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EDITORIAL

Post-traumatic stress disorder and chronic disease: open questions and future directions

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Introduction

A large body of research has now firmly established that traumatic events, such as natural disasters, combat, sexual assault, and child abuse, are frequent occurrences throughout the world and that there are substantial consequences of traumatic event experiences. In most countries, the majority of adults report exposure to at least one traumatic event in their lifetime [1]. PTSD, the paradigmatic stress-related mental disorder, emerges in some persons in response to an unpredictable and uncontrollable traumatic event. PTSD is common with lifetime estimates ranging from 1.7 % in South Korea to 8.8 % in Northern Ireland, and past-year prevalences from a high of 3.8 % in Northern Ireland to a low of 0.2 % in China [2]. Separately, evidence shows that persons who experience traumatic events are more likely to report cardiovascular disease, respiratory disease, and other physical illness [3].

Researchers and health professionals commonly treat the brain and the body as if they are distinct entities, and this approach informs most of the scholarship about the consequences of traumatic events. However, recent advances in our understanding of the relation between PTSD and chronic diseases such as cardiovascular disease and type-2 diabetes suggest this approach is misguided. For example, a recent meta-analysis showed that PTSD and PTSD symptoms are associated with worse self-reported health and health-related quality of life [4]. Rigorous prospective studies have provided evidence that PTSD increases risk of first-onset cardiovascular disease and type-2 diabetes [5, 6]. This evidence, and a comparable body of literature, suggests that PTSD may have profound adverse effects on physical health over the life course. This opens up an important new perspective on the study of the consequences of PTSD and an emerging literature is now informing our understanding of how PTSD may be linked to physical illness.

Two open questions

There are at least two major open questions that limit our understanding of the relation between PTSD and chronic disease.

First, there is the question of the causal relation among trauma, PTSD, and chronic disease. Simply put, does PTSD cause chronic disease, or is there some complex relation among trauma, PTSD, and other chronic diseases. A randomized clinical trial that assesses the consequences to chronic disease of PTSD treatment might shed light on this issue. However, such a study would be impractical and unethical. This suggests that addressing this question must rest on observational data.

Observational data embeds its own particular challenges, particularly temporality and confounding. With regard to temporality, the majority of studies that have documented the relation between PTSD and chronic disease are cross sectional. Rather than PTSD increasing risk of chronic disease, chronic disease may increase risk of PTSD. For example, acute myocardial infarction and stroke have all been associated with increased risk of PTSD [7, 8]. Temporality can be addressed by rigorous prospective epidemiologic studies that exclude persons with chronic

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disease at baseline and examine whether PTSD increases risk of first onset of chronic disease. Confounding is more difficult to address, and may arise if there is a complex causal relation among trauma, PTSD, chronic disease, and other variables. For example, childhood abuse increases risk for the development of PTSD and has been associated with increased risk of chronic disease in the absence of PTSD [9, 10]. Thus, an observed association between PTSD and chronic disease may be due to both conditions being related to childhood abuse.

These two challenges are of interest academically but also have important implications for the mitigation of the consequences of traumatic events. If PTSD truly causes chronic disease, persons with PTSD may benefit from greater surveillance of risk factors and early interventions to prevent the subsequent development of chronic disease. If the PTSD–chronic disease association is explained by other factors, identification of such factors may suggest common potential points of interventions for both PTSD and chronic disease. If the relation is explained by shared genetic risk, this gives clues to the genetic etiology of PTSD and potentially for the comorbidity of PTSD and chronic disease more broadly. Moreover, if PTSD is not causally related to chronic disease, this would suggest treating PTSD, which is important in its own right, would not in an of itself decrease risk of chronic disease.

Second, understanding the mechanistic pathways via which PTSD produces chronic disease remain very much an open question. One possibility is that PTSD alters the health behavior determinants of chronic disease. PTSD is prospectively associated with behavioral risk factors for chronic disease including onset and course of smoking and obesity [11–13]. PTSD has also been associated in cross-sectional studies with significantly reduced likelihood of engaging in positive health behaviors such as physical inactivity and healthy diet, established determinants of chronic disease.

If PTSD increases risk of obesity through adverse effects on health behaviors such as diet and exercise, critical risk factors for many chronic diseases, this implies treatments for PTSD should address key health-related behaviors. PTSD treatments rarely address health-related alterations; lifestyle factors that most strongly influence disease risk—diet, exercise and obesity—are notoriously difficult to change. Identifying 'determinants of determinants'—other factors that may drive these lifestyle factors—may offer new opportunities for intervention to reduce risk of adverse health outcomes. Health behaviors are currently completely outside the scope of PTSD treatments despite the strong evidence that PTSD is correlated with poor physical health.

Another possibility is that PTSD produces neurobiological alterations that increase chronic disease risk. Persons with PTSD, compared to those exposed to trauma but did not develop PTSD, show alterations in inflammatory pathways, lipids and neuroendocrine dysfunction similar to individuals with prevalent cardiovascular disease and type-2 diabetes, and emerging evidence suggests PTSD may be related to accelerated aging [14, 15]. However, few epidemiological studies have measured biomarker levels before and after PTSD onset. Cross-sectional studies documenting an association between PTSD and biomarker elevations cannot determine whether elevations in biomarkers represent vulnerability for PTSD or developed as a consequence of the disorder. Inflammation, in particular, may be a vulnerability factor for psychiatric disorders, with a recent study finding elevations in CRP associated with increased risk of PTSD in a military sample [16].

Directions

Emerging evidence suggests that PTSD increases risk of chronic disease, and this has profound implications for research, practice and our understanding of PTSD as a mental disorder. Open questions of causal structures and of potential mechanistic pathways represent both challenges to the current state-of-the-science and opportunities for innovative scholarship. To advance the science, research is needed that examines whether PTSD onset is accompanied by changes in a broad range of biomarkers for chronic disease. If PTSD alters some biomarkers but not others, this would provide new insight into the pathophysiologic changes that do and do not result from extreme stress. Identification of behavioral and biological alterations produced by PTSD, and whether they lead to disease-related pathophysiological processes can also provide new insight into the neurobiology of PTSD and its relation with chronic disease broadly.

Conflict of interest The authors report no conflict of interest.

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