

## LETTER

# Cannabidiol for functional seizures (psychogenic nonepileptic seizures/attacks) and other stress-associated disorders

To the Editor,

Recently, we published a paper that suggested that *FKBP5* single-nucleotide polymorphisms may play a role in functional seizures (psychogenic nonepileptic seizures/attacks).<sup>1</sup> We also published another paper entitled “*FKBP5* blockade may provide a new horizon for the treatment of stress-associated disorders: An in-silico study” providing a list of the currently available and approved drugs (e.g., fluticasone propionate, prednisolone, dexamethasone, mirtazapine, sertraline, fluoxetine, and citalopram) that could potentially be used for this purpose.<sup>2</sup>

More recently, I read an article entitled: “Cannabidiol alleviates neuroinflammation and attenuates neuropathic pain via targeting *FKBP5*.”<sup>3</sup> In this study, cannabidiol (CBD) was identified as an antagonist of *FKBP5* and *FKBP5* was an endogenous target of CBD.<sup>3</sup> This is a very interesting study that opens a very intriguing avenue for future research.

FK506-binding protein 51 (*FKBP5/FKBP51*) is a gene that encodes *FKBP51* protein and contributes to the regulation of glucocorticoid receptor sensitivity. Mutant variants of *FKBP5* have been associated with reduced glucocorticoid receptor sensitivity, which can lead to decreased hypothalamus–pituitary–adrenal (HPA) axis negative feedback and subsequent maintenance of glucocorticoids in the absence of threats and stress.<sup>4</sup> Accordingly, *FKBP5* polymorphisms have been associated with various stress-associated disorders such as major depression and post-traumatic stress disorder (PTSD), and potentially with functional seizures (psychogenic nonepileptic seizures/attacks).<sup>1,5</sup> Therefore, *FKBP5* blockade may hold promise as a treatment option for stress-associated disorders, including potentially functional seizures (psychogenic nonepileptic seizures/attacks).<sup>2</sup>

At the moment, psychotherapy is considered the best treatment option for patients with functional seizures (psychogenic nonepileptic seizures/attacks). But a large

clinical trial failed to demonstrate that cognitive behavioral therapy (CBT) has a statistically significant advantage compared with standardized medical care alone for the reduction of monthly seizures in these patients.<sup>6</sup> Functional seizures (psychogenic nonepileptic seizures/attacks) have devastating effects on patients' lives<sup>7</sup> and therefore, the scientific community should try to discover efficacious therapeutic options (e.g., a drug) for the treatment of this condition.

In conclusion, the suggestion that CBD is an antagonist of *FKBP5* and *FKBP5* is an endogenous target of CBD could open a new horizon for future research in discovering a treatment option for patients with functional seizures (psychogenic nonepileptic seizures/attacks).

## AUTHOR CONTRIBUTIONS

The sole author had responsibility for all parts of the manuscript.

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I confirm that I have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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## CONFLICT OF INTEREST STATEMENT

Honorarium: Cobel Daruo, Actoverco; Royalty: Oxford University Press (Book publication).

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### REFERENCES

1. Asadi-Pooya AA, Simani L, Asadollahi M, Rashidi FS, Ahmadipour E, Alavi A, et al. Potential role of FKBP5 single nucleotide polymorphisms in functional seizures. *Epilepsia Open*. 2023;8:479–86. <https://doi.org/10.1002/epi4.12716>
2. Asadi-Pooya AA, Malekpour M, Zamiri B, Kashkooli M, Firouzabadi N. FKBP5 blockade may provide a new horizon for the treatment of stress-associated disorders: an in-silico study. *Epilepsia Open*. 2023;8(2):633–40.
3. Wang X, Lin C, Jin S, Wang Y, Peng Y, Wang X. Cannabidiol alleviates neuroinflammation and attenuates neuropathic pain via targeting FKBP5. *Brain Behav Immun*. 2023;111:365–75. <https://doi.org/10.1016/j.bbi.2023.05.008>
4. Zannas AS, Wiechmann T, Gassen NC, Binder EB. Gene-stress-epigenetic regulation of FKBP5: clinical and translational implications. *Neuropsychopharmacology*. 2016;41(1):261–74.
5. Wang Q, Shelton RC, Dwivedi Y. Interaction between early-life stress and FKBP5 gene variants in major depressive disorder and post-traumatic stress disorder: a systematic review and meta-analysis. *J Affect Disord*. 2018;225:422–8.
6. Goldstein LH, Robinson EJ, Mellers JD, Stone J, Carson A, Reuber M, et al. Cognitive behavioural therapy for adults with dissociative seizures (CODES): a pragmatic, multi-centre, randomised controlled trial. *Lancet Psychiatry*. 2020;7(6):491–505.
7. Asadi-Pooya AA. Psychogenic nonepileptic seizures: a concise review. *Neurol Sci*. 2017;38(6):935–40.