A gleam of light at last?

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At the third Oral Evidence Session of the Gibson Parliamentary Inquiry into ME on 7th June 2006, Dr Anthony Cleare from the Section of Neurobiology of Mood Disorder at the Institute of Psychiatry, London, implied that (ME)CFS is not a neuroendocrine disorder. He indicated that in (ME)CFS, cognitive behavioural therapy (CBT) has biological effects, one of which is the normalisation of the disrupted HPA axis. It is noted that even though this is only conjecture, CBT is being promoted nationally as the management regime of choice in (ME)CFS and is the only intervention that carries Government accreditation, even though based on just three RCTs that have shown modest but time-limited improvement in some participants. (In 2001, the [first] York Systematic Review of the relevant literature concluded that: "overall, sufficient research evidence was lacking and the quality was not optimal").

For the benefit of those in the ME community who may be unable to access the literature for themselves, we provide quotations from an important paper by Mark Demitrack in which he considers the role of clinical methodology in studies of therapeutic interventions in (ME)CFS (ref: Clinical methodology and its implications for the study of therapeutic interventions for chronic fatigue syndrome: a commentary. Mark A Demitrack. Pharmacogenomics 2006:7(3):521-528).

"Some observers have noted that the high risk of psychiatric burden is proportional to the number of pure symptoms present. The most extreme view considers these observations to provide convincing evidence that (ME)CFS is, in essence, embedded in the larger nosologic construct of affective disorders. However, the observations of specific protracted fatigue and the absence of substantial psychiatric comorbidity argues convincingly that this is an inappropriate and overly simplistic way of approaching this puzzling condition".

"(Another) major consideration in the approach to clinical therapeutics of (ME)CFS is the fact that it is, by definition, a chronic illness. The magnitude of disease chronicity is a feature that has an important impact on overall treatment responsiveness".

"It is notable that the specific methodology used to ascertain the diagnosis of (ME)CFS, and that used to measure symptom burden and treatment outcome, rarely comes under close scrutiny in studies of therapeutic intervention in this condition. I believe it is crucial that the quality and interpretability of past and future therapeutic studies of (ME)CFS be critically appraised to the extent that they have considered the impact of these issues in their design and conclusions".

“An alternative framework for understanding the biology of (ME)CFS came from the growing body of research in the area of CNS (central nervous system) function in this condition. Reported observations in both the functional alteration of neuroendocrine physiology, as has been seen in the hypothalamic-pituitary-adrenal axis, and observations from neuroimaging studies, have reinforced the view that the peripheral symptoms of the disease may indeed be distal manifestations of a primary disruption in CNS function”.

“It is helpful to consider CFS as a final common pathway expression of an illness that has developed by an accumulation of intrinsic and extrinsic factors. Most authors provide a framework that recognises that a variety of stressors may be precipitants for the development of (ME)CFS. These precipitants likely coincide with inherent vulnerabilities, some of (which) may be genetic and some may be postgenetic, or acquired”.

“In the short term, a pragmatic approach to the development of therapeutics for this condition is likely to be the most fruitful. However, it becomes even more critically important to specify the patient population most likely to benefit from the proposed pragmatic intervention, and exceedingly important to define the specific symptoms, or cluster of symptoms, that may be presumed to benefit from the intervention”.

“It does not seem plausible that any single intervention would be helpful in an undifferentiated majority of patients”.

“It therefore may not be surprising that current treatment options for (ME)CFS appear only modestly effective”.

“Non-response or partial response to treatment is the norm, and more than half of all patients fail to receive any benefit from many interventions”.

“In psychiatric research, several rating scales have been proposed to improve upon the perceived limitations of the HAMD (Hamilton Rating Scale for Depression) but none have clearly risen to the task. Even the most precise tool for the job is essentially useless in the hands of an inept operator. Our group has shown that the measurement error of rating scales can be enormous and can substantially undermine the presumed statistical power of the study”.

“There is ample room for improvement of the methodology for case ascertainment and for symptom measurement in (ME)CFS treatment studies”.

“Most available research has inadequately addressed the methodological complexity and has made unclear presumptions regarding (the) implications for treatment response. This state of affairs seriously limits the conclusions that can be drawn from the information obtained from existing treatment studies”.

“Future research should emphasise the development of improved methods of symptoms assessment”.

“Given that (ME)CFS is an illness that may absorb a significant amount of healthcare services, evaluation of the cost-benefit ratio of potentially effective treatment interventions should be explored”.

“In the face of accumulating evidence, there is increasing realisation that a unitary disease model has been a theoretical and practical impediment to real progress towards effective therapeutics for (ME)CFS. Many treatment studies have, unfortunately, been framed in this manner. Most have also neglected to thoroughly consider the significance of the issues regarding patient selection (and) symptom measurement”.

“(Such new) approaches are more likely to yield homogeneous patient populations. Such studies represent a critical advance in the field, and hold considerable promise for a more reasoned understanding of the nature of the development of (ME)CFS”.