

Chronic depression : an integrative approach to the study of underlying vulnerability factors and psychological treatment

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SUMMARY

Major depressive disorder is a common and highly disabling mental disorder that often takes a chronic course. A depressive disorder is assumed to be chronic when the symptoms of depression persist for two years or longer. Previous research has shown that compared to non-chronic depression, chronic depression is associated with more negative health and economic outcomes, highlighting the importance of effective treatments for chronic depression. Current treatments for chronic depression are available but are often less effective than treatment for episodic forms of depression. Possible reasons for the lack of effectiveness of current treatment approaches might be that current treatment options are too time-limited and too symptom focused. The central question of the current dissertation was if better treatment outcomes could be achieved in long-term psychotherapy for chronic depression that focusses on the underlying vulnerability to chronic depression.

The primary aim of the current dissertation was to test the effects and explore the underlying mechanisms of a long-term integrative treatment approach (schema therapy) for patients with chronic depression. The secondary aim was to further examine underlying neurological and psychological vulnerability factors to (chronic) depression and to determine the stability of psychological vulnerability factors during treatment for depression.

Chapter 1 of this dissertation provides an overview of the diagnostic criteria of a major depressive disorder, the conceptualization of different forms of chronic depression, the prevalence and consequences of chronic depression and a definition and overview of treatment effects of current common treatment approaches to chronic depression. Developmental, psychological and neurological vulnerability factors to (chronic) depression are described. The chapter ends with an outline of the goals of the current dissertation.

In **chapter 2**, the neural correlates of self-referential processing in patients with chronic major depressive disorder were examined. We used functional magnetic resonance imaging (fMRI) during a passive self-referential processing paradigm in patients with chronic major depressive disorder ($n = 17$) and matched healthy controls ($n = 18$). We found that patients with chronic depression had decreased BOLD signal during processing of negative depression related personality traits vs. neutral words in the medial prefrontal cortex. Compared to patients, controls had increased BOLD signal in the dorsolateral prefrontal cortex during processing of positive vs. neutral personality trait words. These findings suggest that chronic depression is characterized by distinct neural processing of emotional self-relevant stimuli in these brain areas. We interpreted these findings in terms of a blunted emotional response in patients with chronic depression.

In **chapter 3**, the default mode network functional connectivity during rest in patients with chronic depression and matched controls before and after a sad mood-induction

was investigated. The mood induction procedure resulted in decreased mood ratings in patients with chronic depression and in non-patient controls. Posterior cingulate cortex (PCC) connectivity with the left parahippocampal gyrus, the left superior temporal gyrus and the left anterior inferior temporal cortex increased in patients with chronic depression, relative to controls, following the sad mood induction. In contrast, PCC connectivity with the left anterior prefrontal cortex and the right precuneus decreased in patients with chronic depression and increased in controls following the sad mood induction. We interpreted these findings in terms of activation of negative latent schemas or rumination of negative thoughts in patients with chronic depression, triggered by the mood induction. Connectivity in non-patient controls following the mood induction was interpreted as indicative of a cognitive control (coping) mechanism possibly preventing non-patient controls from retrieving negative memories and engaging in ruminative thinking.

Next to neurological disturbances underlying chronic depression, we also tested the stability of psychological vulnerability factors during treatment for depression. The study described in **chapter 4** tested the stability of early maladaptive schemas over a course of outpatient treatment for depression as well as the relation of schemas with depressive symptoms in 132 patients with a major depressive disorder. Specific schemas (*failure, emotional deprivation, abandonment/instability*) were found to be related to depressive symptom severity. These schemas, as well as other schemas that were unrelated to depressive symptoms, remained relatively stable over the course of treatment. Our interpretation of these findings was that the underlying vulnerability to depression, in terms of early maladaptive schemas, remains intact following outpatient treatment for depression, highlighting the potential value of addressing these schemas in schema therapy.

Chapter 5 is based on data of a longitudinal cohort study, the *Netherlands Study for Depression and Anxiety*. Based on the data of this study, we investigated the two-year stability of the personality traits neuroticism and extraversion in treated and untreated patients with depression. We found that neuroticism and depressive symptoms decreased in treated and untreated people with depression whereas extraversion did not change significantly. We discuss these findings in terms of the mood-state dependency of neuroticism and concluded that assessment of personality traits in depression is clouded by the current mood state.

The relation between interpersonal problems, the therapeutic alliance and depressive symptoms during cognitive therapy for depression was examined in **chapter 6**. Following a 16 to 20 session course of cognitive therapy, interpersonal distress improved whereas the interpersonal style of depressed patients remained largely stable. Patients who scored high on agency/dominance prior to treatment reported lower quality therapeutic alliance whereas patients who scored high on communion/affection prior to treatment reported higher quality alliance. Patients experiencing higher

interpersonal distress prior to treatment reported higher symptom severity throughout treatment. These findings suggest that interpersonal problems of patients with depression have some predictive validity with respect to the therapeutic alliance and treatment outcomes.

Chapter 7 describes the findings of a meta-analysis quantifying the effects of psychotherapy for depression on improvements in psychosocial functioning. We identified 31 randomized controlled trials comparing the effects of psychotherapy to a control group that also included a measure of psychosocial functioning at post treatment. Psychotherapy resulted in significant improvements in psychosocial functioning at post-treatment with moderate effect sizes. In multivariate meta-regression analyses, the effect size of depressive symptoms, the number of treatment sessions and the treatment format (individual versus group) remained as significant predictors of the effect size for psychosocial functioning. We concluded that psychotherapy has positive effects on psychosocial functioning in depression and that these effects are highly related to, but partly independent from the effects of psychotherapy on depressive symptom severity.

In **chapter 8** the theoretical application of schema therapy for chronic depression is described. Based on our own research and similar studies we argue that chronic depression is characterized by a number of psychological and developmental vulnerability factors (adverse childhood events, personality pathology, cognitive factors, interpersonal factors) and that current treatments for depression might not adequately address these factors. We provide examples of how these factors might be addressed in schema therapy for chronic depression and provide a treatment manual of schema therapy for chronic depression.

The results of a single case-series study of schema therapy for chronic depression are described in **chapter 9**. In this study 25 patients with a chronic major depressive disorder were first assessed during a 6 to 24 weeks baseline period. Following this, patients entered a 12 weeks exploration phase of the study during which schemas were explored, the case-conceptualization was done and treatment goals were set. After the exploration phase, patients received up to 65 sessions individual schema therapy. Of the 25 patients who started with the study, five dropped out during the baseline phase. Of the remaining 20 patients who started with treatment, no one dropped out, 40% responded and 35% remitted. Of the 12 patients who were followed until treatment completion, 58% recovered at the end of the intervention. Mixed model regression analyses contrasting exploration phase and intervention phase effects with the baseline phase yielded significant effects of the intervention on depressive symptom severity, global symptomatic distress and overall wellbeing. These findings provide preliminary evidence for the effectiveness of schema therapy for chronic depression.

In **chapter 10** the underlying mechanisms of change in schema therapy for chronic depression were explored. In particular, we investigated temporal relations between

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change in depressive symptoms during schema therapy for chronic depression and change in negative core-beliefs as well as the relation between change in symptoms and the therapeutic alliance. Our findings have shown that there are no temporal relations between changes in negative core-beliefs and change in depressive symptoms during schema therapy for chronic depression. Instead, changes in negative core-beliefs are concurrently associated with changes in depressive symptoms. Moreover, change in depressive symptoms was unrelated to ratings of the therapeutic alliance but alliance ratings were at least to some degree colored by the current mood state.

In **chapter 11**, the findings of this dissertation are discussed. A number of methodological weaknesses as well as clinical and research implications are discussed. It is argued that depression is characterized by a number of underlying vulnerability factors and that patients with depression might benefit from a focus on these factors. Our findings indicate that schema therapy might be a valuable treatment option for patients with chronic depression and shed some light on the underlying mechanisms of change. The overall conclusion that can be drawn at this point is that schema therapy is a promising treatment for chronic depression but that randomized clinical trials are needed to demonstrate the effectiveness.