At risk of depression and anxiety

Landman-Peeters, Karlien Maria Catharina

AT RISK OF DEPRESSION AND ANXIETY

Studies into the interplay of personal and environmental risk factors

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Karlien Maria Catharina Landman-Peeters
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Promotores	:	Prof.dr. J. Ormel
		Prof.dr. J.A. den Boer
Copromotor	:	Dr. C.A. Hartman
Beoordelingscommissie	:	Prof.dr. S.M. Bögels
		Prof.dr. M. Dekovic
		Prof.dr. W.A.M. Vollebergh

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Chapter 1

Introduction

Depression and anxiety

Depression and anxiety, also referred to as emotional disorders, are common psychiatric problems. The life-time prevalence of diagnosed depression and anxiety disorders (DSM-IV) ranges from 4.6% to 20.8% for depressive disorders (Andrade et al., 2003; Bijl, Ravelli, & Van Zessen, 1998; Kessler et al., 2005; Ormel & Sytema, 1999) and from 10.5% to 28.8% for anxiety disorders (Alonso et al., 2003; Bijl, Ravelli, & Van Zessen, 1998; Kessler et al., 2005). In addition, many individuals report "sub-clinical" depressive and anxiety problems which do not meet DSM-IV criteria but cause suffering none the less (e.g., Kessler et al., 1994, 1997; Roberts et al., 1990). Depression is characterised by depressed mood or loss of interest or pleasure in nearly all activities (e.g., Zahn-Waxler et al., 2006). In addition, depression includes vegetative symptoms (e.g., changes in appetite or weight), cognitive symptoms (e.g., difficulty thinking and concentrating) and/or emotional symptoms (e.g., feelings of worthlessness or guilt). Anxiety is characterised by a sense of apprehension toward the future, continual attentiveness of signs of potential threat and a constant state of preparation and readiness to cope with potential dangers. In order to ward off anxiety, individuals can develop and pursue self-defeating behaviours, for example worry, thought suppression or behavioural avoidance (Barlow, 2000, 2002).

Many individuals with a life-time diagnosis of anxiety or depression experienced their first episodes during respectively late childhood or adolescence and late adolescence or young adulthood (Costello et al., 2003; Kim-Cohen et al., 2003; Lewinsohn et al., 2000; McGee et al., 1992). Depression in childhood is rare with a prevalence of 1%-3% (Cohen et al., 1993; Costello et al., 1996). In adolescence the prevalence of depression increases sharply to near-adult prevalence levels (Kessler, Avenevoli, & Merikangas, 2001; Lewinsohn, Rohde, & Seeley, 1998). Childhood anxiety disorder is more common than childhood depression and, with prevalence rates between 3.5% and 23.9%, almost as common as anxiety disorders in adulthood (Cartwright-Hatton, McNicol, & Doubleday, 2006). From childhood on anxiety disorder is more common in women than in men, while depression becomes more prevalent in women in adolescence (e.g., Hankin & Abramson, 1999; Lewinsohn, Rohde, & Seeley, 1998; Williams et al., 2005).

Etiology of depression and anxiety

Depression and anxiety are so-called multifactorial problems. The probability of developing these problems is influenced by a wide range of risk factors including genetic liability, neurophysiological dysfunctions, predisposing temperament or personality traits,

adverse childhood circumstances, limited interpersonal resources, long-term difficulties and traumatic events (e.g., Brown & Harris, 1978; Goodman & Gotlib, 1999; Hankin & Abela, 2005; Ormel & Neeleman, 2000; Williams et al., 2005). Since about twice as many women than men suffer from depression and anxiety problems, the female gender is often considered a risk factor for depression and anxiety as well.

Current knowledge indicates that the presence or occurrence of any given risk factor in itself is not sufficient to lead to psychiatric disorders such as depression and anxiety, instead the onset of these problems seems to require a combination of several risk factors (Rothman & Greenland, 1998). Risk factors seem to cluster (Bifulco, Moran, & Ball, 2002; Goodyer et al., 1993; Menard, Bandeen-Roche & Chilcoat, 2004; Walsh, MacMillan, & Prescott, 2002), such that, for example, environmental risk factors are more prevalent among those with a higher genetic liability. Besides increasing risk of depression and anxiety by adding to each others effects, risk factors affect each other in such a way that some risk factors mediate or moderate the effect of other risk factors (e.g., Goodman & Gotlib, 1999; Kendler et al., 2002). An example of mediation is that a genetic predisposition to depression and anxiety is thought to operate through the shaping of neurophysiological functions and subsequently the (interpersonal) environment (e.g., Goodman & Gotlib, 1999). An example of moderation is that the impact of stressful events on depression and anxiety is likely to be stronger when social resources are limited (e.g., Cohen & Wills, 1985; Windle, 1992). Many risk factors for depression and anxiety have been identified but the interplay and mechanisms by which risk factors result in depression and anxiety are by no means understood. Extending on existing research, this thesis studies the interplay of several personal and environmental risk factors of depression and anxiety.

ARIADNE

The studies described in this thesis were conducted in the context of the ARIADNE project. ARIADNE stands for 'Adolescents at Risk of Anxiety and Depression; A combined Neurobiological and Epidemiological approach'. ARIADNE's aim is to further our understanding of the etiological mechanisms involved in the onset and course of depression and anxiety disorders. The prospective design incorporates measures of familial liability and neurobiological, neuropsychological, interpersonal and environmental factors in order to examine associations and interplay between risk factors. Participants were adolescent and young-adult offspring of parents (formerly) treated for emotional disorders (for recruitment and sample characteristics see Chapter 2). The research design

adopted in the ARIADNE study has two major advantages: a) the inclusion of adolescents and young-adults increases the chances that we can examine pathways to first onset, b) etiological mechanisms are more likely to surface in high-risk samples since these offer a higher prevalence of and more variation in both risk factors and levels of depression and anxiety than general population samples. Moreover, due to a relatively large sample size of 524 respondents, ARIADNE provides adequate statistical power to formally test the effects and interplay of multiple risk factors.

The present thesis

My work in ARIADNE targeted the etiological role of and interplay between familial liability, gender, temperament, and stress and the extent to which these factors have generic or specific effects on depression and anxiety. As described above, our studies were conducted in a high-risk sample of offspring of parents with a history of emotional disorder. Parental emotional disorder increases offspring risk of these disorders by means of a complex interplay of genetic and environmental effects on offspring emotional health (Downey & Coyne, 1990; Goodman & Gotlib, 1999; Nomura, Warner, & Wickramaratne, 2001; Zahn-Waxler et al., 2006). Goodman and Gotlib (1999) illustrated this intergenerational transmission of risk of depression in an adaptation of general etiological models for depression and anxiety (see Figure 1). This model focuses specifically on maternal depression, but in our opinion it can be used in the wider context of this thesis to illustrate the assumed effects of paternal *and* maternal emotional disorder as well as the interplay of these and other personal and environmental risk factors.

Goodman and Gotlib distinguish between moderators, mediators (or mechanisms), and offspring vulnerabilities in the intergenerational transmission of risk. Moderators are factors that can alter the effect and the prevalence of other risk factors for offspring disorder. Goodman and Gotlib consider temperament, gender and intellectual and social-cognitive skills to be moderators of risk. Besides these offspring characteristics, they identify timing and course of parental disorder and availability and mental health of the other parent as moderators specific to the intergenerational transmission of risk. The mediators in the model are those risk factors through which parental emotional disorder increases offspring risk of psychiatric disorders or mental health problems. These mediators include a) heritability of mental disorder, b) innate dysfunctional neuroregulatory mechanisms, c) exposure to parent's negative and/or maladaptive cognitions, behaviours, and affect, and d) exposure to a stressful environment. Goodman and Gotlib tied these factors to maternal depression, but they are likely to be general risk

factors, that is, the presence of these factors is not always or fully the result of parental disorder. Offspring vulnerabilities include psychobiological dysfunction and deficits or maladaptive styles/tendencies in cognition, affection, or (interpersonal) behaviour. As mentioned above, the studies in the present thesis examined the roles of familial liability, gender, temperament, stress and the extent to which effects are generic or specific for depression and anxiety.

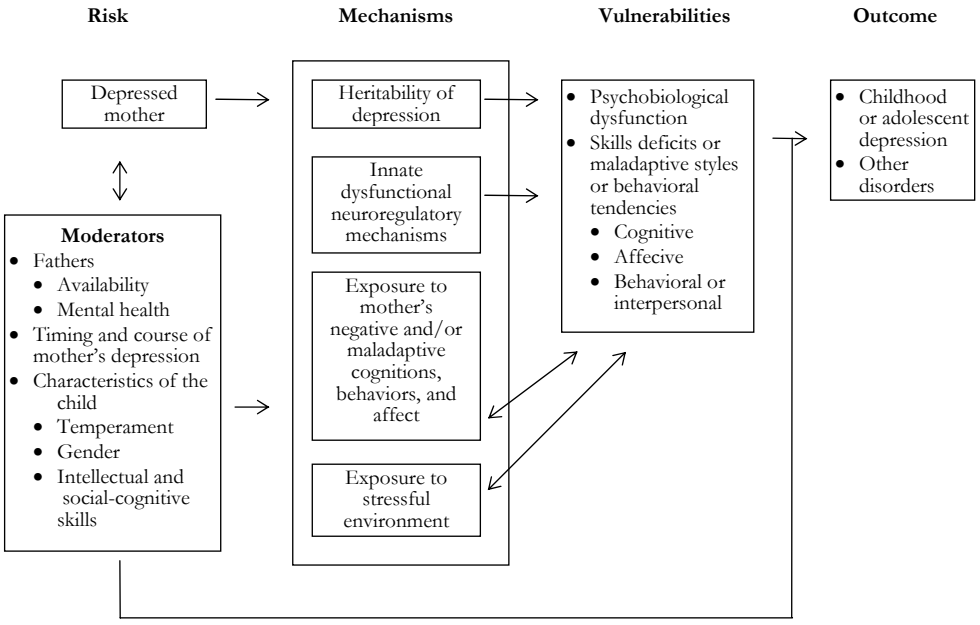

Figure 1 An integrative model for the transmission of risk to offspring of depressed mothers (Goodman & Gotlib, 1999)

Familial liability

The more relatives suffer from emotional disorder, the higher the individual's risk to develop psychiatric problems seems to be (Bijl, Cuijpers, & Smit, 2002; Lewinsohn et al., 2003; Merikangas et al., 1998; Warner et al., 1999; Weissman et al., 2005). For the present thesis familial liability was defined as the number of affected parents. A second affected parent has been found to increase risk of emotional problems in offspring of parents with Major Depressive Disorder (MDD) (e.g., Birmaher et al., 1996; Brennan et al., 2002, Foley

et al., 2001; Marmorstein, Malone, & Iacono, 2004; McCauley, Pavlidis, & Kendall, 2001; Nomura, Warner, & Wickramaratne, 2001; Warner, Mufson, & Weissman, 1995). This operates through both genetic and environmental factors (Brennan et al., 2002; Dierker, Merikangas, & Szatmari, 1999; Nomura, Warner, & Wickramaratne, 2001), probably by both adding genetic and environmental risk and reduction of resources to counterbalance the adverse effects of the disorder in the other parent (Downey & Coyne, 1990; Tannenbaum & Forehand, 1994). According to Goodman and Gotlib the presence of a second affected parent also acts as a moderator. This implies that the effects of parental emotional disorder and associated risk factors, such as adverse familial circumstances, differ according to the presence of a second affected parent. Important in this context are differences in the effects of maternal versus paternal disorder and the relative importance of environmental factors to offspring mental health when genetic risk increases. Maternal emotional disorder is found to be more strongly associated with offspring emotional health and parent-offspring relation quality than paternal emotional disorder (Connell & Goodman, 2002; Field, Hossain, & Malphurs, 1999; Goodman & Gotlib, 1999; Jacob & Johnson, 1997; Johnson et al., 1999; Kendler et al., 2001; Phares & Compas, 1992). While paternal emotional disorder may increase offspring risk when the mother is unaffected, it may not significantly increase offspring risk further when the mother is affected. Environmental risk factors for depression and anxiety are more prevalent among offspring of parents with an emotional disorder than in offspring of unaffected parents (Bifulco, Moran, & Ball, 2002; Goodyer et al., 1993; Walsh, MacMillan, & Jamieson, 2002) and there is evidence that the effect of parental disorder on offspring emotional health is partially mediated by environmental factors such as parent-offspring relationship quality (e.g., Hammen, Brennan, & Shih, 2004; Pilowsky et al., 2006). However, it is not clear whether such environmental factors affect offspring emotional health relatively more or less when genetic risk is higher (e.g., Hammen, Brennan, & Shih, 2004; Pilowsky et al., 2006). In this thesis, we examined the effect of a second affected parent on offspring depression and anxiety and its interplay with parent and offspring gender and parent-offspring relational stress.

Gender

About twice as many women than men suffer from depression and anxiety (e.g., Costello & Angold, 1995; Hankin & Abramson, 1999; Ormel & Sytema, 1999; Williams et al., 2005). This gender difference in anxiety is already found in childhood, while the female preponderance in depression appears in adolescence (e.g., Hankin & Abramson, 1999; Lewinsohn, Rohde, & Seeley, 1998; Williams et al., 2005). Although the gender difference

is consistently reported, it has not been convincingly explained (Bebbington, 1996; Hettema, Prescott, & Kendler, 2001; Hettema et al., 2005; Kendler, Gardner, & Prescott, 2006; Nolen-Hoeksema, Larson, & Grayson, 1999). There is evidence for a greater heritability of depression and anxiety in women (Kendler et al., 2001; Kendler, Gardner, & Prescott, 2002; Lichtenstein & Annas, 2000), but other studies failed to present such evidence (Kendler, Gardner, & Prescott, 2001; Murray & Sines, 1996). Multifactorial studies in adults by Kendler and associates indicate that the underlying structure of the genetic and environmental risk factors for depression and anxiety is similar between men and women (Hettema et al., 2005; Kendler, Gardner, & Prescott, 2002, 2006). This is in line with findings that suggest that risk factors for emotional disorder do not differ between men and women, but that these factors are more prevalent and have a larger impact in women. (Cyranowski et al., 2000; Else-Quest, Hyde, & Goldsmith, 2006; Hankin & Abramson, 2001; Kagan, 2001; Nolen-Hoeksema & Girgus, 1994). Cyranowksi et al. (2000) especially stress the importance of interpersonal relations and interpersonal stressors. According to these authors women develop a greater need for affiliation which makes them especially vulnerable to emotional problems following negative interpersonal events.

Goodman and Gotlib consider offspring gender to be a moderator, implying that associations between risk factors and offspring emotional health are different between sons and daughters. For example, daughters are thought to experience more and be more vulnerable to the (interpersonal) effects of parental emotional disorder than sons (e.g., Davies & Windle, 1997; Hops, 1996). In this thesis we examined the interplay of gender and familial liability and gender differences in the interplay between social support and parent-offspring problems in relation to depression and anxiety problems.

Temperament

Temperament represents basic person characteristics in emotional reactivity and self-regulation (e.g., Rothbart, Ahadi, & Evans, 2000) and affects mental health in interaction with the environment (Dadds & Salmon, 2003; Oldehinkel et al., 2006). Temperament is shaped by the environment to some extent through parenting and other experiences , but it appears to be moderately stable during adolescence and young adulthood (Caspi & Roberts, 2001). In the present thesis, I focus on the temperament domains of negative affectivity, extraversion and effortful control as assessed by the Adult Temperament Questionnaire (Rothbart, Ahadi, & Evans, 2000). Negative affectivity is highly related to the adult personality trait of neuroticism, while effortful control is related to conscientiousness (Rothbart, Ahadi, & Evans, 2000). Neuroticism, extraversion, and

conscientiousness represent the three most salient temperament/personality domains across all major theories of temperament/ personality (e.g., Cloninger, 1986; Eysenck & Eysenck, 1985; McCrae & Costa, 1997; Rothbart, Ahadi, & Evans, 2000). Negative affectivity describes a tendency to experience negative emotions or emotional instability (Eysenck, 1967; Eysenck & Rachman, 1965; John, 1990), extraversion may be described as the tendency to engage in the pursuit of pleasurable experiences (Carver, Sutton, & Scheier, 2000; Depue & Collins, 1999; Derryberry & Tucker, 2006) and effortful control describes the ability to voluntarily regulate attention and behavior (Derryberry, 2002; Rueda, Posner, & Rothbart, 2004). Negative affectivity has a strong positive association with both depression and anxiety (e.g., Caspi et al., 1996; Jorm et al., 2000; Lonigan et al., 1997; Ormel, Oldehinkel, & Brilman, 2001; Roberts & Kendler, 1999) while extraversion has a negative association with emotional problems (e.g., Angst, 1998; Bienvenu et al., 2001a; Brown, Chorpita, & Barlow, 1998; Carver, 2004; Clark, Watson, & Mineka, 1994; Davidson, 1995; Depue & Iacono, 1989; Trull & Sher, 1994). Due to these associations, high negative affectivity and low extraversion are considered to be risk factors for depression and anxiety. Effortful control has been studied less in relation to depression or anxiety, but recent findings show a negative, that is protective, effect of this trait (Eisenberg et al., 2001; Lemery, Essex, & Smider, 2002; Lengua, West, & Sandler, 1998; Lengua, Long, & Smith, 2005; Muris, De Jong, & Engelen, 2004). Temperament characteristics thus are directly associated with risk of emotional disorder, but have also been shown to alter effects of other risk factors (Gothelf et al., 2004; Kendler, Kuhn, & Prescott, 2004a; Ormel Oldehinkel, & Brilman, 2001; Van Os & Jones, 1999) or even each other's effects (Gershuny & Sher, 1998; Muris, 2006; Oldehinkel et al., 2007). In the model of Goodman and Gotlib temperament is proposed to be a moderator in the intergenerational transmission of risk. In the present thesis we examined the interplay of the temperament domains of effortful control, negative affectivity and extraversion, as well as mediation and moderation by these domains in the association between sexual assault and emotional problems.

Stress

Stress can be defined as "environmental events or chronic conditions that objectively threaten the physical and/or psychological health or well-being of individuals of a particular age in a particular society" (Grant et al., 2003, p.449). Since the onset of depression and anxiety disorders is often associated with the experience of stress it 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; Williams et al., 2005). Nonetheless, the majority of individuals that encounter stress do not develop emotional problems (e.g., Hankin & Abela, 2005). The extent to which stress affects emotional health is therefore thought to differ according to its nature, severity or chronicity, as well as to the presence or absence of other stress factors. Moreover, the extent to which events and conditions are appraised as stressful and affecting well being differs according to individual characteristics such as genetic factors, biological processes, temperamental features, cognitive structures, interpersonal interacting styles and emotion regulation (Goodman & Gotlib, 1999; Hankin & Abela, 2005; Williams et al., 2005).

Offspring of parents with emotional disorder encounter more stress, ranging from poverty, parental divorce, disturbed parent-offspring relations and poor family functioning to sexual and physical abuse (e.g., Bifulco, Moran, & Ball, 2002; Downey & Coyne, 1990; Goodman & Gotlib, 1999; Goodyer, 1990; Walsh, MacMillan, & Jamieson, 2002). In addition, parental emotional disorder may increase the extent to which offspring experience stress through its effect on the individual characteristics described above. Goodman and Gotlib therefore consider stress to be a mediator in the intergenerational transmission of risk.

The measures of stress we used in the present thesis concern interpersonal stress, that is stress that occurs in or as a result of interactions between individuals. This type of stress in particular seems to lead to emotional problems (Garber & Flynn, 2001). In this thesis we examined the role of parent-offspring relational stress in the association between familial liability and offspring emotional problems, the interplay of parent-offspring communicational stress and social support, and the interplay of sexual assault and temperament.

Generic and specific effects on depression and anxiety

Several studies indicate that depression and anxiety are transmitted independently within families (Avenevoli et al., 2001; Klein et al., 2003; Weissman et al., 1993), implying that offspring of depressed parents are particularly at risk of depression and offspring of parents with anxiety are particularly at risk of anxiety. Depression and anxiety are however strongly associated. The onset of depression is often preceded by anxiety (e.g., Avenevoli et al., 2001; Cohen et al., 1993) and depression and anxiety are much more often co-morbid than would be expected by chance (e.g., Angold, Costello, & Erkanli, 1999; Brown et al., 2001; Mineka, Watson, & Clark, 1998; Williamson et al., 2005). 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 psychological distress based on broad individual differences in 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 dependent of exposure to environmental factors (Eley & Stevenson, 2000; Kendler et al., 1987, 1992). To fully understand the etiology of depression and anxiety, it is important to distinguish between generic effects of risk factors on psychological distress associated with both depression and anxiety, and specific effects on distress unique for either depression or anxiety. Throughout this thesis we distinguished between offspring depression and anxiety in studying the interplay of familial liability, gender, temperament and/or interpersonal stress.

Outline of this thesis

This thesis continues in Chapter 2 with a description of the ARIADNE data collection procedure and sample characteristics. Chapters 3 through 7 describe empirical studies into the interplay between personal and environmental risk factors.

Chapter 3 examines differences in offspring risk of depression and anxiety disorders according to familial liability and parent and offspring gender. We determined whether a second parent with a history of emotional problems increased risk of depression and anxiety in offspring of depressed parents and whether this effect varied according to whether mother or father was affected and whether offspring were sons or daughters. So far, research on the effect of a second affected parent as well as research formally testing differences in risk according to the parent-offspring gender dyad is scarce.

Chapter 4 examines the role of parent-offspring relational stress in the association between familial liability and offspring emotional problems. Although it is clear that parental emotional disorder is associated with troubled parent-offspring relations, empirical findings concerning the relative contribution to offspring problems in low versus high risk offspring seem contradictory, suggesting either an increased or decreased contribution. We sought to shed further light on these contradictory findings.

In Chapter 5 we examined whether the association between parent-offspring stress and offspring depression and anxiety was buffered by social support and whether this effect was different for male and female offspring. Perceived social support is thought to moderate the association between stress and emotional problems, such that high perceived

social support may decrease the effect of stress on emotional problems. In addition, women are thought to be affected more by social support as well as interpersonal stress. Very few studies have addressed this three-way interaction between gender, stress and support.

Chapter 6 is a longitudinal study into the interplay of the temperament domains of negative affectivity, extraversion and effortful control in relation to depression and anxiety. The aim was to determine whether effortful control could alter the effects of negative affectivity and extraversion on depression and anxiety. So far, only a few studies examined the potentially protective role of effortful control, in particular its subcomponents attentional, inhibitory and activation control.

Chapter 7 describes a study among the female participants of ARIADNE that examined the role of temperament in the association between sexual assault and emotional problems. Although it is widely suggested that sexual assault increases emotional problems partially through altering temperament characteristics (i.e., mediation), empirical studies that formally test this are scarce. In addition we examined whether the association between sexual assault and emotional problems may differ according to temperament (i.e., moderation). Although the literature shows such an effect of temperament on the effect of many stressors, researchers have not considered temperament as a potential moderator of the effect of sexual assault so far.

In the final chapter (Chapter 8), I will discuss our findings and their clinical and research implications.

Chapter 2

ARIADNE: Recruitment and sample characteristics

Inclusion and exclusion criteria

ARIADNE seeks to study the development of depression and anxiety in offspring of parents with a history of such problems. For the study's purposes it was required that one of the parents had a history of depression (that is Major Depressive Disorder [MDD] or Dysthymic Disorder), Panic Disorder (PD) with or without Agoraphobia or Obsessive Compulsive Disorder (OCD). Offspring had to be between 13 and 25 years old. The parents were recruited through mental health facilities in the three northern parts of the Netherlands (i.e., Groningen, Friesland and Drenthe).

Parents and their offspring were not eligible for participation if the parents were diagnosed with Schizophrenia, Schizo-Affective disorder or Post Traumatic Stress Disorder, only had a temporary address, did not master the Dutch language, were assessed only for judicial purposes, or if contact was limited to one consultation. Parental personality disorder was not a exclusion criterion. Information concerning parental borderline disorder, bipolar disorder, reactive depression, psychotic depression, seasonal depression, aggression, and information on heavy substance use or substance abuse was gathered, but such problems were no reason for exclusion. To be included in the study, offspring and parents had to give written informed consent.

Recruitment

The recruitment of the sample is illustrated in Figure 2. Approximately 65000 medical files from 16 mental health facilities (see Table 1) were searched to identify patients eligible for participation the study. All men born between 1941-1965 and all women born between 1941-1967 having received treatment for depression, anxiety indicating panic, PD or OCD after January 1990 were selected, unless it was a priori clear from their file that they did not have children between 13 and 25 years old. This resulted in 6874 individuals (2420 men and 4454 women) who were, based on their medical files, eligible for participation in the study.

The second step in the selection process concerned verification of addresses and checking for double entries due to treatment in more than one facility. The remaining 4470 individuals were sent a letter explaining the aims of the study. This letter also included questions concerning the composition of the nuclear family and age of the children and a request to participate. Of these 4470 individuals, 1189 did not respond, moved out of the area (despite address verification), were deceased or otherwise not

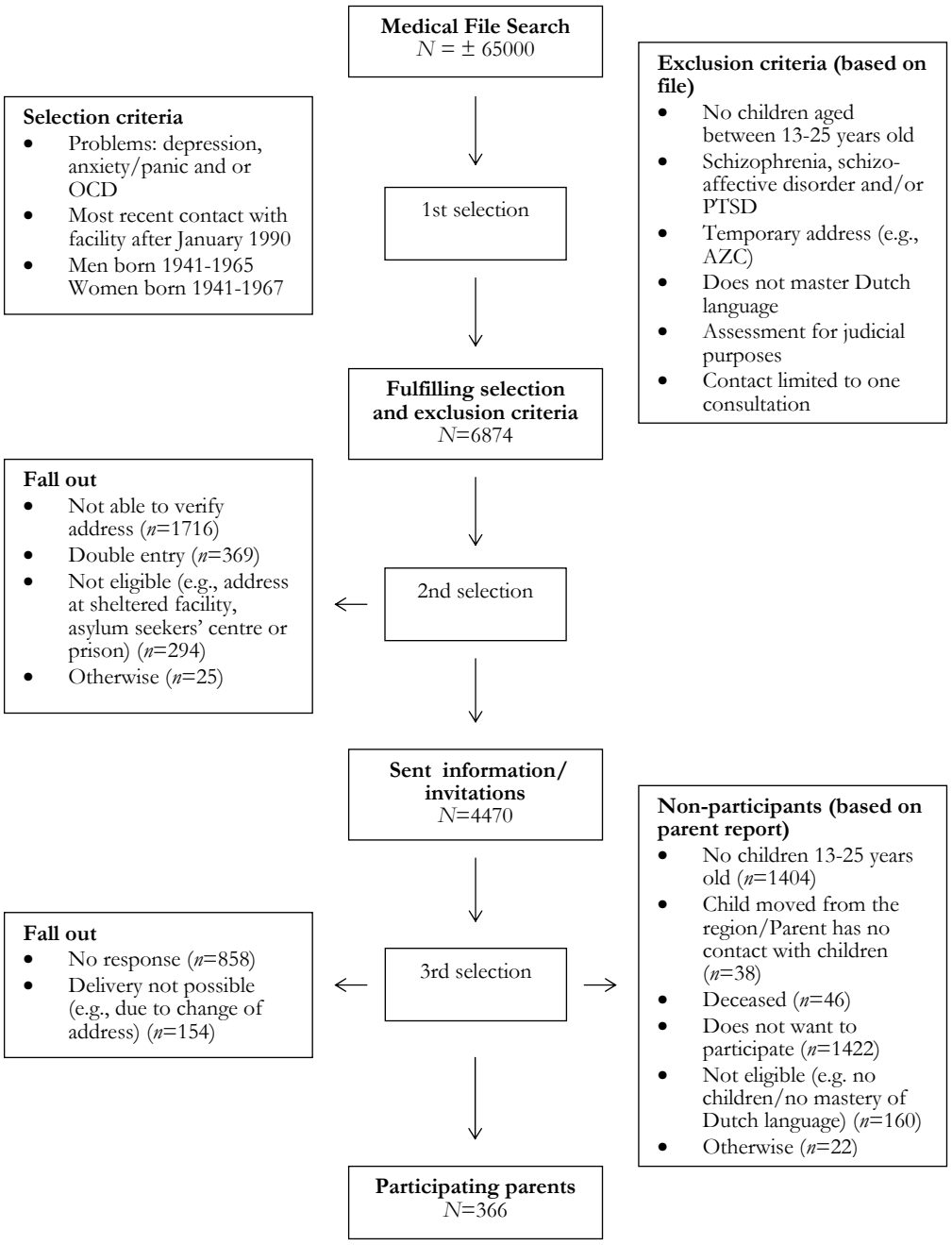

Figure 1 Flow-chart recruitment procedure ARIADNE

eligible for participation, 633 refused to participate without providing information about family composition, 1404 responded that they did not have children between 13-25 years old and 878 individuals had children between 13-25 years old but did not want to participate. Eventually, 366 individuals agreed to participate with one or more children.

Table 1 Participating mental health facilities

Drenthe	Assen	Community mental health center (GGZ Drenthe)
	Assen	Community mental health center (former RIAGG)
	Assen	Outpatient clinic
	Beilen	Psychiatric clinic
	Emmen	Community mental health center (former RIAGG)
	Hoogeveen	Community mental health center (former RIAGG)
	Meppel	Community mental health center (former RIAGG)
Friesland	Drachten	Community mental health center (GGZ Friesland)
	Heerenveen	Community mental health center (GGZ Friesland)
Groningen	Delfzijl	Community mental health center (GGZ Groningen)
	Groningen	Community mental health center (GGZ Groningen)
	Groningen	Psychiatric clinic (University Medical Center Groningen)
	Stadskanaal	Community mental health center (GGZ Groningen)
	Wagenborgen	Community mental health center (GGZ Groningen)
	Winschoten	Community mental health center (GGZ Groningen)

Description of the sample

Offspring were enrolled in the study between June 2000 and September 2002. A sample of 524 offspring (225 males and 299 females) aged between 13 and 25 years old (M= 18.1; SD=3.2) was included in the study. Mean age of the index parents, i.e. those parents who were recruited, was 46.0 years old (SD= 4.8) and in 70.5% of the cases the index parent was the mother. The majority of both parents and offspring (>95%) was of Dutch origin.

Table 2 presents the prevalence of parental MDD, Dysthymia, PD, Agoraphobia and OCD according to DSM-IV criteria. The presence of these diagnoses was assessed by means of the World Mental Health (WMH) Survey Initiative Version of the WHO-CIDI (Kessler & Üstün, 2004). The majority of the index parents had a life-time diagnosis of

depression. Depression and anxiety were comorbid in 50.0% of the index parents, while 37.7% of the parents only had a depression diagnosis and 6.8% only an anxiety diagnosis.

In offspring we assessed the presence of MDD, Dysthymia, PD, Agoraphobia, OCD, Social Anxiety Disorder, Generalized Anxiety Disorder, Separation Anxiety Disorder, and Adult Separation Anxiety Disorder (see Table 2). Of the offspring 31.3% had at least one of these diagnoses, 7.8% had only a depression diagnosis (i.e., MDD and/or Dysthymia), 11.8% an anxiety diagnosis (i.e., any of the anxiety diagnosis described above) and 11.6% had comorbid depression and anxiety. In addition, 3.6% of the offspring reported minor depression, 1.0% reported recurrent brief depression, and 10.1% of the offspring reported having experienced two or more panic attacks (offspring with PD not included). Minor depression incorporates episodes of depression in which dysphoria or anhedonia persisted half the day and/or worst life-time episodes in which at least two symptoms of depression were present (Kessler & Üstün, 2004). Recurrent brief depression incorporates episodes of depression lasting at least three days occurring in most months in a row for an entire year (Kessler & Üstün, 2004). Minor depression and brief recurrent depression can only be diagnosed when MDD or Dysthymia are not present. Of the offspring thus 68.7% had no formal CIDI diagnosis. Note that the CIDI does not establish subclinical differences in depression and anxiety.

Table 2 Prevalence of depression and anxiety disorders

	Index parent (*n*=366)	Offspring (*n*=524)
Major Depressive Disorder	86.9	18.9
Dysthymia	28.4	3.6
Panic Disorder	41.0	7.6
Agoraphobia	28.7	3.2
Obsessive Compulsive Disorder	18.0	6.7
Social Anxiety Disorder	Not assessed	7.4
Generalized Anxiety Disorder	Not assessed	6.3
Separation Anxiety Disorder	Not assessed	4.2
Adult Separation Anxiety Disorder	Not assessed	4.0

Table 3 presents information on family socio-economic status (SES) variables per family at the first measurement wave. Fifty-three families (14.5%) were single-parent families. Educational attainment, occupational level and net yearly income reflect the highest level in the (pair of) parents in the household in which the child lived the largest part of its life. In most families (45.9%) parents completed intermediate general or lower

vocational education, followed by a relatively large percentage of families (28.4%) in which parents completed higher general or vocational education. In most families parents (had) worked in semi-skilled (38.5%) or highly-skilled (31.7%) occupations. In 50.1% of the families the parent who had the highest net year income had an income below or at national average. In 10.4% of the families parents were unemployed, in 45.1% families one parent was employed and in 44.5% families both parents were employed. Information about offspring educational level was gathered at the first measurement wave and was based on the level of secondary education. The different levels were equally represented with 28.8% of the offspring attending or having completed lower general secondary or vocational education (i.e., voortgezet speciaal onderwijs [VSO], individueel voorbereidend beroepsonderwijs [IVBO], voorbereidend beroepsonderwijs [VBO]), 29% intermediate general secondary education (i.e., middelbaar algemeen voortgezet onderwijs [MAVO]), 22.9% higher general secondary education (i.e., hoger algemeen voortgezet onderwijs [HAVO]) and 19.3% pre-university education (i.e., voorbereidend wetenschappelijk onderwijs [VWO]).

Table 3 Percentages of families in SES categories (*n*=366)

Highest parental educational attainment	
Primary education	3.0
Lower vocational education	15.0
Intermediate general or vocational education	45.9
Higher general or vocational education	28.4
Academic or scientific education	7.7
Occupational level	
Not employed	0.3
Non-skilled or low-skilled occupations	7.7
Semi-skilled occupations	38.5
Highly-skilled occupations	31.7
Academic, scientific and executive occupations	21.3
Net yearly income	
Below or at average	50.1
Between average and twice the average	40.2
More than twice the average	5.4

Educational attainment, occupational level and net yearly income are based on the highest educational, occupational and income level in the (pair of) parents. Classification of net yearly income according to the Dutch statistics for 2001 (Centraal Planbureau)

ARIADNE consisted of 4 measurement waves. The studies in this thesis are based on the results obtained at first, second and/or third measurement. At the second measurement wave, approximately one year after the first wave, 487 offspring (93% of the original sample) and at the third measurement wave, approximately two years after the first measurement, 458 (87%) agreed to participate again. At the fourth measurement wave, approximately two years after the third measurement wave, 413 offspring (79%) agreed to participate again.

Currently, 261 offspring participate in a fifth measurement wave within the context of the Netherlands Study on Depression and Anxiety (NESDA). We asked the participants in the fourth measurement wave permission to contact them for participation in future studies in this line of research. The offspring who provided permission were sent information about NESDA. Offspring that wanted to participate were included in NESDA. NESDA will follow participants for eight years.

Chapter 3

Risk of emotional disorder in offspring of depressed parents: Gender differences in the effect of a second emotionally affected parent

Karlien M.C. Landman-Peeters, Johan Ormel, Eric L.P. van Sonderen, Johan A. den Boer, Ruud B. Minderaa, & Catharina A. Hartman. *Depression and Anxiety,* in press.

In offspring of depressed parents a second parent with emotional problems is likely to increase risk of emotional disorder. This effect may however differ between sons and daughters and between offspring of depressed fathers and offspring of depressed mothers. In adolescent and young-adult offspring of parents with Major Depressive Disorder this study examined the effects of a second affected parent, offspring gender, gender of the depressed parent and their interactions on risk of depression and anxiety disorder. We found that daughters had a higher risk of depression and anxiety than sons and that offspring of depressed mothers had a higher risk of anxiety than offspring of depressed fathers. In addition to these main effects, we found an interaction between parent and offspring gender in as much that sons of depressed fathers had the lowest risk of depression and anxiety relative to the other groups. A second affected parent tended to increase risk of depression and significantly increased risk of anxiety. However, this effect of a second affected parent on offspring anxiety was most prominent in daughters when the second affected parent was the father while risk in sons did not increase if the father was affected as well. Our results indicate that paternal and maternal depression similarly and additively increase daughters' risk of emotional disorder, but that sons' risk only increases with maternal depression. Intergenerational transmission of emotional disorder seems strongest when the female gender is involved, either in the form of a daughter or a depressed mother.

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Introduction

Offspring of depressed parents are at increased risk to develop mental health problems, particularly depression and anxiety disorders (further denoted as emotional disorders) (e.g., Biederman et al., 2001; Lieb et al., 2002; Weissman et al., 1993; Wickramaratne & Weissman, 1998). The onset of depression in adolescence and young adulthood is often preceded by anxiety in childhood and early adolescence (e.g., Avenevoli et al., 2001; Cohen et al., 1993) and depression is often co-morbid with anxiety later on (e.g., Angold, Costello, & Erkanli, 1999). Parental depression incorporates a complex interplay of genetic and environmental effects on offspring mental health (Downey & Coyne, 1990; Nomura, Warner, & Wickramaratne, 2001). By examining variation in risk among offspring of depressed parents we can further our understanding of the intergenerational transmission of emotional disorder. In offspring of parents with Major Depressive Disorder (MDD), the present study examined the effect of a second parent with life-time emotional problems on offspring risk.

Depressed patients tend to form relationships with individuals who also suffer from psychiatric problems, which is referred to as assortive mating (e.g., Merikangas et al., 1988). In offspring of depressed parents risk of emotional problems is found to increase when the other biological parent has a history of psychiatric disorder as well (e.g., Brennan et al., 2002; Foley et al., 2001; Marmorstein, Malone, & Iacono, 2004; Nomura, Warner, & Wickramaratne, 2001; Warner, Mufson, & Weissman, 1995). Goodman and Gotlib (1999) formulated four mechanisms by which parental depression can increase offspring risk: a) genetic transmission; b) the development of dysfunctional neuroregulatory mechanisms; c) exposure to the parent's maladaptive affect, behaviour and cognitions; and d) contextual stressors associated with parental depression. Thus, a second affected parent may add to the genetic and environmental risk (Brennan et al., 2002; Dierker, Merikangas, & Szatmari, 1999; Nomura, Nomura, & Wickramaratne, 2001). Offspring with a second affected parent may also be at increased risk since they lack a healthy parent who is able to compensate, genetically and/or environmentally, for the depressed parent's influence on offspring functioning (Downey & Coyne, 1990; Tannenbaum & Forehand, 1994). With respect to the development of emotional disorders, a history of depression or anxiety in the other biological parent seems especially relevant. For the present study we expect that risk of emotional disorder in offspring of depressed parents increases when the other parent has life-time emotional problems as well.

The effect of a second parent may however differ between sons and daughters. From adolescence on, risk of emotional disorders is approximately twice as high in

women than in men (Costello & Angold, 1995; Hankin & Abramson, 1999). This gender difference is thought to be caused (partially) by a greater heritability for depression in women and/or a stronger reactivity to (interpersonal) stress in women (Cyranowski et al., 2000; Hankin & Abramsom, 2001; Shih et al., 2006; Silberg et al., 1999). Among offspring of depressed parents, daughters have a higher risk of emotional problems than sons. This finding may reflect the generally observed gender difference (Garber & Flynn, 2001; Goodman & Gotlib, 1999), such that parental depression increases risk for daughters and sons in a similar way. Above and beyond this, daughters may be more strongly affected than sons by parental depression and/or its correlates (e.g., problems in parent-offspring interaction and family functioning) (e.g., Sheeber, Davis, & Hops, 2002). If we assume the latter, a second parent with emotional disorder may increase risk more in daughters than in sons.

A second parent with emotional problems may further differentially increase risk in offspring of depressed fathers and offspring of depressed mothers. Research indicates that the mechanisms formulated by Goodman & Gotlib (1999) are stronger for maternal than for paternal depression (Connell & Goodman, 2002; Field, Hossain, & Malphurs, 1999; Goodman & Gotlib, 1999; Jacob & Johnson, 1997; Johnson et al., 1999; Kendler et al., 2001). This is reflected in the higher risk of emotional problems in offspring of depressed mothers than in offspring of depressed fathers reported by overviews of the literature (Connell & Goodman, 2002; Phares & Compas, 1992). Assuming that offspring are affected more by maternal than by paternal depression, a second affected parent may add less to the risk of emotional disorder in offspring when this second affected parent is the father.

Given the aforementioned gender differences in offspring and parents it is likely that the effect of a second affected parent differs according to the offspring-depressed parent gender dyad. Several studies included the gender of both offspring and the depressed parent to examine gender differences in offspring emotional disorder (Eberhart et al., 2006; Foley et al., 2001; Hops, 1992; Klein et al., 2005; Nomura, Warner, & Wickramaratne, 2001; Thomas & Forehand, 1991). However, results of these studies are inconsistent. Klein et al. (2005) found effects on depression in both sons and daughters but only of maternal and not of paternal depression. Foley et al. (2001) found that paternal depression increased daughters' but not sons' depression and anxiety, while maternal depression increased depression only in daughters and increased anxiety stronger in daughters than in sons. Thomas and Forehand (1991) found that maternal depression was related to emotional problems in daughters and paternal depression to emotional problems in sons. The findings of Nomura et al. (2001) indicate a reverse pattern in which paternal depression more strongly affected daughters' risk of depression and maternal

depression more strongly affected sons' risk of depression, but they found that paternal and maternal depression similarly increased risk of anxiety disorder in both sons and daughters. Eberhart et al. (2006) found that maternal depression increased risk of depression in both sons and daughters, but paternal depression increased risk only in sons. Hops (1992) reports that associations between parental and offspring depression symptoms were strongest for mothers and daughters, but less consistent and somewhat weaker when fathers or sons were involved. Based on these findings we assume that the effect of a second parent with life-time emotional problems differs according to the depressed parent-offspring gender dyad. Combining our expectations concerning the stronger effect of a second affected parent in daughters and offspring of depressed fathers we hypothesize that a second affected parent increases risk the most in daughters of depressed fathers.

The present examination used data from a Dutch family study among adolescent and young-adult offspring of parents with life-time emotional disorder. For the present study we focused on offspring of parents with MDD to test the following hypotheses: (1) a second parent with life-time emotional problems increases offspring risk of depression and anxiety disorder, (2) a second affected parent increases risk more in daughters than in sons, (3) a second affected parent increases risk more when this second affected parent is the mother than when it is the father, and (4) this latter effect is stronger for daughters.

Methods

Participants

The present study uses data from 349 (154 male and 195 female) offspring between 16 and 25 years old (M=19.8, SD=2.7) from 263 families participating in the Dutch ARIADNE (Adolescents at Risk of Anxiety and Depression; A combined Neurobiological and Epidemiological approach) Study. The study design of ARIADNE has been previously described (Landman-Peeters et al., 2005). Briefly, patients with a) at least one treated episode of emotional disorder between 1990 and 2002, b) no personal history of schizophrenia spectrum diagnoses, and c) biological children aged 13-25 were identified through 16 psychiatric services in the three northern provinces of the Netherlands. Consenting parents and their children were interviewed in person at their home or at the Department of Psychiatry. Only the recruited parent was interviewed and he/she provided information about the other biological parent. Parents and offspring were interviewed by different interviewers. Interviews were conducted by intensively trained and monitored

interviewers with various backgrounds. The Department of Psychiatry at the University of Groningen is an Expert Training Center for the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI).

The 349 offspring came from 263 families where the recruited parent had MDD; 113 offspring had a depressed father and 236 offspring had a depressed mother. Gender ratio and educational level of parents were comparable to findings from a large Dutch population sample concerning individuals with depression (Ten Have et al., 2004). Sixty-nine offspring came from 54 families where the other biological parent had life-time emotional problems as well. The majority of the participants (95%) were white and of Dutch origin.

Measures

Offspring depression and anxiety. Offspring were interviewed with the World Mental Health (WMH) Survey Initiative Version of the WHO-CIDI (Kessler & Üstün, 2004). It is a structured interview to assess mental disorders designed for use by trained interviewers who are not clinicians. By means of computerized algorithms, it provides diagnoses according to accepted criteria such as the International Classification of Diseases (ICD-10) and the Diagnostic and Statistical Manual for Mental Disorders (DSM-IV). The CIDI has been shown to be reliable and valid (Kessler et al., 1994; Lieb et al., 2002; Wittchen, 1994).

To increase sensitivity to offspring problems we assessed a wide range of depression and anxiety disorders. In the present study 44.4% of the offspring had a life-time diagnosis of emotional disorder (i.e. depression and/or anxiety). Depression was present in 30.1% of the offspring. This included the presence of a DSM-IV lifetime diagnosis of MDD (23.5%), Dysthymic Disorder (4.3%) and/or the presence of minor depression (4.9%) or recurrent brief depression (1.1%). Minor depression incorporates episodes of depression in which dysphoria or anhedonia persisted half the day and/or worst life-time episodes in which at least two symptoms of depression were present (Kessler & Üstün, 2004). Recurrent brief depression incorporates episodes of depression lasting at least three days occurring in most months in a row for an entire year (Kessler & Üstün, 2004). Anxiety was present in 33.5% of the offspring. This included a DSM-IV life-time diagnosis of Generalized Anxiety Disorder (7.4%), Obsessive Compulsive Disorder (8.6%), Social Phobia (9.2%), Separation Anxiety Disorder (4.0%), Adult Separation Anxiety Disorder (4.9%), Panic Disorder (8.6%), Agoraphobia (4.0%) and/or the experience of multiple panic attacks (12%).

Parental depression and life-time emotional problems in the other biological parent. For parents identified through psychiatric services we also used the CIDI (Kessler & Üstün, 2004). We assessed life-time Major Depressive Disorder according to DSM-IV (American Psychiatric Association, 1994). These parents were asked about the history of emotional disorder of the other biological parent by means of vignettes of depressive and anxiety disorders based on DSM-IV diagnostic criteria. Only parents who had received treatment for emotional disorder were classified as "affected". In the Netherlands approximately 75% of the individuals with diagnosable depression and/or anxiety disorders seek treatment (Ten Have et al., 2004); we therefore reasoned that the inclusion of this criterion minimised false positive classification and also served as a proxy measure of equal "illness severity" for the two affected parents.

Data analysis

We first calculated the prevalence of depression and anxiety for each combination of offspring gender, gender of the depressed parent and the presence of a second affected parent. As previously mentioned, the 349 offspring came from 263 families. To account for this clustering in families we examined our hypotheses in design-based analyses with families as primary sampling units, using the statistical program STATA 8.0 (StataCorp, 2003).

We examined bivariate associations between our predictor and outcome variables by means of Pearson χ^2-tests. These tests were corrected for the survey design and converted into *F*-statistics (StataCorp, 2003). To test our hypotheses we then conducted logistic regression analyses. This enabled us to simultaneously examine the effects of offspring gender (0=male; 1=female), gender of the depressed parent (0=male; 1=female), the presence of a second affected parent (0=not present; 1=present) and their interactions on the binary outcome measures of offspring emotional disorder. We performed stepwise backward analyses starting with the model including the three-way and all two-way interactions.

Our data indicated that the mean age of offspring with life-time depression (M=20.8, SD=2.7) was significantly higher than the mean age of offspring without life-time depression (M=19.4, SD=2.6) ($t(347)=4.30$, $p<0.001$), but age was not associated with our predictor variables. Age could therefore not be a confounder of associations between predictors and outcome and was not included in our analyses.

Results

Prevalence of depression and anxiety

Prevalence of depression and anxiety are presented for each group of offspring in Table 1.

Table 1 Prevalence of offspring depression and anxiety by offspring gender, gender of the depressed parent and the presence of a second affected parent (total *n*)

	Depressed father		Depressed mother	
	Mother not affected	Mother affected	Father not affected	Father affected
Depression				
Sons	15.6 (45)	12.5 (16)	24.7 (77)	37.5 (16)
Daughters	41.5 (41)	45.5 (11)	30.8 (117)	50.0 (26)
Anxiety				
Sons	8.9 (45)	31.3 (16)	32.5 (77)	18.8 (16)
Daughters	31.7 (41)	54.5 (11)	35.9 (117)	73.1 (26)

Bivariate associations

Daughters had a higher risk than sons of both life-time depression ($F(1,262)=7.98$, $p=0.005$) and life-time anxiety ($F(1,262)=11.10$, $p=0.001$). Compared to offspring of depressed fathers, offspring of depressed mothers had a higher risk of anxiety ($F(1,262)=5.62$, $p=0.019$) but not of depression ($F(1,262)=0.48$, $p=0.491$). Risk of anxiety was also higher in offspring with a second parent with life-time emotional problems ($F(1,262)=7.82$, $p=0.006$) but risk of depression was not ($F(1,262)=2.23$, $p=0.136$).

Logistic regression analyses

Table 2 presents the results of the logistic regression analyses for offspring depression and anxiety. The final model for depression shows that daughters had a higher risk than sons and that offspring of depressed mothers tended to have a higher risk than offspring of depressed fathers, but this latter effect was not significant ($p<0.10$). Similarly, offspring with a second affected parent tended to have a higher risk than offspring without a second affected parent, but this was not a significant effect either ($p<0.10$). The results show a significant interaction between offspring gender and gender of the depressed parent which indicates that sons of depressed fathers had the lowest risk in comparison to the other offspring and that the gender difference in offspring risk of depression was smaller in offspring of depressed mothers than in offspring of depressed fathers (see Figure 1 and

Table 2 Results logistic regression analyses

	Offspring depression			Offspring anxiety		
	B (SE)	*p*	*OR*	*B (SE)*	*p*	*OR*
Offspring gender	1.48 (.48)	.002**	4.41	1.56 (.62)	.012*	4.75
Gender depressed parent	.81 (.44)	.069	2.24	1.59 (.58)	.006**	4.93
Second affected parent	.50 (.30)	.090	1.65	1.54 (.74)	.039*	4.66
Gender offspring × Gender depressed parent	-1.14 (.57)	.045*	.32	-1.41 (.68)	.040*	.24
Gender offspring × Second affected parent	-	-	-	-.59 (1.08)	.585	.55
Gender depressed parent × Second affected parent	-	-	-	-2.27 (.98)	.021*	.10
Gender offspring × Gender depressed parent × Second affected parent	-	-	-	2.90 (1.36)	.033*	18.2

– non-significant interaction effect, not included in the final model; *p<0.05; ** p<0.01

Table 1). The final model did not include interactions with the presence of a second affec ted parent, indicating that the effect of a second affected parent on offspring risk of depression did not differ according to the gender of offspring and/or depressed parent.

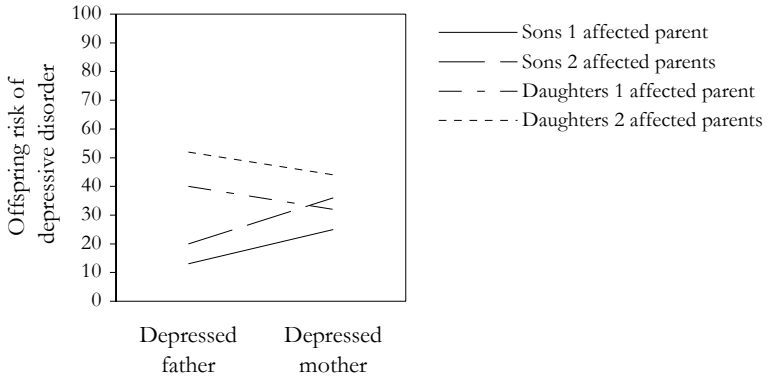

Figure 1 Interaction between offspring gender and gender of the depressed parent in offspring risk of depressive disorder

The final model for anxiety included all main effects and interactions. The main effects indicate that risk of anxiety was higher in daughters, in offspring of depressed mothers and in offspring with a second affected parent. We found two significant two-way interactions: risk of anxiety was lowest in sons of depressed fathers and a second affected

parent increased risk more if this second affected parent was the mother than if it was the father. The third two-way interaction was not significant, suggesting that the effect of a second affected parent did not differ according to offspring gender. However, the significant three-way interaction indicates that the effect of a second affected parent depended on the offspring-depressed parent gender dyad. Figure 2 illustrates that the effect of a second affected parent was strongest in daughters if this second affected parent was the father, while risk of anxiety in sons of depressed mothers did not increase when the father was affected as well.

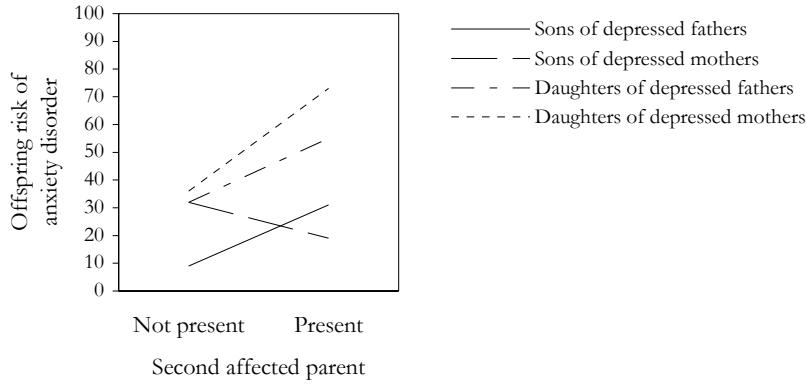

Figure 2 Interaction between offspring gender, gender of the depressed parents, and presence of second affected parent in offspring risk of anxiety disorder

Discussion

In offspring of depressed parents, we examined the effect of a second parent with life-time emotional problems on offspring risk of depression and anxiety. Due to a relatively large sample size, we were able to examine the effect of a second affected parent on offspring according to offspring gender and gender of the depressed parent. We hypothesized that (1) a second affected parent would increase offspring risk of depression and anxiety, (2) a second affected parent would increase risk more in daughters than in sons, (3) risk would increase more if the second affected parent was the mother than if it was the father and (4) that this latter effect would be stronger for daughters. The results for depression did not but the results for anxiety partially did confirm our expectations.

Confirming our first hypothesis, a second affected parent increased offspring risk of anxiety. In line with our third hypothesis, we found that the effect of second affected parent on offspring anxiety was stronger if this was the mother. We did not find confirmation for our second expectation that a second affected parent would increase risk more in daughters than in sons. Although we found that the effect of a second affected parent differed according to the offspring-depressed parent gender-dyad, the differences were not as we expected. Contrary to our expectations, the effect of a second affected parent on daughters' risk of anxiety seemed stronger if this involved the father rather than the mother. We do not know how to explain this. Moreover, our results show that risk in sons did not increase if the second affected parent was the father, while risk in sons and daughters seemed to increase in a similar way if the second affected parent was the mother.

While we found a significant effect of a second affected parent on offspring risk of anxiety, the effect on offspring risk of depression did not reach significance. This seems to contrast with the findings of Nomura, Warner, and Wickramaratne et al. (2001) who found that a second parent with MDD similarly increased offspring risk of depression and anxiety. Our findings are however in line with those of Foley et al. (2001) who reported a stronger effect for offspring anxiety than for offspring depression. Anxiety is suggested to be a prodromal manifestation of depression (Breier, Charney, & Heninger, 1985). Foley et al. reasoned that the effect of a second affected parent was stronger for anxiety than for depression since their sample, similar to ours, consisted of adolescents and young-adults who may have developed anxiety, but may not yet have developed depression. This may have attenuated the possible effect of a second affected parent on offspring risk of depression.

For both depression and anxiety, we found that sons of depressed fathers were at a lower risk than sons of depressed mothers. Risk did not differ between sons of depressed mothers and daughters of either depressed fathers or depressed mothers. This finding seems to combine the higher risks found in daughters and offspring of depressed mothers somewhat. However, instead of a relatively higher risk in daughters of depressed mothers compared to the other offspring in our sample, we found a relatively lower risk in sons of depressed fathers. Furthermore, our findings concerning the effect of a second affected parent indicate that maternal and paternal emotional disorder similarly and additively increase risk of anxiety in daughters, but that risk in sons increases by maternal emotional disorder only. Overviews of the literature (Connell & Goodman, 2002; Phares & Compas, 1992) indicate that the difference between effects of maternal versus paternal emotional disorder is not substantial. However, these overviews did not distinguish between effects in sons and effects in daughters, because studies examining differences between maternal

and paternal depression generally do not include offspring gender (Connell & Goodman, 2002). We formally tested the gender differences by means of interactions and found no difference between maternal and paternal disorder for daughters but did find a difference for sons. The few studies that include both parent and offspring gender report inconsistent results (Eberhart et al., 2006; Foley et al., 2001; Hops, 1992; Klein et al., 2005; Nomura , Warner, & Wickramaratne, 2001; Thomas & Forehand, 1991). Our findings are partially in line with the results of each of these studies. Klein et al. (2005) also found that maternal depression affected risk in both sons and daughters, but these authors did not find an effect of paternal depression. The results of Foley et al. (2001) concerning anxiety are very similar to ours: they found that maternal depression increased risk in both sons and daughters while paternal depression only increased risk in daughters. Their results concerning depression also show that both maternal and paternal depression increased risk in daughters but they did not find effects for sons. Also in line with our findings, Thomas and Forehand (1991) found that maternal depression affected sons, but in contrast with our study, maternal depression did not affect daughters, while paternal depression only affected sons. Similar to our findings, Nomura et al. (2001) found that sons' risk of depression only increased with maternal depression. However, they found that paternal depression increased daughters' risk of depression more than maternal depression, while paternal and maternal depression similarly and additively increased risk of anxiety disorder in both sons and daughters. In line with our results, Eberhart et al. (2006) found that maternal depression increased risk in both sons and daughters, but while we found that paternal depression only increased risk in daughters Eberhart et al. only found an effect of paternal depression in sons. Based on his results Hops (1992) suggested that the intergenerational transmission of depression is stronger for daughters than for sons and stronger for mothers than for fathers. Our results suggest this for both offspring depression and anxiety but clearly more research is needed to find out which results replicate. Our results also indicate that future studies examining differences according to the gender of the depressed parent and/or offspring should take the possible effect of a second parent with an emotional disorder into consideration. In this context it must also be noted that the effect of paternal depression may manifest itself differently in sons (Cummings & Davies, 1994; Marmorstein, Malone, & Iacono, 2004). For instance, Rohde et al. (2005) found that sons of depressed fathers had higher rates of suicidal ideation and suicide attempts than sons of depressed mothers and daughters of depressed fathers or mothers. Moreover, sons were more likely than daughters to develop substance abuse or dependency.

Our results must be considered in the light of four additional limitations. The first limitation is that the offspring in our study were 16-25 years old. Therefore, many may not

have developed anxiety or -in particular- depression yet. This can lead to underestimation of associations. Secondly, information about parental psychiatric history was based solely on the report of one parent. Although accuracy improves with the severity of problems, people generally tend to underreport psychiatric illness in their relatives (Heun, Maier, & Müller, 1997). This will reduce the contrast between offspring without and offspring with a second parent with life-time emotional problems and consequently lead to underestimation of effects. Thirdly, possible differences between groups in severity, chronicity and timing of parental disorder may have affected the strength of associations. The literature suggests that offspring confronted with parental depression early in life and offspring of chronically depressed and/or highly impaired parents are at increased risk (Hammen & Brennan, 2003; Warner, Mufson, & Weissman, 1995). A final limitation is that our data was cross-sectional. We assumed a uni-directional (genetically and environmentally mediated) effect of parental disorder on offspring mental health. However, associations between parental and offspring mental health may have bi-directional origins (Ge et al., 1995), which can only be detected in longitudinal designs.

The experience of depression or anxiety in adolescence or young-adulthood often not only forebodes recurrent episodes in later life, but is also associated with difficulties in the areas of social relationships, education and work. The present paper indicates that offspring risk of depression and anxiety increases when the female gender is involved, either in the form of a daughter or a depressed mother. Early recognition of symptoms reminiscent of depression or anxiety in childhood and appropriate intervention seem important for offspring of depressed parents, particularly for daughters. However, to make this possible, clinical practice should more often inquire after patients' children, especially when it concerns mothers.

Chapter 4

Familial liability and offspring emotional problems: The role of parent-offspring relational stress

Karlien M.C. Landman-Peeters, Catharina A. Hartman, Johan A. den Boer, Ruud B. Minderaa, & Johan Ormel. *Submitted.*

The present study has examined the role of parent-offspring relational stress in the association between familial liability, as indexed by the number of affected parents, and offspring emotional problems. In a Dutch sample of 407 adolescent and young-adult offspring of parents previously treated for depression, we examined (1) whether a second parent with lifetime emotional problems increased parent-offspring relational stress and, via the latter, the emotional problems of offspring, and (2) whether the strength of the association between parent-offspring relational stress and offspring emotional problems differed depending on the number of affected parents. The results have shown evidence for moderated mediation, that is, the association between familial liability and offspring emotional problems was due to (1) a mediation effect by parent-offspring relational stress such that offspring of two affected parents had higher levels of stress than offspring of one affected parent and (2) a moderator effect of familial liability indicated by a stronger association between parent-offspring relational stress and offspring emotional problems in offspring of two versus one affected parent. These findings suggest that parental depression incorporates a complex interplay between genetic and environmental effects on offspring emotional health in which both mediating and moderating influences are involved.

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Introduction

Offspring of depressed parents are at increased risk of developing mental health problems, particularly depression and anxiety (denoted henceforth as emotional problems) (e.g., Biederman et al., 2001; Lieb et al., 2002; Weissman et al., 1993; Wickramaratne & Weissman, 1998). Parental depression incorporates a complex interplay between genetic and environmental effects on offspring emotional health (Downey & Coyne, 1990; Nomura, Warner, & Wickramaratne, 2001), in which mediating and moderating influences are involved.

Parent-offspring relational stress, as indicated by troubled parent-offspring communication, low parental support, and poor family functioning, is found to partly explain (that is, mediate) the association between parental depression and offspring emotional problems (e.g., Brennan et al., 2002; Davies & Windle, 1997; Goodman, 1992; Kane & Garber, 2004; McCarty et al., 2003; Warner, Mufson & Weissman, 1995). Several studies have shown that parents suffering from depression are more critical and less involved in the lives of their children (Downey & Coyne, 1990; Hammen, Brennan, & Shih, 2004; Nomura et al., 2002). Parental depression is also associated with less cohesion and more conflicts within the family (Downey & Coyne, 1990; Nomura et al., 2002; Whaley, Pinto, & Sigman, 1999). Although parent-offspring relational stress is higher during acute episodes of parental depression than after remission, the adverse impact of parental depression on parent-offspring relations and family functioning may persist for up to ten years following remission (Keitner & Miller, 1990; Timko et al., 2002).

While parental depression thus increases parent-offspring relational stress, it may also alter its impact on offspring emotional problems (that is, moderation) (Fendrich, Warner, & Weissman, 1990; Hammen, Brennan, & Shih, 2004; Nomura et al., 2002; Pilowsky et al., 2006). In a community sample, Hammen, Brennan, and Shih (2004) not only found higher levels of parent-offspring relational stress, but also found a stronger association between parent-offspring relational stress and offspring depression in the offspring of depressed parents than was found in the offspring of non-depressed parents. Parental depression seemed to amplify the effect of parent-offspring relational stress. However, the results in research by Weissman and colleagues (Fendrich, Warner, & Weissman, 1990; Nomura et al., 2002; Pilowsky et al., 2006) are at odds with this. Weissman et al. found higher levels of parent-offspring relational stress in offspring of parents who were clinically treated for moderate or severe depression than was found in offspring of non-depressed parents, but this association between parent-offspring relational stress and offspring depression was significant only in the offspring of non-depressed parents (Fendrich, Warner, & Weissman, 1990; Nomura et al., 2002; Pilowsky et

al., 2006). Compared to parents in the Hammen et al. study, the parents in the study of Weissman et al. were more severely depressed (Hammen, Brennan, & Shih, 2004; Pilowsky et al., 2006). The contradictory findings from these studies could be reconciled if we assumed that the severity of parental depression is a measure of genetic liability to emotional problems and that the contribution of environmental factors, such as parent-offspring relational stress, to the development of offspring emotional problems decreased when liability increased. The impact of parent-offspring relational stress on offspring emotional problems would then be less when genetic liability was high.

To our knowledge, variation in risk among offspring of affected parents has not been studied in relation to the effect of parent-offspring relational stress. It therefore remains unclear whether the relative contribution of parent-offspring relational stress to offspring emotional problems depends on the degree of familial liability. Various studies have shown that the risk of emotional problems increases with the number of affected parents (e.g., Brennan et al., 2002; Foley et al., 2001; Marmorstein, Malone, & Iacono, 2004; Nomura, Warner, & Wickramaratne, 2001; Warner, Mufson, & Weissman, 1995). In the present paper, we have examined the role of familial liability, as inferred by the presence of one versus two emotionally affected parents, and also parent-offspring relational stress in the development of offspring emotional problems. Combining the evidence above, we hypothesize moderated mediation, such that (1) the association between familial liability and offspring emotional problems is mediated by higher levels of parent-offspring relational stress and (2) familial liability interacts with parent-offspring relational stress such that the strength of the association between parent-offspring relational stress and offspring emotional problems differs according to level of familial liability. According to Hammen's work a higher familial liability should strengthen the association between parent-offspring relational stress and offspring emotional problems, whereas Weissman et al.'s work indicates that a higher familial liability would weaken it. We tested our hypotheses using longitudinal data from a Dutch sample of 407 adolescent and young-adult offspring from families in which at least one parent had a history of treated depression.

Method

Subjects and Procedure

The present study used data from 407 adolescents and young adults (175 males and 232 females) who participated in the first (T1) and second (T2) waves of assessment of the

Dutch ARIADNE (Adolescents at Risk of Anxiety and Depression; A combined Neurobiological and Epidemiological approach) Study. The study design of ARIADNE has been previously described (Landman-Peeters et al., 2005). Briefly, patients with a) at least one treated episode of emotional disorder, b) no personal history of schizophrenia spectrum diagnoses and c) having biological children aged 13-25 were identified through psychiatric services in the three northern provinces of the Netherlands. At baseline (T1) consenting parents and their children were interviewed in person and were also asked to complete a number of questionnaires. Only the recruited parent was interviewed and he/she provided information about the other biological parent. Approximately one year after the first measurement, offspring were sent a second set of questionnaires for the first follow-up assessment (T2).

At T1 the mean age of the 407 offspring in the present study was 18.35 years (*SD*=3.25). They came from 286 families where the informant parent had been treated for Major Depression Disorder (MDD) with or without co-morbid anxiety. Eighty offspring came from 62 families with two emotionally affected parents. There were no gender or age differences between the groups of offspring with one or two affected parents**.**

Measures

Parent-offspring relational stress. Measurement at T1 included offspring reports on parent-offspring communication, parental support, and family functioning as measures of parent-offspring relational stress.

Parent-offspring communication. We used the Dutch version of the Parent-Adolescent Communications Scales (PACS) (Barnes & Olson, 1995; Jackson et al., 1998). The PACS consists of twenty statements that assess either problems (for example, "My mother/father tends to say things to me that are better left unsaid") or openness (for example, "I feel comfortable with discussing problems with my mother/father") in parent-offspring communication. Participants indicated their degree of agreement with each statement by choosing one of four options: "Strongly agree," "Agree," "Disagree" and "Strongly disagree." Offspring completed a separate PACS for each parent. The scale yields both an Openness and a Problems score. The Openness score is reversed and then added to the Problems score to yield a composite total score. The higher the total score the more problematic the parent-offspring communication. The combined scales here showed a reliability coefficient of 0.89 for Father-Offspring Communication and of 0.90 for Mother-Offspring Communication.

Parental support. The Social Support Questionnaire – short-form (SSQ) (Sarason et al., 1987) was used to collect information about paternal and maternal support. The SSQ was administered during the interview due to the fact that it requires extensive input. This instrument consists of six items that describe different aspects of social support, for example, "Who can you really count on to be dependable when you need help?" and "Who accepts you totally, including both your worst and your best points?" To establish Paternal Support and Maternal Support scales we counted how often participants respectively mentioned their father or mother as providing support. The interviewers stressed that each item on the SSQ tapped a different form of support and, therefore, should be considered separate from the other items.

Family functioning. This was assessed using the Cohesion and Adaptability scales of the Dutch Family Dimension Scales (FDS) (Buurmeijer & Hermans, 1988). The FDS is based on the Family Adaptability and Cohesion Evaluation Scales (FACES) by Olson, Portner, & Lavee (1985). Family cohesion is described as the degree to which family members feel connected and close to each other on an emotional level. This scale consists of twenty-three items, for example, "Our family makes decisions together." Family adaptability is described as the family's ability to change its power structure, roles, and rules in order to adapt to circumstantial and developmental stress. This scale consists of thirteen items, for example, "Rules change in our family." Offspring used a four-point scale ranging from "Never true" to "Always true" to report to what extent the items applied to their family. Internal consistency reliability was 0.87 for the Cohesion scale and 0.84 for the Adaptability scale.

Parent-offspring relational stress index. The previous scales measured the quality of the parent-offspring relationship in the domains of communication, support and family functioning. In order to create a general measure of parent-offspring relational stress we conducted a factor analysis on a Pearson correlation matrix of the six scales described above, using the maximum likelihood estimation method in SPSS version 11.0. Both the scree-test (Cattell, 1966) and the eigen-value-greater-than-one rule (Kaiser, 1960) indicated a single underlying factor with loadings that ranged from |0.591| to |0.696|, with positive loadings for the Father-Offspring Communication, Mother-Offspring Communication and Adaptability scales and negative loadings for the Paternal Support, Maternal Support, and Cohesion scales. After reverse scoring these latter scales, the standardized scores of the six scales were added together. This parent-offspring relational stress index was then used in all subsequent analyses.

Parental disorder. We gathered information about parental emotional disorder at T1. For parents identified through psychiatric services, we used the World Mental Health (WMH)

Survey Initiative Version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI) (Kessler & Üstün, 2004) to assess life-time MDD according to criteria of the Diagnostic and Statistical Manual of Mental Disorders (4th Edition) (DSM-IV) (American Psychiatric Association, 1994). These informant parents were asked about the history of treatment for emotional disorder of the other biological parent by means of vignettes about depressive and anxiety disorders based on DSM-IV diagnostic criteria. Only parents who had received treatment for emotional disorder were classified as "affected." In the Netherlands approximately seventy-five percent of those individuals with a diagnosable depression and/or anxiety disorders seek treatment (Ten Have et al., 2004); we therefore reasoned that the inclusion of this criterion would minimize any false positive classification and also serve as a proxy measure of equal "illness severity" for the two affected parents.

Offspring emotional problems. The DSM-IV Questionnaire (Hartman, 2002; Hartman et al., 2001; Muris, 2006; Muris, Winands, & Horselenberg, 2003) was used to assess offspring emotional problems at T2. Respondents were asked to report on a four-point Likert scale to what extent descriptions of symptomatic behavior accurately described their behavior at the time of measurement. The DSM-IV Questionnaire includes items on a broad range of psychiatric symptoms. The Emotional Problems scale includes thirty-two items, for example "I am often unhappy," "I am low in energy or feel tired for no reason," and "I suddenly become very anxious or panicky for no reason." Internal consistency reliability was 0.94.

Data analyses

Our two key hypotheses were that (1) the association between familial liability and offspring emotional problems is mediated by parent-offspring relational stress and (2) the strength of the association between parent-offspring relational stress and offspring emotional problems is moderated by familial liability. Prerequisites for mediation are that the independent variable, in this case familial liability, is associated with both the outcome and mediator, in this case offspring emotional problems and parent-offspring relational stress, and that the mediator must significantly contribute to the prediction of the outcome variable in an equation in which both the mediator and the independent variable are included (e.g., Baron & Kenny, 1986). Mediation is indicated if the effect of the independent variable decreases when the mediator is included in the regression equation. However, we expected moderated mediation, such that in our model familial liability

would both be the independent variable and the moderator (see Figure 1). Therefore, the interaction between familial liability and parent-offspring relational stress had to be included in the equation as well (cf. Preacher, Rucker, & Hayes, 2007).

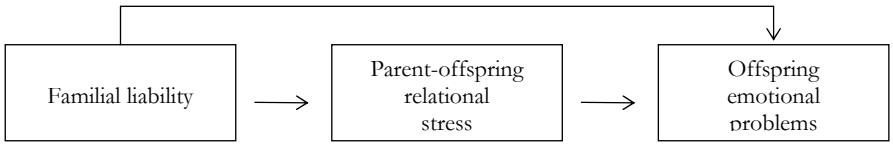

Figure 1 Model of moderated mediation by parent-offspring relational stress in the association between familial liability and offspring emotional problems (see Preacher, Rucker, & Hayes, 2007)

We first examined whether familial liability was associated with both offspring emotional problems and parent-offspring relational stress by testing mean differences between the offspring of one and the offspring of two affected parents. We additionally conducted a regression analysis to examine the extent to which familial liability predicted parent-offspring relational stress. Then we conducted a regression analysis to examine moderated mediation, which consisted of two steps. In the first step we entered familial liability and in the second step we added parent-offspring relational stress and its interaction with familial liability. By means of this second step, we were able to examine the decrease in the effect of familial liability after adding parent-offspring relational stress (that is, mediation) and whether the effect of parent-offspring relational stress differed according to familial liability (that is, moderation). If the interaction between familial liability and parent-offspring relational stress was significant, the interaction effect was then plotted and the association between parent-offspring relational stress and offspring emotional problems was separately examined for the offspring of one and the offspring of two affected parents. If not, mediation was tested using the full sample.

At T1, relatively more offspring of two rather than of one affected parent had moved out of the parental home and were living independently (33.8% versus 22.0%; χ^2=4.81, p=0.028) and had experienced parental divorce (25.0% versus 15.3%; χ^2=4.26, p=0.039). These differences may affect associations between familial liability, parent-offspring relational stress, and offspring emotional problems. Therefore, in the regression analyses we adjusted for the effects of offspring age and gender as well as for offspring residential status and parental divorce.

The 407 offspring came from 286 families. To account for this clustering of observations in families, we conducted design-based regression analyses with families as primary sampling units, using the statistical program STATA 8.0 (StataCorp, 2003). All variables were standardized to improve interpretability and prevent computational problems due to multicollinearity that may occur with variables and their products (Aiken & West, 1991).

Results

Group differences in emotional problems and parent-offspring relational stress

The mean total score for emotional problems was higher in offspring with two affected parents (M= 51.09, SD=14.31) than in offspring of one affected parent (M=46.47, SD=12.27) and this difference was statistically significant ($t(df=405)=2.92$, $p=0.004$). Similarly, the mean parent-offspring relational stress index was higher ($t(df=405)=2.75$, $p=0.006$) in offspring of two affected parents (M=1.22, SD=4.68) than in offspring of one affected parent (M=-0.26, SD=4.21).

Moderated mediation analysis

Our first regression analysis showed that a higher familial liability significantly predicted parent-offspring relational stress (B=0.136 (SE=0.060), p=0.024, 95% Confidence Interval (CI)=0.018-0.254). Thus, after controlling for the effects of offspring gender, age, residential status, and parental divorce, the offspring of two affected parents reported

Table 1 Regression analysis on offspring emotional problems

	B (SE)	95% CI
Step 1		
Familial liability	.146 (.050)**	.048 - .243
Step 2		
Familial liability	.087 (.040)*	.008 - .166
Parent-offspring relational stress	.281 (.049)***	.186 - .377
Familial liability × Parent-offspring relational stress	.100 (.050)*	.001 - .200

Analyses were controlled for the effects of offspring gender, age, and residential status, and parental divorce. All variables were standardized; *** $p<.001$; ** $p<.01$;* $p<.05$

more parent-offspring relational stress than did offspring of one affected parent. The association was not strong: familial liability accounted for only 2% of the variance in parent-offspring relational stress.

Table 1 shows the results of the second regression analysis. This analysis revealed a significant main effect of familial liability in both the first and second step. The inclusion of parent-offspring relational stress and its interaction with familial liability in the second step decreased the effect of familial liability on offspring emotional problems. This indicates that the higher levels of parent-offspring relational stress in offspring of two affected parents could partly explain the higher levels of emotional problems in these children (that is, mediation). In addition, the results showed a significant interaction between familial liability and parent-offspring relational stress. Familial liability moderated the association between parent-offspring relational stress and offspring emotional problems. Regression analyses in the two groups of offspring separately showed a stronger association between parent-offspring relational stress and offspring emotional problems in offspring of two affected parents (B=0.413 (SE=0.100), p<0.000, 95% CI= 0.214-0.612, explained variance 17%) than in offspring of one affected parent (B=0.252 (SE=0.056), p<0.000, 95% CI= 0.141-0.363, explained variance 6%). Figure 2 illustrates the moderator effect of familial liability adjusted for differences in parent-offspring relational stress between offspring of one and two affected parents. The figure indicates that the level of emotional problems is similar in offspring of one versus two affected parents when parent-offspring relational stress is low. However when parent-offspring relational stress is high, offspring of two affected parents show more emotional problems than offspring of one affected parent.

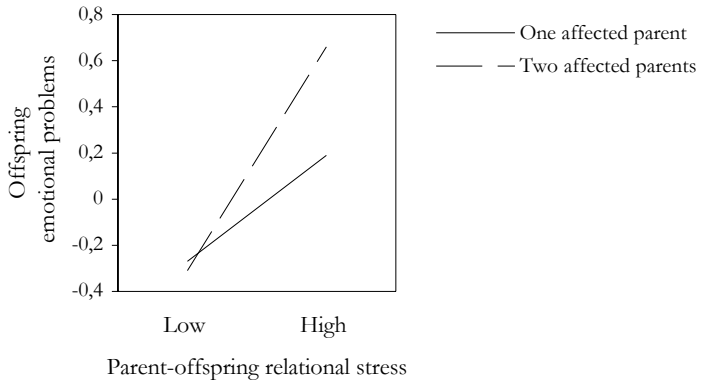

Figure 2 Regression lines for the association between parent-offspring relational stress and offspring emotional problems in offspring of one affected parent and offspring of two affected parents

Discussion

In a sample of adolescent and young-adult offspring of parents with a history of treated depression, we found evidence for moderated mediation by parent-offspring relational stress in the association between familial liability and offspring emotional problems. Higher levels of parent-offspring relational stress in offspring of two affected parents at baseline partly mediated the association between familial liability and offspring emotional problems at one year follow-up, while the effect of parent-offspring relational stress was stronger in the offspring of two than it was in the offspring of one affected parent (that is, moderation).

Our results indicate that increased familial liability incorporates an interplay between increased genetic liability and increased environmental adversity, in this case parent-offspring relational stress. This is in line with the findings of Hammen, Brennan, and Shih (2004) that parental depressive disorder both increased parent-offspring relational stress and strengthened the association between parent-offspring relational stress and offspring depressive disorder. Our findings, however, contrast with the results of Weissman et al. (Fendrich et al., 1990; Nomura et al., 2002; Pilowsky et al., 2006) where parent-offspring relational stress did not make an independent contribution to psychopathology in the offspring of moderately and severely depressed parents. Our results indicate that increased genetic liability strengthens instead of weakens the association between parent-offspring relational stress and offspring emotional problems. Similar to the Weissman et al. study, the parents in the present study received clinical treatment for depression. In contrast though, the Weissman et al. studies used offspring life-time depressive and anxiety disorder as outcomes, whereas we used a dimensional measure of current depression and anxiety symptoms. Similarly, Weissman et al. used dichotomous measures of the quality of parent-offspring relations, where we used an aggregated continuous measure. Our measures may have been more sensitive for the following reasons: a) dichotomous measures statistically attenuate associations between variables, b) dichotomous measures of psychopathological symptoms do not capture high but (still) subclinical levels of emotional problems, and c) dichotomous measures of relationship quality may have less validity as most aspects of parent-offspring relations seem to be a matter of degree rather than of presence or absence. Additionally, our measure was a composite of aspects of the parent-offspring relationship. Factor analysis supported the notion of one general underlying factor. Possibly, this composite captures adversity in parent-offspring relations more accurately than separate measures do. High levels of problems in parent-offspring communication may be compensated by parental

support and family cohesion or vice versa, and, similarly, lack of support from one parent may be compensated by support received from the other parent.

The greater reactivity of offspring of two affected parents to adversity in parent-offspring relations probably reflects an interplay between genetic and environmental factors. Parental depression is thought to genetically and/or environmentally affect offspring neurobiological processes, coping abilities, problem-solving skills, and availability of protective resources (Downey & Coyne, 1990; Goodman & Gotlib, 1999; Hammen, Brennan, & Shih, 2004). In comparison to offspring of one affected parent, offspring with two affected parents may be at increased risk since they lack a non-affected parent who is able to compensate, genetically and/or environmentally, for the affected parents' negative influence on these aspects (Downey & Coyne, 1990).

Our findings should be considered in the context of the following limitations. Firstly, information about parental psychiatric history was based solely on the report of only one parent. Although accuracy improves with the severity of problems, people generally tend to underreport psychiatric illness in their relatives (Heun, Maier, & Müller, 1997). This will reduce the contrast between offspring with one versus two affected parents and, consequently, lead to underestimation of the associations. Secondly, we assumed a unidirectional relationship between parental and offspring emotional problems, but reciprocal associations have been shown, along with offspring emotional problems having a negative impact on parental mental health and parent-offspring relations as well (Ge et al., 1995).

In sum, the findings of the present study indicate that emotional problems in offspring of emotionally disordered parents are increased by the presence of genetic and environmental factors, which act in an additive and interactive fashion. Although we may not be able to decrease genetic vulnerability to parent-offspring relational stress, parent-offspring relations and family functioning can be targeted and improved by prevention and intervention programs.

Chapter 5

Gender differences in the relation between social support, problems in parent-offspring communication, and depression and anxiety

Karlien M.C. Landman-Peeters, Catharina A. Hartman, Gieta van der Pompe, Johan A. den Boer, Ruud B. Minderaa & Johan Ormel (2005).
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Gender differences in the buffer-effect of social support in the relation between stressful circumstances and the development of depression and anxiety disorders are widely assumed, but few studies address this three-way interaction between gender, stress, and support. Data in the present study came from the baseline assessment of the Adolescents at Risk of Anxiety and Depression (ARIADNE) study in 502 adolescent and young-adult children of 356 parents in the Netherlands with a depression, panic disorder and/or obsessive-compulsive disorder. Results indicate that the daughters benefit more from social support than the sons when problems in parent-offspring communication are high, but that this effect holds only for depression symptoms and particularly in relation to problems in father-offspring communication. Social support does not seem to play a role in the development of anxiety.

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Introduction

Although gender differences in the buffer-effect of social support in the relation between stress and depression and anxiety are widely assumed, gender, stress, and support have rarely been studied simultaneously. To our knowledge, two studies explored this issue (Olstad, Sexton, & Søgaard, 2001; Rubin et al., 1992), but did not find a significant three-way interaction. Both studies used normal population samples, while the effects of social support and stress are thought to be most salient in individuals with a higher risk to develop depression and anxiety (Garber & Flynn, 2001). Offspring of parents who suffer from depression and/or anxiety develop these psychiatric problems 2 to 6 times more often than offspring of unaffected parents (e.g., Lieb et al., 2002; Merikangas et al., 1999). The present study explores the three-way interaction between gender, social support and stress in a sample of adolescent and young-adult offspring of patients suffering from depression, panic disorder and/or obsessive-compulsive disorder.

Due to the symptoms of depression and anxiety disorders, interactions between affected parents their offspring can suffer from parental negativity, inattentiveness, criticism, irritability (Johnson et al., 2001; Radke-Yarrow & Klimes-Dougan, 2002), dissatisfaction (Hirschfeld et al., 1997), over-control, and lack of expressed warmth by the parent (Whaley, Pinto, & Sigman, 1999). Garber and Flynn (2001) report that high-risk offspring experience more conflicts with their parents than their peers. The present study focuses on problems in the communication between the adolescent or young-adult and both parents as a measure of stress. We expect that offspring experiencing problematic parent-child communication report more depression and anxiety symptoms than those reporting few or no communication problems.

Social support is considered to be an important environmental factor in the onset and course of depression and anxiety disorders. Higher levels of social support are related to lower levels of depression and anxiety (e.g., Procidano & Walker Smith, 1997; Robinson & Garber, 1995; Sarason et al., 1983), and, although findings remain inconclusive (e.g., Cohen & Wills, 1985; Lepore, Evans, & Schneider, 1991; Monroe, 1983; Monroe et al., 1983; Wade & Kendler, 2000a; Windle, 1992), it is widely assumed that social support also buffers stress (Gottlieb, 1994; Kessler, Price, & Wortman, 1985; Olstad, Sexton, & Søgaard, 2001). The availability of emotional support and the perception that one can rely on one's network when needed appears to decrease the influence of stressful circumstances on the development of psychiatric symptoms (Cohen & Wills, 1985; Kessler, Price, & Wortman, 1985). Increase or onset of psychiatric problems in high-risk young people may be prevented by social support from parents, siblings, members of the extended family, and peers (e.g., Goodman & Gotlib, 2002; Luthar & Zigler, 1991; Phares,

Duhig, & Watkins, 2002). We therefore expect that when social support is available and perceived as sufficient, the extent to which high-risk offspring experience depression or anxiety decreases, not only through its direct influence, but also through its buffering effect.

It is well-established that females are more vulnerable to the development of depression (Cyranowski et al., 2000; Garber & Flynn, 2001; Hops, 1996). Gender differences have been reported in the exposure and reactivity to stressors and social support, giving rise to the assumption that the pathogenic effect of these factors is different for males and females.

Kendler, Thornton, and Prescott (2001) found that males were more sensitive to work problems and divorce or separation, while females were more sensitive to problems in getting along with individuals in their proximal network. Such interpersonal problems are widely reported to result in more symptoms in females than in males (Nolen-Hoeksema, 2001; Seiffge-Krenke, 1995; Wagner & Compas, 1990). Therefore, problems in parent-adolescent communication are expected to affect high-risk daughters more than sons.

Concerning social support, females tend to report larger social networks than males and turn to others for emotional support in stressful circumstances more than males do (Ashton & Fuehrer, 1993; Frydenberg & Lewis, 1993; Seiffge-Krenke, 1995; Taylor et al., 2000). It is therefore argued that females' sense of wellbeing is more strongly influenced by the availability and quality of social support relations (Cyranowski et al., 2000; Flaherty & Richman, 1989). In line with this, research indicates that females report more depression symptoms than males when they experience a lack of social support (Brugha et al., 1990; Slavin & Rainer, 1990), and profit more from support when it is available (Matthews, Stansfeld, & Power, 1999; Taylor et al., 2000). Because females tend to turn to their social support relations when they experience stress, rather than coping by "fight versus flight", they are more likely than males to benefit from available support in confining the consequences of stress (Taylor et al., 2000). Indeed, several authors (e.g., Kaltiala-Heino et al., 2001; Olstad, Sexton, & Søgaard, 2001) have reported that the buffer-effect of support in females seems stronger than that in males. We therefore expect that social support is of greater importance to high-risk daughters than it is to high-risk sons. Assuming that daughters suffer more from problems in parent-offspring communication, but also benefit more from social support than sons, we expect that when problems in parent-offspring communication are high the gender difference in level of symptoms is smaller when social support is available than when it is not.

Research on the effect of social support has mainly focused on depression. It is therefore unclear whether stress, social support, and gender differences play the same role

in the development of anxiety as in the development of depression. Depression and anxiety are considered to be distinct disorders, but probably share a number of risk factors (e.g., Kendler et al., 2003). Examining depression and anxiety symptoms simultaneously gives us the opportunity to explore the specificity of the hypothesised effects (Hammen, 2001, 2002; Wade & Kendler, 2000b). We hypothesise that the effects of gender, problems in parent-adolescent communication, and perceived social support are similar for depression and anxiety symptoms.

In sum, the present study investigates the relations between gender, stress, and social support in their association with depression and anxiety symptoms in a sample of adolescent and young-adult offspring of parents suffering from depression, panic disorder, and/or obsessive-compulsive disorder. We focus on problems in parent-offspring communication and perceived social support. We hypothesise a three-way interaction that shows that when problems in parent-child communication are high, the differences between males and females in levels of symptoms are larger in the situation that perceived support is low than in the situation that perceived support is high. We hypothesise further that this effect holds for both depression and anxiety symptoms.

Method

Participants and procedure

The present study was conducted on data from the base-line assessment of the ARIADNE-study. This is a large prospective study among 524 adolescents and young-adults and 366 parents into the development and course of depression and anxiety disorders among offspring of psychiatric patients. Parents were recruited via psychiatric services in the three northern provinces of the Netherlands. Information about the study was mailed to 4470 patients who were at least once treated for depression, panic disorder, and/or obsessive-compulsive disorder. They were asked to confer with their biological children (aged between 13 and 26 years old) about participation. A total of 1209 parents had children within the age-range and were eligible to participate, 366 agreed to participate (8% of total group; 30% of eligible group) and 843 (19% of total group; 70% of eligible group) refused. Of the 3261 other parents 858 persons did not reply (19%); 420 persons (9.5%) were moved away from the area, deceased or otherwise not eligible for participation; 1404 (31.5%) persons had no biological children within the age-range; and 579 persons (13%) refused to participate without providing information about children.

After consent was obtained, appointments for the individual interviews with parents and offspring were made. Participants were interviewed at home or at the Department of Psychiatry by trained interviewers. Both offspring and parents were interviewed with the Composite International Diagnostic Interview (CIDI) WHO-2000 version (Alonso et al., 2002) to assess clinical depression and anxiety. Parents were also interviewed about the presence of depression, panic, and/or obsessive-compulsive problems in their child's other biological parent. In addition to the interview participants filled in questionnaires. The data in the present study include the DSM-IV questionnaire (Hartman, 2002), the Social Support Questionnaire short-form (Sarason et al., 1987), and the Parent-Adolescent Communication Scales (Barnes & Olson, 1995).

The present study used data from 502 adolescents and young-adults with complete data (215 males and 287 females) between 13 and 25 years old (*M*=18;8, *SD*=3;3). By means of the CIDI, 164 out of the 502 participants were diagnosed with at least one DSM-IV lifetime disorder: 112 with a depression disorder and 114 with an anxiety disorder (38 Panic Disorder; 16 Agoraphobia, 32 Obsessive-Compulsive Disorder, 37 Social Phobia, 30 Generalised Anxiety Disorder, 19 Separation Anxiety Disorder, and 20 Adult Separation Anxiety Disorder). Fifty-nine out of these 164 reported an episode in the month preceding the interview.

The participants came from 356 families (106 fathers and 250 mothers were contacted). Eighty percent of the participants (*n*= 409 participants) had parents with an age-of-onset $\geq$ 10 years before assessment, mean number of years between age-of-onset and assessment was 22 years (*SD*=11;8), 60% of the parents (of 304 participants) reported that they suffered a third or more of their lives (since onset) from depression or anxiety disorders. One hundred forty-seven parents (of 204 participants) reported episodes in the year preceding the interview, 134 parents (of 189 participants) out of 147 reported that this interfered in their personal relationships. Four hundred ninety-five participants (98.6%) experienced parental episodes of depression and/or anxiety during their lives. In 100 families (116 participants) the other biological parent had depression and/or anxiety problems as well, in 72 families (138 participants) only the father, and in 184 families (248 participants) only the mother was affected.

Measures

Depression and anxiety symptoms. Depression and anxiety symptoms were measured by means of the DSM-IV Questionnaire (Hartman, 2002; Hartman et al., 2001). Offspring were asked to report on a 4-point Likert-scale to what extent descriptions of symptomatic

behaviour accurately describe their behaviour at the time of measurement and/or in the preceding 12 months. The DSM-IV Questionnaire includes items referring to depression and a broad range of anxiety disorders. To create scales for depression and anxiety symptoms that differentiate between these problems as much as possible, we conducted a factor analysis with a two-factor solution on the 17 depression and 18 panic and somatization items. We constructed two scales such that only those items were selected which loaded on their own factor with a loading ≥ 0.30 and a difference ≥ 0.20 between this main loading and the additional loading on the other factor. The Depression symptoms scale consists of 14 items, e.g. "I am often unhappy" and "I am low in energy or feel tired for no reason". The Anxiety symptoms scale consists of 16 items, e.g. "I suddenly become very anxious or panicky for no reason" and "I often feel sick to my stomach". Internal consistency reliability is 0.92 for the Depression scale and 0.88 for the Anxiety scale. Participants with a recent episode of depression had a significantly higher mean score on depression symptoms (t=11.20, p<0.001; effect size d=1.72) and participants with a recent episode of anxiety had a significantly higher mean score on anxiety symptoms (t=7.45, p<0.001; effect size d=1.31) than those without a (current) depression and/or anxiety diagnosis. ROC analyses showed that at the optimal cut-off point sensitivity was 0.87 and specificity 0.85 when the depression symptoms score is used to predict recent clinical depression. For anxiety symptoms sensitivity was 0.80 and specificity 0.77 in predicting recent clinical anxiety. The DSM-IV Questionnaire has the advantage that we were able to measure subclinical levels of symptomatology in our high-risk group.

Social support. The SSQ-shortform (Sarason et al., 1987) was used to collect information on two aspects of perceived social support; number of (different) persons from whom support is received and overall satisfaction with social support received from these persons. This instrument consists of six items that describe different aspects of social support, e.g. "Whom can you really count on to be dependable when you need help?" and "Who accepts you totally, including both your worst and your best points?" Subjects report for each item those persons from whom they receive the described support and, on a six-point Likert-scale, their overall satisfaction with the support they experience. These two aspects of perceived social support are combined in one perceived social support score by summing the standard scores of the Number and Satisfaction scales.

This instrument was translated in Dutch for the purpose of this study. The translation procedure incorporated 2 iterations of translations from English to Dutch by the authors and back translations from Dutch to English by an independent researcher blind to the original English version. The SSQ comes with extensive instruction. To

ensure subjects were well informed, the SSQ was administered during the interview so subjects could be instructed orally by the interviewer. The interviewers especially stressed that each item on the SSQ taps a different form of support and, therefore, should be considered separate from the other items.

We consider the items of the SSQ-shortform to be neutral regarding gender, that is, the items do not represent support particularly experienced or preferred by either males or females. Internal consistency reliability was 0.87 for the Number (of support providers) scale, 0.86 for the Satisfaction scale, and 0.84 for the combined scale.

Problems in parent-offspring communication. By means of the Dutch translation of the Parent-Adolescent Communication Scales (Barnes & Olson, 1995; Jackson et al., 1998; Ligthart, 1987) participants reported on the extent to which descriptions of problems (e.g., "My mother/father tends to say things to me that are better left unsaid") and openness (e.g., "I feel comfortable to discuss problems with my mother/father") in the communication with parents apply to their own situation. This was done separately for the father and the mother. The resulting Problems score and Openness score were summed for a total score (Jackson et al., 1998; Ligthart, 1987). By reverse scoring the Openness scale, the summed composite represents the extent to which the participant experiences a problematic communication with his/her biological parents.

The original response option "Do not agree/do not disagree" was removed, leaving four answering categories: "Strongly agree", "Agree", "Disagree", and "Strongly disagree". Reliability-coefficients were 0.91 for the Openness scale and 0.85 for the Problems scale; correlation between these two scales was 0.672 (p<0.001). The combined scale showed a reliability coefficient of 0.93.

Data analysis

Since 95 families participated with two children, 18 with three, and 5 with four children, the data cannot be treated as a sample of 502 independent, interchangeable observations. Members from one family tend be more alike . To account for this dependency or, in other words, variability between both individuals and families, analyses were conducted using hierarchical linear regression. As a first step so-called empty models are fitted for the dependent variables, i.e. depression symptoms and anxiety symptoms. Empty models do not contain predictor variables. Symptomatology is therefore the sum of a general mean, a random effect at the individual level, and a random effect at the family level. Dividing the family-level variance by the sum of family level and individual level variance results in the

intra class correlation coefficient $\rho_{I(Y)}$. This coefficient can be interpreted as the fraction of total variability that is due to the family level (Snijders & Bosker, 1999), in other words, the extent to which family-membership is relevant in predicting symptoms. In contrast, in the Ordinary Least Squares (OLS) empty model symptomatology is the sum of a general mean and general residual individual variance. Comparison of the deviance of the OLS empty model with that of the hierarchical linear empty model shows, by means of a chi-square test, whether the distinction between variability at the family and the individual level provides a better fit to the data. (Deviance is a measure of lack of fit between data and model.)

The following step is the inclusion of the explanatory variables, i.e. gender, perceived social support, and problems in parent-offspring communication. Interactions are calculated as the cross-product of the first order effects. In these analyses, apart from gender, which is a "dummy" variable (male versus female; male is coded 0 and female 1) variable, all the predictor variables are continuous. These variables were transformed into standard scores in order to avoid ambiguities of interpretation as well as computational problems due to multicollinearity that may occur with variables and their products (Aiken & West, 1991).

The extent to which the full model explains variance in adolescent depression and anxiety symptoms (R^2_1) is calculated on the basis of the sums of family level and individual level variance in the hierarchical linear empty model and the full model. Dividing the full-model variance by the empty model variance and deducting the result from 1 gives explained variance R^2_1 (Snijders & Bosker, 1999). Comparison of the deviance of the hierarchical linear empty model and the full model shows, by means of a chi-square test, whether the inclusion of the explanatory variables provides a better fit to the data.

The hierarchical linear regression analyses were conducted on raw data scores. However, the distributions of the depression and anxiety symptom scores were skewed with the tail upwards (skewness= 1.198 and 1.794, respectively). To control for artificial effects all analyses were conducted on logarithmically transformed scores of depression and anxiety symptoms as well.

Results

Table 1 presents means and standard deviations of the different variables for males and females separately. Females report more depression and anxiety symptoms, as well as

problems in the communication with their parents. Males and females do not differ on perceived social support.

Pearson product-moment correlations were negative between perceived social support and depression symptoms (r=-0.271, p<0.001) and perceived social support and anxiety symptoms (r=-0.103, p<0.05). Problems in parent-offspring communication show a positive relation to symptoms, r=0.313 (p<0.001) for the association with depression symptoms and r=0.172 (p<0.001) with anxiety symptoms. Perceived social support and problems in parent-adolescent communication were negatively correlated (r=-0.290, p<0.001). The correlation between depression symptoms and anxiety symptoms was high (r=0.621, p<0.001).

Table 1 Means and standard deviations for males (n=215) and females (n=287)

	Males	Females	*t*	*p*	Effect size *d*
Depression symptoms	21.69 (6.14)	24.57 (7.92)	-4.590	.000***	0.41
Anxiety symptoms	19.33 (4.32)	22.36 (6.49)	-6.282	.000***	0.55
Perceived social support[a]	-.12 (1.60)	.09 (1.60)	-1.408	.160	
Problems in parent-offspring communication	83.01 (13.64)	86.15 (15.77)	-2.335	.020*	0.21

[a] Perceived social support-scores are the sum of standardized scores on the "number" and "satisfaction" scales;
* p<0.05, ** p<0.01, *** p<0.001

Hierarchical linear regression analyses

Intra class correlations $\rho_{I(Y)}$ in the hierarchical linear empty models of depressive and anxiety symptoms were 0.223 for depression and 0.179 for anxiety. Taking variance on the family level into account decreased deviance in depression symptoms significantly with 10.165 (df=1, p<0.01) from 3426.270 in the OLS empty model to 3416.105 in the hierarchical linear regression empty model. Deviance in anxiety symptomatology decreased significantly with 5.361 (df=1, p<0.05) from 3198.163 in the OLS empty model to 3192.802 in the hierarchical linear regression empty model. These results indicate that family membership explains variance in both depressive and anxiety symptoms and that it is necessary to take family membership into account when predicting individual symptoms.

Table 2 shows the results of the multivariate hierarchical regression analyses on depression and anxiety symptoms with gender, perceived social support, problems in parent-offspring communication, and their interactions as explanatory variables.

Regression analyses on the logarithmically transformed scores of depression and anxiety symptoms yielded the same results. The first order effects of gender, satisfaction with social support, problems in parent-offspring communication, and the three-way interaction between these variables were significant for depression symptoms. For anxiety symptoms, only the first order effects of gender and problems in parent-adolescent communication were significant. A first order effect represents the weighted average effect of the predictor coefficient across all observed values of the other predictors (Aiken & West, 1991, p.38).

Table 2 Hierarchical linear regression analyses on depression and anxiety symptoms

	B	*SE B*	β	*t*	*p*
Depression symptoms					
Constant	21.883	.479	-	-	-
Gender	2.330	.623	.173	3.74	.000***
PSS	-1.371	.485	-.206	- 2.83	.002**
PPAC	1.604	.527	.241	3.04	.001**
Gender × PSS	-0.204	.630	-.023	-0.32	.375
Gender × PPAC	0.227	.652	.027	0.35	.363
PSS × PPAC	0.156	.410	.026	0.38	.352
Gender × PSS × PPAC	-0.986	.546	-.123	-1.81	.035*
Anxiety symptoms					
Constant	19.518	.400	-	-	-
Gender	2.742	.522	.244	5.25	.000***
PSS	-0.330	.406	-.059	-0.81	.209
PPAC	0.838	.441	.151	1.90	.029*
Gender × PSS	-0.222	.529	-.030	-0.42	.337
Gender × PPAC	-0.254	.547	-.036	-0.46	.323
PSS × PPAC	0.346	.344	.068	1.01	.156
Gender × PSS × PPAC	-0.487	.459	-.073	-1.06	.145

PSS: Perceived Social Support; PPAC: Problems in Parent-Adolescent Communication;
* $p<0.05$, ** $p<0.01$, *** $p<0.001$

With regard to depression symptomatology these results indicate that a) females experienced more symptoms than males, b) the more social support participants perceived, the less symptoms they reported, c) the more problems reported in parent-offspring communication, the more symptoms they reported, and d) the effect of perceived social support on depression symptoms differed for males and females when

the level of problems in parent-adolescent communication was taken into account. This complete model explained 17.5% of the variance in depression symptoms. Deviance decreased significantly by 92.402 (df=7, p<0.001) from 3416.105 in the hierarchical linear empty model to 3323.703 in the full model.

The results regarding anxiety symptoms indicate that there was no significant gender difference in the buffer-effect of social support. Only two first order effects were significant, indicating that a) more females than males experienced symptoms and b) the more problems in parent-offspring communication, the more symptoms they reported. This complete model explained 9.5% of the variance in anxiety symptoms. Deviance decreased significantly by 47.306 (df=7, p<0.001) from 3192.802 in the hierarchical linear empty model to 3145.496 in the full model. Removal of the three-way interaction and subsequently any of the two-way interactions did not change the findings except for the first order effect of support: when the interaction between gender and support was not entered into the model, the first order effect of support was significant.

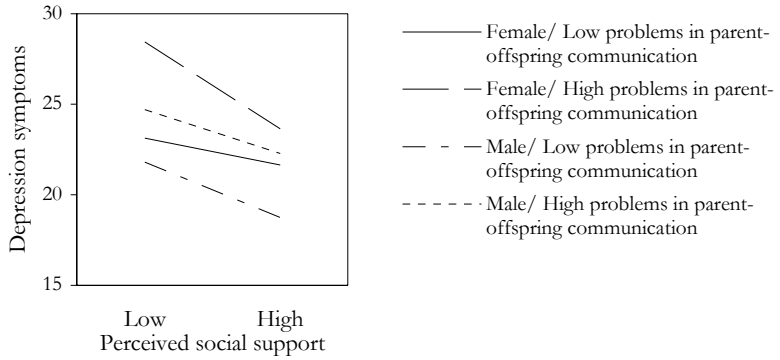

Figure 1 Regression lines for the association between perceived social support and depression symptoms in males and females high and low on problems in parent-offspring communication

Figure 1 shows the regression lines for the effect of perceived social support (PSS) on depression symptoms in males and females in low and high conditions of problems in parent-offspring communication (PPAC). Since our model includes interactions, the regression lines were computed using the *B* instead of the β coefficients (Aiken & West, 1991, p.36). The values of 0 (male) and 1 (female) were used for gender. The values –1 and 1 (representing one standard deviation below and above the mean) were used for respectively the low and high conditions of perceived social support and problems in parent-offspring communication (Aiken & West, 1991, p.13). Figure 1 shows the three

first order effects as described above. The three-way interaction is such that the gender difference depression symptoms is larger for those participants reporting high stress and low support than the gender difference for those participants reporting high stress and high support..

Additional analyses

Check on the effect of participants with current depression and anxiety disorders. Our sample included 164 adolescents and young-adults with a life-time diagnosis of depression and/or anxiety disorder according to DSM-IV. Fifty-nine participants reported an episode of depression and/or anxiety in the month preceding assessment. Being clinically depressed and/or anxious at the time of assessment may have systematically altered these participants' experience of social support and problems in parent adolescent-communication, resulting in much stronger associations for these individuals than for the others and subsequently causing our results for depression symptoms to reach significance. To check whether our results replicate in a nonclinical/subclinical sample, we repeated our analyses with the participants (n=443; 207 males and 236 females) who did not have a current diagnosis. The results with regard to anxiety symptoms were the same as in the full sample. In this analysis, the complete model explains 7.4% of the variance in anxiety symptoms. For depression symptoms findings were similar as well: the three-way interaction remained significant (t=-2.13, p=0.017), although the first order effect of gender just failed to reach significance (t=1.63, p=0.052). The complete model explains 17.9% of the variance in depression symptoms in this analysis.

Check on effects for problems in communication with father and mother separately. The participants rated the communication with their father and mother separately, after which these scores were combined in a total score for problems in parent-offspring communication. However, adolescents and young-adults may be differentially affected by communication problems with father versus mother, and the effect of social support may differ accordingly. We repeated our analyses with the separate scores for fathers and mothers. Results for anxiety symptoms were similar, that is, no significant gender differences in the buffer effect of social support in relation to problems in father-offspring or mother-offspring communication. The full model including problems in father-offspring communication explained 9.2% of the variance in anxiety symptomatology, the model including problems in mother-offspring communication 8.8%. Results for depression symptoms, on the other hand, showed that the three-way interaction was

significant for father-offspring communication problems (t=-1.78, p=0.038), but not for problems in mother-offspring communication (t=-1.12, p=0.131). This difference could not be accounted for by differences in mean, variance or skewness between scores for father-offspring and mother-offspring communication. The full model including problems in father-offspring communication explained 18.1% of the variance in depression symptoms, the model including problems in mother-offspring communication explained 14.4%.

Discussion

In this study we argued that social support might serve as a protective factor in the development of depression and anxiety symptoms in offspring of parents suffering from depression and/or anxiety disorders. We assumed that problems in parent-offspring communication need not result in more symptoms when social support is sufficient. We argued further that this buffer-effect of social support is different for males and females, i.e. when scores on problems in parent-offspring communication are high, the difference between sons and daughters in number of symptoms is smaller in the condition where more support is perceived. Additionally, we assumed that this would hold for both depression and anxiety. We found a significant three-way interaction between gender, support, and stress, but only for depression symptoms. Our expectations are thus partly confirmed. However, certain limitations of our study must be considered.

A first limitation is that our data are cross-sectional. We argued that low perceived social support and problems in parent-offspring communication precede the development of depression and anxiety symptoms. We acknowledge that, since our data are cross-sectional, reciprocal causation between on the one hand perceived support and stress and on the other symptoms cannot be ruled out. Secondly, we relied on self-report data on all measures. Such a single-method approach is sensitive to reporting bias, which can inflate main effects, but it is difficult to see how this can produce a third order interaction effect. Finding the three-way interaction therefore supports the interpretation of our results. A possible third limitation is that our measures of social support and stress are conceptually and empirically related. Parents are important support providers for adolescents and young-adults to such an extent that parental support remains the best indicator of emotional problems in adolescence and young-adulthood (Helsen, Vollebergh, & Meeus, 2000). Therefore, problems in parent-offspring communication must influence the youngster's perception of available support. On the other hand, in multivariate analyses the effects of the variables are adjusted for each other. To substantiate our findings,

replication is needed in a longitudinal or experimental design preferably using multiple informants, multiple methods, and measures that make a clearer distinction between social support and stress. Nonetheless, we found a significant three-way interaction between gender, stress and support, where others did not.

Our sample consisted of offspring of psychiatric patients of whom several already had developed clinical depression and anxiety. In line with Garber and Flynn (2001), we argued that the effect of social support is probably most salient in high-risk individuals. Mechanisms relevant to the development of depression and anxiety are more likely to surface in a high-risk sample, if only because high-risk samples offer more variation in risk factors and symptoms than normal population samples. More variation increases the likelihood of finding associations. However, it might alternatively be argued that the effect that we reported is merely caused by an overly negative state-dependent appraisal by our subgroup of clinically depressed or anxious participants (Robinson & Garber, 1995). In line with our argument regarding reporting bias, results were similar in our additional analysis from which those individuals who experienced a current episode were excluded.

Symptoms of the parental disorder may cause problems in the interaction between parent and child, but these problems are observed in adolescence and young adulthood in general as well (Collins, 1990; Jackson et al., 1998; Steinberg, 1990). Therefore, although sixty percent of the parents did not experience interference of psychiatric symptoms in their interpersonal relations in the year preceding assessment, the quality of parent-offspring communication is relevant to all our participants. Moreover, Garber and Flynn (2001) argued that interpersonal stressors such as interpersonal conflict are more likely to lead to depression than stressors of another nature. Given that it is additionally assumed that interpersonal stress has a larger impact on females, our focus on problems in parent-offspring communication may have contributed to finding a significant gender difference in the effect of perceived social support on stress. Interestingly, though, when the three-way analysis included problems in father-offspring and mother-offspring communication separately, the gender difference in the buffer-effect of social support only was significant in relation to problems in father-offspring communication. This finding is in line with the suggestion of Connell & Goodman (2002) that we should be aware of differential effects from mothers and fathers on offspring symptoms, not only concerning the effects of maternal versus paternal psychopathology, but also concerning quality of parent-offspring relationships. Unfortunately, we did not have large enough groups of offspring with only an affected father versus only an affected mother to conduct reliable analyses that account for the differential effects of paternal versus maternal psychopathology.

Depression and anxiety symptoms are not considered simultaneously very often. Some important work has been done on the specificity of stressful life-events and

circumstances (e.g., Brown, Harris, & Eales, 1996), but in general only depression is considered. Wade and Kendler (2000b) focused primarily on the relation between social support and depression as well, but did an additional analysis on generalised anxiety disorder. Contrary to our findings, they reported that the overall pattern for generalised anxiety disorder is similar to that for depression. In the present study we used measures of depression and anxiety symptomatology that differentiated as much as possible between the two types of problems. This resulted in an anxiety score based on symptoms of primarily Panic Disorder. We consider this scale to be a representation of the "core" elements of anxiety, without the elements that depression and anxiety often share, such as worrying or self-blame. In our opinion, the high correlation between the depression and anxiety scales is more likely to be a reflection of true comorbidity than of measurement inspecificity (Angold, Costello, & Erkanli, 1999; Hartman et al., 2001). Comorbidity of depression and anxiety complicates the efforts to find specific rather than generic risk and protective factors relevant to the development of depression and anxiety. Nevertheless, the present study shows that a first step to get a better insight in the relevance of individual factors is to study depression and anxiety simultaneously, using measures that differentiate between depression and anxiety as much as possible.

In conclusion, our results indicate that the gender difference in the buffer-effect of social support is evident in high-risk participants in relation to depression symptoms, when both the quantity and quality of perceived social support relations and interpersonal stress are considered. The effect of social support on anxiety symptoms was only significant as a first order effect; when the interaction with gender was entered the first order effect was no longer significant. This implies that social support as such is not relevant in relation to anxiety. Research should more often compare vulnerability models rather than individual risk factors. According to Garber and Flynn (2001) the relevance of individual factors can only be established in more complex moderator and mediation models that explore how factors work together in the development of different disorders. The present findings illustrate the importance of considering both the reciprocal relations between etiological factors and multiple disorders.

Chapter 6

Effortful control, neuroticism, and extraversion: Effects on anxiety and depression

Catharina A. Hartman, Karlien M.C. Landman-Peeters, Albertine J. Oldehinkel,
Anne Boomsma, Marijtje A.J. van Duijn, Johan A. den Boer,
Ruud B. Minderaa, & Johan Ormel. *Submitted.*

Individuals proficient in temperamental effortful control appear better able to regulate reactive temperamental traits such as neuroticism and extraversion. The present study investigated whether effortful control, and its sub-components attentional, inhibitory, and activation control, protected against anxiety and depression, directly, or through modulation of the effects of neuroticism and extraversion. We used a longitudinal design and a high-risk sample of adolescent and young adult offspring of parents with an anxiety or mood disorder (n=447). Effortful control protected against depression, through attentional and activation control, and against anxiety in individuals high on neuroticism, through attentional and inhibitory control. Findings were consistent across time and stood firm next to the protective effects of extraversion. Attentional control is discussed in light of the ability to disengage from threats or rumination on loss or failure; inhibitory control in light of cognitive inhibition and free working memory space needed by highly neurotic or extraverted individuals for anxiety regulation; and activation control in light of an orientation towards action and self discipline which attenuates the build-up of further sad affect.

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Introduction

We do not all run the same risk of developing anxiety or mood disorders. Part of this variation in susceptibility depends on our personalities or temperaments. Research has established that neuroticism (similar to negative affectivity, the Behavioral Inhibition System [BIS], and the defense system [cf. Evans & Rothbart, 2007; Carver, 2005; Carver, Sutton, & Scheier, 2000], hereafter referred to as neuroticism) is the strongest and most robust susceptibility trait for anxiety and mood disorders. This holds for adults (e.g., Clark, Watson, & Mineka, 1994; Jorm et al., 2000; Ormel, Oldehinkel, & Brilman, 2001; Roberts & Kendler, 1999) as well as for children (e.g., Caspi et al., 1996; John et al., 1994; Lonigan et al., 1997). Neuroticism may be described as emotional instability or a pervasive tendency to experience negative emotions (Eysenck, 1967; Eysenck & Rachman, 1965; John, 1990) and is thought to relate, in particular, to reactivity of the limbic system (Gray, 1982; Kagan & Snidman, 2004).

Neuroticism tends to predict anxiety and depression alike. More specificity in differentially predicting anxiety and depression has been sought by taking into account a second personality trait, extraversion. Extraversion (similar to the Behavioral Activation System [BAS] and the approach or appetitive system [cf. Carver, 2005; Carver Sutton, & Scheier, 2000], hereafter referred to as extraversion) may be described as the tendency to engage in the pursuit of possible incentives, with sub-components such as reward sensitivity, sociability and eagerness, and is thought to relate, in particular, to reactivity of the dopaminergic system (Carver, Sutton, & Scheier, 2000; Depue & Collins, 1999; Derryberry & Tucker, 2006). Low extraversion is hypothesized to particularly underlie depression while being less relevant for anxiety (e.g., Angst, 1998; Carver, 2004; Clark, Watson, & Mineka et al., 1994; Davidson, 1995; Depue & Iacano, 1989). Empirical findings with regard to such differentiation have nonetheless been mixed, and associations between extraversion and anxiety have been reported as well (Bienvenu et al., 2001a; Brown, Chorpita, & Barlow, 1998; Trull & Sher, 1994). One proposed source for this is the high comorbidity between anxiety and depression, which has often not been controlled for (Middeldorp et al., 2006). Besides, literature suggest that the association between low extraversion and anxiety is, in fact, theoretically sound in case of high neuroticism. That is, the overactive defense system in neurotic individuals who are susceptible for anxiety disorders may reduce approach behavior as a form of reactive self-protection (Derryberry & Rothbart, 1997; Derryberry & Tucker, 2006). Thus, part of the inconsistency in findings may be due to the presence of an interaction between neuroticism and extraversion, which, if not modeled, may sometimes present as a main

effect. Two studies, so far, addressed this interaction, one supporting its presence (Gershuny & Sher, 1998) and one not (Jorm et al., 2000).

A temperamental trait that has more recently come into focus regarding its relation with psychopathology is effortful control (see for two recent overviews, Carver, 2005; Nigg, 2006). The notion of effortful control comes from a body of research by Rothbart and her colleagues (cf. Derryberry & Rothbart, 1997; Rothbart & Bates, 1998) wherein a distinction is proposed between individual differences in reactive traits such as neuroticism and extraversion and individual differences in effortful regulatory traits, subsumed in her model under the name of effortful control (similar to ego resiliency [Block & Block, 1980; Carver, 2005] and related to conscientiousness [Nigg, 2000]). Effortful control can be viewed as a set of relatively deliberate control functions needed for voluntary goal-directed behavior (Derryberry, 2002) similar to the domain of executive functioning as described in the neuropsychological literature (Nigg, 2006). In Rothbart's questionnaires, effortful control is operationalized as the operational efficiency of the executive functions in natural settings (cf. Rueda, Posner, & Rothbart, 2004). Individuals with a high capacity for effortful control are good at sustaining their focus on a task or shifting their attention from one task to another as desired (attentional control), withholding responses which are irrelevant, unintended, or inappropriate (inhibitory control), and executing behavior even if this involves activities which are not particularly pleasurable (activation control). The prefrontal cortex in particular is responsible for such high-level executive processing. Importantly, effortful control can be seen as an important trait for voluntary self-regulation, allowing the individual to break out of their reactive tendencies such as high negative emotionality (neuroticism) and reward sensitivity (extraversion). Recent insights from neuro-imaging studies support this proposition. For example, such studies have shown the importance of the role of the prefrontal cortex in attenuating subcortical limbic activation (Hariri et al., 2003; Ochsner et al., 2004). Similarly, in an epidemiological context, attentional regulation, as one sub-component of effortful control, has been shown to interact with emotionality (Eisenberg et al., 2000). Therefore, ineffective regulation of the motivational response systems by effortful control systems may be an important vulnerability factor for psychopathology (Nigg, 2006).

This appealing idea has been investigated and confirmed mostly for children with externalizing disorders (e.g., Eisenberg et al., 1996; Eisenberg et al., 2000; Eisenberg et al., 2001; Lemery, Essex, & Smider, 2002; Lengua, West, & Sandler, 1998; Nelson et al., 1999). Research on the protective role of effortful control for anxiety and mood disorders is still scarce, and the studies that have been done have yielded less consistent as well as smaller effects relative to the externalizing disorders. This led some investigators to propose that effortful control may be more important for the regulation of anger,

approach, positive emotions and exuberance (Rydell, Berlin, & Bohlin, 2003). Others concluded that the regulation of fear, sadness, avoidance and withdrawal has not received enough explicit study as yet (Carver, 2005). There are nonetheless a number of findings that are suggestive of a protective role of (sub-components of) effortful control against anxiety, or more broadly, internalizing problems. Lengua et al. (1998) reported negative cross-sectional correlations between attentional control and parent and self-rated internalizing symptoms in children. Similarly, Eisenberg et al. (2001) reported diminished effortful control in children with internalizing problems relative to healthy children. Also in a cross-sectional study, Muris, De Jong, and Engelen (2004) showed that attentional control was negatively associated with anxiety in children. In a longitudinal study, Lemery et al. (2002) found negative correlations of inhibitory control and attentional control with father- and mother-rated internalizing problems in children. Also in a longitudinal study, Lengua et al. (2005) showed that inhibitory control was negatively associated with post-traumatic anxiety symptoms following the 9/11 terrorist attack. Importantly, three studies have tested the suggestion put forward by Eisenberg and Morris (2002) and Lonigan, Vasey, and Phillips (2004), among others, that the effects of high neuroticism and low effortful control are mutually enhancing to produce an even worse outcome relative to their separate additive effects. Such an interaction effect was found for adolescents' internalizing problems in a cross-sectional study by Muris (2006) and in a longitudinal study by Oldehinkel et al. (2007), but not in the aforementioned study by Muris, De Jong and Engelen (2004) in children.

The findings as reviewed above show that the question as to which personality or temperament dimensions play a role in anxiety and mood disorders above and beyond neuroticism is far from resolved. In the present study we include the "Big Three", that is, neuroticism, extraversion, and effortful control, with an emphasis on the least investigated trait in relation to anxiety and depression, that is, effortful control. One aim of this study is to investigate whether the protective role of effortful control as it has been found in the handful of studies conducted so far is robust when the possibly protective (i.e., fear reducing or mood elevating) effects of extraversion are included in the model as well. Muris et al. (2004) suggested that one possible source for the mixed findings for effortful control in relation to anxiety may be that extraversion has not been taken into account. To date no studies have investigated the combined influence of neuroticism, extraversion, and effortful control on anxiety. A second aim is to determine whether the protective role of effortful control, additive or in interaction with neuroticism or extraversion, extends to depression, which, as is clear from a recent overview on temperament and psychopathology (Nigg, 2006), has not yet been investigated. A third aim is to clarify the hypothesized protective role of effortful control in terms of the sub-components attention,

inhibition, and activation control. Leading researchers in the field of temperament (Derryberry & Tucker, 2006; Eisenberg et al., 2005a; Nigg, 2000; Nigg, Hinshaw, & Huang-Pollock, 2006) have argued for differentiation among different types of effortful control. With regard to anxiety and depression, some studies focused on attentional control, other studies on inhibitory control, but activation control has not been studied so far, nor has the relevance of these three types of voluntary control been determined within a single study. Not only additive but also interactive effects of neuroticism, extraversion and (sub-components of) effortful control on symptom severity are considered. While the importance of studying interactive effects of personality traits on psychopathology is acknowledged (Klein et al., 2002), still little empirical work has been done in this direction.

Method

Sample

The sample is a high-risk sample. Participants are adolescent and young adult children of parents with a mood or anxiety disorder. They take part in the ARIADNE study, which is short for 'Adolescents at Risk of Anxiety and Depression; A combined Neurobiological and Epidemiological approach'. The participants of the ARIADNE study are followed over time in order to further our understanding of the etiological factors involved in the onset and course of anxiety and mood disorders. They were recruited through their parents who were recruited themselves from 16 psychiatric services in the three northern provinces of the Netherlands. Parents had been treated at least once in their lifetime for a mood or anxiety disorder. Their adolescent and young adult children could participate in the study if they were between 13 and 26 years old. Parents received information about the study by mail and were asked if they had biological children in the appropriate age-range, and if so, to confer with their children about participation in the study. While the parents had a mood or anxiety disorder, there were no in- or exclusion criteria as to whether the adolescents and young adult participants had a psychiatric disorder or not. The study design has been described more extensively by Landman-Peeters et al. (2005). For the purpose of the present study we used the data from three measurement occasions, each with one year apart: temperament measured at baseline (T1) and anxiety and depression outcome variables at one (T2) and two year follow-up (T3). A total of 447 (176 males and 271 females) adolescents and young-adults had complete data on the measures used here. When recruited, their mean age was 18.7 years (*SD*=3.3).

Measures

Psychopathology. Depression and anxiety symptoms were measured with items from the DSM-IV Questionnaire by means of self-report (Hartman, 2002; Hartman et al., 2001; Landman-Peeters et al., 2005; Muris, 2006; Muris, Winands, & Horselenberg, 2003). Participants were asked to report on a 4-point Likert-scale as to what extent descriptions of symptomatic behavior had applied to themselves with regard to the previous 12 month-period, that is, between T1 and T2, and between T2 and T3.

An important methodological challenge is to differentiate between anxiety and depression. Anxiety and depression are often comorbid conditions; hence anxiety and depression scales are often highly correlated. However, apart from this true co-occurrence of anxiety and depression symptoms, measurement is often imprecise such that measures of anxiety often include items that measure depression, and vice versa (cf. Chorpita & Daleiden, 2002; Stark & Laurent, 2001). Therefore, we took great care to tease our measures of anxiety and depression apart. This was done by exploratory factor analyses of the DSM-IV symptom ratings at T1, T2 and T3, respectively, using the maximum likelihood estimation method with oblique (promax) rotation. We selected items that had a main factor loading of at least 0.30 on the appropriate scale and a difference of at least 0.20 between the main loading and the secondary loading if present. To ensure robustness of the findings, these criteria needed to be fulfilled at all three measurement occasions. (Note that while for our substantive analyses we chose a longitudinal perspective, with temperament [T1] predating anxiety and depression outcome measures [T2 and T3], for these factor analyses information of T1 DSM-IV ratings was additionally included for the purpose of constructing subscales that are maximally stable in their differentiation of anxiety and depression).

Table 1 shows the factor solutions of the items that behaved according to these criteria, at T1, T2, and T3. The depression factor consists of items that emphasize sad affect, loss of pleasure, reduced energy, low self-worth, and the absence of positive affect (rescored). The anxiety factor consists of items that emphasize panic-related symptoms and physiological hyper-arousal symptoms that accompany these. Items that were originally included in the analyses but were not retained measured several worries that pertain to Generalized Anxiety Disorder. They did not differentiate between anxiety and depression (high loadings on both the anxiety and the depression factor), which is consistent with the literature (Brown, Chorpita, & Barlow, 1998; Krueger, 1999; Vollebergh et al., 2001).

The items of the depression and anxiety factors that fulfilled the criteria were summed. Internal consistency reliabilities were 0.93 and 0.92 for the Depression scales at

Table 1 Factor loadings on anxiety and depression factors at T1, T2, and T3 (*n*=447)

	T1		T2		T3	
	Factor 1	Factor 2	Factor 1	Factor 2	Factor 1	Factor 2
I was extremely nervous	0.076	0.552	0.137	0.476	0.106	0.566
I had difficulty going places when not accompanied by my parent(s)	-0.081	0.376	0.037	0.295	0.001	0.380
I panicked when I was alone outside the home	-0.123	0.662	-0.042	0.643	-0.239	0.820
I felt panicky when I had to travel on my own (like by car. on the train or on the bus)	-0.153	0.679	-0.210	0.791	-0.167	0.721
I panicked in crowded places	-0.038	0.661	-0.110	0.759	0.008	0.710
I had moments that I had intense fear that I would die	0.066	0.431	0.003	0.550	-0.051	0.535
I feared losing control (such as by doing embarrassing things, fainting, etc.)	-0.077	0.685	-0.059	0.748	-0.069	0.778
I was really concerned about what I felt in my body	-0.019	0.675	0.141	0.508	0.076	0.567
I suddenly became very anxious in situations where most people are not anxious	0.105	0.606	0.044	0.654	-0.016	0.765
I felt dizzy	0.065	0.467	0.195	0.391	0.137	0.472
I was trembling or shaking	0.026	0.535	0.065	0.445	0.073	0.533
I had a feeling that I would suffocate	0.156	0.364	0.161	0.411	0.144	0.450
I suffered from heart palpitations	-0.007	0.598	0.176	0.406	0.141	0.576
I was troubled by numbness or tingling sensations in my arms or legs	0.032	0.358	-0.110	0.542	-0.121	0.636
I felt nauseous	0.044	0.478	0.089	0.464	0.041	0.490
I had stomachaches	0.027	0.499	0.052	0.463	0.209	0.443
I worried a lot that I might be ill	-0.058	0.621	0.035	0.599	0.074	0.564
I felt dejected	0.732	0.155	0.871	0.012	0.830	0.045
I felt like crying	0.616	0.229	0.765	0.078	0.630	0.078
I felt helpless	0.619	0.227	0.764	0.084	0.679	0.218
I felt worthless	0.626	0.234	0.701	0.188	0.728	0.151
I had little faith in my achievements	0.493	0.218	0.452	0.180	0.466	0.205
I felt pessimistic about the future	0.547	-0.010	0.682	-0.085	0.539	0.128
I was low on energy and felt tired without apparent reason	0.461	0.254	0.595	0.143	0.601	0.168
I experienced little pleasure in daily things	0.840	-0.122	0.733	0.026	0.725	0.010
I lost my interest in things or activities	0.670	-0.058	0.653	0.001	0.690	-0.119
I was inactive, I could not get things going, I felt "slowed"	0.549	0.132	0.560	0.086	0.596	0.040
I thought about committing suicide	0.504	0.095	0.492	0.027	0.419	0.085
I was happy (rescored)	0.819	-0.247	0.690	-0.160	0.715	-0.205
I enjoyed things (rescored)	0.710	-0.166	0.647	-0.086	0.720	-0.127
I had enough energy to do my daily duties (rescored)	0.567	0.000	0.500	-0.027	0.546	-0.075
I was optimistic about the future (rescored)	0.728	-0.147	0.658	-0.098	0.686	-0.105
I felt good about myself (rescored)	0.714	-0.016	0.647	-0.023	0.728	-0.085

T2 and T3, repectively. They were 0.89 and 0.90 for the Anxiety scales at T2 and T3, respectively.

Temperament. Temperament was measured by means of the Adult Temperament Questionnaire (ATQ) (Rothbart, Ahadi, & Evans, 2000). Participants rated the items on a 4-point Likert scale with 1 indicating that the item does not at all describe the person and 4 indicating an item to be highly descriptive of the person.

Neuroticism, or negative affectivity in Rothbart's terminology, is associated with potentially threatening or unpleasant stimuli and the experience of negative feelings. The sub-components comprised by the total Negative affectivity scale of the ATQ are Fear (unpleasant affect associated with anticipation of pain or distress), Frustration (unpleasant affect associated with task interruption or the blocking of a desired goal), Reactive sadness (unpleasant affect and lowered mood related to disappointment, loss, and exposure to suffering), and Discomfort (negative affect related to stimulation of visual, auditory, smell/taste and tactile stimulation) (Derryberry & Rothbart, 1988; Evans & Rothbart, 2007). The items pertaining to each of these sub-components were summed. Estimates of the correlation between negative affectivity in the ATQ and measures of Big Five neuroticism are fairly high (around 0.70) (Evans & Rothbart, 2007). Internal consistency reliability was 0.85 for the Negative affectivity scale in our sample.

Extraversion is associated with potentially appetitive stimuli and the experience of positive affect. The different sub-components comprised by the total Extraversion scale are High intensity pleasure (enjoyment related to high levels of novelty and intensity), Sociability (enjoyment derived from social interaction and being in the presence of others), and Positive affectivity (intensity, duration, frequency, rate of onset, and rising intensity of pleasure). Extraversion as operationalized in the ATQ maps fairly well on measures of extraversion of the Big Five model (correlations around 0.65) (Evans & Rothbart, 2007). Internal consistency reliability was 0.82 for the Extraversion scale in our sample.

Effortful control comprises a set of control functions needed for voluntary goal-directed behavior similar to the domain of executive functioning as described in the neuropsychological literature. It is operationalized by the sub-components Attentional control (capacity to voluntary focus as well as shift attention), Inhibitory control (capacity to suppress inappropriate approach behavior), and Activation control (capacity to perform activities that one would rather avoid). Note that inhibitory control, that is, voluntary, flexible control of behavior, is separate from behavioral inhibition, which refers to reactive suppression of behavior motivated by fear or shyness (Carver, 2005; Kagan & Snidman, 2004). Behavioral inhibition is more directly associated with the personality trait of neuroticism and hence a risk rather than a protective factor for psychopathology

(Rothbart & Bates, 1998). Effortful control shows a substantial correlation with conscientiousness of the Big Five model (around 0.60) (Evans & Rothbart, 2007). Internal consistency reliability was 0.84 for the Effortful control scale in our sample. In the present study, we focused specifically on the sub-components of Effortful control. Internal consistencies were 0.80, 0.68, and 0.78 for Attention, Inhibition, and Activation control, respectively.

Statistical analyses

Zero-order correlation coefficients of all relevant measures were calculated for basic insight into patterns of association in the data. Next, we conducted a series of hierarchical regression analyses to examine main and moderating effects of temperament on anxiety and depression. The regression analyses were done in two steps. In step 1 we investigated the main effects of neuroticism, extraversion, and effortful control as measured on T1 on anxiety and depression at T2 and T3. Effortful control was studied both at the aggregated and at sub-component level, that is, attentional control, inhibitory control, and activation control, respectively. In step 2 these analyses were repeated with the inclusion of all two- and three-way temperament interactions in the regression equations. Analyses were done for both T2 and T3 to determine whether effects were consistent across time. In all regression analyses we controlled for gender and age.

Results

Bivariate associations

Zero-order correlations between T1 temperamental traits, gender, age, and T2 and T3 psychopathology are presented in Table 2 for purposes of data description. Both anxiety and depression are highly stable from T2 to T3, depression somewhat less than anxiety. Consistent with this, age is not correlated with anxiety, but shows some positive association with depression. Anxiety and depression are more strongly associated at T2 than at T3, suggesting more differentiation when participants get older. Gender shows a somewhat stronger association with anxiety than with depression, with the higher scores for girls.

Neuroticism at T1 is correlated about equally with anxiety and depression, at T2 and T3, with a minor reduction in magnitude with passing of time. Extraversion at T1 is more strongly correlated with depression than with anxiety, at T2 and T3 also with some reduction across time. The correlations of sub-components of effortful control at T1 with

Table 2 Pearson correlation matrix of T2 anxiety and depression, and T3 anxiety and depression and T1 neuroticism, extraversion, effortful control, gender, and age (*n*=447)

	T2 anxiety	T2 depression	T3 anxiety	T3 depression	T1 neuroticism	T1 extraversion	T1 effortful control	T1 attentional control	T1 inhibitory control	T1 activation control	Gender
T2 anxiety	1.00										
T2 depression	0.63	1.00									
T3 anxiety	0.77	0.49	1.00								
T3 depression	0.55	0.69	0.63	1.00							
T1 neuroticism	0.55	0.54	0.49	0.48	1.00						
T1 extraversion	-0.28	-0.43	-0.22	-0.36	-0.47	1.00					
T1 effortful control	-0.25	-0.29	-0.22	-0.25	-0.39	0.05	1.00				
T1 attentional control	-0.26	-0.29	-0.27	-0.27	-0.45	0.15	0.81	1.00			
T1 inhibitory control	-0.18	-0.11	-0.15	-0.07	-0.30	-0.14	0.73	0.46	1.00		
T1 activation control	-0.11	-0.24	-0.08	-0.22	-0.14	0.10	0.72	0.39	0.22	1.00	
Gender	-0.26	-0.16	-0.23	-0.14	-0.38	-0.01	0.04	0.07	0.16	-0.12	1.00
Age	0.06	0.14	0.05	0.12	0.12	-0.18	0.21	0.14	0.21	0.12	-0.01

Correlations <0.10 were not significant from zero at α=0.05

anxiety and depression are rather stable across time, with similar associations of attentional control with anxiety and depression, inhibitory control somewhat more strongly correlated with anxiety than with depression, and activation control somewhat more strongly correlated with depression than with anxiety.

Neuroticism has a moderate negative correlation with extraversion as well as with effortful control. The latter effect is strongest for attentional control, followed by inhibitory control, and activation control. Extraversion is not correlated with effortful control. The latter null effect constitutes a mixture of small positive correlations with attention and activation control and a small negative correlation with inhibitory control.

Table 3 T2 anxiety and T3 anxiety regressed on T1 temperament variables (*n*=447)

		T2 anxiety		T3 anxiety	
		B	*p*	*B*	*p*
Model neuroticism, extraversion, and effortful control					
Step 1	Neuroticism	.48	.00	.44	.00
	Extraversion				
	Effortful control				
Step 2	Neuroticism	.47	.00	.44	.00
	Extraversion				
	Effortful control				
	Neuroticism × extraversion	-.16	.00	-.11	.00
	Neuroticism × effortful control	-.08	.02	-.08	.05
	Extraversion × effortful control				
	Neuroticism × extraversion × effortful control				
Model neuroticism, extraversion and attentional control					
Step 1	Neuroticism	.49	.00	.41	.00
	Extraversion				
	Attentional control				
Step 2	Neuroticism	.49	.00	.42	.00
	Extraversion				
	Attentional control				
	Neuroticism × extraversion	-.16	.00	-.08	.04
	Neuroticism × attentional control	-.08	.05	-.09	.02
	Extraversion × attentional control				
	Neuroticism × extraversion × attentional control				
Model neuroticism, extraversion, and inhibitory control					
Step 1	Neuroticism	.49	.00	.46	.00
	Extraversion				
	Inhibitory control				
Step 2	Neuroticism	.48	.00	.45	.00
	Extraversion				
	Inhibitory control				
	Neuroticism × extraversion	-.16	.00	-.12	.00
	Neuroticism × inhibitory control	-.13	.00	-.13	.00
	Extraversion × inhibitory control	-.09	.02	-.13	.00
	Neuroticism × extraversion × inhibitory control				
Model neuroticism, extraversion, and activation control					
Step 1	Neuroticism	.49	.00	.45	.00
	Extraversion				
	Activation control				
Step 2	Neuroticism	.48	.00	.45	.00
	Extraversion				
	Activation control				
	Neuroticism × extraversion	-.15	.00	-.10	.01
	Neuroticism × activation control				
	Extraversion × activation control				
	Neuroticism × extraversion × activation control				

Gender and age were part of the regression equation in all analyses; the dependent variables were standardized; cross-products were formed of the *z*-scores of individual predictors in the equation; thus the *B*-coefficients represent the proper standardized solution (see Cohen et al., 2003, p. 283)

Main and interactive effects of temperament on anxiety

Table 3 provides the results of the regression analyses with anxiety at T2 and T3 as the dependent variable. T1 predictors were neuroticism and extraversion with effortful control, attentional control, inhibitory control, or activation control, respectively. Only statistically significant regression coefficients are listed to simplify presentation.

A consistent and substantial main effect for neuroticism was found. Thus, as has repeatedly been shown in previous research, high temperamental neuroticism as measured at T1 predicts later anxiety complaints at T2 and T3. We found no main effects for extraversion or effortful control, nor for any of the sub-components attentional control, inhibitory control, or activation control, respectively. This held both at T2 and T3.

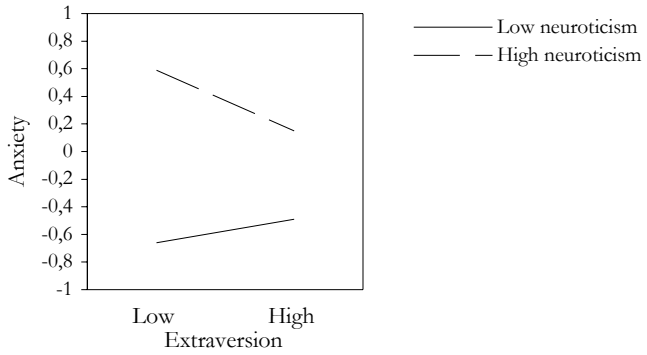

Figure 1 Interaction effect of neuroticism and extraversion on anxiety

There were no three-way but several two-way interaction effects. We found a consistent interaction effect between neuroticism and extraversion on anxiety, at T2. This was replicated for T3 anxiety. To interpret this interaction effect, we plotted the two-way interactions for one standard deviation above and below the mean on neuroticism and extraversion, holding effortful control, or its sub-components, constant at the mean score level. The plots were very similar across all eight analyses. Figure 1 illustrates the interaction between neuroticism and extraversion at T2, at mean levels of effortful control. Adolescents with relatively high neuroticism tend to have less anxiety complaints

when they are extraverted than when they are introverted. Conversely, adolescents with relatively low neuroticism who are extraverted tend to have somewhat more anxiety complaints. Thus, extraversion reduces anxiety in combination with neuroticism, but enhances anxiety somewhat in combination with low neuroticism.

We found a two-way interaction between neuroticism and effortful control on anxiety problems at T2. This effect was replicated for T3 anxiety. Figure 2 illustrates, for T2, at mean levels of extraversion, that individuals with high neuroticism have less anxiety complaints when they have high effortful control than when they have low effortful control. Effortful control is irrelevant for anxiety problems at relatively low levels of neuroticism.

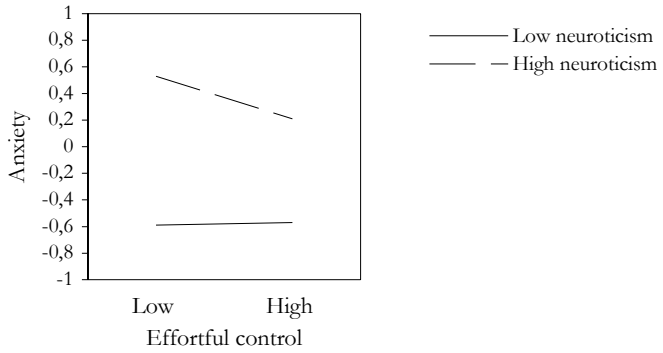

Figure 2 Interaction effect of neuroticism and effortful control on anxiety

Looking subsequently in more detail at the three sub-components of effortful control, the results in Table 3 indicate that this effect holds for attentional control and inhibitory control, but not for activation control. These effects were consistent for T2 and T3. The plots for attentional control and inhibitory control were very similar to those for effortful control (as was illustrated by Figure 2)

At the sub-component level we found one additional interaction between inhibitory control and extraversion. This effect was present both at T2 and T3. Figure 3 illustrates, for T2, that, at average levels of neuroticism, high inhibitory control protects only for anxiety in individuals who are high on extraversion. At low levels of extraversion, individuals with high inhibitory control have similar anxiety scores as those with low inhibitory control.

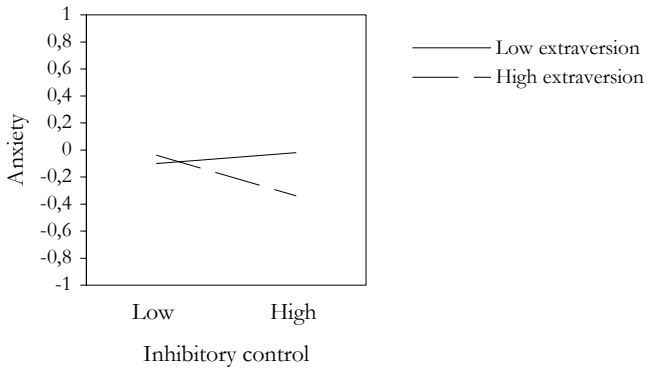

Figure 3 Interaction effect of extraversion and inhibitory control on anxiety

Main and interactive effects of temperament on depression

Statistically significant effects of T1 temperament on T2 and T3 depression are provided in Table 4. Our analyses of the main effects revealed, firstly, an effect for neuroticism on depression symptoms: high neuroticism predicts depression. This effect was consistent for T2 and T3. Secondly, we found a main effect of extraversion, that is, introverted individuals are more likely to experience depression symptoms than extraverted individuals. This effect was present at T2 and T3. Thirdly, we found main effects of effortful control and two of its sub-components, i.e., attentional control and activation control. High effortful control is associated with lower depression scores. Attentional control and activation carry this effect but not inhibitory control. Again, these effects were consistent at both T2 and T3. Together these three main effects indicate that individuals with high neuroticism, low extraversion, and low effortful control have the highest depression scores, while individuals low on neuroticism, high on extraversion, and high on effortful control have the lowest depression scores.

On top of these main effects, we found three-way interaction effects between neuroticism, extraversion, and effortful control, and its sub-components, for all but one analysis (i.e., analysis 4 at T2, β=0.04, p=0.13). These three-way interactions were plotted and showed that the aforementioned main effects can be qualified as follows: The protective effect of extraversion for depression (main effect) is reduced or absent in individuals with low neuroticism and high effortful control. Thus, in those who are least depression prone, high or low extraversion makes little difference. These three-way interaction effects are illustrated by Figure 4 which depicts activation control at T3.

Table 4 T2 depression and T3 depression regressed on T1 temperament variables (*n*=447)

		T2 depression		T3 depression	
		B	*p*	*B*	*p*
Model neuroticism, extraversion, and effortful control					
Step 1	Neuroticism	.35	.00	.33	.00
	Extraversion	-.25	.00	-.19	.00
	Effortful control	-.14	.00	-.11	.03
Step 2	Neuroticism	.33	.00	.33	.00
	Extraversion	-.29	.00	-.23	.00
	Effortful control	-.24	.00	-.22	.00
	Neuroticism × extraversion	-.10	.00		
	Neuroticism × effortful control	-.08	.02	-.08	.05
	Extraversion × effortful control				
	Neuroticism × extraversion × effortful control	-.16	.00	-.20	.00
Model neuroticism, extraversion and attentional control					
Step 1	Neuroticism	.37	.00	.35	.00
	Extraversion	-.23	.00	-.17	.00
	Attentional control	-.11	.02	-.10	.04
Step 2	Neuroticism	.38	.00	.37	.00
	Extraversion	-.27	.00	-.21	.00
	Attentional control	-.16	.00	-.15	.00
	Neuroticism × extraversion	-.14	.00		
	Neuroticism × attentional control				
	Extraversion × attentional control				
	Neuroticism × extraversion × attentional control	-.09	.00	-.09	.00
Model neuroticism, extraversion, and inhibitory control					
Step 1	Neuroticism	.44	.00	.42	.00
	Extraversion	-.22	.00	-.15	.00
	Inhibitory control				
Step 2	Neuroticism	.40	.00	.40	.00
	Extraversion	-.26	.00	-.18	.00
	Inhibitory control				
	Neuroticism × extraversion	-.09	.01		
	Neuroticism × inhibitory control				
	Extraversion × inhibitory control				
	Neuroticism × extraversion × inhibitory control	-.06	.04	-.07	.02
Model neuroticism, extraversion, and activation control					
Step 1	Neuroticism	.39	.00	.36	.00
	Extraversion	-.22	.00	-.17	.00
	Activation control	-.17	.00	-.16	.00
Step 2	Neuroticism	.38	.00	.36	.00
	Extraversion	-.22	.00	-.16	.00
	Activation control	-.21	.00	-.23	.00
	Neuroticism × extraversion	-.09	.01		
	Neuroticism × activation control				
	Extraversion × activation control				
	Neuroticism × extraversion × activation control			-.08	.01

Gender and age were part of the regression equation in all analyses; the dependent variables were standardized; cross-products were formed of the z-scores of individual predictors in the equation; thus the *B*-coefficients represent the proper standardized solution (see Cohen et al., 2003, p. 283)

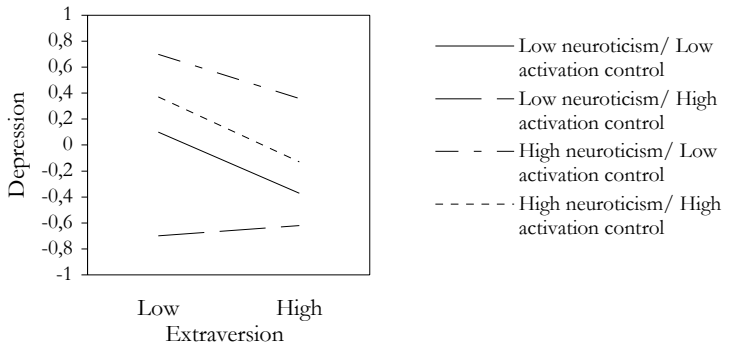

Figure 4 Interaction effect of neuroticism, extraversion, and activation control on depression

Discussion

In the present paper we investigated the simultaneous effects of the "Big Three" in temperament research (cf. Carver, 2005; Nigg, 2000; Rothbart, Ahadi, & Evans., 2000), that is, neuroticism, extraversion, and effortful control, on anxiety and depression. The emphasis was particularly on effortful control, and its sub-components attentional, inhibitory, and activation control. This was done using a longitudinal design in a high-risk sample of adolescent and young adult offspring of parents with an anxiety or mood disorder. We found that effortful control protected against anxiety in individuals high on neuroticism. The protective role of effortful control extended to depression, as a main effect, that is, regardless of someone's stance on neuroticism. In terms of effortful control's sub-components, attentional control and inhibitory control in particular were responsible for the effects on anxiety, while attentional and activation control protected particularly against depression. These effects of effortful control stood firm next to the protective effects of extraversion, which, consistent with the literature, were found for anxiety only in individuals high on neuroticism, and for depression as a main effect. The findings were remarkably robust across the two measurement occasions.

Attentional control was protective for both anxiety and depression. The proposed working would be through the ability to cut off negative emotion by shifting attention from threatening stimuli, worries, or self-depreciating thoughts and focus attention on alternative, affectively neutral or positive thoughts or stimuli (Eisenberg et al., 2005a;

Eisenberg & Fabes, 1992; Rothbart, Ziaie, & O'Boyle, 1992). Indeed, direct evidence of the inability to shift attention away from negative stimuli has been shown by studies using an experimental design in anxious (Derryberry & Reed, 2002; Fox, Russo, & Dutton, 2002) as well as dysphoric (Koster, et al., 2005) participants. Difficulties with disengaging from threatening stimuli perpetuates the continuous processing of this information and hence enhances vulnerability to anxiety disorders (Nigg, 2006). Similarly for depression, rumination can be viewed as a difficulty to volitionally distract one's attention towards something else rather than the unpleasant event (Larsen & Prizmic, 2004; Nolen-Hoeksema, 1993). Present and past studies (Muris, 2006; Oldehinkel et al., 2006) thus suggest that volitional attentional control constrains such biased information processing.

The ability for inhibitory control, which involves down-regulation of irrelevant, unintended, or inappropriate responses, protected against anxiety. This held for those who were high on neuroticism, as well as for those high on extraversion. Inhibitory control was not associated with depression. Although previous studies on temperamental inhibitory control and anxiety did not consider interaction effects, their findings are consistent with ours in showing a protective effect (Lemery, Essex, & Smider, 2002; Lengua, Long, & Smith, 2005). Besides its role in the temperament literature, inhibitory control plays a prominent role in the cognitive literature (Nigg, 2000). Findings on the nature of the association between experimental measures of inhibitory control and anxiety diverge. Better performance (Krikorian, Zimmerman, & Fleck, 2004; Murray & Kochanska, 2002; Thorell, Bohlin, & Rydell, 2004), equal performance (Daugherty, Quay, & Ramos, 1993; Oosterlaan & Sergeant, 1996; Schachar & Logan, 1990), as well as worse performance (Segal, 1996; Tannock, Ickowicz, & Schachar, 1995; Yee & Vaughan, 1996) in anxious respondents relative to normal controls have been reported. Differences in cognitive tasks across these studies likely explain this apparent inconsistency. Better or equal performance for anxious individuals relative to normal controls has been found on relatively pure tasks of response inhibition, such as Go/NoGo and Stop-signal tasks. In contrast, worse performance has been found when inhibition was operationalized in terms of cognitive inhibitory control that involved working memory and control of interfering information. Thus, the neuropsychological literature seems consistent in that anxious individuals are not impaired in primary motor inhibition per se. By contrast, decreased working memory in anxious individuals is consistent with the two major theories on anxiety and cognitive performance by Eysenck and Calvo (1992) and Humphreys and Revelle (1984), respectively. Importantly, our questionnaire measure of inhibitory control (ATQ), operationalized in terms of everyday situations, indeed taps more complex response organization than the interruption of prepared motor responses. For example, the behaviors comprised by the items may require individuals to step out of the immediate

situation, consider long term consequences of the dominant response, consider possible response options, and choose a subordinate response if deemed necessary. This requires interference control, or control over the contents of working memory, working in union with motor control (cf. Mitchell, Macrae & Gilchrist, 2001; Yee & Vaughan, 1996). Consistent with this line of reasoning, inhibitory control using the ATQ (as used here), or the child equivalent measure (CBQ) were shown to be negatively associated with cognitive interference as measured in laboratory tasks (Gerardi-Caulton, 2000; Posner et al., 2002). In sum, our findings of lower anxiety in individuals with higher ability for inhibitory control seem consistent with findings from the cognitive literature as indicated by performance on inhibition tasks that require working memory and interference control. We propose that real-life inhibitory control as measured in the ATQ requires motor control working in concert with working memory. Individuals proficient on this, who are also high on neuroticism may have just that extra bit of oversight so as not to let oneself flood with feelings of anxiety. In the same manner for exuberant, socially outgoing and reward oriented individuals, the ability to control approach tendencies through reflection and motor inhibition may hold positive affective arousal in a more manageable and pleasurable (rather than anxiety evoking) range (Fox & Calkins, 2003).

Activation control measures the capacity to perform mundane actions that have few tangible incentives, yet ought to be done nonetheless. The ability to mobilize and sustain the execution of such less preferred behaviors was found to protect against depression, but not anxiety. While, to our knowledge, the association between temperamental activation control and depression has not been studied before, the present protective effect seems consistent with findings from the broader domain of adult personality research. Firstly, self-discipline, a facet of the higher order personality trait conscientiousness, which taps the ability to begin tasks and complete them despite boredom, shows the highest conceptual overlap with activation control. It has been shown that relative to the other five facets of conscientiousness low self-discipline has the strongest association with depression (Bienvenu et al., 2001b; Rector et al., 2002) as well as with suicidal ideation (Velting, 1999). Secondly, the trait of self-oriented perfectionism (i.e., setting high personal standards; note the distinction from socially prescribed perfectionism that is associated with neuroticism), which overlaps conceptually with activation control, was shown to be negatively associated with depression (Flett, Russo, & Hewitt, 1994). Thirdly, activation control is partly operationalized in the ATQ in terms of control on procrastination. It has been shown that self-discipline and procrastination are highly (negatively) associated (Johnson & Bloom, 1995; Schouwenburg & Lay, 1995; Watson, 2001). Work by Lay and colleagues revealed that the aversiveness of the task was an important aspect of procrastination (Lay & Silverman, 1996), and that dejection rather

than anxiety resulted from procrastination (Lay, 1995). Together these findings suggest that activation control, or the capacity to self-motivate for activities that have few immediate incentives (cf. Cervone et al., 2006) is consistently associated with depression. By extension, low activation control may, in addition to motivational beliefs that nothing will change the situation anyway, underlie the association between depression and passive coping strategies as well (e.g., Matheson & Anisman, 2003). Active coping, like activation control, requires the execution and maintenance of a strategy that runs counter to more easy and automated strategies (Derryberry, Reed, & Pilkenton-Taylor, 2003). Possibly, then, the protective working of activation control is that an orientation towards action and self discipline attenuates the possibility that small set-backs can get on top of one, as such constraining the build-up of further sad affect and passive (and hence sadness enhancing) coping strategies.

While of the same magnitude as in previous studies on the protective effects of effortful control on emotional disorders, current effects are not strong. Although this is not to say that small effects are unimportant (see Shiner & Caspi, 2003, for a clear account of why not) we want to propose two causes as to why the effects of effortful control are likely to be modest. The first cause has to with the complexity of self-regulation and its measurement. As summarized by Derryberry and Tucker (2006), effortful control is only one of many regulatory systems (involuntary attention, central arousal, motor, autonomic, and endocrine systems) all of which influence one another as well as the motivational sub-systems (the defense system or neuroticism, the appetitive system or extraversion) to produce a highly variable behavioral outcome. Put differently, in the present research, there are many unknowns within the individual apart from effortful control that exert their influence. Moreover, research has indicated that the effects of temperament on developmental outcome are rarely direct, but rather, in transaction with the environment (e.g., family environment, life events) (Frick, 2004). Yet even if such contextual factors are brought into the analysis, effects are likely to be small relative to experimental research designs in which negative and positive incentive context can be manipulated and varied, thereby fully gauging temperamental effects (cf. Nigg, 2006). While we currently speculated on the process of how the effects of voluntary attentional, inhibitory, or activation control may take place (e.g., voluntary attentional disengagement, free working memory space for extra oversight, self-discipline and action for defying depression build-up), such mechanisms can be captured directly in experimental designs, presumably with larger effects.

Secondly, we want to point out a possible cause as to why effects are small for anxiety and depression relative to effects reported for externalizing disorders. It has been argued convincingly that all questionnaire measures of effortful control as well as

laboratory executive functioning tasks comprise aspects of executive processes, involving the flexible control of behavior, and aspects of reactive processes, involving reactive behavior motivated by emotions such as fear (Nigg, 2000; Nigg et al., 2005). On a predominantly motivational measure the prediction would be that anxious or depressive individuals have higher scores than individuals from an unaffected comparison group (for example, Kochanska, Coy & Muray [2001] found a *positive* association between reactive behavioral inhibition [i.e., children suppressed behavior in line with prohibitions by their mother] and fearfulness). In contrast, as was hypothesized in this paper, anxious and depressive children would have lower scores relative to an unaffected comparison group on a predominantly executive measure. Thus, in individuals with internalizing problems, executive and motivational control exert opposite influences, and the net effect on measures that tap both aspects is uncertain. In individuals with externalizing problems, however, the motivational (e.g., reduced reactive inhibition such as loosing temper) and voluntary executive (e.g., reduced motor inhibition) components of a measure work in tandem rather than in opposite directions. Thus, although Rothbart's measure of effortful control is thought to be primarily executive, some mixture of reactive and executive control may nonetheless explain attenuation of the effects on anxiety of depression relative to the larger effects found for externalizing disorders.

One important limitation of the present study is that we were unable to differentiate cause and effect. On the one hand it is clear that individuals differ substantially in their capacity of effortful control (Derryberry & Rothbart, 1997; Muraven & Baumeister, 2000; Rothbart et al., 2003). Indeed, the starting point of the temperament approach and also of the present study is that some people have a larger reservoir of effortful control than others and hence that some people are less susceptible to maladjustment than others. On the other hand, it is also well established that anxiety (Eysenck & Calvo, 1992) and depression (Hartlage, Alloy, & Vázquez, 1993) reduce the available resources for executive information processing. We regard it as likely that the reduced effortful control capacities in individuals with high scores on anxiety and depression encompass both the influence of cognitive control on emotional responses and the reverse effect of emotional states on cognitive processes (Campos et al., 1994; Cole, Michel, & Teti, 1994; Fox 1994). Both may play an important role in the chain of events towards the end result of a full-blown disorder. For example, for depression-prone individuals, high on neuroticism and low on extraversion, the self-regulatory challenge is to overcome these reactive tendencies of having frequent negative emotional states and low incentive motivation. While individuals with strong executive capacities in the face of some normal daily disappointment will be able to disengage from the unattainable goal, refocus their attention, and take up the pursuit of another incentive, the emotional state following disappointment may not be so

transient for individuals at risk for depression. They may remain more easily pre-occupied with the lost goal, and become less easily engaged in some distracting other activity that they like (Carver, 2004). This ruminative coping style (Nolen-Hoeksema, 1993) exhausts the already limited cognitive resources that could otherwise be used to effortfully step out of what is to become a downward spiral. The negative contents of their thoughts will prime other negative memories and amplify their passivity and eventually they may become chronically deficient in cognitive resources. Unable to put over the helm, they may abandon all effort, which precipitates a true depressive episode (Hartlage, Alloy, & Vázquez, 1993). A similar chain of cause and effect could be described for anxiety. Obviously, the dynamic nature of such proposed downward spirals could not be tested in the present research. It requires a longitudinal design with much more dense measurement than used here, such as by the experience sampling method (cf. Caprara & Cervone, 2000, p. 333).

A second limitation with regard to our findings is the reliance on self-report measures. This brings along a certain amount of method bias. For measurement of intra-psychic characteristics such as neuroticism or anxiety/depression, other-report is suboptimal relative to self-report. This may even hold for effortful control, in particular attentional control, also not easily observed by others (Eisenberg et al., 2005a). Clearly, the inclusion of objective laboratory measures of (sub-components of) effortful control in future studies would constitute an important addition to self-report measures.

A third limitation is the following. Despite the need for parsing effortful control into more homogenous sub-components (Derryberry & Tucker, 2006; Eisenberg et al., 2005a; Nigg, 2000; Nigg et al., 2006), their theoretical separateness (Cervone et al., 2006; Derryberry, 2002; Evans & Rothbart, 2007), and their relatively low intercorrelations (see Table 2), it is nonetheless uncertain if the current subdivision into attentional, inhibitory, and activation control is the most valid sub-division, and if these three traits are exhaustive. Discussion as to how sub-components of temperamental effortful control map unto facets of conscientiousness in the Big Five personality model, and unto different executive functioning capacities as differentiated in the cognitive literature, has yet to take place.

A fourth limitation concerns the possible limited generalization of our findings beyond a familial high-risk population. Children of parents with an anxiety or mood disorder are a at high risk for developing psychiatric problems through inherited biological vulnerabilities and more than average exposure to varying environmental risks (e.g., parental discord, lack of warmth) (Goodman & Gotlib, 1999). In a similar vein, strong effortful control capacities have a partial genetic basis and partly develop in interaction with a supportive environment (Eisenberg et al., 2005b). Such findings illustrate an

important asset of our study, that is, our high-risk design ensures the maximum possible variance on both etiological and outcome measures. However, a drawback of this high-risk design is that it is in principle possible that our sample identifies susceptibility or protective factors that do not, or play a different role, in the general population. Given these limitations, current findings clearly await replication.

The present results inform treatment because successful treatment of psychopathology requires the ability to self-regulate (Dale & Baumeister, 1999). For example, cognitive therapy involves gaining control over reactive, automated patterns of negative thought (Derryberry, 2002). Similarly, the learning of more adaptive coping strategies requires the activation and sustenance of difficult and tedious behaviors (Derryberry et al., 2003). It has been shown that through training, such effortful control capacities can be strengthened (Rueda et al., 2005; Wells & Matthews, 1994). In fact, they are likely more amenable to change than the reactive temperament traits of neuroticism and extraversion. Apart from training voluntary control, adaptive environmental stimuli to attend to in situations where automatic negative processing predominates need to be learned (Derryberry & Tucker, 2006; Segal, 1996). Thus, the strengthening of effortful control capacities along with a focus on how these can be applied in different situations provide a feasible handle for successful intervention.

Chapter 7

Sexual assault and emotional problems in young women: Conditional effects of temperament

Karlien M.C. Landman-Peeters, Johan Ormel, Johan A. den Boer, & Catharina A. Hartman. *Submitted.*

The long-term response to sexual assault is found to differ between individuals. In a high-risk sample of young women with a history of parental emotional disorders, the present study examined the role of temperament in the association between sexual assault and depression and anxiety problems. History of sexual assault and (facets of) the temperament traits of neuroticism (frustration and discomfort), extraversion (sociability and high pleasure), and effortful control were assessed at baseline and emotional problems at one-year follow-up. The association between moderate sexual assault (i.e., not involving penetration) and emotional problems was strengthened by frustration, whereas the association between severe sexual assault (i.e., involving penetration) and problems was partially mediated by frustration and discomfort. Sociability, high pleasure and effortful control did not moderate or mediate the association. The impact of sexual assault involved the total of emotional problems and not specifically depression or anxiety. We conclude that our results suggest that severe sexual assault predicts emotional problems because it increases temperamental vulnerability to emotional problems, whereas moderate sexual assault leads to emotional problems only in already temperamentally vulnerable individuals

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Introduction

The prevalence of past sexual assault is increased in women who suffer from depression and anxiety (further denoted as emotional problems) (e.g., Bagley & Mallick, 2000; Fergusson, Horwood, & Lynskey, 1996; Katerndahl, Burge, & Kellogg, 2005; Spataro et al., 2004). Studies examining individual differences in the long-term responses to sexual assault generally focus on the influence of factors related to the assault (e.g., severity and duration of the assault or relationship to the perpetrator), coping strategies, experienced blame or control, or family, social, and other contextual factors (Bagley & Mallick, 2000; Jumper, 1995; Mennen, 1993; Whiffen & MacIntosh, 2005; Wyatt & Newcomb, 1990). Although various studies found that temperament characteristics, especially neuroticism, are associated with increased adversity and modify associations between adversity and mental health (Gothelf et al., 2004; Kendler, Kuhn, & Prescott, 2004a; Ormel, Oldehinkel, & Brilman, 2001; Van Os & Jones, 1999), research addressing the role of temperament in the association between sexual assault and emotional problems is limited and typically assumes mediation rather than moderation effects of temperament (Gamble et al., 2006; Pickering, Farmer, & McGuffin, 2004; Roy, 2002; Talbot et al., 2000). Mediation by temperament implies that sexual assault results in emotional problems through its effect on temperament, whereas moderation by temperament means that the impact of sexual assault on emotional problems depends on temperament. The purpose of this study was to examine mediation and moderation by temperament in the association between sexual assault and emotional problems in a sample of young women.

Temperament represents basic person characteristics in emotional reactivity and self-regulation (e.g. Rothbart, Ahadi, & Evans, 2000) and affects mental health in interaction with the environment (Dadds & Salmon, 2003; Oldehinkel et al., 2006). Temperament appears to be moderately stable during adolescence and young adulthood (Caspi & Roberts, 2001). In the present paper, we focus on the temperament domains of negative affectivity, extraversion and effortful control as assessed by the Adult Temperament Questionnaire (Rothbart, Ahadi, & Evans, 2000). Negative affectivity is similar to neuroticism, while effortful control is related to conscientiousness (Rothbart, Ahadi, & Evans, 2000). Neuroticism, extraversion, and conscientiousness represent the three most salient temperament/personality domains across all major theories of temperament/personality (e.g., Cloninger, 1986; Eysenck & Eysenck, 1985; McCrae & Costa, 1997; Rothbart, Ahadi, & Evans, 2000). We used the facets of frustration and discomfort from the domain of neuroticism, sociability and high pleasure from the domain of extraversion, and effortful control. Effortful control consists of the facets of attentional, inhibitory, and activation control. We did not include the neuroticism facets of

fear and sadness or the extraversion facet of positive affectivity as these, due to operational confounding, may be vulnerable for spurious association with measures of emotional problems (Ormel, Rosmalen, & Farmer, 2004). Based on the limited available literature (Gamble et al., 2006; Kendler, Kuhn, & Prescott, 2004a; Pickering, Farmer, & McGuffin, 2004; Roy, 2002; Talbot et al., 2000), we expect that frustration, discomfort, sociability, and high pleasure are relevant in the association between sexual assault and emotional problems. We have no a priori hypothesis for effortful control, but included this domain for exploratory purposes.

Frustration encompasses the amount of negative affect related to the interruption of ongoing tasks or goalblocking. Individuals high on frustration react strongly and aversively when they feel obstructed or interfered with. Discomfort describes unpleasant affect related to stimulation of the senses. Individuals high on discomfort are, for example, bothered by bright light, loud noises, or the feeling of cloth on their skins. As mentioned before, frustration and discomfort represent facets of neuroticism. High neuroticism is thought to represent increased stress sensitivity that predisposes individuals to the development of emotional problems (e.g., Clark, Watson, & Mineka, 1994; Eysenck & Eysenck, 1985; McCrae & Costa, 1997). Statistical tests of mediation or moderation by neuroticism in the association between sexual assault and emotional problems are, to our knowledge, only reported in the studies of Gamble et al. (2006) and Kendler et al. (2004b). Both studies distinguish between moderate and severe assault. Gamble et al. (2006) studied mediation and found that neuroticism partially mediated the association between severe childhood sexual abuse and depressive symptom severity, but found no association between neuroticism and moderate childhood sexual abuse. Kendler et al. (2004b) did not test mediation by neuroticism, but found evidence for a modifier effect of neuroticism in the association between moderate , but not severe, childhood sexual abuse and risk of depression. In the present study we examined frustration and discomfort both as mediators and moderators of the association between sexual assault and emotional problems, distinguishing between moderate and severe sexual assault. Based on Gamble et al. (2006) and Kendler et al. (2004b), we expect that *severe* sexual assault increases emotional problems partly by increasing frustration and discomfort, while the strength of the association between *moderate* sexual assault and emotional problems increases as frustration and discomfort increase.

Sociability describes enjoyment derived from social interaction and being in the presence of others. High pleasure refers to the amount of positive affect related to high intensity-stimuli, situations or activities. As mentioned above, sociability and high pleasure are facets of extraversion (Rothbart, Ahadi, & Evans, 2000). In general, extraversion is negatively associated with emotional problems, especially depression problems (Clark,

Watson, & Mineka, 1994). To our knowledge, no studies examined whether extraversion mediates or moderates the association between sexual assault and emotional problems, but two studies examined the associations between extraversion and sexual assault. Talbot et al. (2000) found that within a sample of women with a history of childhood sexual abuse, those women whose history included both parental abuse and intercourse had relatively low extraversion scores. Talbot et al. (2000) suggest that more severe abuse may decrease extraversion and therefore increase risk of emotional problems. However, Pickering, Farmer, and McGuffin (2004) found a positive association between childhood sexual abuse and extraversion in individuals with a history of depression, suggesting that sexual abuse leads to a more adventurous and sensation-seeking personality or that woman with such personality are more at risk of sexual abuse. We predict that sociability and high pleasure are associated with sexual assault and will examine whether these facets mediate or moderate the association between sexual assault and emotional problems, but have no a priori hypotheses on the direction of effects.

Depression and anxiety can be differentiated by factors that represent low positive affect or hopelessness and physiological hyper-arousal respectively (Brown, Chorpita, & Barlow, 1998; Mineka, Watson, & Clark, 1998). However, when examining possible mechanisms in the development of depression and anxiety it is important to take into account that depression and anxiety are often comorbid (Kessler, 1995) and also share a common factor of psychological distress based on broad individual differences in general problems and negative affect (Brown, Chorpita, & Barlow, 1998; Clark & Watson, 1991). This overlap may conceal that sexual assault or temperament may be specifically associated with either depression or anxiety problems (Clark, Watson, & Mineka, 1994; Ernst, Angst, & Földényi, 1993; Hartman et al., 2007). Therefore, the present study considers whether associations of sexual assault and temperament with emotional problems concern the total of emotional problems, or depression or anxiety problems specifically.

In sum, this article examines mediation and moderation by temperament in the long-term effect of sexual assault on emotional health. We conducted our examinations in a high-risk cohort of adolescent and young-adult women with at least one parent who ever received treatment for depression and/or anxiety disorder. Data on sexual assault were gathered retrospectively at baseline, temperament was assessed at baseline as well, while emotional problems were assessed at one-year follow-up. We distinguished between the effects of severe sexual assault (i.e., involving penetration) and moderate sexual assault (i.e., not involving penetration) and considered whether associations of sexual assault and temperament with emotional problems concerned the total of emotional problems, or depression or anxiety problems specifically.

Method

Participants and Procedure

The present study used data of 278 adolescent and young-adult women from 229 families who participated in the first (T1) and second (T2) assessment waves of the Dutch ARIADNE (Adolescents at Risk of Anxiety and Depression) Study. ARIADNE is a large prospective study into the development and course of depression and anxiety among 520 adolescent and young-adult offspring from 366 families of which one parent had recently received treatment for depression and/or anxiety disorder in a mental health facility in the north of the Netherlands (Landman-Peeters et al., 2005).

At baseline (T1), consenting parents and their offspring were interviewed in person and were also asked to complete a number of questionnaires. Approximately one year later, offspring were sent a second set of questionnaires for the first follow-up assessment (T2).

In our sample, very few men (1.8 %; 4 out of 222) reported sexual assault before T1, therefore we only used data of the women in this study. At T1 these women were between 13 and 25 years old (M =18.2; SD =3.3). Drop outs (n=20) and participants (n=278) did not differ in terms of age and anxiety problems at T1, but dropouts more often reported sexual assault before T1 (40% versus 14%; χ^2=9.47, p=0.002) and tended to report more depression problems at T1 (M= 29.75 (SD=7.99) for dropouts and M=26.26 (SD=8.54) for participants; t(296)= 1.77, p=0.078).

Measures

Sexual assault. At T1, participants were interviewed about their experience of sexual assault. The questions addressing sexual assault were integrated in an interview about a wide range of potentially traumatic events. For this purpose, we used items from the Post Traumatic Stress Disorder section of the World Mental Health (WMH) Survey Initiative Version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI) (Kessler & Üstün, 2004). The questions addressing sexual assault read: "(1) The next two questions deal with sexual assault. The first one is about rape. We define this as someone either having sexual intercourse with you or penetrating your body with a finger or object when you did not want him/her to, either by threatening you or by using force. Did this ever happen to you? (2) Other than rape, were you ever sexually assaulted or molested?" Additional questions addressed the age at which sexual assault occurred for the first time and whether the respondent experienced sexual assault more

than once. We labeled sexual assault involving penetration as "severe sexual assault" and sexual assault not involving penetration as "moderate sexual assault".

Temperament. At T1, temperament was assessed by means of the Adult Temperament Questionnaire (ATQ) **(**Hartman & Rothbart, 2001; Rothbart, Ahadi, & Evans, 2000). Respondents were asked to report on a 4-point Likert scale to what extent temperamental behaviors and cognitions generally applied to them. Frustration was measured by 6 items (e.g., "It doesn't take very much to make me feel frustrated or irritated"), internal consistency reliability (α) for this scale was 0.66. Discomfort was measured by 8 items (e.g., "I'm often bothered by light that is too bright") with α=0.64. Sociability was measured by 6 items (e.g., "I usually like to spend my free time with people") with an α of 0.72. The High pleasure scale consisted of 12 items (e.g., "When listening to music, I usually like to turn up the volume more than other people") and showed an α of 0.65. Effortful control was measured by 24 items and describes the ability to voluntarily regulate attention and behavior (e.g., "It is very hard for me to focus my attention when I am distressed") with α=0.84.

Emotional problems. The DSM-IV Questionnaire (Hartman, 2002; Hartman et al., 2001; Muris, 2006; Muris, Winands, & Horselenberg, 2003) was used to assess depression and anxiety problems at T2. Items in the questionnaire refer to symptoms as used in the Diagnostic and Statistical Manual of mental disorders (4th edition) (DSM-IV) classification system (American Psychiatric Association, 1994). Respondents were asked to report on a 4-point Likert-scale to what extent each symptom (behavior, cognition, feeling) accurately describes their behavior in the months preceding the assessment. The DSM-IV Questionnaire has two advantages for the present study. Firstly, it yields continuous symptom scores, as such measuring also subclinical levels in our high-risk group. Secondly, it has a direct substantive relation to DSM-IV diagnoses (Landman-Peeters et al., 2005).

To create scales for depression and anxiety problems that differentiate between these problems as much as possible, we conducted a factor analysis with a two-factor solution on the depression and anxiety items. We constructed two scales such that only those items were selected which loaded on their own factor with a loading ≥0.30 and a difference ≥0.20 between this main loading and the additional loading on the other factor. The Depression symptoms scale consists of 15 items (e.g., "I am often unhappy", "I am low in energy or feel tired for no reason"). The Anxiety symptoms scale consists of 17 items (e.g., "I suddenly become very anxious or panicky for no reason"). Internal

consistency reliability was 0.94 for the Depression problems scale and 0.90 for the Anxiety problems scale. The Depression and Anxiety scales were standardized and summed to create the scale representing Total emotional problems. The internal consistency reliability of this composite scale was 0.95.

Data analysis

We first examined the bivariate associations between the variables in this study. ANOVA and Dunnett's *t* post-hoc analysis were used to test whether mean scores of the women with a history of severe sexual assault and women with moderate sexual assault were significantly different from those of women without a history of sexual assault. The associations between temperament and emotional problems were examined by means of correlation analysis.

We examined the role of temperament in the associations between sexual assault and emotional problems by means of stepwise regression analyses. All variables were standardized to improve interpretability and prevent computational problems due to multicollinearity that may occur with variables and their products (Aiken & West, 1991). A *p*-value smaller than 0.05 was considered statistically significant. We first examined moderation by temperament. In the first step of the regression analysis, we entered the temperament variables and two dummy variables for sexual assault. The dummy variables represented the effects of moderate sexual assault and severe sexual assault in comparison to no sexual assault. We then examined in the second step whether interactions of sexual assault with temperament were significant by means of forward analysis.

Mediation requires that the mediator is significantly associated with both the outcome and the predictor variable (Baron & Kenny, 1986). In the present study temperament must therefore be associated with both sexual assault and emotional problems to be able to act as a mediator. Potential mediators were identified by means of the results of the ANOVA and correlation analyses. Using stepwise regression analysis, we then examined whether the magnitude of the associations between the sexual assault variables and emotional problems decreased when the potential mediator was added to the regression equation. We tested whether the mediation effect was significant by means of the Sobel test (Baron & Kenny, 1986). Mediation was examined for each temperament variable separately.

To examine whether the associations between sexual assault and temperament are specific for either depression or anxiety, we ran the analyses mentioned above again, but partialled out shared variance by including anxiety problems in the analyses of depression problems and depression problems in the analysis on anxiety problems, respectively. We thus examined associations of sexual assault and temperament with the type of problems

(i.e., unique depression and unique anxiety) rather than the extent to which problems were present.

The 278 respondents in the present study came from 229 families. To account for this clustering of observations in families, we conducted design-based analyses with families as primary sampling units, using the statistical program STATA 8.0 (StataCorp, 2003).

Results

Descriptives and correlations

In total, 39 (14.0%) respondents in our sample reported sexual assault. In 20 of 39 women sexual assault involved penetration. Mean age at first experience was 12.4 years old (*SD*=5.5). This did not differ between women with moderate and women with severe sexual assault.

Table 1 Means (*SD*) of and test-statistics of differences between women with no history of sexual assault and women with a history of moderate sexual assault or severe sexual assault

	No sexual assault	Moderate sexual	Severe sexual assault
Total emotional problems	-.20 (1.65)	.52 (2.26)	1.85 (2.17)***
Depression problems	25.59 (7.72)	28.21 (9.33)	33.25 (9.03)***
Anxiety problems	22.30 (5.80)	25.00 (9.59)	29.90 (10.71)***
Frustration	23.68 (3.90)	24.32 (3.68)	25.65 (3.84)*
Discomfort	18.37 (2.86)	18.47 (2.17)	20.10 (2.59)**
Sociability	18.62 (2.43)	17.05 (3.96)*	17.95 (3.20)
High Pleasure	32.54 (4.62)	33.58 (3.63)	30.80 (5.15)
Effortful Control	60.40 (7.81)	61.47 (7.86)	60.80 (9.04)

Total emotional problems score is sum of standardized depression problems and anxiety problems scores; *p*-values of difference with No sexual assault group; **p*<.05; ***p*<.01; *** *p*<.001

Table 1 presents means on emotional problems and temperament for the women with no history of sexual assault, women with a history of moderate sexual assault and women with a histrory of severe sexual assault. Women with a history of severe sexual assault had significantly more total emotional problems, more depression, and more anxiety at T2, than women without a history of sexual assault. Compared to women without sexual assault, women with severe sexual assault also had higher scores on the

temperament facets of frustration and discomfort. They did not differ on sociability, high pleasure, or effortful control. Women with a history of moderate sexual assault tended to have more total emotional problems and more anxiety, than women without a history of sexual assault, but these differences were marginal and failed to reach significance (p=0.083 and p=0.082 respectively). These women further had a significantly lower mean on the temperament facet of sociability than women without a history of sexual assault, but did not differ on any of the other temperament variables.

Frustration and discomfort were positively correlated with total emotional problems (r=0.415, p<0.001 for frustration and r=0.265, p<0.001 for discomfort), while sociability and effortful control were negatively associated with total emotional problems (r=-0.329, p<0.001 for sociability and r=-0.290, p<0.001 for effortful control). Associations of these facets with the separate measures of depression and anxiety problems were similar. The facet of high pleasure was not significantly associated with the measures of total emotional problems, depression problems, or anxiety problems.

Table 2 Regression coefficients (*SE*) of sexual assault, temperament and interaction from moderation analyses on total emotional problems, depression problems, and anxiety problems

	Total emotional problems	Depression problems (adjusted for anxiety problems)	Anxiety problems (adjusted for depression problems)
Moderate sexual assault	.05 (.05)	.01 (.05)	.05 (.05)
Severe sexual assault	.21 (.05)***	.06 (.07)	.13 (.08)
Frustration	.23 (.07)***	.11 (.07)	.08 (.06)
Discomfort	.12 (.06)*	.00 (.05)	.09 (.05)
Sociability	-.17 (.06)**	-.14 (.06)*	-.03 (.09)
High Pleasure	-.03 (.06)	-.04 (.05)	.03 (.05)
Effortful Control	-.16 (.07)*	-.05 (.07)	-.07 (.06)
Moderate sexual assault × Frustration	.15 (.04)***	-	-
Severe sexual assault × Frustration	.07 (.05)	-	-

Regression coefficients of standardized variables ;* p<.05; ** p<.01; *** p<.001

Moderation analyses

Table 2 presents the results of the moderation analysis on total emotional problems. These results included significant main effects for severe sexual assault, frustration, discomfort, sociability, and effortful control and a significant interaction between moderate sexual

assault and frustration. Severe sexual assault, frustration, and discomfort were associated with higher levels of emotional problems, while sociability and effortful control were associated with lower levels of emotional problems. The effect of moderate sexual assault before T1 depended on frustration scores at T1, such that moderate sexual assault increased emotional problems in women high on frustration, but not in women low on frustration (see Figure 1).

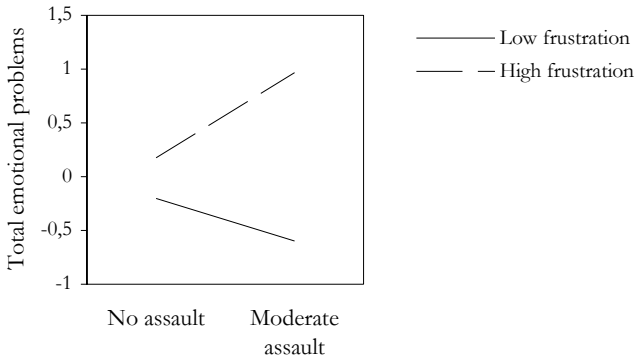

Figure 1 Interaction between moderate sexual assault and frustration in the association with total emotional problems (Low and High Frustration refer to the values of –1 *SD* and +1 *SD*)

The results of analyses that addressed unique depression and unique anxiety show that none of the temperament variables moderated the association between sexual assault and depression or anxiety problems specifically. Moreover, except for the facet of sociability, sexual assault and temperament did not significantly predict depression or anxiety problems beyond the extent that they predicted the extent to which emotional problems were present. Sociability was negatively associated with depression problems when anxiety problems were controlled for, but was not associated with anxiety problems when we controlled for depression problems.

Mediation analysis

The ANOVA analyses showed that women with severe sexual assault, but not women with moderate sexual assault, had significantly more emotional problems than women with no history of sexual assault (see Table 1). Mediation can therefore only be present in the

association between severe sexual assault and emotional problems. Women with severe sexual assault also reported more frustration and discomfort than women with no sexual assault. As frustration and discomfort were significantly associated with emotional problems as well, these facets are potential mediators of the association between severe sexual assault and emotional problems. Data from the women with moderate sexual assault were excluded from the mediation analyses. Furthermore, we did not examine mediation for depression and anxiety specifically, as severe sexual assault was not specifically associated to depression or anxiety problems. Results of the mediation analyses (see Table 3) show that the effect of severe sexual assault on total emotional problems decreased slightly, but statistically significant, by adding either frustration (model 2a) or discomfort (model 2b) to the regression equation. The effect of severe sexual assault further decreased when both facets were added to the regression equation (model 3). The regression coefficients in model 3 indicate that the direct effects of severe sexual assault, frustration, and discomfort on total emotional problems were similar, with severe sexual assault accounting for 5%, discomfort for 4% and frustration for 10% explained variance.

Table 3 Analyses of mediation of the association between severe sexual assault and total emotional problems by frustration and discomfort

	B (*SE B*)	Sobel statistic	Sobel *p*
Model 1			
Severe sexual assault	.29 (.06)***		
Model 2a			
Severe sexual assault	.25 (.06)***		
Frustration	.35 (.06)***	2.03	.042*
Model 2b			
Severe sexual assault	.25 (.06)***		
Discomfort	.24 (.06)***	2.22	.027*
Model 3			
Severe sexual assault	.22 (.06)***		
Frustration	.32 (.06)***		
Discomfort	.19 (.06)**		

Regression coefficients of standardized variables ;* $p<.05$; ** $p<.01$; *** $p<.001$

Discussion

This study examined the role of temperament in the association of sexual assault with emotional problems. So far, only a limited number of studies addressed the associations between sexual assault, temperament and emotional problems (Gamble et al., 2006; Kendler, Kuhn, & Prescott, 2004a, 2004b; Pickering, Farmer, & McGuffin, 2004; Roy, 2002; Talbot et al., 2000). Moreover, these studies typically did not examine or distinguish between mediating and moderating processes. This is important to understand fully the interplay of sexual assault and temperament in their influence on mental health (Whiffen & MacIntosh, 2005). We found that the effect on emotional problems of moderate sexual assault (i.e. not involving penetration), but not severe sexual assault (i.e., involving penetration), was moderated by a temperament that is high on frustration, while the effect of severe sexual assault, but not moderate sexual assault, was partly mediated by both frustration and discomfort. No moderation or mediation effect was found for sociability, high pleasure, and effortful control. We further found that sexual assault was associated with the total of emotional problems and not specifically with depression or anxiety.

The results of our study are in line with both Gamble et al. (2006), who found that neuroticism mediated the association between severe sexual assault and emotional problems, and Kendler, Kuhn, and Prescott (2004b), who found evidence for moderation by neuroticism in the association between moderate childhood sexual abuse and risk of depression. Our results indicate that the effect of moderate sexual assault on emotional problems is stronger in individuals high on frustration. We found that severe sexual assault, frustration, and discomfort were independently and similarly associated with emotional problems. Thus, sexual assault involving penetration seems to be associated with higher levels of emotional problems regardless of the level of neuroticism. In addition, severe sexual abuse is associated with emotional ill-health because it tends to increase neuroticism, as indicated by the mediation effects observed for frustration and discomfort.

In the present study, sociability and high pleasure represented extraversion. In comparison with women with no sexual assault, women with moderate sexual assault had lower sociability, but women with severe sexual assault did not differ from the no assault group. High pleasure was not associated with sexual assault. Our findings are in contrast with the findings of both Pickering et al. (2004) and Talbot et al. (2000). In individuals with a history of depression, Pickering et al. (2004) found a positive association between childhood sexual abuse and extraversion, suggesting that sexual abuse leads to a more sensation-seeking and adventurous personality or that women with this personality are at increased risk to experience sexual abuse. Talbot et al. (2000) found that women with

severe childhood sexual abuse reported lower extraversion than women with less severe sexual abuse. Measures of extraversion generally include assessments of positive affect, which is strongly and negatively associated with emotional problems. Possibly, the result of Talbot et al. was based largely on higher levels of emotional problems in women with severe abuse. Extraversion may not be associated with sexual assault or sexual assault may affect extraversion in both directions, such that extraverted individuals become more extraverted and introverted individuals more introverted, canceling out any effect in our total group.

Sexual assault or temperament may be specifically associated with either depression or anxiety (Clark, Watson, & Mineka, 1994; Ernst, Angst & Földényi, 1993; Hartman et al., 2007). The present findings suggest that the effects of sexual assault does not differentiate between depression or anxiety, but rather is associated with the extent to which emotional problems are present.

The results of the present study should be interpreted in the context of the following potentially significant limitations. First, our sample consisted of adolescent and young-adult daughters of people treated for emotional disorders at least once during their life. Risk to develop emotional problems is higher in offspring of affected parents than in offspring of non-affected parents, partly due to an increased risk to experience stressful life-events, such as sexual assault (Bifulco, Moran, & Ball, 2002; Walsh, MacMillan, & Jamieson, 2002; Young et al., 1997). Higher levels of emotional problems and a higher prevalence of sexual assault may limit the generalizability of our findings. On the other hand, as high-risk populations offer more variance on both risk and outcome variables, mechanisms relevant to the development of depression and anxiety are more likely to surface in such samples (Garber & Flynn, 2001). Secondly, sexual assault that had occurred before T1 was measured retrospectively and at the same point in time as temperament. We therefore cannot rule out memory biases or be sure about the direction of causality. In principle, it is possible that frustration and discomfort increased risk of sexual assault and thus that sexual assault mediated the associations between frustration and discomfort on the one hand and emotional problems on the other. However, in that case one would expect that these facets were associated with both moderate and severe sexual assault, while our findings and those of Gamble et al. (2006) only indicate associations with severe sexual assault. Thirdly, our distinction between moderate and severe sexual assault was based on the distinction between sexual assault involving and not involving penetration and ignored potentially important differences between prolonged and single occasions of sexual assault. We had no reliable information concerning the duration of sexual abuse. Moreover, the relatively small number of women with a history

of sexual assault did not permit further distinctions. Fourthly, attrition between T1 and T2 may have weakened associations.

Assets of the present study are that we investigated temperament as a potential mediator *and* moderator of the association between sexual assault and emotional problems, assessed temperament and emotional problems at different measurement waves, limited potential confounding between measures of neuroticism and extraversion and measures of emotional problems by omitting the temperament scales assessing sadness, fear, and positive affectivity, and examined whether sexual assault is associated with emotional problems in general or depression or anxiety problems specifically.

Sexual assault or abuse in childhood and adolescence, although often associated with other risk factors for emotional problems (e.g., physical and emotional abuse, family environment, and socioeconomic status) (Kendler et al., 2000), has a "unique, diverse, and substantial impact" on emotional problems and risk factors for emotional problems (Kendler, Gardner, & Prescott, 2002). Findings from the present study indicate that the role of temperament in the association between sexual assault and emotional problems is conditional as it depends on the severity of sexual assault. The association between severe sexual assault and emotional problems is partially explained by increased temperamental vulnerability to emotional problems in women with a history of severe sexual assault. In contrast, mild to moderate sexual assault seems to increase emotional problems only in already temperamentally vulnerable individuals.

Chapter 8

Discussion

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). ARIADNE 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 (Cyranowski 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 & Girgus, 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,

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 of 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.

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Samenvatting

Inleiding

Depressie en angst zijn veel voorkomende psychische stoornissen. Het ontstaan van deze stoornissen is gerelateerd aan een breed scala van risicofactoren, zoals genetische kwetsbaarheid, neurofysiologisch disfunctioneren, temperamenteigenschappen, ongunstige gezinsomstandigheden, beperkingen in het sociale netwerk, langdurige moeilijkheden en ingrijpende gebeurtenissen. De aanwezigheid van een enkele risicofactor blijkt echter niet voldoende om depressie en angst te laten ontstaan, dit lijkt veel meer het gevolg van combinaties van meerdere factoren die een optelsom van risico vormen en/of elkaar's effect versterken. Inmiddels zijn er al veel risicofactoren voor angst en depressie bekend, maar het is nog maar ten dele bekend hoe deze risicofactoren op elkaar inwerken en zo al dan niet tot depressie of angst leiden. In de studies beschreven in dit proefschrift wordt het samenspel van een aantal risicofactoren in het ontstaan van depressie en angst onderzocht, het gaat hierbij om combinaties van familiale kwetsbaarheid, geslacht, temperamenteigenschappen en stress. Daarnaast is onderzocht of effecten hetzelfde zijn voor depressie en angst. Samenvattingen van de betreffende studies vindt u hieronder terug.

De studies in dit proefschrift zijn uitgevoerd onder 524 adolescenten en jongvolwassenen uit 366 gezinnen waarvan ouders ooit in de GGZ in behandeling zijn geweest voor een depressie of angststoornis. De deelnemers komen uit de provincies Drenthe, Friesland en Groningen en waren bij aanvang van de studie tussen de 13 en 25 jaar oud. Kinderen van mensen die ooit een depressie of angststoornis hebben gehad hebben een grotere kans dan anderen om zelf deze stoornissen ook te krijgen. De invloed van een stoornis bij de ouder op de geestelijke gezondheid van het kind lijkt te zijn gebaseerd op een verhoogde aanwezigheid van allerlei risicofactoren. Doordat onder kinderen van aangedane ouders in vergelijking met de gemiddelde bevolking risicofactoren en depressie en angst vaker voorkomen kan in deze groep goed worden onderzocht hoe risicofactoren elkaar beïnvloeden in relatie tot deze stoornissen.

Familiale kwetsbaarheid en geslacht

Familiale kwetsbaarheid staat in dit proefschrift voor het aantal ouders met emotionele stoornissen (dat is depressie of angst). Men gaat er van uit dat het risico van kinderen op het krijgen van depressie en angst toeneemt met het aantal ouders dat deze stoornissen

heeft, maar de verschillen tussen kinderen van één aangedane ouder en kinderen van twee aangedane ouders zijn nog niet vaak onderzocht. Daarnaast zijn er aanwijzingen dat de samenhang tussen het vóórkomen van emotionele stoornissen in ouders en kinderen verschillend is voor vaders en moeders en voor zoons en dochters. In verhouding is er echter maar weinig onderzoek gedaan waarin het effect van een stoornis in de vader werd onderzocht. Bovendien zijn uitkomsten van de enkele onderzoeken die rekening houden met zowel het geslacht van de ouders als het geslacht van de kinderen niet eenduidig. In de studie beschreven in Hoofdstuk 3 werd het effect van een tweede ouder met emotionele problemen op het risico voor depressie en angststoornissen in kinderen van depressieve ouders onderzocht. Hierbij werd ook onderzocht of dit effect afhangt van het geslacht van het kind en het geslacht van de depressieve ouder. Uit de resultaten blijkt dat het risico op depressie en angststoornissen het hoogst was in dochters met twee aangedane ouders. Het risico verschilde niet tussen dochters met alleen een aangedane moeder en dochters met alleen een aangedane vader. In zoons lijkt een aangedane vader het risico daarentegen niet te verhogen; het risico was hoger wanneer de moeder was aangedaan dan wanneer de vader was aangedaan en het risico in zoons van aangedane moeders werd niet hoger wanneer de vader tevens klachten had. Voor de klinische praktijk betekenen deze resultaten dat met name kinderen van vrouwen met emotionele problemen en dochters van aangedane ouders een hoger risico hebben om depressie en angst te ontwikkelen. Om te voorkomen dat het verschil tussen de effecten van een depressieve vader en een depressieve moeder op de emotionele gezondheid van de kinderen wordt onderschat zal toekomstig onderzoek naar dit verschil rekening moeten houden met verschillen tussen zoons en dochters en effecten van emotionele problemen van de andere ouder.

Familiale kwetsbaarheid en stress

Men gaat er van uit dat het hogere risico op een emotionele stoornis in kinderen van depressieve ouders gedeeltelijk kan worden verklaard door een grotere blootstelling aan omgevingstress, zoals problemen in de ouder-kind relatie (bijvoorbeeeld communicatie-problemen, gebrek aan steun, en/of gebrekkig gezinsfunctioneren). Deze veronderstelling is gebaseerd op onderzoek naar verschillen tussen kinderen van ouders zonder emotionele stoornissen en kinderen van ouders met zulke problemen. In de studie beschreven in Hoofdstuk 4 werd onderzocht welke rol problemen in de ouder-kind relatie spelen in het

verschil in de mate van emotionele problemen in jongeren met één aangedane ouder en jongeren met twee aangedane ouders. Uit de resultaten blijkt dat de jongeren met twee aangedane ouders zowel meer emotionele problemen als problemen in de ouder-kind relatie rapporteerden dan de jongeren met één aangedane ouder. Daarnaast was de relatie tussen problemen in de ouder-kind relatie en depressie en angst ook sterker in de jongeren met twee aangedane ouders dan in de jongeren met één aangedane ouder. Deze resultaten impliceren dat de toename in depressie en angst bij een toenemende familiare kwetsbaarheid gedeeltelijk lijkt te kunnen worden verklaard door zowel meer problemen in de ouder-kind relatie als een groter effect van deze problemen op jongeren met een hogere familiale kwetsbaarheid. Deze bevindingen verlenen onderbouwing voor de focus op het verbeteren van de ouder-kind relatie in preventieprogramma's die zich richten op het voorkómen van psychische stoornissen bij kinderen van psychiatrisch patiënten.

Geslacht en stress

Depressie en angst komen vaker voor bij vrouwen dan bij mannen. Dit geslachtsverschil zou gedeeltelijk worden veroorzaakt doordat vrouwen vaker stressvolle gebeurtenissen en omstandigheden meemaken dan mannen en ook eerder psychische problemen ontwikkelen door dergelijke stress, met name wanneer het gaat om problemen in de interpersoonlijke sfeer. Wanneer de interpersoonlijke banden goed zijn lijken vrouwen daar echter ook meer van te profiteren dan mannen. Er bestaat een verband tussen sociale steun en depressie en angst, zodanig dat mensen die relatief veel steun ervaren minder depressie en angst hebben dan mensen die weinig steun ervaren. Daarnaast zouden bij mensen die veel sociale steun hebben stressvolle gebeurtenissen of omstandigheden de kans op depressie en angst minder sterk vergroten dan in mensen met weinig steun (het zogenaamde buffereffect van sociale steun). In de studie in Hoofdstuk 5 hebben we onderzocht of er geslachtsverschillen waren in de rol van sociale steun in de relatie tussen stress, in de vorm van problemen in de ouder-kind communicatie, en depressie en angst in de jongeren uit het ARIADNE-onderzoek. Uit de resultaten blijkt dat, in vergelijking met de zoons, de dochters meer depressie en angst en meer problemen in de ouder-kind communicatie rapporteerden. Jongeren met problemen in de ouder-kind communicatie hadden meer depressie en angst, terwijl jongeren met sociale steun minder depressie en angst rapporteerden. Uit de resultaten blijkt verder dat de dochters meer dan zoons van sociale steun profiteerden wanneer ze veel problemen in de ouder-kind communicatie

hadden. Deze resultaten geven aan dat de invloed van problemen in de ouder-kind communicatie dus kan worden gecompenseerd door de sociale steun relaties van het kind, terwijl problemen op beide gebieden geassocieerd zijn met meer depressie en angst. De effecten van de problemen in de ouder-kind communicatie en sociale steun op emotionele problemen lijken sterker voor dochters dan voor zoons. Dit geslachtsverschil is wel eerder onderzocht, maar nog niet eerder aangetoond. Dat we het wel vonden binnen de groep jongeren in het ARIADNE-onderzoek lijkt te impliceren dat het belang van sociale steun in het ontstaan van emotionele problemen groter is voor personen die een hoger risico hebben om deze problemen te krijgen.

Temperament

Temperament beschrijft de manier waarop personen doorgaans reageren op hun omgeving en hun eigen gedachten en gedrag reguleren. Temperament is deels genetisch bepaald, wordt deels gevormd door ervaringen in de omgeving (bijvoorbeeld door de opvoeding of ingrijpende gebeurtenissen), en blijft na de kindertijd over het algemeen gedurende het leven redelijk stabiel. De studies in dit proefschrift hebben zich gericht op de temperamenteigenschappen negatieve affectiviteit, extraversie en 'effortful control'. Negatieve affectiviteit beschrijft emotionele instabiliteit of de neiging om negatieve emoties te ervaren, extraversie staat voor de neiging om op zoek te gaan naar aangename ervaringen en effortful control heeft betrekking op de vaardigheid om vrijwillig het eigen gedrag en de eigen gedachten te reguleren. Hoge negatieve affectiviteit en lage extraversie worden gezien als risicofactoren voor depressie en angst. Effortful control is nog niet veel onderzocht, maar personen die goed in staat zijn hun gedrag en gedachten te reguleren lijken minder kans te hebben om depressie en angst te ontwikkelen. In Hoofdstuk 6 wordt een studie beschreven waarin is onderzocht hoe bovenstaande temperamenteigenschappen elkaar beïnvloeden in relatie tot depressie en angst. De resultaten laten zien dat hoge negatieve affectiviteit depressie en angst voorspelde en dat lage extraversie alleen depressie voorspelde. Hoge effortful control beschermde tegen depressie en, in personen met hoge negatieve affectiviteit, tegen angst. Deze bevindingen zijn relevant voor de klinische praktijk, omdat de effortful control vaardigheden ook betrokken zijn bij het onder controle krijgen van ingesleten reactiepatronen, zoals piekeren en zelfverwijt, en bij de mogelijkheden jezelf te motiveren om te veranderen en te leren anders met dingen om te gaan. Deze vaardigheden kunnen bovendien worden getraind.

Temperament en stress

Temperament wordt verondersteld het effect van gebeurtenissen en omstandigheden op de psychische gezondheid te beïnvloeden, maar ook voor een deel te worden gevormd door ervaringen in de omgeving. In Hoofdstuk 7 wordt een studie beschreven waarin we het samenspel van de temperamenteigenschappen negatieve affectiviteit, extraversie en effortful control met seksueel geweld in de relatie tot emotionele problemen hebben onderzocht. Seksueel geweld is een sterke voorspellende factor voor het ontstaan van depressie en angst. Slachtoffers van seksueel geweld scoren vaak hoger op negatieve affectiviteit. Dit verband wordt uitgelegd als een effect van seksueel geweld op temperament, maar soms ook als een verhoogd risico van personen met hoge negatieve affectiviteit om seksueel geweld mee te maken. Hoewel er is onderzocht of de manier waarop seksueel geweld wordt verwerkt invloed heeft op het effect van deze ervaring op depressie en angst, is er nog niet vaak onderzocht hoe de meer algemene en stabiele temperamenteigenschappen van het slachtoffer de relatie tussen seksueel geweld en emotionele problemen beïnvloeden. Voor de studie in Hoofdstuk 7 gebruikten we de gegevens van de dochters die deelnamen aan het ARIADNE-onderzoek en maakten we een onderscheid tussen verkrachting en aanranding. Uit de resultaten blijkt dat vrouwen die verkrachting hadden meegemaakt hoger scoorden op negatieve affectiviteit dan de vrouwen die aanranding hadden meegemaakt en de vrouwen die geen seksueel geweld hadden meegemaakt, terwijl de laatste twee groepen hierin niet van elkaar verschilden. Dit wijst er op dat het meemaken van seksueel geweld de kwetsbaarheid voor het ontwikkelen van depressie en angst zou kunnen verhogen, indien het gaat om ernstig seksueel geweld. Uit de resultaten blijkt ook dat het verband tussen verkrachting en depressie en angst niet werd beïnvloed door temperamenteigenschappen van het slachtoffer. Aanranding was daarentegen sterker met depressie en angst geassocieerd in vrouwen met hoge negatieve affectiviteit. Dit zou er op kunnen wijzen dat met name de invloed van minder ernstige gebeurtenissen en omstandigheden op de emotionele gezondheid afhangt van de temperamenteigenschappen van de persoon.

Specifieke en generieke effecten voor depressie en angst

Depressie en angst zijn sterk aan elkaar gerelateerd; depressie wordt vaak voorafgegaan door angst en deze stoornissen komen veel vaker samen voor dan op basis van toeval

alleen verwacht mag worden. Depressie en angst zijn van elkaar te onderscheiden door de hopeloosheid en de afwezigheid (nagenoeg) van positieve emoties bij depressie en de fysiologische "overprikkeldheid" in angst, maar worden beiden gekenmerkt door negatieve emoties. Aan depressie en angst zou eenzelfde genetische aanleg ten grondslag liggen, waarbij omgevingsfactoren dan bepalen of deze aanleg zich uit in een depressie of een angststoornis. Om meer te weten te kunnen komen over het ontstaan van depressie en angst hebben we in de verschillende studies bekeken of de effecten van de risicofactoren hetzelfde waren voor depressie en angst of dat ze specifiek waren voor depressie of angst. Uit onze studies blijkt dat sociale steun en de temperamenteigenschap extraversie met name een rol spelen bij depressie en minder bij angst. Seksueel geweld was gerelateerd aan emotionele problemen in het algemeen en niet aan depressie of angst in het bijzonder.

Slotopmerkingen

Met de studies in dit proefschrift hebben we geprobeerd meer te weten te komen over de mechanismen in het ontstaan van depressie en angststoornissen door het samenspel tussen een aantal risicofactoren te onderzoeken. We hebben aanwijzingen gevonden voor geslachtverschillen in de mate waarin familiale kwetsbaarheid het risico op depressie en angst verhoogt, voor een groter effect van interpersoonlijke stress in personen met een hogere familiare kwetsbaarheid, voor geslachtverschillen in het buffereffect van sociale steun, voor een beschermend effect van de vaardigheid het eigen gedrag en de eigen gedachten te reguleren en voor een effect van de neiging negatieve emoties te ervaren op het verband tussen seksueel geweld en depressie en angst. Hoewel dit relevante effecten zijn, zijn het kleine effecten in het gehele ontwikkelingsproces van depressie en angst. Dergelijke effecten lijken relevanter te worden naarmate de kwetsbaarheid voor depressie en angst toeneemt en konden daarom bij uitstek in de hoog risicogroep van de ARIADNE studie onderzocht worden.

De aanwezigheid van een emotionele stoornis in de ouder is één van de sterkste voorspellers voor het ontstaan van depressie en angst. Uit onderzoek is gebleken dat in Nederland ongeveer een derde van het totale aantal kinderen onder de 22 jaar één of twee ouders met een psychische stoornis heeft. Bovendien is deze groep oververtegenwoordigd in de klinieken voor kinder- en jeugdpsychiatrie. Aangezien depressie en angst de meest voorkomende psychische stoornissen onder volwassenen zijn, heeft een grote groep jongeren een verhoogd risico op het ontwikkelen van emotionele stoornissen.

Daarnaast hebben deze jongeren een verhoogde kans om andere psychische en sociale problemen te ontwikkelen. In Nederland zijn er verschillende preventieprogramma's voor kinderen van ouders met psychische problemen, die de kans dat deze kinderen zelf problemen ontwikkelen helpen verkleinen. Het is echter niet haalbaar en wellicht ook niet nodig om alle kinderen van ouders met een emotionele stoornis aan een preventieprogramma te laten deelnemen. Preventie zou zich moeten richten op die jongeren die al wat depressie en angstproblemen hebben, temperamenteigenschappen hebben als hoge negatieve affectiviteit, lage extraversie of lage effortful control, een grotere familiale kwetsbaarheid hebben en/of veel problemen in de ouder-kind relatie ervaren, met name wanneer het om dochters gaat. Een eerste stap in het voorkómen van psychische stoornissen in kinderen van psychiatrisch patiënten is wellicht het informeren naar kinderen bij patiënten die zich aanmelden voor behandeling van depressie of angst.

Nawoord

Hoewel er maar één auteursnaam op de omslag van dit proefschrift vermeld staat, hebben velen door hun inspanningen en steun bijgedragen aan de totstandkoming ervan. Op deze plek wil ik deze personen bedanken.

Het ARIADNE-onderzoek was niet mogelijk geweest zonder de deelnemers. Achter de getallen in de verschillende hoofdstukken gaan jongeren en hun ouders schuil die ieder meerdere uren zijn geïnterviewd en daarnaast ook vragenlijsten hebben ingevuld. Een groot aantal jongeren was ook bereid om voor de vervolgmetingen vragenlijsten in te vullen. Dank voor jullie tijd en openheid.

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Curriculum Vitae

Karlien Landman-Peeters werd op 3 april 1975 geboren te Alkmaar en heeft haar jeugd doorgebracht in Egmond aan den Hoef. Nadat zij haar atheneumdiploma had behaald aan het Petrus Canisius College te Alkmaar, is zij in 1993 Psychologie gaan studeren aan de Rijksuniversiteit Groningen. Zij deed Ontwikkelingspsychologie als hoofdrichting en Sociale Psychologie als nevenrichting. Tijdens haar studie heeft zij met Dr. Sandy Jackson onderzoek gedaan naar de afwegingen en strategieën die adolescenten hanteren bij het maken van een eerste romantisch afspraakje. Haar afstudeeronderzoek naar de samenhang tussen sociale vaardigheden en de grootte van het sociaal netwerk bij jongeren heeft zij uitgevoerd bij Prof.dr. Nicholas Emler aan Oxford University (Engeland). In 1998 behaalde zij haar doctoraaldiploma. Vanaf 1999 werkte zij aan het onderzoek voor dit proefschrift bij de disciplinegroep Psychiatrie van de Rijksuniversiteit Groningen. Hiernaast werkte zij als docent Ontwikkelingspsychologie voor de Stichting Integratieve Psychotherapie Opleidingen, verbonden aan Hogeschool In Holland, en vanaf 2006 voor de Stichting Pedagogische Opleidingen, gelieerd aan de Rijksuniversiteit Groningen. In 2006 werkte ze tijdelijk als onderzoeker bij Accare (Academisch centrum voor kinder- en jeugdpsychiatrie) in Groningen en in 2006 en 2007 heeft ze als docent Onderzoek gewerkt bij de Academie voor Sociale Studies van de Hanzehogeschool Groningen. Vanaf september 2007 is Karlien werkzaam als postdoc bij de disciplinegroep Psychiatrie van de Rijksuniversiteit Groningen.

Karlien is getrouwd met Gerrit Landman; ze zijn samen de ouders van Gijs en Marten.

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