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Salivary testosterone levels and major depressive illness in men

SIR: Davies *et al*'s paper (*Journal*, November 1992, **161,** 629–632) was an interesting attempt to clarify the confusion that exists in the literature about testosterone levels in depressed men. Previous studies measured total testosterone and gave conflicting results. The authors assayed salivary testosterone, as a measure of free testosterone, and found a mean pre-dexamethasone level for the subjects of 133 pmol/l, compared with a mean of 215.1 pmol/l for the controls. Despite a sample size of 12, and the trend towards decreased testosterone observed, it was not suggested that the result could represent a type II error. This was even though they found a significant negative correlation between testosterone levels and both the Hamilton Rating Scale for Depression and the Montgomery and Åsberg Depression Rating Scale. Levitt & Joffe (1988), in a study not referenced by the authors, reported 20% lower free testosterone levels in a cohort of 12 men with major depression according to Research Diagnostic Criteria (RDC). They did consider the findings were possibly due to a type II error.

On the basis of Rubin *et al*'s findings (1989), the authors conclude that the hypothalamic-pituitary-gonadal axis seems to be normal in melancholia, and that the explanation of lower testosterone levels must be elsewhere. We feel this is stated too strongly given the available evidence. Hypercortisolaemia is the main possible explanation put forward by the authors for their findings. Cortisol and dexamethasone do suppress testosterone secretion, as evidenced by the abolition of the correlation, found by the authors, between severity of depression and testosterone post-dexamethasone.

However, although Rubin *et al* (1989) found no abnormality of basal luteinising hormone (LH) and follicle stimulating hormone (FSH), or change in LH and FSH post-gonadotrophin releasing hormone, they did find increased testosterone levels in melancholia, which is in conflict with the authors' findings. Additionally, despite the fact that cortisol suppresses testosterone secretion, testosterone has not been found to negatively correlate the sort of cortisol levels found in depression (Yesavage *et al*, 1985; Levitt & Joffe, 1988; Rubin *et al*, 1989). Similarly, we found little evidence of a corresponding positive correlation between LH and cortisol levels in depressed men ($r_s = 0.143$; Driscoll *et al*, 1991).

The authors' study was also part of an investigation during which dexamethasone suppression tests were carried out. Therefore, presumably the correlation between testosterone and cortisol can be ascertained. This would supply evidence, to either support or refute their hypothesis, that a decreasing salivary testosterone level seen with increased severity of depression is secondary to a corresponding hypercortisolaemia.

Testosterone levels decrease with age, but this phenomena has been observed to be exaggerated in depressed men (Sachar *et al*, 1973; Yesavage *et al*, 1985; Levitt & Joffe, 1988; Rubin *et al*, 1989). The authors' cohort had a mean age of 52.4 years and a large age range (s.d. 12.8 years). If their more severely depressed subjects were also more elderly, then the finding of decreased testosterone levels in severely depressed subjects may possibly be a spurious, but still interesting, finding due to the unexplained relationship between exaggerated decreasing testosterone levels and ageing in depressed men.

Testosterone secretion is stimulated by LH, and testosterone exerts a negative feedback on LH. Although Rubin *et al* (1989) and other workers have found no abnormality of LH secretion in depressed men, we have found LH levels to be significantly raised in a small sample of six men with RDC major depression ($P < 0.02$, two-tailed Mann-Whitney *U* Test; Driscoll *et al*, 1991). This may have been secondary to decreased testosterone levels, but insufficient serum was available to also assay for testosterone. However, LH correlated with the age of the subject ($r_s = 0.77$). Nevertheless, Whalley *et al* (*Journal*, May 1987, **150,** 682–684) found LH to be raised, with no corresponding abnormality of serum testosterone or sex-hormone-binding-globulin, in euthymic men recovered from bipolar manic-depressive illness. Given that hypothalamic endorphins and monoamines are involved in the regulation of pituitary and gonadal sex hormones, the human pituitary gonadotrophin may yet be found to be abnormal in depressed men.

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AUTHORS' REPLY: Some interesting points are raised by Driscoll & Thompson. Firstly, Levitt & Joffe (1988) actually suggested that the small numbers in their study groups might have led to a type I error (not type II error), a point which is difficult to grasp. However, our finding is similar to theirs in that we reported lower mean testosterone levels in the depressed group of men with melancholia ($n=11$) compared with the non-depressed control group ($n=10$). In the light of the thorough study by Rubin *et al* (1989), where blood sampling occurred at 30 minute intervals for 26 hours in 16 endogenously depressed men (according to Research Diagnostic Criteria) and 16 individually matched controls, and no significant differences in total testosterone were found, we hesitate to say that our results may reflect a type II error; more so since (as we stated) Rubin *et al* found testosterone levels to correlate positively with melancholia in the subgroup of six men with melancholia according to DSM–III criteria, and all of *our* patients were melancholic. Because of our small sample, we were particularly stringent in statistical analyses, and a test of significance showed $P=0.025$ for levels of salivary testosterone in the depressed men compared with non-depressed controls.

Secondly, in the depressed group itself we found significantly lower salivary testosterone levels to be associated with more severe depression. One possible cause (of several) suggested was hypercortisolaemia. Having examined the correlation between cortisol and testosterone, there is no support for this. The correlation between cortisol and testosterone was $r=0.042$ ($P=0.9$; $n=11$) before dexamethasone and $r=-0.11$ ($P=0.7$; $n=10$) after dexamethasone. This finding therefore concurs with that of Yesavage *et al* (1985).

Thirdly, is there an age factor? We found no association of testosterone levels with age ($r=-0.26$, $P=0.4$; $n=11$), neither was there an association of depression, as measured by the Hamilton Rating Scale for Depression and the Montgomery and Åsberg Depression Rating Scale, with age ($r=0.08$, NS and $r=0.22$, NS).

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Attitudes to mental illness

SIR: I read with interest the two articles (Brockington *et al*, *Journal*, January 1993, **162**, 93–99; Hall *et al*, *Journal*, January 1993, **162**, 99–108) describing the survey of attitudes to mental illness in Malvern and Bromsgrove. Factor analysis indicated fear of the mentally ill as a main component, but in this case in fact almost 85% of the scores were positive "showing the absence of fear of the mentally ill among most people in the general community" (p. 95). This is a little surprising bearing in mind that a substantial proportion of the literature suggests that members of the 'general public', at least on occasion, view patients and former patients as unpredictable and dangerous. One might have therefore expected at least some ambivalence from subjects in this respect. In spite of the study's sophistication, and its use of vignettes, it may be that an additional design could usefully have complemented their study; for example, the discourse analytic approach advocated by Potter & Wetherell (1987), Gilbert & Mulkay (1984), and others, in which subjects are freely encouraged to express their opinions in dialogue and