



Response to the Letter Concerning the Publication: Neuroimaging in Functional Neurological Disorder: State of the Field and Research Agenda. Perez DL et al. *Neuroimage Clin.* 2021;30:102623

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To the Editor:

We appreciate the opportunity to respond to a letter to the editor from Tuller et al. (2024) regarding our *NeuroImage: Clinical* paper "Neuroimaging in Functional Neurological Disorder: State of the Field and Research Agenda" (Perez et al., 2021). In their letter, Tuller and colleagues raise concerns regarding the following introductory phrase and the linked Stone et al (2010) reference: "this renewed interest

parallels recognition that FND [functional neurological disorder] is the 2nd most common outpatient neurologic diagnosis." While we appreciate there is complexity to epidemiological considerations in FND, we do not agree with the concerns raised. We share our perspective on this matter with the following four points:

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1. The identified sentence pertains to a scene setting statement in the introduction, one that aims to make a brief comment about FND being prevalent, potentially disabling, and driving significant healthcare costs (O'Mahony et al., 2023). By their nature, such brief introductory statements do not generally include nuanced discussion and context. Furthermore, the epidemiology of FND is not the focus of our paper, which reviews multimodal neuroimaging findings and methodologies in the field across evolving case definitions for this condition.
2. The cited Stone et al (2010) article referred to a "psychological / functional" category as the second most common reason for outpatient consultation with a neurologist across 3781 prospective, consecutive consultations in Scotland. Within this category, some of the patients had functional neurological symptoms of seizures, motor difficulties and sensory disturbance. Others were labelled as "functional" and "non-organic" and others received a psychiatric diagnosis like anxiety and depression, but would have had neurological symptoms in order to be referred to a neurology clinic. Some other patients had problems like dizziness and cognitive difficulties likely equivalent to modern diagnoses of functional dizziness and functional cognitive disorder that are now considered part of FND (Hallett et al., 2022). So, the category refers to a broader grouping of functional neurological symptoms that clinical neurologists will recognize, where symptoms arise from a disorder of nervous system functioning rather than an identifiable structural etiology, and which was consistent with work-in-progress diagnostic frameworks in place at the time that the Stone et al (2010) study was performed.
3. The Stone et al (2010) findings have been supported by subsequent publications (Watila et al., 2022; Ahmad and Ahmad, 2016), which used later, arguably more restrictive, diagnostic criteria. For example, an Australian study found that 15 % of a prospective series of 884 patients attending an outpatient neurology clinic were diagnosed with FND (Ahmad and Ahmad, 2016). In this sample, FND was the 3rd most common diagnosis after headache and movement disorders. In a retrospective study of diagnoses in a consecutive series of 1110 patients attending a neurology clinic in person and 845 attending virtually (during the pandemic), FND was found to be the 2nd most common diagnosis in both cohorts with a prevalence of 17.1 % and 12.9 % respectively (Watila et al., 2022).
4. Rank ordering of diagnoses is an inherently complex issue that can vary according to the quality and granularity of diagnostic information available, evolving diagnostic criteria, referral and population biases, and exactly which conditions are combined for comparison, among other considerations.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: D. L.P. has received honoraria for continuing medical education lectures in FND; royalties from Springer for the textbook Functional Movement Disorder and from Elsevier for the textbook Functional Neurological Disorder; is on the editorial boards of *Brain and Behavior* (paid), *Epilepsy & Behavior*, and *The Journal of Neuropsychiatry and Clinical Neurosciences*; has received funding from the NIH and Sidney R. Baer Jr. Foundation for FND research; and is on the FND Society board and American Neuropsychiatric Association advisory council. T.R.N. does expert witness work in personal injury and clinical negligence cases of FND and other disorders; has received financial support for lectures from the FND Society; receives royalties from CRC Press for The Pocket Prescriber textbook series and from Springer for the textbook Functional Movement Disorder; has received grant funding, including for studies related to FND, from the UK National Institute for Health and Care Research (NIHR) and the Medical Research Council (MRC); is co-chair of the FNDS patient liaison committee and on the medical advisory boards of the

charities FND Hope UK and FND Action and a trustee of FND Action. A.A.P. honoraria from Cobel Daruo; royalty: Oxford University Press (Book publication). M.B. receives royalties from CRC Press for Pocket Prescriber Psychiatry 2E and has been awarded fellowships from NIHR and the Wellcome Trust for studies on FND. A.J.C. paid associate editor of *Journal of Neurology, Neurosurgery and Psychiatry*; provides expert testimony in court on a range of neuropsychiatric topics including FND; and is on the FND Society board. Q.D. does medical expert reporting in personal injury and clinical negligence cases, including in cases of FND. M.J.E. does medical expert reporting in personal injury and clinical negligence cases, including in cases of FND; has shares in Brain & Mind (which provides neuropsychiatric and neurological rehabilitation in the independent medical sector, including in people with FND); has received financial support for lectures from the International Parkinson's and Movement Disorders Society and the FND Society; receives royalties from Oxford University Press for his book *The Oxford Specialist Handbook of Parkinson's Disease and Other Movement Disorder*; has received honoraria for medical advice to Teva Pharmaceuticals; receives grant funding, including for studies related to FND, from the National Institute for Health and Care Research (NIHR) and the Medical Research Council (MRC); is an associate editor of the *European Journal of Neurology*; is a member of the international executive committee of the International Parkinson's and Movement Disorders Society and the FND Society board; and is on the medical advisory boards of the charities FND Hope UK and Dystonia UK. A.J.E. has received grant support from the NIH and the Michael J Fox Foundation; personal compensation as a consultant/scientific advisory board member for Neuroderm, Amneal, Acadia, Avion Pharmaceuticals, Acorda, Kyowa Kirin, Supernus (formerly, USWorldMeds), and Herantis Pharma; honoraria for speakership for Avion, Amneal, and Supernus; royalties from Lippincott Williams & Wilkins, Cambridge University Press, and Springer; cofounded REGAIN Therapeutics; co-inventor of the patent "Compositions and methods for treatment and/or prophylaxis of proteinopathies"; and is on the FND Society board. M.H. is an inventor of a patent held by NIH for the H-coil for magnetic stimulation for which he receives license fee payments from the NIH (from Brainsway); is on the Medical Advisory Boards of Brainsway, QuantalX, and VoxNeuro; has consulted for Janssen Pharmaceuticals, and is on the FND Society board. R.A.A.K. receives royalties from Guilford press for a book chapter related to FND; grant funding from the National Health and Medical Research Council, The Medical Research Future Fund for research in FND; provides expert medico-legal opinions on neuropsychiatric disorders, including FND; is on the board of the International Neuropsychiatry Association. M.A.J.T reports grants from the Netherlands Organization for Health Research and Development ZonMW Topsubsidie (91218013) and ZonMW Program Translational Research(40-44600-98-323); has received a European Fund for Regional Development from the European Union (01492947) and a European Joint Programme on Rare Diseases (EJP RD) Networking Support Scheme; furthermore, from the province of Friesland, the Stichting Wetenschapsfonds Dystonie and unrestricted grants from Actelion, Ipsen and Merz. W.C.L. has served on the editorial boards of *Epilepsia*, *Epilepsy & Behavior*, *Journal of Neurology, Neurosurgery and Psychiatry*, and *The Journal of Neuropsychiatry and Clinical Neurosciences*; receives editor's royalties from the publication of Gates and Rowan's *Nonepileptic Seizures*, 3rd ed. (Cambridge University Press, 2010) and 4th ed. (2018); author's royalties for *Taking Control of Your Seizures: Workbook and Therapist Guide* (Oxford University Press, 2015); has received research support from the Department of Defense (DoD W81XWH-17-0169), NIH (NINDS 5K23NS45902 [PI]), VA Providence HCS, Center for Neurorestoration and Neurorehabilitation, Rhode Island Hospital, the American Epilepsy Society (AES), the Epilepsy Foundation (EF), Brown University and the Siravo Foundation; has served on the Epilepsy Foundation New England Professional Advisory Board, the FND Society Board, the American Neuropsychiatric Association advisory council; has received honoraria for the AES Annual Meeting; has served as a clinic development consultant at University of Colorado Denver,

Cleveland Clinic, Spectrum Health, Emory University, Oregon Health Sciences University and Vanderbilt University; and has provided medico legal expert testimony. C.W.M. has received honoraria for continuing medical education lectures in FND, royalties from Springer for a textbook on functional movement disorder, and has received grant support from the Parkinson's Foundation, Alzheimer's Association and the Stony Brook Biomedical Sciences Innovation Fund unrelated to this work. J. P. Staab is supported by grant W81XWH1810760 from the US Department of Defense. J.S. royalties from UpToDate and carries out expert witness work in relation to FND; runs a free website for people with FND, www.neurosymptoms.org; and is on the FND Society board. J.P. Szaflarski, funding: NIH, NSF, DoD, Shor Foundation for Epilepsy Research, UCB Biosciences, NeuroPace Inc., SAGE Therapeutics Inc., Serina Therapeutics Inc., LivaNova Inc., Greenwich Biosciences Inc., Biogen Inc., Eisai Inc., State of AL; Consulting/Advisory Boards: PureTech Health, Biopharmaceutical Research Company, LivaNova Inc., UCB Pharma, AdCel Pharma, iFovea Inc; Editor-in-Chief, *Epilepsy & Behavior Reports* (paid); Editorial board member for *Epilepsy & Behavior*, *Journal of Epileptology* (associate editor), *Journal of Medical Science*, and *Folia Medica Copernicana*; provided expert opinion in medico-legal cases including of FND; has served on the Alabama State Medical Cannabis Study Commission (nominated by Gov. Ivey); serves on the Alabama Medical Cannabis Commission (2021–2025; nominated by Dr. Scott Harris, State Health Officer). S.A. is on the FND Society board.

Data availability

No data was used for the research described in the article.

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