Functional magnetic resonance imaging (fMRI)-A useful tool for the assessment of hypothalamus function?

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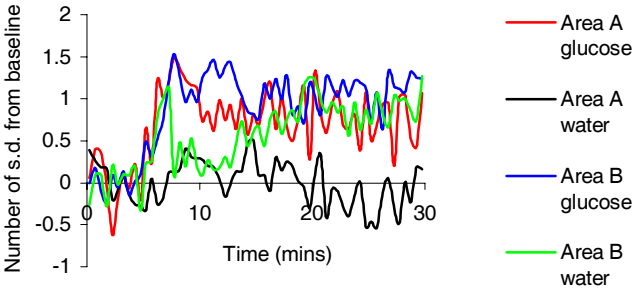
Introduction

In patients with diabetes, tight control of blood glucose is proven to reduce the risk of developing complications. This is, however, difficult to achieve in practice due to the associated increased risk of hypoglycaemia. Some studies using fMRI have implicated the hypothalamus as the centre responsible for regulation of plasma glucose concentration, energy intake and feeding behaviour. Thus, the aim of the present study was to assess whether it is possible to measure activation within the hypothalamus following glucose ingestion and to determine the time course of this activation.

Methods

Initial studies aimed at the analysis of the hypothalamus were undertaken employing a standard fMRI protocol. Previously published findings (obtaining only a single slice) had indicated that the hypothalamus would be readily identifiable with such a protocol (1,2) and thus, to extend coverage of the brain, this was repeated with a multi-slice paradigm. Subsequently, images were obtained using a 1.5 T MRI Philips scanner, T2 -weighted gradient-echo EPI sequence (voxel size = 3x3x3 mm, TR = 10 s, 40 axial slices). A group of 7 healthy individuals aged 25-40 years were recruited and attended on 2 separate occasions. Following an overnight fast, continuous scanning of the individuals was begun. The first 5 mins acted as a baseline at which point, subjects drank either 150ml of water or 75 g of glucose within a 150 ml solution. Scanning continued for a further 25 mins from the beginning of drinking, to give a total scanning time of 30 mins. Subsequently, a separate 3D high-resolution image was obtained at the same orientation to allow anatomical identification. Post acquisition, data analysis was carried out involving; a) Motion correcting the fMRI data and b) Either registering the data to a standard template after which the hypothalamus was located via a standard coordinate system or locating the hypothalamus directly from the fMRI data without the registration stage, using markers (optic chiasm, anterior commissure (AC), mammillary body (MB)). Due to problems that were identified with registration, analysis was only undertaken with areas determined via anatomical markers using a midline sagittal slice. A line was drawn between the MB and AC and a second line drawn perpendicular to the midline of the first. The regions of interest then studied were the upper anterior hypothalamus, an area that would include the paraventricular nucleus (region A) and the lower posterior hypothalamus, an area that would include the ventromedial hypothalamus (region B). Each region was then further subdivided into sub-regions of 2x2 voxels (overlapping each adjacent region by 1 voxel) and the signal time course for each assessed. The ROI with the greatest deviation from baseline for A and B for each subject was then selected for further analysis to assess any general image intensity changes between the water and glucose cases



Results

Figure 1 shows the mean signal change for all subjects in regions A and B for both water and glucose. Data are displayed as the mean of each 30 secs. There was no significant change in signal over the five-minute baseline period for any of the studies. There was a significant increase in signal for Area A glucose ($p= 0.041$) but not for Area A water ($p = 0.886$). Area B glucose showed a trend towards increase but this did not achieve significance ($p= 0.054$). There was no change in signal for Area B water ($p = 0.598$).

Discussion

. The present study has shown that it is possible to measure differences in signal intensity within the hypothalamus following glucose ingestion. Thus, there is the potential to examine the differences in time courses originating from normal and diabetic populations to assess any underlying cerebral processes taking place. However, following analysis of the techniques and the results obtained, it has subsequently become apparent that there are a number of areas that could potentially be limiting the quality of the results obtained. Registering the data to a standard template has generally been found to destroy the anatomical organisation in the region of the hypothalamus. This is partly as a result of it being predominantly cortex characteristic based and hence not necessarily appropriate for fitting deep lying structures of the brain, and partly due to signal loss due to susceptibility in the region of the hypothalamus, resulting in variable edge definition. Thus, ideally, a protocol should be used which has sufficiently high-resolution fMRI images to allow direct identification of the hypothalamus together with a minimization of susceptibility artefacts. The use of SENSE and multi-shot rather than single-shot EPI images have subsequently been assessed with a resolution of 1.6x1.6x1.6 mm, and been found to provide images of sufficient quality. An additional problem has been movement artefacts associated with drinking. In particular, a movement associated with tipping the head (in a z direction) to assist in drinking has been identified as problematic. Attempts to counter this movement with the use of specialist padding fitted to each individual have been partially successful. However, to completely remove any movement artefacts or any potential errors not removed with motion correction software it will be necessary to introduce the relevant solutions intravenously.

References

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