Thermoregulatory activity of the preoptic area in rats is identified with BOLD fMRI

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Introduction

The primary locus for coordination of thermoregulatory information and integration of thermoregulatory responses is the preoptic area (PO) within the hypothalamus (1). In rats, we designed an experimental protocol that modulates body temperature within the physiologically acceptable range and used it as a stimulus for a fMRI experiment to monitor PO activity upon changes in body temperature. BOLD signal intensity changes in the entire brain were also monitored to unravel the general impact of temperature changes on the BOLD contrast. We directed our focus to the role of blood vessels because the hypothalamus is highly vascularized to fullfill its thermoregulatory function. This study is exceptionally relevant for experimental fMRI studies in small anaesthetized animals which suffer from body temperature instabilities causing a drift of the BOLD signal or represent models of impaired vasculature such as in stroke affecting the hypothalamus function.

Material and Methods

Imaging was performed on a 7T MR Solutions (Guildford, U.K.) horizontal MR-system using a customized headphone RF transmission antenna and a circular surface receiver antenna (ϕ:20mm). Rats (male Albino Wistar, n=5) were put on a warm water blanket (Kent, USA) connected to a circulation system (NESLAB instruments, Newington, NH, USA) for experimental modification of the body temperature. The stimulus protocol consisted of a slow increase in T_r from 37°C to 39°C with a subsequent decrease below 38°C after which T_r was increased again up to 39°C followed by a second decrease. Acquisition parameters: 2D FLASH GE with TR/TE=150/14, FOV=20mm, acquisition matrix 128*64, flip angle 35°, averages=1, slice thickness= 1mm.

MR signal changes originate directly from 1) changes in body temperature affecting the BOLD contrast in the blood which is a general effect and from 2) focal neuronal activity as is expected to be present only in the PO. To correct for the generalized effect, we used signal correction algorithms adopted from Peeters and Van der Linden (2). The generalized BOLD changes source from alterations in O2 affinity, blood viscosity and the extent of their contribution is dependent on the local density of the vascular network.

But, despite the fact that the hypothalamus has a lower capillary density than cortical areas, yet larger susceptibility effects contribute to the PO BOLD contrast because large blood vessels run ventrally in the immediate vicinity of the hypothalmus. This creates an imbalance between the large susceptibility effects depicted by the BOLD signal in the PO and its true lower capillary density. Therefore the PO was corrected for changes coming from an adjacent but temperature insensitive area susceptible to equal effects of changes in oxy/deoxy hemoglobin ratios (figure 1) while the cortex (as a controle area lacking any termoreguatory function) was corrected for changes present in the entire brain slice (leaving out the hypothalamus region).

Results

There exists a negative correlation between the body temperature and the BOLD signal of an entire brain slice (figure 2A). An increase of body temperature of 2.2°C results in a BOLD signal intensity drop of 5.4%. The corrected PO signal course (figure 2B) shows a transient increase up to 9% which is initiated at Tr 38.6°C and a plateau is sustained the subsequent decrease from 39.1°C to 37.9°C.

Discussion

It is known that BOLD MRI contrast induced by brain activity reflects a combined effect of local CMRO2, CBF and CBV (4). Our paradigm of changing body temperature added an additional influencing factor *i.e.* increasing temperature reducing the oxygen affinity of hemoglobin resulting in more deoxyhemoglobin. This explains the association of decreasing BOLD signal with increasing body temperature. As a consequence, local neuronal activity as expected in the hypothalamus is masked by susceptibility changes sourcing from local vasculature. In the hypothalamus the contribution of susceptibility effects is large and we succeeded in cutting this back by applying an approved correction algorithm. The resulting PO activity is reflected by a BOLD increase during body warming from 38°C to 39°C and is in accordance with a previous study where we showed that opening of the arteriovasuclar anastomoses in the rat tail, known to be regulated by the PO, is evoked in the same temperature interval (3). The reported study not only contributes in unraveling the thermoregulatory activity of the PO but it sheds a new light on the importance of temperature changes in BOLD fMRI.

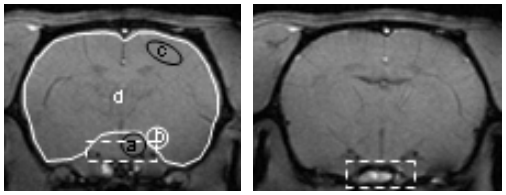

Figure 1: Two adjacent slices. The PO (a) is corrected for a local susceptibility effect sourcing from large vessels running at the ventral side (box) by using the signal intensity of (b), an adjacent thermoregulatory inactive region. The cortex (c) is corrected for the signal of an entire brain slice (d) leaving out the hypothalamus region.

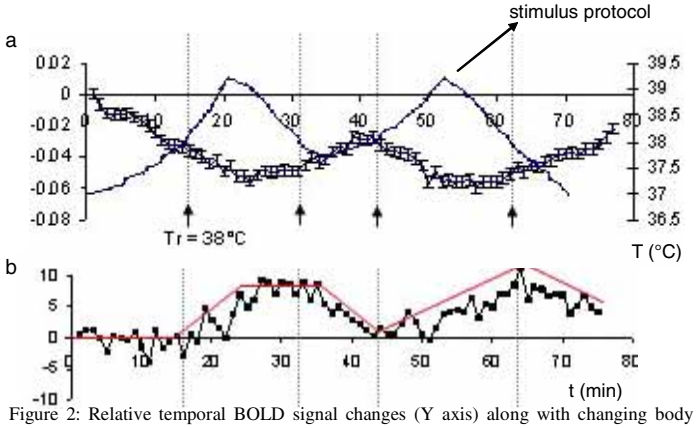

Figure 2: Relative temporal BOLD signal changes (Y axis) along with changing body temperature. In general, an increase in body temperature is associated with a decrease in BOLD as shown in (a) for an entire brain slice. After correction (Material § Methods), PO (b) reveals an increasing BOLD with increasing body temperature higher than 38°C (dashed vertical lines). When cooling down, BOLD decreases.

References:

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2. Peeters RR. 2002 MRI 20(6) 503-510
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