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Brief report

HPA axis hyperactivity and attempted suicide in young adult mood disorder inpatients

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ABSTRACT

Background: Hyperactivity of the Hypothalamic–Pituitary–Adrenal (HPA) axis is a consistent finding in Major Depressive Disorder (MDD) and most prospective studies of HPA-axis function have found that non-suppressors in the dexamethasone suppression test (DST) are more likely to commit suicide during follow-up. The results of studies on HPA-axis function and attempted suicide are less consistent. Suicide attempts are more common among young people than the elderly, whereas suicide is more common among the elderly. The impact of age related changes in HPA-axis system activity in relation to suicidal behaviour across the lifecycle may be of importance.

Methods: The aim of the present study was to investigate the DST results in 36 young adult (30 years or younger) inpatients with mood disorder, with ($n = 18$) and without suicide attempt at the index episode.

Results: The DST non-suppressor rate was 25% among young mood disorder inpatients. DST non-suppression was associated with suicide attempt and post-dexamethasone serum cortisol at 11:00 p.m. was significantly higher in suicide attempters compared to non-attempters. The DST non-suppressor rate was 39% in young adult suicide attempters compared with 11% in non-attempters.

Conclusions: The results add to previous evidence in support of the role of HPA axis hyperactivity and suicidal behaviour. The present findings motivate to include HPA axis measures in the assessment of depression in young adults.

1. Introduction

Mental disorders in young adulthood are common and often co-morbid; the most prevalent lifetime disorders were depressive disorders (17.7%) in a recent national survey (Suvisaari et al., 2008). The burden associated with suicide attempts represented 1.4% of the overall burden of diseases in 2002. It is estimated that this figure will reach 2.4% in 2020.

Suicidal behaviours in young individuals represent an important public health problem. Between 2% and 12% (median 6%) of young people reported a lifetime history of suicide attempt (Beautrais, 2002). Suicide attempts are more common among young people than the elderly, whereas suicide is more common among the elderly. However, the majority of depressed young adults do not make suicide attempts, suggesting that additional factors influence vulnerability to suicidal responses.

Hyperactivity of the Hypothalamic–Pituitary–Adrenal (HPA) axis is well documented among patients suffering from psychiatric disorders, in particular Major Depressive Disorder (MDD) (Bao et al., 2008). Disturbances in the HPA system measured with the dexamethasone test (DST) (non-suppression) have been associated with increased risk of suicide in depressed patients in several prospective studies (Mann et al., 2006; Jokinen et al., 2007). Lester (1992), in an earlier meta-analysis, found that suicide but not suicide attempts were associated with non-suppression on the DST. The relationship between suicide attempts and DST status has

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been less consistent. Targum et al. in 1983 found an association in unipolar depressed inpatients of an abnormal DST with a recent history of suicide attempts.

Two studies found an association between DST non-suppression and seriousness of suicide attempts at baseline (Norman et al., 1990; Targum et al., 1983). In the third study, DST non-suppressors were more likely to make a psychologically, rather than medically, serious attempt during the follow-up (Coryell, 1990). Adolescents who were at risk making suicide attempts during the follow-up displayed significant elevations of cortisol prior to sleep onset (Mathew et al., 2003).

Other studies have shown a relative hypoactivity of the HPA-axis in depressed patients manifesting suicidal behaviour and ideation, the lowest plasma cortisol and corticotrophin responses were found in the patients who recently attempted suicide (Pfennig et al., 2005). Black et al. (2002), in a group of diagnostically heterogeneous mood disorder patients, found a modest association between suicide attempts and DST suppression. Low HPA-axis activity measured with salivary cortisol in suicide attempters at follow-up has recently been reported (Lindqvist et al., 2008).

The age-associated alterations in HPA axis functioning are of importance (Keitner et al., 1992; Heuser et al., 1994; Otte et al., 2005) and the role of HPA axis dysfunction in suicidal behaviour may be different in different age categories with the greatest importance for suicide prediction in the elderly mood disorder inpatients (Jokinen and Nordström, 2008). The impact of age related increase in HPA-axis system activity in relation to changes in occurrence of suicidal behaviour across the lifecycle has not been extensively studied.

The aim of the present study was therefore to investigate DST results and post-dexamethasone serum cortisol levels in young (30 years or younger) mood disorder inpatients with and without suicide attempt in search for associations between HPA axis abnormalities and recent suicide attempt.

2. Methods

2.1. Subjects

This study involved 36 young adult (30 years or younger) psychiatric inpatients (13 men and 23 women, mean age 26, range 20–30, S.D. = 3) admitted to the psychiatric wards at the Karolinska University Hospital between 1980 and 2000 with a DSM diagnosis of mood disorder (unipolar, major depressive disorder, single episode or recurrent, bipolar disorder, depressed or dysthymic disorder). A suicide attempt was defined as a self-destructive act with some degree of intent to die. Eighteen patients had attempted suicide just before admission: 13 women and 5 men. Nine patients had used a violent suicide attempt method, 6 women and 3 men (definition according to Traskman et al., 1981).

Patients with a medical condition or taking medication known to interfere with the results at the time of the DST were excluded. The Regional Ethical Review Board in Stockholm approved the study protocol (Dnr. 2005/1152-31/1).

2.2. Neuroendocrine testing

All DST were performed during the depressive episode and maximum within 15 days after suicide attempt (the mean 8 days). Baseline cortisol was measured on the morning of the test. One mg of dexamethasone was given orally at 11:00 p.m., and plasma cortisol levels were determined from blood samples drawn the following day at 8:00 a.m., 4:00 p.m. and 11:00 p.m. using a commercial radioimmunoassay.

2.3. Data analysis

Group differences were assessed with Chi-square test in categorical variables and with Kruskal–Wallis' test in continuous variables.

Statistical analysis (with JMP V software, SAS Institute Inc., Cary, NC, USA) was conducted to analyze post-dexamethasone serum cortisol levels in suicide attempters and non-attempters using Kruskal–Wallis' test. The p value was set at <0.05.

An ad hoc ROC analysis was used to find optimal thresholds for non-suppressor status to best correlate with suicide attempt.

Receiver-operating characteristic (ROC) curves and tables were created for post DST cortisol levels to establish the optimal cut-off values. ROC areas under the curves (AUCs) were calculated as a measure of the diagnostic performance, and differences were calculated and tested according to the methods of Hanley and McNeil (1983). The cut-off point that optimized sensitivity (proportion of patients correctly identified) and specificity (proportion of controls correctly identified) was used (Altman and Bland, 1994).

3. Results

3.1. Patient characteristics

All analyses were based on a total of $N = 36$ cases. Of the 36 patients with DST results, 9 (25%) had an 8:00 a.m., 4:00 p.m. and/or 11:00 p.m. post-dexamethasone serum cortisol level greater then 5 μg/dl and were considered DST non-suppressors, 27 (75%) patients were suppressors. There was a trend for young women to be non-suppressors (35%) in higher proportion than men (7.7%), ($p = 0.054$).

Men and women or the DST non-suppressor and DST suppressor subjects did not differ in mean age. Eighteen patients hade made a suicide attempt preceding admission; they had a mean age of 26 years.

3.2. Suicide attempt and the dexamethasone suppression test

One major finding was that DST non-suppression distinguished between suicide attempters and non-attempters in the group of young adult depressed inpatients ($p = 0.049$).

39% of young adult suicide attempters were DST non-suppressors compared with 11% of non-attempters. Suicide attempters had significantly higher post-dexamethasone serum cortisol levels at 11:00 p.m. compared with non-attempters ($p = 0.026$, Kruskal–Wallis' test). Post-dexamethasone serum cortisol levels at 8:00 a.m. or 4:00 p.m. did not differ between suicide attempters and non-attempters. In young women the DST non-suppression correlated with non-violent suicide attempt method ($p = 0.048$).

To estimate which threshold level of post-dexamethasone serum cortisol concentration at 11:00 p.m. optimally predicts attempted suicide, we analyzed the ROC curves and ROC