Declaration of Interest

None.

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Letter to the Editor

Plausible explanations for neurocognitive deficits in ME/CFS, aggravation of neurocognitive impairment induced by exertion

We read the review by Cockshell & Mathias (2010) with great interest and compliment the authors for their thorough review of cognitive deficits in Chronic Fatigue Syndrome (CFS). As noted by Thomas & Smith (2009), cognitive impairments can be identified if the appropriate tests and measures are used. However, we would like to make two comments.

First, many studies have established organic aberrations which, at least partially, could account for the neurocognitive deficits seen in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS).

Many aberrations in brain structures and functions have been established in ME/CFS, like hypoperfusion and hypometabolism of brain regions of interest, impaired cerebral oxygenation during exercise, SPECT scan abnormalities in the cerebral cortex, small discrete lesions in the subcortex, a reduction in grey matter, and immunological abnormalities and aberrant proteins in spinal fluid (Lange *et al*. 2005; Chen *et al*. 2008; Twisk & Maes, 2009). In ME/CFS brain activity is significantly more diffuse (Chen *et al*. 2008), possibly as a compensation mechanism (Lange *et al*. 2005).

Hypoperfusion and hypometabolism are plausible explanations for the 'brain fog' often reported by ME/CFS patients. Moreover, a correlation between neurological abnormalities and neurocognitive functioning has been established (Lange *et al*. 2005; Chen *et al*. 2008).

Second, exercise and graded exercise therapy (GET), proposed as a treatment for ME/CFS, are likely to aggravate the cognitive complaints in ME/CFS. The average increase of the prefrontal cortical volume due to cognitive behavioural therapy/GET (CBT/GET), mentioned by Cockshell & Mathias (2010), is very modest (+4.8 ml, S.E. = 2.3 ml, difference in grey-matter volume before intervention: −38.8 ml). The grey-matter volume even declined in a substantial subpopulation.

Inflammation, immunosuppression, immune dysfunction, oxidative and nitrosative stress, mitochondrial dysfunction, apoptosis, infections, channelopathy and a blunted stress response are key pathways in ME/CFS (Twisk & Maes, 2009), as has been confirmed by various gene expression studies.

Since exertion and GET increase inflammation, oxidative and nitrosative stress, and channelopathy, it is not surprising that exercise has a negative impact on the pre-existing cognitive impairments, in large subgroups of patients (Twisk & Maes, 2009).

Several studies show that neurocognitive problems of many ME/CFS patients are aggravated by exercise, e.g. cognitive processing is impaired 24 hours after physically demanding exercise; exertion has a negative effect on simple reaction time and choice reaction time; fatigue-inducing activities cause altered central nervous system signals, which control voluntary muscles; and exertion has a negative impact on perfusion of the left prefrontal lobe and cerebral

oxygenation (Twisk & Maes, 2009). The latter could account for the sustained negative effect of exercise on neurocognitive performance.

We hope that this letter shows the readership that organic aberrations plausibly explain the neurocognitive impairments in ME/CFS, as reported by Thomas & Smith (2009) and Cockshell & Mathias (2010), and that CBT/GET has potential risks, because it can amplify the above-mentioned organic aberrations.

Declaration of Interest

None.

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