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Institutionen för Folkhälsovetenskap

Social Environment and Genetics as Determinants of Depression Occurrence and its Chronicity.
A Longitudinal Survey.

AKADEMISK AVHANDLING
som för avläggande av medicine doktorsexamen vid Karolinska Institutet offentligen försvaras i Föreläsningssal Wangari, Widerströmska huset, Tomtebodavägen 18A

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ABSTRACT

Depressive disorders are a set of heterogeneous disorders whose common characteristics are sadness and lack of interest, but varying regarding other symptoms, response to treatment and probability of recurrence and chronicity. They are a serious public health problem due to high prevalence and disability burden. Depression has a multifactorial causality with several genetic, behavioral and environmental factors playing a putative causal role. Thus, the aim of this thesis was to elucidate the interwoven effects of some environmental stressors, individual's characteristics and some genetic factors on the occurrence and the course of depressive disorders. The subjects were drawn from the PART study (In Swedish: Psykisk hälsa, Arbete och RelaTioner), a longitudinal study with three waves between 1998 and 2010, focused on mental health, work and relations among adult people residing in the Stockholm County, Sweden.

In Studies I and III, the relationship between polymorphisms in COMT and serotonin transporter genes and depressive disorders were explored using a case-control approach. Gene x environment interaction effects on depression risk were addressed focusing on COMT gene, childhood adversities and stressful life events in Study I; and focusing on serotonin transporter gene and objective life events (i.e. loss/separation) in Study III. Significant interactions were found between COMT and family problems during childhood and between serotonin transporter and partner's loss/separation.

In Study II, the association between the psychosocial work environment and depression was scrutinized in a follow-up design of people employed in the same job over three-years. The results showed a strong relationship between inadequate social climate and major depression among women three-years later, while there were no certain effects for the remaining exposure variables. Among men, the findings were controversial: high job demands and inadequate skill discretion appeared as protective factors against depression; thus, more studies using a similar approach are warranted.

In Study IV, the complex inter-relationships among personal characteristics and circumstances over different life periods, and their effects on the chronicity of depression, were explored in a follow-up study of depressed subjects over ten years. It was analyzed using structural equation modeling (SEM). The resulting model revealed two main mechanisms anchored on personality traits: an internalizing pathway and an externalized/adversity pathway; which are in line with studies about the onset of depression.

The effort in this doctoral thesis consisted in putting together some pieces of a big puzzle. It is necessary to develop integrative models from different disciplines (e.g. genetics, neurosciences and epidemiology) in order to elucidate the complex mechanisms behind the depressive disorders.

Keywords: Depressive disorders, COMT gene, Serotonin Transporter, Psychosocial Work Environment, Stressful Life Events, Recurrence, Chronicity