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GHRELIN AFFECTS SLEEP, SECRETION OF CORTISOL AND GROWTH HORMONE AND PSYCHOPATHOLOGY IN PATIENTS WITH MAJOR DEPRESSION

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Introduction: Ghrelin showed antidepressant-like effects in mice. Furthermore, ghrelin influences sleep and the activity of hypothalamic-pituitary-adrenal (HPA) and somatotropic axis in healthy humans as indicated by increased cortisol and growth hormone (GH) plasma levels. Both sleep and the activity of these endocrine axes are disturbed in depression.

Objective: To study the effect of ghrelin on psychopathology, sleep and secretion of cortisol and GH in patients with major depression.

Methods: Depressive symptoms as assessed by a validated self rating scale ('Befindlichkeits-Skala', [well-being scale]), secretion profiles of cortisol and GH and sleep-EEGs were determined in 14 unmedicated patients with major depression (7 women) twice, receiving 50 µg ghrelin or placebo at 2200, 2300, 0000, and 0100 hours.

Results: Overall, depressive symptoms did not change significantly after ghrelin administration (placebo:  $37\pm8$ ; ghrelin:  $33\pm10$ , p=0.178). However, there was an improvement at trend level in men (placebo:  $36\pm9$  to ghrelin:  $30\pm9$ , p=0.093) but not in women. In men, ghrelin was associated with less time awake (placebo:  $149.0\pm11.1$ ; ghrelin:  $88.0\pm12.2$  min, p=0.029) and more non-REM sleep (placebo:  $263.2\pm24.1$ ; ghrelin:  $304.9\pm14.1$  min, p=0.027), in women with less REM sleep (placebo:  $108.6\pm15.7$ ; ghrelin:  $74.1\pm13.8$  min, p=0.031) and longer REM latency (placebo:  $49.9\pm6.5$ ; ghrelin:  $85.6\pm14.1$  min, p=0.019). In both sexes, ghrelin caused strong transient increases of GH and cortisol.

Conclusion: Our study may provide an initial indication that ghrelin can exert antidepressant effects in patients with major depression. Ghrelin strongly affected sleep and secretion of GH and cortisol in a partly different way as previously reported in healthy subjects.