Dynamic T1rho Imaging in Panic Disorder

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Introduction

We have previously reported an increase in the $T_{1\rho}$ relaxation time associated with a visual flashing checkerboard in healthy subjects, which corresponded to a local acidosis measured using ^{31}P spectroscopy [1]. These activity-evoked pH changes are of particular interest in panic disorder since pH may have a central role in this disease [2]. It has been shown by Maddock et al. [3] that subjects with panic disorder have a significant increase in lactate production as compared to controls using a flashing checkerboard paradigm, which suggests that panic disorder subjects exhibit increased acidosis with brain activation as compared to controls. In this work, we hypothesized that dynamic $T_{1\rho}$ imaging would show an increase in the magnitude of the $T_{1\rho}$ response resulting from an increased acidosis. To test this hypothesis, we imaged subjects with panic disorder and matched control subjects using pulse sequences sensitive to pH.

Methods

Thirteen subjects with panic disorder (4 males/9 females, mean age: 31.1, age range: 21-59) and thirteen matched control subjects (4 males/9 females, mean age: 30.3, age range: 23-57) underwent a multi-modal functional imaging study including BOLD, $T_{1\rho}$, and ^{31}P spectroscopic imaging. Informed written consent was obtained from subjects. A visual flashing checkerboard with a temporal frequency of 4 Hz was presented for the functional and spectroscopic imaging using a block design. For BOLD imaging, a 40 second block duration (7 blocks) was used while $T_{1\rho}$ imaging used a 24 sec duration (5 blocks). The BOLD and $T_{1\rho}$ sequences were repeated two and three times, respectively, for each subject. For ^{31}P spectroscopy, the task consisted of three blocks (baseline, activation, baseline) each with a 10min 24sec duration. Imaging was performed on a 3.0T Siemens Trio scanner (Siemens Medical Solutions, Erlangen Germany). Functional $T_{1\rho}$ images were collected using an echo-planar spin-echo sequence (TR/TE=2000/15ms, FOV=240x240mm, matrix size=64x64, and slice thickness/gap=5/1mm) with two spin-lock pulses (10 and 50ms) and B1 frequency of 256 Hz. BOLD imaging was performed by using a T_2^*-weighted echo-planar gradient-echo sequence (TR/TE=2000/30ms, FOV=220x220mm, matrix size=64x64, and slice thickness/gap=4/1mm). The ^{31}P CSI study was collected using a free induction decay acquisition (TR/TE=4000/2.3ms, FOV=240x240mm, matrix size=8x8, slice thickness=30mm, averages=16, vector size=1024). BOLD and $T_{1\rho}$ data were analyzed using standard preprocessing steps including motion correction and spatial smoothing. $T_{1\rho}$ data were preprocessed by first performing motion correction followed by $T_{1\rho}$ map generation. A general linear model was used to generate individual statistical maps and subsequently percent signal change was calculated. BOLD and $T_{1\rho}$ changes were mapped to MNI space and compared between groups. A cluster-wise threshold of $p<0.05$ (corrected for multiple comparisons) was applied to the between group differences. In the subjects with panic disorder, we investigated the relationship between the functional signal changes during the visual activation task and the magnitude of the panic symptoms assessed using the Beck Anxiety Inventory. The ^{31}P data were analyzed using the Siemens Syngo software to determine the chemical shift of the inorganic phosphate (Pi) and phosphocreatine (PCr) peaks in the ^{31}P spectra. Brain pH was estimated using the chemical shift between Pi and PCr in ppm [4].

Results

Fig 1 shows the difference between panic disorder subjects and controls for $T_{1\rho}$ (1A) and BOLD (1B) imaging. The $T_{1\rho}$ imaging shows a significant increase in the $T_{1\rho}$ relaxation rate during visual activity in the cuneus bilaterally and a significant decrease in the anterior cingulate bilaterally in panic disorder subjects as compared to controls. BOLD imaging showed a significantly reduced response in the lingual gyrus in panic disorder subjects as compared to controls. There was a trend ($p<0.06$) toward lower pH measured using ^{31}P in panic subjects as compared to controls in the baseline condition. Significant positive relationships between the Beck Anxiety Inventory and functional $T_{1\rho}$ imaging data was found in panic subjects for the following regions: left middle temporal gyrus,
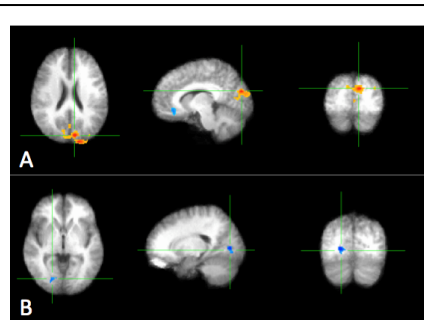

Figure 1. Comparison between panic subjects and controls. A) Difference in T1p response showing an increase in the cuneus and a decrease in the anterior cingulate. B) BOLD data shows a decrease in activation within the right lingual gyrus.
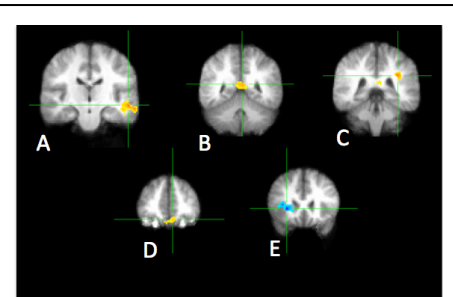

Figure 2. Relationship between the Beck anxiety inventory and the T1p response. A positive relationship is seen in the A) left middle temporal gyrus, B) bilateral posterior cingulate gyrus, C) left inferior parietal lobule, and D) bilateral medial frontal gyrus. A negative relationship is seen in the E) right insula

bilateral posterior cingulate gyrus, left medial frontal gyrus, and left inferior parietal lobule (Fig 2). The right insula had a significant negative relationship. No significant relationships in the panic subjects between symptoms and BOLD data were found. The magnitude of the ^{31}P pH response to the flashing checkerboard was moderately correlated (r=0.23) with the severity of anxiety symptoms in panic disorder subjects.

Discussion and Conclusions

This study shows that dynamic $T_{1\rho}$ imaging may provide new insights into panic disorder. Based on our previous work, the increased $T_{1\rho}$ response may correspond to an increased acidosis within the visual cortex during activation. In addition, the pH estimated by ^{31}P spectroscopy shows an acidosis in the baseline pH measurements. Previous work by Maddock et al. has also shown increased lactate production using a similar visual stimulation paradigm [3]. The relationship between anxiety symptoms and $T_{1\rho}$ response are intriguing. The areas exhibiting a significant positive relationship in this study correspond to regions that responded to CCK-4 induced panic attacks in healthy controls [5]. These results suggest that abnormal pH signaling may play a role in panic disorder.

References

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