Hypertension, a Posttraumatic Stress Disorder?
Time to Widen Our Perspective

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Hypertension has long been suspected of being, in some patients, a psychosomatic disorder. The impact of daily exposure to life stresses, to anger, or to anxiety on high blood pressure has been studied for decades, but these works showed inconsistent results and, as such, mostly failed to confirm the underlying hypotheses.[1] Nevertheless, the role of 2 specific psychological impairments in the development of hypertension is supported by stronger evidence and, as such, deserves further investigation: the repression of the expression of affects[2] and the exposure to intensely traumatic life events.[1]

In particular, posttraumatic stress disorder (PTSD) has been associated with an increased risk of hypertension in a nationally representative US population sample of 4008 subjects (odds ratio, 2.6–2.9 according to the model),[3] and cohorts of 303 223 (odds ratio, 1.6–2.9)[4] and 194 319 (hazard ratio, 1.1–1.3) US veterans deployed in Iraq and Afghanistan.[5] On the other hand, in 3846 wounded US military service members, Stewart et al[6] reported increased incidence rates of hypertension (from 6% to 15%) according to the degree of severity of the initial injury.

In the current issue of *Hypertension*, Howard et al[7] provide further insights into the underlying mechanisms of hypertension in this cohort, by showing a correlation between the chronicity of PTSD (present in a huge proportion of 42% of subjects) and subsequent development of high blood pressure. Interestingly, although both severity of initial injury and duration of PTSD contributed to the risk of hypertension, they appeared to operate at least in part independently.

As mentioned above, the finding of an association between PTSD and hypertension is not limited to veterans after war exposure but has also been documented in the general population.[3] Unfortunately, in the latter, the characteristics of patients with PTSD and hypertension have not been reported in detail. In an insightful article of 1996, Mann[2] reported a history of unusually severe psychological trauma in 8 of 10 patients with severe, paroxysmal hypertension. Although this article, reflecting the experience of the author rather than hard evidence, apparently raised little attention by the time of its publication, nowadays, it is consonant with the experience of physicians seeing patients with refractory hypertension. For example, in our center, 16 of 30 patients with this profile, mostly referred for renal denervation, displayed evidence of various psychological problems or past trauma, including, between others, 2 cases of documented PTSD (1 patient who survived genocide in Rwanda and another who was tortured in Algeria), 2 cases of battered women, and 1 case of child abuse in the family. Interestingly, in patients with uncontrolled hypertension, preliminary data suggest a significant correlation between the number of PTSD symptoms and poor drug adherence,[8] which in turn is frequent in patients with apparently treatment-resistant hypertension.[9]

For these different reasons, we think that evaluation of PTSD as a causative factor of hypertension should not be limited to the specific population of veterans exposed to war-related physical and psychological trauma but deserves to be investigated in patients with other forms of severe, difficult-to-control hypertension. This belief is further reinforced by novel findings from our group presented at the 27th European Meeting on Hypertension and Cardiovascular Protection (Milan, June 16th–19th)[10] showing a high prevalence (17.3% versus 6% in the normal population[11]) of PTSD in a cohort of 35 consecutive patients with refractory hypertension. Whereas drug adherence correlated with the number of traumatic events, the degree of drug resistance correlated with the difficulty to express related emotions. Though at another scale and in a completely different context, these results nicely parallel those obtained by Howard et al[7] in their current article showing an independent effect of (physical) trauma and its psychological consequences (ie, PTSD) on the pathophysiology of hypertension.

On a different note, at the end of their article, Howard et al[7] propose a model for explaining how traumatic events may generate the development of hypertension or other cardiovascular complications. This model is important because it may help physicians understand the role of the trauma. Along the same lines, we would emphasize the concept that inflammatory/metabolic, mental health and behavioral pathways underlying the relation between exposure to a physical (or psychological) injury and subsequent development of hypertension (and possibly hypertension resistance) are probably deeply intertwined. In particular, it has been firmly established that both

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stress and body immune and inflammation-related mechanisms play a crucial role in the pathophysiology of many psychiatric disorders, such as major depression, bipolar disorder, schizophrenia, and autism.[12] Interestingly, exposure to major trauma, such as personal maltreatment or violence, has been found to increase the risk for mental health disorders, and as suggested by Howard et al,[7] this link is mediated by an activation of the immune system.[13] Finally, an additional physiological dimension that was not proposed by the authors would be a stimulation of the sympathetic and renin–angiotensin systems, which may also participate in the development of hypertension, in parallel to the stress and inflammatory systems, and may orient the choice of antihypertensive treatments.[1]

Further insights into the pathophysiology of hypertension in the specific population described by Howard et al[7] and other subsets of hypertensive patients, such as those with treatment-resistant hypertension, may be derived from studies using functional magnetic resonance imaging to dissect changes induced by trauma and hypertension in brain activity, led by interdisciplinary teams involving both experts in hypertension and researchers specialized in the neuroscience of psychopathology.

Finally, the work of Howard et al[7] strengthens the claim that psychological support should be an integral part of the management of some forms of hypertension.[9] As such, beyond its specific teachings for prevention and management of hypertension and cardiovascular complications in military servants, it may help hypertension specialists and more generally all physicians involved in the diagnosis and treatment of this deadly, still uncontrolled disease named hypertension to widen their perspective and incorporate psychological approaches in their armamentarium.

Disclosures

None.

References

1. Mann SJ. Psychosomatic research in hypertension: the lack of impact of decades of research and new directions to consider. *J Clin Hypertens (Greenwich)*. 2012;14:657–664. doi: 10.1111/j.1751-7176.2012.00686.x.
2. Mann SJ. Severe paroxysmal hypertension. An automatic syndrome and its relationship to repressed emotions. *Psychosomatics*. 1996;37:444–450. doi: 10.1016/S0033-3182(96)71532-3.
3. Kibler JL, Joshi K, Ma M. Hypertension in relation to posttraumatic stress disorder and depression in the US National Comorbidity Survey. *Behav Med*. 2009;34:125–132. doi: 10.3200/BMED.34.4.125-132.
4. Cohen BE, Marmar C, Ren L, Bertenthal D, Seal KH. Association of cardiovascular risk factors with mental health diagnoses in Iraq and Afghanistan war veterans using VA health care. *JAMA*. 2009;302:489–492. doi: 10.1001/jama.2009.1084.
5. Burg MM, Brandt C, Buta E, Schwartz J, Bathulapalli H, Dziura J, Edmondson DE, Haskell S. Risk for incident hypertension associated with posttraumatic stress disorder in military veterans and the effect of posttraumatic stress disorder treatment. *Psychosom Med*. 2017;79:181–188. doi: 10.1097/PSY.0000000000000376.
6. Stewart IJ, Sosnov JA, Howard JT, Orman JA, Fang R, Morrow BD, Zonies DH, Bollinger M, Tuman C, Freedman BA, Chung KK. Retrospective analysis of long-term outcomes after combat injury: a hidden cost of war. *Circulation*. 2015;132:2126–2133. doi: 10.1161/CIRCULATIONAHA.115.016950.
7. Howard JT, Sosnov JA, Janak JC, Gundlapalli AV, Pettey WB, Walker LE, Stewart IJ. Associations of initial injury severity and posttraumatic stress disorder diagnoses with long-term hypertension risk after combat injury. *Hypertension*. 2018;71:xxx–xxx. doi: 10.1161/HYPERTENSIONAHA.117.10496.
8. Kronish IM, Lin JJ, Cohen BE, Voils CI, Edmondson D. Posttraumatic stress disorder and medication nonadherence in patients with uncontrolled hypertension. *JAMA Intern Med*. 2014;174:468–470. doi: 10.1001/jamainternmed.2013.12881.
9. Berra E, Azizi M, Capron A, Høieggen A, Rabbia F, Kjeldsen SE, Staessen JA, Wallemacq P, Persu A. Evaluation of adherence should become an integral part of assessment of patients with apparently treatment-resistant hypertension. *Hypertension*. 2016;68:297–306. doi: 10.1161/HYPERTENSIONAHA.116.07464.
10. Berra E, Petit G, Georges C, Capron A, Wallemacq P, de Timary P, Persu A. Twenty-four hour ambulatory blood pressure level is correlated with altered psychological profiles in patients with apparently treatment-resistant hypertension. *J Hypertens*. 2017;35:e129.
11. Frans O, Rimmö PA, Aberg L, Fredrikson M. Trauma exposure and posttraumatic stress disorder in the general population. *Acta Psychiatr Scand*. 2005;111:291–299. doi: 10.1111/j.1600-0447.2004.00463.x.
12. Réus GZ, Fries GR, Stertz L, Badawy M, Passos IC, Barichello T, Kapczinski F, Quevedo J. The role of inflammation and microglial activation in the pathophysiology of psychiatric disorders. *Neuroscience*. 2015;300:141–154. doi: 10.1016/j.neuroscience.2015.05.018.
13. Baumeister D, Akhtar R, Ciufolini S, Pariante CM, Mondelli V. Childhood trauma and adulthood inflammation: a meta-analysis of peripheral C-reactive protein, interleukin-6 and tumour necrosis factor-α. *Mol Psychiatry*. 2016;21:642–649. doi: 10.1038/mp.2015.67.

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