BRIEF REPORTS

Elevated CSF CRF in Suicide Victims

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Introduction

It has been suggested that several indices of enhanced hypothalamic–pituitary–adrenal axis activity, including dexamethasone nonsuppression, may be indicators of suicidal tendencies. However, recent studies have failed to prove that the Dexamethasone Suppression Test (DST) could be a predictor of suicidal behavior (Dam et al. 1985; Ennis et al. 1985; Kocsis et al. 1986; Secunda et al. 1986; Arató et al. 1986a; Modestin and Ruef 1987).

Encouraged by a recent study of Stanley et al. (1985), we resorted to postmortem cerebrospinal fluid postmortem (CSF) analyses as a new research tool in the investigation of completed suicides (Arató et al. 1986b). We found no differences in CSF cortisol and adrenocorticotrophic hormone (ACTH) in suicides and controls. We now report on an extension of that investigation, involving measurement of the concentration of immunoreactive corticotropin-releasing factor (CRF) in CSF.

It is quite plausible that excessive, long-lasting and/or uncontrollable stress could lead to a breakdown of the psychological defensive mechanisms and to the suicidal act. In that case, the measurement of CRF would be a better indicator of stress than ACTH or cortisol levels, as secondary changes of receptor sensitivity at pituitary and adrenal levels could conceal any hyperactivity of the hypothalamic–pituitary–adrenal axis. Depressed patients exhibit blunted ACTH response to ovine (Gold et al. 1984) and human CRF (Holsboer et al. 1984) Gold and coworkers (1984) suggested that CRF hypersecretion may play a crucial role in the pathophysiology of depression. This hypothesis seems to be supported by studies from various centers reporting higher CSF CRF concentrations in depressed patients (Nemeroff et al. 1984; Bissette et al. 1985; Bánki et al. 1987; Roy et al. 1987). Significantly decreased CRF receptor density was found in the frontal cortex of suicide victims, probably due to the down-regulation of CRF binding sites induced by CRF hypersecretion (Owens et al. 1986). Our results, indicating normal CSF cortisol and ACTH, but increased CRF levels in CSF of suicide victims, are in accord with these findings.

Methods

Ten-milliliter cisternal CSF samples were obtained by suboccipital puncture from suicide victims and controls (fatal cardiac arrest) within the first 12 hr after death. Selection was based on sex, age, postmortem interval, and clock time of death. Nineteen matched suicide and control pairs were included in this study. The mean age in the suicide group was 49.1 ± 2.3

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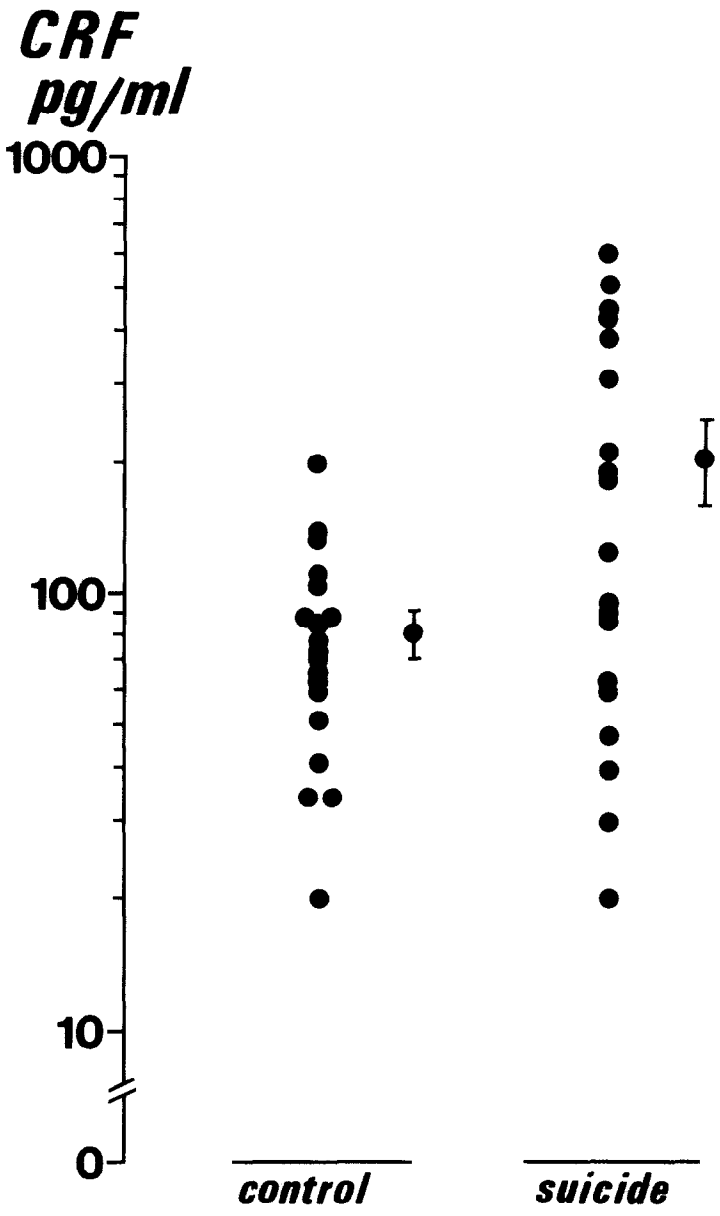

Figure 1. CSF CRF-like immunoreactivity concentrations in 19 matched suicide–control pairs.

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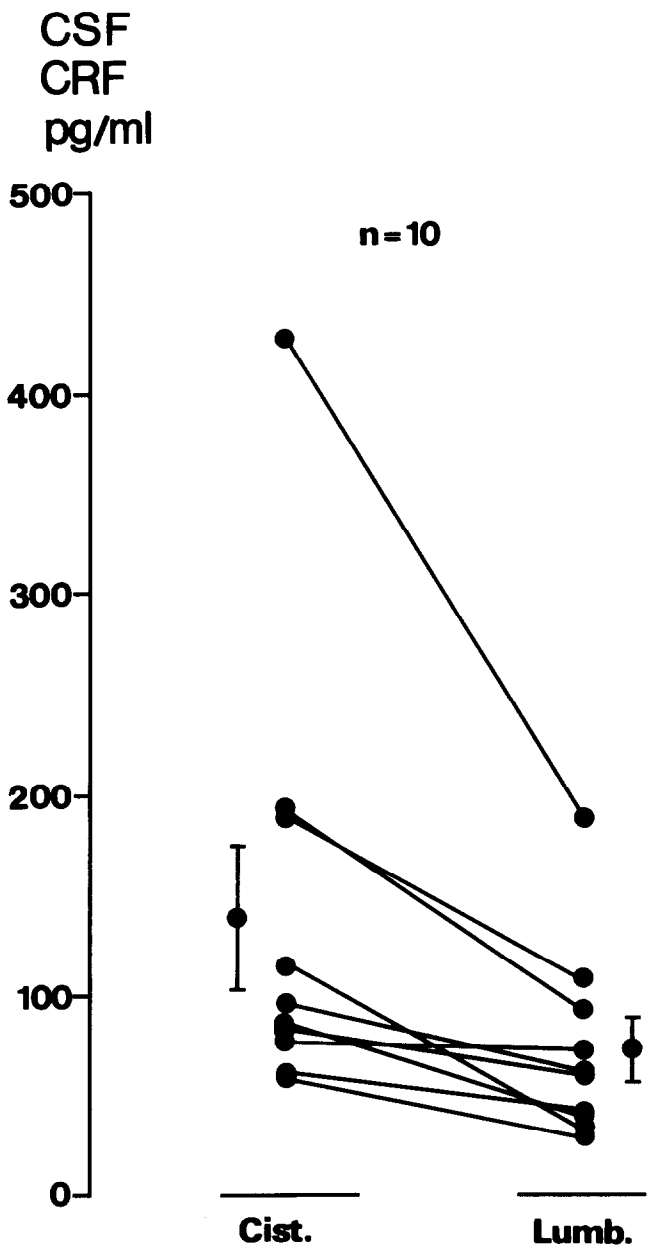

Figure 2. CSF CRF-like immunoreactivity concentrations in the cisternal and lumbar samples obtained at the same time from 10 subjects.

years (±SEM) and in group 51.5 ± 3.1 years. Fourteen men and 5 women were in both groups. The average postmortem intervals were 7.1 ± 0.9 and 6.8 ± 0.7 hr, respectively. The methods of suicide were hanging (13), jumping (2), electrocution (2), and drug overdose (2).

CRF measurements were performed in the Psychoendocrine Laboratory of Duke University, Durham, NC. CRF-like immunoreactivity was determined by a sensitive and specific radioimmunoassay procedure previously described (Nemeroff et al. 1984). In 10 subjects, both 10-ml cisternal and 5-ml lumbar CSF (from the L4–5 interspace) samples were taken in order to investigate the possible craniocaudal gradient for CSF CRF. The group difference was calculated by Student's *t*-test after log-transformation of CRF values.

Results

The individual CRF values in the groups are shown in Figure 1. Significantly higher CRF concentrations were found in the suicide group than in the controls: 207.1 ± 42.1 versus 80.8 ± 9.9 pg/ml ($t = 2.32$, $p < 0.05$).

In interpreting these CSF results it should be noted that cisternal CSF samples were collected, which generally yield higher values than lumbar samples. A consistent craniocaudal gradient for CSF CRF is demonstrated by comparing cisternal and lumbar samples from our 10 subjects (Figure 2).

Discussion

We do not have so-called psychiatric autopsies for these suicide victims, but we have however recently completed retrospective psychiatric assessments on 200 comparable cases of consummated suicide from the same forensic institute. Sixty-one percent of these suffered from a recent episode of affective disorder (Arató et al. 1988). We assume that the elevated CRF concentration found in suicides can be related to their underlying depression and not to the suicidal behavior, as we found no differences in CSF CRF between suicidal and nonsuicidal depressed patients in a clinical investigation (Bánki et al. 1987).

The 19 matched suicide–control pairs included in this analysis were selected from a larger population (44 controls and 22 suicides) whose CSF CRF data were available to us. The two groups were comparable with regard to sex, age, postmortem interval, and clock time of death: these factors thus cannot be responsible for the group differences. The possible influence of these factors on CRF secretion will be investigated later with a larger data base. Interrelationships among CSF cortisol, ACTH, and CRF will also be investigated in a larger population.

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Effects of a Suppression Test Dose of Dexamethasone on Tryptophan Metabolism and Disposition in the Rat

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Introduction

The ratio of circulating tryptophan (Trp) to the sum of the five amino acids (Leu, Ile, Val, Phe, and Tyr) known to compete for the same cerebral uptake mechanism (Trp/CAA ratio) is decreased in depression (DeMeyer et al. 1981; Møller et al. 1986). This ratio, which is a more accurate predictor of brain Trp concentration, and hence 5-hydroxytryptamine (5-HT or serotonin) synthesis, than Trp concentrations alone, is also a predictor of both illness severity (Maes et al. 1987a) and response to antidepressant medication (Møller et al. 1980, 1986). Maes et al. (1987b) showed that both circulating Trp concentration and the Trp/CAA

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