TECHNICAL COMMENTARY

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Hyperarousal

Introduction

Hyperarousal is a core symptom of PTSD, with at least two avoidance symptoms being required for a diagnosis. Hyperarousal symptoms include irritability or aggression, risky or destructive behavior, hypervigilance, heightened startle reaction, difficulty concentrating, and difficulty sleeping.

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 a diagnosis of PTSD. Reviews were identified by searching the databases MEDLINE, EMBASE, and PsycINFO. Hand searching reference lists of identified reviews was also conducted. Reviews with pooled data are prioritised 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. The PRISMA flow diagram is a suggested way of providing information about studies included and excluded with reasons for exclusion. Where no flow diagram has been presented by individual reviews, but identified studies have been described in the text, reviews have been checked for this item. 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, low or very 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, there is a dose dependent response or if results are reasonably 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 low quality evidence finds five clusters of hyperarousal symptoms; irritability/anger, difficulty concentrating, hypervigilance, startle, and sleep difficulty.
- Items relating to irritability/anger include; *I lost my cool and exploded over minor everyday things, I lost my temper, little things made me angry, I felt irritable, I had angry outbursts,* and *I felt that if someone pushed me too far, I would become angry.*
- Items relating to difficulty concentrating include; *I had difficulty paying attention, I was unusually forgetful, I had difficulty concentrating, I had trouble concentrating, I had trouble keeping my mind on what I was doing,* and *I had more trouble than usual remembering things.*
- Items relating to hypervigilance include; *I watched out for danger since the trauma, I was overly alert (for example, checking to see who was around me), I was very aware*

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of my surroundings and nervous about what's going on around me, and *I felt on guard.*

- Items relating to startle include; *unexpected noises made me jump, I was jumpy or easily startled by ordinary noises or movements, I was watchful or on guard, I got startled when there was a sudden noise or movement, unexpected noises startled me more than usual, I was jumpy or startled at something unexpected,* and *I felt jumpy or easily startled*
- Items relating to sleep difficulty include; *my sleep was restless, I had trouble falling asleep, I had sleep problems,* and *I had trouble staying asleep.*
- Moderate to low quality evidence finds a medium-sized effect that people with PTSD and sleep disturbances were significantly more likely to report suicidal behaviours than those without sleep disturbances.
- Moderate to high quality evidence finds small effects of less sleep efficiency, less total sleep time, less slow wave sleep, and more wake time after sleep onset in people with PTSD. Authors report that after adjusting for possible publication bias, the effect sizes for total sleep time, slow wave sleep, and more wake time after sleep onset did not reach statistical significance.

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Del Vecchio N, Elwy AR, Smith E, Bottonari KA, Eisen SV

Enhancing self-report assessment of PTSD: development of an item bank

Journal of Traumatic Stress 2011; 24: 191-9

View review abstract online

Comparison	**Self-report items relating to the PTSD symptom cluster of hyperarousal.**
Summary of evidence	**Moderate to low quality evidence (direct, unclear sample size, unable to assess consistency or precision) finds five clusters of hyperarousal symptoms; sleep difficulty, irritability/anger, difficulty concentrating, hypervigilance, and startle.**

Hyperarousal items assessed on:

Acute Stress Disorder Scale (ASDS), Anxiety and Depression Detector (ADD), Beck Anxiety Inventory – Primary Care (BAI-PC), Seven Symptom Scale - Short Screening Scale for PTSD, Davidson Trauma Scale (DTS) , Detailed Assessment of Posttraumatic Stress (DAPS), Harvard Trauma Questionnaire (HTQ), Impact of Event Scale-Revised (IES-R), Late Effect of Accidental Injury Questionnaire, Los Angeles Symptom Checklist (LASC), Millon Clinical Multiaxial Inventory-III (MCMI-III), MMPI-2 Keane PTSD subscale, Mississippi Scale for Combat Related PTSD, Modified PTSD Symptom Scale (MPSS), National Anxiety Disorder Day Screen, National Women's Study-PTSD module (NWS-PTSD), Penn Inventory, Peritraumatic Distress Inventory (PDI), Posttraumatic Chronic Pain Test (PCPT), Posttraumatic Cognitions Inventory (PTCI), Posttraumatic Stress Scale (PTSS-10,14), Primary Care PTSD Screen (PC-PTSD), Psychiatric Diagnostic Screening Questionnaire (PDSQ), PTSD Checklist (PCL all versions), PTSD Diagnostic Scale (PDS), PTSD Inventory, PTSD Screening and Diagnostic Scale (PSDS), PTSD Symptom Scale-Self-Report (PSS-SR), Problem Checklist, Project IMPACT PTSD Screener, Purdue Posttraumatic Scale (PPS), Responses to Script-Driven Imagery Scale (RSDI), Revised Civilian Mississippi Scale for PTSD (R-CMS), Screen for Posttraumatic Stress Disorder (SPTSS), Short Post-Traumatic Stress Disorder Rating Interview, expanded version (SPRINT-E), Trauma Screening Questionnaire (TSQ), Trauma Stress Schedule (TSS), Traumatic Stress Symptom Checklist (TSSC), Trauma Symptom Checklist-40 (TSC-40), Trauma Symptom Inventory (TSI), UK PTSS-14

275 studies, N not reported

Sleep Difficulty

My sleep was restless

I had trouble falling asleep

I had sleep problems

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I had trouble staying asleep Irritability/Anger I lost my cool and exploded over minor everyday things I lost my temper Little things made me angry I felt irritable I had angry outbursts I felt that if someone pushed me too far, I would become angry Difficulty Concentrating I had difficulty paying attention I was unusually forgetful I had difficulty concentrating I had trouble concentrating I had trouble keeping my mind on what I was doing I had more trouble than usual remembering things Hypervigilance I watched out for danger since the trauma I was overly alert (for example, checking to see who was around me) I was very aware of my surroundings and nervous about what's going on around me I felt on guard Startle Unexpected noises made me jump I was jumpy or easily startled by ordinary noises or movements I was watchful or on guard I got startled when there was a sudden noise or movement Unexpected noises startled me more than usual I was jumpy or startled at something unexpected I felt jumpy or easily startled	
Consistency in results‡	Unable to assess; no measure of consistency is reported.
Precision in results§	Unable to assess; no measure of precision is reported.
Directness of results‖	Direct

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Malik S, Kanwar A, Sim LA, Prokop LJ, Wang Z, Benkhadra K, Murad MH

The association between sleep disturbances and suicidal behaviors in patients with psychiatric diagnoses: a systematic review and meta-analysis

Systematic Reviews 2014; 3: 18

View review abstract online

Comparison	**Relationship between sleep disturbances and suicidal behaviour in people with PTSD.**
Summary of evidence	**Moderate to low quality evidence (small sample, imprecise, direct) finds a medium-sized effect that people with PTSD and sleep disturbances were significantly more likely to report suicidal behaviours than those without sleep disturbances.**
Sleep disturbance and suicide	
A medium-sized effect showed people with PTSD and sleep disturbances were significantly more likely to report suicidal behaviours; 1 study, N = 153, OR = 2.56, 95%CI 1.91 to 3.43, $p < 0.001$	
Consistency in results	Not applicable; 1 study
Precision in results	Imprecise
Directness of results	Direct

Zhang Y, Ren R, Sanford LD, Yang L, Zhou J, Zhang J, Wing YK, Shi J, Lu L, Tang X

Sleep in posttraumatic stress disorder: A systematic review and meta-analysis of polysomnographic findings

Sleep Medicine Reviews 2019; 48: 101210

View review abstract online

Comparison	**Sleep disturbances in people with PTSD vs. controls.**
Summary of evidence	**Moderate to high quality evidence (large samples, precise,**

	inconsistent, direct) finds small effects of less sleep efficiency, less total sleep time, less slow wave sleep, and more wake time after sleep onset in people with PTSD. Authors report that after adjusting for possible publication bias, the effect sizes for total sleep time, slow wave sleep, and more wake time after sleep onset did not reach statistical significance.
Sleep disturbance	
31 studies *Small effects of more sleep disturbance in people with PTSD in;* Less sleep efficiency: N = 1,923, SMD = -0.317, 95%CI -0.504 to -0.131, $p < 0.01$, $I^2 = 63\%$, $Qp < 0.001$ Less total sleep time: N = 2,059, SMD = -0.205, 95%CI -0.352 to -0.059, $p < 0.01$, $I^2 = 46\%$, $Qp < 0.01$ Less slow wave sleep: N = 2,047, SMD = -0.213, 95%CI -0.386 to -0.039, $p < 0.05$, $I^2 = 61\%$, $Qp < 0.001$ More wake time after sleep onset: N = 1,490, SMD = 0.251, 95%CI 0.100 to 0.402, $p < 0.01$, $I^2 = 37\%$, $Qp < 0.05$ Authors report that after adjusting for possible publication bias, the effect sizes for total sleep time, slow wave sleep, and more wake time after sleep onset did not reach a statistical significance. Sex, age, PTSD severity, type of controls, medication status, adaptation night, polysomnographic scoring rules, and study location were factors that contributed to heterogeneity between studies.	
Consistency in results	Inconsistent
Precision in results	Precise
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, OR = odds ratio, *p* = statistical probability of obtaining that result, Q = statistical test for heterogeneity, SMD = standardised mean difference, 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[6].

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† 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). A receiver operating characteristic (ROC) curve represents sensitivity/specificity pairs corresponding to different cut-off values. A guide for interpreting the area under the curve (AUC) statistic is; 0.90 to 1.00 = excellent, 0.80 to 0.90 = good, 0.70 to 0.80 = fair, 0.60 to 0.70 = poor, and 0.50 to 0.60 = fail.

Weighted mean difference scores refer to mean differences between treatment and comparison groups after treatment (or occasionally pre to post treatment) and in a randomized trial there is an assumption that both groups are comparable on this measure prior to treatment. Standardized 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. 0.2 represents a small effect, 0.5 a moderate effect, and 0.8 and over 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 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. Unstandardized (*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. Standardized 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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