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7

7. SUMMARY AND GENERAL DISCUSSION

7.1 Summary of 'Personality and Psychotic Disorders'

In Chapter 1 background was provided on psychotic disorders, the GROUP study and FFM personality traits. Three models of inter-relations between personality and psychopathology were elucidated. Briefly recapitulated: *the vulnerability model* assumes that personality contributes to the development of a disorder (Figure 1), *the pathoplasty model* assumes that personality indirectly affects the manifestation of a disorder (Figure 2), and *the scar model* assumes that the disorder affects personality (Figure 3). Also, the two main aims of the current thesis were presented. These aims were: (1) to examine whether FFM personality traits contribute to the vast heterogeneity found in expression of psychotic disorders, and (2) to better understand how FFM personality traits may be connected to symptom expression in patients with psychotic disorders, i.e. to relate our findings to the different models of inter-relations between personality and psychopathology.

In Chapter 2 the second aim was addressed, by examining whether change in psychotic symptom levels predicted change in FFM personality traits in patients with psychotic disorders, which would be indicative of 'scarring'. Our main findings were

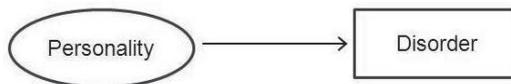


Figure 1. The vulnerability model

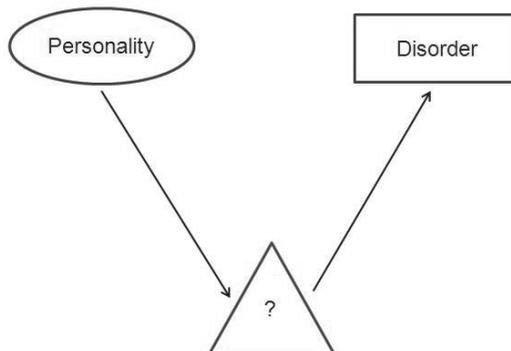


Figure 2. The pathoplasty model



Figure 3. The scar model

that changes in positive and disorganization symptom levels did not affect any FFM trait. Changes in negative symptoms predicted changes in Neuroticism and (inversely) in Extraversion and Openness, but this was due to symptomatic overlap between negative and depressive symptoms. When correcting for depressive symptoms, only a trend-level change in Openness remained. These findings indicate limited support for the scar model in regard to psychotic disorders; negative symptoms may ‘scar’ levels of Openness. Depressive symptoms, however, may affect Neuroticism levels and Extraversion levels, consistent with findings reported in the general population (Fanous et al., 2007; Jylha et al., 2009; Ormel et al., 2004a).

In Chapter 3 levels of FFM personality traits and relations with (subclinical) psychotic symptoms were examined in patients with psychotic disorders, their siblings and control subjects. Siblings of patients with psychotic disorders were found to have levels of Neuroticism intermediate to patients and controls. This finding suggests that levels of Neuroticism increase with the familial risk for psychosis, which is in line with the vulnerability model. However, we did not correct for depressive symptoms in this study. As siblings of patients with psychotic disorders are more likely to suffer from depression compared to control subjects (Klaassen et al., 2013), and as depression may affect Neuroticism levels, we cannot rule out that the higher level of Neuroticism in siblings reflect a state-effect from depression. Alternatively, higher levels of Neuroticism may reflect higher levels of (distress from) subclinical positive symptoms, although the findings regarding clinical positive symptoms discussed in the previous chapter decrease the likelihood of this possibility. In sum, it is not yet possible to rule out potential ‘scarring’ from (subclinical) symptomatic states on levels of Neuroticism. On the other hand, there is also evidence that that Neuroticism represents a vulnerability factor for onset of psychotic symptoms, independent from depressive and subclinical psychotic symptom levels (Krabbendam et al., 2002; Barrantes-Vidal et al., 2009).

Further findings in this study were that subclinical and clinical psychotic symptoms show different associations with FFM personality traits. Subclinical positive symptoms were found to be (cross-sectionally) associated with higher Neuroticism and higher Openness levels, in all three groups, with stronger relations in patients. In regard

to clinical symptoms in patients, Agreeableness was inversely related to all types of psychotic symptom levels (positive, negative, disorganization, excitement and emotional distress); Neuroticism was related to emotional distress; and lower Extraversion and lower Openness (trend-level) to negative symptoms. The findings reported in Chapter 2 indicate that lower Agreeableness cannot be accounted for by a possible state-effect from psychotic or depressive symptoms, which implies that other explanations are warranted in order to explain the relationship with clinical symptom severity. Several possibilities will be discussed hereafter (section 7.2.2).

In Chapter 4, first the factor structure of the Yale-Brown Obsessive-Compulsive scale (Y-BOCS) (Goodman et al., 1989), a standard measure for obsessive-compulsive symptoms (OCS), was examined in patients with psychotic disorders. Our findings indicated an optimal fit for the originally proposed, two-factor scoring structure, consisting of (1) obsessions and (2) compulsions. Our findings also indicated that, contrary to Y-BOCS assumptions, more resistance to OCS is not always a sign of health. This finding is not unique for patients with psychotic disorders, as it has been reported before in patients with primary obsessive-compulsive disorder (Deacon and Abramowitz, 2005; Storch et al., 2005; Woody et al., 1995). In the second part of this chapter, associations between FFM personality traits and a liability for OCS were examined in patients with psychotic disorders and their siblings. Presence of a current major depressive episode was an exclusion criterion for study participation. Patients and siblings with OCS (resp. 25% and 11.4%) showed higher Neuroticism compared to their counterparts without OCS, also when controlling for (subclinical) psychotic symptoms. Additionally, higher Neuroticism was found to be related to OCS severity in both groups. These findings are in line with the vulnerability model, but further prospective studies are needed in order to affirm this hypothesis. Presently, it cannot be ruled out that the Neuroticism levels may be affected ('scarred') by the presence of OCS.

In Chapter 5 the relative contribution of Neuroticism, Extraversion, Agreeableness and adult attachment styles to subjective quality of life in patients with psychotic disorders was investigated. FFM personality traits were found to contribute to all (the physical, psychological, social and environmental) domains of quality of life in patients with psychotic disorders, over and above the impact of positive, negative and depressive symptoms. These findings suggest that FFM traits make an independent and significant contribution to quality of life, which is in line with the pathoplasty model.

Finally, in Chapter 6, FFM personality traits were identified as possible mediators between childhood traumatic experiences and current functional outcome in patients

with psychotic disorders. In general, higher levels of traumatic experiences were found to be related to lower quality of life, more social withdrawal and a higher likelihood of an at face-value 'unfavorable' personality profile (higher Neuroticism and lower Extraversion, Openness, Agreeableness and Conscientiousness). However, patients with an at face-value 'favorable' personality profile (lower Neuroticism, and higher Extraversion, Openness, Agreeableness and Conscientiousness) consistently showed better social functioning and quality of life, irrespective of their level of childhood traumatic experiences. This could not be accounted to socio-demographic or illness related variables. These findings suggest that individual differences, as reflected by FFM personality traits, independently and significantly contribute to manifestation of illness in patients with psychotic disorders, which is in line with the pathoplasty model.

7.2 General discussion

7.2.1 Neuroticism and vulnerability for psychopathology

The results of the studies described in this thesis show that particularly higher Neuroticism is associated with more severe symptom expression in patients with psychotic disorders: higher Neuroticism is found to be associated with higher levels of emotional distress, higher risk and severity of comorbid OCS and higher levels of subclinical psychotic symptoms. However, conceptual overlap between Neuroticism and internalizing symptoms (depressive and anxiety symptoms) may explain part of these relations. Along the same lines, Ormel et al. criticized the use of Neuroticism as an explanatory concept in the etiology of psychopathology, due to its alleged non-informative nature (Ormel et al., 2004b). The authors state that Neuroticism scores may reflect a person's characteristic level of distress, and even prospective associations with internalizing pathology may be considered to be largely tautological, since scores on any characteristics with substantial within-subject stability will predict that characteristic and its related variables at any point in time; in other words: one's general level of negative emotions will 'predict' corresponding levels of negative emotions. According to the authors, the circularity of this process of reasoning can only be avoided when knowledge becomes available about the determinants and mechanisms that produce high Neuroticism scores.

In the last years, progress has been made in this area, from both a biological and psychological standpoint, from a wide range of disciplines (van Winkel et al., 2008; Jacobs et al., 2011; Ormel et al., 2013). We will discuss some of these findings, focusing

on supposed affective and cognitive/behavioral components of Neuroticism, for both internalizing and psychotic pathology.

Regarding affect, Neuroticism has been found to be closely linked to several emotional states and dynamic patterns of reactivity sampled in the context of everyday life, for instance with use of diary techniques such as the Experience Sampling Method (Myin-Germeys et al., 2009). Higher Neuroticism was found to be expressed in emotional reactivity to stress (Bolger and Schilling, 1991; Gunthert et al., 1999; Mroczek and Almeida, 2004; Suls and Martin, 2005; Jacobs et al., 2011), increased negative affect (Mroczek and Almeida, 2004; Suls and Martin, 2005; Miller et al., 2009; David et al., 1997), decreased positive affect (Jacobs et al., 2011; David et al., 1997) and negative affect instability (Jacobs et al., 2011; Miller et al., 2009). The typically modest inter-correlations between most of these factors, suggest that they reflect largely independent emotional processes (Jacobs et al., 2011). It is likely that these components differ with regard to involved genes, brain processes and environmental factors, and hence differ in their relationship with psychopathology (Ormel et al., 2013). A study using cross-twin, cross-trait analyses and bivariate structural equation modelling showed that unique, non-shared environmental factors drive the relation between Neuroticism and decreased positive affect; the relation with increased negative affect instability on the other hand was concluded to be driven by both shared genetic factors as well as individual-specific environmental factors (Jacobs et al., 2011).

The high emotionally-reactive phenotype represented by higher Neuroticism scores may be further aggravated by cognitive/behavioral components, such as ineffective coping skills (Gunthert et al., 1999; Suls and Martin, 2005). The relation between Neuroticism and acute internalizing pathology has been reported to be mostly 'direct'; which was interpreted as a result of biological vulnerability and/or childhood developmental factors, and partly 'indirect': mediated by coping (Mirnic et al., 2013).¹

Similar mechanisms have been proposed in order to explain part of the relationship between Neuroticism and psychotic pathology. Both negative affect (Horan et al., 2008; Krabbendam and van Os, 2005; Krabbendam et al., 2005b; van Rossum et al., 2011) and higher stress-reactivity (Myin-Germeys et al., 2001; Myin-Germeys and

¹ By contrast, the authors found most of the inverse relations between internalizing pathology and Extraversion, which is strongly associated with positive affect (Wilt et al., 2012), and Conscientiousness, which is associated with better recovery from negative affect (Javaras et al., 2012), to be mediated by coping. Agreeableness and Openness were found to be unrelated to internalizing pathology this study, in line with meta-analytic findings (Kotov et al., 2010).

van Os, 2007; Docherty et al., 2009) have been identified as potential vulnerability markers for psychotic onset and symptom exacerbation. Part of the relation between Neuroticism and psychosis may be mediated by the emotional response to the initial subclinical psychotic experiences and by use of coping styles (Krabbendam et al., 2005a). However, psychosis liability and the liability to develop dysfunctional emotional appraisal have also been found to share substantial common genetic origin (Jacobs et al., 2005; Lataster et al., 2009). Moreover, non-affective psychotic disorders and non-psychotic affective disorders show so much non-specific similarity in risk-factors, that some have proposed a paradigm shift from diagnostic categories to cognitive, emotional and social endophenotypes (Weiser et al., 2005).

7.2.2 Agreeableness and vulnerability for psychotic symptoms

In their recent review on the current status on the biological and psychological basis of Neuroticism, Ormel et al. recommend that Neuroticism should be 'deconstructed', not only in levels of affect and reactivity to events, but also, among others, into inner-focused anxious distress versus outer-focused irritable distress, as these components may result from different neurobiological substrates (Ormel et al., 2013). This distinction in internalizing and externalizing facets of Neuroticism is in line with studies further examining the factor structure of the FFM (DeYoung et al., 2007). The specific externalizing facets of Neuroticism, angry hostility and impulsiveness, have been found to be related to lower Agreeableness, and both are related to negative affect instability (Miller et al., 2009). Although a premise of the FFM is that the five domains are relatively independent, it is not uncommon that Neuroticism and Agreeableness show moderate (inverse) correlations (Suls and Martin, 2005). The angry hostility facet of Neuroticism has even been argued to better fit the Agreeableness than the Neuroticism domain (Ashton and Lee, 2005). The overlap between higher Neuroticism and lower Agreeableness may explain why both have been found to be related to psychotic symptom severity (Lysaker et al., 2003). Interestingly, the findings of our cross-sectional study presented in Chapter 3 and the findings of earlier prospective studies (Gleeson et al., 2005; Lysaker and Taylor, 2007) provide indication that Agreeableness may be more strongly related to psychotic symptom severity and symptom exacerbation than Neuroticism. An obvious potential confounder of this relation would be substance abuse, which is associated with lower Agreeableness in both the general population (Ruiz et al., 2008; Kotov et al., 2010) and patients with schizophrenia (Reno, 2004). However, as active substance abuse was an exclusion criterion in the study by Lysaker

et al. (2007), this makes this pathoplastic explanation less likely, at least in their study. Lysaker et al. also included only patients characterized by stable medication use, making poorer medication adherence also a less likely explanation. In the same line, antisocial personality traits, which are strongly associated with lower Agreeableness (Ruiz et al., 2008), have been identified as a risk factor for schizophrenic relapse, independent from substance abuse and medication adherence (Dingemans et al., 1998). Gleeson et al. (2005) describe several alternative hypotheses how lower Agreeableness may represent structural tendencies in behavior, cognition and affect, that elicit higher levels of stress, facilitate social isolation and reduce opportunities for disconfirmation of psychotic interpretation, which may increase patients' vulnerability for symptom exacerbation. Future studies are warranted in order to investigate to what extent lower Agreeableness and higher Neuroticism are related to psychotic symptom exacerbation due to shared or unrelated determinants.

7.2.3 Limitations

Each of the studies included in the current thesis is subjective to its specific limitations, which are discussed in the corresponding chapters. Here some general limitations will be discussed. One of the major limitations is that most studies have a cross-sectional design, which means that caution should be applied regarding conclusions of causality. More prospective studies are required in order to investigate causal directions in the relationship between personality and psychotic disorders, particularly aimed at ruling out potential state-effects. As the third assessment period of the GROUP study recently was completed, more prospective studies will shortly be feasible using the present sample.

Second, the current cohort study design entailed that we assessed levels of FFM personality traits in patients with psychotic disorders after onset of illness. Although there is evidence that higher Neuroticism (Goodwin et al., 2003; Krabbendam et al., 2002; Lonqvist et al., 2009) and lower Extraversion (van Os and Jones, 2001) are precursors of onset of illness in patients with psychotic disorders, as far as we are aware no studies to date have compared pre- and post-onset levels of FFM personality traits in individuals who experienced a psychotic episode. As a psychosis is often experienced as a very disruptive, potentially even traumatic experience, perhaps especially when experienced for the first time, it is possible that 'scarring' occurred in the very first phases of illness. Additionally, it is possible that multiple psychotic episodes may have a cumulative effect on FFM personality traits over time, over the longer course of illness.

Although there is evidence that (equivalents of) Neuroticism levels are fairly consistent across samples reflecting different symptomatic states (inpatients vs. outpatients), as well as recent-onset and chronic stages of psychotic illness (Horan et al., 2008), it is unknown whether this is also the case for the other FFM traits. Lower Agreeableness (Gleeson et al., 2005) and lower Extraversion (Jonsson and Nyman, 1991) have also been identified as possible risk factors for psychotic relapse. If there is a cumulative effect of FFM traits over the more malignant course of illness, and the same traits represent risk factors for unfavorable outcome, this mechanism may contribute to relapse proneness, potentially resulting in a vicious circle.

A third limitation may be the generalizability of our findings to all patients with psychotic disorders, due to selection bias. Patients who are able to give informed consent to participate in a demanding study may be a relatively well functioning group. The finding that psychotic symptom severity was generally clustered at the lower values in the present sample emphasizes the likelihood of this limitation. Although it is hard to envision how selection bias could completely be avoided, perhaps comparison of subgroups with different levels of psychotic symptom severity or functional impairment may have shown a greater impact of psychotic illness on some of the outcome of the present studies. We recommend that future studies differentiate between patients with different levels of illness severity.

Fourth, self-report measures were used frequently in our studies, among others for the measurement of FFM personality traits. Self-report measures are by definition subjective to self-report bias. Nevertheless, there is little indication that patients with psychotic disorders are more subjective to self-report bias in this area compared to individuals from the general population, for two reasons. For one, the reliability and factor structure of the FFM in patients with schizophrenia has been reported to be highly comparable to a normative sample (Bagby et al., 1999). Additionally, another study reported that patients with schizophrenia presented FFM scores comparable to clinician's estimation, although patients with poor insight may overestimate their level of Extraversion (Bell et al., 2007). The latter study, however, used an atypical method for assessing clinicians' estimation of patients' FFM traits, namely interviews designed to assess symptoms and functioning in psychotic disorders. Use of a third-person version of a standard measure for FFM traits, as has been utilized in a study comparing self and spouse rating of FFM traits in the general population (Costa, Jr. and McCrae, 1988), would provide an assessment of self vs. other ratings with better construct

validity. A different approach altogether would be the use of diary techniques which sample experiences in the context of everyday life, such as the Experience Sampling Method (Myin-Germeys et al., 2009) mentioned earlier in this chapter (section 7.2.1). This method has been used in a subsample of the third assessment period of the GROUP study, allowing for combination of methods in the present sample.

Fifth, according to several personality-theorists, the lexical approach to personality, which the FFM is ultimately based on, has its own limitations. Two of these limitations, the limited explanatory power of lexically derived personality dimensions and overlap between some of the FFM domains, were mentioned earlier in this chapter (section 7.2.1 and 7.2.2). Other criticisms involve concerns regarding the use of adjectives as personality variables, the use of lay observers for assessing personality and the lack of similar strategies used in other sciences. We refer to Ashton and Lee (2005) for an elaborate discussion of and retorts to these criticisms.

7.2.4 Strengths

On the other hand, the FFM also possess a major advantage in regard to use in patients with psychotic disorders compared to other personality measures. To our knowledge, the FFM is the only model of personality to date which has demonstrated adequate psychometric properties in patients with psychotic disorders (Bagby et al., 1999), and, more specifically, stability over time despite fluctuations of psychotic symptoms (Kentros et al., 1997; Beauchamp et al., 2006). The results of our study discussed in Chapter 2 contribute evidence in support of this strength.

A second strength of the studies presented in the current thesis is that we widened the scope beyond Neuroticism and Extraversion to the other FFM traits. Many previous studies of FFM traits in patients with psychotic disorders focused solely on Neuroticism or on Neuroticism and Extraversion (Dinzeo and Docherty, 2007). This widening of scope, for instance, led to the finding discussed previously in this chapter that further research on the nature of the relationship between lower Agreeableness and psychotic symptom severity is warranted.

Third, use of a model of normal personality as opposed to models of abnormal personality, enabled us to not only focus on vulnerability but also on protective factors. The results discussed in Chapter 6 demonstrated that FFM traits may represent protective factors in adult patients with psychotic disorders. Further 'deconstruction' of the FFM traits may help to identify resilience factors in patients with severe mental illness, which is a highly understudied area of research.

Fourth, although only a subsample of the GROUP study participated in FFM assessment, the sample size still exceeded many previous studies of patients with psychotic disorders. This may have allowed us to discover relations which may have otherwise stayed obscured in previous studies due to less statistical power, for instance the ‘scarring’ of negative symptoms on Openness levels discussed in Chapter 1.

Finally, the inclusion of siblings of patients with psychotic disorders in the studies examining links between FFM traits and psychopathology may be considered a strength. Siblings share part of patients’ genetic and environmental factors, without psychotic disorder-related confounding factors, such as medication use, social stigma and secondary consequences of illness in regard to objective life conditions (such as housing and job status). Similar relations between FFM traits and (subclinical) psychopathology in patients and siblings contra-indicate that the relations are caused by these potentially confounding factors.

7.3 Clinical implications

Assuming that certain FFM traits are risk factors for symptom expression after onset of illness, the question arises how to best translate this to clinical practice. One option would be the direct targeting of harmful mechanisms underlying the FFM trait(s). For instance, clinicians may offer stress management training or anxiety reducing medication for patients who are more vulnerable to stress (Docherty et al., 2009), or cognitive behavior therapy for patients who are more likely to employ cognitive biases that facilitate social isolation or interpersonal conflict. However, it is not yet clear to what extent FFM personality traits can be modified by therapy. The few studies that have investigated this issue focused solely on Neuroticism in patients with depressive disorders (Tang et al., 2009; Zinbarg et al., 2008), and results are not conclusive.

An alternative option is use of FFM traits to help select the type of treatment from which patients are most likely to benefit. Empirical support for this strategy in regard to patients with psychotic disorders comes from a recent study, in which different FFM traits were found to predict change in active coping strategies for different forms of therapy: benefit from cognitive behavioral therapy was found to be most strongly associated with patients’ level of Conscientiousness, while benefit from the more interactive skills training for symptom management was found to be most strongly related to patients’ level of Extraversion (Beauchamp et al., 2013).

Furthermore, knowledge of patients’ FFM traits may be useful for selecting specific therapeutic strategies. For one, it may help clinicians in anticipating likely pitfalls in

therapy. For instance, as lower Agreeableness has been reported to be associated with a lower quality of working alliance in the treatment of patients with psychotic disorders (Johansen et al., 2013), therapists may anticipate that the formation of a solid therapeutic relationship may require more time and effort for this group. Miller describes several examples how levels of FFM traits may be indicative of specific pitfalls for therapy, along with links with expected clinical presentation of patients and expected preferences for interventions (Miller, 1991). Knowledge of patients' personality traits may also help clinicians in forming a conceptualization of the cause and nature of presented problems. For instance, the social stigma of psychiatric illness may be particularly painful for patients with a high need for social conformity, which may be a feature of high Agreeableness, and cognitive problems associated with the aftermath of a psychotic episode may be particularly distressing for patients with the high striving levels often seen in individuals with high levels of Conscientiousness.

7.4 Conclusion

The results of the current thesis provide support that normal personality traits as conceptualized by the FFM contribute to the vast heterogeneity in symptom expression in patients with psychotic disorders. The found relations between FFM personality traits and functional outcome (subjective quality of life and social functioning) are relatively robust, since these relations survive correction for current symptom severity. The findings regarding the relations with symptomatic outcome (subclinical psychotic symptoms, psychotic symptoms and comorbid OCS) should, however, be considered to be preliminary, as the extent to which the FFM traits may be affected by state- or even scar-effects is not yet fully examined. Also, 'deconstruction' of the FFM traits, particularly lower Agreeableness and higher Neuroticism, is required in order to better understand the nature of the etiological processes involved, for instance by discriminating between mechanisms which may involve levels of affect and reactivity, and between internalizing and externalizing processes. Although, through this, new and intriguing questions and directions for future research arose, the findings presented in the present thesis highlight that relations between FFM personality traits and symptom expression in patients with psychotic disorders cannot be explained by manifestation of psychotic illness alone. This is contrary to the long-held belief, starting with Bleuler and Kraepelin, that a psychotic disorder irreversibly 'damages' the personality. Our hope is that, in time, attention to individual differences as reflected by patients' personality traits may help identify those at the risk of an unfavorable course, and contribute to diminishing this risk through person-tailored therapeutic interventions.

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