DOI: 10.1002/trc2.12419

LETTER



Could cerebrospinal fluid leak contribute to the link between traumatic brain injury and dementia?

Dear Editor,

We read with interest the fascinating research conducted by Schievink and colleagues on the link between cerebrospinal fluid (CSF) leak and symptoms of behavioral variant of frontotemporal dementia (bvFTD), an early-onset dementia.¹ This study found that CSF venous fistula, a type of spinal CSF leak, is found in \approx 40% of their included patients with symptoms of bvFTD and spontaneous intracranial hypotension or brain sagging. Nine patients were found to have CSF venous fistula on imaging. Surgical ligation of the spinal CSF leaks resolved bvFTD symptoms in all of these nine patients. It was positive to see that, once identified, correction of CSF venous fistula could reverse such serious and devastating symptoms.

Previous evidence suggests that patients with a history of traumatic brain injury (TBI) are at elevated risk of dementia diagnosis. For example, a population-based study in Taiwan found that, even after adjusting for factors such as socioeconomic status and presence of comorbidities, the risk of developing dementia of any type is 1.7-fold greater among patients with a history of TBI as compared to those without.² This study further identified that the association between TBI and dementia was stronger in younger patients, thus indicating a potential link to early onset dementia.² Similar findings were demonstrated by another study in Sweden. This 33-year follow-up study found that TBI was strongly associated with an increased risk of non-Alzheimer's types of early-onset dementia.³ The association was significant even after adjustment for covariates among those with only one mild TBI, as well as for those with two or more mild TBIs, and those with one severe TBI.³

The underlying mechanism between TBI and dementia is currently unclear. However, the findings of Schievink et al. provide insight into one potentially causal pathway to explain at least some of the observed association. Because CSF leaks are identified in $\approx 1\%$ to 3% of all TBIs in adults,⁴ individuals with a history of TBI may thus be at risk of dementia symptoms and diagnosis partly due to spinal CSF leaks and intracranial hypotension.

In individuals with a history of TBI, the presence of chronic and persistent headaches may suggest spinal CSF leaks and intracranial hypotension.⁵ Future study in individuals with dementia and a history of TBI may benefit from screening for the presence chronic headaches. If, in individuals with past TBI, higher odds of headache are found in

individuals with dementia as compared to those without dementia, then further imaging studies in the select individuals with headaches could be conducted to assess for the presence of frontotemporal dementia brain sagging syndrome and CSF leaks, and thus possibly provide evidence for one of the links between TBI and dementia.

ACKNOWLEDGMENTS

This work did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CONFLICT OF INTEREST STATEMENT

None of the following authors have any proprietary interests or conflicts of interest related to this submission. Author disclosures are available in the supporting information.

> ZhiDi Deng¹ Esme Fuller-Thomson²

¹Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Alberta, Canada

² Institute for Life Course & Aging, Factor-Inwentash Faculty of Social Work, University of Toronto, Toronto, Ontario, Canada

Correspondence

Esme Fuller-Thomson, Director of the Institute for Life Course & Aging, Factor-Inwentash Faculty of Social Work, Cross-appointed to the Faculty of Medicine, University of Toronto, 246 Bloor St. W., Toronto, ON M5S 1V4, Canada. Email: esme.fuller.thomson@utoronto.ca

REFERENCES

- Schievink WI, Maya M, Barnard Z, et al. The reversible impairment of behavioral variant frontotemporal brain sagging syndrome: Challenges and opportunities. Alzheimer's & Dementia: Translational Research & Clinical Interventions. 2022;8(1):e12367.
- Wang H-K, Lin S-H, Sung P-S, et al. Population based study on patients with traumatic brain injury suggests increased risk of dementia. J Neurol Neurosurg Psychiatry Res. 2012;83(11):1080-1085.
- Nordström P, Michaëlsson K, Gustafson Y, Nordström A. Traumatic brain injury and young onset dementia: a nationwide cohort study. *Ann Neurol.* 2014;75(3):374-381.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made. © 2023 The Authors. *Alzheimer's & Dementia: Translational Research & Clinical Interventions* published by Wiley Periodicals LLC on behalf of Alzheimer's Association.



- 4. Oh J-W, Kim S-H, Whang K. Traumatic cerebrospinal fluid leak: diagnosis and management. *Korean J Neurotrauma*. 2017;13(2):63.
- 5. Schievink WI. Spontaneous spinal cerebrospinal fluid leaks and intracranial hypotension. JAMA. 2006;295(19):2286-2296.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.