, humid environments. When the environmental temperature is above the core body temperature, sweating is the only physiological way for humans to lose heat. High temperatures pose serious stresses for the human body. Temperatures above 40ºC can be life threatening. The brain itself can't tolerate temperatures above 40.5ºC.

Hyperthermia happens when the body produces or absorbs more heat than it can dissipate. It is usually caused by prolonged exposure to high temperatures.

Hyperthermia, during which the body temperature rises above the 37ºC set point, differs from having a fever. During fever the hypothalamus changes the body's temperature set point. This higher baseline temperature helps to fight infection as internal processes run faster, organs work more quickly, and antibodies are synthesized more rapidly. In addition many microbes are weakened or killed by an increased heat level.

High temperatures are known to damage sperm. Recently, researchers discovered that children run an increased risk of brain cancer when their father had been exposed to excessive heat from for instance a sauna or an electric blanket, prior to their conception.

Experimentally, hyperthermia is used to treat some kinds of cancer. Raising temperature causes apoptosis, programmed cell death. Hyperthermia therapy is applied locally to damage and kill cancer cells.

Hypothermia occurs when the body temperature sinks below the required temperature for normal metabolism and bodily functions. This can already start at about 2ºC below the set point temperature. It is usually caused by prolonged exposure to cold air or water.

A slightly lower body temperature may have a positive effect, as chemical processes including aging slow down. In a study, transgenic mice were given a gene that elevated the hypothalamic temperature. This made the hypothalamus lower the body temperature by 0.3 to 0.5ºC. The transgenic mice lived substantially longer than normal mice, males about twelve percent and females about twenty percent.

The effect on humans hasn't been studied. Many stories are known of children fallen into cold water and having been revived even after being unconscious for over an hour. In cold water, metabolism is lowered and the brain can withstand a longer period of hypoxia. The low temperature appears to prevent cellular damage that occurs when blood flow and oxygen are lost for a time.

Most cellular processes are strongly temperature dependent. Even a small drop in temperature seems to encourage cell membrane stability. This helps to prevent an influx of unwanted ions during an ischemic insult and helps minimize disruption to the cellular environment.

Temperature also influences synaptic function. At lower temperatures synaptic vesicle recycling is substantially slower. In addition, cooling reduces the efficacy of neurotransmitter release. Research on rat hippocampal slices showed a decline in extracellular synaptic potentials and a reduction in transmitter release.

Hypothermia may thus decrease the release of detrimental neurotransmitters and other toxic substances. It also lowers the brain's need for nutrients, including oxygen and glucose. Rewarming after cooling has been shown to trigger dendritic spine proliferation on mature neurons, which can be a sign for synaptic plasticity.

Therapeutic hypothermia is being used for medical treatments, although there is no consensus yet on its effectiveness. Cooling techniques include a cap that blows cold air across the scalp, a chilling nasal spray, and an icy lung injection. Targeting only the brain is the preferred method, as cooling the whole body increases the risk of infection and pneumonia. A drop in temperature of about 4ºC is necessary.

Brain cooling appears to have therapeutic potential for epilepsy, stroke, asphyxia, and other neurological diseases. It also prevents brain damage after heart attacks and can control intracranial pressure after an ischemic stroke as it reduces swelling. Cooling is an interesting technique for treatment of focal epilepsy. When applied very close to the epileptogenic focus, cooling terminates neocortical seizures.

In baby’s deprived from oxygen at birth, cooling the brain helps to prevent brain damage as it stops apoptosis. The method only works for moderate brain injuries. It may also be an option to reduce the negative effects of anesthesia. Anesthetic drugs trigger apoptosis and anesthesia during brain development may contribute to behavioral and developmental delays. Further study is necessary to find out whether the normal, healthy apoptosis process during brain development will start up again after terminating hypothermia.

Thermoregulation and emotion

A strong relationship exists between body temperature and performance in humans. Cognitive function is improved by increasing body temperature slightly above normal and reduced by a slight decrease. An increased temperature enhances working memory, subjective alertness, and visual attention. This could be explained by the fact that changes in brain temperature alter synaptic function. A higher temperature results in faster transmission.

These effects concern only very small changes within the optimal thermal zone. Extreme heating or cooling impairs performance.

An interesting research link would be the effect of living in extreme warm or extreme cold climates. It appears that this may impair cognitive performance despite the protective environments humans have been able to construct. What can be done to protect the developing brain from these extremes?

Temperature also affects human emotion. This is most clear in high ambient temperatures, which are known to generate more aggression. Heat waves result in elevated numbers of deaths, suicides and murders.

But there also appears to be a link between body temperature and emotion. The hypothalamus has a function in both thermoregulation and emotion. Some behavioral and physiological aspects, such as shivering, panting, and sweating, occur not only during thermoregulation, but with certain emotions as well, for instance fear and anxiety or excitement. Thermo sensitive neurons in the hypothalamus also change their activity in response to emotional stimuli. Facial muscles may play a role in this link between temperature and emotion. When they stretch or tighten the blood flow in the cavernous sinus changes. This raises or lowers the temperature of the blood flowing in the brain and activates neurons in the hypothalamus. Variations in the cerebral temperature might influence the release or blocking of emotion-linked neurotransmitters. Blowing air in the nasal cavity gives an emotional response: warm air generates aversive feelings and cool air pleasant feelings. People with a nasal congestion feel discomfort. Packing of the nasal airways results in severe distress in spite of the fact that sufficient oxygen is reaching the brain via mouth breathing. A failure to cool the cavernous sinus via air intake in the nasal cavity may be the cause for these negative feelings.

Further research should give more insight into the contribution of brain temperature to emotion. There might exist a link with depression. The neurotransmitter serotonin plays a role in both depression and thermoregulation. Maybe brain temperature in individuals suffering from depression is higher than normal, which would add to negative feelings.

References

BBC health news, http://news.bbc.co.uk/2/hi/health.

Coren, Stanley. *Sleep Thieves, an eye-opening exploration into the science and mysteries of sleep*. New York (US): Free Press Paperbacks, 1997, pp 57 and 169.

Gazzaniga, Michael and Richard Ivry and George Mangun. *Cognitive neuroscience, the biology of the mind* 3rd ed. New York (US): W.W. Norton & Company, 2009, p 82-84.

Kandel, Eric and James Schwartz and Thomas Jessell. *Principles of Neural Science* 4th ed. New York (US): McGraw-Hill, 2000, pp 893, 896, 945 and 998-1002.

Kirov, S. and L. Petrak, J. Fiala and K. Harris. *Dendritic spines disappear with chilling but proliferate excessively upon rewarming of mature hippocampus*. Neuroscience, 2004.

Micheva, Kristina and Stephen Smith. *Strong effects of subphysiological temperature on the function and plasticity of mammalian presynaptic terminals.* Journal of Neuroscience, 2005.
Passlick-Deetjen, Jutta and Eva Bedenbender-Stoll. *Why thermosensing? A primer on thermoregulation*. Nephrol Dial Transplant, 2005.
Saper, Clifford. *Hypothalamus*. www.scholarpedia.org, 2009.
ScienceDaily. *Cooling the brain prevents cell death in infant mice exposed to anesthesia*. www.sciencedaily.com, 2008.
Steinberg, Gary. *Brain cooling shows promise as technique to prevent long-term stroke damage*. Journal of Neurosurgery, 2001.
Vroon, Piet. *Wolfsklem*. Amsterdam (NL): Ambo, 1992, pp 98-100.
Wikipedia, www.wikipedia.com
Wright, Kenneth and Joseph Hull and Charles Czeisler. *Relationship between alertness, performance and body temperature*. American Journal of Physiology, 2002.
Yang, X.F. and D.W. Duffy, R.E. Morley and S.M. Rothman. *Neocortical seizure termination by focal cooling: temperature dependence and automated seizure detection*. Epilepsia, 2002.
Yang Xiao-Feng, and Yannan Ouyang, Bryan Kennedy and Steven Rothman. *Cooling blocks rat hippocampal transmission by a presynaptic mechanism*. Journal of Physiology, 2005.
Zajonc, R.B. and Sheila Murphy and Marita Inglehart. *Feeling and facial efference: implications of the vascular theory of emotion*. Psychological Review, 1989.

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