



The Assessment and Treatment of Individuals with History of Traumatic Brain Injury and Post-Traumatic Stress Disorder: A Systematic Review of the Evidence

EXECUTIVE SUMMARY

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PREFACE

VA's Health Services Research and Development (HSR&D) Service works to improve the cost, quality, and outcomes of healthcare for our nation's veterans. Collaborating with VA leaders, managers, and policy makers, HSR&D focuses on important healthcare topics that are likely to have significant impact on quality improvement efforts. One significant collaborative effort is HSR&D's Evidence-based Synthesis Program (ESP). Through this program, HSR&D provides timely and accurate evidence syntheses on targeted healthcare topics. These products will be disseminated broadly throughout VA and will: inform VA clinical policy, develop clinical practice guidelines, set directions for future research to address gaps in knowledge, identify the evidence to support VA performance measures, and rationalize drug formulary decisions.

HSR&D provides funding for four ESP Centers. Each Center has an active and publicly acknowledged VA affiliation and also serves as an Evidence Based Practice Center (EPC) supported by the Agency for Healthcare Research and Quality (AHRQ). The Centers will each generate three evidence syntheses annually on clinical practice topics of key importance to VHA leadership and policymakers. A planning committee with representation from HSR&D, Patient Care Services (PCS), Quality Enhancement Research Initiative (QUERI), Office of Quality and Performance (OQP), and the VISN Clinical and Quality Management Officers, has been established to identify priority topics and key stakeholder concerns and to ensure the quality of final reports. Comments on this evidence report are welcome and can be sent to Susan Schiffner, ESP Program Manager, at Susan.Schiffner@va.gov.

This report is based on research conducted by the Minneapolis Veterans Affairs Medical Center, Minnesota Evidence Synthesis Program, and the Center for Chronic Disease Outcomes Research under contract to the Department of Veterans Affairs. The findings and conclusions in this document are those of the author(s) who are responsible for its contents; the findings and conclusions do not necessarily represent the views of the Department of Veterans Affairs. Therefore, no statement in this article should be construed as an official position of the Department of Veterans Affairs.

This report is intended as a reference and not as a substitute for clinical judgment.

This report may be used, in whole or in part, as the basis for development of clinical practice guidelines and other quality enhancement tools, or as a basis for reimbursement and coverage policies. The Department of Veterans Affairs endorsement of such derivative products may not be stated or implied.

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BACKGROUND

United States (U.S.) Veterans Affairs (VA) and Department of Defense (DoD) healthcare facilities are increasingly serving a large population of Operation Enduring Freedom and Operation Iraqi Freedom (OEF/OIF) veterans who have sustained traumatic brain injury (TBI), suffer from post-traumatic stress disorder (PTSD), or have both a history of TBI and current PTSD (TBI/PTSD). Mild TBI (mTBI) is considered the most common form of TBI. Uncertainty exists regarding the long-term health outcomes of mTBI as well as the validity of criteria used to assess for a history of this injury. Symptoms that may be attributable to mTBI are similar to symptoms of PTSD. It is unknown whether findings from civilian populations with both a history of mTBI and PTSD (mTBI/PTSD) are applicable to individuals with combat-related mTBI/PTSD. Current evidence-based practices to screen, diagnose, prospectively evaluate, and treat mTBI symptoms or PTSD may be less accurate or effective if and when these conditions co-occur. Thus, there is a need to develop an evidence base to identify best practices to define, diagnose, evaluate, and manage patients with mTBI/PTSD, particularly in U.S. veterans of OEF/OIF. We conducted a systematic literature review to address the following key questions:

- 1) What is the prevalence of comorbid TBI and PTSD? Does the reported prevalence vary by study population, trauma etiology, TBI severity (mild versus moderate and severe), or methods of case ascertainment?
- 2a) What is the relative accuracy of diagnostic tests used for assessing mTBI when mTBI is comorbid with PTSD?
- 2b) What is the relative accuracy of diagnostic tests used for assessing PTSD when PTSD is comorbid with mTBI?
- 3a) Are there psychosocial or pharmacological therapies used for treatment of mTBI and PTSD simultaneously?
- 3b) Are therapies for treatment of mTBI effective when mTBI is comorbid with PTSD? Is there evidence of harms?
- 3c) Are therapies for treatment of PTSD effective when PTSD is comorbid with mTBI? Is there evidence of harms?

This review was conducted as part of the VA Evidence Synthesis Program (ESP). The topic was nominated by the Minneapolis VA Evidence Synthesis Program Center. The report was intended to serve as an evidence-base to guide recommendations of a June 2009 VA Consensus Conference on the Diagnosis and Management of mTBI, PTSD, and pain as well as to inform healthcare practice and policy within the VA. Our key questions, scope, and work plan were refined in collaboration with a Technical Advisory Panel comprised of clinical, research, and health policy experts in TBI and PTSD.

METHODS

Literature Search

We searched the PubMed, PsycINFO, and REHABDATA databases to identify peer reviewed articles published in text journals between 1980 and June, 2009 that included patients with both a history of TBI and PTSD. Titles, abstracts, and articles were reviewed and data were extracted by investigators with knowledge of the subject area and trained in critical analysis of the literature. We attempted to assess the prevalence of TBI/PTSD in predefined patient subgroups and, for mTBI/PTSD, evaluate the quality, applicability, and strength of diagnostic accuracy studies focusing on relevance to U.S. OEF/OIF veterans using STARD and QUADAS checklists. We evaluated results from intervention trials using modifications of GRADE criteria.

Active Research

We contacted investigators of currently funded research, representatives from related VA workgroups, and authors of recently published relevant studies to collect information about ongoing research pertinent to each key question.

RESULTS

We screened 1107 references and performed a detailed full text review of 358. From these, 31 unique studies (37 references) met inclusion criteria. We also included a large telephone survey of a national sample of OEF/OIF veterans conducted by the RAND Corporation and published after peer review on their website. We excluded studies if they focused on subjects less than age 18 years of age, did not enroll individuals with probable TBI history or probable PTSD, or did not present results in a manner that addressed the key questions. The primary findings are described below.

Key Question #1

In addition to the RAND survey, 31 unique observational studies met inclusion criteria and reported prevalence of TBI/PTSD. Sample sizes ranged from 10 to 2525, though only five enrolled 200 or more subjects. No studies were U.S. population-based, though several reports focused on U.S. veterans of OEF/OIF, a key population for this report. The two largest published studies and the RAND report each evaluated approximately 2000 U.S. soldiers and veterans of OEF/OIF. Twenty-one published studies enrolled subjects with a history of mTBI (eight exclusively, including the two large studies that included U.S. veterans); the remaining described moderate and severe TBI or did not report TBI severity. Studies varied widely in their design, construction of the cohort, timing and method of case ascertainment, and definition of disease/injury. Many studies did not report patient demographic characteristics, trauma types, or frequency of pain or mental health disorders other than PTSD. When these descriptive details were included, there was considerable variation across studies but prevalence of TBI/PTSD was generally not stratified by these potentially important variables. These factors made it impossible to pool results and greatly weakened the strength of the evidence.

Mean age of subjects ranged from 25 to 52 years and proportion female from 0% to 83%. The percent of individuals of white race ranged from 16% to 92% in the seven studies reporting race/ethnicity data. Of the 1,965 individuals included in the RAND survey, 88% were men, 66% were white (22% black), and the median age was 30 years. “Combat” (blast and non-blast) injuries accounted for most of the trauma in the eight studies involving U.S. military personnel and veterans. This was true of the RAND study as well, which was conducted with a large population of individuals previously deployed as part of OEF/OIF. Among the remaining studies involving non-veteran civilians, motor vehicle crashes were the most frequent sources of trauma.

The majority of included studies had highly selected study populations (e.g., 18 of 31 studies were based on samples in which all participants had a history of TBI and another was based on a group of patients with PTSD). Across studies, there was wide variation in the prevalence of TBI/PTSD by study population (for example, from 0% among medical patients recruited from a single-center Neurology Department to 70% in a clinical sample of patients with obsessive-compulsive disorder); trauma types (32% to 66% of participants with combat-related TBI); TBI severity (0% to 89% among individuals with mTBI and 0% to 19% among those with severe TBI); and methods of case ascertainment (5% to 66% among participants responding to self-report inventories of PTSD symptoms and 8% to 70% among those assessed through structured clinical interviews). In the RAND cohort, the prevalence levels of probable TBI history and PTSD were 19.5% and 13.8%, respectively; the prevalence of probable TBI/PTSD was 6.6%.

Key Question #2

There were no published studies addressing the relative accuracy of diagnostic tests used for assessing history or symptoms of mTBI or PTSD when one condition co-occurs with the other.

Key Question #3

There were no published studies that evaluated the effectiveness and harms of treatments for co-management of mTBI/PTSD. There were no studies that examined effectiveness of treatments specifically for PTSD or mTBI symptoms in individuals with both conditions.

Active Research:

Responses were received from 30 individuals. We identified four ongoing studies that will report prevalence of TBI/PTSD, five studies on assessment of mTBI/PTSD, three studies that address both prevalence and assessment of mTBI/PTSD, and six studies on treatment of mTBI/PTSD. One of the treatment studies identified is a randomized, controlled trial.

FUTURE RESEARCH NEEDS

Long-term prospective observational studies are needed that use standardized validated measures of both history and symptoms of TBI and PTSD to determine prevalence, severity, and long-term outcomes of TBI/PTSD, especially in veterans with history and symptoms of mTBI. Among

military personnel, pre-deployment as well as post-deployment assessment should be completed using objective measures that limit ascertainment, recall, or reporting bias. Outcomes data should be stratified by clinically relevant patient characteristics, trauma etiology and severity, and time from trauma. Diagnostic accuracy studies are needed that utilize established quality methods. Randomized controlled treatment trials in populations of interest are required to evaluate the effectiveness and harms of potential therapeutic options, especially among individuals with mTBI history.

CONCLUSIONS

Reported prevalence of TBI/PTSD varies widely, likely depending on patient characteristics, trauma etiology and severity, and the disease/injury definition used and time and method of ascertainment. There is no information on the relative diagnostic accuracy of commonly used tests to assess history and symptoms of mTBI or PTSD when the conditions are co-occurring, though the prevalence of co-occurrence is likely to depend most closely on diagnostic methods, definitions, and timing of ascertainment. There is no information on the effectiveness and harms of therapies in adults with mTBI/PTSD. The reported active research studies are inadequate to address key questions 2 and 3 assessed in this review.