

Reviewer comments:

Comment: 1) The introduction is quite short and could benefit from being fleshed out further, including providing information about the clinical utility of better understanding the neurobiology of delayed onset.

Response: We expanded the paragraph on the clinical utility of neurobiological insights into delayed expression of PTSD: “A proper understanding of the neurobiological basis for delayed expression of PTSD is clinically useful since it has implications for diagnostic assessment in both treatment and forensic settings and in the context of litigation. Specifically, neurobiological models of PTSD may explain variability in the progressive increase in PTSD symptoms over time following exposure to trauma that characterizes PTSD with delayed expression. Neurobiological mechanisms and systems are likely to play a central role in determining the duration of the prodromal phase, the presence of prodromal symptoms and mental and physical disorder comorbidities.”

Comment: 2) The first citations are not provided until line 10 of the introduction, yet earlier sentences require references. Please provide citation when defining a term or providing information from another source. There are other instances (e.g., first paragraph in Neuroinflammatory Mechanisms) in which no citations are provided but there should be references.

Response: We added references in the parts of the text that were indicated by the reviewer and checked adequate referencing throughout.

Comment: 3) It is unusual to provide a Figure (#2) in the concluding remarks. All figures should be provided in the results section and the discussion/concluding remarks should not provide new information but rather discuss the results in further detail.

Response: We moved the figure from the discussion section to the results section.

Comment: 4) Please provide additional limitations of your study. The focus of the review is on delayed onset and therefore this is not a limitation of the study but rather its focus.

Response: We agree and clarified the study limitations, which now read:

“Limitations of the current scoping review are inherent to the use of titles and abstracts for the screening of study eligibility, as not all potentially relevant findings may have been reported in study titles or abstracts. However, we minimized the risk of inadvertently excluding relevant findings by using a broad search strategy and including review studies besides primary studies.”

Comment: 5) Similar to the introduction, it would be helpful if the discussion/conclusion could link these findings to the clinical implications of presentation and treatment (pharmacological, psychological, etc).

Response: Following this suggestion, we elaborated on diagnostic and treatment implications: “These findings have implications for diagnostic assessment in both treatment and forensic settings. Delayed expression of trauma and stressor-related disorders requires careful individual assessment of the trauma history, intervening stressors, and development of symptoms of mental and physical disorders. In addition to PTSD, other specific trauma- and stressor-related disorders and mental and physical disorder comorbidities need to be evaluated with regard to the potential causal link between traumatic exposure and delayed symptoms, while taking into account the frequently substantial etiological overlap.

Subthreshold PTSD symptoms may indicate clinically significant distress and functional impairment. Findings from a Korean cross-sectional study among 45,698 active firefighters indicated that the presence of subthreshold PTSD symptoms was associated with suicidal behavior, depression, alcohol use problems, and functional impairment [48]. Assessment of a history of TBI is mandatory in help-seeking, trauma-exposed individuals, specifically in soldiers and veterans, who are at increased risk of PTSD with delayed expression [2-4], as this may be associated with delayed expression of PTSD [28]. Foreseeable stressors and resource losses, including

unemployment and physical impairments, may be an effective target for secondary prevention of psychological distress. Pharmacological prevention of PTSD following exposure to potentially traumatic events is not generally recommended, and there is insufficient evidence to recommend selective, indicated pharmacological prevention [49]. Emerging evidence supports selective prevention with hydrocortisone [50], a corticosteroid drug with immunosuppressive effects. Our data provide support for exploring the preventive potential of normalizing immune reactivity by pharmacological means.”

Science editor comments:

Comment: (1) The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s)

Response: Done

Comment: (2) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.

Response: The picture was made by the first author to visually summarize findings from the current review. We now uploaded all Figures as .pptx files.

Comment: (3) PMID numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout.

Response: We revised the reference list accordingly.

Other editorial comments:

We made sure to spell out abbreviations in accordance with the Journal style and checked the language.