Delineation of the Functional Neuroanatomy of Induced Anxiety: A fMRI Study Using the Intravenous Caffeine Model

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INTRODUCTION

Common anxiety disorders include panic disorder, obsessive compulsive disorder, post-traumatic stress disorder, and social phobias. The brain circuitry associated with anxiety remains to be fully elucidated. Investigators have used a number of imaging modalities including positron emission tomography for imaging the brain during induced anxiety states. We report here the first fMRI study of an intravenous caffeine model of anxiety in the human brain.

METHODS

The model of anxiety used in this study consisted of intravenous (i.v.) infusion (slow push, lasting 30 seconds) of caffeine (3.5 mg/kg) based on the method described by Nickell and Uhde[1]. Six normal healthy volunteers abstaining from caffeine for ≥ 2 weeks prior to the study underwent the i.v. caffeine challenge protocol. 128 Echo Planar BOLD functional MR images (TE=60msec) were acquired every 3 seconds on a 1.5T GE Horizon scanner equipped with Echospeed gradients. 64 scans were obtained pre-infusion, followed by 64 scans in the post infusion phase. Anxiety rating scales were also obtained for the subjects following the protocol.

Standard data analysis methodology included the generation of statistical maps (non-parameterized KS test Z-scores) comparing the pre- and post-caffeine functional images. The statistical maps were then superimposed on the high resolution anatomical images of the individual subjects. No motion correction was performed on the image series, as motion detection analysis showed minimal in plane and through plane motion (<1mm) in these motivated subjects.

RESULTS

The statistical maps in 5 of the 6 subjects showed activation in the superior temporal cortex, the amygdala and the anterior cingulate. Figure 1 shows examples of these statistical maps superimposed on anatomical images.

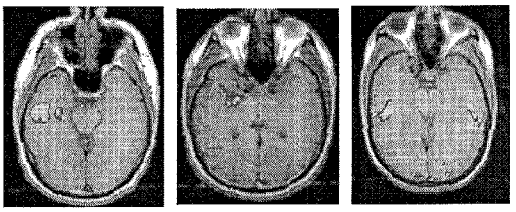

Fig 1. Map of the brain regions activated in the i.v. caffeine model of anxiety. Maps calculated as the Z-scores for non-parametric KS test between the pre- and post-caffeine groups of images.

Figure 2 shows a typical signal intensity time course for a single activated pixel in the amygdala. The figure shows an approximately 5% increase in the signal intensity from this region of the brain after the infusion of caffeine. All subjects reported increased anxiety and experienced olfactory hallucinations, typical of the i.v. caffeine challenge paradigm.

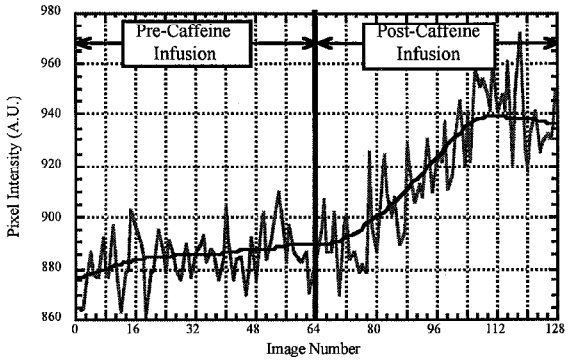

Fig 2. Intensity time course graph of an activated pixel in the amygdala.

DISCUSSION

Regions of the brain previously implicated in the functional neuroanatomy of anxiety, including the superior temporal cortex, the amygdala and the anterior cingulate [2,3], were consistently activated in this fMRI study. These initial findings indicate that fMRI will be a valuable tool for mapping the CNS circuitry of induced anxiety states and in the investigation of anxiety disorders and their effective treatment. Studies are ongoing to further establish the role of functional MRI in the study of anxiety including the correlation of these findings with regional cerebral blood flow via $^{15}O_2$-PET in these same subjects.

REFERENCES

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