Assessment of human brain temperature during brain activation and hypercapnia by ^{1}H MRS

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Introduction Due to rapid ATP turnover and high cerebral metabolic rate of oxygen ($CMRO_2$), brain exerts high baseline heat production. The majority of heat is dissipated via the cerebral blood flow (CBF), and indeed, venous blood leaves the brain at a higher temperature than found in the incoming blood (1). Infrared scanning during craniotomy has revealed reproducible temperature increases of ~0.05 to 0.7 ^{o}C in human brain cortex (2,3). Invasive animal experiments indicate that sensory stimulations (4,5) result in brain temperature (T_{brain}) changes in either direction depending on anatomical localizations. A model of human brain temperature distribution predicts that temperature varies within the brain tissue and activation influences local temperature according to anatomical site (6). In this model, the baseline blood-to-brain tissue temperature gradient determines the direction of temperature change by activation induced perfusion increases. To clarify the effects of CBF on brain temperature (a) focal brain activation and (b) hypercapnia can be performed. Hypercapnia increases CBF without effect on $CMRO_2$, whereas brain activation leads to an increase in both CBF and $CMRO_2$. In the present study ^{1}H MRS was used to for estimation of brain temperature exploiting the frequency difference between N-acetyl aspartate (NAA) and water (Δf) at 3T in healthy volunteers during the two different conditions (a and b above).

Methods 7 healthy male volunteers (aged 24 to 51 y) gave informed consent before enrolling in the study. All MR scanning was done using a Philips Achieva 3T scanner with a SENSE headcoil for signal reception. For visual stimulation (6 volunteers) black/white checkerboard stimulation at 8 Hz was projected onto a screen in the scanner bore. T_2*-weighted fMRI was acquired from 5 axial 4 mm thick slices covering the visual cortex using single-shot gradient echo EPI and the acquisition parameters were as follows: TR 2000 ms, TE 30 ms, 128x128 data matrix, SENSE factor of 2. BOLD activation area was revealed using the Philips routine. Single voxels (17x17x10 mm^3) were positioned according to activation maps so that the volume 1 (V1) was entirely with the BOLD activated brain and volume 2 (V2) on border of the BOLD activated area. For hypercapnia (5 volunteers) inspired CO_2 ($FICO_2$) was 5% in air (purged to a heating humidifier) through a non-rebreathing circuitry (Hans Rudolph Inc, Kansas City, USA). End-tidal CO2 ($ETCO_2$) was monitored on line. ^{1}H MRS spectra from three volumes (Fig. 1) were acquired using a SENSE headcoil and the acquisition parameters as follows: TR 1600 ms, TE 60 ms, SW 1500 Hz, 2048 data points, NS 32, water suppression power set to about 50% of the power required for full suppression of water signal. Time series of 5 spectra were acquired for visual stimulation and visual stimulation of 54 sec was delivered during the third spectral acquisition. Two baseline spectra were acquired before exposure to FICO2 of 5% for for duration of two MRS spectra (104 sec), followed by four post-hypercapnia MRS acquisitions. FIDs were processed offline by exponential functions corresponding to 0.5-1.4 Hz line-broadening before Fourier transformation. Lorenzian lines were fitted using the software obtained from MRSTools Inc (Kuopio, Finland). Ten minutes before entering the magnet, body temperature was measured in each subject at three sites; oral cavity, tympanum and skin overlying the course of the temporal artery using an infrared scanner (Exergen; MA, USA). These measurements were repeated immediately after the scanning session. Temperature in the scanning suite was 21.3±0.2 ^{o}C. Wilcoxon matched-pairs signed-ranks test was used for statistical analysis. The two pre-stimulation or pre-hypercapnia spectra were averaged for common control values in each condition.

Results Fig. 1 shows the BOLD activation volume and positioning of the three ^{1}H MRS voxels (V1-V3). BOLD signal increased during visual stimulation by 5.8±1.9%. Line width for water and NAA peaks were 9.1±1.7 and 7.1±1.4 Hz, respectively and the signal-to-noise ratio for NAA was 18.9±4.4. All these spectral characteristics conform spectral quality requirements for accurate T_{brain} measurement (7). The baseline Δf translate to average T_{brain} in V1, V2 and V3 of 36.4±0.6, 36.4±0.3 and 36.2±1.7 ^{o}C, respectively. Fig. 2 shows ΔT_{brain} in V1 and V2 during the visual stimulation. In V1 the T_{brain} decrease during stimulation by 0.14±0.10 ^{o}C approached significance ($p<0.07$). In V2 T_{brain} changes were much less obvious (p values >0.65).

During $FICO_2$ of 5%, $ETCO_2$ reached a level of 9±1 mmHg above the baseline. T_2*-weighted signal intensity increased by 4.8±1.8% by 100 sec of hypercapnia throughout the gray matter as a sign of increased CBF. T_{brain} decreased by 0.37±0.57 ^{o}C during the first minute of hypercapnia followed by return to baseline over time (Fig. 2) The mean body temperature was 36.6±0.4 ^{o}C before and 36.8±0.1 ^{o}C after the MR scans

Conclusions The ^{1}H MRS results indicate a tendency towards a slight decrease in T_{brain} during visual stimulation in the visual cortex. This observation is at variance with the T_{brain} changes on the surface of the brain determined by infrared spectroscopy (2,3). The tendency towards lower T_{brain} in the brain parenchyma during activation is likely to be due to increased CBF, because hypercapnia, which is known to be associated with increased CBF, results in decrease in T_{brain} for a considerable length of time. Our preliminary data agree with the conclusions by Yablonskiy and co-workers (8) concerning activation induced T_{brain}. Whether there is heterogeneity in the T_{brain} response to activation as predicted by the model of Collins et al (6), remains to be seen.

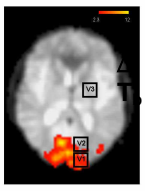

Fig.1 BOLD activation map and localization of V1,V2 and V3

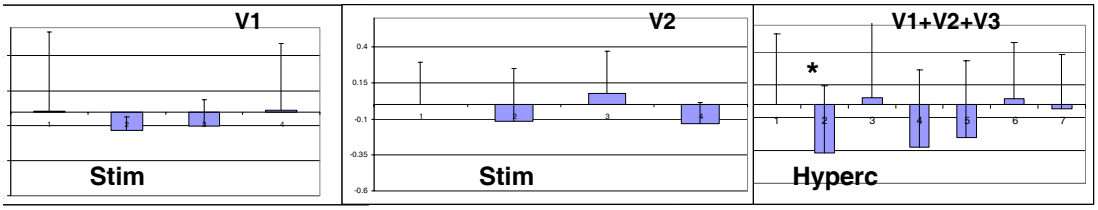

Fig. 2. Changes in T_{brain} during visual stimulation (Stim) in V1 and V2 and during hypercapnia (Hypec) in V1+V2+V3.*$p<0.02$

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