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Depression in the elderly. A study from the perspective of daignostic classification, etiology, biological correlates and remission
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Eugen Kahn about his teacher, Emil Kraepelin: "He never tired of telling us that our science was only beginning. He taught us not to overestimate our findings. Anything might be ephemeral. Any step may be undone by new 'facts'; yet the step was not in vain as it was inevitable on the endless road to better, but never complete knowledge". (xix, Kahn. E. "Emil Kraepelin: February 15, 1856-October 7, 1926- February 15, 1956" Am J Psychiat. 1956, 113:289-294)

This last chapter starts with a concise summary of the findings presented in this study, and a discussion of its strengths and limitations. This will be followed by some reflective comments on the conclusions of the study given its limitations and on the potential merits for medical practice and research.

Summary

The number of elderly in the population is rising, in absolute and relative numbers as well, and will continue to do so in the decades to come. This is probably one of the reasons for the growing popularity of the elderly population in social, psychological and medical research. Depression is one of the most prevalent disorders in later life. Taking Hippocrates, who already described the phenomenon of melancholia some 2500 years ago. As a starting point, the first chapter provides a short historical overview of depression and an outline of this thesis, which discusses issues of diagnostic classification, etiology and prognosis of depression in the elderly (chapter 1).

Chapter 2 describes the design, subjects and measures of the study that provided the basis of the thesis. The study combined a cross-sectional (case-control) and a longitudinal approach. Subjects were recruited from eligible participants of the Groningen Longitudinal Aging Study (GLAS), which was held on 1993; and from mental health care outpatients. GLAS subjects were selected either by screening questionnaire or identified as having depressive symptoms by their general practitioner (GP). Apart from an extensive diagnostic evaluation, variables

were measured from both the psychosocial and the biological domain. Depressive subjects were measured at study entrance, than followed every two months until remission up to a maximum of two years. After remission or, if remission did not occur within the study period, two years, they were measured for the second time (chapter 2).

Depressive states not meeting criteria for major depression have received much attention during the past years (Angst & Merikangas 1997;Angst & Merikangas 2001;Judd et al. 1994;Judd, Akiskal, & Paulus 1997;Sartorius et al. 1993). In the elderly the prevalence of these depressive symptoms is relatively high as compared to major depression (Beekman 1996). Discussions focus on the continuity issue, in other words, on the question whether subthreshold depressive syndromes exist on a continuum with major depression or rather form a latent qualitative distinction (Solomon, Haaga, & Arnow 2001). In our study of depressed elderly, major, minor and symptomatic depression shared considerable associations. Variables that are considered part of, or an expression of, vulnerability for depression, such as neuroticism, mastery, chronic somatic diseases, familial depression and recurrence of depression, did not differ significantly between minor and major depression. Furthermore, most variables did not differ between symptomatic depression and the other categories either, whereas there was a major distinction between the control group of non-depressed elderly and the depressive groups (chapter 3).

Subjects who were signalled by their GP or received mental health care treatment had higher anxiety comorbidity rates than subjects from the general population. One reason might be that comorbid anxiety caused patients or their environment to seek for help earlier than those with only depressive symptoms, or that the combination with anxiety made the GP more alert on a mental disorder (chapter3).

In elderly, use of medication is relatively high. Chronic polypharmacy (the use of two drugs or more) exists in one-third of the elderly (Veehof et al. 1999). In addition, depressive symptoms are often masked by somatic symptoms in the elderly (Mulsant & Ganguli 1999). The depressed elderly in our study, especially those with subtreshold depressive complaints (called symptomatic depression) that were not detected as such by their general practitioner, used more 'somatic' medication than those without depression or with more severe or recognized depressive syndromes. They also used more 'somatic' medication with depression as a possible side-effect (Dhondt A.D.F et al. 1999). This might indicate that elderly persons with depressive symptoms which are not recognized by their GP, express their depressive symptoms in a more somatic idiom compared to the other groups, or that their depressive symptoms were a side-effect of their 'somatic' medication (chapter 4).

Chapter 5 and 6 explore different etiological pathways leading to depression. It was possible to divide our group of depressed elderly in three subgroups with different etiological pathways: 1) early-onset depression with longstanding psychobiological vulnerability, 2) late-onset depression as a reaction to severe life stress, and 3) late-onset depression associated with vascular risk factors (chapter 5). The finding of vascular risk factors as an etiological factor for late-life depression is consistent with the etiological model of late life depression described by Alexopoulos et al. (1997). The role of vascular risk factors was further explored in a group of subjects of whom data from the GLAS baseline measure were available. Consistent with the findings in chapter 5, we found that vascular risk factors played their etiologic role especially in depressive episodes that seem to appear "out of the blue", in other words, were not preceded by a stressful life event. Furthermore, vascular risk did not act as a psychosocial stressor or a vulnerability factor that modifies the risk associated with life

stress, but seemed to represent an independent pathway to depression. An unexpected and as yet not understood finding was that vascular risk factors had a protective effect on the negative influence of life stress on the onset of depression in this group of subjects. However, this might have been a chance finding.

Depression has often been associated with a change in activity of the hypothalamic-pituitary-adrenal axis. Findings of elevated cortisol levels have been replicated, but not consistently. We investigated effects of severity and duration of the depression on 24-hour urinary cortisol levels. Because of exclusion criteria, the group we studied in this report was relatively small compared to those used in other chapters. In this group of depressed elderly, we found no hypersecretion of cortisol as compared to the control group but rather evidence for cortisol hyposecretion in persons, especially males, suffering from chronic depressive symptoms. (chapter 7).

A small subgroup of the depressed elderly was asked to donate blood for immunologic measures. At the moment this thesis was written, only data of the relatively newly discovered Natural Killer-T cell had become available for analysis. Depressive disorder was associated with a substantial increase of NK-T-cells, indicating an activation of the immune system. This increase was absent in the subgroup that used antidepressive medication (chapter 8).

The prognosis of depression in the elderly is according to the literature generally not very good: about 33 % are recovered after two years (Cole, Bellavance, & Mansour 1999). In our study, 29.3% of the depressed elderly had remitted completely within two years. Severity of the depression and living alone had a negative influence on the speed of remission. The results further suggest that treatment improved the prognosis of relatively severe depressions, but not the prognosis of mild depression. The score on the Geriatric Depression Scale was a better predictor of prognosis and treatment response than the diagnosis obtained by a semi-structured diagnostic interview (chapter 9).

Strengths and limitations

The study presented in this thesis has some notable strengths, which are listed below.
- The composition of the sample offered the opportunity to compare depressed elderly in the general population, general practitioners' patients and the mental health care outpatients; and hence could investigate and control for effects of recognition and treatment.
- Diagnosis was based on a diagnostic interview that handles the symptoms of depression in great detail. Because the interview was semi-structured, interviewers could elaborate on a symptom until they had enough information to decide whether it was present in a clinically significant level. Subclinical symptoms levels were documented as well, which made it possible to diagnose the category of symptomatic depression.
- The course of the depressive episode was carefully charted by bimonthly (telephone) interviews followed by a second standardized diagnostic interview.
- Assessment of a variety of putative vulnerability indicators for depression made it possible to provide a broad overview of factors associated with late-life depression and to examine interrelationships between (domains of) vulnerability factors.

On the other hand, the generalizability of the results of the study is limited by a number of shortcomings: