

Trajectories of PTSD Symptoms and Predictive Factors of Trajectory Membership: A Step Toward Identifying Veterans at Risk

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The article “Latent Trajectories of Trauma Symptoms and Resilience: The 3-Year Longitudinal Prospective USPER Study of Danish Veterans Deployed in Afghanistan” by Andersen and colleagues¹ examines trajectories of posttraumatic stress disorder (PTSD) symptoms from predeployment to 2.5 years postdeployment and the predictive factors of trajectory membership among a sample of Danish soldiers deployed to Afghanistan. Iraq and Afghanistan veterans face a number of psychological, physical, and social challenges perideployment and postdeployment. One of the most prevalent mental health diagnoses seen in these veterans is PTSD.² As the authors note, identified heterogeneous trajectories of PTSD symptoms suggest that the presence or absence of a PTSD diagnosis may not be capturing the complex nature of posttraumatic stress responses. This point evokes the clinical concern that perideployment and postdeployment diagnostic screenings alone are not sufficient in determining appropriate prevention and treatment efforts.

The authors identified 6 PTSD symptom trajectories. There was a resilient trajectory, with low symptom levels across all assessments, and 5 symptom fluctuation trajectories. One symptom fluctuation trajectory displayed “a very low symptom level from before deployment to 3 months after deployment, followed by a rise in symptom level starting at the 7-month assessment and continuing to rise through the 2.5-year assessment,”^{1(p)} and was deemed the “late-onset trajectory.” The identification of the late-onset PTSD symptoms trajectory in veterans seems to be of particular significance when considering the adequacy of diagnostic screens. Among Operation Iraqi Freedom–Operation Enduring Freedom (OIF–OEF) US combat infantry units who screened positive for a mental disorder, only 23%–40% sought mental health care.³ Yet the recent Institute of Medicine report⁴ projects that this cohort will require extensive services in the coming years and decades. A significant factor in treatment initiation and retention among OIF–OEF veterans is severity of PTSD symptoms.⁵ Thus, veterans who are at risk of worsening PTSD symptom severity may not seek out treatment in a timely manner as a result of their current mild symptom presentation. This

postponement of treatment is unfortunate, considering that there is the possibility that early intervention would be useful in preventing this symptom trajectory. Indeed, there is some evidence to suggest that PTSD can be prevented by early provision of modified versions of prolonged exposure.^{6,7} Further, without knowledge of PTSD symptom trajectories, screeners may not even recommend treatment or appropriately timed follow-up screenings. Of note, Veterans Health Administration, Department of Defense guidelines recommend that veterans be reassessed for PTSD 3 to 6 months after their return from deployment⁸; however, the assessments are still based on diagnostic screenings, and there is no process for identification of those at greatest risk and, thus, most in need of continued monitoring. Other studies have found that, if PTSD is present at 3 months posttrauma, it is likely to remain so without intervention.⁹ However, in this sample, veterans were not stable 3 months after their return home. Andersen and colleagues¹ assessed the index trauma and discovered that, for those with PTSD 2.5 years after their return home, the index trauma was most likely postdeployment. As the authors note, the PTSD at 2.5 years may be in response to this intervening index trauma rather than deployment trauma. Again, this presents an important area for continued assessment.

Research suggests that mathematical predictive models are informative,^{10,11} but the field is not yet at a developmental stage to prospectively predict an individual’s likely response and trajectory given certain experiences and predispositions. Of course, identifying the probable symptom trajectories of veterans by assessing current symptom presentation alone is not feasible. The consideration of predictive factors is important. For instance, a recent study¹² found that genetic risk predicted PTSD posttrauma and that an early intervention seemed to mitigate genetic risk. There is an urgent push to identify biomarkers of PTSD, which would help toward detecting risk factors. By assessing predeployment vulnerabilities and deployment and postdeployment stressors as possible predictors of symptom fluctuation and late-onset PTSD symptoms, Andersen and colleagues¹ confirmed many well-identified predictors within a veteran population displaying heterogeneous PTSD symptom patterns. More specifically, predeployment exposure to traumatic events, higher neuroticism, and higher depression and perideployment exposure to dangerous mission environments increased the risk of belonging to the symptom-fluctuation trajectory. Membership in the late-onset PTSD symptoms trajectory was predicted by predeployment emotional problems and exposure to

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more traumatic events prior to deployment. Additionally, exposure to more traumatic events at postdeployment was a predictive factor specific to the late-onset PTSD symptoms. Veterans within the late-onset PTSD symptoms trajectory were exposed to a higher proportion of “accidents . . . , life threatening disease . . . , robbery involving a weapon . . . , threat of death or serious bodily harm . . . , intimate partner abuse . . . , and other life threatening or physically damaging events”^{1(p)} than the resilient group. This information could be used to develop predictive measures of PTSD symptom trajectories. Again, if the authors had genetic information on the veterans, this might account for a large proportion of the variance.

The reported connection between exposure to additional postdeployment traumatic events and the late-onset PTSD symptoms is important when considering prevention and treatment approaches and requires further exploration. The authors discuss a fear reinstatement hypothesis put forth by Bryant et al.¹³ This explanation is speculative and would depend on whether the individual did indeed have a strong fear response to a deployment-related trauma that had not fully resolved or left him or her more sensitized to high fear to a subsequent trauma. Incomplete extinction has been associated with resistance to extinction,¹⁴ which probably also accounts for the difficulty some with PTSD continue to experience. In a recent study¹⁵ comparing D-cycloserine, alprazolam, or placebo combined with virtual reality exposure therapy in veterans with PTSD, those who displayed good emotional learning in sessions profited more from the addition of D-cycloserine, a cognitive enhancer, and also displayed lower startle response and cortisol reactivity following treatment. If the fear reinstatement hypothesis is accurate, it implies we need to identify those at risk early and conduct effective extinction therapy to both help with the deployment-related stress response and protect for response to future stressors. Another approach is to consider clinical anecdotal evidence and research findings¹⁶ that demonstrate that a significant percentage of OIF–OEF veterans engage in risk-taking behaviors postdeployment. There are different explanations as to why this is the case. For instance, Killgore et al¹⁷ found that various combat experiences, such as exposure to violent combat and killing another person, predicted engagement in risky behaviors upon returning from deployment. Risky behaviors, such as substance dependence and driving at high speeds, may increase the risk for exposure to traumatic events.¹⁸ It is possible that risky behaviors contributed to the probability of experiencing a traumatic event postdeployment in the late-onset PTSD trajectory group. Thus, in order to prevent worsening of PTSD symptoms among these veterans, screening of risky behaviors and reintegration education and care are also very important to consider.

Importantly, in this sample, the authors were better at predicting who would not develop PTSD. The great majority in this sample (78%) was classified as “low-stable.” This is good news in that the majority of war fighters do not end up with chronic PTSD. However, this leaves 22% with likely

PTSD or subthreshold PTSD for whom we must improve prediction.

Andersen and colleagues¹ have produced noteworthy findings that have the potential to move the field away from the less than ideal diagnostic system in the process of determining appropriate prevention and treatment. Better assessment should include indications of pathology or distress based on not only self-report but also clinician ratings of patient-reported symptoms. Now, it is up to researchers and clinicians to translate information about trajectories of PTSD symptoms and the predictive factors of trajectory membership into useful tools to be used in clinical practice.

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REFERENCES

- Andersen SB, Karstoft K-I, Bertelsen M, et al. Latent trajectories of trauma symptoms and resilience: the 3-year longitudinal prospective USPER study of Danish veterans deployed in Afghanistan. *J Clin Psychiatry*. 2014;75(9):1001–1008.
- Seal KH, Bertenthal D, Miner CR, et al. Bringing the war back home: mental health disorders among 103,788 US veterans returning from Iraq and Afghanistan seen at Department of Veterans Affairs facilities. *Arch Intern Med*. 2007;167(5):476–482.
- Hoge CW, Castro CA, Messer SC, et al. Combat duty in Iraq and Afghanistan, mental health problems, and barriers to care. *N Engl J Med*. 2004;351(1):13–22.
- Institute of Medicine. *Treatment for Posttraumatic Stress Disorder in Military and Veteran Populations: Final Assessment*. Washington, DC: National Academies Press; 2014.
- Harpaz-Rotem I, Rosenheck RA, Pietrzak RH, et al. Determinants of prospective engagement in mental health treatment among symptomatic Iraq/Afghanistan veterans. *J Nerv Ment Dis*. 2014;202(2):97–104.
- Bryant RA, Sackville T, Dang ST, et al. Treating acute stress disorder: an evaluation of cognitive behavior therapy and supportive counseling techniques. *Am J Psychiatry*. 1999;156(11):1780–1786.
- Rothbaum BO, Kearns MC, Price M, et al. Early intervention may prevent the development of posttraumatic stress disorder: a randomized pilot civilian study with modified prolonged exposure. *Biol Psychiatry*. 2012;72(11):957–963.
- Veterans Health Administration, Department of Defense. *VA/DoD Clinical Practice Guideline for the Management of Post-Traumatic Stress, Version 2.0*. Washington, DC: Veterans Health Administration, Department of Defense; 2010.
- Rothbaum BO, Foa EB. Subtypes of posttraumatic stress disorder and duration of symptoms. In: Davidson JRT, Foa ED, eds. *Posttraumatic Stress*

- Disorder: DSM-IV and Beyond*. Washington, DC: American Psychiatric Press; 1993:23–35.
10. Galatzer-Levy IR, Ankri Y, Freedman S, et al. Early PTSD symptom trajectories: persistence, recovery, and response to treatment: results from the Jerusalem Trauma Outreach and Prevention Study (J-TOPS). *PLoS ONE*. 2013;8(8):e70084.
 11. Ursano RJ, Colpe LJ, Heeringa SG, et al; Army STARRS collaborators. The Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS). *Psychiatry*. 2014;77(2):107–119.
 12. Rothbaum BO, Kearns MC, Reiser E, et al. Early intervention following trauma mitigates genetic risk for PTSD in civilians: a prospective, emergency department study. *J Clin Psychiatry*. In press.
 13. Bryant RA, O'Donnell ML, Creamer M, et al. A multisite analysis of the fluctuating course of posttraumatic stress disorder. *JAMA Psychiatry*. 2013;70(8):839–846.
 14. Lee JL, Milton AL, Everitt BJ. Reconsolidation and extinction of conditioned fear: inhibition and potentiation. *J Neurosci*. 2006;26(39):10051–10056.
 15. Rothbaum BO, Price M, Jovanovic T, et al. A randomized, double-blind evaluation of D-cycloserine or alprazolam combined with virtual reality exposure therapy for posttraumatic stress disorder in Iraq and Afghanistan War veterans. *Am J Psychiatry*. 2014;171(6):640–648.
 16. Strom TQ, Leskela J, James LM, et al. An exploratory examination of risk-taking behavior and PTSD symptom severity in a veteran sample. *Mil Med*. 2012;177(4):390–396.
 17. Killgore WDS, Cotting DI, Thomas JL, et al. Post-combat invincibility: violent combat experiences are associated with increased risk-taking propensity following deployment. *J Psychiatr Res*. 2008;42(13):1112–1121.
 18. Koenen KC, Harley R, Lyons MJ, et al. A twin registry study of familial and individual risk factors for trauma exposure and posttraumatic stress disorder. *J Nerv Ment Dis*. 2002;190(4):209–218.