TECHNICAL COMMENTARY

All therapies for complex PTSD

Introduction

Complex PTSD usually arises from chronic interpersonal violence or abuse. It is conceptualised as the core symptoms of PTSD (re-experiencing the trauma, avoidance of traumatic reminders, and exaggerated startle and hypervigilance) plus disturbances in self organisation, affect dysregulation, negative self-concept, and relationships. These disturbances are proposed to be associated with sustained, repeated or multiple forms of traumatic exposure (e.g., genocide campaigns, childhood sexual abuse, child soldiering, severe domestic violence, torture or slavery), reflecting loss of resources under conditions of prolonged adversity. People with complex PTSD may also show high levels of depression, psychological distress, dissociation, and substance misuse.

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 review topics were found, only the most recent and comprehensive 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 four systematic reviews that met our inclusion criteria[3-6].

- Moderate to low quality evidence found large effects of improved PTSD symptoms with psychological treatments pre- to post-treatment in adult women with a history of childhood abuse. The effect was medium sized in women with complex PTSD and large in women with non-complex PTSD when compared to usual care or waitlist control conditions.
- Moderate quality evidence found a medium-sized improvement in PTSD symptoms with group-based trauma interventions compared to usual care in people with complex PTSD and a history of interpersonal trauma or abuse.
- Moderate quality evidence found both specific-to-trauma and non-specific-to-trauma treatments improved PTSD symptoms in people with complex and non-complex PTSD. The effect was greater with

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specific interventions than with non-specific interventions and was greater in people with non-complex PTSD than in people with complex PTSD.

- For individual psychological therapies, moderate quality evidence found CBT, exposure therapy, and EMDR all improved PTSD symptoms in people with complex PTSD when compared to standard care/waitlist (all large effects). CBT, exposure therapy, and EMDR also improved disturbances in relationships, affect dysregulation, and negative self-concept when compared to standard care/waitlist (all medium to large effects). Only CBT and EMDR improved PTSD symptoms when compared to non-specific therapies (medium-sized effects). Only CBT improved relationships (small effect), and only EMDR improved negative self-concept (medium to large effect) when compared to non-specific therapies.

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Dorrepaal E, Thomaes K, Hoogendoorn AW, Veltman DJ, Draijer N, van Balkom AJLM

Evidence-based treatment for adult women with child abuse-related Complex PTSD: A quantitative review

European Journal of Psychotraumatology 2014; 5: 23613

View review abstract online

Comparison	**Effectiveness of psychological therapies (mostly CBT with psychoeducation, cognitive therapy and/or restructuring, affect regulation skills training, and exposure therapy) vs. waitlist or usual care for PTSD symptoms in women with a history of childhood abuse.** **Length of treatment ranged from 12 to 24 weeks or 14 to 27 sessions with a duration of 60-120 minutes each.**
Summary of evidence	**Moderate to low quality evidence (large sample, indirect) found large effects of improved PTSD symptoms with psychological treatments pre-post-treatment in people with and without complex PTSD. The effect was medium sized for complex PTSD and large for non-complex PTSD when compared to control conditions.**
PTSD symptoms	
7 RCTs, N = 482 *Large effects of improved PTSD symptoms with psychological treatments pre-post-treatment in people with and without complex PTSD;* Complex PTSD: $d = 1.2$, $p < 0.01$ Non-complex PTSD: $d = 1.8$, $p < 0.01$ *The effect was medium sized for complex PTSD and large for non-complex PTSD when compared to control conditions;* Complex PTSD: $d = 0.6$, $p < 0.01$ Non-complex PTSD: $d = 1.4$, $p < 0.01$	
Consistency in results‡	Not reported
Precision in results§	Not reported
Directness of results‖	Indirect; mixed treatment and/or control conditions.

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Gerger H, Munder T, Barth J

Specific and nonspecific psychological interventions for PTSD symptoms: a meta-analysis with problem complexity as a moderator

Journal of Clinical Psychology 2014; 70: 601-15

View review abstract online

Comparison	**Effectiveness of specific (consistent, standardised, face-to-face, individual, and trauma-focussed) vs. nonspecific psychological therapies (using a range of techniques and not trauma or PTSD focussed) for complex and non-complex PTSD.**
Summary of evidence	**Moderate quality evidence (large overall sample, some inconsistency, precise, indirect) found both treatments improved PTSD symptoms in people with complex and non-complex PTSD (medium to large effects). The effect was greater with specific interventions than with non-specific interventions and was greater in people with non-complex PTSD than in people with complex PTSD.**

PTSD symptoms

Pre-post-treatment analyses showed both clinical groups (complex and non-complex PTSD) improved with specific (large effects) and non-specific (medium-sized effects) interventions;

Specific interventions for complex PTSD: SMC = -1.09, 95%CI -1.38 to -0.79, $p < 0.05$

Specific interventions for non-complex PTSD: SMC = -1.63, 95%CI -2.11 to -1.15, $p < 0.05$

Non-specific interventions for complex PTSD: SMC = -0.82, 95%CI -1.19 to -0.45, $p < 0.05$

Non-specific interventions for non-complex PTSD: SMC = -0.71, 95%CI -1.02 to -0.40, $p < 0.05$

A small effect showed improved symptoms with specific interventions vs. non-specific interventions;

All patients: 18 RCTs, N = 1,274, SMD = -0.43, 95%CI -0.64 to -0.23, $p < 0.001$, $I^2 = 58\%$

A large effect of improved symptoms was found with specific interventions vs. non-specific interventions for non-complex PTSD, and a small effect was found for complex PTSD;

Complex PTSD: 12 RCTs, N unclear, SMD = -0.23, 95%CI -0.32 to -0.04, $p < 0.05$, $I^2 = 34\%$

Non-complex PTSD: 6 RCTs, N unclear, SMD = -0.87, 95%CI -1.20 to -0.53, $p < 0.05$, $I^2 = 33\%$

When analysis of complex PTSD was restricted to studies with structural equivalence of interventions, the effect between specific and nonspecific psychological interventions was reduced to a non-significant effect (SMD = -0.11, $p = 0.28$).

There were no significant associations between the effect size and study methodological quality or credibility of the nonspecific psychological intervention.

Consistency in results	Inconsistent for overall analysis, consistent for complex and non-

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	complex PTSD analyses.
Precision in results	Precise
Directness of results	Indirect; mixed treatment and/or control conditions.

Karatzias T, Murphy P, Cloitre M, Bisson J, Roberts N, Shevlin M, Hyland, Maercker P, Ben-Ezra A, Coventry M, Mason-Roberts P, Bradley S, Aoife Hutton P

Psychological interventions for ICD-11 complex PTSD symptoms: Systematic review and meta-analysis

Psychological Medicine 2019; 49: 1761-75

View review abstract online

Comparison	**Effectiveness of psychological therapies vs. standard care/waitlist or non-specific controls in people with complex PTSD.**
Summary of evidence	**Moderate quality evidence (mixed sample sizes, mostly inconsistent and imprecise, indirect) found CBT, exposure therapy, and EMDR all improved PTSD symptoms when compared to standard care/waitlist (large effects). Only CBT and EMDR improved PTSD symptoms when compared to non-specific therapies (small to medium-sized effects).** **CBT, exposure therapy, and EMDR also improved disturbances in relationships, affect dysregulation, and negative self-concept when compared to standard care/waitlist (medium to large effects). Only CBT improved relationships (small effect), and only EMDR improved negative self-concept (medium to large effect) when compared to non-specific therapies.**

PTSD symptoms

The following therapies showed large effects of improved PTSD symptoms when compared to standard care/waitlist;

CBT with or without exposure: 27 RCTs, N = 1,672, g = -0.90, 95%CI -1.11 to -0.68, $p < 0.001$, I^2 = 76%

Exposure therapy: 6 RCTs, N = 436, g = -1.05, 95%CI -1.52 to -0.58, $p < 0.001$, I^2 = 71%

EMDR: 4 RCTs, N = 197, g = -1.26, 95 CI -2.01 to -0.51, p = 0.001, I^2 = 79%

The following therapies showed small to medium-sized effects of improved PTSD symptoms when compared to non-specific therapies;

CBT with or without exposure: 9 RCTs, N = 731, g = -0.37, 95%CI -0.66 to -0.09, p = 0.011, I^2 =

71% EMDR: 3 RCTs, N = 135, *g* = -0.69, 95 CI -1.35 to -0.03, *p* = 0.041, I^2 = 70% Exposure therapy had no significant effect on PTSD symptoms when compared to non-specific therapies. Authors report that childhood-onset trauma was associated with poorer outcomes than adult-onset trauma.
Disturbances in relationships
The following therapies showed medium-sized effects of improved relationships when compared to standard care/waitlist; CBT with or without exposure: 16 RCTs, N = 880, *g* = -0.66, 95%CI -0.84 to -0.48, *p* < 0.001, I^2 = 45% Exposure therapy: 4 RCTs, N = 268, *g* = -0.59, 95%CI -1.12 to -0.07, *p* = 0.028, I^2 = 73% EMDR: 4 RCTs, N = 178, *g* = -0.76, 95 CI -1.35 to -0.16, *p* = 0.012, I^2 = 70% *Only CBT showed a small improvement in relationships when compared to non-specific therapies;* CBT with or without exposure: 3 RCTs, N = 207, *g* = -0.32, 95%CI -0.60 to -0.03, *p* = 0.029, I^2 = 0% Exposure therapy and EMDR had no significant effect on disturbances in relationships when compared to non-specific therapies.
Affect dysregulation
The following therapies showed large effects of improved affect regulation when compared to standard care/waitlist; CBT with or without exposure: 3 RCTs, N = 115, *g* = -1.42, 95%CI -2.20 to -0.65, *p* < 0.001, I^2 = 71% EMDR: 1 RCT, N = 23, *g* = -1.64, 95 CI -2.56 to -0.72, *p* < 0.001 CBT with or without exposure and EMDR had no significant effect on affect regulation when compared to non-specific therapies. No study assessed exposure therapy on affect dysregulation.
Negative self-concept
The following therapies showed medium to large effects of improved negative self-concept when compared to standard care/waitlist; CBT with or without exposure: 9 RCTs, N = 601, *g* = -0.82, 95%CI -1.19 to -0.44, *p* < 0.001, I^2 = 79% Exposure therapy: 3 RCTs, N = 233, *g* = -0.73, 95%CI -1.03 to -0.43, *p* < 0.001, I^2 = 21% EMDR: 1 RCT, N = 83, *g* = -0.61, 95 CI -1.04 to -0.17, *p* = 0.006 *Only EMDR showed a medium to large improvement in negative self-concept when compared to non-specific therapies;* EMDR: 2 RCTs, N = 109, *g* = -0.78, 95 CI -1.56 to -0.01, *p* = 0.049, I^2 = 75% CBT with or without exposure had no significant effect on negative self-concept when compared to

non-specific therapies. No study assessed exposure therapy on negative self-concept outcome compared to non-specific therapies.	
Consistency in results	Mostly inconsistent
Precision in results	Mostly imprecise
Directness of results	Indirect; mixed control conditions

Mahoney A, Karatzias T, Hutton P

A systematic review and meta-analysis of group treatments for adults with symptoms associated with complex post-traumatic stress disorder

Journal of Affective Disorders 2019; 243: 305-21

View review abstract online

Comparison	**Effectiveness of group-based trauma interventions vs. usual care/waitlist for people with complex PTSD and a history of interpersonal trauma and abuse.**
Summary of evidence	**Moderate quality evidence (large sample, inconsistent, precise, indirect) found a medium-sized effect of improved PTSD symptoms with group-based trauma interventions compared to usual care.**
PTSD symptoms	
A medium-sized effect showed group-based trauma interventions improved PTSD symptoms more than usual care; 24 RCTs, N = 2,229, g = -0.66, -0.94 to -0.37, $p < 0.0001$, $I^2 = 86\%$ Depression, psychological distress, and dissociation also improved with group-based trauma interventions. Trials with older participants reported significantly lower effect sizes than trials with younger participants. There were no significant differences in effect sized when group trauma memory processing was compared to psychoeducation, nor when trauma-focussed group interventions were compared to non-trauma-focussed group interventions.	
Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	Indirect; mixed treatment conditions.

Explanation of acronyms

CBT = cognitive behavioural therapy, CI = confidence interval, *d* or *g* = Cohen's d and Hedges' g, standardised mean difference, EMDR = eye movement desensitisation and reprocessing, 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, SMD = standardised mean difference between groups, SMC = standardised mean change within groups, vs. = versus

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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[7].

† 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[7].

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[8]. 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[7];

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

§ 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[9].

‖ 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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