CAN HYSTERIA BE DIAGNOSED WITH CONFIDENCE?[1.]

CONFLICTS IN BRITISH RESEARCH, 1998

INTRODUCTION

1998 will long be remembered in the UK as the year in which sufferers from Myalgic Encephalomyelitis (ME/CFS), so long misinterpreted by the media as an imaginary illness, finally took matters into their own hands and challenged the endorsement of that view by the Royal College of Physicians, Psychiatrists and General Practitioners [2.] and the medical press [1.]. After enduring unprecedented difficulties in obtaining standard health care, sickness benefit, insurance, pension and educational rights, two separate patient initiatives emerged, organised by more chronically and severely affected who had previously been overlooked: (1) A petition, supported by 12,502 signatures and calling for withdrawal of the Royal Colleges' guidelines on ME/CFS, was presented to Lady Jay (Minister for Health) in the House of Lords on 26.11.97. (2) Following a meeting organised by the most severely affected patients in the Grant Committee Room on the House of Commons on 14.4.98 and attended by some 52 MPs. An Early Day Motion on the recognition of Myalgic Encephalomyelitis was tabled by 18 MPs in the House of Commons on 27.7.98 which cautioned that the new 'Expert Committee on ME/CFS' announced by government on 17.7.98, should take evidence from a board section of medical and other interest groups and have the power to question and influence current thinking on the disease.

RESEARCH RELATING TO ME/CFS IN THE UK - SOME PUBLICATIONS IN 1998

The power of British Research to change the present climate of opinion will undoubtedly depend upon its rating in respect of:

(a) Scientific integrity and determination to seek out the causes, as well as the effects of the illness (+)

(b) The relevance of such work to diagnosis and management (+)

(c) Whether the study sample includes severely and chronically ill patients, seldom seen outside general (family) practice (+).

(d) Whether the conclusions drawn are obviously influenced by the personal prejudices of the investigators (-)

1. RICHARDSON J, COSTA DC.
Relationship between SPECT Scans and buspirone tests in patients with ME/CFS. Journal of Chronic Fatigue Syndrome 1998; 4(3) in press.

INTRODUCTION

It has been suggested that one of the major effects of persistent virus infection in disorders such as ME/CFS is upon the hypothalamus - a sub cortial area of the brain which maintains body homeostasis and regulates the output of pituitary hormones such as prolactin. The purpose of this study was to correlated, by non invasive methods, evidence of cellular dysfunction at the site (demonstrated by SPECT scans) and of associated neuroendocrine disturbance, (demonstrated by biochemical assay) in patients with chronic enteroviral infection (shown to persist by repeated laboratory investigation). Buspirone, an anxiolytic drug which promotes the release of prolactin from the pituitary, by means of its effect upon serotonin (5HT) receptors, provides a convenient test of hypothalamic function in this respect.

METHODS:

1. PATIENT SELECTION - Patients were selected from a large number with a provisional diagnosis of ME/CFS which had been referred over the years to Dr Richardson, by doctors from all parts of the UK, requesting confirmation. 39 of these subjects (17 males and 22 males) were included in this study following screening: (a) by subjective account of symptoms using the Newcastle Research Group (NRG questionnaire tested and used in family practice over 4 decades and, with modifications, in widespread use over the UK. This differentiates central (brain) from peripheral (muscle) fatigue and recognises cognitive disturbance. In addition the CDC (1994) and Oxford (1991) criteria as well as the Hamilton Score (to exclude Psychiatric illness) were used, (b) by clinical examination and other objective tests), (c) by evidence of a recent positive buspirone test and of persistent enteroviral infection as demonstrated by the repeated presence of enteroviral group antibody in the blood.

2. CONTROL GROUP: a comparable control group was selected from family members (not necessarily blood relatives) who were asymptomatic and who underwent clinical scoring and examination, and buspirone at the same time.

3. BUSPIRONE STIMULATION STUDIES: performed by Dr Richardson. Blood samples were taken at 10 pm, 9 am and after administration of 50 mgms of buspirone, one hour later (10 am) and analyses at the Department of Biochemistry, Queen Elizabeth Hospital, Gateshead using the IMX system (Abbot Laboratories) NB further details of this test and of diurnal cortisol and prolactin levels are reported elsewhere [3].

4. SPECTS SCANS: were performed by Dr D C Costa at the Institute of Nuclear Medicine, University College, London, Medical School using Tc-99m-HMPAO intravenously, followed 15-30 minutes later by data acquisition, using a brain dedicated triple head gamma camera (GE NEUROCAM). (NB - all patients in this study had been ill for prolonged periods, some for over a decade while one had made a partial recovery, thus the results reported do not necessarily reflect the range of clinical severity in this illness).

5. RESULTS: (a) Buspirone tests - a significant rise in prolactin levels (250% and upwards) one hour after buspirone administration was recorded in 26/39 patients (67%) but below this level in the comparison group. (b) SPECTS SCANS - 39 patients (100%) showed hyperfusion in some area of the brain, 35 patients (90%) in subcortical areas (Brain stem and/or basal ganglia) and 30 patients (70%) in temporal, parietal or frontal lobes. (NB 'Hypoperfusion' indicates uptake of radioactive material due to metabolic problems in local brain cells rather than any diminution of blood supply to the brain in general.).

6. CONCLUSION: (a) In ME/CFS, history and clinical examination still remain the corner stone of diagnosis but completion of the buspirone test and SPECTS scan provide basic complementary evidence. (b) The implications of this study for treatment are (I) that it should encourage a more sympathetic attitude to the ME/CFS patient (ii) that the findings should be pursued in relation to possible reparative treatment bearing in mind that, in neurological conditions, healing and repair are notoriously imperfect.

COMMENTS: This study, by family doctor with more than 4 decades of research experience into the effects of virus infection and subsequent organ pathology as well as diagnosis, treatment and prognosis, addresses in a very simple way the seldom recorded problem of patients who are chronically and severely ill with ME/CFS.

RESEARCH RATING: (+)(+)(+)

2. CHAUDHURI A, BEHAN WMH, BEHAN PO. Chronic Fatigue Syndrome. Proc Roy Coll Physicians Edinb. 1998: 28: 150-163

INTRODUCTION

This comprehensive review, mainly of the work done by Professor Behan's team in Glasgow begins with EPIDEMIOLOGY which, it is pointed out, has become a numbers game depending upon which ever 'CFS' definition is in vogue, and that the disease, in endemic or epidemic form, presents with a 'flu like respiratory or gastrointestinal illness in 80% of cases'. A very thorough and detailed account is then given of symptoms, laboratory and other investigations. Despite some minor inconsistencies with previous advise, the review is especially valuable for this section and for its 89 references to world literature.

RESEARCH IN GLASGOW: The main interest lies in the many aspects of innovative research into the organic basis of ME/CFS, pioneered by the Glasgow team or reported from elsewhere. These include:

MUSCLE AND EXERCISE: ultrastructural abnormalities in mitochondria (awaiting confirmation) enzyme deficiencies and defects in type II muscle fibres (not related to deconditioning) are recorded. A claim is made of the first ever objective test for post exertion muscle fatigue, by demonstration of a rapid decline in thigh muscle tone at 4 and 24 hours after exercise while resting every expenditure in ME/CFS is unusually high, possible because of diversion to metabolically over active tissue elsewhere which decreases the amount available for physical activity.

NERVE CONDUCTION AND EMG TESTS: At least 1/3 of ME/CFS patients have abnormal tests and 75% of those experiencing 'jitter; where two muscle fibres are tested simultaneously, may suffer malfunction at the muscle membrane in the motor end plate rather than in the nerve.

CARDIOVASCULAR SYSTEM: Neurally mediated hypotension (NMH) in ME/CFS patients is attributable to abnormal cardiac reflexes. An innovative Glasgow study (using Thallium-20 SPECT scans) into the common complaint of 'coronary type' chest pain with negative ECG in these subjects, discloses abnormal leakage of ions (atom particles which influence nerve transmission) through the cell membrane. This can be demonstrated in 75% of ME/CFS subjects even in the absence of chest pain and appears to be identical to the so-called 'Syndrome X' in which skeletal muscle is likewise affected.

NEUROIMAGING: Using SPECT scans of the brain, this team confirms hypoperfusion (diminished metabolism) involving Temporal lobes and other areas above and below the cortex, in adults and children. These findings are in line with research published by COSTA in the US and at least 5 other teams in the USA and South America.

HYPOTHALEMAIC AND NEUROENDOCRINE STUDIES: Pioneering observations have been made in Glasgow, relating to dysfunction of the hypothalamic/pituitary/adrenal axis and maladaptation to stress, while Professor Dinan (a research associate) has noted smaller than normal adrenal glands in ME/CFS. A variety of abnormalities relating to hyper and hypersensitivity to neuro transmitters has been research by this

team and elsewhere. These problems undoubtedly underlie the exceptional sensitivity of ME/CFSs sufferers to toxins, antidepressants and anticholinergic agents.

TOXINS: This research team is one of the few which have investigated the close relationship between the neurological effects of chronic low dose organosphosphate poisoning and similar symptoms in ME/CFS. These compounds are potent inhibitors of neural anticholinesterase and, even a minute amount, may cause cardiac arrhythmia in patients developing chronic fatigue after poisoning by insecticides or similar agricultural products.

GENETICS, IMMUNOLOGY, VIROLOGY: These studies appear to have rather negative and disappointing research projects for the team. Despite recognising family clustering of ME/CFS, there appears to be no genetic basis as yet, while no diagnostic pattern can be discerned in a variety of nonspecific immunological findings, except possibly an allergic predisposition. While recognising the clinical identity between ME/CFS and post polio fatigue and despite the identification of a variety of mutated enteroviruses in 41% of patients by a different virology in Glasgow, Professor Behan's associated have announced no persistence of infection in ME/CFS by enteroviruses, herpes viruses (including EBV) retroviruses or measles - however their enthusiasm has been kindled again by the finding that enteroviruses (like HIV) can damage sodium and calcium ion channels in cell membranes (see cardiovascular system) as can many toxins.

TREATMENT: After testing a wide range of agents ranging from nutritional supplements and immune manipulators to anti depressants, the team concludes that treatment remains largely symptomatic.

THE FUTURE: Attention should not be directed to the ion channel leakage and neurochemical disturbances which threaten homeostasis in ME/CFS.

COMMENT: There is a certain disappointment at the rather random and seemingly disconnected subject matter of this review, which doe not make for easy reading (unlike the sequential and clearly linked reports emerging from the US team researching the late effects of polio who are not so well funded). Moreover, some pejorative allusions to the seriously disabled young people with ME/CFS (who, it is alleged, imagine their symptoms) demeans not only this famous and world renowned team but also the prestigious journal which prints them.

RESEARCH RATING (+)(+)(+)(-)

3. A Research Portfolio on Chronic Fatigue (FOX, R. ed: on behalf of the Linbury Trust). Royal Society of Medicine Press Ltd, 1 Wimpole Street, London WIM 8AE. 1998

INTRODUCTION

The distribution of this portfolio at the Stephen Strauss lecture reception , Royal College of Physicians, London on 16.7.1998 coincided with a new initiative by the retiring UK Chief Medical Officer to promote research, via a committee of experts, on the management of ME/CFS. Stephen Strauss is well known in the USA for his interest in this subject, but perhaps better known in the UK for his public appreciation of the Royal College's report on this illness (CR54 1996) which he applauded as 'the finest contemporary position statement in the field' [4]. The Linbury Trust has, since 1991, been the foremost UK supporter of research into ME/CFS, having invested some £4 million in grants. If any change is to expected in the advice given to ME/CFS sufferers by the new expert committee in the future, it is important to examine the type of research funded at present.

THE LINBURY RESEARCH PROGRAMME

Of the 19 current or past Linbury Trust grant holders invited to contribute to this portfolio, 12 are psychiatrists (63%) while 9 of the 13 subjects covered in this booklet (70%) including all 3 papers on treatment, have psychiatrists or psychologists as authors. Of the remaining 4 authors outside this profession, not all van be deemed free of prejudice in favour of a 'psychiatric dimension' to the illness. The psychiatrist invited to supply the 'Editorial Afterword' to this portfolio has produced a master piece of circular reasoning in diagrammatic form supporting this 'psychiatric dimension', as follows: Patients with ME/CFS are psychologically predisposed to masattribute their symptoms of fatigue to physical causes, obliging them to reduce activity which leads to deconditioning and depression which, in turn perpetuated their chronic fatigue and increases their depression. Now read on:-

A. CONTRIBUTIONS BY PSYCHIATRIST AND PSYCHOLOGISTS:

1. EPIDEMIOLOGY (S, WESSELY); This subject was apparently invented following the first 'XFS' definition in 1998 and takes no account of the many previous seminal papers detailing the progress of this illness from sporadic cases to endemic clusters and them to epidemics of international importance. In his own words, the author vases his ideas upon a 'paper and pencil exercise' conducted amongst 15,000 GP registered patients in the South of England who were asked only about muscle pain and fatigue. The ridiculous prevalence estimate thus calculated, was translated by the RCP report (CR54 1996) into one million sufferers in the UK - about twice the prevalence recorded even in the most occupational predisposed professions (eg Health Care and Teaching). Professor Wessely dismisses any connection with common virus infections apart from EBV, virus meningitis and Q Fever - a rickettsial zoonosis, rare in the UK! There is a general dislike expressed within this 'psychiatric dimension', of a search for 'causes' which are said to be futile and may prevent recovery. (In the RCP guidelines, SPECT

SCANS and laboratory investigation for enteroviruses are specifically excluded from their list of useful tests).

2. PSYCHOLOCIAL ASPECTS (CHALDER);
3. COGNITIVE FUNCTION THERAPY (JOYCE);
4. GRADED EXERCISE (WHITE);
5. COGNITIVE BEHAVIOUR THERAPY (SHARPE);
6. ANTI DEPRESSANTS (WEARDEN & APPLEBY) - all follow this well known path but with commendable honesty in respect of the expense of cognitive behaviour therapy (a-do-it-yourself manual is proposed) and the uncertain outcome of graded exercise and anti depressant therapy, of which the cost along (currently £239 million p.a. for the 4 million UK patients already taking them) would bankrupt the National Health Service!

B OF THE 3 NON ;PSYCHIATRIC' SUBJECTS HANDLED BY PSYCHIATRISTS:

7. NEUROIMAGING (DAVID and COX) think there is no mileage in this and though COSTA's research is interesting, it needs conformation!
8. NEURO CHEMISTRY (CLEARE) and
9. NEUROENDOCRINE ABNORMALITIES (SCOTT and DINAN). These contributions are refreshingly different and well researched, though it is still disappointing to find that SCOTT and DINAN's innovative research, relating maladaptation of the hypothalamic, pituitary/adrenal axis to stress, is feebly ascribed to a psychological dimension. Can a life threatening failure of adrenal function really be ascribed to 'inactivity'?

C. OF THE 4 NON PSYCHIATRIC GRANT HOLDNG RESEARCH GROUPS

10. MUSCLE. (JACHSON and McARDLE) write an interesting and well research paper but, sadly conclude that a vicious circle of biochemical changes in muscle is caused by mental and physical insults leading to inactivity, muscle pain and exercise intolerance;
11. IMMUNOLOGY. (CASH and GIMENEZ) disclose the fact that their quest for an immunological marker for ME/CFS has, so far, been in vain;
12. CARDIAN RHYTHMS. (WILLIAMS and WATERHOUSE) have somewhat neglected the major homeostatic role of the hypothalamus in this respect and, in suggesting deficiency of pineal function in ME/CFS, point to melatonin and light therapy as a cure. One wonders if this will need to be for life and lead to sun-bed deconditioning!; Finally;
13. VIROLOGY. (CLEMENTS) pursues a steady and well organised path to provide evidence of organic pathology in ME/CFS and finds that some 41% of patients studied harbour mutated atypical enteroviruses though some have evidence of a new infection while others are infected by more than one strain. This steady and painstaking work may well be in the forefront of progress to diagnosis, prevention and management in the future.

COMMENTS

While the contributions in this portfolio vary remarkably in quality and some fulfil all the desirable aims of research into ME/CFS, the overall impression is a triumph of the 'psychiatric dimension' over common sense and experience.

RESEARCH RATING (+)(+)(+)(-)(-)(-)

THE WAY FORWARD

It is encouraging to note than in increasing number of the Linbury grants since 199, yet to be completed, include a higher proportion of investigations into organic causes of this illness, 2 devoted to ME/CFS in children and one to alternative therapies. However, knowledge is freedom and eternal vigilance on the part of patients with this disheartening illness as well as those doctors who try to support them is the price of it. The Linbury Trust now urges Government Research Councils and the National Health Service to fund this work. If so, they would be wise to consult research teams with wider practical experience of those patients who are seriously and chronically affected and who have special knowledge of the problems faced by children and adolescents, if we are not to enter the 2nd millennium with less knowledge than we had already gained in the first.

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