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Mini Review

Magnetic Resonance Spectroscopy Thermometry: A Paradigm for Monitoring Core Brain Temperature Response in Functional Spectroscopy Studies

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Abstract

Magnetic Resonance Spectroscopy (MRS) predominantly measures brain metabolism, and in recent times, has attracted research interest for interrogating brain function. Brain activation paradigms mostly used in such functional MRS studies have involved the use of a visual stimulus at a frequency of about 8 Hz. It is suspected that sustained visual stimulation at such a frequency could have physiological consequences such as headaches for research volunteers. This paper highlights the utility of MRS thermometry in measuring brain temperature changes associated with functional MRS experiments, and how this method could be routinely incorporated in standard functional MRS acquisitions. The proposed paradigm does not affect the data acquisition times of functional MRS, which is desirable for clinical studies.

Keywords: *Magnetic Resonance Spectroscopy (MRS); Thermometry; Core Brain Temperature; Functional Spectroscopy*

Background

The human brain carries out high levels of metabolic activity during its function, and the energy used for metabolism is ultimately transformed into heat. All physiochemical activities occurring in neurons are therefore influenced by heat, often measured as temperature. Even under resting conditions, brain temperature is reported to fluctuate over a relatively wide range, between 2°C and 4°C [1]. As a thermoregulator of body temperature, the brain detects changes in temperature of the environment, codifies the information and adjusts internal body temperature through effector mechanisms to either produce or lose heat to the environment depending on the estimated temperature condition of the environment [2,3]. Through these thermoregulatory and metabolic activities, the brain is reported to consume about 20% of the total body's oxygen intake when at rest [4].

There is mounting evidence to show that the temperature of the environment has some effect on brain temperature, metabolism [5], cognition [6,7] and general function [8]. Motor activity like exercise increases brain metabolism which is thought to moderately elevate core brain temperature without affecting cognitive function [5]. On the contrary, extreme high environmental temperature (which is external to the core body temperature) is reported to decrease cognitive function [6,7], which might be modified by different time scales [6]. Kiyatkin [1] presents a comprehensive review about the mechanisms underpinning temperature fluctuations in the brain.

Brain temperature monitored with thermocouples is reported to be higher than core body temperature during exercise, with or without hyperthermia, due to increased heat storage in the brain [9]. In addition, the negative effect of hyperthermia on human brain function and its sensitivity to heat is significantly reduced during head cooling [10]. These observations further confirm the role of the brain in regulating motor activities, in addition to other physiological activities in the body. Brain temperature changes may serve as a clinical indicator to many health conditions such as brain injury, stroke, trauma, headache, epilepsy, neurodegenerative and mood disorders. Centrally-mediated mechanisms of brain temperature regulation are often targeted as plausible explanation to brain temperature changes. However, little is reported about the spatial and temporal distributions of brain temperature fluctuations [11]. This is where nuclear magnetic resonance (NMR) based techniques, such as functional magnetic resonance spectroscopy, become useful.

Functional magnetic resonance spectroscopy

Brain metabolism and function are simultaneously assessed by functional magnetic resonance spectroscopy (fMRS). In its implementation, a pulse sequence on a magnetic resonance imaging (MRI) scanner acquires spectral data by exploiting the blood oxygenation level dependent (BOLD) contrast mechanism of neural response to a controlled external stimulus [12,13]. Due to the sensitivity of the technique to motion artefacts, motor neuroactivation paradigms are often undesirable; visual neuroactivation involving a stable human subject is often preferred. Spectral response to the stimulus is often recorded from the visual cortex region of the brain [12-14].

In the presence of the stimulus, neural activity increases above baseline state which is associated with increased cerebral blood flow, cerebral blood volume and metabolic rate of oxygen consumption [15]. This effect modifies magnetic susceptibility around the brain region being activated, causing the acquired spectral width to reduce, and its area and height to increase, relative to the baseline condition [12-14]. Due to its ability to acquire functional information in addition to the standard neurometabolite profile, it has been suggested that fMRS should be the technique of choice in studies aiming to elucidate detailed brain function [16], which includes thermoregulation.

Magnetic resonance spectroscopy thermometry

The necessity for brain temperature monitoring in fMRS is due to the fact that such experiments can potentially cause significantly elevated core brain temperature and other undesirable physiological effects, if not well controlled. The intensity and duration of neuroactivation could impact brain temperature and potentially induce headaches after data acquisition. In the measurement of core brain temperature, the spectra may be recorded without a stimulus; however, the effect of the stimulus on core brain temperature fluctuations may also be assessed. In both cases, the technique is known as magnetic resonance spectroscopy thermometry.

Magnetic resonance spectroscopy thermometry is a temperature measuring technique that is based on a shift in the resonance frequency of the water peak away from the spectral peak of N-acetyl aspartate [17-20]; indeed, other studies have used the creatine and choline spectral peaks as well [21-23]. The frequency difference is then calibrated into a temperature value using various calibration or regression equations [21]. Both single-voxel [17,18,21] and spectroscopic imaging [19,20] techniques have been applied in brain temperature studies employing magnetic resonance spectroscopy.

Core brain temperature monitoring in functional spectroscopy

In contrast to elevated core brain temperature caused by hotter environments, sustained visual stimulation has been observed to rather reduce visual cortex temperature [24,25]. Even though initial neural activation may raise physiological state and brain temperature above baseline limits and even above body temperature [25], continuous stimulation increases cerebral blood flow to the activated neurons, thus helping carry away the heat generated at that location. This brings down the temperature level below the initially increased temperature level. At the end of the neuroactivation, core brain temperature rises again back to baseline value, indicating brain warming post-neuronal activation [25].

It is important to mention that metabolite concentrations in brain tissue are not affected by neuroactivation [26]. However, contrary to the suggestion of reduced visual cortex temperature, a marginally elevated visual cortex temperature has been observed elsewhere [26]. The plausible explanation to this finding was that an increase in heat production would be required to balance the cooling effects of the increased blood flow. The condition for this to occur is that the amount of heat increase should be greater than or at least equal to the amount of heat produced by the complete metabolism of the increased glucose utilization that accompanies activation.

Sukstanskii and Yablonskiy [27] explain further that core brain temperature is influenced by the balance between metabolic heat production, heat removal by blood flow, and heat conductance. An offset balance results in temperature changes if there is a disproportional local increase in blood flow as compared with oxygen consumption during functional brain activity. They demonstrated that within deep brain structures, neuroactivation is associated with temperature decreases in regions of elevated blood flow (activated regions) and is associated with temperature increases in regions of reduced blood flow (deactivated regions). They concluded that superficial brain regions may show an exact opposite of this temperature effect, particularly because they are cooler than incoming arterial blood due to heat exchange with the environment.

Future Direction

Brain temperature measurement from already acquired magnetic resonance spectroscopy is straightforward and does not require additional data collection time. In fact, retrospective data acquired with or without neurostimulation can be processed to quantify the frequency offset between the water peak and the spectral peak of any one of N-acetyl aspartate, creatine or choline, and then apply published calibration models [17-21] to convert the frequency offset to temperature. This then offers an opportunity to monitor brain temperature in every functional spectroscopy study, that has the potential of causing fluctuations in core brain temperature.

Conclusion

This article presents insights into the role of magnetic resonance spectroscopy in measuring brain metabolism and function. The potential effect of functional spectroscopy on brain temperature fluctuations is discussed, for which reason there is the need for future studies to consider monitoring the effect of neuroactivation on core brain temperature changes using magnetic resonance spectroscopy thermometry, which does not require additional data acquisition time in the MRI scanner.

Conflict of Interest

The author has no conflict of interest to declare.

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