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Stress related disorders and physical health

PTSD is associated with diverse physical conditions

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Post-traumatic stress disorder (PTSD) and other stress related disorders are common and associated with considerable distress, psychiatric comorbidity, and reduced functioning.¹ Less well recognised is the substantial physical comorbidity associated with these conditions, highlighting an ongoing tendency to a dualistic view of mind and body.² Song and colleagues' (doi:10. 1136/bmj.l5784) concerning finding that people with stress related disorders are at significantly heightened risk of life threatening infections³ challenges this notion and adds to previous research suggesting overlapping mechanistic pathways between mental and physical health.⁴

PTSD is strongly associated with poor physical health. A recent summary of reviews⁵ identified increasingly robust evidence confirming a link between PTSD and various physical conditions, including gastrointestinal, dermatological, musculoskeletal, neurological, and cardiorespiratory disorders. One meta-analysis found a 27% increase in the rate of cardiac events or cardiac specific mortality in people with PTSD after adjusting for depression and personal, clinical, and psychosocial factors.⁶ In a previous study, Song and colleagues found that people with PTSD had a 46% higher risk of developing an autoimmune disorder than people without PTSD.⁷

The true nature of the relation between physical health and stress related disorders is difficult to tease out; various biological, psychological, and social factors are likely contributors. For example, a significantly increased risk of type 2 diabetes in people with PTSD disappears after controlling for obesity.⁵

The high comorbidity of PTSD with physical symptoms and syndromes that are often difficult to explain on the basis of physical disease alone is well recognised.⁸ Somatic symptoms, whatever their cause, are common, particularly among people with more complex stress related disorders. DESNOS (disorders of extreme stress not otherwise specified) was proposed as a new diagnosis for a previous iteration of the Diagnostic and Statistical Manual for Mental Disorders (fourth edition), with somatisation as a diagnostic criterion.⁹ Although not accepted, the features of DESNOS, including "somatic complaints" were included as "associated descriptive features" of PTSD that "may occur."

Common pathways

Various mechanisms have been suggested to explain observed associations between stress related disorders and physical disorders. Key among them is a disturbed hypothalamic-pituitary-adrenal axis, with reduced cortisol levels or receptor resistance leading to heightened adrenergic tone and excessive inflammation.⁵ Song and colleagues argue that their

results are consistent with this hypothesis and the resultant overproduction of inflammatory cytokines.³

Some researchers have argued that PTSD might be a systemic illness or one that has systemic manifestations,⁴ others that it is an immunological disorder.¹⁰ A systematic review of inflammatory markers and PTSD found PTSD to be associated with increased levels of interleukin 6, interleukin 1 β , tumour necrosis factor α , and interferon γ .¹¹

The largest genome-wide analysis of PTSD,¹² including more than 30 000 people with PTSD and 170 000 controls, provided heritability estimates of 5-20%, similar to those for depression. Heritability is likely to be polygenic, but loci associated with PTSD include one that influences immunity and inflammation and might explain some of the excess physical morbidity seen in people with PTSD.

Song and colleagues' methodology is strong but they correctly acknowledge some limitations and an inability to determine causality.³ As with many cohort studies of PTSD, not controlling for exposure to trauma and lack of standardised assessment of the PTSD phenotype give further cause for caution when interpreting the results.

Their finding of increased risk in those with younger age of PTSD onset is important and consistent with the known association between adverse childhood experiences, particularly multiple adverse childhood experiences, and poor subsequent physical and mental health.¹³ It could be that people with more complex presentations of stress related disorders are particularly vulnerable. The introduction of Complex PTSD as a parallel diagnosis to PTSD in the newly created grouping of disorders specifically associated with stress in the International Classification of diseases (11th revision)¹⁴ provides an opportunity to further explore this possibility.

Finding that treatment with selective serotonin reuptake inhibitors seems to be protective against life threatening infection is also important, and it emphasises the need for effective treatment of PTSD. Drug treatments for PTSD tend to be less effective than psychological treatments, and recently updated guidelines highlight the increasing number of evidence based approaches available.¹⁵

Firm conclusions about the associations between stress related disorders and physical health would be premature, but mounting evidence suggests that carefully designed studies to identify common or related mechanistic pathways could be fruitful in the future. PTSD, with its high level of physical comorbidity, is a major public health concern; a holistic biopsychosocial approach to research and management of PTSD, coproduced with patients and families, is likely the best way to help people with this common and debilitating condition.

- 1 Bisson JI, Cosgrove S, Lewis C, Roberts NP. Post-traumatic stress disorder (Clinical Review). *BMJ* 2015;51:h616110.1136/bmj.h6161.
- 2 Demertzi A, Liew C, Ledoux D, et al . Dualism persists in the science of mind. *Ann N Y Acad Sci* 2009;1157:1-9. 10.1111/j.1749-6632.2008.04117.x 19351351
- 3 Song H, Fall K, Fang F, et al . Stress related disorders and subsequent risk of life threatening infections: a population-based sibling-controlled cohort study. *BMJ* 2019;367:l5784.
- 4 Mellon SH, Gautam A, Hammamieh R, Jett M, Wolkowitz OM. Metabolism, metabolomics, and inflammation in posttraumatic stress disorder. *Biol Psychiatry* 2018;83:866-75. 10.1016/j.biopsych.2018.02.007 29628193
- 5 Ryder AL, Azcarate PM, Cohen BE. PTSD and physical health. *Curr Psychiatry Rep* 2018;20:116. 10.1007/s11920-018-0977-9 30367276
- 6 Edmondson D, Kronish IM, Shaffer JA, Falzon L, Burg MM. Posttraumatic stress disorder and risk for coronary heart disease: a meta-analytic review. *Am Heart J* 2013;166:806-14. 10.1016/j.ahj.2013.07.031 24176435
- 7 Song H, Fang F, Tomasson G, et al . Association of stress-related disorders with subsequent autoimmune disease. *JAMA* 2018;319:2388-400. 10.1001/jama.2018.7028 29922828
- 8 Gupta MA. Review of somatic symptoms in post-traumatic stress disorder. *Int Rev Psychiatry* 2013;25:86-99. 10.3109/09540261.2012.736367 23383670
- 9 American Psychiatric Association. *Diagnostic and Statistical Manual for Mental Disorders*. 4th ed. American Psychiatric Association Press, 1994.
- 10 Wang Z, Caughron B, Young MRI. Posttraumatic stress disorder: an immunological disorder? *Front Psychiatry* 2017;8:222. 10.3389/fpsy.2017.00222 29163241
- 11 Passos IC, Vasconcelos-Moreno MP, Costa LG, et al . Inflammatory markers in post-traumatic stress disorder: a systematic review, meta-analysis, and meta-regression. *Lancet Psychiatry* 2015;2:1002-12. 10.1016/S2215-0366(15)00309-0 26544749
- 12 Nievergelt CM, Maihofer AX, Klengel T, et al . International meta-analysis of PTSD genome-wide association studies identifies sex- and ancestry-specific genetic risk loci. *Nat Commun* 2019;10:4558. 10.1038/s41467-019-12576-w 31594949
- 13 Hughes K, Bellis MA, Hardcastle KA, et al . The effect of multiple adverse childhood experiences on health: a systematic review and meta-analysis. *Lancet Public Health* 2017;2:e356-66. 10.1016/S2468-2667(17)30118-4 29253477
- 14 World Health Organisation. *ICD-11 International Classification of Diseases 11th Revision*. WHO2018; <https://icd.who.int>
- 15 Bisson JI, Berliner L, Cloitre M, et al . The International Society for Traumatic Stress Studies new guidelines for the prevention and treatment of posttraumatic stress disorder: methodology and development process. *J Trauma Stress* 2019;32:475-83. 10.1002/jts.22421 31283056