High Sensitivity and Specificity in Brain Injury Diagnostic Method Using Statistical Parametric Mapping of Resting FDG Positron Emission Tomography

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ABSTRACT

Estimates place the annual rate of traumatic brain injury in the USA at around 1.78 million. The majority of these are classified as mild traumatic brain injury (mTBI). Traditional CT and MR imaging protocols used to detect skull fractures, intracranial bleeding, and lesions often show no structural damage after mTBI. While most mTBI patients recover within 3 to 6 months, there are those who continue to experience postconcussive symptoms with no structural evidence of injury. The purpose of this experiment is to examine the sensitivity and specificity of PET imaging in conjuction with Statistical Parametric Mapping in distinguishing mTBI patients from controls. Three blind raters distinguished between PET scan images from 15 controls and 18 chronic mTBI patients with 97% sensitivity and 100% specificity. Despite the small sample and rater sizes, the high sensitivity and specificity values suggest that PET imaging could provide valuable information about mTBI in research and perhaps in clinical contexts.

INTRODUCTION

Traumatic brain injury is an important health concern. Estimates place the annual rate of traumatic brain injury in the USA at around 1.78 million cases. Those who sustain traumatic brain injuries may be at risk of developing neurocognitivie and psychiatric complications. Most traumatic brain injuries are classified as mild (mTBI), the least severe of three categories, which also include moderate and severe.

The majority of mTBI patients recover within 3 to 6 months, but there are those who continue to experience postconcussive symptoms despite showing no structural evidence of injury with computed tomography (CT) or magnetic resonance imaging (MRI). In light of this, there is potential for FDG PET imaging techniques to detect changes in brain metabolism following mTBI.

FDG PET imaging works by introducing the radioactive isotope fludeoxyglucose into the body, which is then taken up along with glucose. This radioactive isoptope emits positrons that travel in opposite directions and are detected by a ring of tomographs surrounding the subject. A 3D representation of the spatial distribution of the isotope is then constructed from the information gathered by the detectors. In this way, FDG PET is used to measure the uptake of glucose throughout the brain.

Studies have shown changes in glucose metabolism and uptake after mTBI both in global and in specific regions such as the anterior cingulate and corpus callosum despite large variations in experimental design. Hypometabolism is the most common reported finding; although, increased metabolism in various regions has also been reported.

This experiment investigates the sensitivity and specificity of resting FDG PET imaging in conjunction with the MATLAB package Statistical Parametric Mapping in distinguishing chronic mTBI patients from controls.

METHODS

Subjects This study comprises PET scan images from 15 controls (mean age 31.3 ± 11.1 yrs, 8M, 3F) and 18 chronic mTBI clinical referrals (mean age 34.9 ± 18.7, yrs, 5F, 13M). Controls were screened for any neuropsychological and psychiatric abnormalities using CPT, PAI, WCST, and MicroCog.

METHODS

PET Imaging All subjects were imaged with a Siemens HRRT scanner (FWHM=2.5mm). Subjects were at rest during injection with 2-deoxy-2-(18F)flouro-D-glucose and during image acquisition.

Statistical Parametric Mapping - Normalization (SPM5) HRRT interfiles obtained from the scanner were converted to SPM Analyze format using HRRT2SPM. Files underwent spatial normalization in SPM-5

Statistical Parametric Mapping - Z-map generation (SPM8) Scans were normalized to similar voxel amounts using the image calculator in SPM-8, and a multivariable linear model design factoring in age and gender was created to compare FDG uptake against the control group. Contrast overlays showing areas of significant increases or decreases ($p = 0.1$, voxel threshold = 30) were created for all controls and mTBI subjects. The contrasts were then superimposed onto their respective scans in VINCI to create Z-maps.

Rating and Sensitivity and Specificity Identifying information was removed from all Z-maps. 3 blind raters rated the Z-maps as either "Brain Injured" or "Control". Sensitivity was calculated by dividing the number of true positivies by the sum of the true positives and false negatives. Specificity was calculated by dividing the number of true negatives by the sum of the true negatives and false positives.

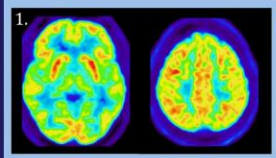
RESULTS

The average calculated sensitivity was 97 ± 0.03% and the average specificity was 100 ± 0%

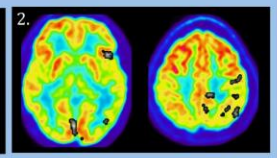
Sensitivity and Specificity Results

	Sensitivity	Specificity
Rater 1	0.94	1
Rater 2	1	1
Rater 3	1	1
Average	0.97	1
Standard Devation	0.03	0

1.



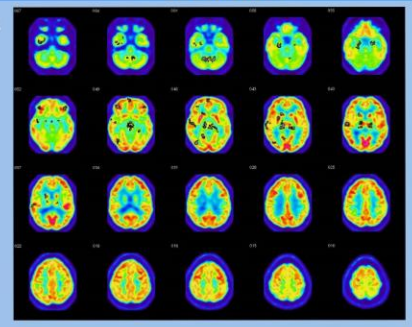
2.



The table above shows the results of each rater. Image 1 shows the PET scan of control subject with a contrast overlay. Image 2 shows the PET scan of an mTBI subject with a contrast overlay. The areas of gray designate areas of abnormal FDG uptake compared to the controls.

RESULTS

3.



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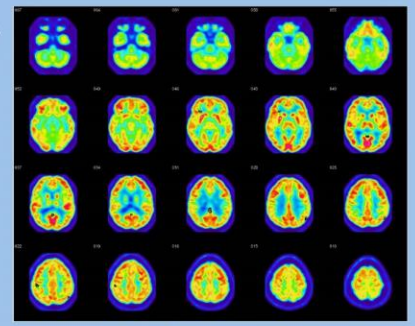

Image 3 shows an example of an mTBI scan overlaid with a positive contrast. Image 4 shows an example of an mTBI scan overlaid with a with negative contrast.

CONCLUSIONS

Three blind raters distinguished between mTBI and control Z-maps with very high sensitivity and specificity, suggesting that PET in conjunction with SPM can identify changes in glucose metabolism following mTBI. Longitudinal studies that combine multiple PET scans at various times after mTBI injury may shed light on metabolic changes in those who experience persistent postconcussive symptoms.

REFERENCES

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