Hypocortisolism in recurrent affective disorders

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Akademisk avhandling

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Avhandlingen kommer att försvaras på svenska.

Fakultetsopponent: Professor Marie Åsberg, Institutionen för kliniska
vetenskaper, Karolinska institutet.
Bipolar disorders and recurrent depressions are two common psychiatric disorders with a lifetime prevalence of approximately 1% and 8%, respectively. Despite treatment these patients suffer from affective symptoms up to 50% of the time, resulting in lower well-being. The average life length is also reduced with 10-15 years, mainly attributable to suicide and cardiovascular disease. Increased stress is one of many factors that have been shown to be linked to an increased risk for developing affective disorders and some comorbid somatic conditions such as metabolic disturbances and cardiovascular disease. An increased stress level is known to cause hyperactivity of the hypothalamic-pituitary-adrenal-axis (HPA-axis) with increased cortisol secretion. Hyperactivity of the HPA-axis (or hypercortisolism) is one of the most replicated neurobiological findings in depression. In other stress-related disorders it has however been shown that prolonged stress over long periods of time can lead to a state of low HPA-axis activity, hypocortisolism. Since persons with recurrent affective disorders such as bipolar disorder and recurrent depression are exposed to a high degree of recurrent and chronic stress it could be expected that in addition to hypercortisolism, a state of hypocortisolism could also develop in these disorders, potentially exerting an influence upon the psychological and somatic well-being among these patients.

The major aim of this thesis was to evaluate whether hypocortisolism is related to relevant psychiatric and somatic phenotypes in recurrent affective disorders.

In bipolar disorder, individuals with hypocortisolism exhibited a higher degree of depression and low quality of life compared to patients with normal HPA-axis activity. In recurrent depression, individuals with hypocortisolism exhibited shorter leukocyte telomere length than patients with normal or high HPA-axis activity, which is an indication of an accelerated aging process. In a sample of both bipolar and recurrent depression patients, hypocortisolism was associated with an increased proportion of obesity, dyslipidemia, and metabolic syndrome compared with patients with normal or high HPA-axis activity. Patients with recurrent depression showed a higher occurrence of hypocortisolism than the control sample representative of the general population. Patients with bipolar disorder showed a similar occurrence of hypocortisolism as the control sample. Among bipolar disorder patients with a low degree of lifetime with lithium prophylaxis, there was an inverse correlation between age and HPA-axis activity. In contrast, among patients with a higher degree of lifetime with lithium prophylaxis as well as among the controls, there was no correlation between age and HPA-axis activity. Accordingly, hypocortisolism was most common among older patients with a low degree of lifetime with lithium prophylaxis.

In conclusion, hypocortisolism in both recurrent depression and bipolar disorder was associated with multiple clinically-relevant phenotypes. Additionally, it was shown for bipolar disorder patients that increasing age was a risk factor for hypocortisolism and that prophylactic lithium treatment was a protective factor. It is argued that the protective effect of lithium towards the HPA-axis is attributable to its mood-stabilizing effect, which in turn reduces the chronic stress level. These results provide new insight into the role of hypocortisolism and chronic stress in recurrent affective disorders warranting further studies and hopefully providing clues to improved treatment strategies.

Key words Affective disorders, Bipolar disorder, Cortisol, Depression, HPA-axis, Hypercortisolism, Hypocortisolism, Lithium, Metabolic syndrome, Obesity, Quality of life, Recurrent depression, Stress, Telomeres