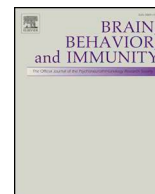




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Letter to the Editor

Autonomic and inflammatory disturbances do not seem to explain symptoms in chronic fatigue



I thank Valenti and Garner for their reflections on our recent paper (Kristiansen et al., 2019) on post-infectious chronic fatigue, including their suggested hypotheses: 1) That autonomic and inflammatory disturbances and inflammatory-autonomic interactions are underlying causal factors for symptoms, and 2) That therapies enhancing parasympathetic activity might inhibit inflammatory activation and thereby improve symptoms.

While I agree that autonomic and inflammatory disturbances are interesting topics for further chronic fatigue studies, I consider existing evidence to count against the suggested hypotheses. For instance, in our recent study, there are no strong associations between autonomic/inflammatory alterations and patients' symptoms; rather, we found a striking discrepancy between the severe symptom burden and functional disability, and the subtle disturbance of biological markers (Kristiansen et al., 2019). More importantly, a previous randomised controlled trial of the sympathetic inhibitor and parasympathetic stimulator drug *clonidine* in chronic fatigue syndrome adolescents demonstrated attenuated sympathetic and inflammatory activity in the intervention group; however, neither symptoms nor function improved (Sulheim et al., 2014). Thus, it seems that autonomic and inflammatory disturbances – while likely present in chronic fatigue and chronic fatigue syndrome – should be regarded secondary phenomena unrelated to patients' complaints, rather than causal factors explaining these complaints. If so, parasympathetic activation might have anti-inflammatory effects without affecting patients' symptoms of having a chronic inflammatory disorder.

In more general terms, chronic fatigue and chronic fatigue syndrome seem to be characterized by a discrepancy between subjective experiences and objective measurements (Cvejic et al., 2016). Disturbances of interoception, such as sensitization of sensory processing,

might explain such a phenomenon (Brosschot, 2002; Nijs et al., 2012), and might be a fruitful avenue for further research.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.bbi.2019.05.037>.

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