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Prediction of cortisol response to dexamethasone from age and basal cortisol in normal volunteers: A negative study

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Abstract. The dexamethasone suppression test (1 mg at 23 h and 4 P.M. blood collection) was performed in 22 normal subjects. In contrast to a previous study using 0.5 mg dexamethasone and a 8–9 A.M. post-dexamethasone blood sample, age and basal cortisol level did not significantly predict postdexamethasone cortisol levels.

Key words: Dexamethasone suppresion test – Cortisol – Aging

In a recent study, Branconnier et al. (1984) found that serum cortisol levels following a dexamethasone suppression test (DST) could be accurately predicted in normal subjects from a multiple linear regression equation when both age and pre-dexamethasone serum cortisol levels were used in combination as regressors. This study used a dexamethasone dose of 0.5 mg, whereas the generally employed dosage is 1 mg; moreover, post-dexamethasone samples were collected at 8–9 A.M. whereas the most discriminant time for identifying cortisol nonsuppression is 4 P.M. (Carroll, 1982). Since adjustment of the DST for age and pre-dexamethasone serum cortisol levels could represent an improvement in the DST procedure, we replicated the study of Branconnier et al. (1984), using 1 mg DST and a 4 P.M. post-dexamethasone collection.

Methods

Subjects. The study included 22 normal subjects (8 males and 14 females, with age ranging from 19 to 63 years; mean age = 38.9 + 13.5). All subjects were carefully screened for any medical illness and for personal and first degree relative history of psychopathological disorders. Moreover, no subject took any drugs (including oral contraceptives) for at least 1 month and all had a body weight not differing by more than 20% from the ideal weight. All subjects were fully informed regarding the study and gave informed consent.

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DST procedure. The DST was performed according to the simplified procedure described by Carroll (1982). At 8 A.M. on day 1, 10 ml of venous blood was collected. Subjects were given dexamethasone 1 mg orally on the same day at 11 P.M. A second blood sample was collected the following day at 4 P.M. Blood was immediately centrifuged and serum was stored at −20° C until analysis.

Cortisol assay. Plasma cortisol was measured by direct radioimmunoassay (RIA) from samples of 25 µl, 40-fold diluted, and heated at 60° C for 30 min. RIA used ^{125}I-cortisol (Farmos Diagnostica, Finland) and anticortisol antiserum (made against the 3-CMO-BSA conjugate), as described previously (Sulon et al. 1978). All samples were processed in duplicate within the same assay, with a maximal intra-assay coefficient of variation of 4.3% and a detection limit of 1.0 µg/dl.

Data analysis. Post-dexamethasone serum cortisol level was used as the dependent variable in a multiple linear-regression model. Independent variables consisted of the predexamethasone cortisol level, gender, and age. A stepwise solution was employed and the entry and deletion criteria for independent variable were set at a statistical significance level of $P < 0.05$ for the partial r^2.

Results

Serum cortisol level was significantly lower following DST: 1.74 + 2.15 µg/dl versus 14.05 + 7.06 µg/dl, $T = 12.6$, $P < 0.0001$. According to the cortisol cutoff level defined by Carroll et al. (1981) (5 µg/dl), two subjects were nonsuppressors (9.1%).

The stepwise solution to the multiple linear-regression analysis revealed that neither age [$r^2 = 0.003$, $F(1,21) = 0.2$, NS], nor predexamethasone serum cortisol level [$r^2 = 0.01$, $F(1,23) = 0.1$, NS] accounted for a significant proportion of the variation in the post-dexamethasone serum cortisol level. The partial r^2 for gender did not reach statistical significance level either [$r^2 = 0.007$, $F(1,21) = 0.1$, NS]. Therefore, no regression equation was obtained.

Discussion

In contrast to the study of Branconnier et al. (1984), these data do not show that post-dexamethasone serum cortisol level can be accurately predicted in normal subjects from a multiple linear regression equation when both age and predexamethasone serum cortisol level are used in combination as regressors. This discrepancy may result from the differences in the methodology used: 0.5 mg dexamethasone and blood sampling the next day at 8–9 A.M. in the study of Branconnier et al. (1984); 1 mg dexamethasone and blood sampling at 4 P.M. the next day in our study. Our results confirm the lack of correlation found in normal subjects between age and response to dexamethasone (Tourigny-Rivard et al. 1981; Stokes et al. 1984). The influence of age in depressive patients is controversial. While the initial studies on the DST did not show any age-related effect (Carroll et al. 1981; Asnis et al. 1982), more recent studies found a significant correlation between post-dexamethasone cortisol values and age (Asnis et al. 1981b; Davis et al. 1984; Fogel et al. 1985; Stokes et al. 1984). However, most results suggest a lack of correlation between pre- and post-dexamethasone cortisol levels both in normal subjects and in depressive patients (Asnis et al. 1982; Halbreich et al. 1984, 1985a, b; Holsboer et al. 1984; Stokes et al. 1984; Brown et al. 1985). In fact, the activity of the hypothalamic-pituitary-adrenal (HPA) system can be divided into various functions with a complicated set of stimulus-response and feedback mechanisms (Keller-Wood and Dallman 1984). The absolute levels of cortisol represent the overall activity of the system which may be abnormally elevated (as is the case in some depressed patients). The DST represents only an exogenous intervention in one HPA regulatory mechanism – the delayed feedback mechanism. It has already been reported that there is only a partial overlap between an abnormally high set point (cortisol hypersecretion) and an abnormality of feedback mechanism (DST nonsuppression) (Asnis et al. 1981a; Holsboer et al. 1984; Stokes et al. 1984; Brown et al. 1985; Halbreich et al. 1985a, b).

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