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14. ABSTRACT

Traumatic brain injuries (TBI) are a common occurrence from roadside blasts of improvised explosive devices (IEDs). In the proposed cross-sectional study, we aim to apply neurobehavioral testing and advanced MRI techniques [task-activated functional MRI (fMRI) and diffusion tensor imaging (DTI)] to gain a comprehensive understanding of the neural changes underlying blast-related MTBI. We will accomplish this goal by conducting advanced neuroimaging (task-activated fMRI and DTI fiber tracking) and neurobehavioral testing (computerized assessment and standard neuropsychological testing) on 60 chronic trauma patients: 15 military MTBI patients who have experienced blast injuries, 15 civilian MTBI patients with mechanical closed head injuries, 15 military and 15 civilian patients with orthopedic injuries. Year one of the project has been devoted to the development of the necessary infrastructure for the execution of this complex multisite study. A number of development tasks have been undertaken, including hiring and training a new coordinator in Houston, developing uniform procedures for analysis of image data in Cleveland and Houston, and further developing the avenues for recruitment of subjects. We have recruited 32 subjects and acquired imaging and cognitive data from 25 of these subjects. We are satisfied that the accrual of data is of high reliability and integrity. Over the next year, we will continue recruitment, acquisition of data, and data analysis across the two study sites.

15. SUBJECT TERMS
Blast-related traumatic brain injury (TBI), fMRI, DTI, cognition

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INTRODUCTION

Traumatic brain injuries (TBI) are a common occurrence from roadside blasts of improvised explosive devices (IEDs). Like civilian TBI, blast-related TBI can result from mechanical forces in which objects in motion strike the head or the head is forcefully put into motion and strikes an object. TBI from exposure to an explosive blast may also result from a third cause: barotrauma. Blasts produce wave-induced changes in atmospheric pressure, which in turn produce characteristic injuries to vulnerable bodily regions at air-fluid interfaces, such as the middle ear. It is unknown whether the neural and cognitive sequelae of blast-related TBI differ from those resulting from mechanically-induced TBI commonly observed in civilian accidents. Understanding the potentially unique sequelae of blast-related TBI is critical for accurate diagnosis and designing effective pharmacological and neurorehabilitation interventions.

In the proposed cross-sectional study, we aim to apply neurobehavioral testing and advanced MRI techniques [task-activated functional MRI (fMRI) and diffusion tensor imaging (DTI)] to gain a comprehensive understanding of the neural changes underlying blast-related MTBI. This will be accomplished by comparing neurobehavioral and neuroimaging findings obtained from military personnel who have experienced a blast injury with those obtained from civilians who have experienced TBI from motor vehicle accidents and from military and civilian control participants with orthopedic injuries. We will accomplish this goal by conducting advanced neuroimaging (task-activated fMRI and DTI fiber tracking) and neurobehavioral testing (computerized assessment and standard neuropsychological testing) on 60 chronic trauma patients: 15 military MTBI patients who have experienced blast injuries, 15 civilian MTBI patients with mechanical closed head injuries,15 military and 15 civilian patients with orthopedic injuries.

BODY

Year two of the project was devoted to the development of the necessary infrastructure for the execution of this complex multisite study. A number of development tasks have been undertaken to train new personnel for the study and to develop cross-platform analyses to provide reliability in image analysis. All of these goals have been accomplished and the analysis of imaging data is beginning. While there have been problems over the year, each of them has been successfully managed to the exacting standards of the Principal Investigators. This meticulous work has laid the groundwork for high integrity in data collection. Details regarding each of these tasks are provided below, broken down by category.

Staff Recruitment, Employment, Organization, Training. We have no changes in personnel.

Neuropsychological and Neurobehavioral Measures
We are in the process of collecting brain imaging data and data on all outcome measures. In an attempt to measure effort, the Word Memory Test has been added to the battery. All forms have been scored and entered into an Access database. All electronic files have been backed up on a local drive.

MRI

- Brain Imaging Protocols: Combining brain imaging data across two research sites is a considerable technical challenge. Extensive work has been done to establish a good matching of the scan parameters and to confirm the acquisition of comparable, high quality images for the Cleveland Clinic and Houston HNL scanners (all are Siemens 3T Trio MRI scanners).

- fMRI, DTI, and MRI Volumetric Data Acquisition: As of 8/31/2010, the Cleveland Clinic site has imaged 12 military TBI subjects, 2 military orthopedic injury control subjects, 2 civilian TBI subjects, and 1 civilian orthopedic injury control subjects. All image data are placed on a secure server at Cleveland Clinic and are then transferred and archived at the image analysis laboratories in both Houston and Cleveland.

- fMRI Data Analysis: All fMRI datasets have been checked for image quality, with no task runs being excluded due to scanner artifact and few excluded due to motion. Current efforts for processing and analysis of the data are focused on the development of different, but complementary image analysis procedures at the Houston and Cleveland sites to provide convergent validation of the results. The Cleveland site is using procedures they have developed around the AFNI (Analysis of Functional Neuroimaging) suite of programs and Houston center is using SPM (Statistical Parametric Mapping) software. Data from four cases have been processed and subjected to analysis at both sites using these different approaches. Initial results suggest a favorable degree of convergence, but there are still some inconsistencies in the results that likely reflect between-site differences in image processing (e.g., smoothing and normalization), contrast definition, threshold setting procedures, and the methods used for image display. On 9/1/2010 the imaging researchers discussed these issues on a conference call and agreed to a number of methodology changes that would allow a more direct comparison of results from the two sets of processing and analysis procedures, while still retaining the strengths of these individual approaches. These modifications were evaluated during a conference call on 10/13/2010.

- DTI, Volumetric MRI Data Analysis: We are up to date in the analysis of MRI volumetric data of brain regions. In addition we are in the process of analyzing the DTI data.

- Cleveland Recruitment: We have recruited 15 military TBI subjects, 3 military OI, 5 civilian, and 3 civilian OI subjects.

KEY RESEARCH ACCOMPLISHMENTS

At this point in the project, the key accomplishments have been the recruitment of 26 (43%) of the subjects, and scanning of 17 of these subjects (28% of total sample) in Cleveland. This solid foundation permits us to make continued and consistent progress in data analysis. We anticipate a productive and efficient process based on the painstaking and meticulous work that has been put in to this point. To summarize, key accomplishments have been:

- Standardization of imaging protocols across the Houston and Cleveland sites.
- Recruiting a total of 26 subjects in Cleveland.
- Development, testing, and implementation of comparable fMRI data analysis strategies for both the Houston and Cleveland sites
- fMRI, volumetric MRI, and DTI scanning completed for 17 subjects.
- Initial development of complementary procedures for analysis of the fMRI data.

REPORTABLE OUTCOMES

Given that the initial goals have been to develop the mechanisms by which we will conduct the project, the products of our labor are not yet tangible. While engaged in recruitment and acquisition of data, we have devoted time to set up comparable image analysis procedures in Cleveland and Houston, attending to detail, ensuring the integrity and reliability of the data we will use to arrive at the reportable outcomes.
We are engaged in data analysis while we are enrolling additional patients. We anticipate that we will have reportable outcomes within the next year.

CONCLUSION

The first year of the project was devoted to creating a viable infrastructure to support the collection of data across multiple sites. The second year of the project was devoted to the recruitment of subjects. Cleveland has completed recruitment of the military TBI subjects and made significant progress in recruitment of the civilian subjects. The military OI subjects are the most challenging group to recruit.

REFERENCES

Given that we are not yet reporting data, we have no references at this time.