TECHNICAL COMMENTARY

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POST-TRAUMATIC STRESS DISORDER LIBRARY

Illness onset

Introduction

Differences are observed in the age of onset of mental disorders, which may be influenced by genetic and/or environmental factors. While most individuals develop symptoms of PTSD within three months of the trauma, some symptoms can appear later and persist for months and sometimes years. Understanding the factors associated with age at the onset of symptoms could lead to better understanding of the disorder and earlier and improved intervention strategies for patients.

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 three systematic reviews that met our inclusion criteria[3-5].

- Moderate to high quality evidence finds the average age of onset of PTSD is 26.6 years, with no differences between males and females.
- Moderate quality evidence finds the overall median prevalence of PTSD tends to reduce over time, from 28.8% at one-month post trauma to 17% at 12 months post trauma. Median prevalence post non-intentional (accidental) trauma also decreases over time (30.1% to 14%), while median prevalence post intentional (non-accidental) trauma is lower initially and increases over time (11.8% to 23.3%).
- Moderate to high quality evidence suggests around 24.5% of people diagnosed with PTSD had a delayed onset, with most experiencing earlier milder symptoms. The prevalence of delayed-onset PTSD is highest in professional groups and those who experienced combat trauma.

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De Lijster JM, Dierckx B, Utens EMWJ, Verhulst FC, Zieldorff C, Dieleman GC, Legerstee JS

The age of onset of anxiety disorders: A meta-analysis

Canadian Journal of Psychiatry 2017; 62: 237-46

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Comparison	**Age of onset of PTSD.**
Summary of evidence	**Moderate to high quality evidence (large sample, inconsistent, appears precise, direct) finds the average age of onset of PTSD is 26.6 years, with no differences between males and females.**
Age of onset	
The average age of onset of PTSD is around 26.6 years; 12 studies, N = 1,459, mean age = 26.6 years, 95%CI 22.1 to 31.0, Q*p* < 0.0001 Prospective studies reported an earlier age of onset. There was no moderating effect of sex.	
Consistency in results‡	Inconsistent
Precision in results§	Appears precise
Directness of results‖	Direct

Santiago PN, Ursano RJ, Gray CL, Pynoos RS, Spiegel D, Lewis-Fernandez R, Friedman MJ, Fullerton CS

A Systematic Review of PTSD Prevalence and Trajectories in DSM-5 Defined Trauma Exposed Populations: Intentional and Non-Intentional Traumatic Events

PLoS ONE 2013; 8: e59236

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Comparison	**Prevalence of PTSD over time and onset after intentional vs. non-intentional traumatic events. Intentional traumas are those that involve deliberate infliction of harm, while non-intentional traumas are accidental.**

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Summary of evidence	**Moderate quality evidence (large study size, unable to assess consistency or precision, direct) finds the median prevalence of PTSD tends to reduce over time, from 28.8% at one month to 17% at 12 months. Median prevalence post-non-intentional trauma exposure also decreases over time (30.1% to 14%), while median prevalence post-intentional trauma exposure is lower and increases over time (11.8% to 23.3%).**
Onset of illness	
The overall prevalence of PTSD post-trauma; 35 studies 1 month: medium = 28.8%, mean = 25.4% 3 months: medium = 17.8%, mean = 18.8% 6 months: medium = 14.9%, mean = 16.1% 12 months: medium = 17.0%, mean = 17.7% *The prevalence of PTSD post-non-intentional trauma;* 14 studies 1 month: medium = 30.1%, mean = 28.0% 3 months: medium = 17.8%, mean = 18.8% 6 months: medium = 12.9%, mean = 14.4% 12 months: medium = 14.0%, mean = 14.8% *The median prevalence of PTSD post-intentional trauma;* 21 studies 1 month: medium = 11.8%, mean = 23.6% 3 months: medium = 17.1%, mean = 18.9% 6 months: medium = 19.0%, mean = 18.3% 12 months: medium = 23.3%, mean = 23.1%	
Consistency in results	Unable to assess; no measure of consistency is reported.
Precision in results	Unable to assess; no CIs are reported.
Directness of results	Direct

Utzon-Frank N, Breinegaard N, Bertelsen M, Borritz M, Eller NH, Nordentoft M, Olesen K, Rod NH, Rugulies R, Bonde JP

Occurrence of delayed-onset post-traumatic stress disorder: a systematic

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review and meta-analysis of prospective studies **Scandinavian Journal of Work, Environment & Health 40: 215-29** View review abstract online	
Comparison	**Prevalence of delayed-onset PTSD (>6 months post-trauma).**
Summary of evidence	**Moderate to high quality evidence (large sample, inconsistent, appears precise, direct) suggests around 24.5% of people diagnosed with PTSD had a delayed onset, with most experiencing earlier subclinical symptoms. The prevalence of delayed-onset PTSD is highest in professional groups and those who experienced combat trauma.**
Delayed-onset PTSD	
39 prospective studies, N = 30,210 Overall prevalence of PTSD = 19.7%, 95%CI 15.8 to 24.2%, I^2 = 90% Overall prevalence of delayed-onset PTSD = 5.6%, 95%CI 4.3 to 7.3%, I^2 = 91% Proportion of delayed-onset PTSD relative to all cases of PTSD = 24.5%, 95%CI 19.5 to 30.3%, I^2 = 94% Subgroup analyses showed delayed-onset PTSD was higher among professional groups compared to non-professional victims (37.6% vs. 20.3%). It was also higher in those exposed to combat than other trauma types (39.9% vs. 17-26%). There were no moderating effects of early (1-6 months after the trauma) vs. late (>9 months after the trauma) baseline assessment, assessment tool, or other study methods. Authors report that most people with delayed-onset PTSD experienced early subclinical symptoms.	
Consistency	Inconsistent
Precision	Appears precise
Directness	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, *p* = statistical probability of obtaining that result, Q = test for heterogeneity

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[6].

† 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[6].

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[7]. 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[6];

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

§ 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[8].

‖ 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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