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Fluoxetine and graded exercise in chronic fatigue syndrome

Sir: First, may we congratulate Wearden *et al* (1998) on completing such an important and technically difficult study of chronic fatigue syndrome (CFS). We wondered whether the authors were able to give further data which might explain the relatively modest results with fluoxetine and which are also relevant to the commentary on this study (Deale *et al*, 1998).

Many patients in such studies may have long illness durations and in this case the median duration of fatigue symptoms for all patients was over two years. It was unclear how long the duration of mood symptoms was, bearing in mind that major depression and dysthymia were important components of the psychiatric comorbidity in 46% of patients.

These issues are important as, in our experience at a multi-disciplinary CFS clinic, most patients will have been offered a range of antidepressants before referral to tertiary care and it is possible that these mood symptoms may have become refractory to treatment (Scott, 1988). This might partly explain the very modest response to fluoxetine seen and is an alternative explanation to that suggested by Deale *et al* (1998). The neuroendocrine hypothesis of CFS is indeed of great interest but not all of these findings have been consistently replicated (Yatham *et al*, 1995), which may point to heterogeneity in this patient group.

Deale, A., Chalder, T. & Wessely, S. (1998)

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Author's reply: Drs Lynch and Fraser raise an important question concerning the duration of symptoms of depression in our trial of fluoxetine in patients with CFS (Wearden *et al*, 1998) and in other CFS trials. Unfortunately, we do not have data on the duration of depressive symptoms, although symptoms of depressive or anxiety disorder preceded symptoms of fatigue in only nine (7%) of the 136 patients with CFS. In our paper we showed that patients with depressive disorders at baseline randomly allocated to fluoxetine or placebo tended to improve over the six-month period, which does not support the assertion that there was a substantial proportion of patients in our sample with difficult-to-treat chronic depression.

Possibly one reason why fluoxetine was shown overall to have a modest effect over six months is because there was a differential effect of fluoxetine on CFS patients with or without any depressive diagnosis at baseline. The 26 patients with any DSM-III-R depressive disorder randomly allocated to fluoxetine showed a mean improvement between baseline and six months of 3.2 (95% CI 1.6–4.8) on the Hospital Anxiety and Depression (HAD) scale depression score and 3.5 mlO₂/kg per min (95% CI 1.3–5.7) on the Functional Work Capacity (FWC) measure. The 20 patients with any DSM-III-R depressive disorder randomly allocated to placebo showed a mean improvement over the same time scale on the HAD depression scale of 1.7 (95% CI 0–3.3) and FWC measure of 0.3 mlO₂/kg per min (95% CI –1.9–2.4). The 42 patients without DSM-III-R depressive disorder randomly allocated to fluoxetine showed a mean improvement of 0.9 (95% CI –0.1–1.9) on the HAD depression scale and 0.2 mlO₂/kg per min (95% CI –1.1–1.5) on the FWC measure. The 48 patients without DSM-III-R depressive disorder randomly allocated to placebo showed a mean improvement of 0.9 (95% CI 0.04–1.9) on the HAD depression scale and 1.4 mlO₂/kg

per min (95% CI –0.1–3.0) on the FWC measure. Although this is a *post-hoc* analysis which must be treated with great caution, it suggests that fluoxetine has a modest effect on depression and functional work capacity in depressed CFS patients only. Fluoxetine provides no benefit over placebo in the treatment of CFS patients with no depression.

As we suggested in the discussion section of our paper, the overall effect of fluoxetine on depression in the whole sample is dependent on the proportion of patients in the sample with a diagnosis of depression.

Wearden A. J., Morriss, R. K., Mullis, R., et al (1998) Randomised, double-blind, placebo-controlled treatment trial of fluoxetine and graded exercise for chronic fatigue syndrome. *British Journal of Psychiatry*, **172**, 485–490.

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Chromosome 22q11 deletions and aggressive behaviour

Sir: We thank Lachman & Papolos (1998) for their interest in our paper on the prevalence of velo-cardio-facial syndrome (VCFS) in a population of subjects with idiopathic learning disability (Murphy *et al*, 1998) and agree that aggressive behaviour was a feature of the clinical presentation of both patients reported. Lachman & Papolos (1998) suggest that, as the low-activity catechol-O-methyltransferase (COMT) allele is associated with violence in schizophrenia, hemizygosity for this allele may be the common denominator that leads to aggression in individuals with VCFS and schizophrenia.

To test this hypothesis, we genotyped the COMT codon 158 polymorphism in both individuals with VCFS and schizophrenia reported in our study (Murphy *et al*, 1998). Both individuals were found to be hemizygous for the low-activity COMT allele. Consequently, our results lend support to the hypothesis proposed by Lachman & Papolos (1998) that hemizygosity for the low-activity COMT allele may be a determinant for aggressive behaviour in individuals with schizophrenia with or without VCFS.

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Murphy, K. C., Jones, R. G., Griffiths, E., et al (1998) Chromosome 22q11 deletions. An under-recognised

cause of idiopathic learning disability. *British Journal of Psychiatry*, **172**, 180–183.

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Slow progress in improving practice of electroconvulsive therapy

Sir: The recent article by Duffett & Lelliott (1998), concerning electroconvulsive therapy, highlighted the poor progress made in improving some areas of practice in this field, despite two previously well-publicised

audits and recommendations made by the Royal College of Psychiatrists.

It was heartening that only 7% of respondents identified the anaesthetic service as “poor”, and that there were occasional problems in only 15% of cases. The standards of anaesthetic practice are governed by recommendations published regularly by the Association of Anaesthetists and have been discussed in the anaesthetic press (Dunkley, 1995; Watts, 1996).

Regular audit in the form of Confidential Enquiry into Perioperative Deaths reports has resulted in a fall in the number of anaesthetic-related deaths due to continuous change in practices. The low morbidity and mortality associated with electroconvulsive therapy (Pearman *et al*,

1990) may explain the lack of incentive to change practice shown by some institutions and the slow impact made by the Royal College of Psychiatrists.

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Dunkley, C. J. A. (1995) Anaesthetic assistance during electroconvulsive therapy. *Anaesthesia*, **50**, 1009.

Pearman, T., Loper, M. & Trieryl, L. (1990) Should psychiatrists administer anaesthesia for ECT? *American Journal of Psychiatry*, **147**, 1553–1556.

Watts, J. (1996) Anaesthetic assistance during electroconvulsive therapy. *Anaesthesia*, **51**, 609.

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One hundred years ago

The Mental Affections of Children – Idiocy, Imbecility, and Insanity

By William W. Ireland, MD Edin. London: J. & A. Churchill. Edinburgh: James Thin. 1898. Pp. 435. Price 14s.

Dr. Ireland's former work on Idiocy and Imbecility was in its time the best English work on the subject and the present treatise will be welcomed by all interested in the subject. Some chapters are reintroduced with necessary modifications from the older work, but a great part is entirely new. Dr. Ireland commences with a general discussion of the causation of idiocy, in which he gives the chief place to neurotic heredity, considering alcoholism a less important factor *per se* than is generally held. He strongly combats the view that idiocy is to be looked on as an example of reversion to a lower type in the evolutionary scale. Dr. Ireland makes the following classification based on pathological grounds: (1) Genetous idiots, including the well-known “Mongolian” group; (2) microcephalic; (3) hydrocephalic; (4) eclamptic; (5) epileptic; (6) paralytic; (7) traumatic; (8) inflammatory; (9) sclerotic (10) syphilitic; (11) cretins; and (12) idiots by deprivation.

This classification is convenient, notwithstanding that from the point of view of symptoms the groups are much less definite. The fullest descriptions are of the genetous idiots and of the microcephalic. The general peculiarities of feature and of physical and mental development are very clearly given, although Dr. Ireland has been rather sparing in illustrating his descriptions from photographs of his cases. Individual and striking cases are described in detail, and there are some useful though rather brief accounts of the conditions of the nervous system found after death. Medical treatment in these cases calls for little remark, and Dr. Ireland has no belief in surgery for relieving the mental condition. Craniectomy, he believes – and we agree with him – to be useless for the relief of microcephaly, the operative procedure being “founded on an incorrect pathology”. The chapter on Cretinism is a little disappointing. There is an admirable chapter on a subject which usually is passed over – Insanity in Children and Insane Idiots. The sensory deficiencies of idiots are described, but no mention is made of the excessive development of the powers of smell which has been recorded by others. The mental limitations of idiots and the

best methods of educating them are described and a short account is given of the laws bearing on the subject. The book concludes with an interesting chapter on “Wolf Boys” – boys who are found wild and are supposed to have been fostered by wild animals. When serving in the army in India Dr. Ireland had opportunities of inquiring almost at first hand into several supposed instances. He believes that some were imposters but that most were idiots who had been exposed by their parents in the woods. He quotes some delightful stories of boys, reminding one of Kipling's Jungle Book hero Mowgli, but it is clear that Dr. Ireland is sceptical as to the truth of most of them.

Dr. Ireland is so well known as an interesting writer that expectation as to the quality of the book was pitched high and was not disappointed. It is the best account we have of an extremely difficult subject and is worthy of the great reputation and long experience of the author.

REFERENCE

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