TECHNICAL COMMENTARY

Traumatic brain injury

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Introduction

Traumatic brain injury (TBI) is defined as an alteration in brain function, or other evidence of brain pathology, caused by an external force. Brain injury can have severe consequences on physical, cognitive, and affective functioning and may lead to long-lasting limitations in these domains. Studies have demonstrated that both civilian and military patients with TBI of various severity levels can develop PTSD, even when a person cannot recall the details of the traumatic event.

Method

We have included only systematic reviews (systematic literature search, detailed methodology with inclusion/exclusion criteria) published in full text, in English, from the year 2010 that report results separately for people with PTSD. Reviews were identified by searching the databases MEDLINE, EMBASE, and PsycINFO. When multiple copies of reviews were found, only the most recent version was included. We prioritised reviews with pooled data for inclusion.

Review reporting assessment was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist that describes a preferred way to present a meta-analysis[1]. Reviews with less than 50% of items checked have been excluded from the library. Note that early reviews may have been guided by less stringent reporting checklists than the PRISMA, and that some reviews may have been limited by journal guidelines.

Evidence was graded using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group approach where high quality evidence such as that gained from randomised controlled trials (RCTs) may be downgraded to moderate or low if review and study quality is limited, if there is inconsistency in results, indirect comparisons, imprecise or sparse data and high probability of reporting bias. It may also be downgraded if risks associated with the intervention or other matter under review are high. Conversely, low quality evidence such as that gained from observational studies may be upgraded if effect sizes are large or if there is a dose dependent response. We have also taken into account sample size and whether results are consistent, precise and direct with low associated risks (see end of table for an explanation of these terms)[2]. The resulting table represents an objective summary of the available evidence, although the conclusions are solely the opinion of staff of NeuRA (Neuroscience Research Australia).

Results

We found two systematic reviews that met our inclusion criteria[3-20].

- Moderate quality evidence found the prevalence of PTSD after a TBI was around 24%. Rates were higher in males than females, in samples with TBI than other physical injuries, in military samples exposed to a blast than civilians exposed to a motor vehicle accident, and in studies from the USA than other countries. There have been no differences found in the rates of PTSD in people with a mild versus moderate-severe TBI.

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Loignon A, Ouellet MC, Belleville G

A systematic review and meta-analysis on PTSD following TBI among military/veteran and civilian populations

Journal of Head Trauma Rehabilitation 2020; 35: E21-E35

View review abstract online

Comparison	**Prevalence of PTSD following a traumatic brain injury (TBI) vs. no TBI in military and civilian samples.**
Summary of evidence	**Moderate quality evidence (large samples, inconsistent, imprecise, direct) found the prevalence of PTSD after a traumatic brain injury was around 24%. Rates were highest in samples with more males, in samples with TBI rather than another physical injury, in military samples exposed to a blast rather than civilians exposed to a motor vehicle accident, and in studies from the USA.**

Prevalence of PTSD after a TBI vs. no TBI

Samples with TBI

Both: 31 studies, N = 20,586, prevalence = 23.9%, 95%CI 19.9% to 28.5%

Military: 19 studies, N = 13,861, prevalence = 36.8%, 95%CI 29.2% to 49.2%

Civilian: 12 studies, N = 6,725, prevalence = 15.7%, 95%CI 11.9% to 20.4%

Samples without TBI (with another injury or unknown status)

Both: 31 studies, N = 20,586, prevalence = 11.7%, 95%CI 9.0% to 15.1%

Military: 19 studies, N = 13,861, prevalence = 10.8%, 95%CI 7.0% to 6.2%

Civilian: 12 studies, N = 6,725, prevalence = 12.4%, 95%CI 8.9% to 17.1%

People with TBI were significantly more likely to have a diagnosis of PTSD than people without TBI;

OR = 2.68, 95%CI 2.00 to 3.70, $p < 0.001$, $I^2 = 94.2\%$

Civilians with TBI were significantly more likely to have a diagnosis of PTSD than those without TBI;

OR = 1.26, 95%CI 1.00 to 1.60, $p = 0.046$, I^2 not reported

Military with TBI were significantly more likely to have a diagnosis of PTSD than those without TBI;

OR = 4.18, 95%CI 2.90 to 6.00, $p < 0.001$, I^2 not reported

Studies with more males rather than females, had a greater risk of PTSD in samples with TBI.

Studies from the United States rather than other countries, had a greater risk of PTSD in samples with TBI.

Studies with an unknown injury comparison group rather than another physical injury comparison group, had a greater risk of PTSD in samples with TBI.

Studies of people with TBI from blast injuries rather than motor vehicle accidents had a greater risk of PTSD. There were no significant moderating effects of time since injury, TBI severity, study design, diagnostic tool for assessing PTSD or TBI, age, sample size, or study quality.

Consistency in results	Inconsistent
Precision in results	Imprecise
Directness of results	Direct

Van Praag DLG, Cnossen MC, Polinder S, Wilson L, Maas AIR

Post-Traumatic Stress Disorder after Civilian Traumatic Brain Injury: A Systematic Review and Meta-Analysis of Prevalence Rates

Journal of Neurotrauma 2019; 36: 3220-32

View review abstract online

Comparison	**Prevalence of PTSD in civilians with a traumatic brain injury (TBI).**
Summary of evidence	**Moderate quality evidence (large sample, direct) finds the median prevalence of PTSD in civilians with a traumatic brain injury is around 15.6%. There were no differences in rates of PTSD between people with mild or moderate/severe TBI.**

Prevalence of PTSD in civilians with a TBI
31 studies N = not reported, prevalence = 15.64%, 95%CI 12.88% to 18.40%, I^2 = 82% There were no differences in rates of PTSD between people with mild or moderate/severe TBI (13.5% vs. 11.8%).

Consistency in results	Inconsistent
Precision in results	Appears imprecise
Directness of results	Direct

Explanation of acronyms

CI = confidence interval, I^2 = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), N = number of participants

Explanation of technical terms

* Bias has the potential to affect reviews of both RCT and observational studies. Forms of bias include; reporting bias – selective reporting of results; publication bias - trials that are not formally published tend to show less effect than published trials, further if there are statistically significant differences between groups in a trial, these trial results tend to get published before those of trials without significant differences; language bias – only including English language reports; funding bias - source of funding for the primary research with selective reporting of results within primary studies; outcome variable selection bias; database bias - including reports from some databases and not others; citation bias - preferential citation of authors. Trials can also be subject to bias when evaluators are not blind to treatment condition and selection bias of participants if trial samples are small[21].

† Different effect measures are reported by different reviews.

Prevalence refers to how many existing cases there are at a particular point in time. Incidence refers to how many new cases there are per population in a specified time period. Incidence is usually reported as the number of new cases per 100,000 people per year. Alternatively some studies present the number of new cases that have accumulated over several years against a person-years denominator. This denominator is the sum of individual units of time that the persons in the population are at risk of becoming a case. It takes into account the size of the underlying population sample and its age structure over the duration of observation.

Reliability and validity refers to how accurate the instrument is. Sensitivity is the proportion of actual positives that are correctly identified (100% sensitivity = correct identification of all actual positives) and specificity is the proportion of negatives that are correctly identified (100% specificity = not identifying anyone as positive if they are truly not).

Weighted mean difference scores refer to mean differences between treatment and comparison groups after treatment (or occasionally pre to post treatment) and in a randomised trial there is an assumption that both groups are comparable on this measure prior to treatment. Standardised mean differences are divided by the pooled standard deviation (or the standard deviation of one group when groups are homogenous) that allows results from different scales to be combined and compared. Each study's mean difference is then given a weighting depending on the size of the sample and the variability in the data. Less than 0.4 represents a small effect, around 0.5 a medium effect, and over 0.8 represents a large effect[21].

Odds ratio (OR) or relative risk (RR) refers to the probability of a reduction (< 1) or an increase (> 1) in a particular outcome in a treatment group, or a group exposed to a risk factor, relative to the comparison group. For example, a RR of 0.75 translates to a reduction in risk of an outcome of 25% relative to those not receiving the treatment or not exposed to the risk factor. Conversely, a RR of 1.25 translates to an increased risk of 25% relative to those not receiving treatment or not having been exposed to a risk factor. A RR or OR of 1.00 means there is no difference between groups. A medium effect is considered if RR > 2 or < 0.5 and a large effect if RR > 5 or < 0.2[22]. lnOR stands for logarithmic OR where a lnOR of 0 shows no difference between groups. Hazard ratios measure the effect of an explanatory variable on the hazard or risk of an event.

Correlation coefficients (eg, r) indicate the strength of association or relationship

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between variables. They can provide an indirect indication of prediction, but do not confirm causality due to possible and often unforseen confounding variables. An r of 0.10 represents a weak association, 0.25 a medium association and 0.40 and over represents a strong association. Unstandardised (*b*) regression coefficients indicate the average change in the dependent variable associated with a 1 unit change in the independent variable, statistically controlling for the other independent variables. Standardised regression coefficients represent the change being in units of standard deviations to allow comparison across different scales.

‡ Inconsistency refers to differing estimates of effect across studies (i.e. heterogeneity or variability in results) that is not explained by subgroup analyses and therefore reduces confidence in the effect estimate. I^2 is the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance) - 0% to 40%: heterogeneity might not be important, 30% to 60%: may represent moderate heterogeneity, 50% to 90%: may represent considerable heterogeneity and over this is considerable heterogeneity. I^2 can be calculated from Q (chi-square) for the test of heterogeneity with the following formula[21];

$$I^2 = \left(\frac{Q - df}{Q}\right) \times 100\%$$

§ Imprecision refers to wide confidence intervals indicating a lack of confidence in the effect estimate. Based on GRADE recommendations, a result for continuous data (standardised mean differences, not weighted mean differences) is considered imprecise if the upper or lower confidence limit crosses an effect size of 0.5 in either direction, and for binary and correlation data, an effect size of 0.25. GRADE also recommends downgrading the evidence when sample size is smaller than 300 (for binary data) and 400 (for continuous data), although for some topics, these criteria should be relaxed[23].

‖ Indirectness of comparison occurs when a comparison of intervention A versus B is not available but A was compared with C and B was compared with C that allows indirect comparisons of the magnitude of effect of A versus B. Indirectness of population, comparator and/or outcome can also occur when the available evidence regarding a particular population, intervention, comparator, or outcome is not available and is therefore inferred from available evidence. These inferred treatment effect sizes are of lower quality than those gained from head-to-head comparisons of A and B.

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