

Further discussion of a preliminary study of sleep quality in functional neurological disorders: A reply to Professor Kawada.

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We would like to thank Prof. Kawada for his interest in our manuscript (1), which describes a preliminary investigation of sleep quality in people with functional neurological disorders (FND). Below we respond to Prof. Kawada's comments.

1. Prof. Kawada writes, "...the authors did not explain the opposite direction in beta values of anxiety and depression by a regression analysis". While our paper focuses on the relationship between sleep and FND-related functional impairment, Prof. Kawada is correct in noticing that, in step 4 of the regression analysis (in Table 2 of Graham & Kyle, 2017(1)), anxiety becomes negatively associated with FND-related functional impairment when depression is entered into the model. We attribute this effect to shared variance between anxiety and depression, with depression being a strong predictor of FND-related functional impairment. Variance inflation factors (2.03 and 2.39) and tolerance statistics (0.49 and 0.42) suggested that it would be acceptable concurrently to include both depression and anxiety. However, we agree that a principal components analysis of depression and anxiety items could be used to derive an alternative factorial solution that could subsequently be entered into the regression model.
2. Prof. Kawada remarks that, "Percentages of medications in anti-depressants and benzodiazepines were 52.7% and 9.3%, and the difference of prescription rate would partly contribute to the result". We agree that medication use may co-vary with FND-related functional impairment. In addition, it may also act as a proxy for severity of sleep disturbance and/or distress, which was captured by our questionnaires. Consistent with our aims, we focused on self-reported sleep disturbance in this first study but we concur that future studies, using appropriate designs, should investigate a range of potential intermediate pathways linking sleep to functional impairment and other outcomes in FND.
3. A statement is made regarding the age range of our sample: "The authors handled relatively young patients with having FND-related functional impairment". In contrast, the age range of our online sample (M= 40.42 years, SD = 10.83) was commensurate with those of previous large FND cohort studies (M= 39.1; M = 37.2, SD =13.7) (2, 3) and our clinical sample (M= 37.85, SD = 15.96). In addition, FND have variable age of onset, are not generally progressive, and can spontaneously remit. Therefore, 'age' or 'years with FND' are less likely to be indicators of symptom severity or symptom-related functional impairment than in progressive neurological conditions.
4. Finally, Prof. Kawada writes "In addition, difference of clinical symptoms and stages in several neurological disorders would also be related to the results. As the number of samples

was limited, stratified analysis would be difficult to conduct". We agree that it would be interesting to stratify the sample by FND symptom constellations (for example, those with non-epileptic seizures and those with functional motor disorders) and symptom severity, but as Dr Kawada notes our sample size and composition does not permit this. Clearly sleep disruption is associated with most mental and physical health problems. Nonetheless, we should not assume that sleep disruption always represents a consequence of some "primary" condition, such as depression. Rather there appears to be a complex bi-directional relationship between sleep and symptom severity in many conditions (4), and sleep often interacts with co-morbidities and medications.

In summary, we welcome Prof. Kawada's useful comments on our paper. We hope our work will stimulate others to investigate sleep in FND and to build upon these preliminary findings.

1. Graham CD, Kyle SD. A preliminary investigation of sleep quality in functional neurological disorders: Poor sleep appears common, and is associated with functional impairment. *Journal of the neurological sciences*. 2017;378:163-6.
2. Stone J, Warlow C, Sharpe M. The symptom of functional weakness: a controlled study of 107 patients. *Brain*. 2010;133(5):1537-51.
3. Duncan R, Graham CD, Oto M, Russell A, McKernan L, Copstick S. Primary and secondary care attendance, anticonvulsant and anti-depressant use and psychiatric contact 5–10 years after diagnosis in 188 patients with psychogenic non-epileptic seizures. *J Neurol Neurosurg Psychiatry*. 2014;jnnp-2013-306671.
4. Buysse DJ. Sleep health: can we define it? Does it matter? *Sleep*. 2014;37(1):9-17.