On Brain Temperature Regulation - From Rats to Humans: Size Matters

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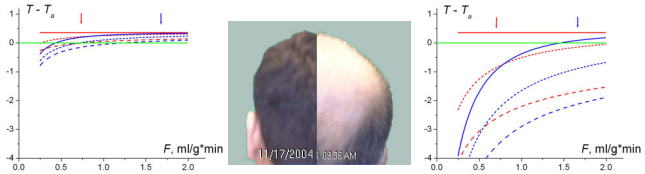
Introduction: Numerous studies of functional activation-induced changes in brain temperature in animals and humans have demonstrated a great variety of responses. Both increases and decreases in temperature were registered. Besides, a magnitude of the effect ranges from several milli-degrees to degree of Centigrade. The nature of this variability has not been understood yet and caused much discussion at the ISMRM meetings. This subject is important as temperature affects brain metabolism and may influence brain response to functional activation. Changes in the temperature can also alter the fMRI signal decay rate [1], hence should be taken into account in the interpretation of fMRI data, especially attempting quantification of brain hemodynamic responses. Herein, we propose a quantitative analytical theory of brain temperature regulation in humans and small animals and demonstrate that in small animals, as compared to humans, heat exchange with the environment can reduce brain temperature to the level below that of the body, globally reversing the sign of brain temperature response upon functional activation. In addition to the "size", other parameters crucially influencing "temperature effect" are blood flow and the intensity of heat exchange with the environment.

Theory: Our analysis is based on a standard bio-heat equation for temperature distribution $T(\mathbf{r})$, $k\nabla^2 T-\beta(T-T_a)+q=0$, with the boundary condition at the surface, $-k\,\partial T/\partial \mathbf{n}=h\cdot(T-T_e)$. Here k is the tissue thermal conductivity, $\beta=\rho\rho_b c_b F$, ρ is the tissue density, ρ_b and c_b are the density and specific heat of blood, T_a is the arterial blood temperature, F is blood flow, q is the rate of metabolic heat production, T_e is the ambient temperature and h is the effective heat transfer coefficient from brain to environment; $\partial/\partial\mathbf{n}$ is the derivative along the normal to the surface. Since we are interested in a general picture of the temperature distribution and its dependence on the brain size, we consider brain as a sphere of radius R. In this model, a solution to the bio-heat equation can be written in the form: $T(r)=T_a+T_m-(T_a+T_m-T_e)\cdot Z^{-1}\cdot\sinh(r/\Delta)/r,\qquad Z=\sinh(R/\Delta)+(k/hR)\cdot\left[R/\Delta\cdot\cosh(R/\Delta)-\sinh(R/\Delta)\right],\qquad (1)$

where, $T_m=q/\beta$ is a positive metabolic temperature shift from the arterial temperature due to the internal brain heat generation; $\Delta=(k/\beta)^{1/2}$ is a flow-dependent characteristic length. Under normal conditions in humans and rats, Δ is about 3.5 and 2 mm, respectively (normal gray matter blood flow is 0.67 and 1.7 ml/g/min in humans and rats, correspondingly). It means that the temperature distribution in the normal human brain ($R\approx 7\text{cm}$) is practically homogeneous, $T=T_a+T_m$, except of the surface "screening shell" of thickness $\Delta<<R$ [2]. In small animals, like rats, the shell's thickness is comparable with the brain radius $R\sim 1\text{cm}$ and, therefore, the temperature distribution in the brain is substantially inhomogeneous. The metabolic temperature shift under normal conditions, is about 0.3-0.4°C [1]. According to Eq. (1), major parameters defining temperature distribution in the brain are: brain size R, blood flow F, and effective heat transfer coefficient h. A standard value of h, typically used in literature for radiation contribution, is $4\cdot10^{-4}\text{W/(cm}^2\cdot\text{°C)}$. However, there are other physical mechanisms contributing to heat exchange (evaporation, heat conduction through skull and CSF, blood flow through the scalp etc. - see quantitative analysis in [2]). In Figure, we show the flow dependence of the difference between the brain and body (arterial blood) temperature $\Delta T=T-T_a$ (°C) in the center of the brain (solid lines), at the brain surface (dashed lines) and on the border of the screening shell (distance Δ from the brain surface, short-dashed lines) for humans (red lines), $R_h=7\text{cm}$, and for rats (blue lines), $R_r=1\text{cm}$, for two values of the parameter h: $4\cdot10^{-4}\text{W/(cm}^2\cdot\text{°C)}$ (left panel), and $3\cdot10^{-3}\text{W/(cm}^2\cdot\text{°C)}$ (right panel). These parameters roughly correspond to a hair-covered head and a bold head. We also used $T_a=37°C$, $T_e=23°C$, $k=5.65\cdot10^{-3}\text{W/(cm}\cdot\text{°C)}$. The green line corresponds to $\Delta T=0$. Positions of physiological parameters for humans and rats are indicated by the red and blue arrows, respectively.



Discussion: One can see that at the center of the human brain, ΔT is practically independent of blood flow and h and is equal to T_m. For rats, however, the result is very different – temperature in the center of the brain can be readily decreased below arterial temperature by either increasing heat exchange with the environment or decreasing the blood flow (i.e. anesthesia). Temperature at the surface of human and rat brain dramatically depends on h : for $h=4\cdot10^{-4}\text{W/(cm}^2\cdot\text{°C)}$ surface variation of ΔT doesn't exceed several tens of °C, whereas for $h=3\cdot10^{-3}\text{W/(cm}^2\cdot\text{°C)}$, this variation reaches several degrees of Centigrade.

Conclusion: As temperature of incoming arterial blood under normal physiological conditions is cooler than the brain temperature, and oxygen consumption increases in functionally-activated brain regions less than the blood flow [3], brain temperature locally decreases upon functional activation [1]. This effect can be reversed near the brain surface where temperature falls below arterial temperature [4]. Equation (1) predicts conditions when such a reversal effect can be realized as function of the relevant parameters. It is demonstrated herein that in the same subject under different physiological and especially external conditions, one can expect substantially different brain temperature response to functional activation.

Acknowledgement: Supported by NIH grant R01 NS 41519

References: 1. D. A. Yablonskiy, J. J. H. Ackerman, M. E. Raichle, PNAS **97**, 7603 (2000). 2. A. L. Sukstanskii, D. A. Yablonskiy, J. Therm. Biol. **29**, 583 (2004). 3. P. Fox, M. Raichle, Proc. Natl. Acad. Sci. USA **83**, 1140 (1986). 4. C. M. Collins, M. B. Smith, R. Turner, J Appl Physiol **97**, 2051 (2004).