Neuroendocrine Studies in Patients with Affective Disorders

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Akademisk avhandling

som med vederbörligt tillstånd av Rektor vid Umeå universitet för avläggande av medicine doktorsexamen framläggs till offentligt försvar i Föreläsningssal A, Psykiatriska kliniken, Målpunkt F, Plan o, Norrlands universitetssjukhus, torsdagen den 28 mars, kl 09:00.

Avhandlingen kommer att försvaras på engelska.

Fakultetsopponent: Professor Wieslaw J. Cubala, Medical University of Gdańsk, Polen

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Abstract

Background
Affective disorders are common and a major cause for increased disability and mortality worldwide. Exogenous stressors and biological variables, including neuroendocrine factors, are assumed to contribute to an increased vulnerability to mood dysregulation. Affective disorders are highly heterogeneous and different neuroendocrine systems may play differential roles in the phenotypic expression of affective disorders in men and women.

Aims
The overall aim of this thesis was to study three neuroendocrine systems in relation to underlying behavioral endophenotypes (personality traits, self-directed and interpersonal violence, and psychiatric symptoms) in patients with affective disorders.

Methods
In Study I oxytocin plasma levels were assessed in 101 general psychiatric outpatients and followed-up in 36 patients after one month. Patients underwent diagnostic, symptomatic, and personality trait assessments.

In Study II insulin and glucagon levels in plasma and cerebrospinal fluid (CSF) were assessed in 28 patients hospitalized after a recent suicide attempt and 19 healthy controls. Study persons were assessed regarding lifetime violence expression, psychiatric diagnoses and symptoms.

In Study III serum levels of allopregnanolone, progesterone and estradiol were assessed in 14 women with severe postpartum depression and psychosis who, as previously reported, responded with rapid symptom remission during sublingual estradiol treatment. Hormonal and symptomatic assessment were performed before and after 4 weeks of estradiol treatment. 28 healthy postpartum controls were included for baseline comparison.

Results
I) Plasma oxytocin levels were positively associated with personality traits of impulsiveness (monotony avoidance) and negative emotionality (psychic anxiety) with potential gender differences.

II) Patients after suicide attempt had higher insulin (plasma and CSF) and lower glucagon levels (CSF) than healthy controls. Insulin levels (plasma and CSF) were higher and glucagon levels (plasma) were lower in patients and controls with higher levels of prior violence expression.

III) Serum allopregnanolone decreased in women with postpartum depression and psychosis during estradiol treatment. The ratio between allopregnanolone and progesterone was significantly lower in patients than in healthy controls at baseline and it remained unchanged after symptom remission.

Conclusion
Behavioral endophenotypes, rather than categorical diagnoses, of affective disorders were associated with neuroendocrine variation in three different cohorts of patients with affective disorder. Hormonal variation pointed towards an association with trait, rather than state like facets of affective behavior, constituting potential vulnerability markers for affective dysregulation.

Keywords
Affective disorder, Suicide attempt, Postpartum depression, Postpartum psychosis, Personality traits, Violence, Oxytocin, Insulin, Glucagon, Allopregnanolone, Progesterone, Estradiol