Psychoneuroendocrinology, Vol. 6, No. 4, pp. 355 – 357, 1981.
Printed in Great Britain.

0306 – 4530/81/040355 – 03 $02.00/0
Pergamon Press Ltd.

SHORT COMMUNICATION

THE EFFECT OF AMPHETAMINE ON PLASMA CORTISOL IN PATIENTS WITH ENDOGENOUS AND NON-ENDOGENOUS DEPRESSION

MICHAEL FEINBERG,* JOHN F. GREDEN and BERNARD J. CARROLL

Mental Health Research Institute and Clinical Studies Unit, Department of Psychiatry, University of Michigan, Ann Arbor, MI 48109, U.S.A.

(*Received* 30 *April* 1981; *in final form* 1 *June* 1981)

SUMMARY

Amphetamine sulphate (0.1 mg/kg, i.v.) produced no consistent change in plasma cortisol levels in 21 depressed patients. Seven patients with endogenous depression (melancholia) were matched with seven patients with non-endogenous depression; there was no difference in the cortisol response to amphetamine between these two groups.

Key Words—Amphetamine; cortisol; depression; melancholia.

BIOLOGICAL research in depressed patients has included studies of endocrine function and studies of biogenic amine function. Some investigators have combined these approaches by testing the endocrine responses of depressed patients to stimuli affecting biogenic amines. Sachar *et al.* (1980) administered dextroamphetamine sulphate (0.1 mg/kg, i.v.) to depressed patients and found that previously elevated plasma cortisol concentrations were suppressed to baseline levels by this drug. We gave the same dose of dextroamphetamine sulphate to 21 depressed patients and found no such suppression of cortisol levels.

Our patients were studied as part of an evaluation of biological markers for endogenous depression (ED; melancholia). They gave informed consent for all procedures, which had been approved by The Human Use Committee of University Hospital. Each patient was fully evaluated clinically as described by Carroll *et al.* (1980), and both clinical and RDC (Research Diagnostic Criteria, Spitzer *et al.*, 1975) diagnoses were made. Fourteen patients received diagnoses of ED, unipolar or bipolar. We selected seven of these patients by matching them for age and sex with a separate group of patients who suffered from non-endogenous depression (ND; 'neurotic' depression). All patients were free of psychotropic drugs for at least two weeks before amphetamine was given. Each test procedure began at about 0800 hr, with patients in a basal state, when a cannula was inserted into an antecubital vein. Clotting was prevented by slow infusion of normal saline with heparin. We drew blood samples, using a three-way stopcock, every 15 min for 120

*Reprint requests to: Michael Feinberg, Mental Health Research Institute, 205 Washtenaw Place, Ann Arbor, MI 48109, U.S.A.

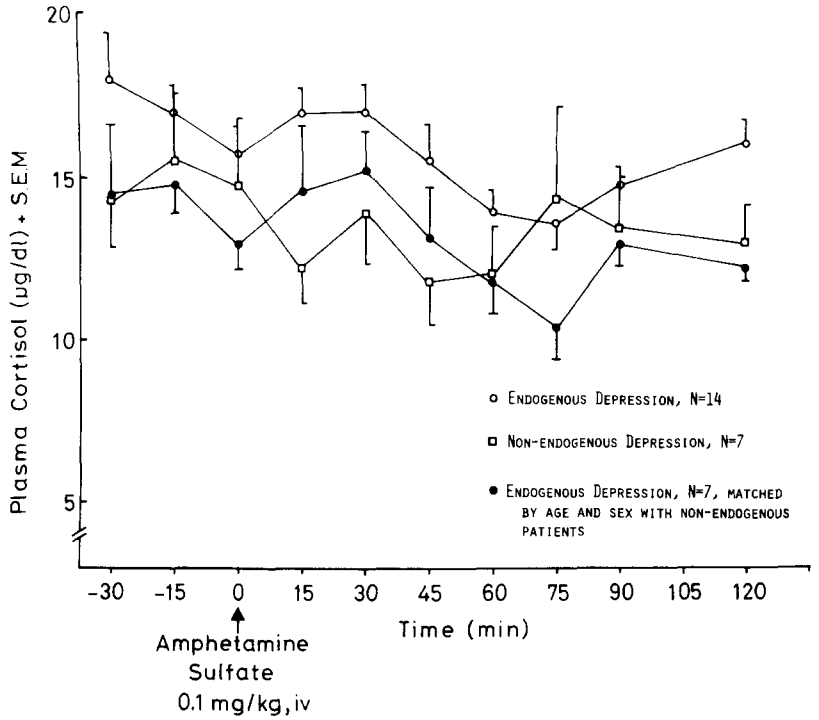

FIG. 1. Plasma cortisol values (mean ± S.E.) before and after amphetamine, 0.1 mg/kg, i.v. The subjects were patients suffering from endogenous or non-endogenous depression.

min, beginning 30 min after insertion of the cannula. We gave amphetamine (0.1 mg/kg, i.v.) 60 min after inserting the cannula. Data analysis was done using the Michigan Interactive Data Analysis System (MIDAS); the method for profile analysis is from Morrison (1967).

The mean age (± S.D.) of the 14 ED patients was 47.4 ± 16.0 yr; there were two men and 12 women. There were two men and five women in the ND group. Their mean age was 37.4 ± 7.8 yr, and the seven matched ED patients had a mean age of 37.1 ± 8.0 yrs. None of the ND patients had an abnormal response to dexamethasone, according to the criteria of Carroll *et al.* (1981). Eight of the 14 ED patients had an abnormal response; these included six of the seven unmatched ED patients and two of the matched patients.

The mean plasma cortisol values are plotted in Fig. 1, where the vertical bars represent the standard error of the mean. The data for the 14 ED patients, the seven ND patients, and the seven (of the 14) ED patients who are matched to the ND patients are plotted separately. Profile analysis shows that the three curves are parallel, and that the unmatched ED patients had higher plasma cortisol levels than did the other 14 patients. There was no such difference between the ND patients and the matched ED patients. The analysis also shows that all three plots are parallel to the abscissa; there is no evidence for a decrease in plasma cortisol after amphetamine.

We also examined the data of each individual patient for evidence of amphetamine-induced secretion of cortisol, using the criteria of Weitzman *et al.* (1971) to define a secretory episode. They defined a secretory episode as occurring when the plasma cortisol concentration rose in a successive sample by at least 2 μg/100 ml and when the next concentration was also higher than the initial one. The episode was considered to have terminated at the first time point when the concentration fell by at least 1 μg/100 ml, provided that the fall was consistent for the next sampling points. Four ED patients may have had secretory episodes during the test, but these would have begun 60 min or more after amphetamine and continued past the time of the last sample (120 min after amphetamine). One ND subject may have had an episode beginning 15 min after amphetamine and lasting 75 min. These possible secretory episodes in ED patients are not in accord with a steady decrease in plasma cortisol after amphetamine.

We thus were not able to confirm the results of Sachar *et al.* (1980), having found no steady decrease in mean plasma cortisol concentration after amphetamine in either group. We also found no increase in cortisol after amphetamine, which is not in accord with the results of Brown *et al.* (1978) in normal subjects or those of Checkley (1979) in depressed patients. However, we used a lower dose of amphetamine than was used in either of these studies, which suggests that we might have found an effect of amphetamine on plasma cortisol had we used a higher drug dose. This hypothesis is supported by some of the results of Brown *et al.* (1978), who noted almost no effect on plasma cortisol of a lower dose of amphetamine (10 mg, p.o.). However, we would expect our results to confirm those of Checkley (1979) that ED patients show no response at all to amphetamine, rather than a decrease in plasma cortisol. We believe that we can draw no conclusions about the neurotransmitter abnormality in endogenous depression from the effects of this dose of amphetamine on plasma cortisol.

This work was supported in part by the Michigan Department of Mental Health and by NIMH grant MH 28294. We thank Mr. James Ritchie and his staff for the cortisol assays. We also thank Drs. J-P. De Vigne, Z. Kronfol and E. Young for helping with catheter studies.

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