TECHNICAL COMMENTARY

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Exposure therapy

Introduction

Exposure therapy helps people confront their fears in a safe environment. Although avoidance might help reduce feelings of fear in the short term, over the long term it can make the fear become even worse. Exposure therapy helps break the pattern of avoidance and fear. Prolonged exposure therapy consists of 9 to 12 90-minute sessions. Sessions one and two include information gathering and psychoeducation. The later sessions include repeated imaginal exposure to the index trauma and assignment of in-vivo exposure homework to avoided trauma cues.

In vivo exposure involves directly facing a feared object, situation, or activity. Imaginal exposure involves vividly imagining the feared factors, while virtual reality exposure uses technology to imitate the feared factors. Interoceptive exposure involves deliberately bringing on any physical sensations that are feared, though harmless.

Exposure therapy can be paced in different ways. Graded exposure is where the feared factors are ranked according to difficulty, with the mild factors exposed first. Flooding also uses this hierarchy but begins with the most difficult tasks. Systematic desensitisation combines exposure with relaxation to associate the feared factors with being relaxed.

Exposure therapy can help weaken previously learned associations between feared factors and bad outcomes. It can help show people that they can confront their fears and manage feelings of anxiety. People can learn to attach more realistic beliefs about the feared factors, and they can become more comfortable with the experience of fear.

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).

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Results

We found six systematic reviews that met our inclusion criteria[3-8].

- Moderate quality evidence found large effects of reduced PTSD and depressive symptoms, and more loss of PTSD diagnosis, with exposure therapies than with waitlist or usual care. There was a medium-sized effect of greater improvements in PTSD and depressive symptoms with prolonged exposure therapy than with relaxation.
- Moderate quality evidence found large effects of reduced PTSD symptoms and general subjective stress with prolonged exposure therapy compared to control conditions. These effects remained, but were reduced, at the 12-months follow-up. Larger effects were found when the comparison was with waitlist/no treatment than when the comparison was with a psychological placebo (e.g., treatment as usual). There were no differences in symptoms between prolonged exposure therapy and active treatments (e.g., cognitive therapies).
- Moderate quality evidence found medium-sized effects of improved PTSD and depression symptoms with virtual reality exposure therapy compared to inactive controls (no treatment, treatment as usual, waitlist, and attention placebo). More treatment sessions were associated with larger effect sizes, and effects remained for up to 12 months. There were no differences in symptom improvements between virtual reality exposure therapy and active controls (CBT, prolonged exposure, or present-centred group therapy).
- Moderate to low quality evidence found large effects of reduced PTSD symptom severity with narrative and prolonged exposure therapies compared to waitlist/no treatment in children and adolescents. At 1-4 months post-treatment narrative exposure therapy continued to show a large effect in children and adolescents.
- Moderate quality evidence found factors associated with uptake of prolonged exposure therapy or trauma-focussed CBT were (in descending order of effect); adaptability of staff workflow to CBT, veteran affairs service connection, staff familiarity with trauma-focussed CBT, mental health referral source, patient interest in trauma-centred treatment, Vietnam veterans, older age, increased PTSD severity, comorbid depression, female gender, black or racial-ethnic minority, and previous psychotherapy.

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Deng W, Hu D, Xu S, Liu X, Zhao J, Chen Q, Liu J, Zhang Z, Jiang W, Ma L, Hong X, Cheng S, Liu B, Li X

The efficacy of virtual reality exposure therapy for PTSD symptoms: A systematic review and meta-analysis

Journal of Affective Disorders 2019; 257: 698-709

View review abstract online

Comparison	**Effectiveness of virtual reality exposure therapy vs. control conditions (active and inactive) for PTSD symptoms in adults with PTSD.** **Active controls included cognitive behaviour therapy (CBT), prolonged exposure, and present-centred group therapy. Inactive controls included no treatment, treatment as usual, waitlist, and attention placebo.**
Summary of evidence	**Moderate quality evidence (small to medium-sized samples, consistent, mostly precise, indirect) found medium-sized effects of improved PTSD and depression symptoms with virtual reality exposure therapy compared to inactive controls (no treatment, treatment as usual, waitlist, and attention placebo). More treatment sessions were associated with larger effect sizes, and effects remained for up to 12 months. There were no differences in symptom improvements between virtual reality exposure therapy and active controls (CBT, prolonged exposure, or present-centred group therapy).**

PTSD symptoms

Small-medium effects of improved PTSD and depression symptoms with virtual reality exposure therapy vs. controls;

PTSD: 10 RCTs, N = 309, $g = 0.327$, 95%CI 0.105 to 0.550, $p < 0.01$, $I^2 = 48\%$, $p = 0.46$

Depression: 7 RCTs, N = 209, $g = 0.373$, 95%CI 0.110 to 0.637, $p < 0.01$, $I^2 = 49\%$, $p > 0.05$

Meta-regression showed more treatment sessions were associated with larger effect sizes.

Subgroup analysis showed the effects were medium-sized when compared to inactive controls, but not-significant when compared to active controls;

PTSD, inactive controls: 5 RCTs, N = 175, $g = 0.567$, 95%CI 0.270 to 0.863, $p < 0.01$

PTSD, active controls: 6 RCTs, N = 239, $g = 0.017$, 95%CI -0.412 to 0.445, $p = 0.939$

Depression, inactive controls: 4 RCTs, N = 176, $g = 0.548$, 95%CI 0.204 to 0.892, $p = 0.002$

Depression, active controls: 3 RCTs, N = 138, $g = 0.124$, 95%CI -0.286 to 0.535, $p = 0.553$

The pre-post treatment effect for improvement in PTSD symptoms was medium-sized at 3-month follow-up; 6 RCTs, N not reported, g = 0.697, 95%CI 0.262 to 1.133, p < 0.01 *The pre-post treatment effect for improvement in PTSD symptoms was large at 6-month follow-up;* 6 RCTs, N not reported, g = 0.848, 95%CI 0.324 to 1.372, p < 0.01	
Consistency in results‡	Consistent where reported
Precision in results§	Mostly precise
Directness of results‖	Indirect; mixed control conditions

DiMauro J

Exposure therapy for posttraumatic stress disorder: A meta-analysis

Military Psychology 2014; 26: 120-30

View review abstract online

Comparison	**Effectiveness of exposure therapy vs. virtual reality exposure therapy for PTSD symptoms in adults with PTSD.**
Summary of evidence	**Moderate to high quality evidence (large sample for exposure therapy, small sample for virtual reality exposure therapy, inconsistent, precise, direct) found a large effect of improved PTSD symptoms pre-post treatment with exposure therapy, and a medium-sized effect with virtual reality exposure pre-post treatment.**
PTSD symptoms	
There was a large effect of improved PTSD symptoms pre-post treatment with exposure therapy, and a medium-sized effect with virtual reality exposure; Exposure therapy: 22 studies, N = 617, SMD = 1.06, 95%CI 0.84 to 1.29, p < 0.001 Virtual reality exposure therapy: 6 studies, N = 60, SMD = 0.69, 95%CI 0.35 to 1.02, p < 0.001 There was no moderating effect of sex.	
Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	Direct

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Forman-Hoffman V, Middleton JC, Feltner C, Gaynes BN, Weber RP, Bann C, Viswanathan M, Lohr KN, Baker C, Green J

Psychological and Pharmacological Treatments for Adults With Posttraumatic Stress Disorder: A Systematic Review Update

Agency for Healthcare Research and Quality Comparative Effectiveness Reviews (US)
Report No.: 18-EHC011-EF: 2018-SR-01

View review abstract online

Comparison	**Effectiveness of exposure therapies vs. inactive control conditions (waitlist or usual care) or active controls (relaxation) for PTSD symptoms in adults with PTSD.**
Summary of evidence	**Moderate quality evidence (large or small samples, inconsistent, precise, indirect, or direct) found large effects of reduced PTSD and depressive symptoms, and more loss of PTSD diagnosis, with exposure therapies than with waitlist or usual care. There was a medium-sized effect of greater decreases in PTSD and depressive symptoms with prolonged exposure therapy than with relaxation.**
PTSD symptoms	
Large effects showed reduced PTSD and depressive symptoms, and more loss of PTSD diagnosis, with exposure therapies than with waitlist/treatment as usual; PTSD symptoms: 13 RCTs, N = 885, SMD = -1.23, 95%CI -1.50 to -0.97, I^2 = 67.5% Depressive symptoms: 10 RCTs, N = 7,152, SMD = -0.76, 95%CI -0.91 to -0.60, I^2 = 19% Loss of PTSD diagnosis: 6 RCTs, N = 409, RD = 0.56, 95%CI 0.35 to 0.78, I^2 = 91% *There were medium-sized effects of greater decreases in PTSD and depressive symptoms with prolonged exposure therapy than with relaxation;* PTSD symptoms: 3 RCTs, N = 155, SMD = -0.45, 95%CI -0.78 to -0.13 Depressive symptoms: 3 RCTs, N = 155, SMD = -0.39, 95%CI -0.71 to -0.07	
Consistency in results	Inconsistent, apart from depressive symptoms.
Precision in results	Precise
Directness of results	Indirect for inactive controls (mixed control conditions), direct for active controls.

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Mavranezouli I, Megnin-Viggars O, Daly C, Dias S, Stockton S, Meiser-Stedman R, Trickey D, Pilling S

Research Review: Psychological and psychosocial treatments for children and young people with post-traumatic stress disorder: a network meta-analysis

Journal of Child Psychology and Psychiatry, and Allied Disciplines 2020; 61: 18-29

View review abstract online

Comparison	**Effectiveness of exposure therapies vs. waitlist/no treatment for PTSD symptoms in children and adolescents (up to 18 years old).**
Summary of evidence	**Moderate to low quality evidence (large overall sample, unclear consistency, imprecise, indirect) found large effects of reduced PTSD symptom severity with narrative and prolonged exposure therapies compared to waitlist/no treatment. At 1-4 months post-treatment narrative exposure therapy continued to show a large effect.**
PTSD symptoms	
Network meta-analysis included 29 RCTs, N = 1,960 *Narrative exposure and prolonged exposure showed large effects of improved PTSD symptoms post-treatment compared to waitlist/no treatment;* Narrative exposure: SMD = -1.49, 95%CrI -2.25 to -0.74 Exposure/prolonged exposure: SMD = -1.34, 95%CrI -2.15 to -0.51 At 1-4 months follow-up, narrative exposure continued to show a large effect.	
Consistency in results	Authors report no inconsistency between direct and indirect evidence. Consistency between individual study results is unclear.
Precision in results	Imprecise
Directness of results	Indirect; network meta-analysis

Powers MB, Halpern JM, Ferenschak MP, Gillihan SJ, Foa EB

A meta-analytic review of prolonged exposure for posttraumatic stress disorder

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Exposure therapy

Clinical Psychology Review 2010; 30: 635-41 View review abstract online	
Comparison	**Effectiveness of prolonged exposure therapy vs. control conditions for PTSD symptoms in adults or adolescents with PTSD.**
Summary of evidence	**Moderate quality evidence (large samples, inconsistent, precise, indirect) found large effects of reduced PTSD symptom severity and general subjective stress with prolonged exposure therapy compared to control conditions. These effects remained, but were reduced, at the 12-months follow-up. Larger effects were found when the comparison was with waitlist/no treatment than when the comparison was with a psychological placebo (e.g., relaxation, treatment as usual). There were no differences in symptoms between prolonged exposure and active treatments (e.g., cognitive therapies).**
PTSD symptoms	
Large effects showed prolonged exposure outperformed control conditions on; Reduced PTSD symptoms: 13 RCTs, N = 675, $g = 1.08$, 95%CI 0.69 to 1.46, $p < 0.001$ Reduced general subjective distress: 13 RCTs, N = 666, $g = 0.77$, 95%CI 0.53 to 1.01, $p < 0.001$ The average participant receiving prolonged exposure fared better than 86% of the control participants at post-treatment on PTSD symptoms, and 79% of the control participants at post-treatment on subjective distress. These effects remained, but were slightly reduced, at 12 months follow-up. There were no moderating effects of time since trauma, publication year, dose, study quality, or type of trauma. *Larger effects of improved symptoms were found when comparing prolonged exposure with waitlist/no treatment than when comparing prolonged exposure with a psychological placebo;* Waitlist: 7 RCTs, N not reported, $g = 1.51$, 95%CI 1.12 to 1.90, $p < 0.05$ Psychological placebo: 8 RCTs, N not reported, $g = 0.65$, 95%CI 0.29 to 1.01, $p < 0.05$ *There were no significant differences in symptoms between prolonged exposure and other active treatments (cognitive processing therapy, cognitive therapy, eye movement desensitisation and reprocessing, or stress inoculation training);* 6 RCTs, N = 262, $g = -0.07$, 95%CI -0.42 to 0.28, $p = 0.69$	
Consistency in results	Authors report data are inconsistent.
Precision in results	Precise
Directness of results	Indirect; mixed control conditions.

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Van Den Berk Clark C, Moore R, Secrest S, Tuerk P, Norman S, Myers U, Lustman P, Schneider F, Barnes J, Gallamore R, Ovais M, Plurad J, Scherrer J

Factors associated with receipt of cognitive-behavioral therapy or prolonged exposure therapy among individuals with PTSD

Psychiatric Services 2019; 70: 703-13

View review abstract online

Comparison	**Factors associated with uptake of prolonged exposure therapy or trauma-focussed CBT.**
Summary of evidence	**Moderate quality evidence (large samples, inconsistent, some imprecision, direct) found factors associated with uptake of prolonged exposure therapy or trauma-focussed CBT were (in descending order of effect); adaptability of staff workflow to CBT, veteran affairs service connection, staff familiarity with trauma-focussed CBT, mental health referral source, patient interest in trauma-centred treatment, Vietnam veterans, older age, increased PTSD severity, comorbid depression, female gender, black or racial-ethnic minority, and previous psychotherapy.**

Factors increasing uptake

There was increased rates of treatment initiation with (in descending order of effect);

Adaptability of staff workflow: 2 studies, N = 63,052, OR = 4.66, 95%CI 1.60 to 7.72, $p < 0.05$

Veteran affairs service connection: 3 studies, N = 631,067, OR = 2.30, 95%CI 2.18 to 2.42, $p < 0.05$

Staff exposure to trauma interventions: 3 studies, N = 693,796, OR = 2.30, 95%CI 2.09 to 2.52, $p < 0.05$

Mental health referral source: 2 studies, N = 61,452, OR = 2.28, 95%CI 1.05 to 3.50, $p < 0.05$

Interest in trauma-centered treatment: 1 study, N = 476, OR = 2.13, 95%CI 1.37 to 3.30, $p < 0.05$

Vietnam veteran: 3 studies, N = 964, OR = 1.58, 95%CI 1.00 to 2.15, $p < 0.05$

Older age: 9 studies, N = 645,407, OR = 1.56, 95%CI 1.51 to 1.61, $p < 0.05$

Increased PTSD severity: 6 studies, N = 1,890, OR = 1.46, 95%CI 1.13 to 1.78, $p < 0.05$

Comorbid depression: 9 studies, N = 288,486, OR = 1.21, 95%CI 1.14 to 1.29, $p < 0.05$

Female gender: 8 studies, N = 288,848, OR = 1.18, 95%CI 1.08 to 1.27, $p < 0.05$

Black or racial-ethnic minority: 9 studies, N = 288,470, OR = 1.16, 95%CI 1.03 to 1.28, $p < 0.05$

Previous psychotherapy: 5 studies, N = 274,206, OR = 1.01, 95%CI 1.01 to 1.02, $p < 0.05$

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Consistency in results	Authors report results are inconsistent, although including only high-quality studies reduced heterogeneity for sex, race, military era, and staff training.
Precision in results	Some imprecision
Directness of results	Direct

Explanation of acronyms

CI = confidence interval, *d* or *g* = Cohen's d and Hedges' g, standardised mean difference, I^2 = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), N = number of participants, RCT = randomised controlled trial, SMD = standardised mean difference, *p* = statistical probability of obtaining that result, 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[9].

† 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[9].

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[10]. 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[9];

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

§ 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[11].

‖ 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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