Memory Disturbances and Dexamethasone Suppression Test in Major Depression

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Introduction

A large body of research has shown cognitive disturbances in major depression (Blaney 1986; Niederehre and Yoder 1989).

The dexamethasone suppression test (DST) yields pathological results in about 50% of major depressive patients (Carroll et al 1981). Interestingly, several studies showed a relationship between hypothalamo–pituitary–adrenal (HPA) overactivity and cognitive impairment in depressed patients (Brown and Shuey 1980; Reus 1982; Rubinow et al (1984), Winokur et al 1987; Siegel et al 1989; Wolkowitz et al (1990). These results remain controversial, however, possibly due to methodological differences both in the DST procedure and in the selection of cognitive instruments (Caine et al 1984; Georgotas et al 1986). Two major hypotheses regarding the relationship of cognitive impairment and abnormal DST are possible: (1) that an abnormal DST identifies a subgroup of depressives with a form of illness also characterized by more severe cognitive deficit; and (2) that the abnormality in the HPA axis, perhaps even the elevated cortisol level itself, *cause* the cognitive impairment. In this context, our purpose was to assess the relationships between HPA activity and memory performance using a sophisticated and well-validated test, the Rey Memory Profile (PRM) (Rey 1966).

Methods

Subjects

The sample comprised 16 inpatients with a major depressive syndrome as per DSM-III criteria, with 3 patients diagnosed with bipolar disorder, depressed, and the remainder with major depressive disorder classified as single episode in 3 cases and recurrent in 9 cases. Ten patients were melancholic and none exhibited psychotic features. There were ten women and six men, with a mean age (± SD) of 45.9 ± 10.6 years. None presented clinical evidence of dementia or cognitive-impairing disease beyond the depressive episode. The educational level was classified into four groups: primary school (n = 5), junior high school (n = 6), senior high school (n = 3), or college (n = 2).

DST

Within the 2 weeks following admission, the DST was performed according to a method modified from Carroll et al (1981): pre-DST cortisol was determined at 8 AM, oral dexamethasone (1 mg) was administered at 11 PM, and post-DST cortisol was collected at 4 PM on the following

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Received November 26, 1990; revised May 28, 1991.

0006-3223/91/$03.50

day. Cortisol was measured by radioimmunoassay (RIA) (Ansseau et al 1987). Nonsuppression was defined by a post-DST cortisol level higher than 5 μg/dl.

Memory Assessment

During the same period, memory abilities were assessed by the PRM, which comprises seven subtests evaluating visual knowledge (subtest 1), automatic visual learning (subtest 2), voluntary and effortful learning with visual assistance (subtests 3, 4, and 5), direct free recall (subtest 6), and delayed free recall (subtest 7) and yields a total score.

Data Analysis

The relationships between cortisol and memory data were assessed by Spearman rank correlation coefficient, using pre-DST and post-DST cortisol, as well as the *RATIO* of pre-DST and post-DST cortisol (adaptation of the Cortisol Suppression Index; Bernstein and Chung 1984) and the difference (*DELTA*) between pre-DST and post-DST cortisol. Because age and educational level influenced cognitive performance as measured by PRM total scores ($r = -0.69$, $p = 0.01$, and $r = 0.72$, $p = 0.01$, respectively), DST suppressors and nonsuppressors were compared by covariance analysis using age and educational level as covariates.

Results

Age did not show any significant correlation with cortisol measures.

Following DST, ten patients showed normal cortisol suppression and six were nonsuppressors. The memory performance of these two groups did not significantly differ.

As shown in Table 1, pre-DST cortisol level and PRM subtest 3 exhibited a positive correlation, whereas post-DST cortisol was unrelated to memory scores. RATIO and DELTA measures were positively correlated with subtests 3 and 6 and with PRM total score. Moreover. DELTA measures tended to correlate with subtests 2, 5, and 7.

Discussion

Despite its obvious limitations, particularly in light of small sample size and numerous statistical tests, this study, showing significant relationships between memory disturbances and several indexes of cortisol nonsuppression after DST, is in agreement with several previous reports (Rubinow et al 1984; Siegel et al 1989; Wolkowitz et al 1990). In addition to those studies, our results suggest that HPA assessments that include both basal and post-DST cortisol levels (DELTA and RATIO) are better correlated with memory processes than isolated post-DST levels.

In our study, the DST status (suppressor

Table 1. Spearman Rank Correlation Coefficients and p Values Between Cortisol Measures and Memory Performance[a]

	PRM subtest number							PRM total score
	1	2	3	4	5	6	7	
Pre-DST cortisol	0.09	0.27	0.57	0.27	0.39	0.34	0.33	0.47
	NS	NS	0.02	NS	NS	NS	NS	NS
Post-DST cortisol	0.36	0.01	−0.10	−0.01	−0.08	−0.26	−0.10	−0.13
	NS	NS	NS	NS	NS	NS	NS	NS
Pre-DST/post-DST	−0.16	0.27	0.49	0.30	0.34	0.56	0.31	0.47
cortisol RATIO	NS	NS	0.06	NS	NS	0.02	NS	0.07
Pre-DST − post-DST	−0.13	0.45	0.61	0.33	0.42	0.61	0.45	0.56
cortisol DELTA	NS	0.08	0.01	NS	0.10	0.01	0.10	0.02

[a]NS = $p > 0.10$.

versus nonsuppressor) did not seem to be sensitive enough to differentiate memory profiles, confirming a previous report by Caine et al (1984) that used a similar sample size. In contrast, with a larger sample, Winokur et al (1987) showed differences between suppressors and nonsuppressors regarding memory deficit at admission, but they eliminated patients who exhibited post-DST cortisol levels between 1.5 and 6.0 μg/dl.

The relationship between HPA overactivity and cognitive disturbances remains controversial, however (Georgotas et al 1986). Some of the many factors that might account for the discrepancies in the literature include heterogeneity of the depressive population (e.g., both our study and Rubinow's work had included bipolars as well as unipolars), and the different cognitive measures employed (e.g., memory versus cognitive flexibility versus other cognitive functions). Moreover, the DST procedure is far from being standardized, for example, Siegel et al (1989) used 0.5 mg dexamethasone and Georgotas et al (1986) 1 mg dexamethasone. We also used particular indexes to assess HPA overactivity and particularly a modified version of the cortisol suppression index (Bernstein and Chung 1984) with the ratio of 8 AM pre-DST to 4 PM post-DST instead of 8 AM pre-DST to 8 AM post-DST or 4 PM pre-DST to 4PM post-DST.

The relationship of cognitive impairment and HPA overactivity can be interpreted in two different ways. First, HPA overactivity could characterize a subtype of severe depression associated with cognitive problems. Second, HPA overactivity could be responsible for memory disturbances. Supporting this latter hypothesis, a recent study showed that the administration of exogenous corticosteroids altered cognitive functions and memory (Wolkowitz et al 1990).

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