Chapter 8

Discussion
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Introduction

Many personal and environmental risk factors for depression and anxiety have been identified. It is also clear that the presence or occurrence of a single risk factor in itself is not sufficient to lead to the onset of depression and anxiety disorders. Instead, the impact of any given risk factor seems to depend on the presence of other risk factors (e.g., Ingram & Luxton, 2005; Rothman & Greenberg, 1998). The aim of this thesis was to extend our knowledge on this interplay of personal and environmental risk factors. In successive chapters we examined the interplay of familial liability and gender (Chapter 3), familial liability and stress (Chapter 4), gender and stress (Chapter 5), several facets of temperament (Chapter 6) and temperament and stress (Chapter 7). In this final chapter I discuss our findings and their implications for future research and clinical practice. Before I do so, two points should be noted.

Firstly, in the studies presented in this thesis we focused on offspring depression and anxiety. However, problems in offspring of parents with an emotional disorder are not likely to be limited to emotional problems alone. Research indicates increased risk of externalizing problems, such as aggressive behavior or drug/alcohol use or abuse, in these offspring as well (Avenevoli & Merikangas, 2006; Cummings & Davies, 1999; Downey & Coyne, 1990; Goodman & Gotlib, 1999; Kane & Garber, 2004). This also may hold for somatic problems. For example, Wyman et al. (2007) found evidence that parental stress, such as mental health problems, is associated with natural killer cell activity in offspring, such that offspring of parents experiencing high stress were more often physically ill than offspring of parents experiencing low stress. In addition, factors outside the domains of psychiatric and physical health, such as school performance or social functioning, may be affected by parental disorder (Conger, Patterson, & Ge, 1995; Ge et al., 1995). ARIDNE includes measures of such offspring problems, but these were beyond the scope of this thesis. Thus, the reader of this thesis should be aware that in our studies those offspring of parents with an emotional disorder that did not report depression and anxiety may have had other problems instead.

Secondly, a number of variables used in our studies were assessed retrospectively and/or at the same measurement occasion. Particularly in these instances, we can not be certain of the direction of causality in the associations between predictor and outcome variables. In addition the associations we found may be bi-directional, with mutual influences between predictor and outcome variables.
Familial liability

Throughout this thesis we defined familial liability as the number of affected parents. In the context of our high-risk sample this meant we distinguished between offspring with one and offspring with two parents with a history of depression and/or anxiety. In line with the few other studies on this topic (Brennan et al., 2002; Foley et al., 2001; Marmorstein, Malone, & Iacono, 2004; Nomura, Warner, & Wickramaratne, 2001; Warner, Mufson, & Weissman, 1995), we found that the presence of a second affected parent increased life-time risk of emotional disorder (see Chapter 3) and current level of emotional problems (see Chapter 4). In our study, the information concerning emotional problems in the second parent was provided by the informant parent and did not incorporate formal DSM-IV diagnoses. The associated unreliability may have reduced the size of the effects.

The number of studies on the effect of a second affected parent are limited. In addition, the available studies are not fully comparable concerning the kind of problems that were assessed in the second parent. Individuals with mental health problems tend to have marital partners who also have mental health problems. While partners often have the same kind of problems, they may suffer from different disorders as well (Dierker, Merikangas, & Szatmari, 1999; Foley et al, 2001; Merikangas et al., 1988). The type of disorder which offspring may develop is likely to differ according to the nature of the problems in the other parent (Foley et al., 2001). In Chapter 3 we found that a second affected parent increased offspring risk of anxiety disorders, while it only tended to increase offspring risk of depression. We examined whether our finding could have resulted from the fact that some of the “second” parents had anxiety but not depression problems. However, when we excluded offspring of which the other parent only had anxiety or controlled for the presence of parental anxiety, we found the same results. A second affected parent may thus particularly increase offspring risk of anxiety. Alternatively, our finding may also originate from the age of our sample. Since the age of onset of depression is on average 5 till 10 years later than that of anxiety disorders (Ernst, 1992; Weissman et al., 1997), many of the offspring may have developed anxiety but no depression yet. In the examination of the intergenerational transmission of risk researchers should be aware whether and how the nature of problems in the other parent and how the age of their sample may influence findings of increased risk in offspring with increasing familial liability.

Our results indicate that it is important to inquire after the children when patients present themselves for treatment and be available to provide help especially if both
parents have mental health problems. Research by Ge et al. (1995) indicates bi-directional effects between parent and offspring emotional problems, while Bögels and Siqueland (2006) report beneficial effects for both offspring and parents when offspring were treated. Helping the offspring may thus not only prevent (severe) problems in offspring but may also help parents to recover.

**Familial liability and gender**

Goodman and Gotlib (1999) proposed that both the presence of a second affected parent and offspring gender act as moderators in the intergenerational transmission of risk (see Chapter 1). Consequently, the effect of a second affected parent may differ between daughters and sons. In addition, the impact on offspring emotional health is thought to differ between paternal and maternal disorder (Connell & Goodman, 2002; Phares & Compas, 1992). How these gender differences in parents and offspring combine has rarely been investigated. Our results in Chapter 3 indicated that the impact of a second affected parent differs according to both offspring and parent gender. While a second affected parent increased risk in daughters and in sons of depressed fathers, we found that a father with emotional problems did not increase risk in sons of depressed mothers. In addition we found that sons with only an affected father had a lower risk than sons with only an affected mother. Risk did not differ between daughters with only an affected father or only an affected mother. Our findings imply that paternal and maternal emotional disorder may similarly and additively increase risk of depression and anxiety disorders in daughters, while risk in sons may only increase with maternal emotional disorder.

Until the 1980’s, research into the intergenerational transmission of risk of emotional disorder focused almost exclusively on the effect of an affected mother (Kane & Garber, 2004; Phares & Compas, 1992). To date the number of studies focusing on maternal emotional health is still larger than the studies examining the effect of paternal disorder. A review (Phares & Compas, 1992) and a meta-analysis (Connell & Goodman, 2002) of the available studies on the difference in the effect of maternal versus paternal disorder indicate that the impact of maternal disorder is larger than the impact of paternal disorder, but also that the difference is not large. However, the review and meta-analysis could not differentiate between effects on sons and daughters since very few studies examined effects of paternal and maternal disorder for sons and daughters separately.

Those studies that did examine differences in risk according to the parent-offspring gender dyad (Eberhart et al., 2006; Foley et al., 2001; Hops, 1992; Klein et al., 2005;
Nomura, Warner, & Wickramaratne, 2001; Thomas & Forehand, 1991) provide inconclusive results. Our findings are in line with Hops’ (1992) conclusion that the intergenerational transmission of depression is stronger for daughters than for sons and stronger for mothers than for fathers, but further extend on this finding by indicating that especially sons of affected fathers have a lower risk compared to the other three parent-offspring gender dyads.

Our results indicate that associations between parental and offspring emotional problems are affected by emotional problems in the other parent. Risk in daughters with two affected parents was considerably higher than risk in daughters with one affected parent, while risk in sons of affected fathers only increased when the mother was affected as well. Future studies examining gender differences should therefore account for the effects of a second affected parent either by only including offspring with one affected parent or by distinguishing between offspring of two healthy parents, offspring with one and offspring with two affected parents.

Gender is often considered as a risk factor, but gender can only serve as a proxy representing factors characteristic to or more prevalent in women. We can offer three explanations of our finding that maternal emotional disorder increases risk in both sons and daughters whereas paternal disorder only increases risk in daughters. Firstly, there is evidence that some of the genes associated with emotional disorder may be linked to the X-chromosome (Brummett et al., 2003; Yu et al., 2005). This could explain a higher risk in women than in men and, since sons get their X-chromosome from their mother and not from their father, also our finding that paternal depression does not increase risk in sons. A second explanation is formed by the combination of a) the relatively larger role of the mother compared to the father in shaping the child’s environment, beginning before birth up to late childhood and early adolescence (Connell & Goodman, 2002), b) the finding that fathers seem better able than mothers to compensate for their disorder in the contact with their children (Field, Hossain, & Malphurs, 1999) and c) the higher sensitivity to relational stress in daughters (Cryanowski et al., 2000; Hankin & Abramson, 2001; Nolen-Hoeksema & Girgus, 1994). While a and b can explain that maternal emotional disorder increases risk in both sons and daughters, c will have the effect that paternal disorder increases risk in daughters but not in sons. A final explanation for the absence of an effect of paternal problems on emotional problems in sons can be that sons of affected fathers may develop other problems than depression and anxiety, such as substance use or dependency (Cummings & Davies, 1994; Marmorstein, Malone, & Iacono, 2004; Rohde et al., 2005).

Adopting longitudinal designs that follow children from early childhood through the different developmental phases into adulthood, may enlighten us concerning the
differential roles of paternal and maternal disorder in the development of mental health problems in their sons and daughters. Such a design can also more easily account for differences according to the developmental timing and chronicity of the parental disorder. Research indicates that offspring risk is higher when children are confronted with parental disorder early in life and for longer periods of time (Hammen & Brennan, 2003; Warner, Mufson, & Weissman, 1995). ARIADNE includes retrospective assessments of timing and chronicity of parental disorder. Associations of these factors with offspring risk will be examined and reported on in forthcoming studies.

Our finding on the interplay of familial liability and gender is relevant to clinical practice by giving evidence that especially offspring of affected women and daughters are at increased risk to develop depression and anxiety.

Familial liability and stress

In Chapter 4 we examined the interplay of familial liability and parent-offspring stress in the association with offspring emotional problems. In their model of the intergenerational transmission of risk, Goodman and Gotlib (1999) proposed that stressful parent-offspring relationships partially mediate the association between parental and offspring emotional health. Parental emotional disorder would thus increase offspring risk of depression and anxiety through the effects of the parental disorder on the quality of the parent-offspring relationship. By extension, the effect of a second affected parent on offspring emotional problems would be mediated by higher levels of parent-offspring stress. Our results in Chapter 4 provide evidence for this idea. Offspring with a second affected parent reported more parent-offspring stress than offspring of one affected parent and these higher levels of parent-offspring stress partially mediated the association between familial liability and offspring emotional problems. In addition, Goodman and Gotlib proposed that a second affected parent acts as a moderator of the association between parent-offspring stress and offspring emotional health. A second affected parent would strengthen the association between parent-offspring stress and offspring emotional health. Similar levels of parent-offspring stress would then result in more emotional problems in offspring of two than in offspring of one affected parent. In contrast to this idea, however, research by Weissman and colleagues (Fendrich, Warner, & Weissman, 1990; Nomura et al., 2002; Pilowsky et al., 2006) indicated moderation in the reverse direction, that is, the association between parent-offspring stress and offspring emotional problems was less strong in offspring with
a depressed parent than in offspring without a depressed parent. This finding implies that the association between parent-offspring stress and offspring emotional problems would be less strong in offspring of two affected parents than in offspring of one affected parent. Our findings in Chapter 4 are consistent with moderation as proposed by Goodman and Gotlib, that is, we found a stronger association between parent-offspring stress and offspring emotional health in offspring with two affected parents than in offspring with one affected parent. The mediation and moderation effects in our study are also in line with the effects found by Hammen, Brennan, and Shih (2004) who studied the role of parent-offspring stress in the difference in risk of depression between offspring of unaffected parents and offspring of affected parents. Very few studies examined both mediation and moderation effects in the association between parental disorder, parent-offspring stress and offspring problems. In addition, the results of these studies seem inconclusive. Our study not only adds to the knowledge concerning the interplay between familial liability, parent-offspring stress and offspring problems, but also extends current knowledge by examining differences within a high-risk sample. Since the number of studies on this subject is still limited, the finding that a higher familial liability strengthens the association between stress and offspring emotional problems needs further replication.

In our study we used the quality of the parent-offspring relationship to examine the interplay of familial liability, that is the number of affected parent, and stress in the association with offspring problems. It may be worthwhile to use stressors less directly related to parental symptoms to further examine the interplay of familial liability and stress (i.e., mediation and moderation). In addition, research into the role of familial liability may be extended with measures of familial liability that are more refined, for example measures incorporating the presence of emotional problems in siblings or grandparents. Such measures of familial liability may even serve as proxy’s of genetic liability, especially when they incorporate information about age of onset, chronicity and severity of the relative’s disorder (Wals et al., 2003).

Our findings provide further justification for the focus on the parent-offspring relationship in programs aimed to prevent problems in offspring of parents with depression and anxiety problems (Avenevoli & Merikangas, 2006; Bool et al., 2002). Although we may not be able to decrease vulnerability to parent-offspring relational stress, parent-offspring relations and family functioning can be targeted and improved by prevention and intervention programs.
**Gender and stress**

Stress is an important factor in many etiological models of depression and anxiety (e.g., Brown & Harris, 1978; Goodman & Gotlib, 1999; Hankin & Abela, 2005; Ormel & Neeleman, 2000). One of the explanations offered for the gender difference in depression and anxiety, also by Goodman and Gotlib (1999), is that stressful events and circumstances are more prevalent among women and that women are more vulnerable to the effects of stress, especially interpersonal stress (Cyranowski et al., 2000; Hankin & Abramson, 2001; Nolen-Hoeksema & Gergus, 1994). Due to this assumed greater sensitivity to interpersonal circumstances, women may however also profit more than men when interpersonal relations are available and provide support (Matthews, Stansfeld, & Power, 1999; Taylor et al., 2000). The presence of social support is associated with lower levels of depression and anxiety problems (e.g., Procidano & Walker Smith, 1997; Robinson & Garber, 1995; Sarason et al., 1983). In addition, social support is widely assumed to be able to act as a buffer against the effects of stressful events or circumstances (Gottlieb, 1994; Kessler, Price, & Wortman, 1985; Olstad, Sexton, & Søgaard, 2001). Due to gender differences in the effect of interpersonal stress, the interplay between parent-offspring stress and social support may differ between daughters and sons. In Chapter 5 we examined the interplay of gender, parent-offspring communication stress and social support. The social support measure in Chapter 5 combined the total number of people providing support as well as the quality of the support. Daughters reported more depression, anxiety and parent-offspring stress than sons. Offspring experiencing problems in the parent-offspring relation reported more depression and anxiety while high social support was associated with less depression and anxiety. In line with our expectations we found that the daughters benefited more from social support than the sons when problems in parent-offspring communication were high.

We found a significant three-way interaction between gender, stress and support where other studies did not. This may be explained by the nature of our design. Mechanisms in the development of depression and anxiety are more likely to surface in high-risk samples since these samples offer more variance in both predictor and outcome measures (Garber & Flynn, 2001). Furthermore, our findings in Chapter 4 suggest that the impact of interpersonal stress is also stronger in high-risk individuals.

Our findings in Chapter 5 indicate that the effect of parent-offspring communication stress can be compensated by social support, but also that problems in
both domains increase risk of depression and anxiety. The three-way interaction with
gender however suggests that this may be more true for daughters than for sons.

**Temperament**

Temperament is associated with emotional health. In general individuals with high
negative affectivity report more depression and anxiety than individuals with low negative
affectivity (e.g., Clark, Watson, & Mineka, 1994; Jorm et al., 2000). Extraversion and
effortful control, on the other hand, are negatively associated with emotional problems,
such that individuals with high extraversion or effortful control in general have less
depression and anxiety than individuals with low extraversion or effortful control (e.g.,
Angst, 1998; Carver, 2004; Clark, Watson, & Mineka, 1994; Davidson, 1995; Depue &
Iacano, 1989; Eisenberg et al., 2001; Lengua, West, & Sandler, 1998; Muris, De Jong, &
Engelen, 2004). We examined the associations between negative affectivity, extraversion
and effortful control on the one hand and depression and anxiety on the other in the
Chapters 6 and 7. The associations we found are similar to those reported in the literature.
The results in Chapter 6 showed that the association between the temperament traits on
the one hand and depression and anxiety on the other were stable with increasing time
intervals between assessment of temperament and depression and anxiety.

In Chapter 6 we examined interactions between the separate traits of negative
affectivity, extraversion and effortful control in the relation with depression and anxiety.
While extraversion was not directly associated with anxiety, we found a significant
interaction indicating that high extraversion decreased both depression and anxiety in
individuals with high negative affectivity. Extraversion includes the sub-trait of sociability.
A possible explanation of the interaction between negative affectivity and extraversion is
that the tendency to seek and enjoy social contact also implies the ability to activate the
social support network and that social support not only limits the effects of stressful
events or circumstances (Chapter 5), it also limits the effects of a general tendency to
experience negative affect.

The results in Chapter 6 also included an interaction between effortful control and
negative affectivity in relation to anxiety. This interaction indicates that individuals with
high negative affectivity experienced less anxiety if they had high effortful control than if
they had low effortful control. These findings suggest that a tendency to experience
negative affect increases risk of anxiety particularly in those individuals who are less able
to regulate their mood by focusing their attention on something else or to refrain from
irrelevant, unintended or inappropriate responses.
The protective role of effortful control is relevant for clinical practice. The capacities represented by effortful control are involved in gaining control over automated tendencies, such as worrying or self-blaming, and motivating oneself to change and learn more adaptive coping strategies (Derryberry, 2002; Derryberry, Reed, & Pilkenton-Taylor, 2003). Moreover, these capacities can be strengthened through training (Rueda et al., 2005; Wells & Matthews, 1994).

The etiological relevance of the association between temperament, especially the trait of negative affectivity, and emotional problems is not undisputed. Particularly negative affectivity, but extraversion as well, shows conceptual overlap with emotional problems (Ormel, Rosmalen, & Farmer, 2004). Accordingly, many measures of negative affectivity and extraversion include items that are very similar to or the opposite of items that are used to assess depression and anxiety. Individuals experiencing depression and anxiety evidently report, respectively more or less of this behavior. In Chapter 7 we have tried to prevent such conceptual confounding by excluding the sub-traits fear and sadness of negative affectivity and positive affect of extraversion. The remaining facets of frustration, discomfort, sociability, and high pleasure showed weaker associations with emotional problems (i.e., the sum of depression and anxiety problems) than we found for negative affectivity and extraversion, although the differences were small. The origins of the strong association between temperament and emotional problems and the question how this should be interpreted will probably remain subject to discussion until we have objective non-self-report measures of negative affectivity. Meanwhile, more longitudinal research starting in childhood and incorporating simultaneous measures of both temperament and emotional problems is needed to examine to what extent temperament can serve as a predictor of depression and anxiety.

Researchers mainly seem to study direct associations between temperament and emotional health, but temperament is thought to affect mental health in interaction with the environment. Temperament characteristics may therefore explain why environmental factors do not affect emotional health similarly across individuals. We examined the interplay of stress and temperament in Chapter 7.

Temperament and stress

Of the different temperament traits, negative affectivity has been shown to moderate the effect of stressful events or circumstances on depression and anxiety (Gothelf et al., 2004; Kendler, Kuhn, & Prescott, 2004; Ormel, Oldehinkel, & Brilman, 2001; Van Os & Jones,
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1999). The experience of sexual assault is strongly associated with the presence of depression and anxiety (e.g., Bagley & Mallick, 2000; Fergusson, Horwood, & Lynskey, 1996; Katerndahl, Burge, & Kellogg, 2005; Spataro et al., 2004). Although there are studies that examine whether the effect of sexual assault differs according to the manner in which victims cope with this experience (e.g., Frazier, 2003; Valentine & Feinauer, 1993) temperament in the sense of basic and stable characteristics of the individual has not very often been studied in relation to sexual assault. The few available studies report positive associations between negative affectivity and sexual assault (Gamble et al., 2006; Kendler, Kuhn, & Prescott, 2004a; Roy, 2002; Pickering, Farmer, & McGuffin, 2004; Talbot et al., 2000). Although it can not be ruled out that negative affectivity increases risk of sexual assault, researchers generally assume that it is more likely that the experience of sexual assault increases negative affectivity. Negative affectivity is thus thought to mediate the association between sexual assault and emotional problems. Given that the authors of the only study reporting an interaction effect of sexual assault and temperament did not foresee and also question this result (Kendler, Kuhn, & Prescott, 2004a), researchers do not seem to consider the possibility that negative affectivity may also moderate the effect of sexual assault. In Chapter 7 we examined both mediation and moderation by temperament in the association between sexual assault and emotional problems. We distinguished between moderate and severe sexual assault, that is between assault involving penetration and assault not involving penetration. Research indicates that assault involving penetration is more strongly associated with emotional problems than assault not involving penetration. Based on the available literature (Gamble et al., 2006; Kendler, Kuhn, & Prescott, 2004) we assumed that the role of negative affectivity differs according to the severity of the sexual assault. We conducted our analyses using data from the daughters in our sample. Our findings confirmed our expectations. Negative affectivity partially mediated the association between severe sexual assault and emotional problems while it moderated the association between moderate sexual assault and emotional problems. The women with high negative affectivity and a history of moderate sexual assault reported more emotional problems than the women with low negative affectivity and a history of moderate sexual assault. We did not find mediation or moderation by extraversion or effortful control. Our study, just like almost all studies on sexual assault, used retrospective reports on sexual assault. We are therefore unable to determine the direction of causality. In addition we were not able to distinguish between prolonged and single occasions of sexual assault. Combined with the fact that only a very limited number of studies on the effect of sexual assault formally test mediation and moderation effects of temperament, our finding is in need of replication. Nonetheless, we feel we may conclude that severe assault increases emotional problems irrespective of temperamental
characteristics, but also increases vulnerability for emotional problems by affecting temperament, while the effect of moderate sexual assault on emotional health depends on temperamental vulnerability.

The concept of temperament represents innate individual differences in emotional and behavioral dispositions that are co-shaped by the early life environment and relatively stable over time. The results in Chapter 7 indicate that the experience of very stressful events may alter individual basic tendencies of reacting to and interacting with the environment.

**Generic and specific effects on depression and anxiety**

Depression and anxiety can be distinguished from each other by low positive affect or hopelessness in depression and physiological hyper-arousal in anxiety (Brown, Chorpita, & Barlow, 1998; Mineka, Watson, & Clark, 1998), but they share a common factor of general negative affect (Brown, Chorpita, & Barlow, 1998; Clark & Watson, 1991). Behavior-genetic and several family studies (Eley & Stevenson, 2000; Kendler et al., 1987, 1992; cf. Middeldorp et al., 2005; Thapar & McGuffin, 1997) indicate that depression and anxiety share an underlying genetic risk. This underlying risk may be differentially expressed as depression or anxiety depending on exposure to different environmental factors (Kendler et al., 1987, 1992; Eley & Stevenson, 2000). To increase our knowledge on the specificity of effects, we examined the interplay of personal and environmental risk factors separately for depression and anxiety.

As discussed earlier, the results in Chapter 3 showed that a second affected parent increased offspring risk of anxiety significantly, but the effect did not reach significance for offspring depression. It may be that the association between parental and offspring depression is so much stronger than the association between parental depression and offspring anxiety that the presence of a second affected parent adds less to offspring risk of depression than to offspring risk of anxiety. However, instead of interpreting our finding as a specific effect for anxiety, we think that these results more likely reflect that many of the younger offspring in our sample already developed anxiety but no depression yet.

The results in Chapter 5 showed a gender difference in the buffer-effect of social support in the association of parent-offspring communication stress with depression but not in the association with anxiety. In addition, the association between social support and depression was stronger than the association between social support and anxiety. If we assume that the tendency to seek and enjoy social contact, that is part of extraversion, also
implies the ability to acquire and activate a social support network, the results for social support are in line with the differential effect of extraversion as found in Chapters 6 and 7. Low extraversion is hypothesized to particularly underlie depression while being less relevant to anxiety (e.g., Angst, 1998; Carver, 2004; Clark, Watson, & Mineka, 1994; Davidson, 1995; Depue & Iacono, 1989). Low social support may similarly be more relevant in the development of depression than of anxiety. On the other hand these findings may reflect the tendency of individuals with depression to withdraw from social contact. Assuming that the association between social support and depression is bi-directional, the presence of social support seems more important for both the prevention and treatment of depression than of anxiety.

The results in Chapter 7 showed that sexual assault was associated with emotional problems in general, but not specifically with either depression or anxiety. The results in Chapter 6 indicated that effortful control acted as a direct protective factor for depression and as an indirect protective factor for anxiety if individuals had a tendency to experience negative affect.

Across the separate studies, we tried to establish the specificity of effects in several ways. In Chapter 3 we conducted separate analyses for offspring depression and offspring anxiety disorders. About 50% of the offspring with a diagnosis had both a depression and an anxiety disorder. Although, based on current DSM-IV nomenclature, this overlap points to true comorbidity, it may have limited the possibility to detect differential effects for depression and anxiety. In Chapters 5, 6 and 7 we conducted separate analyses on dimensional measures of depression and anxiety derived from factor analysis that distinguished between depression and anxiety as much as possible. Nonetheless depression and anxiety problems were still strongly associated. Given that our dimensional measures are based on what distinguishes anxiety and depression, that is low positive affect and physiological hyper-arousal, this association was probably based on comorbidity or true overlap given the common component of depression and anxiety, i.e. general negative affect, rather than on measurement confounding. In Chapter 7 we included depression as a predictor of anxiety and anxiety as a predictor of depression to control for comorbidity and the common factor of negative affect. Although adjusting for strongly associated variables may leave too little variance to detect smaller effects, this strategy is maybe best fit to detect directional effects that hold specifically for depression and not anxiety, and vice versa. On the other hand limiting conceptual and measurement overlap may be enough: we found a specific association between (components) of extraversion and depression in both the unadjusted (Chapter 6) and adjusted analyses (Chapter 7) and the unadjusted analyses in Chapter 5 also differentiated between depression and anxiety in that social support seems less relevant to anxiety than to depression.
Concluding remarks

The present thesis sought to extend our knowledge on some of the mechanisms in the etiology of depression and anxiety by examining the interplay of personal and environmental risk factors in a sample of offspring of parents with a life-time diagnosis of depression or anxiety. By examining differences within a high-risk sample and formally testing moderation and mediation effects we were able to provide further evidence for differences in risk of depression and anxiety according to the parent-offspring gender dyad, increased impact of interpersonal stress in individuals with a higher familial liability, gender differences in the buffer-effect of social support, the interplay between temperament characteristics, and the interplay between temperament and stress. While being relevant, mediation and moderation effects in the etiology of depression and anxiety seem to be small. Such effects may be less likely to surface in studies using normal population samples. The use of high-risk samples may be a prerequisite for detecting mechanisms in the development of emotional disorder.

Probably because it incorporates a complex interplay of many genetic and environmental effects on offspring functioning, parental emotional disorder is one of the strongest predictors of depression and anxiety. Our research has learned us that to be able to study the mechanisms in the intergenerational transmission of risk, research needs assessments of psychopathology in both parents. Due to developmental changes in offspring vulnerabilities, chronicity, severity and timing of the parental disorder must be considered in relation to the offspring’s developmental phase as well. Moreover, parental and offspring problems seem to affect each other. Ideally, the intergenerational transmission of risk should be studied in longitudinal designs that start when offspring are relatively young and assess both parent and offspring functioning at regular intervals.

Bool et al. (2002) estimated that in the Netherlands about one third of the total number of children under the age of twenty-two have one or two parents with a psychiatric disorder. Moreover, offspring of parents with a psychiatric disorder are over-represented in pediatric in-patient services (Bool et al., 2002). Given the fact that depression and anxiety are amongst the most prevalent mental health problems in adults, a large group of young individuals (in both absolute and relative terms) are at increased risk of emotional disorder. Mental health services in the Netherlands offer several prevention programs specifically aimed at offspring and families of psychiatric patients (Bool et al., 2002; Van Doesem, Frazer, & Dhondt, 1995). Research on the effectiveness of these programs is scarce, but both Dutch (Van Doesem, Frazer, & Dhondt, 1995) and international reports (Beardsley et al., 1996; 1997a; 1997b; Clarke et al., 2001) indicate promising results. Prevention can reduce the incidence of new cases up to 19% (Cuijpers,
Van Straten, & Smit, 2005) and possible an even higher percentage in high-risk groups (Cuijpers, 2003). However, two points have to be noted. Firstly, it is not feasible and may also not be necessary to enroll all offspring of parents with a history of emotional disorder in prevention and intervention programs. Although risk is increased, many of these offspring do not develop emotional problems. Moreover, risk differs considerably within these offspring. A first criterion for prevention interventions should be the presence of prodromal symptoms (Cuijpers, 2003). In addition, our findings indicate that prevention should focus on offspring with high familial liability and offspring experiencing disturbed parent-offspring relations or family functioning, while the literature further indicates a focus on offspring of parents with chronic and severe mental health problems (Goodman & Gotlib, 1999; Hammen & Brennan, 2003; Warner, Mufson, & Weissman, 1995).

Secondly, it may be difficult to identify the offspring that are at risk. Psychiatric patients with children may be reluctant to present themselves for treatment or reveal details of their family live out of fear to encounter doubt about their parenting skills that (in some cases) may eventually lead to extensive control by youth services or the loss of parental authority (Ackerson, 2003; Nicholson, Sweeney, & Geller, 1998). In addition, clinical practice indicates that inquiring after the children of patients is not (yet) part of the standardized intake procedures of mental health services. Psychiatrists, psychologists, and other individuals involved in the treatment and care of psychiatric patients should maybe act more on the notion that these patients’ children represent the larger part of the next generation of individuals in need of mental health care.