Theoretical Model of Human Brain Temperature Distribution During Functional Activation

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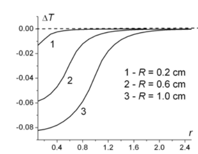
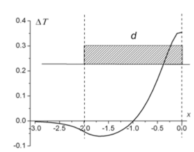
Introduction: Temperature distribution in the brain changes upon functional activation. This effect should be taken into consideration in fMRI because it leads to changes in the brain metabolism and, as a result, to changes in the R_2^* decay rate of fMRI signal [1]. A basic analytical theory of this phenomenon was developed in [1], where it was shown that a disproportional increase in the blood flow as compared to oxygen consumption within an activated area [2] results in modification of the tissue energy balance and consequently in changes of temperature distribution in the activated area. As shown in [1], in deep brain regions, functional activation leads to corresponding temperature decrease. However, this situation may be different if an activated area is close to the brain surface [3]: heat exchange with the environment may lead to inhomogeneous temperature distribution in the vicinity of the surface and may actually result in activation-induced temperature increases rather than decreases. This conclusion was reached in [3] by means of a rather sophisticated computer model of human brain temperature regulation. Recently, we have proposed a simple analytical model of human brain temperature regulation [4] that captures major mechanisms affecting temperature distribution in a human head. Herein we utilize this model to theoretically analyze how the size and position of the activated area influence the temperature change in the brain during functional activation and also how this change depends on the relationship between changes in the blood flow and oxygen consumption.

Theoretical Approach: Our analysis is based on the standard bio-heat equation for temperature T distribution: $k\nabla^2 T - \beta(T - T_a) + q = 0$, where 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, and q is the rate of metabolic heat production. At rest, the temperature distribution in the normal human brain is practically homogeneous, $T = T_0 = T_a + T_{m0}$, except of the surface "screening shell" of thickness $\Delta = \kappa_0^{-1}$, $\kappa_0 = (\beta_0/k)^{1/2}$ [4], where $T_{m0} = q_0/\beta_0$ is a positive metabolic temperature shift (MTS) from the arterial temperature due to the internal brain heat generation. Under normal conditions in humans Δ is about 2-3 mm. From this perspective, it is convenient to divide the brain at rest into two areas – a *temperature homogeneous core* and a *screening shell* where temperature distribution is substantially inhomogeneous.

Functional Activation in the Temperature Homogeneous Core: First, we consider an activated area as a sphere of radius R positioned in the homogeneous core of the brain. Upon functional activation, the parameters F and q in the activated area increase, $F_1 > F_0$, $q_1 > q_0$, and a temperature distribution becomes non-uniform: $T(r) = T_a + T_{m1} - (T_{m1} - T_{m0}) \cdot A_1 \cdot \sinh \kappa_1 r / r$ within the activated area, and $T(r) = T_a + T_{m0} + (T_{m1} - T_{m0}) \cdot A_2 \cdot \exp[-\kappa_0 (r - R)]/r$ outside. Here r is a distance from the center of the activated area, $T_{m1} = q_1/\beta_1$, $\kappa_1 = (\beta_1/k)^{1/2}$, $A_{1,2}$ are coefficients depending on $\kappa_{0,1}$ and R. The parameter $\Delta = \kappa_0^{-1}$ defines a characteristic size of the temperature inhomogeneity in the surrounding tissue. In the human brain, this size (2-3 mm) may be comparable with the size of the activated area. The change in the temperature distribution $\Delta T(r) = T(r) - T_0$ is shown in Fig.1 for typical values of the parameters: $T_a = 37°C$, $k = 5.65 \cdot 10^{-3}\,\mathrm{W/(cm \cdot °C)}$, $q_0 = 15.6 \cdot 10^{-3}\,\mathrm{W/cm^3}$, $F_0 = 1.2 \cdot 10^{-2}\,\mathrm{ml/(g \cdot sec)}$ and different radii of the activated area. We also assumed that upon activation, blood flow and metabolic heat generation increased by 50% and 10%, respectively. These parameters correspond to MTS $T_{m0} = 0.36°C$ and $T_{m1} = 0.26°C$. It is important to note that i) temperature in the activated area decreases; ii) temperature decreases also in a surrounding tissue of thickness Δ; iii) the absolute value of the temperature change crucially depends on the relationship between the size of an activated area R and the parameter Δ: if the activated area is bigger than Δ (curve 3), the temperature within the area practically coincides with $T_a + T_{m1}$; if, however, $R < \Delta$ (curve 1), the temperature only slightly deviates from T_0. Curve 2 represents an intermediate case.



Functional Activation near the Brain Surface: In first approximation, near the brain surface, temperature distribution can be considered as a one dimensional problem [4]. Consider the activated area (dashed in Fig. 2) of length d located in the vicinity of the brain surface ($x = 0$). The boundary condition to the bio-heat equation at the surface is used, $-kT'(0) = h \cdot (T(0) - T_e)$, where T_e is the ambient temperature and h is the effective heat transfer coefficient. In the brain at rest, the temperature monotonically increases from the surface to the center ($x < 0$), $T_0(x) = T_a + T_{m0} - A \cdot \exp(\kappa_0 x)$, where the coefficient A depends on h, κ_0 and T_e [4]. The temperature change upon activation, $\Delta T(x) = T(x) - T_0(x)$, is shown in Fig. 2 for the same values of parameters as above and, $h = 3 \cdot 10^{-3}\,\mathrm{W/(cm^2 \cdot °C)}$, $T_e = 20°C$, $d = 2\,\mathrm{cm}$. As we see, due to the surface effects, the temperature may increase upon activation in one region (deeper in the brain) and decrease in others (close to surface). Although our model is one-dimensional and doesn't include detail information on the brain structure, its comparison with that developed in [3] demonstrates a good quantitative agreement.



Conclusion: We have developed an analytical theory of brain temperature regulation and changes during functional activation. Our analysis shows that the size and the position of the activated area influence the temperature change in the brain both quantitatively and qualitatively. The temperature effect substantially depends on heat exchange with the environment and the relationship between changes in the blood flow and oxygen consumption. Predicted complex response of brain temperature to functional activation may shed a light on previously observed variability in the temperature changes in human and animal brains upon functional activation.

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