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Letter to the Editor

Anti-neural antibody response in patients with post-treatment Lyme disease symptoms versus those with myalgic encephalomyelitis/chronic fatigue syndrome

To the Editor

Post-treatment Lyme disease symptoms (PTLDS) and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) have several clinical features in common, including fatigue, musculoskeletal pain, and cognitive difficulties (Gaudino et al., 1997). Immunologic mechanisms have been suspected to play a role in both PTLDS and ME/CFS. However, biomarkers for the two conditions are currently lacking, creating a barrier to better understand them. In a previous study published in BBI, we developed a semi-quantitative immunoblot assay to compare antibody reactivity to neural antigens in a group of PTLDS patients and controls (Chandra et al., 2010). Inclusion/exclusion criteria were previously described (Chandra et al., 2010). We found a significantly increased level and frequency of IgG anti-neural antibody reactivity in the PTLDS patients (41 of 83; 49.4%) both in comparison to patients who had been treated for Lyme disease previously but did not have residual symptoms (5 of 27; 18.5%) and to healthy controls who never had Lyme disease (3 of 20; 15.0%) ($p < 0.01$ for both comparisons). The anti-neural antibody response in the patients with PTLDS was independent of serologic positivity for antibodies to *Borrelia burgdorferi* (the etiologic agent of Lyme disease).

Using the same methodology in a new analysis, we screened plasma samples from 51 ME/CFS patients (36 female; mean [SD] age, 51.2 [11.7] years) and 53 age- and gender-matched healthy controls (40 female; mean age, 50.0 [13.6] years), provided by the SolveCFS BioBank (Irlbeck et al., 2014). This study was approved by the Institutional Review Board of Columbia University Medical Center. The ME/CFS and control sample sizes in this study provided greater than 90% power, with $\alpha < 0.05$, to detect the same frequencies of antibody reactivity previously observed in the PTLDS patients and associated controls (Chandra et al., 2010). ME/CFS patients met the Fukuda or the Canadian criteria for this condition (Carruthers, 2007; Fukuda et al., 1994) and lacked histories suggestive of Lyme disease. Screening questionnaires were used to evaluate the general health of the unaffected controls and to confirm that that they did not meet ME/CFS case definition criteria. In contrast to the findings of our prior study on PTLDS patients (Chandra et al., 2010), we found no significant difference in the prevalence of anti-neural antibody reactivity between ME/CFS patients (4 of 51; 7.8%) and healthy controls (7 of 53; 13.2%) ($p = 0.5$).

Although often detectable (Chandra et al., 2010), it is unclear whether the presence of anti-neural antibodies has a role in the pathogenesis of certain PTLDS manifestations. If these antibodies do play a role, it would appear that the cause of the somewhat similar symptoms in ME/CFS is different. A potential limitation of the methodology employed in this and in our prior study (Chandra et al., 2010) is that it primarily detects reactivity to prominently expressed neural proteins and can miss reactivity to some minor proteins or non-protein antigens. Further inquiry into B cell activation mechanisms and autoantibody response may be useful to gaining a better understanding of differences between PTLDS and ME/CFS, and might provide potential markers for the identification of disease subsets.

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Disclaimer and potential conflicts of interest

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