Psychoneuroendocrinology (2008) 33, 1061—1068

available at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/psyneuen

Salivary cortisol and suicidal behavior—A follow-up study

Daniel Lindqvist [a,*], Anders Isaksson [b], Lil-Träskman-Bendz [a], Lena Brundin [a]

[a] Department of Clinical Sciences, Section of Psychiatry, Kioskgatan 19, Lund University Hospital, SE-221 85 Lund, Sweden
[b] Department of Clinical Chemistry, Lund University Hospital, SE-221 85 Lund Sweden

Received 3 March 2008; received in revised form 9 May 2008; accepted 11 May 2008

KEYWORDS
HPA-axis;
Salivary cortisol;
Suicide attempt;
Follow-up;
Major depressive disorder;
Corticotrophin-releasing hormone

Summary
Introduction: Hyperactivity of the hypothalamic—pituitary—adrenal (HPA)-axis is a common finding in major depressive disorder. Similar studies on suicide attempters are less abundant, and the results are divergent. The main aim of the present study was to investigate HPA-axis parameters by the time of a suicide attempt and at follow-up in search for associations between HPA-axis function and suicidal behavior.
Methods: Thirty-five suicide attempters and 16 non-suicidal controls were admitted to a psychiatric ward between the years of 1986 and 1992. Corticotrophin-releasing hormone (CRH) in cerebrospinal fluid and urinary cortisol were obtained for the suicide attempters. The patients were followed up approximately 12 years after the index admission. Cortisol was measured in saliva, and additional suicide attempts and current psychiatric symptoms were registered.
Results: At follow-up, evening salivary cortisol was lower in suicide attempters compared to controls. Low cortisol levels at follow-up were associated with severe psychiatric symptoms. Among women, repeated suicide attempts were associated with low morning and lunch salivary cortisol, and in this subgroup we also found significant correlations between salivary cortisol at follow-up, and CRH as well as urinary cortisol at index.
Conclusion: We found evidence for an association between low HPA-axis activity and suicidal behavior. This could be due to long-lasting and severe psychiatric morbidity, which in turn has exhausted the HPA-axis of these patients. The potential role of hypocortisolism should be given more attention in studies on suicidal patients.

1. Introduction

Finding biological measures in order to predict suicidal behavior is an important task in psychiatric research. Disturbances of the hypothalamic—pituitary—adrenal (HPA)-axis are well documented among patients suffering from psychiatric disorders, in particular major depressive disorder (MDD) (Bao et al., 2008). The majority of studies indicate a hyperactivity of the HPA-axis in patients with an ongoing depression (Plotsky et al., 1998; Pariante, 2003; Claes, 2004). However, low HPA-axis activity has been suggested in depression with atypical features (Antonijevic, 2006), as

* Corresponding author. Tel.: +46 46 173840; fax: +46 46 173844.
E-mail address: Daniel.Lindqvist@med.lu.se (D. Lindqvist).

0306-4530/$ — see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.psyneuen.2008.05.012

well as in multiepisodic and chronic depressive disorders (Shah et al., 1998; Oldehinkel et al., 2001; Watson et al., 2002; Ehnvall et al., 2004). Among suicide attempters, patients with Axis II personality disorders display lower cortisol levels than the ones without such a diagnosis (Westrin et al., 2003). There is also evidence of HPA-axis hypoactivity in the pathophysiology of stress- and fatigue-related disorders (Heim et al., 2000).

In previous studies, our research group has reported lower levels of corticotrophin-releasing hormone (CRH) in cerebrospinal fluid (CSF) of suicide attempters with MDD, compared to non-MDD suicide attempters. Patients with repeated suicide attempts had lower CSF-CRH than non-repeaters (Traskman-Bendz et al., 1992). A subset of these patients was followed up after a mean of 7 months, and the CRH levels remained on an unchanged low level (Westrin et al., 2001). We have also found a negative correlation between suicidal intent and post-dexamethasone cortisol levels in serum among suicide attempters with MDD, indicating an inverse relationship between suicidality and HPA-axis drive in this patient group (Lindqvist et al., 2008). Low 24-h urinary cortisol is associated with adverse events during early life in the same patient material (Sunnqvist et al., 2008). In line with these results, studies from other groups also demonstrate that suicidal patients may display decreased levels of cortisol (Secunda et al., 1986; Pfennig et al., 2005). However, in contrast some studies indicate that HPA-hyperactivity is associated with suicidal behavior (Lopez-Ibor et al., 1985; Westrin and Nimeus, 2003) and completed suicide (Yerevanian et al., 2004; Coryell et al., 2006; Jokinen et al., 2007). As evident from the above, there is abundant evidence of a disturbed HPA-axis activity in suicide victims and attempters, and there is a great need for a more detailed understanding of these changes.

The aim of the present study was therefore to investigate cortisol and CSF-CRH in suicide attempters in search for associations between HPA-axis abnormalities and suicidal behavior—and this time in a long term follow-up situation. Based on our previous findings, our main hypothesis was that HPA-axis activity would remain low in suicide attempters with MDD. We also hypothesized that the severity of psychiatric symptoms would correlate negatively with salivary cortisol levels.

2. Methods

2.1. Index period

2.1.1. Suicide attempters

The 40 suicide attempters participating in the present study were originally admitted to the medical intensive care unit of the Lund University Hospital between the years of 1986 and 1992 (index-period). Within a few days, they were referred to a psychiatric ward of the Lund University Hospital, specialized in mood disorders and suicidal behavior. A suicide attempt was defined as: ''situations in which a person has performed an actually or seemingly life threatening behavior with the intent of jeopardizing his/her life or to give the appearance of such intent, but which has not resulted in death'' (Beck et al., 1972). The diagnoses were set according to the Diagnostic and Statistical Manual of Mental Disorders, 3rd edition (American Psychiatric Association, 1987). Two psychiatrists set the diagnoses after a consensus discussion.

2.1.2. Sampling for biochemical analyses

At index, 16 of the 40 suicide attempters agreed to undergo lumbar puncture. Lumbar punctures were performed after a medication free period of 16 $\pm$ 7 days from admission to the psychiatric ward. Occasional doses of benzodiazepines were allowed during this period. Blood samples were screened for antidepressants, neuroleptics, and benzodiazepines on the day of the lumbar puncture. None of the patients had any detectable levels of antidepressants or neuroleptics, but benzodiazepines were detected in seven (41%) of the suicide attempters. Lumbar punctures were performed as previously described by Traskman-Bendz et al. (1992). Twenty-four hour urine samples were collected during three consecutive days for 24 of the 40 suicide attempters.

2.1.3. Analyses of biochemical markers

CRH levels were determined in CSF using radioimmunoassays (RIA), as previously described (Traskman-Bendz et al., 1992). Cortisol was measured in 24 h urine samples using a RIA (Orion Diagnostica Cat. No.: 68548, Espoo, Finland). Three urine samples were collected on consecutive days, and the average of these values was used for statistical analysis.

2.2. Follow-up

2.2.1. Patients and psychiatric evaluations

Follow-up was conducted approximately 12 years after index admission (1999—2002). Sixty patients (40 suicide attempters and 20 non-suicidal controls) participated in the follow-up. The sample of non-suicidal controls consisted of patients who received psychiatric inpatient care during the same time period (1986—1992) as the group of former suicide attempters, but had no history of suicide attempt prior to that time. The controls were matched with the suicide attempters at index according to diagnosis, time of hospitalisation, gender and age.

At follow-up, the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (American Psychiatric Association, 1994) was used for diagnostics. All patients were assessed for Axis II personality disorders. Semi-structured interviews were conducted by a psychiatrist and a resident of psychiatry, and included information on suicidal attempts during the follow-up time, as well as assessments of current psychiatric symptoms. For the latter purpose the comprehensive psychopathological rating scale (CPRS) (Asberg et al., 1978) was used. The CPRS consists of 65 items, rated from 0 to 3 defined points with halfsteps. The first 40 items are reported and the last 25 are observed by the psychiatrist. The reliability and validity of the CPRS have been proved (Jacobsson et al., 1978; Asberg and Schalling, 1979). The Montgomery—Åsberg depression rating scale (MADRS) (Montgomery and Asberg, 1979) is a subscale extracted from the CPRS. It contains 10 items that assess severity of depression, rated 0—6 points on each item. The MADRS has also been tested for validity and reliability (Von Knorring and Strandman, 1978; Maurer et al., 1984).

Thirteen (37%) of the suicide attempters and eight (50%) of the controls received antidepressants, nine (26%) suicide