CORRESPONDENCE

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γ-Melanotropin and β-Endorphin After Dexamethasone

To the Editor:

Dysregulation of the hypothalamic–pituitary–adrenal axis exists in a substantial percentage of patients with major depressive disorder. This dysregulation has been most often studied using the Dexamethasone Suppression Test (DST); in addition to the finding of an abnormal adrenal response to the DST (elevated postdexamethasone plasma cortisol levels), certain patients also have disturbances at the level of the pituitary corticotroph, as reflected by plasma levels of either adrenocorticotrophic hormone (ACTH) or β-endorphin (βE). What is perhaps unexpected is that a subset of depressed patients manifest a disturbance of either the adrenal or the pituitary secretory product, but not both (Fang et al. 1981; Yerevanian et al. 1983; Matthews et al. 1986). One possible explanation that has been suggested for this apparent dissociation of adrenal and pituitary responsiveness to dexamethasone involves the secretion of γ-melanotropin (γ_3MSH). This peptide is found in the amino-terminal domain of proopiomelanocortin, the ACTH/βE precursor. This peptide has significant endocrinological effects, potentiating ACTH-induced steroidogenesis at the adrenal cortex (Pedersen et al. 1980; Al-Duijaili et al. 1981). If this peptide were differentially released by the corticotroph, it might explain the discrepancy between postdexamethasone cortisol and ACTH or βE responses. We undertook a preliminary study to determine if postdexamethasone γ_3MSH could be measured in human plasma, and if it is released concomitantly with or dissociated from the peptides of the carboxy-terminal domain (βE or ACTH).

The postdexamethasone responses of βE and γ_3MSH were determined in seven individuals. Each subject was unremarkable in medical history and examination, manifested no abnormalities on laboratory testing of thyroid, renal, hepatic, and pancreatic function, had normal complete blood counts and had negative urine drug screening. Diagnoses were by DSM-III criteria (APA 1980): two subjects were schizophrenic, two had major depressive disorder, and three were free from psychiatric illness. Written informed consent was obtained from each participant. The study protocol involved an overnight oral DST with plasma collection for peptide determination by radioimmunoassay (RIA); this protocol has been previously described (Matthews et al. 1986). Briefly, on the night prior to study, each subject received 1 mg oral dexamethasone. Intravenous catheters were inserted at 2:30 PM on the following day; blood was obtained at four time points between 3:30 and 4:30 PM, and each sample was assayed in triplicate for γ_3MSH and βE. Values utilized for analysis were the means of these four determinations. Plasma collection, peptide extraction, and the βE RIA were essentially as described by Matthews et al. (1986). γ_3MSH was assayed by an RIA (antiserum courtesy Dr. H. Vaudry) that we have recently developed and described for use in human plasma (Meador-Woodruff et al. 1987).

Postdexamethasone plasma levels of γ_3MSH and βE were found to be highly correlated ($n = 7$, $df = 5$, $r = 0.90$, $p < 0.01$). To further validate the cosecretion and high degree of correlation between circulating levels of these two peptides, plasma levels of γ_3MSH and βE were also determined in a group of 33 rats; the two peptides were again significantly correlated ($n = 33$, $df = 31$, $r = 0.061$, $p < 0.001$).

These results suggest that γ_3MSH and βE are concomitantly secreted from the pituitary in humans following dexamethasone. Additionally, these data, as well as the rat data, replicate previous work that has demonstrated that γ_3MSH and either ACTH or βE are coreleased in a variety of situations, both in humans and lower animals (Nakao et al. 1980; Baird et al. 1982; Pederson et al. 1982; Hale et al. 1984). These findings add to the growing body of literature that indicates that the major proopiomelanocortin domains (ACTH, γ_3MSH, and βE) appear to be concomitantly secreted at rest, as well as following stimulation and inhibition of the anterior pituitary. The dissociation that has been observed between the adrenal (cortisol) and pituitary (ACTH and βE) responses to dexamethasone in a subpopulation of de-

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pressed patients does not appear to be accounted for by the differential secretion of γ_3MSH. It is more likely that this dissociation of pituitary and adrenal responses to dexamethasone in certain patients is the result of differential regulatory events in these two endocrine organs. It should be emphasized that these results are preliminary, however, and will require replication in a larger population.

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Folic Acid and Cognition in the Elderly Depressed

To the Editor:

Sommer and Wolkowitz (1988) found an association between low RBC folic acid (FA) and poorer cognitive function in elderly demented patients. Cognitive dysfunction was measured by the Mini-Mental State (MMS) (Folstein et al. 1975). We were interested to discover if a similar relationship could also be detected between plasma FA and cognitive impairment in elderly depressed patients.

Fifteen patients (2 men, 13 women) with a mean age of 70.3 ± 6.1 years (range 63–82) were examined. All patients met DSM-III (APA 1980) criteria for a major depressive episode. Patients had mild cognitive impairment, which was defined as an MMS score below 27 (normal 30 points). The mean MMS score was 23.7 ± 3.1. The mean plasma FA was 8.1 ± 4.2 ng/ml (normal range 2.5–17.5 ng/ml). Scores of the MMS were not significantly correlated with FA levels ($r = 0.30$). Therefore, we could not confirm the findings of Sommer and Wolkowitz (1988) in our elderly depressed patients. This might be due to the fact that cognitive impairment in our patients was less severe than in their demented patients. It could also be because we determined plasma folic acid instead of RBC folic acid.