

**The Aetiology of Emotional Symptoms in Children and Adolescents:
Depression and Anxiety in Twins**

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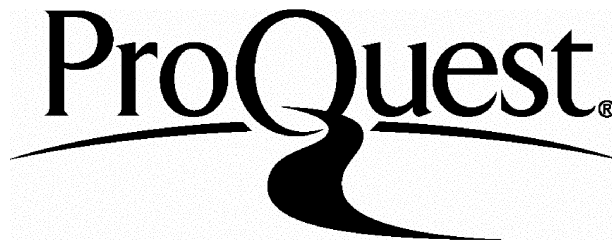
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Abstract

The Children's Depression Inventory (CDI) and the State-Trait Anxiety Inventory for Children (STAIC) were completed by 395 twin pairs aged 8 to 16 years. Eighty-nine pairs of these twins and their mothers were then visited and interviewed to ascertain whether there had been any major life events or ongoing experiences in the preceding twelve months. These events and experiences were rated for various aspects of impact on the child.

As the CDI and the STAIC are highly correlated the first stage of the analysis was a second order factor analysis of the items on the two questionnaires which resulted in two relatively independent factors of depression and anxiety ($r = .27$). The second stage of the analysis was the genetic analyses of scores on these two factors. Within-pair similarity for depression scores was found to be due to genetic factors ($a^2 = .54$), whereas for within-pair similarity on anxiety symptoms the common environment was the significant parameter ($c^2 = .44$). Extremes analyses found that the same factors appeared to contribute to extreme scores of depression ($h^2_g = .46$) and anxiety ($c^2_g = .40$) as those responsible for individual differences. Multivariate model-fitting revealed that the covariation between depression and anxiety was entirely accounted for by a shared genetic factor ($r_g = 1.0$).

The second section considered the relationship between the life events and experiences data and the depression and anxiety scores. Loss events were found to be associated with depression and danger events with anxiety. Negative experiences were found to be significantly associated with both depression and anxiety. Experiences characterised by schoolwork problems and friendship problems were significantly related to depression.

These results imply that while the genetic factors for depression and anxiety in children and adolescents are largely shared, the environmental influences are specific, resulting in the particular manifestation of the symptomatology.

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Table of Contents

Abstract	2
Acknowledgements	3
Table of Contents	4
List of Tables and Figures	10
Introduction	15
Chapter 1: Literature Review Part I	17
Depression and Anxiety in Children and Adolescents: The Concepts	
Section 1.1: Theories of Depression and Anxiety	17
1.1.1: Theories of depression	17
1.1.1.1: Psychological theories	17
1.1.1.2: Physiological theories	19
1.1.2: Theories of Anxiety	20
1.1.2.1: Social theories	20
1.1.2.2: Cognitive theories	21
1.1.2.3: Physiological theories	22
Section 1.2: Phenomenology of Depression and Anxiety	23
1.2.1: Presentation of depression	23
1.2.1.1: Behavioural symptoms of depression	24
1.2.1.2: Cognitive schema in depression	25
1.2.1.3: Biological features of depression	25
1.2.2: Prevalence of depression in children and adolescents	27
1.2.2.1 Prevalence of depressed mood	28
1.2.2.2 Prevalence of depressive disorders	29
1.2.2.3 Effects of gender on prevalence of depression	30
1.2.3: Continuity between depression in childhood and adulthood	31
1.2.4: Presentation of anxiety	32
1.2.4.1: Behavioural symptoms and anxiety	32
1.2.4.2: Cognitive schema in anxiety	34

1.2.4.3: Biological features of anxiety	35
1.2.5: Prevalence rates of anxiety in children and adolescents	36
1.2.5.1 Prevalence of anxious mood	36
1.2.5.2 Prevalence of anxiety disorders	36
1.2.5.3 Effects of gender on prevalence of anxiety	37
1.2.6: Continuity between anxiety in childhood and adulthood	37
Section 1.3: The Assessment of Depression and Anxiety	38
1.3.1: Rating-scales	38
1.3.1.1: Self-report	39
1.3.1.2: Parent-report	40
1.3.1.3: Teacher-report	40
1.3.2: Clinical interviews	41
1.3.3: Parent-child agreement in ratings of depression and anxiety	41
Chapter 2: Literature Review Part II	43
Genetic Studies of Depression and Anxiety	
Section 2.1: Behaviour Genetic Theory and Design	43
2.1.1: Family study design	43
2.1.1.1: Assortative mating	44
2.1.2: Twin study design	45
2.1.2.1: Zygosity determination	47
2.1.2.2: Representativeness	48
2.1.2.3: Equal environment assumption	49
2.1.3: Adoption study design	51
2.1.3.1: Representativeness	52
2.1.3.2: Selective placement	52
Section 2.2: Genetic Studies of Depression	53
2.2.1: Studies with adults	53
2.2.1.1: Evidence from family studies	53
2.2.1.2: Evidence from twin studies	53
2.2.1.3: Evidence from adoption studies	57
2.2.1.4: Evidence from molecular genetics	59
2.2.2: Genetic Studies of Depression in Children and Adolescents	61

2.2.2.1: Evidence from family studies	61
<i>Top-down studies</i>	62
<i>Bottom-up studies</i>	63
2.2.2.2: Evidence from twin studies	65
Section 2.3: Genetic Studies of Anxiety	67
2.3.1: Anxiety in Adults	67
2.3.1.1: Evidence from family studies	67
2.3.1.2: Evidence from twin studies	70
2.3.1.3: Evidence from molecular genetics	73
2.3.2: Anxiety in Children and Adolescents	74
2.3.2.1: Evidence from family studies	74
<i>Top-down studies</i>	74
<i>Bottom-up studies</i>	75
2.3.2.2: Evidence from twin studies	77
Chapter 3: Literature Review Part III	79
Environmental Factors, Depression and Anxiety	
Section 3.1: The Assessment of Life Events	79
3.1.1: Ascertaining potentially predictive events	80
3.1.1.1: Reporter bias	80
3.1.1.2: Events preceding onset	80
3.1.1.3: Independence	81
3.1.2: Reliability	81
3.1.2.1: Test-retest reliability	81
3.1.2.2: Agreement between multiple respondents	82
3.1.2.3: Inter-rater reliability	84
3.1.3: Fall-off in reporting	85
3.1.4: Defining events	86
3.1.5: Quantification of stress	87
3.1.5.1: Short-term and long-term impact	88
3.1.6: Long-term experiences	88
3.1.7: Background factors	89
3.1.8: Time involved	89

Section 3.2: Depression and Environmental Factors	89
3.2.1: Life events and depression	91
3.2.2: Vulnerability factors and depression	95
3.2.2.1: The social approach	95
<i>Studies with adults</i>	95
<i>Studies with children</i>	97
3.2.2.2: The cognitive perspective	102
3.2.2.3: Genetic vulnerability factors	105
Section 3.3: Anxiety and Environmental Factors	106
3.3.1: Life events and anxiety	106
3.3.2: Vulnerability factors and anxiety	108
3.3.2.1: The social approach	108
<i>Studies with adults</i>	108
<i>Studies with children</i>	109
3.3.2.2: The cognitive approach	110
Section 3.4: Genotype-Environment Correlations	111
3.4.1: Heritability of life events	112
3.4.2: Heritability of family relationships	115
3.4.2.1: Perceived family relationships	115
3.4.2.2: Observed family relationships	118
3.4.3: Heritability of measures of friendship	119
3.4.4: Heritability of social support	121
Chapter 4: Literature Review Part IV	125
The Aetiology of Depression and Anxiety in Children and Adolescents	
Section 4.1: Comorbidity between Depression and Anxiety	125
4.1.1: Comorbidity as artifact	127
4.1.1.1: Symptom overlap	127
4.1.1.2: Anxiety within depression	130
4.1.1.3: Stages of one illness	132
4.1.2: Explanations of comorbidity	134
4.1.2.1: Overlapping risk factors	134
4.1.2.2: Comorbid syndrome has a specific risk factor	139

4.1.2.3: One disorder leads to the other	141
Section 4.2: Conclusions and Hypotheses	142
Chapter 5: Methodology	145
Section 5.1: Methodology of Main Study	145
5.1.1: Selection of the sample	145
5.1.2: Zygosity determination	148
5.1.3: Assessment of life events and long-term experiences	148
5.1.4: Rating the life events and long-term experiences	149
Section 5.2: Reliability Study	151
5.2.1: Methodology	151
5.2.1.1: Subjects	151
5.2.1.2: Procedure	151
5.2.2: Results	152
5.2.2.1: Equality of mother-report for both twins	152
5.2.2.2: Inter-rater reliability of elicitation	153
5.2.2.3: Inter-rater reliability of ratings: Rater 1 vs. rater 2	154
5.2.2.4: Inter-rater reliability of ratings: Raters 1 & 2 vs. rater 3	157
5.2.2.5: Inter-rater reliability of best estimated ratings: Raters 1 and 2 vs. rater 3	160
Section 5.3: Analysis of Twin Data	162
5.3.1: Model-fitting with twin data	163
5.3.2: Group heritability analyses	168
Chapter 6: Results	171
Section 6.1: Phenomenology of Depression and Anxiety	171
6.1.1: Prevalence rates	171
6.1.2: Creating refined measures of depression and anxiety	172
6.1.3: Effects of age, sex and SES on prevalence	178
Section 6.2: Genetic Analyses of Depression and Anxiety	180
6.2.1: Univariate genetic analyses	181
6.2.1.1: Child reported data	181
6.2.1.2: Parent reported data	184

6.2.2: Multivariate genetic analyses of child-reported depression and anxiety	185
6.2.3: Group heritability analyses	192
6.2.4: Bivariate group heritability analyses	194
6.2.5: Multivariate genetic analyses of depression and anxiety: Child- and parent-report	195
6.2.6: Effects of age and sex on the univariate genetic analyses of child-reported depression and anxiety	198
6.2.7: Effects of age and sex on the bivariate genetic analyses of depression and anxiety	204
Section 6.3: Associations Between Depression, Anxiety, Life Events and Long-Term Experiences	209
6.3.1: Baseline rates of life events and LTEs	209
6.3.2: Associations between caseness and life event data	214
6.3.3: Associations between caseness and LTE Data	218
6.3.4: Interaction effects of event and LTE scores on caseness	223
6.3.5: Confounding factors	225
Chapter 7: Discussion of Main Results and Conclusions	232
Section 7.1: Producing Refined Measures of Depression and Anxiety	232
Section 7.2: Genetic Analyses of Depressive and Anxious Symptoms	233
Section 7.3: Environmental Factors, Depression and Anxiety	238
Section 7.4: Limitations of the Study	242
Section 7.5: Implications of the Study	245
References	247
Appendix 1: Children's Depression Inventory, State-Trait Anxiety Inventory for Children, Child Behaviour Checklist, Twin Similarity Questionnaire	273
Appendix 2: Rated Life Events and LTEs	283

Tables and Figures

Table 5.2.2.1a: Comparing Mean Levels of Events and LTEs Reported by the Mother for the First and Second Twin	153
Table 5.2.2.2a: Eliciting Events from the Child Interviewer 1 Compared to Interviewer 2	154
Table 5.2.2.3a: Independence Ratings for Child and Parent Reported Events and LTEs: Rater 1 Compared to Rater 2	155
Table 5.2.2.3b: Inter-rater Reliability of Events, Rater 1 Compared to Rater 2: Dimensions of Loss, Danger, and Negative Impact	156
Table 5.2.2.3c: Inter-rater Reliability of LTEs, Rater 1 Compared to Rater 2: Dimensions of Loss, Danger, and Negative Impact	157
Table 5.2.2.4a: Independence Ratings for Child and Parent Reported Events and LTEs: Raters 1 and 2 Compared to Rater 3	157
Table 5.2.2.4b: Inter-rater Reliability of Events, Raters 1 and 2 Compared to Rater 3: Dimensions of Loss, Danger, and Negative Impact	159
Table 5.2.2.4c: Inter-rater Reliability of LTEs Raters 1 and 2 Compared to Rater 3: Dimensions of Loss, Danger, and Negative Impact	160
Table 5.2.2.5a: Independence Ratings for Best Estimated Events and LTEs: Raters 1 and 2 Compared to Rater 3	161
Table 5.2.2.5b: Best Estimated Events - Raters 1 and 2 compared to Rater 3: Dimensions of Loss, Danger, and Negative Impact	161
Table 5.2.2.5c: Best Estimated LTEs - Raters 1 and 2 compared to Rater 3: Dimensions of Loss, Danger, and Negative Impact	161
Figure 5.3.1a: Univariate Genetic Analysis of Twin Data	163
Figure 5.3.1b: Univariate Genetic Analysis of Twin Data with Dominance Effects	164
Figure 5.3.1c: Cholesky Decomposition: Bivariate Model	165
Figure 5.3.1d: General and Specific Factors Model: Trivariate Case	166
Figure 5.3.1e: Causal Model in which Variable 1 Causes Variable 2	166
Table 6.1.2a: Factor Analysis of the CDI and STAIC-Trait	173

Table 6.1.2b:	Second Order Factor Analysis of the CDI and STAIC-Trait Factors	174
Table 6.1.2c:	Factor Analysis of the Items Representing Depression and Anxiety from the CBCL	177
Table 6.1.2d:	Second Order Factor Analysis of the CBCL Factors	177
Table 6.1.3a:	Comparison of Mean Scores for Depression and Anxiety for Children, Adolescents, Males, and Females	178
Table 6.1.3b:	Logit Analysis of Sex and Age effects on Depressive Symptoms	179
Table 6.1.3c:	Logit Analysis of Sex and Age effects on Anxiety Symptoms	179
Table 6.2.1.1a:	Univariate Genetic Analysis of Depression Dimension	182
Table 6.2.1.1b:	Univariate Genetic Analysis of Anxiety Dimension	182
Table 6.2.1.1c:	Univariate Genetic Analysis of CDI total score	182
Table 6.2.1.1d:	Univariate Genetic Analysis of STAIC-TRAIT total score	183
Table 6.2.1.1e:	Univariate Genetic Analyses of Depression and Anxiety in Children and Adolescents	183
Table 6.2.1.2a:	Univariate Genetic Analyses of CBCL Anxiety/Depression Syndrome	184
Figure 6.2.2a:	Full Model for the Bivariate Genetic Analysis of the Depression and Anxiety Dimensions	186
Table 6.2.2a:	Correlation matrices for Depression and Anxiety Dimensions, and for CDI and STAIC-Trait	187
Figure 6.2.2b:	Final Model from the Bivariate Genetic Analysis of the Depression and Anxiety Dimensions	187
Figure 6.2.2c:	General and Specific Factors Model for Depression and Anxiety	189
Figure 6.2.2d:	Final Model from the Bivariate Genetic Analysis of the CDI and STAIC-Trait	189
Figure 6.2.2e:	Causal Model in which Anxiety Causes Depression	191
Table 6.2.2b:	Final Solutions from Causal Models	191

Table 6.2.3a:	Group Heritability Estimates for the Stage 1 Data	192
Table 6.2.3b:	Group Heritability of CDI Scores with Cut-Off of 13	193
Table 6.2.4a:	Bivariate Heritability Estimates for Depression and Anxiety Dimensions and for the CDI and STAIC-Trait	194
Figure 6.2.5a:	General and Specific Factors Model, Child- and Parent- Reported Depression and Anxiety	195
Table 6.2.5a:	Correlation Matrices for Child- and Parent-Reported Depression and Anxiety Dimensions	196
Figure 6.2.5b:	Final Model for Child- and Parent-Reported Depression and Anxiety	197
Table 6.2.6a:	Correlation Matrices for Transformed Depression and Anxiety Dimensions, divided by Age-Group and Zygosity	198
Table 6.2.6b:	Univariate Genetic Analysis of Transformed Depression Dimension: Main Effects of Age	199
Table 6.2.6c:	Free and Fixed Four Group Models Main Effects of Age on Depression	199
Table 6.2.6d:	Models for Anxiety - Sample Divided by Age-Group	200
Table 6.2.6e:	Free and Fixed Four Group Models Main Effects of Age-Group on Anxiety	201
Table 6.2.6f:	Correlation matrices for Depression and Anxiety Dimensions, divided by Sex and Zygosity	202
Table 6.2.6g:	Models for Depression - Sample Divided by Sex	202
Table 6.2.6h:	Free and Fixed Four Group Models Main Effects of Sex on Depression	203
Table 6.2.6i:	Models for Anxiety - Sample Divided by Sex	203
Table 6.2.6j:	Free and Fixed Four Group Models Main Effects of Sex on Anxiety	204
Figure 6.2.7a:	Final Model from the Cholesky Decomposition of the Transformed Depression Dimension and the Anxiety Dimension: Younger Children only	205

Figure 6.2.7b:	Final Model from the Cholesky Decomposition of the Transformed Depression Dimension and the Anxiety Dimension: Older Children only	205
Table 6.2.7a:	Main Effect of Age on the Cholesky Decomposition of Depression and Anxiety	206
Figure 6.2.7c:	Final Model from the Cholesky Decomposition of the Transformed Depression Dimension and the Anxiety Dimension: Boys only	207
Figure 6.2.7d:	Final Model from the Cholesky Decomposition of the Transformed Depression Dimension and the Anxiety Dimension: Girls only	207
Table 6.2.7b:	Main Effect of Sex on the Cholesky Decomposition of Depression and Anxiety	208
Table 6.3.1a:	Baseline Rates of Life Events and LTEs Comparison with Sandberg et al. (1993)	210
Table 6.3.1b:	Percentage of Families from Each SES Group	211
Table 6.3.1c:	Percentage of Younger, Older, Male and Female Children	211
Table 6.3.1d:	Mean Number of Life Events and LTEs in Families of Higher and Lower SES	212
Table 6.3.1e:	Mean Number of Life Events and LTEs in Younger and Older Children	213
Table 6.3.1f:	Mean Number of Life Events and LTEs in Male and Female Children	213
Table 6.3.2a:	Independent T-Tests of Negative Event Scores for Cases and Controls	216
Table 6.3.2b:	Paired T-Tests of Negative Event Scores for Probands and their Co-Twins	216
Table 6.3.2c:	Independent T-Tests of Loss and Danger Scores for Cases and Controls	217
Table 6.3.2d:	Paired T-Tests of Loss and Danger Scores for Probands and their Co-Twins	218

Table 6.3.3a:	Independent T-Tests of Negative LTE Scores for Cases and Controls	219
Table 6.3.3b:	Paired T-Tests of LTE Scores for Depressed Probands and their Non-Depressed Co-Twins	219
Table 6.3.3c:	Independent T-Tests of Friendship, School-work, Family Relationship and Family Structure Problems for Cases and Controls	221
Table 6.3.3d:	Paired T-Tests of Friendship, School-work, Family Relationship and Family Structure Problems for Probands and their Co-Twins	221
Table 6.3.4a:	Interaction Effects of Independent Negative Life Events and LTE Types on Caseness	223
Table 6.3.4b:	Logit Analysis of Interaction Effects of Independent Negative Life Events and LTE Types on Caseness	224
Table 6.3.5a:	Testing for Associations Between Sex and the Event and LTE Measures Associated with Depression	226
Table 6.3.5b:	Testing for Associations Between Sex and LTE Type	226
Table 6.3.5c:	Testing for Associations Between Age-Group and the Event and LTE Measures Associated with Anxiety	227
Table 6.3.5d:	MZ and DZ Correlations for the Event and LTE Variables that were Associated with Depression and Anxiety	228
Table 6.3.5e:	MZ and DZ Probandwise Concordance Rates for the Binary LTE Variables that were Associated with Depression	229
Table 6.3.5f:	Bivariate Group Heritability Estimates for Anxiety and Depression and the Best Estimated Events and LTE Data	229
Table 6.3.5g:	Prevalence Rates of the LTEs in Co-Twins of Depressed MZ and DZ Probands	230

Introduction

This thesis is divided into three main sections. These are the literature review, the methods of the study, and the results and discussion. The literature review discusses the theories, phenomenology, assessment and aetiology of depression and anxiety in children and adolescents. In particular, behaviour genetic studies of depression and anxiety, and studies of environmental influences on depression and anxiety are reviewed in detail. As much of the literature that has formed the basis of the work with children and adolescents was conducted with adults, many of the studies reviewed here used adult subjects. However, this should be seen as informing the reader about the background on which the study of depression and anxiety in children and adolescents is founded.

Chapter 1 reviews the traditional theories of depression and anxiety. Following this are sections on the phenomenology and prevalence of depression and anxiety, and the assessment of these states. Chapter 2 begins with an introduction to behaviour genetic theory. This is followed by two sections reviewing the behaviour genetic studies of depression and anxiety. Within each of these the adult literature is reviewed first followed by the literature on genetic studies of child and adolescent depression and anxiety. Chapter 3 discusses the assessment of environmental influences implicated in depression and anxiety, and then reviews the literature investigating such influences in adults and in children and adolescents. This chapter ends with a discussion of genotype-environment correlations. In chapter 4, the co-occurrence of depression and anxiety (comorbidity) is discussed in terms of all of these aetiological factors. This chapter ends by summarizing the conclusions of the literature review and the resulting study hypotheses.

Chapter 5 describes the methods of the study, including the reliability study of the interview, the Psychosocial Assessment of Childhood Experiences (PACE).

The final section of this chapter describes the techniques used in analysing twin data.

Chapter 6 presents the results in three sections which address the issues discussed in chapters 1,2 and 3 respectively. Thus the first of these presents the prevalence rates of depressive and anxious symptoms, the production of refined measures of depression and anxiety, and the effects of age, sex and SES on scores on these measures. The results from the genetic analyses of depressive and anxious symptoms are described in the second section. The chapter concludes with the analyses investigating the associations between life events, long-term experiences and depressive and anxious symptoms. Finally, Chapter 7 discusses the main findings and implications of the study.

Chapter 1: Literature Review Part I

Depression and Anxiety in Children and Adolescents: The Concepts

Section 1.1: Theories of Depression and Anxiety

There are two types of theory which have traditionally been applied to the phenomena of depression and anxiety. These are psychological theories (social theories, cognitive theories, and behavioural theories), and physiological theories. All these types of theory and the evidence for them are discussed throughout this literature review. The aim of this section is briefly to introduce the varied theories of depression and anxiety in order to provide a general background on which a more detailed overview of their aetiology can be built. These theories will be discussed first with reference to depression and then with reference to anxiety. As the social, cognitive and behavioural theories of depression involve a considerable amount of over-lapping constructs these will be covered together. The more recent application of behaviour genetics theory to depression and anxiety is discussed in chapter 2.

1.1.1: Theories of depression

1.1.1.1: Psychological theories

Brown and Harris' (1978b) book "The Social Origins of Depression" introduced two major concepts in the aetiology of depression which have been the subject of much subsequent research. These were vulnerability factors and provoking agents. Their theory predicted that any individual who experienced a provoking agent (or life event) would be more likely to become depressed than an individual who did not

suffer such a life event. In addition to this, an individual who had also experienced a vulnerability factor would be substantially more likely to become depressed in the presence of a provoking agent than someone who had not experienced a vulnerability factor. However, a vulnerability factor alone was not a risk factor for depression. Provoking agents were events such as death of a loved one, illness of a loved one, losing one's job, or marital conflict and breakdown. The four factors which were found to act as vulnerability factors to depression in adult women were loss of mother before the age of 11, lack of employment outside the home, more than 3 children under the age of 14 living in the home, and lack of a good marital relationship. In Brown and Harris' (1978b) theory, cognitive factors such as self-esteem, helplessness and hopelessness were seen as mediators of these environmental influences.

Seligman's theory of Learned Helplessness (1974, 1985; reviewed in Seligman and Peterson 1986) considered cognitive factors as mediators of the effects of social events on depression in children as well as adults. Early work with dogs by Seligman and colleagues showed that exposure to uncontrollable shocks resulted in three types of deficit. First there was a lack of motivational deficit, ie. the animals failed to make as many attempts to escape. Secondly, there was a cognitive deficit in that even when an occasional successful escape attempt was made, this pattern was not learned. Thirdly, the animals showed an emotional deficit in which they failed to respond to the shocks with an emotional response but merely sat passive and accepting. The key factor in producing this state of "learned helplessness" was felt to be the uncontrollability of the situation. Seligman argued that this state of learned helplessness is the central construct in depression in humans.

Abramson, Seligman and Teasdale (1978 reviewed in Seligman and Peterson 1986) extended this theory to include the notion of attribution. In this theory three dimensions of attribution were seen as central to the creation of learned helplessness and depression. The first of these was that the uncontrollable event be seen as related to the characteristics of the individual (ie. internal as opposed to external). If this was the case then self-esteem would be reduced with the growth of

the helplessness. Secondly, the uncontrollable event, if attributable to conditions which persist over time would be seen as stable, and the resulting helplessness would be “non-transient”. Finally, if the event was seen as global, i.e. could happen in a variety of situations, not just this one, then helplessness was likely to be pervasive. Thus the attribution of an uncontrollable event as internal, global and stable was seen as resulting in poor self-esteem and non-transient, pervasive helplessness.

Similar cognitive schemas were put forward in Beck’s (Beck & Clark 1988) Information Processing Perspective. This described the depressed individual as having a negative view of the self, the world, and the future. This view would lead to selective processing involving overgeneralisation of negative information. Systematic distortions in the processing of information would result in the apparent confirmation of the individual’s negative view of the self, world and future. Thus a vicious cycle would be set up, with appraisal of negative information as “pervasive, global, and exclusive”. The depressed person would view himself as inadequate and worthless, the world as presenting insurmountable hurdles, and the future as bleak and hopeless. Such a position could also be brought about through lack of positive reinforcement as proposed in Lewinsohn’s behavioural learning theory (1974, discussed in Harrington 1993).

1.1.1.2: Physiological theories

Physiological theories of depression try to explain the relationship between abnormal aspects of depressed subjects’ physiology, and their behavioural symptoms. The disturbances of mood, sleep, appetite, and autonomic activity seen in depressed patients suggest dysfunction of the hypothalamus (Kazdin 1990) and septo-hippocampal system (Gray 1988). The septo-hippocampal system was described by Gray as the mediator between external stimuli and internal biological changes. This model proposed that the septo-hippocampal system is responsible for comparing internally generated plans with the actual outcome. It was predicted

that a mismatch between the expected and observed outcome, especially when continuous and uncontrollable, would result in activation of the septo-hippocampal system. This in turn would result in the depletion of neurotransmitters such as noradrenaline and serotonin.

Serotonin is involved in the regulation of appetite so poor functioning of this transmitter may account for the appetite changes. In addition to this, noradrenaline and serotonin regulate the neuroendocrine agents that control pituitary function and hormonal responses (Kazdin 1990). Neurotransmitter deficits can therefore lead to dysfunction of hormones. Two hormones which are abnormal in depressed individuals are cortisol and growth hormone. Cortisol interacts with stress to produce disordered circadian rhythms, which may account for the sleep disturbances seen in depressed patients. Thus the different levels of abnormality of physiology in depressed patients account for many of the behavioural symptoms seen in these patients.

In summary, theories of depression emphasise the role of external stressors such as life events, and internal mediating processes. These processes include cognitive components such as attributions and learned helplessness, and biological components such as the septo-hippocampal system. Thus the outcome from this process is a combination of both cognitive deficits and abnormal physiological features.

1.1.2: Theories of anxiety

1.1.2.1: Social theories

Bowlby's (1973) Attachment Theory discussed the relationship between poor attachment in infancy and anxiety disorders. In particular Bowlby discussed the school phobic child in terms of anxious attachment. In this situation, the child was

seen as not wishing to be parted from his attachment figure, rather than specifically not wanting to go to school per se. This led to the consideration of school phobia of this type as a form of Separation Anxiety Disorder, and was described as being triggered by fear that while apart from the attachment figure some event would befall either the child or the attachment figure. Other types of anxiety can similarly be seen as related to fears of certain events occurring or of certain situations.

Social learning theories advocate the role of conditioning in the acquisition of anxiety. Such theories hypothesise that an individual may learn to fear a stimuli because in the past this stimuli has been associated with a threat (Strange 1992). In addition to this, an individual may learn to fear an object because they see others displaying fear of that object. In this way phobias may be transmitted across the generations from parent to child. For example a parent with social phobia is likely to teach a child, whether they mean to or not, that contact with other individuals is a threatening situation and one to be avoided. Such theories suggest that parental anxiety disorders may function as a factor of the rearing environment that result in the familial association seen in these disorders. This offers an alternative to the theory that such familiarity is as a result of genetic factors.

1.1.2.2: Cognitive theories

Cognitive theories tend to stress the relationship between threat and anxiety. For example Eysenck's (1992) Hypervigilance Theory of Anxiety emphasises selective processing of threat stimuli from all the stimuli available. A similar theory put forward by Beck and Clark (1988) discussed anxiety in terms of selectivity in the processing of threat cues with an exaggerated estimate of vulnerability. Negative appraisals of the situation were described as being selective and specific, referring only to the particular threat situation to which that individual was vulnerable. Thus this theory emphasised not only hypervigilance to threat, but a specificity of threat, such that only certain classes of feared stimuli would provoke anxiety in any particular individual.

Similarly, Endler and Edwards' (1988) Multidimensional Interaction Model of Anxiety hypothesised that areas of high trait anxiety, for example anxiety about social situations, would lead to high state anxiety when confronted with that particular situation type. This theory proposed that there would be an interaction of cognitive vulnerability (trait anxiety) with specific stressors to produce state anxiety.

1.1.2.3: Physiological theories

The predominant neuropsychological theory of anxiety is that of Gray (1988). The central feature in this theory was the "behavioural inhibition system". As discussed earlier, this system was described as assessing the environment for potentially threatening stimuli. An important feature of this system therefore was the comparison of expected and observed outcomes in order to search for threatening mismatches. Gray (1988) proposed that the brain system responsible for the "behavioural inhibition system" is the septo-hippocampal system. The activation of this system would lead to the inhibition of current behaviour and increased readiness for action accompanied by extreme awareness of the environment. The septo-hippocampal region governs the noradrenergic and serotonergic systems which are found to be abnormal in anxious patients.

A further region of the brain Gray (1988) discussed in his theory of anxiety was the role of the amygdala in "fight or flight" behaviours. The amygdalas are activated by serotonin levels, so it can be seen how the functioning of the septo-hippocampal system is related to that of the amygdala via the neurotransmitter serotonin. This underlines once again the role of this transmitter in anxiety.

In summary, theories of anxiety describe this state as a pervasive fear, of separation or of specific stimuli. This is coupled with hypervigilance to fear-inducing stimuli, a process which may be governed by the septo-hippocampal system. In conclusion, theories of depression and anxiety while emphasising

different aspects of social and cognitive factors, suggest overlapping biological mechanisms are involved. It may be that these account for their common co-occurrence. The co-occurrence of depression and anxiety is discussed in more detail in chapter 4.

Section 1.2: Phenomenology of Depression and Anxiety

This section describes the presentation, prevalence and continuity from childhood to adulthood of depression and anxiety. Although the presentation of depression and anxiety in adults is described, this section focuses on a review of the more directly relevant literature pertaining to children and adolescents. Depression is covered first followed by anxiety.

1.2.1: Presentation of depression

Depression can be considered at two levels. The first of these is mood or symptom, the second is syndrome or disorder. A description of the presentation of the disorder necessarily includes a description of the mood and symptoms involved so in this way both levels of classification will be considered. The presentation of a psychiatric disorder is best described in terms of three categories of features. The first of these is the behavioural features or symptoms that are used to make a diagnosis. Much of the research literature uses a system of classification called the Diagnostic and Statistical Manual of Mental Disorders (DSM). The most recent edition of this is DSM-IV, but as this was only published in 1993, studies from the 1980s and early 1990s have used DSM-III and DSM-III-R. However, in this section the classification of depressive and anxiety disorders under DSM-IV will be

described. The second type of feature of depressive and anxiety disorders is the accompanying cognitive schema, and the third is the physiological abnormalities.

1.2.1.1: Behavioural symptoms of depression

The presentation of depression in children and adolescents has been found not to differ much from that of depression in adults (Mitchell, McCauley, Burke, & Moss 1987). Depressive disorders can be classified into unipolar and bipolar disorders, a distinction which rests upon the presence or absence of mania. Depression with mania is referred to as bipolar depressive disorder. Unipolar depression can be further classified into Major Depressive Disorder (MD) and Dysthymic Disorder (DD). Although studies involving subjects with bipolar disorder are included in this literature review the project has only considered consider unipolar depressive symptoms and for this reason unipolar depressions are discussed in greater detail.

The DSM-IV classification of MD includes the following symptoms of which at least five must be present for most of the time during a two week period: depressed mood (or irritable mood in children), markedly diminished interest or pleasure in all or nearly all aspects of life, significant weight change, sleep disturbances, psychomotor agitation or retardation, fatigue or low energy, feelings of worthlessness or excessive inappropriate guilt, poor concentration, and recurrent thoughts of death and ideation about suicide. Taken individually these can be thought of as what is referred to as depressive symptomatology. The DSM-IV classification of DD involves very similar symptomatology of which three symptoms must be present more of the time than not, for at least two years. However, the additional symptoms of low self-esteem or self-confidence, and feelings of pessimism and despair give the definition a more cognitive base.

1.2.1.2: Cognitive schema in depression

As with the behavioural features of depression, in children from approximately 8 years of age, the cognitive schema are the same as those in adults (Harrington 1993). These children express feelings of worthlessness, low self-esteem, a negative view of the self, world and future, and the attribution of negative events as internal, global and stable (Beck 1987). In addition to this, many theories have focused on the feelings of uncontrollability termed learned helplessness, which is also seen in the child and adolescent depressed population (Abramson, Seligman, & Teasdale 1978 reviewed in Seligman, Peterson, Kaslow, Tanenbaum, Alloy, & Abramson 1984). These cognitive schema are thought to be the mediators between vulnerability factors, stressors and depression (Brown & Harris 1978b).

1.2.1.3: Biological features of depression

Investigations of biological markers for depression have tended to focus on neurotransmitters and neuroendocrine systems, both of which are said to reflect central nervous system functioning (Puig-Antich 1986).

Abnormalities in four monoamine neurotransmitters have been discussed in the aetiology of depression. These are norepinephrine, noradrenaline, dopamine and serotonin. Specifically, it appears that receptor uptake of these transmitters may be altered in depressed subjects. Tricyclic antidepressants (eg. imipramine) are thought to act by increasing sensitivity of the receptors (Davison & Neale 1986; Strange 1992; Brown, Steinberg, & van Praag 1994).

Rogeness et al. (1990) found that children with depressive disorders had higher levels of norepinephrine than children with conduct disorder. In addition, there is considerable evidence for abnormal serotonin levels in depressed children and adolescents, but this evidence is contradictory in that the results can be interpreted as demonstrating either decreased or increased serotonergic activity (Rogeness,

Javors, & Pliszka 1992). Dopaminergic functioning has not been demonstrated to be consistently different in children with depression as compared to other groups (Rogeness, Javors, & Pliska 1992). These data can be seen as consistent with Rogeness, Javors and Pliska's (1992) hypothesis that depression in children is associated with high levels of serotonin and norepinephrine but low to normal levels of dopamine.

One unresolved issue in this area is the lack of response of depressed young people to tricyclic antidepressants (eg. Puig-Antich et al. 1987). Several explanations have been offered for this lack of response (Harrington 1993). The first of these is that there may be methodological weakness in the studies carried out so far. These could include factors such as the level of dosage given. Second, early-onset disorders appear to differ from later onset, specifically they appear to have a higher heritable component (Weissman, Warner, Wickramaratne, & Prusoff 1988). Third, the systems involved in the physiology of depression may be subject to developmental changes.

Two neuroendocrine systems which are under the control of serotonin have been found to be abnormal in depressed adults. These are cortisol, and growth hormone. A test of the relationship between cortisol secretion and MD (the dexamethasone suppression test - DST) involves analysing levels of cortisol after administration of dexamethasone. A review of 14 studies revealed sensitivity of the DST for diagnosing MD in children of 69.6% and specificity of 69.7%, and corresponding levels of 47.1% and 80.2% for adolescents (Casat, Arana, & Powell 1989). The more recent evidence suggests that the DST is not able to discriminate between children and adolescents with a depressive disorder, another psychiatric disorder, or no known disorder (Birmaher, Dahl, Ryan et al. 1992; Birmaher, Ryan, Dahl et al. 1992; Tyrer et al. 1991).

Growth hormone secretion in childhood depression has been extensively studied by Puig-Antich and his colleagues. Their results show that in a similar manner to depressed adults, prepubertal children with endogenous depression will

hypo-secrete growth hormone in response to insulin induced hypo-glycemia. Also, depressed children secrete significantly more growth hormone during sleep than normal and psychiatric non-depressed controls (Puig-Antich & Rabinovich 1986; Puig-Antich 1986).

Research on depression has also focused on abnormalities of sleep. Reviews of the literature on sleep EEGs have been shown abnormalities in a variety of ways in adults with depressive disorders. These include a decrease in slow-wave sleep, a decrease in sleep efficiency, a shortening of latency to the first rapid eye movement (REM) period, an increase in REM density, and an abnormal temporal distribution of REM sleep during the night (Puig-Antich 1986, Stein, Wilson, Uhde 1994). However, the evidence for abnormal sleep EEGs in child and adolescent subject with depressive disorder is inconclusive. The abnormalities described above that are seen in adult depressives are not found in young subjects, but different abnormalities are seen. However, there is considerable variance with age in these measures throughout adulthood, so it may be that the unusual sleep EEG patterns in depressed children are due to their age rather than their depression (Puig-Antich 1986; Puig-Antich & Rabinovich 1986). This area is in need of further research.

Overall, there are several aspects of the physiology of a depressed individual which are abnormal. These abnormalities could be caused by genetic factors, and as such the investigation of genetic factors as part of the aetiology of depression is an important area of work.

1.2.2: Prevalence rates of depression in children and adolescents

Estimates of prevalence of depression differ depending on the level of depression which is being identified. As discussed above there are two levels at which depression can be considered. First, the assessment of mood or symptoms usually

involves identifying individuals who endorse a single item pertaining to the most salient feature of depression, ie. feelings of sadness, or who score above a specific cut-off score on a set of symptom items describing depressed mood. Second, at the level of disorder, a diagnosis must be made either by clinical interview or by a research interview which identifies the presence or absence of symptoms that meet the criteria for depression. The effects of age or pubertal status, sex and the interaction of these two factors on prevalence rates are also discussed.

1.2.2.1: Prevalence of depressed mood in children and adolescents

Achenbach (1991a, 1991b, 1991c) investigated the prevalence of depressed mood by analysing the percentage of non-referred children aged 4 to 18 ($N = 2,110$) for whom the single item "sad, unhappy or depressed" was endorsed. This produced rates of depressed mood of 10% to 20% for parent-report and on the self-report measure (only those aged 11-18 years, $N = 1,054$) the rates were 20% to 40%. There was a trend in the data for the older children to score higher than the younger children. In the self-reported data this reached significance, but age accounted for less than 1% of the variance in the scores. Rutter, Graham, Chadwick, and Yule (1976) found that in their community sample of 183 14-15 year-olds the one item frequency on self-report of "often feel miserable or depressed" was between 20.8% and 23.0%. Petersen, Compas, Brooks-Gunn, Stemmler, Ey, and Grant's (1993) review of 14 studies found the median rate of depressed mood in adolescence was 35%.

An alternative method of assessing mood is to identify symptoms that tend to cluster together. This approach is taken by Achenbach, whose "syndrome" of "anxious/depressed" behaviour can be thought of as a measure of anxious and depressed mood. The cut-off chosen for a measure such as this is entirely arbitrary. In this case the cut-offs were designed to select the highest scoring 5% of the population (Achenbach & Edelbrock 1983; Achenbach 1991a, 1991b, 1991c). Age effects have been shown for this syndrome. Achenbach, Conners, Quay,

Verhulst, and Howell (1989) conducted an ANCOVA in which they looked for main effects of age on the syndrome anxious/depressed. A main effect of age was found, with the adolescents (12-16) scoring more than the children (6-11). However age accounted for less than 1% of the variance in the syndrome score.

A more rigorous test of depressed mood is whether the child scores above a cut-off that has been designed to give maximum sensitivity and specificity for identifying clinical cases. Such cut-offs are referred to as clinical cut-offs. An example of a study investigating prevalence of depressed mood in this way is that of Stavrakaki, Williams, Walker, Roberts, and Kotsopoulos (1991) who assessed 326 children aged 10-11 years with the Children's Depression Inventory (CDI) (Kovacs 1981, 1985). They found that between 1% and 2% of the children scored above the cut-off of 19.

In summary, the levels of children and adolescents who express depressed mood is between 10% and 40%. However, the number who score in the clinical range for depressed mood is far lower, only 1% to 2% in children aged 10 to 11. This is similar to the rates found for depressive disorder as illustrated below. The effects of age are consistent in child- and parent-report in that adolescents report and are reported to have higher levels of depressive symptoms than children.

1.2.2.2: Prevalence of depressive disorders in children and adolescents

Rates of depressive disorder in community or school list samples of children are found to be in the region of 1% to 3% (Fleming, Offord, & Boyle 1989; Anderson, Williams, McGee, and Silva 1987; Flemming & Offord 1990). Rates of depression for adolescents from epidemiological studies in various countries have been found to be between 3% and 6% (Fleming, Offord, & Boyle 1989; Fleming, Boyle, & Offord 1993; Garrison, Addy, Jackson, McKeown, & Waller 1992; Goodyer & Cooper 1993; Kashani, Orvaschel, Rosenberg, & Reid 1989;

McGee, Feehan, Williams, & Anderson 1991). Thus it appears that depression is more common in adolescents than in children.

There have been suggestions that the increased rates of depression in adolescence as compared to children is due to biological changes at puberty. A study by Angold and Rutter (1992) investigated this issue in a sample of 3,519 8- to 16-year-old psychiatric patients. Both boys and girls showed higher levels of depression in the older children, but when age was controlled for, pubertal status did not explain any further proportion of the variance. It appears therefore that it is age, rather than pubertal stage that effects rates of depression in children and adolescents.

1.2.2.3: Effects of gender on prevalence of depression in children and adolescents

In the child and adolescent literature on depression, it is commonly cited that girls are more likely than boys to endorse a single item of depressed mood (Achenbach 1991a, 1991b, 1991c; Rutter, Graham, Chadwick, & Yule 1976), to score more on depression scales (Stavrakaki, Williams, Walker, Roberts, & Kotsopoulos 1991; Garrison, Addy, Jackson, McKeown, & Waller 1992; Achenbach, Conners, Quay, Verhulst, & Howell 1989; Ferdinand, Verhulst, & Wiznitzer 1994) and may be more likely to be diagnosed with a depressive disorder (McGee, Feehan, Williams, & Anderson 1991). However the picture is somewhat complicated by what appears to be an interaction of age with sex on prevalence of depression, such that in a pre-pubertal depressed population, two-thirds of the sample will be boys, and one third girls, but after puberty only one third of depressed adolescents are boys (Rutter, Tizard, & Whitmore 1981; Angold & Rutter 1992; Ferdinand, Verhulst, & Wiznitzer 1994).

1.2.3: Continuity between depression in childhood and adulthood

The first issue to consider when investigating the issue of continuity of disorder from childhood to adulthood is the re-occurrence rates in children with depressive disorders. These have been found to be high in several studies (Kovacs, Feinberg, Crouse-Novak, Paulauskas, Pollack, & Finkelstein 1984; Nolen-Hoeksema, Seligman, & Girgus 1992; Quinton, Rutter, & Gulliver 1990; Harrington, Fudge, Rutter, Pickles, & Hill 1990).

Furthermore, the similarity of depression childhood and adolescence to that seen in adults has been illustrated in the rates of depressive disorder in the relatives of depressed subjects (Harrington et al. 1993). The prevalence of depressive disorders in 128 interviewed relatives of a depressed proband group was significantly higher than that in the 151 interviewed relatives of the control group (47% as compared to 32%, $p < 0.01$, odds ratio = 1.9). Rates of any of the other psychiatric disorder categories were not significantly different between the two groups. In addition to this the prevalence rate for female relatives of depressed children was 59% as compared to that for male relatives which was 32% (odds ratio = 3.1, $p < 0.01$). The sex of the proband had no effect on the prevalence rates in the relatives. This demonstrates the similarity of depression in young people to depression in adults, in that there are higher levels of depression in the relatives of depressed than non-depressed young people, and the female relatives are more strongly affected than the males.

One final issue to consider here is the finding that early onset depressive disorders have a stronger familial loading (Weissman et al. 1986; Kupfer, Frank, Carpenter, & Neiswanger 1989; Weissman, Warner, Wickramaratne, & Prusoff 1988; for a review see Strober 1992). This suggests that while there is substantial continuity from childhood depressive disorders to these disorders in adulthood, there may be different aetiological factors involved in such cases from those which begin in

adulthood. As such, while it is clearly important to review evidence from adults, that which considers early-onset cases may be more relevant.

In summary, childhood and adolescent depression closely resembles adult depression in behavioural, cognitive, and biological aspects. Also from around the age of 12 years onwards, females are significantly more likely to become depressed than males. There is also considerable continuity from depression in childhood to depression adulthood.

1.2.4: Presentation of anxiety

1.2.4.1: Behavioural symptoms and anxiety

In 1980, when DSM-III was published, there was a major change in the nosology of the anxiety disorders. In place of the diagnostic category "anxiety neurosis" were the two disorders "Panic Disorder" (PD) and "Generalised Anxiety Disorder" (GAD). In DSM-IV there are the following anxiety disorders: Panic Disorder (PD) with or without Agoraphobia, Agoraphobia without Panic Disorder, Specific Phobia, Social Phobia, Obsessive-Compulsive Disorder (OCD), Post-Traumatic Stress Disorder (PTSD), and Generalised Anxiety Disorder (GAD). As research into the anxiety disorders has concentrated on PD and GAD, it will mainly be these two disorders that are discussed below.

PD involves at least one panic attack accompanied by worry for at least a month about the possible re-occurrence of the attack. A panic attack involves discrete periods of extreme fear or discomfort involving at least four of the following symptoms: pounding heart, sweating, trembling, sensations of shortness of breath, feelings of choking, chest pain, nausea, feeling dizzy, derealisation, fear of losing control, fear of dying, numbness, and chills or hot flushes. The addition of Agoraphobia refers to feelings of inability to escape from one's situation.

GAD involves at least three of the following symptoms being present more days than not for a period of at least six months: restlessness, being easily fatigued, difficulty in concentration, irritability, muscle tension, and sleep disturbance. The worry or anxiety is not specific.

Phobias involve persistent and marked fears of specific objects or situations. This is accompanied by considerable attempts to avoid the provoking situation. Forced endurance of the feared situation causes acute and extreme distress. OCD involves recurrent thoughts or repetitive actions, and PTSD involves recurrent intrusive and distressing reliving of the stressful event to which the individual was subjected.

The anxiety disorders of childhood are also numerous. They include Separation Anxiety Disorder, Specific Phobias, Social Phobias (including school phobia), Obsessive-Compulsive Disorder (OCD), Post-Traumatic Stress Disorder (PTSD), and Overanxious Disorder (OAD).

SAD is the classic childhood anxiety disorder. It involves excessive anxiety concerning separation from major attachment figures including persistent reluctance to go to sleep without the presence of the attachment figure, or to go out including going to school as this means leaving the attachment figure. It is important to note that the fear is related to leaving the attachment figure, not to going to school per se which is more likely to be seen in phobics. This is illustrated in a study by Last and Strauss (1990) which showed that mothers of children with SAD and school refusal were significantly more likely to have a history of school refusal themselves than mothers of children with phobic school refusal. This is interpreted as showing the importance of the role of poor mother-child interaction in SAD children, as compared to the specific event or situation related aetiology of phobic school refusal. However, this could also be interpreted as suggesting specificity of the genetic factors involved in SAD. Physical symptoms such as

headaches and nausea when separation is imminent or current are also seen in SAD.

Interestingly, the temperamental characteristic “behavioural inhibition” which refers to being shy, timid, and constrained in unfamiliar surroundings has been shown to be associated with later anxiety disorders (Hirshfeld et al. 1992).

The other anxiety disorders present in a very similar manner in childhood and adolescence to how they present in adults. OAD is the childhood version of GAD, involving unspecific excessive worry and fearful behaviour. Samples of children with OAD tend to be significantly older and more symptomatic, with higher levels of additional anxiety disorders than samples of children with SAD (eg. Last, Hersen, Kazdin, Finkelstein, & Strauss 1987).

Although PD is not generally thought of as a disorder of childhood and adolescence, a paper by Moreau and Weissman (1992) which critically reviewed 63 articles relating to PD in children and adolescents concluded that this disorder also occurs in this age-range and presents in a very similar way to PD in adults.

1.2.4.2: Cognitive schema in anxiety

The predominant maladaptive schema present in anxiety disordered individuals is hypervigilance to danger and threat (Beck and Clark 1988). More specifically, particular hypervigilance is seen with reference to the particular stimulus which arouses the individual's fear (Endler & Edwards 1988).

Anxiety disorders in childhood, and particularly SAD are thought to be related to poor attachment in infancy which results in persistent fears about leaving the attachment figure and about new social situations (Bowlby 1973).

1.2.4.3: Biological features of anxiety

Several neurotransmitters have been implicated in anxiety. These include GABA, noradrenaline, norepinephrine, and serotonin. GABA is the inhibition transmitter, so low levels of this transmitter lead to an increase in behavioural inhibition and a parallel increase in levels of arousal and anxiety levels in anxious patients (Gray 1988; Strange 1992). The activation of the behavioural inhibition system, (the septo-hippocampal system) results in high levels of serotonin and noradrenaline. Anxiolytic drugs are thought to lower levels of anxiety by acting on the behavioural inhibition system in that they reduce the stress-induced levels of noradrenaline and serotonin and this lowers their anxiety-inducing effects (Gray 1988). Similar behavioural changes to those seen in patients taking anxiolytics are seen in individuals with lesions in the septohypocampal region, offering further support for this hypothesis.

Due to the apparent overlap between the physiological aspects of depression and anxiety the antidepressant imipramine has been tested in the treatment of school phobia and panic symptoms. This drug is thought to alleviate the serotonin abnormalities seen in adult patients with depression or anxiety. Some studies have found this to be an effective treatment (Gittelman-Klein & Klein 1971; Deltito & Hahn 1993; Ballenger, Carek, Steele, & Cornish-McTighe 1989), while others have not (Klein, Koplewics, & Kanner 1992; Bernstein, Garfinkel, & Borchardt 1990), suggesting that this is an area that requires further investigation.

Increased urinary norepinephrine has been demonstrated in children with behavioural inhibition (Kagan, Reznick & Snidman 1987). As described earlier stable inhibition has been shown to be associated with later anxiety disorders (Hirshfeld et al. 1992). Furthermore, Rogeness, Javors, Maas, and Macedo (1990), who investigated levels of plasma norepinephrine in children, found that norepinephrine function is higher in children with SAD as compared to children with conduct disorder.

Once again there appears to be an overlap between the physiological aspects of depression and anxiety. This issue will be considered further in Chapter 4.

1.2.5: Prevalence rates of anxiety in children and adolescents

As with the section on prevalence rates in depression, this section will be divided into studies of mood and studies of disorder. As Achenbach's syndrome "anxious/depressed" encompasses both anxiety and depression this will not be discussed further.

1.2.5.1: Prevalence of anxious mood in children and adolescents

The prevalence of symptoms of SAD, PD, OAD, and fear in children and adolescents ranges from 10% to 30% depending on the type of symptom under study (Bell-Dolan, Last, & Strauss 1990; King, Gullone, & Ollendick 1992; Moreau & Weissman, 1992; Stavrakaki, Williams, Walker, Roberts, & Kotsopoulos, 1991). These symptoms tend to be more prevalent in younger rather than older children (Bell-Dolan, Last, & Strauss 1990; King, Gullone, & Ollendick 1992).

1.2.5.2: Prevalence of anxiety disorders in children and adolescents

Prevalence of anxiety disorders in children and adolescents may also be age-related. A sample of 70 8-year-olds (Kashani, Orvaschel, Rosenberg, & Reid 1989) found prevalence of anxiety disorders to be 25.7% using child interviews, whereas two samples of 11-year-olds (Anderson, Williams, McGee & Silva 1987; McGee, Feehan, Williams, & Anderson 1992) found rates to be in the region of 6-10%. Studies of adolescents have produced estimated prevalence rates in the region of 10-20% (McGee, Feehan, Williams, & Anderson 1991;

Kashani, Orvaschel, Rosenberg, & Reid 1989; Kashani & Orvaschel 1990). Although these data show no clear pattern, they are suggestive of there being age effects on prevalence of anxiety disorders in children and adolescents.

1.2.5.3: Effects of gender on prevalence of anxiety in children and adolescents

Numerous studies have reported higher mean anxiety and fear scores for girls than boys (King, Gullone, & Ollendick 1992; Stavrakaki, Williams, Walker, Roberts, & Kotsopoulos 1991; Bell-Dolan, Last, & Strauss 1990). Furthermore this gender effect appears also to be present in the prevalence of anxiety disorders (McGee, Feehan, Williams, & Anderson 1991; Kashani & Orvaschel 1988; Kashani & Orvaschel 1990; Anderson, Williams, McGee, & Silva 1987) in that these are more commonly reported in girls than in boys.

1.2.6: Continuity between anxiety in childhood and adulthood

Although there have been no published prospective longitudinal studies of anxiety disorders from childhood through to adulthood, there have been several studies which have investigated the presence of anxiety symptoms or disorders in the histories of adult patients with anxiety disorders (Gittelman-Klein, & Klein 1971; Hoehn-Saric, Hazlett, & McLeod 1993; Swedo, Leonard, & Rapoport 1992; Lipsitz et al. 1994). These studies have all found that there were significantly inflated rates of anxiety in the childhood's of the anxious adults. However, they all suffer from the same methodological limitation which is that the data is retrospective and is thus likely to be subject to reporter bias. The current psychological status of the subjects could well be acting as a confounding factor in the relationship between current and retrospectively reported childhood rates of anxiety.

Deltito & Hahn (1993) considered the presentation of anxiety disorders in a three generation family pedigree. All 14 genetically related members of the family had an anxiety disorder. In the children this was school phobia, which was also present in the histories of all the older family members. The adult manifestation of anxiety was PD. This case study, although somewhat anecdotal, gives some further evidence for the continuity from school phobia in childhood to PD in adulthood.

This section has shown anxiety to be a fairly common problem in children and adolescents that may persist into adulthood.

Section 1.3: The Assessment of Depression and Anxiety in Children and Adolescents

This section discusses the assessment of depression and anxiety in children and adolescents, and is divided into two main sections which cover assessment by rating-scales and assessment by clinical interview. The issue of assessment of depressed and anxious symptoms and disorders in adults is not discussed as this would involve excessive repetition of several aspects of this topic. Suffice to say that similar advantages and disadvantages of these two methods are present in the assessment of adult psychiatric symptoms and disorders. A third section discusses parent-child agreement on ratings of depression and anxiety.

1.3.1: Rating-scales

In children and adolescents self-report measures of depression and anxiety are commonly completed by three types of reporter. These are the child, a parent or a teacher. As will be seen there are advantages and disadvantages to all three sources of information.

1.3.1.1: Self-report

The main advantage of the use of self-report for symptoms such as depression and anxiety is that as these are internalising symptoms they may not be noticeable to anyone but the child. The use of self-report can lead to the identification of covert behaviours and thoughts. However, the main disadvantage of this method of assessment is the problem of cognitive ability to cope with the task. An important issue in the use of self-report scales is the consideration of the age at which a child becomes able to comprehend and complete the task accurately. This depends not only on age but on cognitive development. To complete a self-report questionnaire pertaining to the presence or absence, frequency and timing of internalising symptoms the child needs to have obtained a certain level of reading and language comprehension, of temporal awareness, and awareness of his or her own thoughts, emotions and behaviours. Between the ages of 8 and 10 a child developing normally will have acquired the capacity to function at a high enough level to cope with these requirements (Harrington 1993). However at the age of 8, reading and comprehension skills may not be adequate to complete the task alone, so studies of younger children tend to require the presence of either a teacher or parent to aid the completion of the questionnaire. However, even in the presence of such help, child report from younger children cannot be expected to provide a totally accurate picture, so the additional collection of information from another source is always advisable. In older children and adolescents self-report is likely to be the most accurate and useful source of information, and in this age-range it is possible to consider information from this source alone as valid.

The main problem with the self-report measures of symptoms of depression and anxiety in children and adolescents that are currently available is that they are all highly correlated with one another. For example the Children's Depression Inventory (CDI) (Kovacs, 1981, 1985) and the Trait scale from the State-Trait Anxiety Inventory for Children (STAIC) (Spielberger, 1973) have been shown to correlate with one another to the level of .62 (Norvell, Brophy, & Finch, 1985). The Revised Children's Manifest Anxiety Scale (RCMAS) (Reynolds & Richmond,

1978, 1979) has been found to correlate with the CDI to a similar extent ($r = .64$) (Ollendick & Yule, 1990). These high correlations are largely due to considerable overlap in the symptoms of depression and anxiety defining these disorders, and thus in the items on questionnaires measuring them.

1.3.1.2: Parent-report

The main advantage of parent-report over self-report is for younger children, where estimation of the duration of symptoms is difficult for the child as concepts of time may not be fully developed, and the parent may thus be the only source of information of this type. However, although the parent sees their child in a number of different situations, they can only detect overt depressed or anxious behaviour such as sleeping and eating problems, irritability and crying. They are often unable to detect many of the covert symptoms. Furthermore, parents are poor at distinguishing between symptoms of depression and anxiety (Achenbach 1991b). In addition to this there may be a bias due to the parents' own affective state. For these reasons parent-report alone provides an incomplete picture of internalising symptoms, and should ideally be coupled with information from at least one other source.

1.3.1.3: Teacher-report

The use of the teacher as a source of information regarding the child's internalising symptoms allows for the identification of overt symptoms, especially behaviour problems, seen in the school environment. However, clearly the teacher can only identify overt symptoms, and only those seen at school. For this reason teacher report should form part of a wider assessment of internalising symptoms in children and adolescents.

1.3.2: Clinical interviews

The advantages of the clinical interview over questionnaire measures are numerous. The interviewer can probe in response to the subjects answers in order to clarify the responses given, the identification of symptom severity is possible, as is the accurate timing and duration of symptoms. Such information can result in diagnoses according to criteria such as DSM-IV. However, diagnostic interviews are very time consuming and such a detailed level of information is not always necessary. As with questionnaire measures children may not always be reliable reporters, especially younger children, so it is essential to interview additional central figures in the child's life in the younger age-ranges.

Clinical interviews can vary in a number of ways including whether it is a structured or semi-structured interview, whether the interviewer is a clinician or a lay interviewer, whether the child, parent or both are interviewed, and which classification system is used. Such differences result in quite varied reliability and validity figures for the different clinical interviews available (see Silverman 1991 and Hodges 1993). There is as yet no definitive marker for depressive disorder or for anxiety disorders, so diagnoses are still to a certain extent subjective.

1.3.3: Parent-child agreement in ratings of depression and anxiety

Agreement between self-report and parent-report of internalising symptoms in children and adolescents is notoriously poor. Numerous studies have revealed poor parent-child agreement for ratings of both depression and anxiety (Barrett et al. 1991; Renouf and Kovacs 1994; Angold, Weissman, John et al. 1987; Engel, Rodrigue & Geffken 1994; Moretti, Fine, Haley, and Marriage 1985). The level of agreement may alter with the age of the child, but the data on this developmental process are mixed, and suggest that it depends on the nature of the symptoms to be identified (Barrett et al. 1991; Renouf and Kovacs 1994; Angold et al. 1987).

In conclusion, this discussion has revealed various advantages and disadvantages in the available methods of assessing depression and anxiety in children and adolescents. With these limitations in mind it is now possible to review the evidence for a genetic basis to these affective states.

Chapter 2: Literature Review II

Genetic Studies of Depression and Anxiety

Section 2.1: Behaviour Genetic Theory and Design

During the past two decades there has been increasing recognition of the necessity to study the role that both genes and the environment play in producing behaviour. Behaviour genetics is the study of the origin of behaviours within genetically sensitive designs. Measurable aspects of the individual's behaviour are referred to as behavioural phenotypes. There are three designs that have been used to study behavioural phenotypes in this way. These are family studies, twin studies and adoption studies.

2.1.1: Family study design

This methodology utilises families to estimate the “familiality” of a phenotype. If an individual with a certain phenotype is more likely to have relatives with that phenotype then this is said to be a familial characteristic. Evidence of this kind tends to be reported as the “morbid risk” for relatives of probands (individuals with the phenotype of study) as compared to the morbid risk for relatives of normal controls. The morbid risk is the percentage of individuals in the relatives of the affected group who themselves show that phenotype. Family studies can therefore provide data on whether a certain phenotype consistently runs in families, in which case there may be genes involved in the aetiology of that phenotype. The familiality estimates can be seen as the upper limit for any potential genetic influence. However, data of this kind cannot specify whether it is the genes shared within the families or the environment shared by family members that are resulting

in the within-family resemblance seen. For these specific estimates to be made, twin or adoption data are required.

One issue which must be considered here impacts not only on family studies but on all genetic research. This is assortative mating, which refers to the tendency for people to mate with phenotypically similar individuals to themselves.

2.1.1.1: Assortative mating

This process effects the distribution of genes throughout the population, and is thus an important issue for behaviour geneticists. For characteristics which are polygenic this can result in increased genotypic variability (Plomin, DeFries, & McLearn 1990). This can be explained mathematically in that there will be less regression to the mean expression of that characteristic than there would be if mating were entirely random. For single gene characteristics the effect of assortative mating will be to reduce heterogeneity in that homozygotes will tend to mate with homozygotes, and those that mate with heterozygotes will produce some homozygotes as well as heterozygotes (Plomin, DeFries, & McLearn 1990). Investigations of assortative mating with regard to anxiety and affective disorders produced varying results and have been criticised for using unstandardised methods of assessment and unmatched control samples (Heun & Maier 1993). In order to address these criticisms Heun and Maier (1993) used a standardised interview (Lifetime Version of the Schedule for Affective Disorders and Schizophrenia: SADS-L) (Spitzer & Endicott 1977) to examine rates of psychiatric disorder in the spouses of patients with psychiatric disorders as compared to the spouses of healthy controls matched for age, sex and educational level. Their results indicate that spouses of patients do not have significantly more psychiatric disorders than spouses of healthy controls. A study by Colombo, Cox and Dunner (1990) found no evidence for assortative mating for patients with anxiety disorders.

Thus it appears that assortative mating is not a crucial issue for behaviour genetic studies for anxiety or depressive disorders.

2.1.2: Twin study design

Twin studies can ascertain the proportion of variance in a phenotype that is due to genetic and environmental factors. This is made possible by the occurrence of two types of twins in the human population which result in two types of genetic relatedness coupled with identical rearing families. The first type of twins are monozygotic (MZ) twins who originate from the same fertilised egg, and are thus genetically identical. The second type of twins are dizygotic (DZ) twins, who are created by the simultaneous fertilisation of two eggs. Thus these twins will like other siblings, share on average 50% of the genes which are free to vary in humans. Both members of the twin-pair must have been reared by the same family in this design, so that the rearing environments can said to be equally similar for MZ and DZ pairs, in that they are children growing up at the same age in the same family. Two types of genetic factors can be estimated from twin studies. The first of these is known as an “additive” genetic factor (A). These are genes for which the effects simply add up in proportion to how many copies of the genes there are in the individual genotype (0, 1, or 2). The other type of genetic factor is genetic “dominance” (D). This is where one type of allele is dominant over another and the alleles at a certain locus may not therefore simply add up in their effects. For MZ twins, the within-pair correlation for both of these aspects of genotype is 1.0, as these twins are genetically identical. For DZ twins however, the within-pair correlations for additive and dominance genetic effects are 0.5 and 0.25 respectively. It is the difference in correlation of genetic factors for MZ and DZ twins which is at the base of the twin methodology.

In the twin design environmental factors refer to those factors in the aetiology of the phenotype which are non-genetic. There are two types of environmental factors

which can be estimated from twin studies. The first of these is “common” or shared environment (C). This refers to aspects of the environment which act in such a way as to make members of the same family similar to one another. In both MZ and DZ twins the within-pair correlation for this factor will be 1.0, as it is by definition those aspects of the environment shared by both twins. Non-shared or “specific” environmental factors (E) refer to those environmental factors which are not shared by family members, but are specific to the individual, creating within-family differences. As one would expect the within-pair correlation for this factor is 0.0, as these are features of the environment not shared by the twins.

There are three levels of data analysis which can be conducted using twin pairs. The first of these is to contrast the MZ and DZ phenotypic correlations (if the phenotype is measured continuously) or concordance rates (if the phenotype is binary). Two types of concordance rates are used in this field: pairwise and probandwise concordance. Both of these are only calculated when the sample consists of pairs where at least one member is affected. The pairwise concordance rate is calculated to be the number of concordant pairs in the sample divided by the total number of pairs. The probandwise concordance rate is the number of affected individuals in concordant pairs divided by the total number of affected individuals. If the MZ correlation or concordance rate is more than the DZ correlation or concordance rate this implies that genetic influences are involved in that phenotype. A rough estimate of the heritability of a phenotype that is measured as a continuous variable is to double the difference between the MZ and DZ correlations (see Chapter 5 for a more detailed explanation). It is not possible to obtain such an estimate of heritability from concordance rates.

The advent of model fitting techniques has allowed for more sophisticated analyses of this type of data resulting in specific estimates of heritability (a^2 or h^2), common environmentality (c^2) and specific environmentality (e^2). These terms are the squared path co-efficients in the model from the latent factors A, C, and E to the measured phenotype. If the estimate of C is non-significant and can be dropped

from the model then dominance effects can also be calculated (d^2). (See Chapter 5 for a more technical description of this process).

Finally, there is one further use of twin data. This is the estimation of heritability of extreme phenotypes. For example, heritability of depression scores across the normal range may not be of as much interest to the researcher as the heritability of very high depression scores. If this is the case, then a multiple regression procedure described in the methodology section is used to calculate “group heritability” (h^2_g) (DeFries & Fulker 1985, 1988). Group heritability is defined as the extent to which the difference between the mean score of a high scoring group and the mean score of an unselected population is heritable (see Chapter 5 for a more detailed explanation).

Having presented the theory behind the twin design, it is now of importance to discuss three design issues. These are zygosity determination (MZ versus DZ), representativeness, and the “equal environments assumption” (EEA) (the assumption that MZs experience as similarly equal environments to each other as members of DZ pairs).

2.1.2.1: Zygosity determination

There are two predominant methodologies for assigning zygosity. The first and more accurate of these is to do a blood test. This can then be subjected to various levels of analysis. At the basic levels, blood group can be ascertained, and if this is not identical, the twins are clearly DZs. At the most advanced level, the DNA can be examined and genetic markers compared. The second and more common method is to use questionnaires which ask about the physical similarity of the twins and the tendency for other people to confuse them (including members of their own families). Questionnaires of this type have been shown to have an accuracy of zygosity determination of about 95% (Goldsmith 1991). Although this means that in

a study using this method of zygosity determination alone, 5% of twins pairs will be wrongly assigned, in large data sets this will not dramatically alter the results.

2.1.2.2: Representativeness

Two specific issues are considered here. These are whether twins are representative of the general population and whether there are biases in volunteer samples.

There are two well-documented differences between the twin population and the singleton population. The first of these is that twins are on average born at 37 rather than 40 weeks, and are generally of lower birth-weights than singletons. However the available evidence suggests that optimum gestation is 38 weeks for twins, and any differences in birth-weight disappear by early childhood (for a review see Rutter & Redshaw 1991). The second of these differences refers to the development of language in twins. Significant delay in language development in twins has become a well-replicated finding, leading to fears that twin children may not be representative of the singleton child population (Rutter & Redshaw 1991). However, as there has been no suggestion in the literature that language development is related to symptoms of anxiety and depression in middle childhood and adolescence this issue will not be considered further.

There are two features on which volunteer samples of twins differ from the general population of twins. These are percentage of MZs and percentage of female pairs. While in the general population of twins the ratio of MZ female:MZ male:DZ female:DZ male is 1:1:1:1, in volunteer samples this tends to be closer to 4:2:2:1. This was demonstrated in a review of 14 volunteer twin samples by Lykken and Tellegen (1978). This bias means that in particular the DZ male pairs are likely to be unrepresentative of the whole twin population. Another source of bias in twin studies of psychiatric disorder is whether the twins are recruited from a population or a clinic sample, as the latter requires treatment seeking, which, as will be

discussed, can alter heritability estimates. For these reasons, and also due to the preponderance of psychiatric disorders in females, one of the largest current twin studies involves adult female pairs only from a population rather than clinic sample (Kendler and colleagues). In general the trend is now to try to recruit population based samples, to reduce bias in the sample.

2.1.2.3: Equal environment assumption

As discussed above, an important feature of the twin design is the assumption that twins within MZ pairs experience environments as similar to that of their co-twin as twins in DZ pairs. This assumption has often been challenged due to the physical similarity of the twins resulting in assumptions that it is impossible to treat MZ twins as differently as DZ twins are treated. These challenges have been dismissed with evidence from 4 types of studies. The first of these illustrates that parents treat MZ twins more similarly than DZ twins because twins from an MZ pair exhibit more similar behaviours and thus elicit more similar responses. The second type of evidence comes from studies which look perceived zygosity (where either the twins or their parents mistakenly believe MZ twins to be DZs). The third and fourth types of evidence come from studies which illustrate that physical similarity and similarity of treatment have no influence on similarity of twins for various outcome measures.

Lytton (1977) used direct observation of 46 male twin pairs aged 2½ years and their parents to test the EEA. He found that while parents do treat MZ twins more similarly in some respects they do not systematically introduce greater similarity of treatment of MZ twins in the actions which they themselves (the parents) initiate. Thus for parent-initiated actions which should in theory most strongly violate the EEA, there was no effect of zygosity.

An analysis of four parentally unrecognised MZ twin pairs (parents thought they were DZs) by Scarr (1968) revealed that it was the twin-pairs' actual rather than perceived zygosity which the parents were responding to. This gives further

evidence for the hypothesis that parents respond to, rather than create, differences and similarities in their twins. A similar analysis of 25 pairs of parentally unrecognised MZ twins by Goodman and Stevenson (1991) provides further evidence for the relevance of actual zygosity over perceived zygosity. The 25 parentally unrecognised MZ twin-pairs were found to be as similar to each other on measures of maternal and paternal warmth and criticism as the correctly classified MZ pairs (N = 70).

An extended analysis of this kind was conducted on 158 adult female twin pairs in which at least one of the twins disagreed with the project-assigned zygosity (Kendler, Neale, Kessler, Heath, & Eaves 1993a). Perceived zygosity (included in a model-fitting analysis as a form of specified common environment) was not a significant influence on within-pair similarity for five psychiatric disorders including major depression (MD), generalised anxiety disorder (GAD), and phobia.

Hettema, Neale, and Kendler (1995) went on to investigate the influence of physical similarity on within-pair similarity for the same five disorders. Physical similarity was treated as a specific form of common environment and was found not to have a significant influence on MD, GAD or on phobias. As it is the physical similarity of MZ twins that is most commonly cited as evidence against the equal environments assumption, this study provides important evidence suggesting that for internalising disorders at least, this factor is not a significant methodological issue.

The influence of childhood and adulthood similarity of treatment on within-pair similarity of depressed and anxious symptoms and disorders has been investigated in multiple papers by Kendler and colleagues (Kendler, Heath, Martin, & Eaves 1986; Kendler, Neale, Kessler, Heath, & Eaves 1992b, 1992c, 1992d). The measure of similarity of treatment included ascertaining how often as children the twins shared the same room, had the same playmates, were dressed alike, and were in the same classes at school. No consistent relationship was found between

similarity of treatment during childhood or adulthood and twin resemblance on any of the measures of depression and anxiety.

Finally, Morris-Yates, Andrews, Howie, and Henderson (1990) conducted a factor analysis of 343 adult same-sex twins responses to questions about the similarity of their social environment in childhood. This resulted in two factors corresponding approximately to imposed and elicited similar treatment. The authors also questioned the twins about what level of similarity they would have preferred, and compared this to what level of similar treatment they perceived themselves as having had (too much, neutral, or too little). The data show that MZ twins had more similar treatment imposed on them, and that they would have preferred less similar treatment. However this increased similarity of treatment did not have any relationship with subsequent (current) levels of neuroticism, anxiety or depression.

In summary, there is now a considerable body of evidence in favour of the equal environments assumption, some of which particularly refers to the study of depression and anxiety.

2.1.3: Adoption study design

The adoption study design allows the comparison of genetically related individuals reared in different environments. A particularly powerful variant of this design uses reared apart twins as in the Swedish Adoption/Twin Study of Aging (SATSA). The within-pair correlation of reared apart MZ twins is a direct measure of genetic influence on the phenotype of interest. The advantage of the adoption design is that it has more power to detect environmental influences than the twin design. However there are two issues which must be discussed when considering the adoption methodology as a tool for behaviour genetics. The first of these is representativeness and the second is selective placement.

2.1.3.1: Representativeness

It has been suggested that adoptive families may represent supernormal environments which could make them unrepresentative of the general population. Furthermore, the biological families may also be unrepresentative of the general population. However, Plomin, DeFries, & McClearn (1990) have argued that as long as means and variances for relevant characteristics in both sets of parents are available, adjustments can be made if necessary in the interpretation of the data. In the Colorado Adoption Project (CAP) (Plomin, DeFries, & Fulker 1988) both the adoptive and biological families were found to be representative of the general population on a variety of cognitive and demographic measures.

2.1.3.2: Selective placement

This refers to the tendency for adoption agencies to attempt to match the adoptive family to the biological family on various characteristics. These can include characteristics as diverse as physical appearance and SES. This results in a potential correlation of the genotype and environments of the adoptive family with that of the biological family, and an overestimation of environmental influences. This can be overcome in a number of ways. One approach is to allow the latent variable of biological parents' genotype to correlate with the latent variable of the adoptive parent's environment. Another way is to include a specific common environment term referred to as "correlated" environment. This factor is shared by both members of a biological sibling pair or a twin pair that have been reared apart, and refers to those aspects of their environment that are likely to be correlated and therefore make them resemble one another.

Either of these methods allows the researcher to control for selective placement. This issue is however becoming of less importance as adoption agencies now tend not to favour selective placement as this leads to unrealistic expectations on the part of the adoptive parents as to the similarity of the child to themselves.

As can be seen from this brief overview, there are three methodologies available to behaviour geneticists. All of these designs have been utilised in the study of depression and anxiety, although adoption data is scarce. It will become clear from the following review that these techniques are as informative in their identification of environmental factors as they are in their identification of genetic factors.

Section 2.2: Genetic Studies of Depression

2.2.1: Studies with adults

2.2.1.1: Evidence from family studies

Several studies have demonstrated the familiarity of MD by comparing rates of the disorder in relatives of individuals with MD to rates in relatives of normal controls (Leckman, Merikangas, Pauls, Prusoff, & Weissman 1983; Weissman, Gershon, Kidd et al. 1984; Weissman et al. 1986; Kupfer, Frank, Carpenter, & Neiswanger 1989). The rates of MD without exception have been higher in the relatives of the depressed groups.

An interesting feature of many of these studies is that early age of onset appears to be associated with a higher familial loading (Weissman, Gershon, Kidd et al. 1984; Weissman et al. 1986; Kupfer, Frank, Carpenter, & Neiswanger 1989; Weissman, Warner, Wickramaratne, & Prusoff 1988).

2.2.1.2: Evidence from twin studies

While familial evidence is important in investigating the factors involved in the transmission of depression, they cannot untangle the two familial factors, namely genes and common environment. For this one must look to twin research. An early

twin study (N = 151 pairs) of affective disorders estimated heritability of MD to be .54 and common environment to be .03 (Torgersen 1986a). Although model-fitting was not conducted in this analysis these results suggest that an AE model would produce the best fit to the data. Such a model has subsequently been found to fit data on depressive symptoms and disorders in several subsequent studies. A notable team of researchers in this area is the group involved with the Virginia Twin Study, an adult female twin population register in America, and the evidence from this set of studies is very informative. Early work by this team (Kendler, Heath, Martin, and Eaves 1987) looked at 3,798 pairs of twins, the results from which suggest that there is a genetic predisposition to symptoms of depression that also predisposes the subject to anxious symptomatology, and that it is specific non-shared environmental factors that then result in the symptoms of depression being manifested. Andrews, Stewart, Allen, and Henderson (1990) found a genetic contribution to neuroticism and to symptoms depression, but not to any affective disorders (N = 466 twin pairs). This suggests that while symptoms of depression are partly explained by genetic factors, the aetiological factors for depressive disorders are somewhat more complex than those for depressive symptoms, and may not involve genetic factors. Mackinnon, Henderson, and Andrews (1990) looked at genetic and environmental factors contributing to lability (within-group variability over time) and level of anxious and depressive symptomatology and trait neuroticism using 466 adult twin pairs. Their findings confirmed the above results that there is a substantial impact of genetics on level of symptomatology, but also found that there was no genetic or shared environment impact on lability of depressive symptoms or neuroticism.

Further to this work Silberg et al. (1990) factor analysed replies on the "Centre for Epidemiologic Studies-Depression scale" (CES-D) producing four factors. These were depressed affect and interpersonal sensitivity, positive affect, a general depression factor, and a somatisation, poor concentration and poor motivation factor. They fitted a full ACE model to the 4 factor scores as well as to all 20 items of the CES-D. The resulting models for the four factors had genetic and non-shared environment terms accounting for 33-55%, and 45-67% respectively of the

variance in factors 1 and 2, whereas the variance in factors 3 and 4 was, contrary to the results of Kendler, Heath, Martin, and Eaves (1987), Andrews, Stewart, Allen, and Henderson (1990), and Mackinnon, Henderson, and Andrews (1990) accounted for only by common environment (26-38%) and non-shared environment (62-74%) terms. The model with all twenty items contained one shared genetic term, one shared common environment term, and 4 specific non-shared environment terms. The genetic factor contributed in a small way to the variance in depressive symptoms, but it was largely the non-shared environment terms that accounted for the variance in these symptoms. This is again suggestive of there being a general genetic predisposition to depressive symptomatology, with specific environmental impacts resulting in the specific manifestations of that symptomatology.

The stability of depressive symptomatology, and the contributions of genetic factors to this stability was examined in two twin/family samples by Kendler et al. (1994) (N = 30,445 individuals). Heritability of depressive symptoms was estimated at between 30% and 37%, and genetic factors accounted for more than half of the variance in a stable trait-like report of depressive symptoms. Common environmental factors were not found to be important for liability to or stability of depressive symptoms. Interestingly, the final model predicting depressive symptomatology contained not only an additive genetic component, but also a dominance genetic component (D), and an effect of assortative mating, as well as the specific environment factor. The parameter estimates for A, D, and E respectively were 16%, 21% and 63% for one sample and 22%, 8% and 70% for the other sample. In both samples, genetic factors accounted for about a third of the variance in depressive symptoms, and also accounted for all the within-pair similarity. Common environment terms were not required in either data set, hence the possibility of considering a dominance term.

Kendler, Neale, Kessler, Heath, and Eaves (1992e) using a sample of 1,033 female twin pairs confirmed and extended the conclusions from Kendler, Heath, Martin, and Eaves (1987) to MD. In this study it was found that while genetic

factors contributed to the presence or absence of a life-time ever diagnosis of MD this same genetic factor also contributed to the presence or absence of a life-time ever diagnosis of generalised anxiety disorder (GAD) and it was specific non-shared environmental factors that resulted in the particular disorder manifested by the subject. Kendler, Neale, Kessler, Heath, and Eaves (1992b) assessed the sample by interview, from which 9 commonly used definitions of MD were diagnosed with varying prevalence rates for a life-time ever diagnosis of MD of 21% to 45%. For all definitions ACE, ADE, and AE models were fitted to the data. The results in general supported an AE model, with common environment explaining little if any of the variance in MD in adult female twins. These estimates do not take account of the unreliability of the measures, which is incorporated into the non-shared environment term. Kendler, Neale, Kessler, Heath and Eaves (1993e), by using data from two time-points were able to re-calculate these estimates incorporating error of measurement into the structural equation model. This model produced a heritability estimate of 71% for a life-time ever diagnosis of MD, with a specific environmental factor accounting for the other 29% of the variance. As the authors summarise "more than half of what was considered environmental effects when life-time history of MD was analysed on the basis of one assessment appeared, when two assessments were used, to reflect measurement error." Thus test-retest reliability figures are clearly of paramount importance in looking at the heritability of depressive symptoms and disorders.

Another article by Kendler, Neale, Kessler, Heath, and Eaves (1993d) again using longitudinal data, investigated the stability of one-year prevalence of MD over time. They found that the genetic factors influencing liability to MD over a period of a year were stable over time, with the same genetic factor impacting on MD at time 1 as MD at time 2, whereas the rest of the variance in MD at time 1 and time 2 was accounted for by non-shared environmental factors that were specific to each time point. The stable genetic factor accounted for 43% of the variance in liability to MD at both time points, and the transitory non-shared environment factors accounted for 57% of the variance at both time-points.

Tambs, Harris, and Magnus (1995) investigated the heritability and environmentality of anxious/depressed symptoms in a large (N = 2570 pairs and 724 single responders) population sample of twins aged 18-25 years. The authors found that there was no worsening of fit when the sexes were constrained to fit the same model. This resulted in a heritability estimate of 43% for their anxious/depressed symptom score. This is a rather higher heritability estimate than that found in Tambs and Moum (1993), an entire population sample, where the upper limit was given as 22%.

An issue which has confounded some of these results is that of treatment seeking. This formed part of a coping strategy described as "problem solving" which was found to be heritable (Kendler, Kessler, Heath, Neale, & Eaves 1991). This emphasises the need to use population samples rather than clinical samples in behaviour genetics research.

The message to be taken from this review is that it is highly probable that depressive symptoms and major depression are heritable, but that the level of heritability calculated can be contaminated by certain aspects of the measurement or sampling criteria.

2.2.1.3: Evidence from adoption studies

The adoption methodology using the biological and adoptive families of adopted probands and controls is the most powerful method for assessing the impact of the environment on individuals. The results based on this design also implicate substantial genetic factors influencing levels of depressive symptoms and disorders.

Mendlewicz & Rainer's (1977) adoption study of manic-depressive disordered probands and their biological and adoptive relatives was the first adoption study of any affective illness. This study found there to be far higher levels of

psychopathology in the biological relatives than in the adoptive relatives of the subjects. Taking any affective disorder, the percentages of diagnoses in the adoptive and biological relatives were 28% and 12% respectively ($p < 0.025$). This result clearly demonstrated the importance of genetic factors in this area, and further adoption studies have since been carried out.

A slightly later study of 48 adoptees with MD by Cadoret, Gorman, Heywood, & Troughton (1985) showed there to be 15% and 28.6% (males and females respectively) MD in the adoptees with affective disorder present in their biological first-degree relatives, as compared to levels of 7.0% and 13.9% for the adoptees who did not have affective disorder in their biological relatives. This difference is not significant, but is in the expected direction.

Wender et al. (1986) investigated the frequency of psychiatric disorders in the biological and adoptive relatives of 71 adult adoptees with mood disorders and 71 matched controls. They found that levels of completed suicide in particular, but also bipolar and unipolar affective disorder were considerably and significantly higher in the biological relatives of the probands than in any other group (15% vs. 1%, 20% vs. 5%, and 8% vs. 1% for the biological and adoptive relatives on the three psychopathology measures respectively). They do not use their data to calculate heritability estimates for these disorders, but the evidence points to a substantial genetic component relating to mood and affective disorders.

Bergeman, Plomin, Pedersen, and McClearn (1991) of the Swedish Adoption/Twin Study of Aging (SATSA) considered 424 older twins (age at least 50 years) reared together and apart. Fourteen percent of the variance in depression was accounted for by a genetic factor that was totally shared with perceived social support, explaining 65% of the covariance between these two factors. Another genetic factor specific to the depression score was included in the model but did not account for any of the variance. This implies that perception of social support is governed by the same genetic factors as depression, and as such may merely be part of the symptomatology of depression. This has grave implications for the use

of self-perceptions of support when investigating support as a vulnerability or risk factor for depression. This issue will be discussed further in due course. Similar heritability estimates of depressive symptomatology were obtained by Gatz, Pedersen, Plomin, Nesselroade, and McClearn (1992) who sent the Centre for Epidemiologic Studies-Depression scale (CES-D) (Radloff 1977; Weissman, Sholomskas, Pottenger, Prusoff, & Locke 1977) to 481 monozygotic and dizygotic twin pairs reared together or apart who were involved with the SATSA. Genetic factors explained 16% of the variance in the total score, and 19% of the variance in the Psychomotor Retardation and Somatic Complaints subscale, but heritability was very low for the Depressed Mood and Well-being subscales. Significant age-group effects were found in this study, with heritabilities greater in twins aged 60 years or older as compared to those under 60. This suggests that there may be different aetiological factors involved in the creation of depressive symptoms at different times of life. The implications of this are that heritability of depressive symptomatology must be seen in a developmental perspective, which is particularly important when considering children and adolescents. There may thus be advantages to analysing data from children and adolescents as two separate groups.

2.2.1.4: Evidence from molecular genetics

This evidence largely concerns the genetics of bipolar rather than unipolar depressive disorder. Studies investigating the molecular genetics of depression have attempted to establish the mode of transmission of this disorder and candidate loci for the gene or genes involved. Segregation analyses consider the pattern of affected individuals within families. Such analyses can address the hypotheses that there is no familial transmission, that there is no single major locus of inheritance and that there is no polygenic inheritance (Moldin, Reich, & Rice 1991). Although the hypothesis that there is no familial transmission has been rejected in several studies (Crowe, Namboodiri, Ashby, & Elston 1981; Goldin, Gershon, Targum, Sparkes, & McGinniss 1983; Tsuang, Bucher, Fleming, &

Faraone 1985) the evidence for the two hypotheses addressing the type of inheritance has been ambiguous (Crowe, Namboodiri, Ashby, & Elston 1981; Goldin, Gershon, Targum, Sparkes, & McGinniss 1983; Tsuang, Bucher, Fleming, & Faraone 1985; Cox et al. 1989; Price, Kidd, & Weissman 1987). A review of six segregation analyses found that only one was able to reject the hypothesis that there is no single major gene involved in depression, but this study also found that the transmission probabilities differed significantly from expected Mendelian values (Price, Kidd, & Weissman 1987). Thus it is unclear whether this disorder is governed by one major gene or is polygenic. Studies of specific genetic markers may help to clarify this situation.

Two methods have been used in the study of genetic markers associated with depression. Linkage studies test whether a particular allele or marker is co-inherited with the expression of the disorder of interest. Studies of genetic association compare the frequency of a particular marker in a sample of subjects with the condition of interest to a sample of controls (McGuffin 1988). Although several studies have produced interesting results, many of these have not been replicated. For example linkage to chromosome 11 (Egeland et al. 1987) was not replicated by Kelsoe et al. (1989) in their analysis a larger sample from the same pedigree. Further studies have also failed to replicate this finding in a number of different pedigrees (Hodgkinson et al. 1987; Mendlewicz et al. 1987; for a review see Mendlewicz 1994). In addition, while one study found an association between manic-depressive illness and the tyrosine hydroxylase (TH) gene on chromosome 11 (Leboyer, Malafosse, Boularand et al. 1990), this finding was not replicated (Gill et al. 1991).

Linkage to two sites on the X-chromosome have been demonstrated in bipolar affective disorder (Baron et al. 1987, Mendlewicz et al. 1987), but it is now known that the distance between these two loci is so great that it is unlikely that the same gene would be linked to both. A subsequent exploration of this region of the X-chromosome with multiple DNA markers has further reduced the likelihood of there being X linkage for manic-depression (Baron et al. 1993).

Furthermore, although linkage and association studies have suggested a relationship between major depression and bipolar affective disorder and the human leukocyte antigens (HLAs) on chromosome 6 (Weitkamp et al. 1981; Matthysse & Kidd 1981; Stancer et al. 1988), this has not been supported in other studies (Goldin, Clerget-Darpoux, & Gershon 1982; Targum, Gershon, Van Eerdewegh, & Rogentine 1979).

Finally, a recent study by Ogilvie et al. (1996) compared rates of three alleles of the serotonin transporter gene on chromosome 17 in a depressed group (MD or bipolar affective disorder) and a control group. There was a significant difference between the two groups which was largely explained by the over-representation of one of the alleles in the subjects with MD. This is an exciting finding, particularly as this relates to a specific neurotransmitter which is known to be involved in depression. However this finding will need to be replicated.

In summary, although molecular genetic studies have been unable to produce unambiguous evidence for the mode of transmission of depressive disorders or for specific loci involved in these conditions, this is an area that is currently developing at a rapid pace.

2.2.2: Genetic Studies of Depression in Children and Adolescents

2.2.2.1: Evidence from family studies

These can be divided into those where the authors have investigated the children of adult probands (top-down studies), and those where the child was the proband, and levels of disorder in the adult (and child) relatives were analysed. This latter type of study is referred to as a bottom-up study.

Top-down studies

Weissman, Leckman, Merikangas, Gammon, and Prusoff (1984) compared the children of their depressed group with the children of a control group for levels of depression in the children. The depressed adults were classified into four groups: those with no additional anxiety disorder, those with agoraphobia, those with panic, and those with generalised anxiety disorder. In these groups the rates of depression in their children were 13.2%, 22.2%, 26.3%, and 9.4% respectively. The rate of depression in the children of the normal controls was 0.0%. There is clearly a familial transmission of depression from parent to child, that is complicated by its involvement with various anxiety disorders. Biederman, Rosenbaum, Bolduc, Faraone, & Hirshfeld (1991) looked at the levels of anxiety and depressive disorders in children (aged 4 to 20 years) of parents with MD without anxiety disorder (N = 12 children), PD and Agoraphobia with MD (N = 25 children), PD and Agoraphobia alone (N = 14 children), any other psychiatric disorder (N = 23 children), and healthy controls (N = 47 children). For the five groups the rates of MD in the children were 16.7%, 20.0%, 35.7%, 17.4%, and 0.0% respectively. The levels of MD were significantly higher in all the psychiatric groups than the normal controls. These data give further support to the hypothesis that depression is a familial disorder.

Weissman, Warner, Wickramaratne, and Prusoff (1988) went on to look more closely at the effects of age of onset of depression in 133 probands and 82 controls on the levels and age of onset of depression in their children. Children of parents with early onset MD (before 20 years of age) had the highest risk of developing MD themselves. Nearly all of these cases were children whose onset was pre-pubertal. That is to say early onset MD in parent probands tended to lead to pre-pubertal onset of MD in their children. There was a 14 fold increased risk of onset of MD before age 13 in the children of parent probands whose onset was before 20 years, compared to a 5.6 or 3.0 fold increase when the onset in the parent was between the ages 20-29 or over 30 respectively. This suggests a separate process for MD in pre-pubertal children, which may have a much higher genetic loading than the

genetic loading for depression in adolescents. All groups including the control group had highly increased levels of MD in the children after the age of 15. It is thus of great importance to look at these issues separately for children and adolescents. This finding was extended in a later paper by Warner, Mufson, and Weissman (1996) who found that offspring of early-onset probands with MD, panic or both (onset before the age of 30 years) were at significantly higher risk for depressive and anxious disorders than the offspring of never psychiatrically ill controls. This study also investigated the influence of psychiatric illness in the coparent, ie. the parent not identified as a proband in the study. The results provide evidence for the association between depression and alcoholism in that offspring of coparents with a diagnosis of alcohol abuse were at higher risk for depression and anxiety as compared to offspring of coparents without a diagnosis of alcohol abuse.

Early onset depression (before 32 years) was also considered in a paper by McGuffin, Katz, and Bebbington (1987). This study of 83 families found that although there was a significant association between early onset of depression in the proband and higher rates of illness in the relatives this difference disappeared when lifetime prevalence or morbid risk to age 65 were taken into account. This suggests that the findings relating to early age of onset may be due to the fact that younger subjects have not fully moved through the period of risk for disorder. However, it is possible that the relatively high age of cut-off for early-onset in this study (32 years) resulted in the weakening of the findings relating to this issue. Further studies of this factor are clearly required. Interestingly, early age of onset is also associated with a significantly more lengthy recovery Kovacs, Feinberg, Crouse-Novak, Paulauskas, and Finkelstein (1984).

Bottom-up studies

Harrington et al. (1993) looked at the prevalence of psychiatric disorders in the first-degree relatives of 80 children with depressive disorder, and 80 non-

depressed controls. The results are presented as odds ratios, which range between 1.6 and 1.9 for the varying definitions of depression in the adult relatives. There were also higher levels of depression in the female than in the male relatives. The authors propose that these results support the validity of depression in children as resembling depression in adults, and are also supportive of the theory that depression is a heritable disorder.

A further family history study of pre-pubertal MD (Puig-Antich et al. 1989) compared the family histories of 48 pre-pubertal children with MD to those of 20 children with non-affective psychiatric disorders and 27 normal controls. The relatives were also assessed by the FH-RDC method except for the mothers who were directly interviewed. Compared to the normal controls, the familial rates of psychiatric disorders, especially MD were significantly higher in the MD group. This evidence is supportive of the validity of the category of MD being used in pre-adolescent children, and confirms the findings from the adult data that MD tends to aggregate in families.

Kutcher and Marton (1991) interviewed 259 first-degree relatives of 73 adolescents (aged 13 to 19) with unipolar depression, bipolar depression and normal controls. Both bipolar and unipolar depression were significantly more common in the bipolar and unipolar groups than in the control group. The figures were 14.8%, 5.2% and 1.2% respectively for bipolar depression in the relatives, and 18.5%, 20.0% and 3.6% for unipolar depression in the relatives.

The following two studies did not identify either child or parent as the proband but investigated whole families and a whole population. Tambs' (1991) family study investigated anxious and depressive symptoms in nuclear families (N = 8,096). The univariate results produced estimates of heritability of 0.43 for both depressive and anxious symptoms. Tambs and Moum (1993) examined the clustering of depressive and anxious symptomatology in an entire Norwegian adult population sample of 61,286 persons. They chose not to distinguish between the symptoms of depression and anxiety, stating that "in a normal population sample little is gained

by classifying anxiety and depression separately". This narrow approach, unnecessary in such a large sample, meant that the authors prevented themselves from finding any differences in the familial aspects of anxious and depressive symptomatology. The study included evidence from a large number of differentially related children, adolescents and adults. Their heritability based on family data for these symptoms was given an upper limit of 22%. This is somewhat lower than most of the heritability estimates for depressive and anxious symptomatology from twin studies, (and also from Tambs 1991) and the authors suggest that this is due to increased similarity of the environment of monozygotic twin pairs resulting in artificially inflated heritability estimates. This seems unlikely in the light of the evidence for the equal environment assumption. However, the heritability estimates produced by this type of research must be taken as pointing one in a certain direction rather than producing absolute figures, particularly, one must not take one set of results in isolation. Tambs and Moum's (1993) heritability estimate for anxious-depressed symptomatology of 22% is a similar pattern, if not absolute level to other research in this area. The most interesting finding from this study is the increasing resemblance between relatives with decreasing age differences. The authors conclude that this suggests age-specific genes and age-specific environmental factors which warrant further investigation.

2.2.2.2: Evidence from twin studies

Wierzbicki (1987) looked at within pair similarity of 20 monozygotic and 21 dizygotic twin pairs for level and lability of depressed mood as assessed by self- and parent-report. For the parent rating, the heritability estimates of the level and lability of the total score were .35 and .94 respectively. The heritability estimates for the level and lability of depressed mood rated by the child were rather higher, .94 and .85 respectively. These results are suggestive of substantial genetic contributions to both level and lability of depressed mood in children and adolescents as rated by parent- or self-report.

Further evidence for this genetic factor is provided by Rende, Plomin, Reiss, and Hetherington (1993). This study was the first to look at the heritability of individual differences and extreme scores on the Children's Depression Inventory (Kovacs 1981, 1985), completed by children aged 9 to 18 years, using the DeFries and Fulker (1985, 1988) regression method. Individual heritability was estimated at .34, while common environment was not significant. For the extreme group estimates, probands were taken as being those with a score of 13 or more on the Children's Depression Inventory (CDI). This resulted in a group heritability of .23 which was not statistically significant. The common environment estimate for extreme group membership was .44, a substantial and significant component. However the method used to calculate this parameter has subsequently been criticised and an alternative method is now used to calculate group common environmentality (see Chapter 5).

A paper by Thapar and McGuffin (1994) further explores the heritability of depressive symptomatology in children and adolescents. This study involved 316 families with twins aged 8 to 16 years and produced a heritability estimate for parent-reported depressive symptoms based on the Mood and Feelings Questionnaire (Costello & Angold 1988) of 79%. Self-reported depressive symptoms also measured using the MFQ were only obtained for the adolescents (N = 100) and produced a heritability estimate of 70%.

In conclusion, both depressive symptoms and depressive disorders have been shown to be not only familial, but heritable, in children, adolescents and adults. A particularly interesting and important finding that is clear from the family data in this review is that the early onset depression is likely to be associated with higher heritabilities than late onset depression. This may account for the high heritabilities found in the few twin studies of children and adolescents that have been conducted.

Section 2.3: Genetic Studies of Anxiety

Much of the literature relevant to the heritability of anxiety as a symptom or a disorder, also considers the heritability of depression. For this reason many of the studies reviewed below will have been discussed in the previous section, and will be reviewed here in less detail. Anxiety disorders are classified in DSM-IV into three main categories. These are Agoraphobia and Panic Disorder (PD), Phobias, and Generalised Anxiety Disorder (GAD). Research into the heritability of anxiety disorders has concentrated on PD and GAD. The findings on these two disorders are different as will be seen below.

As with the data on depression, the results are divided into those from adult studies and those from studies using children and adolescents. Family studies will be reviewed first, followed by twin studies. There are no adoption studies of anxiety symptoms or disorders.

2.3.1: Anxiety in adults

2.3.1.1: Evidence from family studies

Two family studies by Leckman, Merikangas, Pauls, Prusoff, and Weissman (1983) and Leckman, Weissman, Merikangas, Pauls, and Prusoff (1983) found that there was a familial component to anxiety disorders, but this was shared to a certain extent with MD. Harris, Noyes, Crowe, and Chaudhry's (1983) direct interview family study of 60 adults with Agoraphobia, PD or no psychiatric illness found that 32%, 33%, and 15% respectively of the relatives also had an anxiety disorder. The transmission was not specific to Agoraphobia, in that equal numbers of relatives presented with PD as Agoraphobia, although less presented with GAD (8%, 9%, and 5% respectively). However in the PD group the relatives were far more likely to present with PD itself rather than Agoraphobia or GAD (21%, 2%, and 7%

respectively). A further direct interview family study by Crowe, Noyes, Pauls, and Slymen (1983) compared relatives of subjects with PD with or without Agoraphobia, and controls (N = 82). Percentages of PD in the relatives were 17.3% and 1.8% respectively, demonstrating the additional familial risk for relatives of subjects with Agoraphobia as well as PD. Rates of GAD were equal in both groups, which strongly suggests separate aetiological factors for PD and GAD.

Noyes et al. (1986) went on to clarify the relationship between PD and Agoraphobia. Relatives of their PD group (N = 40 probands) showed 17.3% PD and 1.9% Agoraphobia, whereas relatives of Agoraphobic group (N = 40 probands) showed 8.3% PD and 11.6% Agoraphobia. Relatives of non-anxious controls (N = 20 controls) showed 4.2% PD and 4.2% Agoraphobia. Probands and relatives with Agoraphobia reported more severe disorders in terms of symptom severity, earlier onset, more frequent complications, and a less favourable outcome than the probands and relatives with PD. These factors, alongside the pattern of disorders in the relatives of the two groups, suggest that Agoraphobia is a more serious variant of PD.

Another family study of PD is that of Maier, Lichtermann, Minges, Oehrlein, and Franke (1993), in which the relatives of 40 PD probands with or without Agoraphobia and 80 controls were interviewed. In the relatives of the proband group, 7.9% were diagnosed with PD, as compared to 2.3% of the relatives of the controls. In this data set, the addition of Agoraphobia to the diagnosis of the proband did not alter the risk of PD with or without Agoraphobia in the relatives. However there was not an Agoraphobia only proband group so direct comparison of these data with those from Noyes et al. (1986) is not possible.

Although the relationship between these two disorders is clearly close, how close is their relationship to GAD? The following study investigated this issue. Noyes, Clarkson, Crowe, Yates, and McChesney (1987) interviewed the relatives of adults with GAD (N = 20 probands), PD (N = 40 probands), and Agoraphobia (N = 40 probands), and found their relatives all had higher levels of anxiety disorders than

the relatives of the control group (N = 20) (30.1%, 25.7%, 27.7%, 13.3% respectively). The relatives of the GAD group had significantly higher levels of GAD than any other disorder (19.5% as compared to 0.0% to 4.1%) and significantly higher levels of GAD than any of the other groups (19.5% as compared to 3.5% to 5.4%). Also relatives of the PD and Agoraphobia groups had higher levels of PD (14.9% and 7.0% respectively) and Agoraphobia (1.7% and 9.4% respectively) than the relatives of the GAD group (4.1% PD, and 3.3 % Agoraphobia). As with their previous studies, relatives of the PD group showed PD most commonly, and more commonly than GAD or Agoraphobia, whereas the agoraphobic group's relatives showed equal levels of PD and Agoraphobia, and lower levels of GAD. These results suggest that while all three disorder are clearly familial, GAD does not share the aetiological factor that PD and Agoraphobia share.

This conclusion is strengthened by findings from a study by Mendlewicz, Papadimitriou, and Wilimotte (1993). The age-corrected morbidity risk for PD was found to be significantly greater in relatives of subjects with PD (N = 122) than relatives of subjects with GAD (N = 102) or controls (N = 130) (13.2, 3.3, and 0.9 respectively).

Other anxiety disorders which have been investigated using family studies are phobias, and posttraumatic stress disorder. Fyer et al. (1990) interviewed 49 first-degree relatives of 15 simple phobics and 181 first-degree relatives of 59 never-mentally-ill acquaintances. Thirty-one percent of the phobics' relatives as compared to 11% of the comparison group's relatives received a life-time diagnosis of simple phobia. This transmission was specific to simple phobia in that rates of PD, social phobia, OCD, GAD, non-simple phobic anxiety, MD, alcoholism and drug use disorder were not significantly higher in the relatives of the case group as compared to the relatives of the controls. Simple irrational fears that did not reach DSM-III-R criteria did not increase the risk for simple phobia in relatives. Thus phobias appear to be another distinct aetiological category.

Davidson, Swartz, Storck, Krishnan, and Hammett (1985) conducted a family study of 36 individuals with posttraumatic stress disorder (PTSD). First degree relatives of this group showed high levels of psychopathology. Notably, 20% showed depression, 22% anxiety disorders and 60% alcoholism. In comparison with the family histories of a depressed group and an anxiety disordered group previously collected, the PTSD group's relatives most closely resembled those of the anxiety disordered group. This group may be harder to classify aetiologically due to the very nature of the disorder, that it is a response to an extreme environmental influence.

2.3.1.2: Evidence from twin studies

Considering anxiety at the symptom level briefly, Kendler, Heath, Martin, and Eaves' (1987) adult female twin study of 3798 pairs investigated anxious and depressive symptomatology. They found that anxiety symptoms were heritable in that genes were influencing the overall level of symptomatology, but it was specific environmental influences that resulted in anxious as opposed to depressed symptoms being expressed. Similarly Mackinnon, Henderson, and Andrews (1990) looked at the heritability of level and lability of trait neuroticism, symptoms of anxiety and symptoms of depression in adult twin pairs (N = 462 pairs). Their data suggested that level of neuroticism is highly heritable (.67 in females, .46 in males), with an AE model giving the best fit. Level of anxiety symptoms was found to follow a similar pattern of heritability. However lability of neuroticism and anxiety could be entirely accounted for by environmental factors.

Symptoms of panic-phobia were considered using two twin-family samples (3965 volunteer twins and their first degree relatives and 1433 twins and first degree relatives from a population sample) by Kendler, Walters, Truett et al. (1995). Heritability estimates using all of the subjects were between .26 and .38 for the males and between .15 and .16 for the females. Using the volunteer twins only, the proportion of variance in panic-phobia symptoms due to genetic factors was

estimated to be 41% for males and 35% for females. These estimates are somewhat higher for the females than those using all the family members, suggesting that the twin method may at times over-estimate heritability. No common environment factors were required so dominance terms were estimated. For the males, 38% of the variance was due to dominance, and only 3% was due to additive genetic factors. In contrast, 35% of the variance in females was accounted for by additive genetic factors, and a dominance term was not required. This suggests that there may be some sex specificity in the precise genes that are involved in the aetiology of panic-phobia symptoms. A further analysis conducted on the twins from each of the samples in which the effects of error of measurement were removed by including test-retest figures in the model resulted in heritabilities of 73% and 47% for the males and 24% and 30% for the females (volunteer and population samples respectively). It is clear from these analyses that the aetiology of panic-phobia symptoms involves genetic factors, but these may be different for males and females.

Moving on to consider the evidence at the disorder level we turn to twin studies of PD, Agoraphobia and other phobias, and GAD. In 1983 Torgersen investigated genetic factors in anxiety disorders using a small twin sample ($N = 85$ same sex pairs). The monozygotic co-twins showed levels of anxiety disorders five times as high as the levels in the DZ co-twins for the PD/Agoraphobia/panic attack group. However levels were equal in the monozygotic and dizygotic co-twins of the GAD group. This adds to the conclusions from the family data and suggests that while PD, Agoraphobia and panic attacks show some heritability, and possibly some shared genetic aetiology, GAD is a distinct disorder, with a distinct aetiology that may not involve genetic factors to a large extent.

Torgersen (1990) further investigated anxiety disorders in a sample of 177 adult twin pairs. The probandwise concordance rates for monozygotic twins for an anxiety disorder without panic attacks was 34%, whereas for dizygotic twins it was 17%. For anxiety disorder with panic attacks, concordance levels were 22% and 0% respectively. These results suggest a genetic component to the aetiology of

anxiety disorders with or without panic attacks. We have a conflict here than as to whether GAD is a heritable disorder or not. Further studies were required to clarify this issue.

Andrews, Stewart, Allen, and Henderson (1990) looked at the level of anxiety disorder using 446 adult twin pairs. This study found that there was a possible genetic contribution to their category "Major Anxiety" which included PD, Agoraphobia, Social Phobia, and OCD. There was, however no suggestion in the data of a genetic contribution to GAD.

Another team to investigate this disorder was Kendler, Neale, Kessler, Heath, and Eaves (1992c). In this paper results were presented from a genetic analysis of 1-month GAD and 6-month GAD diagnosed by interview in 1033 female twin pairs. They found GAD to be moderately familial, and this was explained by genetic factors for the 1-month GAD with or without PD (heritability around 30%). However the results were less clear cut for the 6-month GAD, for which a genetic factor explained within pair similarity only when the disorder was accompanied by PD. Thus heritability may not be an important aetiological factor for GAD, but clearly is for PD, resulting in a heritability being found for GAD only when accompanied by PD. However, conflicting conclusions are reached when one considers a further paper (Kendler, Neale, Kessler, Heath, and Eaves 1992e), in which for all definitions of GAD (1-month, and 6-month GAD, lifetime diagnoses with or without hierarchy) the same model produced the best fit. This model contained a genetic factor shared by MD and GAD, with environmental influences specific to each disorder. Thus it is clear that while PD and Agoraphobia do not share genetic factors with GAD, GAD may still be a heritable disorder, in that it appears to share a heritability factor with MD.

Considering PD in greater detail, Kendler, Neale, Kessler, Heath, and Eaves (1993) point out that treatment seeking is very low in this particular disorder, but has been a requirement of all previous studies investigating its aetiology. Within their population twin sample of adult females (N = 2163 women) varying definitions

of PD were used, with all subjects being diagnosed at each level. However as the affected sample was rather small (236 by the most broad lifetime diagnosis), the authors were unable to reject out-right the model which fitted slightly less well (usually the CE model) than the model of best fit (usually the AE model). Heritability ranged from 30% to 40% for all but one of the definitions of the disorder, using a multiple threshold model, which suggested that the narrower and broader definitions were at different points on a continuum for symptomatology.

Turning now to twin studies of phobias, Kendler, Neale, Kessler, Heath, and Eaves (1992d) analysed the genetic epidemiology of phobias diagnosed by interview in 2163 adult women who were twins. They found there were common and specific AE factors for the four phobias: Agoraphobia, social phobia, situational phobia, and simple phobia. Heritability estimates ranged from 30% to 40%.

In summary, PD and Agoraphobia have been shown to be heritable in adults, with figures for heritability estimates in the region of 30% to 40%. The two disorders appear to be variants of one disorder, with Agoraphobia perhaps being the more serious manifestation of the disorder. The picture for GAD is less clear, in that alone it appears not to be heritable, although it is certainly familial, but in studies which combine the investigation of GAD with MD, GAD is found to share genetic factors with MD. This issue will be further discussed in the section on comorbidity. It looks likely however that this disorder will be shown to be genetically mediated to a certain extent, but this genetic factor is clearly different from that which is responsible for PD and Agoraphobia.

2.3.1.3: Evidence from molecular genetics

As with the study of depressive disorders molecular geneticists have considered the mode of inheritance of anxiety disorders and the evidence for linkage and associations with particular genetic markers. The available data have concentrated on PD which is not surprising as this has been shown far more consistently to be

heritable than GAD. The studies considering mode of inheritance of PD have produced contradictory evidence with some studies suggesting autosomal dominance and others suggesting polygenic transmission (Torgersen 1988; Woodman 1993; Weissman 1993).

Linkage analyses of PD have tended to exclude rather than confirm a role for the loci that have been studied thus far. For example, a study by Crowe, Noyes, Wilson, Elston, & Ward (1987) tested for linkage between 29 genetic markers and PD in 26 families. One locus on chromosome 16 was suggestive of linkage. However further analyses by this team (Crowe, Noyes, Samuelson, Wesner, & Wilson 1990) failed to confirm this finding. The Tyrosine Hydroxylase locus was also investigated with reference to PD in 14 pedigrees (Mutchler, Crowe, Noyes, & Wesner 1990) but this linkage was rejected.

Thus, as with the molecular genetic studies of depressive disorders, the mode of transmission and the role of specific loci for anxiety disorders is ambiguous.

2.3.2: Anxiety in Children and Adolescents

2.3.2.1: Evidence from family studies

Top-down studies

Weissman, Leckman, Merikangas, Gammon, and Prusoff (1984) conducted a family study looking at the children of probands with MD, with or without anxiety disorders. The children of probands with MD and Agoraphobia, MD and PD, or MD and GAD showed levels of anxiety and phobic disorders (0% to 36.8%) considerably higher than those in the children of the normal controls (1.2% to 2.3%). This shows cross-generational familial resemblance for anxiety disorders, that share some aetiological factors with MD in the parents.

More specifically Turner, Beidel, and Costello (1987) investigated 59 children aged 7-12 years. The children were of probands with anxiety disorders, probands with dysthymia, children of never mentally ill parents, and normal school children. The children of the anxiety probands were found to report more anxiety (STAIC) (Spielberger 1973) and fear symptoms (FSSC-R) (Ollendick 1983) than the children of normal controls, and than normal school children. The authors state that anxiety disordered parents' children were 7 times more likely to receive a diagnosis of an anxiety disorder than the control group children, but this figure does not take into account the different sizes of the two groups. If the figures are compared as percentages, the children of the anxiety disordered group were 5 times more likely to have received a diagnosis of anxiety disorder than the controls, and twice as likely as the children of the dysthymic group.

Biederman, Rosenbaum, Bolduc, Faraone, and Hirshfeld (1991) looked at the levels of anxiety and depressive disorders in children (aged 4 to 20 years) of parents with various psychiatric disorders. Of interest here are the findings for the children of the parents with PD and Agoraphobia alone (N = 14 children), PD and Agoraphobia with MD (N = 25 children), any other psychiatric disorder (N = 23 children), and healthy controls (N = 47 children). For the four groups the rates of any anxiety disorder in the children were 21.4%, 48.0%, 21.7%, and 10.6% respectively. Thus the levels of anxiety disorders were higher in all the psychiatric groups than the normal controls, and were particularly high in the "PD, Agoraphobia and MD" group.

Bottom-up studies

Livingston, Nugent, Rader, and Smith (1985) looked into the family histories of children with severe depression (N = 12) or anxiety (N = 11). Less than a third of the relatives of the anxious children were not diagnosed as having some form of psychiatric disorder, but the familial transmission did not seem to be very specific,

with the family histories of depressed children being very similar to that of the anxious children.

A study of mothers' of children with SAD, OAD or a non-anxiety non-affective psychiatric disorder by Last, Phillips, and Statfeld (1987) found that percentage of mothers with SAD as children was not significantly different between the three groups. However there was specificity for OAD, in that the mothers of the OAD group were significantly more likely to have suffered from OAD themselves as children than were the mothers if either of the other two groups. One weakness of this study is that the mother diagnoses were made from retrospective questionnaire information which could be biased by the mother's attitude to the anxiety symptoms in her child, and also by her own current symptomatology. However this does provide some preliminary evidence for OAD being a familial disorder.

Last, Hersen, Kazdin, Orvaschel, and Perrin (1991) carried out a family study of children with anxiety disorders (N = 94), Attention Deficit Hyperactivity Disorder (ADHD) (N = 58), and never psychiatrically ill subjects (N = 87). The relatives of the anxious group had higher levels of anxiety disorders than the relatives of the ADHD and control groups (34.6%, 23.5%, and 16.3% respectively). More specifically, the children with OAD had the highest levels of anxiety disorders in their relatives (3.8% to 29.0% and 2.7% to 23.7% respectively as compared to 0.0% to 11.0% in the relatives of the "other anxiety disorder" group). In particular, relatives of the overanxious group were much more likely to have PD than relatives of the SAD and "other anxiety disorder" groups (11.5%, 2.7%, and 0.0% respectively). Contrary to the authors' expectations there appeared not to be any specificity for SAD and OAD. Nor was there any close relationship between OAD and GAD.

Rosenbaum et al. (1991) investigated the notion that behavioural inhibition is a crucial factor in anxiety. The study looked at the parents (N = 75) and siblings (N = 45) of 22 children who were behaviourally inhibited at 21 months of age and 2 comparison groups of 19 children found to be uninhibited, and 20 normal controls.

This group had previously demonstrated that behavioural inhibition at 2 years is associated with social avoidance at 7 years (Kagan, Reznick, & Snidman 1988). While there was no increased risk for anxiety disorders in the siblings of the inhibited group, the parents of these children showed significantly higher levels of childhood, and adulthood anxiety disorders. The results are particularly striking for social phobia, where the percentages of social phobic parents of the inhibited, uninhibited and normal control group children are 17.5%, 0.0%, and 2.9% respectively. This suggests that behavioural inhibition may be a feature through which familial resemblance for anxiety disorders and particularly social phobias (and in children perhaps separation anxiety disorder) is transmitted. Due to the lack of data on anxiety disorders in the sample children themselves it is difficult to make any further conclusions from this data.

These results are strongly suggestive of there being a familial factor, though not necessarily a genetic factor, for anxiety disorders in children and adolescents. Next we turn to twin analyses.

2.3.2.2: Evidence from twin studies

Stevenson, Batten, and Cherner (1992) investigated the heritability of fears in 319 child same-sex twin-pairs aged 8 to 18 years. The total fear score (from the Fear Survey Schedule-Revised) (Ollendick 1983) was found to have a heritability estimate of 29%, with some specific fear factors showing higher heritability, and some showing negligible heritability. Group heritabilities for the fear factors and for the total fear score were of similar magnitude to the individual heritabilities, suggesting that extreme fears are just one end of a fear continuum, with the same aetiological factors accounting for the scores at any point on that continuum. Shared environmental influences were also important in accounting for within pair similarity. The non-shared environment factor was particularly important for fear of medical procedures, and the authors suggest that this could be because such experiences are by their nature generally non-shared, so the environmental factors

responsible for the fear they produce would be due in large part to non-shared environmental influences. Fear of failure, which as the authors note, is the fear dimension most closely related to social fear has a large common-environment factor, which suggests that such fears are learned in the family setting.

Thapar and McGuffin's (1994) twin study of anxiety in 376 pairs of twins aged 8 to 16 used the Revised Children's Manifest Anxiety Scale (R-CMAS) (Reynolds & Richmond 1978, 1979) to look at the heritability of anxious symptomatology. This scale was completed by the parents for both the children and the adolescents, and the adolescents also filled a self-report version. Surprisingly the results from these two data sets are very different. The parent report of anxious symptomatology was found to have an estimated heritability of 59%, but the self-report measure had no significant genetic component. Amongst the authors reasons for this discrepancy is the suggestion that the parents are rating an enduring trait, whereas the self-report is reflecting current state. This possibility could be tested by using the Spielberger State-Trait Anxiety Inventory for Children (STAIC) (Spielberger 1973) which specifically measures these two aspects of anxiety symptoms separately. Other suggestions include the lack of power in such a small sample, and the effect of age-group on heritability, however the parent ratings of the adolescent sample alone had enough power to detect a genetic component, which was of a higher magnitude than that detected in the parent ratings for the entire sample.

In conclusion, anxiety disorders in children also are strongly familial but the precise nature of this factor is not clear. It seems likely that as childhood anxiety is commonly associated with social anxiety and fears that common environmental influences will be of central importance here.

Chapter 3: Literature Review Part III

Environmental Factors, Depression and Anxiety

Section 3.1: The Assessment of Life Events

Life events can be assessed using either self-report or interview measures. Initial research in this area tended to rely on self-report measures many of which have been based on the Social Readjustment Rating Scale by Holmes and Rahe (1967). The more recent use of interviews inspired by the construction of the Life Events and Difficulties Schedule (LEDS) by Brown and Harris (1978a) has raised several questions regarding the accuracy of self-report measures, which are central to the whole issue of assessment of life events (Paykel 1983; Brown 1989; Goodyer 1990a; Rutter & Sandberg 1992). Although much of the research in this field has involved adults reporting on their own life events, some research has involved children and adolescents. This has been of four types. First, there are the studies in which children and adolescents were asked to complete self-report forms about stressful life events (eg. Mullins, Siegel, & Hodges 1985; Rende & Plomin 1991a; Nolen-Hoeksema, Seligman, & Girgus 1992; Gore, Aseltine, & Colton 1992; Tisher, Tonge, & Horne 1994; Loss, Beck, & Wallace 1995). Secondly, there are studies in which parents were interviewed about their children's life events (eg. Goodyer, Kolvin, & Gatzanis 1985; Goodyer, Wright, & Altham 1990a, 1990b). Thirdly, there are studies in which both the child and a parent were interviewed (eg. Monck & Dobbs 1985; Glen, Simpson, Drinnan, McGuinness, & Sandberg 1993; Sandberg et al. 1993), and finally there are studies in which only the child was interviewed (eg. Hammen 1988). These studies, like those using adults, have strengths and weaknesses, and these issues require discussion.

In considering the assessment of life events in adults, children and adolescents, eight issues will be covered. These are the ascertainment of potentially predictive events, reliability, fall-off in reporting, definition of events, quantification of stress, the inclusion of long-term experiences, background factors, and time involved. Within each section the findings from the adult data will be discussed first, followed by those from the more limited data using children and adolescents.

3.1.1: Ascertaining potentially predictive events

3.1.1.1: Reporter bias

One possible confounding factor in life events research is that individuals may try to “explain away” their own or their child’s symptoms by exaggerating their report of an event that they see as causal (Brown 1989). In this way psychiatric illness might result in a bias in the reporting and rating of life events. In order to obtain information about events which are independent of the illness and of the individual about whom the events are being reported two techniques are used. These are only collecting events that precede onset of the illness, and only analysing events which are thought to be independent of the behaviour of the subject.

3.1.1.2: Events preceding onset

Dating of events is more reliable when obtained through interview, as the interviewer uses discussion of events by which to anchor timings, for example birthdays or Christmas. This results in greater accuracy of timing of events. However, even using this methodology agreement between two reporters about the timing of an event may not always coincide (eg. Monck & Dobbs 1985). For this reason, much research now uses the concept “independence” first utilised by Brown and Harris (1978b).

3.1.1.3: Independence

The term “independence” refers to whether the event is likely to have been brought about by any aspect of the subjects behaviour. If this is unlikely the event is said to be independent of the subject. An example of this is death of a relative or close confidant (excluding murder or careless accidents). By analysing only independent events, it is possible to investigate the association of events and symptomatology, with some certainty that the symptoms did not cause the events. Without accurate timing of the events and onset, it is not however possible to test a causal hypothesis.

The next issue to be considered is the reliability of life events assessments.

3.1.2: Reliability

Reliability of self-report and interview measures of life events tends to be of two types, test-retest reliability, and agreement between multiple reporters (eg. parent and child). Also, for the interview method, inter-rater reliability is crucial.

3.1.2.1: Test-retest reliability

A review by Paykel (1983) found test-retest correlations for total scores on self-report measures to range from a lower limit of 0.07 to an upper limit of 0.90, with most figures being in the 0.6 range. In contrast, the test-retest reliability figures given as percentage concordance for a specific event for the two interview studies presented were 0.70 and 0.95. The first of the studies also calculated the test-retest reliability for the total scores and found the correlation for this to be approximately 0.2 higher than the percentage concordance for specific events. This, Paykel argued, suggests that the reliability for specific events from self-report measures

would be between 0.00 and 0.70 which is considerably lower than that from the interview method.

The studies reviewed by Paykel were all studies of adults. The only test-retest study of child and parent reported life events is that of Glen, Simpson, Drinnan, McGuinness, and Sandberg (1993) who conducted a reliability exercise using a new interview called the Psychosocial Assessment of Childhood Experiences (PACE). In this test-retest study of 15 parent-child pairs, percentage concordance for life events reported at time one and life events reported at time 2 was 0.46 for child report and 0.54 for parent report. The comparable data for long-term experiences are 0.58 and 0.55. This suggests that children are not much less reliable as reporters than their parents. Test-retest reliability of ratings by the respondent and by the interviewer of events and long-term experiences that were reported at both times produced kappas of between 0.51 and 0.86 for the individual variables rated, with most in the range 0.65 to 0.75. Test-retest reliability for the independence ratings of the events and long-term experiences were between 88% and 93% agreement for independence from child for events reported by mother or by child.

3.1.2.2: Agreement between multiple respondents

In adult studies the use of multiple raters usually means that the spouse or partner of the subject is also involved as a reporter. When multiple raters are used agreement is found to be greater in those studies that used interview methods rather than questionnaires (Paykel 1983; Brown 1989). In three studies of children and adolescents, the child as well as a parent was used as a reporter, and parent-child agreement was investigated.

The first of these is the study by Loss, Beck, and Wallace (1995), who assessed 88 mother-child pairs in which the children were either 9 or 12 years old. The measure used was Coddington's Life Events Record (Coddington 1972) which is an

adaptation for use with children from the Social Readjustment Rating Scale (Holmes & Rahe 1967). This measure was analysed in terms of reported life change units, and total impact of life events. The correlation between the mothers' and the children's reports of life change units was modest ($r = 0.28$, $p < 0.01$), as was the correlation for the total impact scores for those events ($r = 0.34$, $p < 0.001$). This suggests that on a measure such as this children and mothers report different events.

The second study of relevance here is that of Glen, Simpson, Drinnan, McGuinness, and Sandberg (1993). They found that parent-child agreement over the presence or absence of an event was 42.7% at time 1 and 42.0% at time 2. This suggests again that parents and children are reporting quite different events, and data should therefore always be collected from both.

Finally, a study by Monck and Dobbs (1985) specifically investigated agreement between 67 mother and daughter pairs for life events assessed using an adapted version of the LEDS (Brown & Harris 1978a). The daughters were aged between 15 and 20 years old. Of the total number of events reported, 59.4% were reported by both informants. Another 28.4% were reported by the daughter only and another 12.2% by the mother only. A very similar pattern of results for the severe events was also found. The daughters were more likely to report all the events collected from either informant than the mothers were (40% of daughters reported all events as compared to 13% of mothers), and this difference was also seen for the severe events although it was less significant (49% and 34% respectively). The girls over 17 themselves reported a larger proportion of the total events collected about them (ie. including those reported only by the mother) than the girls under 17 (57% and 27% respectively), but this difference did not show with the severe events alone. For the mothers, those with girls of less than 17 reported more of the total severe events recorded for their daughter (73% as compared to 31%), but this difference was not seen when all the events were considered. These results confirm the importance of obtaining both mother and child report of events.

A similar issue is explored in a study by Rende and Plomin (1991) which investigated agreement between parents and 7-year-old children on their perception of the stressfulness of events that had occurred in the past year, as reported by the parents on the Social Readjustment Rating Scale for elementary school children (Coddington 1972). Parent ratings of the upsettingness of life events were significantly higher for 5 out of the 25 categories of life event. The children did not perceive any of the events as being significantly more upsetting than the parents. The mean composite stress score from the parent report was significantly higher than that from the child report (4.08 compared to 3.17, $p < 0.001$). The partial correlation between child and parent composite stress scores controlling for the number of events is only 0.21 ($p < 0.01$). This illustrates how different child and parent perceptions of the upsettingness of life events are, and implies that ratings obtained from parents only over-estimate the level of stress experienced by the child, confirming the importance of obtaining data from both the child and a parent.

3.1.2.3: Inter-rater reliability

Paykel (1983) presents inter-rater reliability for the Interview for Recent Life Events, a list of 64 events administered as a semi-structured interview and rated in the manner of Brown & Harris' (1978a) interview. Inter-rater reliability for agreement over the occurrence of an event was 95%. Agreement for the rating of independence was 87% for zero or one-point difference on a five-point scale. Agreement for objective negative impact was 76% for zero or one-point difference, also on a five-point scale. This suggests that it is possible to obtain very high inter-rater reliability for such interview measures.

Glen, Simpson, Drinnan, McGuinness, and Sandberg (1993) also presented inter-rater reliability of 70 child reported events and 67 parent reported events. The reliability was very high, with kappas ranging from 0.85 to 1.00 for the individual variables rated by the interviewers. This confirms the finding that raters can be

trained in such a way as to produce reliable ratings from an interview of life events such as those discussed above.

A second approach to assessing the accuracy of a measure of life events is to investigate the rate of “fall-off” in the reporting of events.

3.1.3: Fall-off in reporting

Reports of life events are subject to a phenomena called “fall-off”. This is a process by which fewer and fewer events are recalled the further into the past the interview asks about. In particular, individuals tend to under-report events when using self-report measures, and this increases as the time period moves further into the past (Monroe & Wade 1988). Approximately 4-5% per month fall-off is found in self-report measures, but only 1-3% occurs with trained interviewer’s using Brown’s methodology (Paykel 1983). Fall-off in the first six months tends to be considerably lower than that in the second 6 months. This can be illustrated by comparing the rate of fall-off in interview studies that only asked about the previous six months (rate of fall-off 8-9% over the whole 6 month period), as compared to a study that interviewed about events from a twelve month period (fall-off over the twelve months was 34%) (Paykel 1983).

As with the adult literature, fall-off is also reported in the child and adolescent literature. Monck and Dobbs (1985) found that almost twice the level of events were reported for the immediately preceding 6 months than for the 6 months before that. The most marked fall-off in reporting was seen for recall of events that occurred more than 30 weeks previously.

This suggests that it is unwise to make any firm conclusions from data on life events reported as happening more than a year before the interview. This effects studies of disorder in particular, because the case group is often required to report on the

twelve months preceding onset, which may itself be several months before the time of the interview. Such studies should perhaps concentrate on a shorter time-period, for example six months.

3.1.4: Defining events

Another issue of importance is that on a check-list, life events may be interpreted in many ways and this is left up to the respondent. For example, moving house could mean to a less desirable home, it could be unplanned and enforced, it could be associated with family breakdown, with a change of neighbourhood, loss of friends and change of school. By contrast it could be expected and planned for, involving a larger more desirable new home, with no family breakdown, no change in neighbourhood, social circle or school. Interview measures provide a far more detailed appraisal of the event and as such are able to assess the information given regarding the surrounding situation from which to make impact ratings.

Circumstantial information is also used to rate the particular quality of the event, sometimes defined in terms of threat or danger as compared to loss (eg. Brown & Harris 1978b; Finlay-Jones & Brown 1981). The former category refers to events that are threatening to the individual's family, health, finances, friends, self-esteem or any other area of importance. Loss events include exits which are defined as when a person loses someone from their social sphere (Paykel 1969). Loss events can also refer to events such as the loss of employment or of the subjects home. Finally loss can refer to something less tangible, for example trust, if a partner is found to have been cheating, or a child to have been lying. These concepts can only be rated if adequate information about the surrounding circumstances of the event are collected, which means that an interview is required.

3.1.5: Quantification of stress

For similar reasons, quantification of stress is also more accurate when interview procedures are used. The method used by Brown and Harris (1978a) was to have the interviewer make a judgement about the contextual threat the event posed for the subject. This will be referred to as contextual negative impact in order not to use the term threat, which is used here to refer specifically to events involving threat or danger to the individual as discussed above. A rating of contextual negative impact involves inquiring as to the circumstances surrounding the event, and rating the impact of the event as being that which one would expect for any person with those surrounding circumstances. Any details from the respondent about their reaction to the event or any symptoms or emotions that followed it are not incorporated into this rating. Paykel (1983) has argued that such ratings may be subject to bias from the interviewer who knows that the respondent became ill after the event. However if the interviewer is adequately trained, such information should not bias the rating.

Quantification of stress can be achieved in several other ways, although as will be seen, these are less reliable. One method by which the rating of severity of impact of an event can be obtained is simply adding up the total events score, but this only provides a very rough and inaccurate rating of stress. An improvement on this method is achieved by weighting the events (eg. Holmes & Rahe 1967). These two types of quantification presume simple additivity is appropriate to the investigation of life events, but Brown and Harris (1978, 1989) have argued that events are not simply additive and should not be treated in this way. A more elaborate method used both with self-report measures and with interviews is to ask the respondent to give their impression of the impact of the event. However, if the respondent rates the impact of the event themselves, this rating is purely subjective, and as such may be influenced by the subsequent illness. As Brown (1989) discusses, emotion must play a critical role in the assignment of meaning to a particular event. For example, as discussed earlier, an individual may try to justify their symptoms by emphasising the negative aspects of an event that they see as causal. Such a bias can produce a link

where in fact none was present. In self-report measures the timing of the impact is often not clear, for example, immediate impact could mean the moment the event happened or any point during the day during which it happened. The impact of an event as it occurs is usually greater than that which is felt shortly after the event, but in a self-report measure it may not be clear exactly what the subject is required to rate. For this reason Brown incorporates the concepts of short-term and long-term impact into his methodology.

3.1.5.1: Short-term and long-term impact

As the impact of an event may be short lived or may be more long-term, the rating of the impact at the time of the event, and about one to two weeks later allows for such information to be collected. Short-term impact is the rating made for the impact of the event at the time it happened. If an event is still having an impact on the individual one to two weeks later, it is said to involve long-term impact. Severe events are those that are rated as moderate or severe on the long-term negative impact rating.

3.1.6: Long-term experiences

Discrete events are not the only type of stressor which can be measured within the context of life events research. Long-term difficulties such as poor housing or marital conflict can also be regarded as stressors, and yet are not events. These long-term experiences were defined in Brown and Harris (1978b) as ongoing stressful situations lasting at least a month. A similar approach was taken by Glen, Simpson, Drinnan, McGuinness, and Sandberg (1993). In many available self-report measures, such difficulties tend to be rated and collected as if they were life events with no distinction between stressors that are acute and those that are chronic. As such factors are likely to act in different ways, this could mask the effects of one or other type of factor in any analyses.

3.1.7: Background factors

In addition, interviews can collect information about background factors such as SES, housing, quality of family relationships, and death of attachment figures at any stage in the subjects life. All of these factors are potential predictive factors for depression and anxiety and as such are of interest.

3.1.8: Time involved

Interview methods are very expensive in terms of time. The LEDS can take up to a morning to complete, the PACE requires approximately two hours for the mother interview and one hour with the child. This means that for large scale projects, for example those looking at the heritability of life events where large sample sizes are required, self-report measures may be essential. However, if such data is obtained, the weaknesses described above cannot be ignored.

In conclusion, interviews provide detailed, accurate, reliable information from which extensive ratings can be made of the precise nature of the event. For these reasons, studies which used such interviews are given more weight in the following literature review.

Section 3.2: Depression and Environmental Factors

The model on which this review of environmental factors, depression and anxiety is based is that of Brown and Harris (1978b). As discussed in Chapter 1, this model has two main concepts. Firstly there are acute stressful life events (also referred to as risk factors or provoking agents) from the individual's recent past, which are seen as triggers that result in psychopathology in the individual. However, not all individuals who experience such life events become ill, and this is explained by the additional presence or absence of vulnerability factors. Vulnerability factors are

features of the individual's earlier environment that interact with stressful life events increasing the likelihood of a psychiatric outcome. This model predicts that the risk of psychopathology in a sample experiencing vulnerability factors but not life events should be no higher than the population risk for this disorder. The risk for a sample experiencing one or more life events but no vulnerability factor should be higher than either of these groups. Finally, the risk is predicted to be highest in a sample where the individuals have experienced both vulnerability factors and recent stressful life events. This pattern of associations is known as a multiplicative interaction.

A multiplicative interaction can be detected in a regression analysis, by including an "event x vulnerability" interaction term into the equation. If this term is a significant predictor of psychopathology in addition to the predictive power of the "event" term alone, and the "vulnerability" term does not have any predictive power, this is support for the above hypothesis. However in this type of analysis the dependent variables are frequently binary variables, requiring the use of logistic regression, which, as Kendler, Kessler, Walters et al. (1995) point out produces a specific problem. This is that the use of log transformed data alters the nature of multiplicative interactions such that they become additive. In their own words "What is a multiplicative interaction in the probability model becomes (to a first approximation) simply additive in the logistic model". Thus in the following review of the literature, where many of the studies have used logistic regression, the results must be interpreted with caution, and the possibility of underlying multiplicative interactions not ruled out. However, the important feature of Brown and Harris' theory (1978b) was that a vulnerability factor alone has no predictive power.

An additive interaction is one where subjects experiencing a vulnerability factor alone are at as high a risk for psychopathology as subjects experiencing a life event alone. Subjects who experience both types of factor are at a higher risk than either of these groups, but the increased burden of the two factors is simply additive. Such vulnerability factors cannot be seen as true vulnerability factors as defined by Brown and Harris (1978b), but are still of interest as predictors of psychopathology.

3.2.1: Life events and depression

It is a well replicated finding that subjects (children, adolescents and adults) report higher levels of life events in the period of time preceding onset of depression, and during the course of the illness, than comparison groups report for a similar period of time, and that individuals with depressive disorders or with high levels of depressive symptoms report more life events than individuals without depressive disorders or with low levels of depressive symptoms (Paykel et al. 1969; Brown & Harris 1978b; Finlay-Jones & Brown 1981; Kashani, Holcomb, & Orvaschel 1986; Rodgers 1990; Garrison, Addy, Jackson, McKeown, & Waller 1992; Goodyer, Wright, & Altham 1987, 1988; Mackinnon, Henderson, & Andrews 1990; Goodyer, Cooper, Vize, & Ashby 1993; Tisher, Tonge, & Horne 1994). There are two possible reasons for this association between depression and life events. Firstly, the depression could cause the subject to over-report negative life events, thus leading to an artificial inflation of the relationship between depression and life events, or second, the relationship could be a real one, with life events being a genuine component in the aetiology of depression.

In order to choose between these two alternative hypotheses Fergusson and Horwood (1984) used structural equation modelling on their longitudinal data. Their sample consisted of 1103 adult women, who completed a self-report measure of depression and a reduced version of the Social Readjustment Rating Scale (Holmes, & Rahe 1967) which asked about life events in the previous 12 months. These measures were collected at two time points, two years apart. They fitted a model to their data, in which there were two pathways of interest. One path led from the depressed symptoms at time 2 to the life events at time 2 (this tests whether current depression affects the reporting of the life events). The other led from the life events reported at time 1 to life events at time 2 and then to the depressed symptoms at this time, testing whether the life events are causally related to the depression. Their results suggest that while the presence of depressive symptoms does have an effect on self-report of life events, the path leading from life events to the depressive

symptoms is of greater magnitude. Thus the relationship between life events and depression is at least in part due to the fact that life events are involved in the aetiology of depression.

Another important point to establish is whether the raised levels of life events are as a result of the depression. Considering the life events preceding onset of the disorder is one way of considering this issue, and studies which have been conducted in this way find that life events prior to onset are predictive of caseness (Paykel et al. 1969; Finlay-Jones & Brown 1981; Goodyer, Wright, & Altham 1988; Goodyer, Cooper, Vize, & Ashby 1993). However, if the cases are not recent onset cases, or are simply expressing high levels of symptomatology this approach is not possible, and the interview tends to concentrate on the twelve months preceding interview. In studies of this kind, another way in which to establish whether the relationship between life events and depression is true is to make use of the concept of "independence" introduced earlier. By dividing the events into those which are likely to be independent of the behaviour of the subject, and those which are primarily related to the behaviour of the subject, one can then analyse only those events over which the subject had little or no control. When this is done the relationship still holds true even for the independent events which were not caused by the subject (Goodyer, Kolvin, & Gatzanis 1985; Finlay-Jones & Brown 1981; Goodyer, Kolvin, & Gatzanis 1986; Goodyer, Wright, & Altham 1988).

The association between life events and depression is not affected by sex or age (Goodyer, Kolvin, & Gatzanis 1986) and is strengthened the more life events there are reported (Goodyer, Kolvin, & Gatzanis 1987).

Specifically, depression is associated with loss events, particularly exit events as shown in Paykel et al. (1969). In this study, depressed adult subjects (N = 185) were significantly more likely to report an exit event for the six months preceding onset than the control subjects (N = 185) in the six months preceding interview (26% and 5% respectively). Similar results have been found in child data (Goodyer, Kolvin, &

Gatsanis 1985; Weller, Weller, Fristad, & Bowes 1991; Kranzler, Shaffer, Wassrman, & Davies 1989).

In particular the role of loss in depression is often compared to threat or danger events which are strongly implicated in the aetiology of anxiety. This distinction has been drawn by many authors (Freud 1959 discussed in Smith & Allred 1989; Bowlby 1973, 1980; Brown & Harris 1978b). Finlay-Jones and Brown (1981) considered the impact of loss and danger type events on psychopathology in 164 young women interviewed with the LEDS (Brown & Harris 1978a). The specificity of loss events to depression was highly significant. Sixty-five percent of the depressed subjects (N = 17) reported at least one severe loss in the year preceding onset as compared to 10% in the control group (N = 119). Mixed cases (N = 15) were significantly more likely to have experienced both a severe loss and a severe danger event in the twelve month period than the depressed group, the anxious group or the controls (60%, 35%, 8%, and 2% respectively).

The specificity of loss events to depression as compared to “maladjustment” was shown in a study of children by Berney et al. (1991). This study compared groups of children and adolescents with endogenous depression or with depression with negative cognitions to a group of children and adolescents with non-depressive psychiatric disorder. The comparison group was described as maladjusted, including an element of antisocial behaviour in one-third of the cases, but no further details (eg. presence or absence of anxiety disorders) are given. Of the three groups, the percentage of children who's mothers' reported at interview a severe negative exit event was 22%, 38%, and 13% respectively. The difference between the depression with negative cognitions and the maladjusted group was significant ($p < 0.05$). This demonstrates the importance of loss events in the aetiology of depression, but without an anxious comparison group and a normal comparison group the results are not as informative as they might be.

The measures of life events in the studies of children reviewed thus far have all relied on parent report. One study in which the children report on life events themselves is that of Loss, Beck, and Wallace (1995). This study of 88 nine- and twelve-year-old children found that children with CDI (Kovacs 1981, 1985) scores of more than 19 rated themselves as having experienced significantly higher levels of life events (on the Life Events Record, Coddington 1972) in the preceding twelve months than the children in the "non-distressed" group, those with scores below 19 on the CDI. Also, distressed children and their mothers had more mutually endorsed life events than the non-distressed group. These results confirm the findings from the above studies that use the mother as the rater of life events.

While the effects of life events, and in particular loss, have been shown to be considerable, it remains unclear why some children respond to undesirable life events with a depressive disorder, while others remain psychologically well. As discussed earlier, underlying vulnerability factors could account for differences in reactions to stressful life events. The majority of work into vulnerability factors associated with depression has concentrated on social vulnerability factors and these will be reviewed first. A related area of work has been to consider cognitive factors that act as mediators in the relationship between social vulnerability factors, life events and depression. This area will be covered briefly. Finally there is new data that suggests that certain genetic factors may act as vulnerability factors that predispose the individual to psychiatric disorder in the presence of a stressful life event.

3.2.2: Vulnerability factors and depression

3.2.2.1: The social approach

Studies with adults

Brown and Harris (1978b) described four vulnerability factors which increased the chances of a woman developing depression in the presence of a life event or difficulty. These were lack of full-time or part-time employment outside the home, lack of a good marital relationship, presence of three or more children under 14 at home, and parental loss before the age of 11. In their later work this became referred to as early loss and a rating of parental loss before age 17 is brought in. These factors acted in such a way that their presence without a stressor did not constitute a risk for depression, but in the presence of a stressor, depression was the probable outcome. The only exception to this was lack of employment outside the home which only acted in this way when in conjunction with another vulnerability factor. This vulnerability factor has not been the subject of further enquiries or replication so will not be discussed. In order to illustrate the relationship between these vulnerability factors, stressors and depression Brown and Harris (1978b) provided the following statistics comparing various groups. Firstly, only 1% of those women with a vulnerability factor became depressed as compared to 11% of those with a provoking agent. Secondly, of the women who experienced one provoking agent and one vulnerability factor 12% developed depression, as compared to 3% of the women with two vulnerability factors and no provoking agent. Thus these two types of factors acted in quite different ways. A vulnerability factor will interact with a stressor to produce the outcome of depression.

The four vulnerability factors for depression in adult women developed in Brown and Harris (1978b) have been subject to the criticism that these were not truly multiplicative interactions and that all the factors were independent predictors of depression (Tennant & Bebbington 1978), but these criticisms were dismissed by

Brown and Harris (1978c). Since this time further studies have found loss of a parent to be associated with depression, though not to act as a true vulnerability factor (Alnæs & Torgersen 1988, 1989a, 1989b; Kendler, Neale, Kessler, Heath, & Eaves 1992a).

It seems that loss is associated with depression in adulthood, but how is this vulnerability transmitted? One possibility that has been investigated is that the effects of loss are felt indirectly through the resulting "lack of care" experiences after such a loss. Parental indifference, institution rearing and premarital pregnancy have suggested that a downward cycle of events set up by the initial loss of a parent can result in depression (Quinton, Rutter, & Liddle 1984; Harris, Brown, & Bifulco 1986; Bifulco, Brown & Harris 1987; Harris, Brown, & Bifulco 1987).

Social support has been demonstrated to be associated with depression (Finlay-Jones 1989). Furthermore, lack of a supportive relationship, the use of "turning to others" as a coping strategy and perceived support have all been demonstrated to interact with recent stressful life events in producing depression (Brown, Andrews, Harris, Adler, & Bridge 1986; Kendler, Kessler, Heath, Neale, & Eaves 1991; Kessler, Kendler, Heath, & Eaves 1992).

However, it must be noted that it is possible that perceived lack of social support may merely be a symptom of depression. This hypothesis is supported by results from Bergeman, Plomin, Pedersen, and McClearn (1991) who found that the genetic factors involved with depression were entirely shared with those involved in the perception of social support. In the light of this finding, the above results must be interpreted with caution.

The evidence for three or more children living at home being a vulnerability factor for depression has become less clear with the passage of time. Both Brown and Harris (1986) and Rodgers (1990) found that having three or more children did not appear to act as a vulnerability factor for depression in women. Brown and Harris (1986)

theorised that the changing social climate (notably control over pregnancy and the resulting increased choice for parenthood) caused this factor no longer to be the stressor it was earlier in the century.

Studies with children

Having discussed the work of Brown and Harris (1978b) and the subsequent research into depression in adult women that it inspired, it is now possible to move on to the more specific area of interest here which is depression in children and adolescents. There are six similar environmental factors which have received attention in the child and adolescent literature on depression. These are lifetime exits (of attachment figures), poor family relationships, peer problems, academic problems and lack of achievement, maternal depression, and early hospitalisation and illness. The majority of the studies reviewed below are cross-sectional, and their data has tended to be used to test for associations between environmental influences and symptomatology or caseness. In many of these studies the environmental factors are discussed as predicting depression in that they account for a certain proportion of the variance in the variance of symptoms. However in order to test for true prediction or causality of symptoms longitudinal data is required. The few studies that present longitudinal data or that test for interactions with stressful life events are reviewed in greater detail. Much of this data comes from an extensive series of papers by Goodyer and colleagues. The papers from 1988 to 1991 all used the same sample. This was a case-control sample of 100 case children aged 7 to 16, classified as predominantly depressed or predominantly anxious, and 100 matched community controls. The six areas outlined above will now be reviewed, concluding with three papers that investigate multiple risk factors.

First, lifetime exits have been shown to be associated with both depression and anxiety (Goodyer & Altham 1991a). Furthermore, Reinherz, Stewart-Berghauer, Pakiz, Frost, Moeykens, and Holmes' (1989) 10-year longitudinal study of 404

children assessed at ages 5, 9, and 15, found death of a parent was a predictor of later depression. However this was only in the girls, for whom this variable accounted for 5% of the variance in CDI scores (Kovacs 1981, 1985) at age 15. One of the most common forms of lifetime event which children are exposed to is divorce. A prospective study of initially intact families by Block, Block, and Gjerde (1988) showed that families in which divorce subsequently occurred were characterised by unsupportive parenting. This concept is similar to the construct "lack of care" investigated as a vulnerability factor for depression by Bifulco, Brown, and Harris (1987). Thus the risk of depression after loss of parent(s) through divorce may be mediated by earlier, and subsequent, lack of parental support.

Second, lack of support has also been shown to be associated with high levels of depressive symptoms in adolescent inpatients (Barrera & Garrison-Jones 1992). In addition, there are well replicated associations between depression and dysfunctional family relationships (Rutter, Graham, Chadwick, & Yule 1976; Puig-Antich, Kaufman, Ryan, Williamson, Dahl, Lukens, Todak, Ambrosini, Rabinovitch, & Nelson 1992), high Expressed Emotion (EE) (Rutter & Brown 1966) (Schwartz, Dorer, Beardslee, Lavori, & Keller 1990; Asarnow, Goldstein, Tompson, & Guthrie 1993), and insecure parental attachment, poor maternal bond and maternal discipline (Armsden, McCauley, Greenberg, Burke, & Mitchell 1990; Tejerina-Allen, Wagner, and Cohen 1994).

Third, support from confidants and peers, self-ratings of perceived popularity, and quality of friendships have been found to be associated with depression and loneliness (Reinherz, Stewart-Berghauer, Pakiz, Frost, Moeykens, & Holmes 1989; Armsden, McCauley, Greenberg, Burke, & Mitchell 1990; Parker, & Asher 1993; Goodyer, Wright, & Altham 1989). Interestingly, when Goodyer, Wright, and Altham (1990a) explored the relationship between recent life events and friendship problems in 12 months prior to onset, they found that friendship problems and life events exert independent additive influences on psychiatric disorder in the child. Further evidence that poor friendships are involved in the aetiology of depression is the

finding that poor friendships are also a significant predictor of recovery status (Goodyer, Germany, Gowrusankur, and Altham 1991).

Fourth, there is considerable evidence that shows depression in school-age children to be associated with poor school performance and academic problems (Rutter, Graham, Chadwick, & Yule 1976; Carlson & Cantwell 1983; Petersen, Compas, Brooks-Gunn, Steemler, Ey, & Grant 1993; McGee, Feehan, Williams, & Anderson 1991, Puig-Antich et al. 1993).

Goodyer, Wright, and Altham (1990b) looked at recent social achievements (success rated relative to expectancies of the mother and child in the categories of education, sports, art/craft/technology, and community achievements) which fell in the same time-frame as recent social adversities (life events, and poor friendships). Independent effects on caseness were found for the events measure and also for one interaction term (achievements x friendships) which exerts a multiplicative interaction on the likelihood of being a case. This factor was only significant for cases, implying that the effects of poor friendships are enhanced in a multiplicative manner by lack of achievements, but that in the absence of poor friendships, lack of achievement is not a significant predictor for depression.

Fifth, it is a common finding that adults with affective disorders have children with affective disorders, and children with affective disorder have parents with affective disorders (Tambs & Moum 1993; Puig-Antich, Goetz, Davies, Kaplan, Davies, Ostrow, Asnis, Twomey, Iyengar, & Ryan 1989; Harrington, Fudge, Rutter, Bredenkamp, Groothues, & Pridham 1993; Weissman, Warner, Wickramaratne, & Prusoff 1988; Hammen 1990). Although many of these studies investigated shared genetic factors, part of this association may be due to the particular environment that a depressed mother creates for her child.

Life events and maternal depression have been found to have independent additive effects on depression in the child (Goodyer, Wright, & Altham 1988; Goodyer,

Cooper, Vize, & Ashby 1993; Fergusson, Horwood, & Lynskey 1995; Tisher, Tonge, & Horne 1994; Hammen, Burge, & Adrian 1991). There is however, a strong possibility that this association is however an artifact, and that life events as reported by the mother are biased by her depression.

This was investigated in a study by Loss, Beck, and Wallace (1995) who explored the effects of maternal depression on the mothers' agreement with her child on a rating of life change. They found that mothers with scores above the mean on the Beck Depression Inventory (BDI) (Beck, Ward, Mendelson, Mock, & Erbaugh 1961) agreed significantly less well with their children's ratings on a self-report questionnaire measure of life change than mother's who scored below the mean ($r = .16$ compared to $r = .33$). This suggests that mother's depression may reduce her accuracy as a reporter of her child's life events. However, parent-child agreement for life events was fairly low for both normal and depressed mothers, emphasising once again the importance of obtaining such information from both the child and the mother.

Sixth, multiple admissions to hospital were found to be associated with a teacher rating of emotional disturbance in a study of 10-year old children (Quinton & Rutter 1976). This relationship was strongest in those families at high psychosocial disadvantage, a composite measure including six features which were living in a broken home, maternal psychiatric disturbance, father having a police conviction, child having been in the care of the local authority, serious overcrowding in the home, and father in an unskilled or semi-skilled occupation. This underlines the importance of many of the factors previously discussed and shows how multiple factors can interact to contribute to depression. More recently, Reinherz, Stewart-Berghauer, Pakiz, Frost, Moeykens, and Holmes' (1989) longitudinal study of 404 adolescents found that serious illness between birth and five years of age accounted for 3% of the variance in depressive symptoms ($p < 0.005$).

Finally we come to three studies that investigate multiple risk factors of various different types. The first of these is Goodyer and Altham (1991 part 2) who considered several vulnerability factors within their 1988 sample. The factors were lifetime exit events excluding those in the last 12 months (as reported by the mother at interview), maternal distress, lack of good maternal confiding relationship, recent friendship difficulties, and lack of recent achievements (the latter two both reported by child and mother). Recent stressful life events were also included in the regression analyses. Thus it can be seen that this paper covers many of the factors discussed above. Of the 100 cases, only 3 had not experienced any of these adversities, whereas 35 of the 100 controls had not. All of the social factors were required in the regression equation, as were lifetime exit events. As with other work by this team, sex and pubertal status were considered, but neither was predictive of caseness.

Another study which simultaneously considered multiple vulnerability factors is Cohen, Brook, Cohen, Velez, and Garcia (1990). This was a longitudinal study with a random community sample of 423 adolescents aged 13-18 at follow-up. The follow-up measure was the CBCL (Achenbach & Edelbrock 1983). This was to be the dependent variable with multiple predictor risk variables measured at the initial time-point eight years previously. The risk measures were too numerous to give full details, but they covered four main areas. These were biological (eg. early illness and hospitalisation), context (eg. SES, social isolation, residential instability), family (eg. parental mental health, low maternal availability, broken family), and parent-child interaction (eg. parental involvement and inattention, rules and punishments). For the internalising scale on the CBCL six of the risk factors were significant predictors when all other factors were controlled for. These were biological risk, social isolation, parental mental illness, mother and step-father type home, maternal inattention (which surprisingly had a negative relationship with internalising score), and lax, inconsistent rules. The authors then analysed the data using a new analysis which they name net regression. This technique was used to assess whether any of the factors were significantly better predictors for any one group (internalising,

externalising, drug abuse) over and above the level of prediction for the other groups. The only risk factor that was specific in this way to the internalising group was social isolation. This confirms the association of friendship difficulties with childhood depression.

The third study is that of Seifer, Sameroff, Baldwin, and Baldwin (1992). This was a longitudinal study of 152 children (aged 4 at time 1 and aged 13 at time 2) assessed with a multitude of measures. Fifty children were designated as being high risk, the other 102 as low risk (using a composite measure of disadvantage including variables such as maternal mental illness, low level of parental education and occupation, father not present in household, four or more children in the family, disadvantaged minority ethnic background, rigid parenting values, and poor quality mother-child interaction in a laboratory teaching task). The dependent variable of interest here was change in social-emotional competence, or adjustment, as reported by the child at age 13. None of the child reported change in adjustment was accounted for by mother reported variables. However there were several child reported variables that accounted for significant proportions of the variance in change of adjustment according to the child report. Positive change in adjustment for both the high and low risk groups was predicted by perceived competence in both the school and social arenas, and by having lower levels of unknown or external locus of control and by lower levels of life events for both the low and high risk groups. Thus it can be seen that many protective factors are reversals of vulnerability factors, even in the presence of high levels of background risk factors.

3.2.2.3: The cognitive perspective

This refers to the holding of certain dysfunctional attitudes that result in the individual being more likely to become depressed. Studies interested in considering how cognitive factors mediate the relationship between vulnerability factors, stressors

and depression consider such factors as self-esteem or self-concept, and attributions or helplessness.

Low self esteem has been shown to be a good predictor of depression (Reinherz et al. 1989). In addition to this, self-esteem has been shown to be related to positive change in adjustment over time (Seifer, Sameroff, Baldwin, & Baldwin 1992). However, the two studies which consider an interaction between low self-esteem and life events have produced conflicting results.

Brown, Andrews, Harris, Adler, and Bridge (1986) looked at low self-esteem as a vulnerability factor for depression. Three hundred and fifty-three adult women took part in a 2-stage study of support, self-esteem, life events and onset of depression. Low self-esteem was significantly related to onset of depression when in combination with a stressful life event, but was not related to onset of depression without the presence of a provoking agent (33% vs. 4% respectively). This suggests that low self-esteem is a vulnerability factor for depression. This is compatible with the hypothesis that self-esteem mediates the effects of previous vulnerability factors; but this was not tested in this study.

A similar study by Hammen (1988) reported on longitudinal data from 79 children aged 8 to 16 of mothers with major depression, chronic medical illness and no known illness. In predicting diagnosable depression or CDI scores (Kovacs 1981, 1985) at follow-up, the initial diagnosis and stress threat were significant, as was the measure of self concept. However the "stress threat x self-concept" interaction was non-significant in predicting diagnosable depression or CDI scores. As this analysis was conducted using a hierarchical multiple regression, one must conclude that, at least in this sample, self-concept was an independent predictor of depression.

Learned helplessness as an attributional style, has been shown to predict later symptoms of depression in children (Seligman, Peterson, Kaslow, Tanenbaum, Alloy, & Abramson 1984; Seligman, & Peterson 1986; Mullins, Siegal, & Hodges

1984; Seifer, Sameroff, Baldwin & Baldwin 1992) and was described as being the end result for a child who experiences either the absence of a mother figure, an unresponsive mother, or stimulus deprivation (Seligman 1975, reviewed in Brown & Harris 1978b, and in Kazdin 1990). This can be seen to parallel Brown and Harris' later findings that it is primarily lack of care following loss of mother that is a vulnerability factor for depression rather than the loss itself (Harris, Brown, & Bifulco 1986, Harris, Brown, & Bifulco 1987, Brown & Harris 1993a). Furthermore, Armsden, McCauley, Greeburg, Burke, and Mitchell (1990) found that poor parent attachment was not only significantly related to current depressive states, but was also associated with attributional style.

Hammen, Adrian and Hiroto (1988) looked specifically at the attributional style of 79 children aged 8 to 16. They tested the hypothesis that in the presence of a negative life event, a negative explanatory style would increase the likelihood of the child having an expectation of uncontrollability (hopelessness) which would then lead to depression. Diagnostic status at follow-up was taken to be the dependent variable in a logistic regression with initial diagnosis, attributional style, stress threat, and an "attribution x stress" interaction as the predictors. In their analyses the authors found that in the prediction of diagnosable depression only initial diagnosis and stress threat were significant predictors, there was no predictive value to attributional style or to the interaction term. This suggests that attributional style may not be a mediator of vulnerability to depression in children and adolescents. However this is a relatively small sample and the results would need to be replicated before one could fully reject the hypothesis.

Age-related changes were explored in another longitudinal study by Nolen-Hoeksema, Girgus, and Seligman (1992) who investigated the interrelationships between children's depressive symptoms, attributional style, negative life events, and social and achievement helplessness as rated by teachers. The sample for this study consisted of between 255 and 508 school children investigated at 9 time points over a 5 year period, at the beginning of which they were 9 years old. In a

predictive analysis, depressive symptoms were found to be best predicted by depressive symptoms at an earlier time-point. In the younger children (9 to 10 years) negative life events also predicted later depressive symptoms, and as the children grew older, a negative explanatory style became predictive of depressive symptoms. Those children that were depressed showed less improvement or more deterioration in their explanatory style over time. A similar effect was seen for social and achievement helplessness but this was a less consistent result. This supports the theory that a cycle is set up of negative life events leading to a negative explanatory style, resulting in depressive symptoms which themselves produce a worsening of social and achievement helplessness and a more negative set of attributions about self.

This section has shown that negative attributions and feelings of hopelessness are predictors of depression. Also, these negative cognitions can mediate the effects of vulnerability factors such as poor attachment, so that in the presence of a severe negative life event, there is a high risk of depression. The relationships between all these factors may vary with age, but this finding requires confirmation.

3.2.2.4: Genetic vulnerability factors

Kendler, Kessler, Walters et al. (1995) produced a ground-breaking analysis of the relationship between genetic liability, stressful life events and major depression in adult women. The research was conducted on a large population based sample of female adult twins. High genetic risk (monozygotic twin, co-twin with MD versus dizygotic twin, co-twin unaffected) led to a significant increase in the risk of suffering from MD. Stressful life events also significantly increased the risk of onset of MD. In a logistic regression, these two factors did not have a multiplicative interaction effect, but as described earlier this could have been due to the use of logistic regression, so the authors analysed the data using a probabilistic scale. Interestingly they found an interaction effect that had been masked by the log transformation of the data. The

authors summarise that "Genetic factors influence the risk of onset of major depression in part by altering the sensitivity of individuals to the depression-inducing effect of stressful life events".

In summary, factors such as loss of an attachment figure, family relationship problems, friendship problems, academic problems, maternal depression and early illness are predictive of depression in children and adolescents. These associations may be mediated by a number of social, cognitive and genetic factors.

Section 3.3: Anxiety and Environmental Factors

There is a lack of evidence in this area when compared to the literature on environmental factors and depression. Much of the evidence pertaining to the relationship between the environment and internalising disorders does not distinguish between anxious and depressive symptoms, or between anxiety and depressive disorders. For this reason the literature of this type that was reviewed in the preceding sections will not be reviewed here again.

3.3.1: Life events and anxiety

Anxiety disorders, including panic disorder and agoraphobia have been shown to be associated with high levels of negative life events preceding onset of the disorder (Finlay-Jones & Brown 1981; Faravelli 1985; Last, Barlow, & O'Brien 1984).

As with the data on depression and environmental factors it is necessary to show that these increased levels of life events are not due to the disorder. This is illustrated in the above studies, all of which considered the period of time *preceding* onset. In addition to this many studies have shown increased levels of stressful life

events in anxious subjects even when only independent events were analysed (eg. Finlay-Jones & Brown 1981, Goodyer, Wright, & Altham 1987, 1988, 1990a, 1990b).

The specificity of loss events to depression is paralleled by a similar specificity to the type of life events that provoke anxiety, namely danger or threat events. Awareness of this has been noted in the literature for many decades. Freud (1959, in Smith & Allred 1989) argued that danger or threat of losing someone who is highly valued leads to anxiety, and that an actual loss of this kind results in depression. Bowlby (1973, 1980) agreed with this distinction, but pointed out that there were many other types of threat that could result in anxiety. Brown and Harris (1978b) found there to be such specificity of life events in their adult female sample. Levels of severe non-loss events (ie. danger) were significantly higher in the anxious and depressed group than in the depressed and borderline anxious group or depressed only groups. Mixed cases were more likely to have reported both loss and non-loss events as compared to the controls. The purely depressed group and the depressed and borderline anxiety group reported significantly more loss events than the depressed and anxious group. More recently in Finlay-Jones and Brown (1981) and in Finlay-Jones (1989) danger was found to be significantly associated with onset of anxiety. Seventy-seven percent of the anxious cases (N = 13) reported a severe danger event in the twelve months preceding onset as compared to 47% of the depressed cases (N = 17) and 12% of the controls (N = 119). Exposure to both severe loss and danger was significantly related to the onset of mixed anxiety-depression. Finally, Last, Barlow, and O'Brien (1984) found the majority of events reported by agoraphobics to be interpersonal conflict and endocrine or physiological events, both of which have large components of threat. However, these events also included elements of loss, and bereaved children have been shown to have elevated levels of anxiety (Kranzler, Shaffer, Wassrman, & Davies 1989). This is likely to be due to the fact that some types of event such as bereavement while being predominantly characterised by loss are also surrounded by circumstances which are threatening. This emphasises the need to rate events for both loss and threat or danger on dimensions, rather than categorising them into one or the other.

3.3.2: Vulnerability factors and anxiety

Having shown the importance of life events and particularly threat to anxiety we can now turn to the types of factors that may act as vulnerability factors for anxiety when in conjunction with a stressor, or that may simply be alternative types of predictor.

3.3.2.1: The social approach

Studies with adults

Two of Brown and Harris' (1978) vulnerability factors have been considered with reference to the onset of an anxiety disorder in adulthood. These are loss of a parent in childhood, and lack of a confiding relationship.

Loss of a parent and more general major losses in childhood have been demonstrated to be associated with anxiety disorders in adulthood (Alnæs & Torgersen (1988, 1989; Kendler, Neale, Kessler, Heath, & Eaves 1992a; Torgersen (1986b). However, Brown and Harris (1993a) found that loss of mother before age 11 did not contribute much further variance to the measure of current anxiety once early adversity (parental indifference, physical and sexual abuse) had been taken into account.

Finlay-Jones (1989) also considered "lack of confiding relationship" as a potential vulnerability factor for anxiety. This variable was not only found not to act as a vulnerability factor for anxiety but was not even a predictor of anxiety. His findings suggest that lack of this type of relationship results specifically in depression.

Thus of the four vulnerability factors for depression from Brown and Harris (1978b), only early loss of parent has been demonstrated to be a potential vulnerability factor for later anxiety.

Studies with children

The literature on vulnerability factors for anxiety in childhood is also somewhat limited, but several potential factors have been investigated. These are lifetime exits, family relationships, poor friendships, lack of achievements, and maternal depression.

Lifetime exits excluding those in the past 12 months were shown to be associated with caseness for anxiety as well as depression in the studies by Goodyer and Altham (1990a, 1990b).

Poor family relationships have been demonstrated to be associated with anxiety disorders when assessed in terms of poor parental attachment (Armsden, McCauley, Greenburg, Burke, & Mitchel 1990), EE (Stubbe, Zahner, Golstein, & Leckman 1993), competitive parenting (Krohne & Hock 1991), and inconsistent parenting (Kohlmann, Scumacher, & Streit 1988).

Friends are another major source of support for children, and as such it has been hypothesised that poor friendships could result in anxiety. This hypothesis has received considerably less attention than that with depression as the outcome. However, the available evidence suggests that poor friendships may be involved in the aetiology of anxiety in children independent of the presence of stressful life events (Goodyer, Wright, & Altham 1989, 1990). Furthermore, the enhancing effect of lack of achievement in the presence of poor friendships reported by Goodyer, Wright and Altham (1990) was as likely to lead to anxiety as depression.

Finally, as with depression, maternal distress, poor confiding in the mother's own relationships and life events were found to have an additive effect on the likelihood of the child becoming anxious (Goodyer, Wright, & Altham 1988). Similarly, when Fendrich, Warner, and Weissman (1990) looked at the associations between various family risk factors, parental depression and depression in the child (N = 220)

they found that if either parent was depressed this was a considerably more powerful predictor of anxiety disorder in the child than any of the family risk factors (odds ratios of between 3.04 and 3.99 when in association with any one of the five family risk factors).

3.3.2.3: The cognitive approach

The common theme in cognitive theories of anxiety is hypervigilance to threat. This is illustrated in Eysenck's (1992) cognitive theory of anxiety. Brown, Harris, and Eales (1993b) suggest but do not test a pathway from early adversity to later anxiety via cognitive predispositions, for example physical abuse leading to a cognitive vulnerability to physical danger. This specificity of cognitive vulnerability and the roles of trait as opposed to state anxiety forms the centre of many of the theories of cognitive mediators to anxiety.

The selective attention to threat stimuli described in Eysenck's Hypervigilance Theory of Anxiety (1992). This hypervigilance to threat stimuli is demonstrated in experiments involving subliminal presentation of threat words and the Stroop colour naming task in which selective attention is paid to threat stimuli by anxious patients. Specificity of trait anxiety to threat stimuli is also emphasised in Endler and Edwards' (1988) Multidimensional Interaction Model of Anxiety. This model is illustrated with evidence from Endler and Okada's (1975, in Endler & Edwards 1988) subjects, who were shown to respond with state anxiety to stress events that interacted with the corresponding trait vulnerability. Female students were found to have increased levels of state anxiety after a physical danger stress or the threat of such a stress (eg. an electric shock) if they showed high levels of trait anxiety on a physical danger dimension. This offers some support for Brown, Harris, and Eales' (1993b) hypothesis.

A similar view is put forward in Beck and Clark's Content-Specificity Theory (1988), which is illustrated with evidence from three types of studies reviewed by Beck and Clark (1988). The first of these show a significant bias in anxious patients to interpret ambiguous situations as threatening. The second type of evidence comes from studies which demonstrate that in dichotic listening tasks, anxious subjects will selectively attend to the fear or threat words in the unattended channel. Finally, specificity of threat subject was also demonstrated in some studies, for example physical threat words were only selectively attended to by subjects with physical worries, and spider-related words were selectively attended to by spider phobics. In addition to this, Beck, Brown, Steer, Eidelson, and Riskind (1987) demonstrated that patients diagnosed with an anxiety disorder scored significantly higher on the measure of anxious cognitions than a group with depressive disorder. This confirmed Beck and Clark's (1988) theory that the cognitions for anxiety were specific to anxiety.

The available evidence appears to support the hypothesis that anxious patients are over sensitive to threat stimuli, especially those that are specifically related to the particular area of fear for that individual. Such oversensitivity may be the result of early experiences, and may act as a mediator in the presence of a stressor to produce anxiety.

Section 3.4: Genotype-Environment Correlations

A recent area of study of the environment has been to consider the impact of genes on measures of the environment (Plomin 1994a). If an environmental measure, (as yet usually the family environment) is treated as a dependent variable in a genetically sensitive design, then estimates of heritability can be calculated, and these have been found to account for a significant proportion of the variance in some measures. This creates a new possibility for the interpretation of the relationship between environmental factors, depression and anxiety. It may be found that some

of this relationship is accounted for by genetic factors, and that measures of the environment are in fact measures of aspects of the individuals' genotype. Features of the environment associated with depression and anxiety which have been considered in a behaviour genetic design are life events, family relationships, friendships, and social support.

3.4.1: Heritability of life events

Wierzbicki (1989) investigated frequency and impact of pleasant and unpleasant events and life experiences using self-report measures completed by 41 adult MZ pairs, and 29 adult same-sex DZ pairs. On all sub-scales the MZs resembled one another more closely than the DZs, and the heritability estimates were significant for frequency of both pleasant and unpleasant events, level of pleasantness and total impact of pleasant events, and number and total impact of life experiences. Had their sample been larger it is likely that all aspects of these measures would have had significant heritability estimates. The heritability estimates for frequency of pleasant and unpleasant events and number of life experiences were 34%, 32%, and 41% respectively. The paper concluded that these results illustrated a genetic influence on frequency of engagement in, and emotional response to mood-related events. It is difficult to clarify whether this is an appropriate conclusion, as the measures were not described in any detail and concepts such as the independence of the events from the individual's behaviour were not measured. However this does give some preliminary evidence for the hypothesis that the heritability of depression and anxiety described earlier may be in part due to the heritability of the life events and experiences associated with these types of symptoms.

Further support for this hypothesis comes from the work of the Swedish Adoption/Twin Study of Ageing (SATSA). Plomin, Lichtenstein, Pedersen, McClearn, and Nesselroade (1990) investigated 399 pairs of older adult twin pairs, both MZ and DZ, reared together and apart. The measure used was the Social

Readjustment Rating Scale (SRRS) (Holmes & Rahe 1967). The correlation between the members of the MZ pairs reared apart gives a direct estimate of genetic influence. For total number of life events this figure was .49, and for number of undesirable life events it was .45. The reared apart MZ correlation for events classified as “controllable” (ie. non-independent) was .54, whereas for “uncontrollable” (ie. independent) events the correlation was .22. This suggests that as one would expect, it is controllable, non-independent events that are most highly heritable. The low DZ correlations suggested dominance rather than additive genetic influences, so the model fitting included estimates of this parameter. Heritability of total number of life events was estimated to be 40% which was a non-additive genetic component. For undesirable events heritability was estimated to be 36%, and this was again a non-additive genetic component. An additive genetic component was required for uncontrollable events, the heritability estimate for these events being 18%, but for the controllable events a non-additive genetic term was required, resulting in a heritability estimate of 43%. These results confirm the findings from the reared apart MZ correlations and give further support to the hypothesis that life events are heritable, particularly those under the control of the individual.

This issue was also considered in a study by Kendler, Neale, Kessler, Heath, and Eaves (1993d). This study of self-reported life events from 2,315 adult female twin pairs found that correlations for number of life events within the monozygotic pairs consistently exceeded the correlations for total number of life events in the dizygotic pairs. When the life events were categorised into “network” events (those relating to members of the subjects social network) and “personal” events (those relating directly to the subject) an interesting contrast emerged. For all three classes of network event (death, illness/injury and crisis) the model of best fit was a CE model, with common environment accounting for between 32% and 45% of the variance. In contrast, for four of the six personal event categories, an AE model provided the best fit, with heritability estimates of between 14% and 39%. Interpersonal events were found to fit a full model with heritability estimated at 18%, and work events were

found to fit a CE model with common environment accounting for 29% of the variance. The authors suggest that any influence of common environment on personal events tended to be influences from enduring family environment, and they conclude that personal events are largely governed by genetic factors rather than common environment.

The only study of the heritability of life events in children and adolescents is that of Thapar and McGuffin (1996 in press). In this study parent-reported life events were obtained for 287 twin pairs (aged 8 to 17 years) from a community sample. Model-fitting was conducted treating the males and females as two groups. For the total life events scores a CE model produced the best fit for both males and females. Parameter estimates were 83% and 76% for c^2 for the males and females respectively. For the total number of independent events a CE model produced the best fit for males with c^2 estimated at 95%, whereas for the females a full ACE model was required with estimates of 15% for h^2 and 76% for c^2 . This suggests that events in children as reported by parents are not strongly influenced by genetic factors. However the total negative impact scores were found to be heritable, with estimates of h^2 of 54% and 16% for the boys and girls respectively. Estimates for c^2 were 31% and 70% respectively. This suggests that while the total number of events, or even the total number of independent events is unlikely to be influenced by genetic factors, the number of negative events is likely to be governed by genetic factors to quite a substantial level. The study also obtained self-reported life-events for the adolescents in the sample ($N = 126$, age-range not given). For these reports, an AE model produced the best fit for total number of events, total number of independent events, and total negative impact. The increased role of genetic factors in the child-reported events may be due to the fact that this is a child-based design, and thus has more power to detect genetic influences on the child-reported data. This issue is discussed further below.

The implications of these results are that genes may be acting as a confounding factor in the analysis of life events and depression or anxiety. Further investigation of this issue using child and adolescent subjects is required.

3.4.2: Heritability of family relationships

The studies estimating the heritability of parent-child interactions and sibling-sibling interaction can be divided into those that study perceived relationships and rely on self-report measures, and those that observe family interactions as a direct measure of family relationships.

3.4.2.1: Perceived family relationships

The first study to consider this issue was that of Rowe (1981). In this study, 89 adolescent twin pairs (mean age 17.3 years) completed self-report measures of their perceptions of their mothers' and fathers' behaviour towards them. The results are given for a scale of parental "acceptance-rejection", and two of parental "control". The monozygotic correlations were significantly higher than the dizygotic correlations for the acceptance-rejection scale suggesting that this measure would require a genetic factor (parameter estimates not given). In contrast the control scales appeared only to require environmental factors due to the similarity of the MZ and DZ correlations. These results held for ratings of both mothers and fathers.

Rowe (1983) replicated these findings with a separate sample of adolescents. Perception of family environment of 416 adolescents was assessed using another self-report measure. The sample included 59 monozygotic twin pairs, 31 dizygotic pairs including 11 of opposite-sex, 52 pairs of same-sex siblings and 66 pairs of opposite-sex siblings. Two second-order factors measuring different aspects of perceived family environment were obtained. These were "acceptance-rejection" and

“restrictiveness-permissiveness”. Acceptance-rejection was found to fit an AE model (parameter estimates not given), whereas the model of best fit for the restrictiveness-permissiveness scale was a CE model. This confirms the role of genetic factors in acceptance-rejection in family relationships, and the role of common environment in control.

Further confirmation of this distinction comes from a study by Plomin, Reiss, Hetherington, and Howe (1994). This paper reports on findings from the Non-shared Environment Adolescent Development project (NEAD) which includes 707 pairs of siblings with a wide range of genetic relatedness due to the inclusion of both never-divorced and step-families, from which twins, full, half and unrelated siblings were recruited. The children (aged 10 to 18) and their parents completed a battery of self-report measures of parent-child interaction and also sibling interaction. The estimates of heritability from this study are numerous due to the unusual design of this study, from which varying comparisons of genetic relatedness were possible, resulting in multiple estimates of heritability. For this reason, individual estimates will not be given, but the range gives an appropriate reflection of the specific results. For the child reported parent-child interaction, positivity, negativity and monitoring all required A terms (estimates of heritability ranging from 25% to 56%), with the exception of maternal negativity for which the estimate of heritability was 23% but this was non-significant. The parent reported measures were more similar to the results from Rowe (1981, 1983). Positivity and negativity had estimates of heritability ranging from 18% to 53%, whereas estimates of heritability of monitoring were very low, ranging from 1% to 13%. For sibling interaction, the estimates of heritability ranged from 10% to 36%, again showing significant involvement of genetic factors in measures of the perceived family environment. One notable feature of the results from this study is that the E terms are exceptionally small, and rarely reach significance. This means that not only has the study achieved a very low level of error of measurement, but that the aetiological factors of these measures of the family environment are almost entirely familial, with non-shared environment playing very little role in the aetiology of family interactions.

It is interesting to note that parental measures of control have been found to have low or non-significant estimates of heritability (Rowe 1981, 1983; Plomin, Reiss, Hetherington, and Howe 1994) whereas child-report of parental control shows a significant influence of heritability (Plomin, Reiss, Hetherington, and Howe 1994). There are three related reasons for these findings. The first is discussed by Lytton (1991), and is the issue of the child's role in aspects of the parent-child relationship. Lytton argues that factors such as warmth are likely to be related more to the child's own characteristics than to the choice of the parent. In contrast, parents are more likely to have a "conscious, purpose-driven programme" for controlling any child's behaviour. Thus this aspect of the parent-child relationship is likely to be more similar for different siblings in one family than other aspects of the relationship such as warmth. This then may account for the low heritability of parent rated control in these studies. The second and related issue of relevance here is that these studies are using a child-based genetic design. This means that the results have more power to detect behavioural differences caused by the child's genotype than behavioural differences caused by the parents genotype which is only inferred in the child-based design. This is because the design rests on the genetic relatedness of the two types of twin, whereas the relatedness of the children to their parents is always 0.5. As such any choice the parent makes over control, due to their own genotype, is only an indirect genetic effect in the children. Therefore a child-based genetic design will have less power to parent-initiated behaviours than those initiated by the child. Thirdly, the child's report of parental control is their own perception of this aspect of their relationship, and this will be influenced by their own characteristics. For this reason the influence of the child's genotype on their perception of the control in the parent-child relationship is likely to be significant even though this influence was not found in the parent-report of this aspect of parenting.

3.4.2.2: Observed family relationships

Much of the work in this area has involved interaction between mothers and their infants and young children. Adoption data from Plomin and his colleagues has revealed genetic influences on various aspects of mother-infant interaction. These include mothers' "naming of objects for her child", total "mother-child interaction" score, and particularly "maternal responsivity/involvement" and "variety in daily stimulation" (see Plomin 1995 for a review). Further adoption data from this team which investigated mothers and children aged 1, 2, and 3 years revealed genetic influences on "maternal affection/attention", and on "maternal intrusiveness" (at 3 years only), whereas no genetic influence was found for the factor "maternal verbal responsiveness".

One study investigating this issue in older children and adolescents is that by O'Connor, Hetherington, Reiss, & Plomin (1995), who analysed data from 10-minute discussions around problem and conflict areas between each of two children aged 10 to 18 years and each of their parents (ie. four pairs per family) from 675 families. Heritability estimates for positivity, negativity and control toward the child were 18%, 24% and 24% respectively for fathers and 18%, 38% and 0% for mothers. Estimates of heritability for positivity and negativity from the children were 64% and 52% respectively for interaction with fathers, and 59% and 48% for interaction with mothers. These estimates are higher from the children because of the child-based genetic design, which, as discussed above, has more power to detect genetic factors that reflect genetically based differences in behaviour of the child rather than those of the parent.

In summary, it appears that some features of family interactions such as monitoring and control may not be influenced by genetic factors and can therefore be interpreted as genuine measures of the environment. However this is not the case for some features of family interaction such as positivity and negativity which appear to be influenced by genetic factors which may therefore be confounding the

relationship between family interactions and outcomes in the child such as depression or anxiety.

3.4.3: Heritability of measures of friendship

Daniels and Plomin's (1985) study of 198 sibling pairs aged 12 to 28 years from adoptive and non-adoptive families investigated within-pair similarity for type of friendship group. The peer group scales were "college" peer group, "delinquent" peer group and "popular" peer group. Genetic factors were found to be involved in the extent to which one sibling was more likely to be a member of a particular group than the other sibling. However, the genetic factors only accounted for 2%, 2%, and 6% of the variance in the peer group scales respectively. This suggests that it is largely environmental factors that are involved in the aetiology of peer group membership, and that as such, measures of friendship may be regarded as fairly pure environmental factors.

The heritability of these peer-group characteristics (college, delinquent and popular) were investigated further in a study of 104 pairs of adult twins aged 18 to 75 years (mean age = 35.24 years) by Baker and Daniels (1990). Retrospectively reported similarity of peer-group characteristics were significantly higher for MZ than DZ twins. This alone is suggestive of genetic influences on peer-group characteristics. Considering both this data and the adoption data described above, the authors found that not only were the MZ pairs consistently more similar for each of the peer-group characteristics than the DZs, but similarly, the biological siblings were consistently more similar than the adoptive siblings. The authors conclude that this measure may be governed by genetic factors more than previously thought. There are three main implications of these conclusions being reached when the twin design was utilised as compared to the adoption data. The first of these is that there may be an influence of non-additive genetic effects (eg. dominance or genotype-environment interactions) on the measures of peer group membership. This type of

influence is more identifiable in the twin design, because the correlation for dominant genetic factors is only 0.25 for DZ pairs, as compared to 1.0 for MZ pairs. In the adoption design there is less difference in the magnitude of the correlation for dominance effects in the different types of sibling (0.25 for biologically related siblings and 0.0 for biologically un-related siblings). Secondly, that this may be a violation of the equal environments assumption. However, the authors argue that the MZ twins who were more similar on these measures were not significantly more similar on the measures of current adult personality. Thus any past experiences of friendship were not significantly related to current personality, and the equal environment assumption appears to have held. Thirdly, the authors suggest that the older age-range of the twins as compared to that of the adoptive and non-adoptive siblings could account for the lowered influence of non-shared environment due to the retrospective nature of the data. These two studies taken together suggest that caution is still required with regard to viewing measures of peer group membership as a pure measure of the environment.

Manke, McGuire, Reiss, Hetherington, and Plomin (1995) utilised 701 same-sex sibling pairs aged 10 to 18 years from the NEAD project to investigate the influence of genotype on quality of best friendships as rated by the adolescents, and type of peer-group as rated by the parents (college orientation, delinquency, and popularity). For the measure of positive interactions with best friends there was an estimate of heritability of 31%, whereas for negative interactions with best friends the variance was almost entirely accounted for by non-shared environment. The models for peer-group membership as reported by each parent all contained significant heritability estimates ranging from 49% to 85%. This shows substantial genetic influence on quality and type of friendships as assessed by self- and parent-report respectively. This further emphasises the need for caution when investigating friendships and peer-group membership as a measure of the environment.

3.4.4: Heritability of social support

Bergeman, Plomin, Pedersen, McClearn, and Nesselroade (1990) investigated the genetic and environmental influences on social support in a sample of 424 pairs of twins aged 50 years and above from SATSA. Within-pair correlations for quantity of supportive relationships were entirely accounted for by “shared” environment (for reared together twins) and “correlated” environment (trait-relevant experiences in the current environment in twins reared together, or those that have been re-united, and selective placement in twins reared apart). In contrast to this, within-pair similarity for perceived support was entirely accounted for by additive genetic factors with an estimated heritability of perceived support of 30%.

Kessler, Kendler, Heath, Neale, and Eaves' (1992) data from 821 female twin pairs found that perceived support from relatives, perceived support from friends and access to a confidant all had significant heritability estimates (28%, 32%, and 50% respectively). The estimates for the perceived support were both of additive genetic factors, whereas heritability of access to a confidant was due to non-additive genetic effects. Within-pair similarity for perceived spouse support was entirely due to the common environment ($c^2 = 24\%$).

In summary, these studies have provided substantial evidence for there being genetic influences on social support. For this reason the relationship between such measures and outcomes such as depression, may be mediated by the same genetic factors. These results suggest that genotype-environment correlations must be considered in the aetiology of outcomes such as depression and anxiety.

Three types of genotype-environment correlation were described by Plomin, DeFries, & Loehlin (1977) who named them passive, reactive and active. A passive genotype-environment correlation occurs when a child is genetically related to his or her parents. The parents provide elements of both the genotype and the environment, therefore the child's genotype is related to the environment. A reactive

or evocative genotype-environment correlation occurs because a child's genotype evokes certain types of responses from others. An active genotype-environment correlation is caused by the child's genotype effecting his or her selection of the environment.

These correlations were further discussed in the context of a developmental model by Scarr & McCartney (1983) and Scarr (1992). The authors argue that the active genotype-environment correlation is the most direct measure of the effects of genotype on the environment because the individual is actively selecting their own environment. In this model it was predicted that gene-environment correlations would largely be of the passive kind during infancy, with a decline during childhood, during which the active type would increase. In this way, the degree of influence of genotype over environment would increase with time, as the active kind took over. The evocative or reactive type would remain relatively constant over time. This model would predict for example that heritability of peer-interaction would be substantial and significant reflecting active choice of peers by the individual. As discussed earlier, some studies have found substantial heritability estimates for various aspects of friendships, so the developmental theory of Scarr and McCartney (1983) and Scarr (1992) has had some support

Specific types of genotype-environment correlations can be investigated in a number of ways. One way is to compare the correlation between environmental measures and outcome in individuals from non-adoptive and adoptive families. This identifies passive genotype-environment correlations. A second approach is to correlate the measured environment of adopted children with the characteristics of their biological parents. This results in a measure of combined passive and evocative genotype-environment correlations. Finally, a multivariate genetic analysis of the correlations between environmental measures and outcome can identify the aggregated genotype-environment correlation of all three types. An analysis of this kind with depression in the adolescent as the outcome variables was conducted by Pike, McGuire, Hetherington, Reiss, and Plomin (1996). The NEAD sample was used and

a multivariate genetic analysis looking at the relationship between parental positivity, negativity and monitoring and adolescent depression was conducted. A genetic factor shared between maternal negativity and adolescent depression was found to account for 10% of the variance in adolescent depression, and 58% of the variance in maternal negativity. This shared genetic factor accounted for approximately 70% of the correlation ($r = 0.33$) between these two measures.

Bergeman, Plomin, Pedersen, and McClearn's (1991) study considered the possibility of there being shared genetic influences on perceived support and on depression. They found that the correlation between their measure of perceived support and the measure of depression was entirely accounted for by a shared genetic factor. This factor accounted for 12% of the variance in perceived support, and 14% of the variance in depression. Sixty-five percent of the correlation between these two measures was calculated to be due to this shared genetic factor. This confirms the above finding that the association between measures of the environment and depression must be interpreted with caution as it looks increasingly likely that this finding is confounded by shared genetic factors that can account for a substantial proportion of the covariance of the two measures.

An extended analysis of this kind is presented in a paper by Kessler, Kendler, Heath, Neale, and Eaves (1992) which examined the shared genetic and environmental influences on various aspects of perceived support and depression in a sample of 821 adult females twin pairs. In this analysis two possible models accounting for the relationship between perceived support and depression are tested. The first of these is the "mediation" model where the influence of the A, C, and E terms that influence support are only influencing depression through the influence of support on depression. In this model the support measure mediates the effects of these three factors on depression. The second model is a "spuriousness" model in which the A, C, and E terms that are predicting support are shared with the measure of depression, as in the two analyses discussed above. The only measure of support which was found to fit the latter model was perceived relative support. Perceived

spouse support, perceived friend support and access to a confidant all fitted the model in which the effects of the A, C, and E, terms that impact on support only impact on depression indirectly through the impact of support on depression. This is an important finding because it suggests that although variation in many measures of the environment appears to be governed by genetic factors, these measures are likely still to be genuine predictors of measured outcome variables. As such, these measures remain valid tools for assessing the aetiology of outcomes such as depression and anxiety. In addition to this, however, it is also clear that the aetiology of variation in environmental measures deserves further attention.

In conclusion it is clear that some environmental factors are strongly influenced by familial factors, including genetic factors, and as such, environmental measures must be regarded within the context of an interactional model.

Chapter 4: Literature Review Part IV

The Aetiology of Depression and Anxiety in Children and Adolescents

Section 4.1: Comorbidity between Depression and Anxiety

The issue of comorbidity is pertinent to the whole field of child psychiatry (see Caron & Rutter 1991 for a review), but for the purposes of this thesis, comorbidity between depression and anxiety will be discussed. Comorbidity occurs when two disorders are present in the same individual and is an area that has only recently begun to be extensively studied. This concept is particularly important when studying the aetiology of depression and anxiety because of the high proportion of cases (adults and children) that show both disorders (eg. Bernstein & Garfinkel 1986; Andersen, Williams, McGee, & Silva 1987; Kovacs 1989; Leckman, Merikangas, Pauls, Prusoff, & Weissman 1983; Leckman, Weissman, Merikangas, Pauls, & Prusoff 1983; Maier, Lichtermann, Minges, Oehrlein, and Franke 1993). The study of one of the conditions without reference to the other produces at best unclear, and quite possibly misleading, results. This is because the aetiological factors for the two disorders may not be the same, and by not discriminating between cases of pure depression, pure anxiety and comorbid depression and anxiety the researcher cannot hope to provide information that is specific to either disorder. Indeed in striving to understand the complex relationship between these two disorders, research in this field has developed a greater understanding of the aetiology of each of them. Thus the discussion of comorbidity between depression and anxiety will involve the consideration of all of the aetiological factors reviewed thus far, and is the culmination of this review.

For there to be true comorbidity the depression and anxiety must both be at disorder level. However, it is also of interest to explore the relationship between depressive and anxious symptoms, which are also found frequently to be correlated (Achenbach, Connors, Quay, Verhulst & Howell 1989; Norvell, Brophy, & Finch, 1985; Ollendick & Yule 1990). In exploring this issue two types of explanation of comorbidity will be considered. The first type regards comorbidity between depression and anxiety simply to be a function of the way the disorders are defined. Specifically there are three ways in which comorbidity can be seen to be artifactual. The first of these is that there is diagnostic overlap between the two types of disorder as in DSM-IV. This means that there will necessarily be symptoms of anxiety in a patient with MD for example, and such associations are not true comorbidity. Associated with this is the fact that self-report measures of depressive symptomatology contain symptoms of anxiety, and vice versa. Secondly, comorbidity may be falsely created by artificial subdivisions of disorder, such that comorbidity is implied simply by the presence of two sub-types of the same disorder. Thirdly, it is possible that anxiety and depression are merely different stages of one disorder.

The second type of explanation endeavours to explain comorbidity between depression and anxiety in terms of the aetiological factors that result in each disorder. There are four explanations of this kind (Caron & Rutter 1991). The first of these is that depression and anxiety have shared risk factors, the second, an extension of this, suggests overlapping risk factors. Thirdly there is the possibility that there is a unique risk factor specific to the comorbid case, and finally, there is the view that one disorder actually leads to the other. This is different from suggesting that the two are alternate manifestations of one disorder because the relationship implied here is causal, i.e. the earlier disorder causes that later disorder.

4.1.1: Comorbidity as artifact

4.1.1.1: Symptom overlap

A mistake that is often made when considering comorbidity is to misinterpret the symptom overlap between depressive and anxiety disorders. For example fatigue, sleep disturbance and irritability are all symptoms of both MD and GAD according to DSM-IV criteria. As Hershberg, Carlson, Cantwell & Strober (1982) state, "Children with diagnosed anxiety and depressive disorders complain of many of the same symptoms." This leads to item overlap between rating scales, which therefore lack discriminant validity and need greater specificity (Brady & Kendall 1992). This problem results in falsely high levels of "comorbidity". Several studies have revealed the considerable similarity of questionnaires relating to depression on the one hand, and anxiety on the other. This rating scale overlap is often misinterpreted. For example Norvell, Brophy & Finch (1985) found a significant relationship between results from the Children's Depression Inventory (CDI) (Kovacs 1981, 1985) the Revised Children's Manifest Anxiety Scale (RCMAS) (Reynolds & Richmond 1978, 1979) and the State-Trait Anxiety Inventory for Children (STAIC) (Spielberger 1973), as completed by 30 hospitalised emotionally disturbed children. This finding was said to show "a significant relationship between anxiety and depression". This is a typical error of interpretation where comorbidity is concerned. What Norvell et al. were seeing was clear evidence of the considerable overlap between questionnaires attempting to assess different disorders. This issue could be clarified by use of pure depression and pure anxiety factors within such questionnaires. If there were subjects who reported high levels on both factors, then this group could be said to be showing comorbid symptoms of depression and anxiety. Another possibility would be to remove any items pertaining to disorders other than the target disorder from self-report measures.

There is one theory of depression and anxiety that may have come up with a solution to this problem of symptom overlap. This is the theory of "negative

affectivity" (Watson & Clark 1984, Kendall & Watson 1989, Clark & Watson 1991). This theory makes use of two concepts. The principal component is that of negative affectivity, which encompasses several aspects of negative affect such as negative mood and cognitions, and also low self-esteem. The second concept is "positive affectivity" which distinguishes between the subsets of depression and anxiety within the overall construct of negative affectivity. Positive affectivity is a quality that is completely missing in sufferers of major depressive disorders, who express high levels of anhedonia (loss of pleasure) whereas anxiety disordered patients have normal levels of positive affectivity. The two types of disorder are also distinguished by the physiological arousal present in cases with an anxiety disorder. Thus the two disorders are seen as separate disorders both of which have this major component negative affectivity.

A twin/family study of 810 individuals considering negative and positive affect by Baker, Ceas, Gatz, and Mellins (1992), found that the variance in negative affect as measured by the Affect Balance Scale was accounted for entirely by an "AE" model with a heritability of 58%, whereas positive affect required a purely environmental "CE" model. Thus familial resemblance for positive affect was entirely due to common environmental factors. These results are very interesting in the light of Watson and Clark's (1984) paper and suggest that data from subjects suffering from pure depression should fit an "AE" model, but data from comorbid or pure anxiety cases should require a full "ACE" model. The evidence reviewed earlier offers some support for this hypothesis.

Ollendick and Yule (1990) also investigated the relationship between depression and anxiety in the light of Watson and Clark's (1984) theory. They obtained a moderately high significant correlation ($r = .64$) between depression and anxiety symptom ratings using the CDI (Kovacs 1981, 1985), and the RCMAS (Reynolds & Richmond 1978, 1979) on 327 British and 336 American children aged between 8 and 10. However, high levels of comorbidity were revealed between social anxiety and depression, not global anxiety. This suggests that in this particular age group

Watson and Clark's (1984) notion of negative affectivity is applicable only to the relationship between social anxiety and depression. It may be that at this age social anxiety and poor self-esteem are the central components of what is shared between depression and anxiety, and it is variables pertaining to these two concepts that tend to cause such high levels of overlap of symptomatology on self-report measures.

Another approach to this problem is to test whether there is only one factor underlying symptoms of depression and anxiety, or whether there are two. Two studies have tested one and two-factor models. Feldman (1993) used confirmatory factor analysis on data from 981 adults collected from four different studies to test whether the correlation between the scores on multiple self-report measures of depression and anxiety was best accounted for by one underlying factor or two correlated underlying factors. The results for the four data sets were mixed, and although they were interpreted as giving support for the one-factor model, there was not sufficient evidence that the two-factor model fitted the data less well. A further study using confirmatory factor analysis to explore the structure of self-reported depressed and anxious symptoms in 273 children aged 8 to 12 years found evidence for two distinct constructs of depression and anxiety (Crowley & Emerson 1996). Ten measured variables were entered into the analysis and both a one-factor and a two-factor model were tested. The data consisted of five sub-scales from the CDI (Kovacs, 1981, 1985), the Reynolds Children's Depression Scale (RCDS) (Reynolds 1989), three subscales from the RCMAS (Reynolds & Richmond, 1978, 1979) and the STAIC-Trait (Spielberger 1973). The fit of the two-factor model was significantly better than that for the one-factor model ($\Delta\chi^2 = 160.5$, $df = 1$, $p < .001$) suggesting that it is possible to identify distinct constructs of depression and anxiety from child-reported data. This study demonstrates that it is possible to distinguish between depression and anxiety in child-reported data even though there is considerable symptom over-lap between the two.

4.1.1.2: Anxiety within depression

Some researchers choose to resolve the issue of overlap by considering anxiety and depression as essentially one disorder, and see the separate classification of depression and anxiety as unnecessary. This position will be considered next.

An example of this is the study by Bernstein and Garfinkel (1986). This study of 26 early adolescent chronic school refusers found very high levels of depressive disorders (69%), and fairly high levels of anxiety disorders (62%) and comorbid depressive and anxiety disorders (50%). Multiple self-report measures of depression and anxiety were used to compare symptomatology in the three groups. Two particular comparisons are of interest here. Firstly, the children and adolescents with anxiety disorder alone reported lower levels of anxiety symptoms on all the measures than the groups with depressive disorder or with mixed anxiety-depression, although some of these differences did not reach significance. The anxiety disordered group also reported lower levels of depressive symptoms than both the pure depressed group and the mixed group. These results suggest that pure anxiety is a milder form of depressive disorder. In addition to this, those patients with severe anxious symptomatology also reported severe depressive symptoms indicating that severe anxiety disorders may be clinically indistinguishable from depressive disorders.

Further evidence for this hypothesis comes from the study of 106 children and adolescents aged 5 to 17 by Strauss, Last, Hersen and Kazdin (1988) using the STAIC (Spielberger 1973), the RCMAS (Reynolds & Richmond 1978, 1979), the Fear Survey Schedule for Children-Revised (FSSC-R) (Ollendick 1983) and the CDI (Kovacs 1981, 1985). As with Bernstein and Garfinkel (1986) they found their comorbid anxiety and depressive disordered group to be more anxious and fearful than the group with a "pure" anxiety disorder. In addition, the anxiety disordered group only scored significantly higher than the psychopathological control (consisting of children with conduct disorder, attention deficit disorder with

hyperactivity, oppositional disorder, and/or adjustment disorder) group on the state scale from the STAIC and not on any of the other measures of anxiety or fear, whereas the comorbid group scored significantly higher than the control group on all the measures used. This strengthens the hypothesis that the pure anxiety group are not expressing symptoms of the severity of those in the anxiety and depressive disordered group in that the only feature of these children's disorders that is significantly different from the psychopathological control group is high levels of current anxiety.

The evidence that anxiety is merely part of depression, and the two disorders are simply subdivisions of one disorder has led many researchers to describe them as one phenomenon. An example of this is Achenbach, Connors, Quay, Verhulst & Howell (1989) who suggest that at the symptom level it is not possible to distinguish between the two. In their research they therefore use the factor "anxious/depressed". A related issue is whether it is truly helpful to classify variations within each of these disorders as separate disorders. For as Caron and Rutter (1991) point out "the apparent overlap between supposedly different disorders may not represent comorbidity as it is usually conceptualised". In particular, an important question to ask at this point is whether subdivisions of depressive and anxiety disorders are appropriate to children and adolescents. The available evidence suggests that the current extensive subdivisions may be unnecessary in this age group. This is illustrated in a study by Last, Hersen, Kazdin, Finkelstein & Strauss (1987), who found that half of their sample of 73 inpatient children with separation anxiety also had overanxious disorder and 95% of this comorbid group also had another anxiety diagnosis. The children with separation anxiety disorders tended to be somewhat younger than those with overanxious disorders, but this could reflect age effects on patterns of manifestation rather than a difference between two distinct disorders. This leads on to the next possibility to be considered, that the various anxiety and depressive disorders could simply be alternate manifestations or stages of one disorder.

4.1.1.3: Stages of one illness

Anxiety pre-dates depression in many cases of adult psychiatric illness (Dealy, Ishiki, Avery, Wilson & Dunner 1981; Dobson 1985; Rohde, Lewinsohn, Seeley 1991; Brown & Harris 1993a) so the two syndromes could therefore be considered as different stages or manifestations of one disorder. For example an individual may suffer from anxiety when an unpleasant event is imminent, later responding to the actual event with depression. This hypothesis is discussed by Bowlby (1973, 1980) who theorised that disrupted attachment bonds set off a process that results at a first stage in separation anxiety disorder (SAD). As the child comes to realise the loss of the attachment figure this disorder progresses into depression. In a more general sense, threat of loss is seen as anxiety provoking, whereas actual loss is described as provoking depression. A particularly clear example of this specificity comes from the study by Finlay-Jones and Brown (1981) discussed earlier. Anxious cases were significantly more likely to report a severe danger event in the twelve months preceding onset as compared to depressed cases and normal controls. In contrast, depressed subjects were significantly more likely to report at least one severe loss in the year preceding onset as compared to the anxious group and the control group. Finally, comorbid cases were significantly more likely to have experienced both a severe loss and a severe danger event in the twelve month period than the depressed group, the anxious group or the controls (60%, 35%, 8%, and 2% respectively). This specificity of loss and threat or danger events provides a theoretical basis for the finding that anxiety pre-dates depression, since threat of loss usually precedes actual loss.

This relationship has also been found in depression and anxiety in children and adolescents. An example of this is a study by Strauss, Lease, Last & Francis (1988) of 23 children (aged 5 to 11) and 32 adolescents (aged 12 to 19) with overanxious disorder (OAD). The authors noted several developmental differences in their samples. Firstly while the younger group tended to show comorbid SAD or attention deficit disorder (ADD) with the OAD, the older group tended to have

comorbid simple phobias and MD alongside their OAD. The older age group was more symptomatic on self-report measures of anxiety, depression and fearfulness, particularly the STAIC (Spielberger 1973) scores, the worry factor from the RCMAS (Reynolds & Richmond 1978, 1979) and the CDI (Kovacs 1981, 1985).

In the light of Bowlby's (1973, 1980) theory Kovacs, Gatsonis, Paulauskas, and Richards (1989) conducted a longitudinal study of 104 children aged 8 to 13 years to investigate the association of anxiety and depressive disorders in this age-group. They found that of the children with depression and a comorbid anxiety disorder, two thirds had developed the anxiety disorder first. Also, in the children with depression, if an anxiety disorder developed it tended to do so between the ages of 9 and 11, and at the latest by the age of 12 years.

Additional evidence for this developmental framework is provided by Hershberg, Carlson, Cantwell, and Strober (1982) who found in a sample of 102 children and adolescents aged 7 to 17 that the anxious group was pure, and younger than the depressed group, which was not pure. Similarly Stavrakaki, Vargo, Boodoosingh & Roberts (1987) reported that in their sample of children aged 6 to 16 with depressive or anxiety disorders the children with both disorders tended to be older than the children with anxiety disorders alone. Stavrakaki et al. concluded that the two should be considered as developmental variations of one syndrome.

The evidence of these three sections suggests that anxiety and depressive disorders could be alternative manifestations of one underlying disorder. The course of the illness and developmental stage of the child are two factors which result in different manifestations of the disorder. We come now to examine the possible aetiological mechanisms by which the comorbidity between depression and anxiety is produced.

4.1.2: Explanations of comorbidity

As outlined earlier, four explanations have been offered for the comorbidity between two disorders (Caron & Rutter 1991). These are that they share all their aetiological factors, that the factors for one overlap with the factors for the other, that the comorbid state has a unique set of aetiological factors, and that one disorder leads to the other. It is clear from the discussion above that anxiety and depression are highly unlikely to share all of their aetiological factors, and there is no evidence to support this hypothesis. For this reason, only the other three positions will be considered below. The evidence for these positions is not reviewed separately for children and adolescents, as the aim of this section was to bring together all the previously reviewed data into a coherent strategy from which to design the current study.

4.1.2.1: Overlapping risk factors

The most logical explanation for the temporal relationship between these two disorders is that they share common aetiological factors, and that alternative manifestations are as a result of specific factors over and above the common factors, for example age or developmental stage. These factors could either be genetic or environmental. Family studies can reveal a familial factor that may be environmental or genetic while twin or adoption designs are needed to identify the relative magnitude of common environmental and genetic factors. In practice, the evidence comes from twin designs, as adoption data is very scarce. Studies of the biological aspects of depression and anxiety can investigate whether there are overlapping brain processes which mediate the effects of any shared genetic factors. Finally, environmental factors are explored by studies of association, and these are considered for potential overlap.

The evidence from family studies reveals substantial shared familiarity of depression and anxiety. For example a study of adults identified that the risk of MD was significantly higher in relatives of subjects with PD than relatives of normal controls (Maier, Lichtermann, Minges, Oehrlein, & Franke 1993). In addition, levels of MD have been found to be higher in the children of adults with an anxiety disorder as well as a depressive disorder as compared to the children of parents with either an anxiety or a depressive disorder alone (Leckman, Weissman, Merikangas, Pauls, & Prusoff 1983; Weissman, Leckman, Merikangas, Gammon, & Prusoff 1984; Biederman, Rosenbaum, Bolduc, Faraone, & Hirshfeld 1991). A study by Rende, Wickramaratne, Warner, and Weissman (1995) found that sibling resemblance for depression was of a very similar magnitude in groups of children whose parents had MD and children of parents who did not have MD. In contrast sibling resemblance for anxiety and for mixed anxiety-depression was considerably higher in the group whose parents had MD. This implies that the effects of the risk from parental depression may be seen in the presence of childhood anxiety rather than depression, and that these two types of disorder must therefore share common aetiological factors. Finally, the relatives of children with SAD or OAD were found not to differ in level or type of affective disorder in their relatives as compared to a group of children with MD (Livingston, Nugent, Rader, & Smith 1985).

However, there does appear to be some specificity of the factors involved in anxiety over and above those that are shared with depression as demonstrated in the following study. In Turner, Biedel, and Costello's (1987) family study, 59 children (aged 7-12 years) of two groups of probands, one with anxiety disorders (N = 14), the other with dysthymia (N = 13), and children of normal controls (N = 16) were interviewed. The children of the anxiety disordered group were 5 times more likely to have received a diagnosis of anxiety disorder than the controls, and twice as likely as the children of the dysthymic group. Of the 7 children of the anxiety disordered group who received a DSM-III diagnosis only one was diagnosed with a depressive disorder, suggesting considerable specificity of the

factors that result in anxiety disorders. Taken with the results above these data imply that while depression and mixed anxiety-depression share some aetiological factors, pure anxiety has a specific set of aetiological factors not involved with depression.

The evidence from twin studies provides more specific results that can distinguish between shared genetic and shared environmental factors for depression and anxiety. Kendler, Heath, Martin and Eaves (1987) used multivariate genetic analysis of anxiety and depression data from 3798 pairs of adult twins to show that genes act largely in an unspecific way, influencing the overall level of psychiatric symptoms. They also found the environmental factors to have specific effects for symptoms of depression, and symptoms of anxiety. Kendler, Neale, Kessler, Heath and Eaves (1992e) went on to report on cases of comorbid clinical major depression (MD) and generalised anxiety disorder (GAD) amongst a sample of 1033 female twins. Genetic factors for MD and GAD were completely shared, but common environment played no role in the aetiology of either disorder. Non-shared environmental experiences resulted in the particular manifestations of MD or GAD. The finding that the genetic factors for these two disorders are entirely shared has subsequently been extended to a sample including males as well as females, and a high proportion of individuals hospitalised for MD (Roy, Neale, Pedersen, Mathe & Kendler 1995).

Mackinnon, Henderson and Andrews (1990) used a similar technique to look at liability (variation in level) of anxiety and depressive symptoms in 462 adult twin pairs. They reached a conclusion that fits well with the Kendler et al. (1987,1992e) data. "Gene action would effectively 'set' an individual's general level of symptoms with life events and other environmental exposures being responsible for variations about this level."

It is interesting to note that as recently as 1988, Hamilton in an authoritative review book of this field (Last & Hersen 1988) pronounced that "Even more to the point, all

investigators agree that the genetic factors for depression are distinct from those for anxiety states." This shows how rapidly knowledge is expanding in this field.

As became clear in the discussion of the phenomenology of depression and anxiety several neurotransmitter functioning abnormalities have been demonstrated in both depression and anxiety, and may thus be mediating the effects of shared genetic factors. For example norepinephrine levels are abnormal in children with stable behavioural inhibition, and in both anxious and depressed children (Kagan, Reznick & Snidman 1987; Rogeness, Javors, Maas, and Macedo 1990). Furthermore, anxiolytics and tricyclic antidepressants work in part by reducing noradrenaline which is found to function abnormally in both depressed and anxious patients (Davison & Neale 1986; Strange 1992; Gray 1998). Tricyclic antidepressants are also thought to effect receptor uptake of serotonin, a neurotransmitter which is found to be abnormal in both depressed and anxious patients. As discussed earlier this had led to researchers to test the use of tricyclic antidepressants in the treatment of anxiety as well as depression, but these studies have not produced consistent results (Gittelman-Klein & Klein 1971; Deltito & Hahn 1993; Ballenger, Carek, Steele, & Cornish-McTighe 1989; Klein, Koplewics, & Kanner 1992; Bernstein, Garfinkel, & Borchardt 1990). These shared physiological features may be mediating the effects of any shared genetic factors.

Having discussed the evidence for shared familial factors, and more specifically for shared genetic factors, the evidence for environmental factors that are associated with both depression and anxiety is now reviewed.

Stressful life events have been found to be predictive of both depression and anxiety in adults (Finlay-Jones & Brown 1981; Faravelli 1985; Last, Barlow, & O'Brien 1984; Paykel et al. 1969; Brown & Harris 1978b; Rodgers 1990; Mackinnon, Henderson, & Andrews 1990) and in children (Garrison, Addy, Jackson, McKeown, & Waller 1992; Goodyer, Wright, & Altham 1988; Goodyer, Cooper, Vize, & Ashby 1993; Tisher, Tonge, & Horne 1994; Sandler, Tein, & West

1994). Specifically loss of a parent appears to be predictive of both depression and anxiety in adulthood (Brown & Harris 1978b; Torgersen 1986; Alnæs & Torgersen 1988, 1989; Kendler, Neale, Kessler, Heath, & Eaves 1992a). These relationships may be mediated by lack of care following loss of parent (Brown & Harris 1993; Brown, Harris, & Eales 1993). Thus loss of parent in childhood is a risk factor shared by both depression and anxiety, and may therefore sometimes account for the comorbidity between the two. It must be noted that this factor specifically relates to loss of parent in childhood, as recent loss remains a specific factor for depression. In addition, lifetime exits excluding those in the last twelve months are predictive of both depression and anxiety in children and adolescents (Goodyer & Altham 1991a).

Quality of attachment and family relationships in families of depressed and anxious children have also been investigated with respect to levels of depression and anxiety in the children. Armsden, McCauley, Greenburg, Burke, and Mitchel (1990) showed that depressed children had poorer attachments to their parents than non-depressed children, and that the additional presence of separation anxiety disorder was also associated with poorer attachments. Several other studies have revealed a relationship between family relationships including measures of expressed emotion and depression and anxiety in the child (eg. Stubbe, Zahner, Golstein, & Leckman 1993; Fendrich, Warner, & Weissman 1990; Krohne & Hock 1991; Kohlmann, Scumacher, & Streit 1988; Tejerina-Allen, Wagner, & Cohen 1994; Schwartz, Dorer, Beardslee, Lavori, & Keller 1990; Asarnow, Goldstein, Tompson, & Guthrie 1993; Barrera & Garrison-Jones 1992).

Poor friendships and lack of recent achievements have also been found to be associated with depression and anxiety in children and adolescents (Goodyer, Wright & Altham 1989, 1990).

In summary, there are both genetic and environmental factors that are involved in the aetiology of both depression and anxiety in adults. Factors such as these

explain the high levels of comorbidity seen between these two types of symptoms and disorders. As Caron & Rutter (1991) point out "variable expression is a well recognised feature of many genetic disorders" and extrapolating from the adult data, it looks increasingly likely that there are shared genetic factors and environmental factors that are causal for both depression and anxiety, and that different manifestations appear in response to developmental stage, different aspects of life events, or other environmental factors.

4.1.2.2: Comorbid syndrome has a specific risk factor

Some researchers while agreeing that depression and anxiety may share some of their risk factors regard comorbid depression and anxiety as a unique syndrome that has specific aetiological factors that are not shared with the other two disorders. Family and genetic research can help clarify this issue. If the family history of pure depressed, pure anxious, and comorbid groups are dissimilar, the comorbid syndrome should be regarded as separate, and the reverse is also true. Also if the family histories of those with comorbid depressive and anxiety disorders are more similar to the family histories of probands with depressive disorder alone or anxiety disorder alone, then the single disorder can be regarded as a precursor to the comorbid state. Genetic research can establish whether risk factors (either environmental or genetic) are shared or different for the two disorders as well as the comorbid condition.

There is some evidence for subjects with mixed anxiety-depression constituting a distinct group from individuals with pure anxiety. A twin study found relatives of individuals with mixed anxiety-depression to be at a higher risk for depression and mixed anxiety-depression but not for pure anxiety (Torgersen 1990a). A study of children and adolescents found that the depressive and anxiety disordered group scored significantly higher than the anxiety disordered group on the STAIC

(Spielberger 1973), the RCMAS (Reynolds & Richmond 1978, 1979) and the FSSC-R (Ollendick 1983) (Strauss, Last, Hersen, & Kazdin 1988).

In contrast to these two studies, another family study by Leckman, Merikangas, Pauls, Prusoff & Weissman (1983) found that relatives of anxiety and depressive disordered probands were at much higher risk for depression, mixed depression-anxiety and pure anxiety than relatives of probands with depressive disorder alone. The authors suggest that comorbid depression-anxiety is aetiologically distinct from pure depression. Also, as described earlier, Kovacs, Gatsonis, Paulauskas, & Richards (1989) found that the children in their study who were comorbid with both a depressive disorder and an anxiety disorder were significantly younger at onset than those with just a depressive disorder. Kovacs et al. suggest that this early onset could be revealing a greater vulnerability in these children. Recovery from the depression seemed to be effected by comorbid anxiety in a variety of ways, depending on whether there was secondary dysthymia and whether the depression itself was primary or not. These two studies imply that comorbid depression and anxiety could be a distinct disorder from depression.

All these studies interpret their findings as evidence for there being a distinct construct of comorbid anxiety-depression. However, some suggest that this condition is distinct from pure anxiety, the that it is distinct from pure depression. No study has found that twins or relatives of probands with mixed anxiety-depression showed significantly higher levels of mixed anxiety-depression specifically. It seems more probable that due to the shared genetic aetiology of these disorder, a mixed anxiety-depression state is often seen, and that this is a more severe variant than either of the pure states, thus carrying with higher risk for relatives. Structural equation modelling analyses need to be conducted so that the impact of shared and specific genetic and environmental factors may be ascertained. There may yet be good evidence for a specific factor relating only to the mixed anxiety-depression syndrome.

4.1.2.3: One disorder leads to the other

There is little data available to support a hypothesis such as this. One study has examined "neurotic behaviour" as a potential vulnerability factors for depression (Rodgers 1990). The measure consisted of various neurotic behaviours such as bed-wetting at age 6, introversion, non-attendance at school, and menstrual pain assessed more than 20 years before the depression was assessed. This composite score was found to be a classic vulnerability factor for depression in that it interacted significantly with recent stressful life events to produce depression. This suggests that anxiety may be related to an increase in risk for depression in later life. Further evidence for this possibility comes from a longitudinal study by Reinherz, Stewart-Berghauer, Pakiz, Frost, Moeykens, and Holmes (1989). Anxiety assessed at age 9 was found to be a risk factor for depression at age 15, accounting for 6.8% of the variance in this measure. However, other types of evidence suggest that the hypothesis that anxiety causes depression does not fully explain the relationship between the two. In particular it is well documented that although anxiety frequently pre-dates depression, it also can post-date depression, and that depression can occur without an anxiety disorder having preceded it (Kovacs, Gatsonis, Paulauskas, & Richards 1989). This longitudinal study of anxiety and depressive disorders in children aged 8 to 18 found that of the children with depression and a comorbid anxiety disorder, although two thirds had developed the anxiety disorder first, one third had not. Also, the anxiety "often persisted after the depression had remitted".

A novel approach was taken to the problem of comorbidity by Neale and Kendler (1995). In this study various models were fitted to cross-sectional data on MD and GAD. Two of the models fitted included terms specific to both MD and GAD and also included a path leading from one measured variable to the other. These two variations of the causal model as well as a number of other models were fitted to the data. The model in which MD caused GAD provided a good fit to the data. In addition to this a model in which there was reciprocal causation also provided a

good fit to the data. This is an interesting approach to the problem and allows one to test causal hypotheses using correlational data. However these results require replication before MD can be regarded as causing GAD, especially as theory and the literature would predict a causal relationship in the other direction.

In conclusion, while there are factors that are involved in the aetiology of both depression and anxiety, there also appear to be factors that are specifically related to anxiety. In order to clarify the relationship between depression and anxiety in children and adolescents twin data is required that can model the various possibilities outlined above.

Section 4.2: Conclusions and Hypotheses

The aim of this literature review was to introduce the issues which led to the design of this study. Therefore in this concluding section the most salient points of this review will be re-iterated and the design issues that they led to discussed. The first point that came through in the review was that depressive and anxious symptoms affect a substantial minority of the child and adolescent population. It is clear that these symptoms can lead to disorders which have been shown to have considerable continuity into adult life. These states can have serious implications for the individual. At the symptom level, depression and anxiety are associated with poor self-esteem and pessimistic attitudes about the self, the world and the futures, which can put the child at a considerable disadvantage compared to his or her non-depressed, non-anxious peers. At the disorder level, depression can lead to as extreme an outcome as suicide, and separation anxiety more often than not results in serious discontinuity in education due to school refusal. For these reasons amongst others it is important to attempt to explain the aetiology of these symptoms, in the hope that greater knowledge of this kind will result in an improvement in the

predicting of children likely to suffer from such symptoms, and a corresponding improvement in the care offered to these children.

A crucial issue in this area is whether it is possible to distinguish between depressive and anxious symptoms. Measures of depression and anxiety in children and adolescents have been demonstrated to be highly correlated, and thus identifying aetiological factors that are shared by both or distinct to one or other is problematic. Although it is unlikely to be possible to distinguish between depression and anxiety in parent-reported data, this may be feasible with self-reported data.

Two main categories of aetiological factors have been explored. The first of these is genetic factors. The adult evidence shows the substantial role that genetic factors play in both depression and panic. In contrast anxiety appears not to be strongly governed by genetic factors. The available evidence suggests that the same factors are also involved in extreme group membership for these types of symptoms. The comorbidity between depressive and anxiety disorders appears to be entirely accounted for by shared genetic factors. Investigations into the biological aspects of depression and anxiety suggest that neurotransmitter functioning may be altered in these individuals, and this may be the expression of the genetic factors involved in the aetiology of these states. The evidence concerning the aetiology of depression and anxiety is more limited for child and adolescent subjects. However, the available data suggests that as in adults genetic factors will be significant for depression, but anxiety symptoms may be more strongly influenced by the common environment. There is no published multivariate genetic analysis of depression and anxiety in children and adolescents.

Studies of association have been reviewed that explored the role of the environment, and it has been found that while some environmental factors may lead either to depression or anxiety, others play a more unique role.

Specifically, in adults, loss events are related to depression, whereas threat events are implicated in anxiety. Furthermore, while loss of a confidant is a vulnerability factor for depression, it has not been found to be associated with anxiety. Some of the environmental factors involved in depression and anxiety in adults have been explored with reference to children and adolescents, but the specificity to depression and anxiety of events characterised by loss and threat or more ongoing situations such as friendship problems has not been considered in this age-range.

This review led to the following specific hypotheses. First, that factor analysis of the items from two self-report questionnaires of depressive and anxious symptoms, completed by children and adolescents would result in purer dimensions of depression and anxiety that were less correlated than the total scale scores. Second, that genetic rather than common environmental factors would be significant in predicting individual differences depression scores, whereas common environmental rather than genetic influences would be central to the aetiology of individual differences in anxiety. Third, that the same factors would account for extreme scores on these dimensions as account for individual differences. Fourth, that shared genetic factors would account for the correlation between depression and anxiety, whereas environmental influences would account for the specific manifestations of the symptomatology. A related hypothesis to be tested was whether one type of symptom caused the other. Fifth, that loss events in the past twelve months would be associated with current depressive symptomatology but not current anxious symptomatology, and that threat or danger events in the past year would be associated with current anxious symptomatology but not current depressive symptoms. Finally, it was hypothesised that ongoing stressful situations such as family relationship problems, academic problems, and friendship problems would be associated with depression and possibly with anxiety. These were the hypotheses that this study set out to address.

Chapter 5: Methodology

Section 5.1: Methodology of Main Study

This study was designed to assess the contribution of genetic and environmental factors to depression and anxiety in childhood and adolescence. For this reason twin pairs were utilised as the subjects. The twins were recruited from the Register for Child Twins held at the start of the study at the Institute of Child Health. The study was a two-stage study in which the children were screened for high or low levels of depressive and anxious symptomatology, and a proportion of the stage 1 sample were visited and a semi-structured interview was conducted to ascertain information relating to life events during the preceding twelve months.

5.1.1: Selection of the sample

There were 748 pairs of twins aged 8 to 16 years on the Register for Child Twins at the start of the study. All of these children and adolescents were sent two self-report questionnaires, the CDI (Kovacs 1981, 1985) and the STAIC (Spielberger 1973), and the parents were sent the Child Behaviour Checklist (CBCL) (Achenbach 1991a, 1991b) (see Appendix 1). The accompanying letter stressed the importance of the twins completing these measures independently, and the parent completing the CBCL about each child independently. Furthermore, it was suggested that for the younger children a parent might need to read the questions out to each child if their reading was not quite developed enough to complete the questionnaire alone. These instruments have been widely used in the field of child psychology and psychiatry. Their reliability and validity is summarised below.

Test-retest reliability for the CDI over a period of a week was found to be .38 for 69 normal children and .87 for 30 emotionally disturbed children (Saylor, Finch, Spirito, & Bennett 1984). Stability over a 3 to 4 week interval for a variety of samples has been estimated at between .43 and .72 (Kovacs 1981, 1985; Fundudis et al. 1991), and over a 6 month period at .80 (Seligman et al. 1984). Split half reliability and Chronbach's alpha coefficients for the CDI of between .57 and .94 have been reported (Kovacs 1981, 1985; Saylor, Finch, Spirito, & Bennett 1984; Seligman et al. 1984). Chronbach's alpha coefficient represents the mean of the correlations between all possible half sets of the items on a scale (Achenbach 1991b). The validity of this measure was demonstrated in a study in which children with diagnosed depression were shown to score significantly more on the CDI (Kovacs 1981, 1985) than children with DD, conduct disorder or any other psychiatric disorder (Moretti, Fine, Haley, & Marriage 1985), and than children with an anxiety disorder (Hodges 1990).

The test-retest reliability of the STAIC-Trait scale is adequate (.65 to .71 over a six-week interval), and the test retest of the state scale is not surprisingly somewhat lower than this (.31 to .47 over a six week interval) (Spielberger 1973). The internal consistency (Chronbach's alpha) of the two scales was calculated to be between .78 and .87 (Spielberger 1973). A study by Perrin and Last (1992) found that in their sample of 213 boys aged 5 to 17 years, the Modified State-Trait Anxiety Inventory for Children (STAICM) (Fox and Houston 1983) (an extended version of the STAIC with added somatic anxiety questions) distinguished anxiety disordered children from controls, but failed to distinguish between anxiety disordered children and those with Attention Deficit Hyperactivity Disorder (ADHD). The weakness of this measure may have been due in part to the inclusion of children as young as five in this study. As discussed above, most self-report measures are designed to be completed by children aged at least 8 years. However, children with an anxiety disorder have been shown to score significantly higher on the STAIC (Spielberger 1973) than children with a depressive disorder (Hodges 1990).

The test-retest reliability over a one week period for the anxious/depressed syndrome on the CBCL was calculated to be .86 (Achenbach 1991b) for a sample of mothers of 72 non-referred children. Stability of scores on this syndrome over a two-year period (from age 6 to age 8) was calculated to be .67 in a sample of children taking part in a longitudinal study including low birthweight and normal birthweight children (Achenbach 1991b). Internal consistency (Chronbach's alpha) for this syndrome ranged from .86 to .88 for girls and boys aged 4 to 18 years (Achenbach 1991b).

The two self-report measures were then used to categorise the twin-pairs into case and control pairs that could then be visited for the second stage of the study. The parent-report measure was not used to select children onto the second stage as the literature suggests that by the age of 8 children are more accurate reporters of their internalising symptoms than their parents (Angold, Weissman, John et al. 1987; Moretti, Fine, Haley, Marriage 1985). Cut-offs of one standard deviation above the mean were used for the CDI and the Trait and State scales of the STAIC. As the two stages of this project ran approximately four months apart over an 18 month period the cut-offs for the CDI and STAIC had to be decided in advance of the completion of stage 1 in order to select families to be invited to take place in the second stage of the study. Thus cut-offs of one standard deviation above the mean were calculated from the available data set ($N = 126$ pairs) and used for recruitment onto the second stage. These were 17 for the CDI, 44 for the STAIC-Trait, and 37 for the STAIC-State. The level of one standard deviation above the mean was chosen because this would allow for the study of children expressing levels of symptomatology well above average, but still within the normal range. Case pairs were defined as pairs in which at least one child scored above the cut-off on at least one of the CDI and the STAIC-Trait. The STAIC-State was not used to identify case pairs because this measures very transient feelings. For a pair to be classified as controls, both members had to score below both of these cut-offs, and in addition to this, they were both required to score below the cut-off on the STAIC-State as well. Thus there was a group in which the pairs were

neither cases or controls, in which the children scored below the cut-offs for the CDI and the STAIC-Trait, but above the cut-off on the STAIC-State. The two self-report measures were also completed at the time of the interview.

5.1.2: Zygosity determination

Zygosity was diagnosed using the "Twin Similarity Questionnaire" (Cohen, Dibble, Grawe & Pollin 1973) (see Appendix 1), The cut-off from the questionnaire for diagnosis of zygosity was chosen after three raters compared photographs with scores on the questionnaires. This cut-off was the same as that recommended as the lower limit for diagnosing twin pairs as definitely MZ by Cohen, Dibble and Grawe (1973).

5.1.3: Assessment of life events and long-term experiences

The interview used to ascertain life events and long-term experiences (LTEs) experienced during the previous twelve months was the Psychosocial Assessment for Childhood Experiences (PACE) (Sandberg et al. 1993; Glen et al. 1993). This interview was based on the principles of the Life Events and Difficulties Schedule (LEDS) (Brown & Harris 1978a) and was constructed specifically to obtain life events and LTEs impacting on children from interview with both the mother and the child. The interview was conducted with each of the twins about themselves, and with the mother about each of the twins. A different interviewer was used to interview each of the twins, but only one (the author) was used to interview the mother about both twins. This was because a single visit was being made on which all the interviews were conducted and having built up a rapport with the mother it worked more productively to retain one interviewer for the whole of the mother interview. The mother interview was re-constructed for use with mothers of twins in that the questions covering

family details that would be identical for each child were re-written into one section that was completed once only, whereas the section containing child centred questions was completed twice, once with reference to one twin and once with reference to the other. The interviews were conducted by the author and another Ph.D. student, both of whom undertook extensive training in the use of the interview with the first author of the interview (Dr. Seija Sandberg).

The events and LTEs collected from the mother and those collected from the child were discussed by the two interviewers involved and combined into one set of data described as the best estimated data. In this data set any events or LTEs which on discussion were thought unlikely to have occurred or unlikely to have occurred in the previous twelve months were excluded.

5.1.4: Rating the life events and long-term experiences

The life events obtained from the child and mother interviews were written up individually by the interviewers and each event was rated on a number of variables. The events were first rated for independence from the behaviour of the child and independence from the behaviour of the rest of the family. An event could be either “probably or definitely independent” of the child or family or “probably or definitely behaviour related”.

Ratings from zero to three were made on 6 variables measuring various aspects of the quality of the life event. These were loss of attachment figure, loss of a valued idea, risk of loss of attachment figure, trauma as a witness, physical jeopardy, and psychological challenge. Of these 6 variables the meaning of two require brief explanation. Loss of a valued idea was applicable to events that resulted in losses of a less tangible kind than the loss of an attachment figure. For example the failure of a school entrance exam and thus the loss of a future possibility would be rated as loss of an idea. Starting to

menstruate would also be rated for loss of an idea, the idea being the "continuity of childhood". Psychological challenge referred to events where the child had to overcome some hurdle, for example taking an exam would be rated on that variable. Two dimensions were created from these variables for the independent events. The first of these was loss, which was made up of loss of an attachment figure and loss of a valued idea. The second dimension was danger and was constructed from the variables risk of loss of attachment figure, physical jeopardy, psychological challenge and trauma as a witness. The term danger is used in order to clarify comparison with Finlay-Jones and Brown's (1981) results, but events rated as danger events in either the current study or that of Finlay-Jones and Brown (1981) are not necessarily implying actual danger to the individual, and may be more easily understood if thought of as threat. Thus for each child total independent loss and total independent danger scores were created.

Four further variables were used to assess the impact of the event on the child. In this methodology negative impact remaining two weeks after the event (long-term negative impact) is also rated on a scale of zero to three. Events which are rated as moderate or high on this variable are said to be severe negative events and it is these events which have been shown to be predictive of depressive disorder in adult women (Brown & Harris 1978b; Finlay-Jones & Brown 1981) and mood disorders in children (Goodyer et al. 1985). For each child the total number of severe independent negative events was calculated, as was the total long-term negative impact score per child for all independent events. In addition to this, the score given for the long-term negative impact variable is approximately reflected in the total of the scores given for the 6 variables mentioned earlier. Thus in this analysis, events which scored 2 or more on either the dimension of loss or that of danger were said to be severe loss and severe danger events. For each child the total number of independent severe loss and independent severe danger events was calculated. In summary therefore the data from the independent events was utilised in 6 ways, total long-term negative impact, total loss, total danger, and number of

severe negative events, number of severe independent loss events and number of severe independent danger events per child. See Appendix 2 for some examples of rated life events and long-term experiences.

Section 5.2: Reliability Study

5.2.1: Methodology

5.2.1.1: Subjects

The subjects were 16 pairs of same sex twins recruited from the Register of Child Twins. All same sex twins aged 8 to 16 who were on the register and lived in London were contacted to ask them to take part in the reliability study. Of these 23 pairs 2 had moved and were untraceable, 4 declined to take part, 3 did not reply, and 13 took part. One other family wrote to say they would take part too late to be involved. In order to recruit 3 more pairs to the reliability study, 8 families in Kent were invited to take part. Of these 2 declined, 3 did not reply and 3 took part in the study. The final 16 pairs consisted of 5 child (8 to 11 years) male pairs, 4 adolescent (12 to 16 years) male pairs, 4 female child pairs and 3 female adolescent pairs.

5.2.1.2: Procedure

Sixteen child-twin pairs and their mothers were interviewed using the PACE (Sandberg et al. 1993). In order to achieve this reliability exercise, within each family visited, one of the child interviews was recorded and rated afterwards by the other interviewer. The mother interview pertaining to this same child was also rated by the interviewer not conducting the interview. Thus the data from each family consisted of two child interviews one of which had been rated by

both interviewers, resulting in three sets of child data. There was also the same combination of data from the mother interviews. After these ratings had been made, 10 of the child data sets and 10 of the mother data sets were re-rated by Dr. Sandberg, in order to achieve validity of the interviewer's ratings. Thus the interviewers' ratings were compared to each other and also to this "gold standard" rating. There was also the best estimated data described earlier. During "best estimation", any events or long-term experiences that seemed after discussion to be unlikely to have taken place during the past 12 months were removed, as were any which were deemed by the raters after discussion not to have reached criteria high enough to be regarded as a genuine event or experience. This process was conducted with ten child-mother pairs, by the two interviewers. These ten best estimated data sets were then re-rated and thereby validated by Dr. Sandberg. All these data sets were then subjected to reliability calculations which are presented in the following section.

The variables included in this reliability exercise are the independence of the event or LTE from the child, and the dimensions of loss, danger and negative impact described in the methodology section.

5.2.2: Results

5.2.2.1: Equality of mother-report for both twins

This study was designed such that the mothers were to be interviewed about their first born twin first, followed by the second born twin. As this interview had never been used with twins before it was important to ascertain whether the mother would report a different number of events and experiences for the first twin she spoke about as compared to the second. In order to answer this question paired t-tests were conducted comparing the mean number of events or experiences reported by

the mother for twin 1 and twin 2. The results of these t-tests are given in Table 5.2.2.1a.

Table 5.2.2.1a: Comparing Mean Levels of Events and LTEs Reported by the Mother for the First and Second Twin

Twin	Data Set	Mean	SD	t	df	p
First	Events	3.38	2.31	1.46	15	ns
Second	Events	2.75	1.92			
First	LTEs	1.69	1.08	0.81	15	ns
Second	LTEs	1.56	1.03			

These results show that there were no significant mean differences in number of events or LTEs reported by the mother for the twin she spoke about first as compared to the one discussed second. As such the process of interviewing the mother about both twins consecutively was not likely to be a source of over- or under-reporting of events or LTEs for either twin.

5.2.2.2: Inter-rater reliability of elicitation

The second question pertaining to the interviewing process itself concerned the eliciting of information from the subjects. Did the two interviewers elicit significantly different numbers of events and long-term experiences? Independent t-tests were conducted comparing mean number of events and LTEs elicited by interviewer 1 (TE) and interviewer 2 (BH).

The results in Table 5.2.2.2a show that there were no significant differences in the mean number of events and LTEs elicited by interviewer 1 and interviewer 2.

Table 5.2.2.2a: Eliciting Events from the Child
Interviewer 1 Compared to Interviewer 2

Interviewer	Data Set	Mean	SD	t	df	p
1	Child-Reported Events	2.88	1.82	0.61	30	ns
2	Child-Reported Events	3.38	2.71			
1	Parent-Reported Events	2.75	1.57	-0.83	30	ns
2	Parent-Reported Events	3.38	2.55			
1	Child-Reported LTEs	1.00	0.89	0.85	30	ns
2	Child-Reported LTEs	0.75	0.78			
1	Parent-Reported LTEs	1.44	0.96	-1.02	30	ns
2	Parent-Reported LTEs	1.81	1.11			

5.2.2.3: Inter-rater reliability of ratings: Rater 1 vs. rater 2

The fundamental question in the analysis of an inter-rater reliability study is how closely do the two raters agree on their ratings of the same information? In order to answer this question all the interviews were taped and rated by the other interviewer. To analyse this data, the ratings requiring a judgement made by rater 1 (TE) were compared with those made by rater 2 (BH). For the independence ratings this was conducted with the event or LTE as the unit of analysis, as only those events and LTEs deemed to be probably or definitely independent of the behaviour of the child were to be analysed in the main study. The independence variable was binary, with one value meaning “probably or definitely independent of the child”, and the other meaning “probably or definitely related to the behaviour of the child”, so a kappa was used to compare the two sets of ratings. These are given in Table 5.2.2.3a.

Table 5.2.2.3a: Independence Ratings for Child and Parent Reported Events and LTEs: Rater 1 Compared to Rater 2

Data Set	Kappa	p
Child Reported Events	0.73	<.001
Child Reported LTEs	0.75	<.01
Parent Reported Events	0.72	<.001
Parent Reported LTEs	1.00	<.001

These kappas are all approaching or greater than 0.75, and as such demonstrate excellent inter-rater reliability of the independence ratings (Fleiss 1981).

For the ratings of long-term negative impact (for events only), negative impact on child (for LTEs only) and the dimensions of loss and danger (for events and LTEs), the analyses were conducted with the child as the unit of analysis. As these variables were continuous, intraclass correlations and paired t-tests were conducted. The intraclass correlations tested for differences in rank between the two sets of data, whereas the t-tests ascertained whether there were differences in the mean level of the scores. The results from these sets of analyses are given in Tables 5.2.2.3b and 5.2.2.3c.

The intraclass correlations of the scores from rater 1 and rater 2 for each child on each of these broad dimensions are very high apart from the dimension of loss in child reported LTEs. This was due partly to very low levels of loss LTEs being reported in the child interview. This was partly because loss more commonly occurs as an event, and partly because the children tended to report events rather than LTEs. So, with a sample of this size, there was very little data on child-reported loss LTEs, thus the variance on this dimension and the reliability for these data was very low. In addition to this there were also problems with the definition of the variable "loss of an idea" which was one of the two variables forming the dimension of loss. For this reason, the two raters clarified the definition of this

variable and visited ten more families. When the total loss and number of high loss scores from the child-reported LTEs from these ten further interviews were calculated, there was 100% agreement between the raters for both variables.

There was only one variable in which there were significant differences in the mean levels of the scores as rated by the two raters, and this was the number of high negative impact LTEs from the parent-reported interviews. This was the only one of 24 t-tests which gave a significant difference between the means at the .05 level, and as such could be regarded as a chance finding. However, in order to clarify that this was the case, the ten further interviews used to check on the reliability of the child reported loss LTEs were also used to check on this variable. The intraclass correlation for number of high negative impact LTEs from parent-report in these ten interviews was .625, and the t-test was non-significant ($t = -.80$, $df = 8$, $p = ns$). This confirms that the significant finding for this variable in the original data set was probably a chance finding.

Table 5.2.2.3b: Inter-rater Reliability of Events, Rater 1 Compared to Rater 2:
Dimensions of Loss, Danger, and Negative Impact

Data Set	Dimension	Intraclass Correlation	t-value	DF	p
CR events	Total Loss	.80	0.29	12	ns
CR events	Total Danger	.82	-0.44	12	ns
CR events	Total Negative Impact	.85	-0.67	12	ns
CR events	No. of High Loss	.63	0.00	12	ns
CR events	No. of High Danger	.66	0.00	12	ns
CR events	No. of High Negative Impact	.90	0.00	14	ns
PR events	Total Loss	.94	0.40	14	ns
PR events	Total Danger	.86	-0.96	14	ns
PR events	Total Negative Impact	.91	-0.76	14	ns
PR events	No. of High Loss	.84	0.32	14	ns
PR events	No. of High Danger	.74	-0.56	14	ns
PR events	No. of High Negative Impact	.79	0.82	14	ns

Note: CR = child-reported; PR = parent-reported

**Table 5.2.2.3c: Inter-rater Reliability of LTEs, Rater 1 Compared to Rater 2:
Dimensions of Loss, Danger, and Negative Impact**

Data Set	Dimension	Intraclass Correlation	t-value	DF	p
CR LTEs	Total Loss	.18	-1.51	8	ns
CR LTEs	Total Danger	.53	1.47	8	ns
CR LTEs	Total Negative Impact	.65	-0.29	8	ns
CR LTEs	No. of High Loss	.20	-1.41	8	ns
CR LTEs	No. of High Danger	.65	2.00	8	ns
CR LTEs	No. of High Negative Impact	.83	-1.00	14	ns
PR LTEs	Total Loss	.80	1.24	13	ns
PR LTEs	Total Danger	.73	1.38	13	ns
PR LTEs	Total Negative Impact	.92	1.00	13	ns
PR LTEs	No. of High Loss	.76	1.00	13	ns
PR LTEs	No. of High Danger	.53	0.37	13	ns
PR LTEs	No. of High Negative Impact	.78	2.65	14	<.05

Note: CR = child-reported; PR = parent-reported

5.2.2.4: Inter-rater reliability of ratings: Raters 1 and 2 vs. rater 3

The next stage was to compare the ratings of the two interviewers with those of Dr. Sandberg (rater 3). The independence ratings were once again analysed using a kappa and show an excellent level of inter-rater reliability.

**Table 5.2.2.4a: Independence Ratings for Child and Parent Reported Events and
LTEs: Raters 1 and 2 Compared to Rater 3**

Data Set	Kappa	p
Child Reported Events	0.82	<.001
Child Reported LTEs	0.93	<.001
Parent Reported Events	1.00	<.001
Parent Reported LTEs	0.82	<.001

The reliability of the dimensions was again calculated with intraclass correlations and paired t-tests. For the child-reported LTEs, the ratings for "number of high danger events" per child were in perfect agreement as can be seen from the intraclass correlation, so a t-test could not be conducted. The results comparing the ratings of rater 1 and 2 with rater 3 for the child-and parent-reported events and LTEs are given in Tables 5.2.2.4b and 5.2.2.4c.

As can be seen from these tables, at this level of analysis the reliability is very high. There was however an overall tendency for raters 1 and 2 to give lower scores than rater 3, and three of these differences reached statistical significance. The three dimensions that showed a significant difference between raters 1 and 2 and rater 3 were "total negative impact" and "number of high negative impact" in the child-reported events and "number of high negative impact" in the parent-reported LTEs.

The unreliability of the negative impact ratings for the child reported events was due to the problems with the variable measuring long-term negative impact. On discussion it became clear that there was a specific misunderstanding between raters 1 and 2 and rater 3. The long-term negative impact rating was defined by rater 3 as being the same as the impact at the time of the event for events where there was a major change in the child's life, for example death of a relative. This was because there was unlikely to be any real change in level of adaptation to the event after a period of only two weeks. However raters 1 and 2 had been dropping the long-term negative impact ratings down at least one point from the short-term impact ratings for almost all events. It was agreed that for events of this nature, where there was a major change in the child's world, the long-term negative rating should be left the same as that for the short-term impact rating.

For similar reasons, raters 1 and 2 had been under-rating the negative impact of LTEs particularly in the parent-reported data, as compared to rater 3. It was decided that although all of these results suggested that the ratings in the current study were likely to be somewhat lower than those made by Dr. Sandberg this

would if anything lower the chances of finding associations with caseness. In addition to this, the most important feature of this reliability exercise was to check that the same events and LTEs were rated as highly negative by all three raters, ie. that the rank was the same. This information is obtained from the intraclass correlations which are all excellent.

Table 5.2.2.4b: Inter-rater Reliability of Events, Raters 1 and 2 Compared to Rater 3: Dimensions of Loss, Danger, and Negative Impact

Data Set	Dimension	Intraclass Correlation	t-value	DF	p
CR Events	Total Loss	.85	-1.31	7	ns
CR Events	Total Danger	.95	-1.16	7	ns
CR Events	Total Negative Impact	.96	-1.87	7	ns
CR Events	No. of High Loss	.79	-1.16	7	ns
CR Events	No. of High Danger	.88	-2.05	7	ns
CR Events	No. of High Negative Impact	.95	-1.50	9	ns
PR Events	Total Loss	.92	-1.26	7	ns
PR Events	Total Danger	.98	-0.55	7	ns
PR Events	Total Negative Impact	.96	-2.97	7	<.05
PR Events	No. of High Loss	.97	1.00	7	ns
PR Events	No. of High Danger	.86	1.00	7	ns
PR Events	No. of High Negative Impact	.95	-2.53	8	<.05

Note: CR = child-reported; PR = parent-reported

Table 5.2.2.4c: Inter-rater Reliability of LTEs Raters 1 and 2 Compared to Rater 3: Dimensions of Loss, Danger, and Negative Impact

Data Set	Dimension	Intraclass Correlation	t-value	DF	p
CR LTEs	Total Loss	.95	-1.00	5	ns
CR LTEs	Total Danger	.90	1.58	5	ns
CR LTEs	Total Negative Impact	.95	-1.00	5	ns
CR LTEs	No. of High Loss	.66	-1.00	5	ns
CR LTEs	No. of High Danger	1.00	N/A	N/A	N/A
CR LTEs	No. of High Negative Impact	.95	-1.00	8	ns
PR LTEs	Total Loss	.74	-1.00	7	ns
PR LTEs	Total Danger	.84	0.00	7	ns
PR LTEs	Total Negative Impact	.97	-1.53	7	ns
PR LTEs	No. of High Loss	.66	-1.00	7	ns
PR LTEs	No. of High Danger	.87	-1.00	7	ns
PR LTEs	No. of High Negative Impact	.91	-1.00	8	<.05

Note: CR = child-reported; PR = parent-reported

5.2.2.5: Inter-rater reliability of best estimated ratings: Raters 1 and 2 vs. rater 3

The last set of data to be analysed was the best estimate data, the amalgamation of the child and parent reported data. It was the best estimated data that was to be analysed in the main study, and as such these ratings are the ones that are most directly relevant. In Table 5.2.2.5a are the kappas comparing the independence ratings from the best estimates done by raters 1 and 2 with those done by rater 3. These kappas are excellent and confirm the high reliability of the independence ratings. The intraclass correlations and paired t-tests for the comparisons between the best estimations done by raters 1 and 2 and by rater 3 are given in two further tables.

Table 5.2.2.5a: Independence Ratings for Best Estimated Events and LTEs:
Raters 1 and 2 Compared to Rater 3

Data Set	Kappa	p
Best Estimated Events	0.86	<.001
Best Estimated LTEs	1.00	<.001

Table 5.2.2.5b: Best Estimated Events - Raters 1 and 2 compared to Rater 3
Dimensions of Loss, Danger, and Negative Impact

	Intraclass Correlation	t-value	DF	p
Total Loss	.81	-0.61	7	ns
Total Danger	.70	0.00	7	ns
Total Negative Impact	.52	-0.53	7	ns
No. of High Loss	.62	-0.55	7	ns
No. of High Danger	.59	-1.00	7	ns
No. of High Negative Impact	.69	-1.00	7	ns

Table 5.2.2.5c: Best Estimated LTEs - Raters 1 and 2 compared to Rater 3
Dimensions of Loss, Danger, and Negative Impact

	Intraclass Correlation	t-value	DF	p
Total Loss	.85	-1.96	9	ns
Total Danger	.97	-0.56	9	ns
Total Negative Impact	.75	-1.46	9	ns
No. of High Loss	.65	-0.56	9	ns
No. of High Danger	.92	1.50	9	ns
No. of High Negative Impact	.78	-2.45	9	ns

These results confirm the reliability of the dimensions and allow for confidence in interpreting the results of the main study.

The final section of this methodology chapter presents a more technical description of the analysis of twin data than that given in Chapter 2.

Section 5.3: Analysis of Twin Data

The use of twins in behaviour genetics research rests on the fact that while identical or monozygotic twins (MZs) share their entire genome, fraternal or dizygotic twins (DZs) share on average only 50% of the genes which are free to vary in humans. These genetic factors account for some of the similarity within pairs of twins. The rest of the within-pair similarity is attributed to common environmental factors. These are by definition any factors which are not additive genetic factors, but which make the twins similar to one another. In other words, at this level of analysis these factors are indistinguishable from genetic dominance or other non-additive genetic effects. Factors within the environment which make twins different from one another are known as non-shared environmental influences.

Thus the variance in the phenotype can be divided into that which is attributable to additive genetic (A), common environmental (C) and non-shared environmental (E) factors as in the equation below.

$$V_p = A^2 + C^2 + E^2$$

The contribution of each of the three factors to the variance in the phenotype is estimated from the within-pair correlations for that phenotype, which can only be accounted for by shared genetic and shared common environmental factors, as in the following equations.

$$r_{MZ} = A^2 + C^2$$

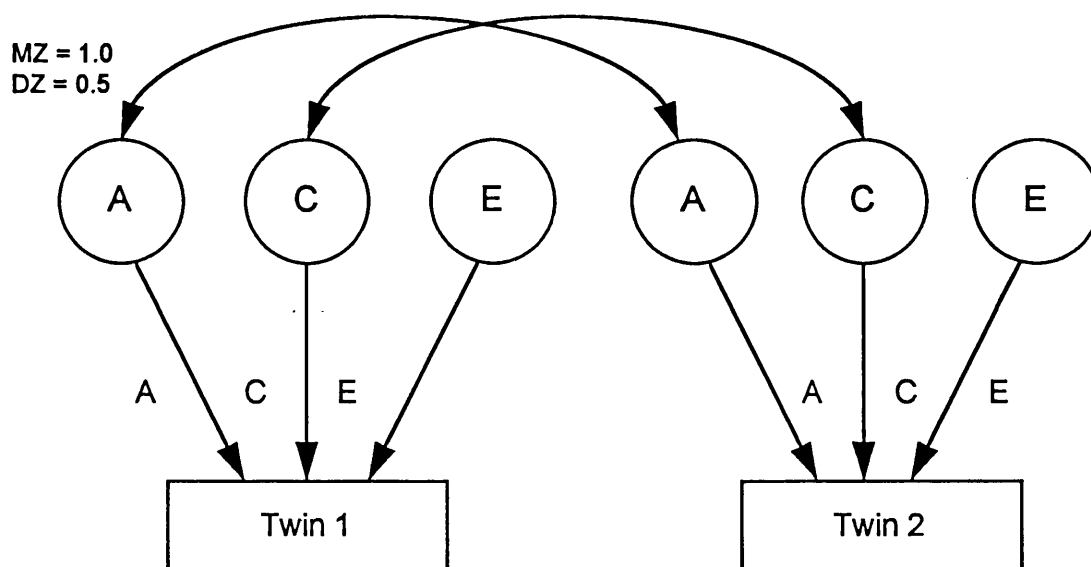
$$r_{DZ} = \frac{1}{2}A^2 + C^2$$

From these simultaneous equations it can be seen that if the MZ and DZ correlations for the phenotype are available, then the A, C, and E terms can be estimated. However, this very simple technique cannot take into account the variance within the data sets and also does not allow one to test whether a certain parameter differs significantly from zero. In order to incorporate these two aspects into the analysis model-fitting is required.

5.3.1: Model-fitting with twin data

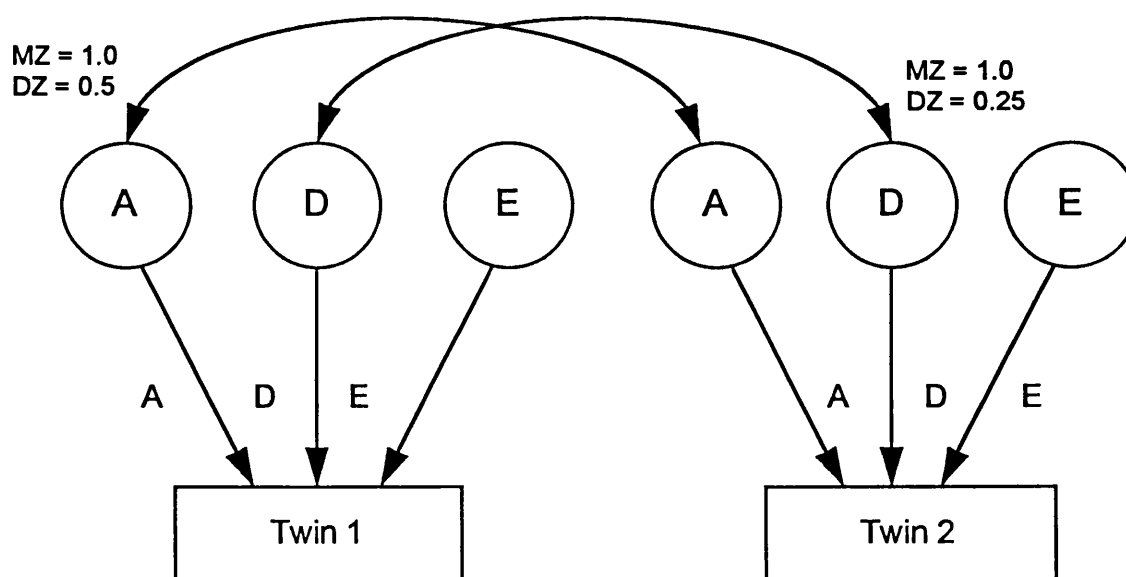
In model-fitting analyses the model is constructed and then tested against the variance-covariance matrices for the MZ and DZ twins. The simple univariate model is given in Figure 5.3.1a.

Figure 5.3.1a: Univariate Genetic Analysis of Twin Data



Chi-square is used to test the fit of the model with the data provided. Parameters that appear not to be significantly contributing to the fit of the model are dropped, and the change in chi-square between the two models is calculated. If the change is not a significant deterioration of fit for the number of degrees of freedom gained, then the parameter can be dropped. According to the rule of parsimony the model of best fit is said to be that which contains the fewest parameters without significant deterioration of fit. In this process of model-fitting, if the C term can be dropped without significantly worsening the fit of the model then genetic dominance (D) can be introduced. The within-pair correlation for dominance for MZ pairs is 1.0, and for DZ pairs it is 0.25, as in Figure 5.3.1b.

Figure 5.3.1b: Univariate Genetic Analysis of Twin Data with Dominance Effects



There are several other measures of fit as well as the chi-square, and the two used in this study are the Comparative Fit Index (CFI) and Akaike's Information Criterion (AIC). The CFI has an upper limit of one, and levels above 0.9 suggest an adequate fit to the data (Dunn, Everitt, & Pickles 1993). The AIC

takes into account not only the goodness of fit of the model, but also the number of parameters being estimated. The model of best fit is that with the lowest value, which should ideally be negative (Williams & Holahan 1994).

Multivariate models can also be fitted to the data in which there are sets of factors that influence variance in just one of the variables, and sets of factors that influence variance in more than one of the variables and also the covariance between these two variables. The three types of multivariate model utilised in the analysis of this data set are the Cholesky decomposition, the general and specific factors model, and the causal model (Neale & Kendler 1995). These are illustrated below, with data from just one of the twin pair being included in the model for reasons of space. The Cholesky decomposition is illustrated in the bivariate case (Figure 5.3.1c), the general and specific factors model in the trivariate case (Figure 5.3.1d), and the causal model in the bivariate case (Figure 5.3.1e).

Figure 5.3.1c: Cholesky Decomposition: Bivariate Model

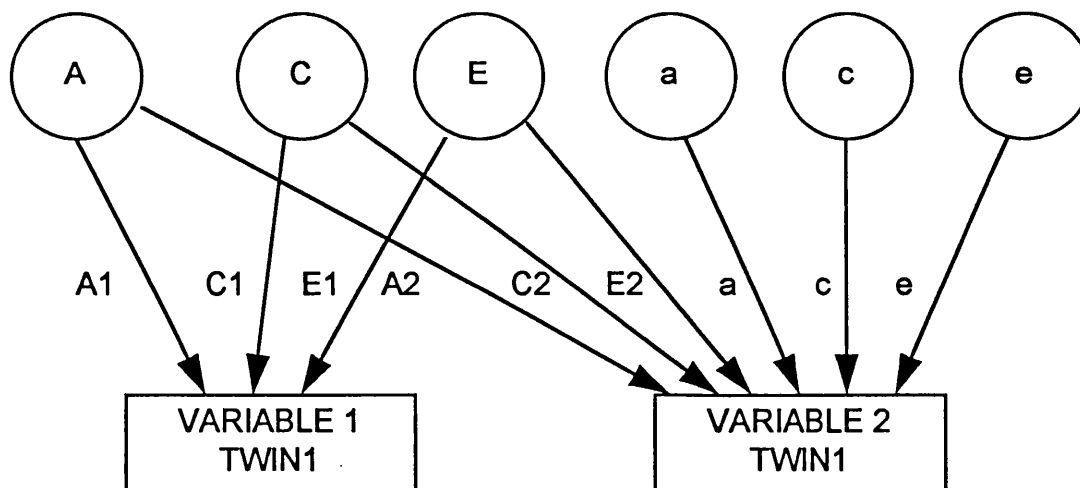


Figure 5.3.1d: General and Specific Factors Model: Trivariate Case

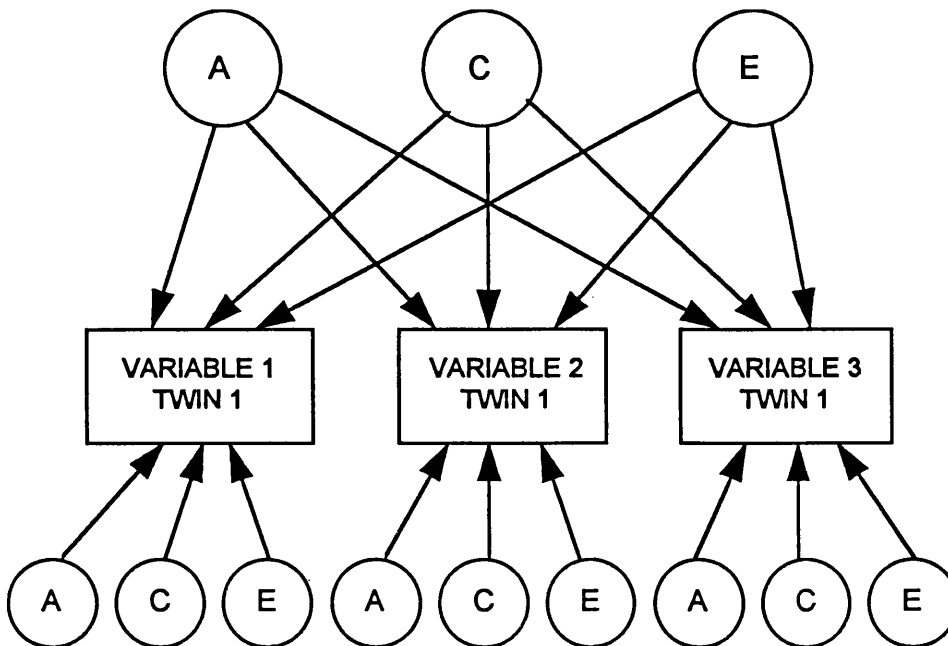
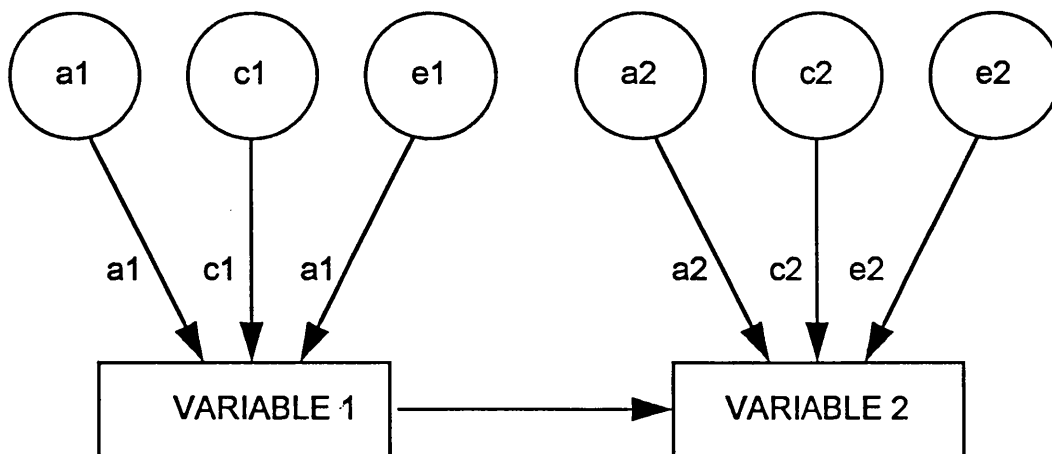


Figure 5.3.1e: Causal Model in which Variable 1 Causes Variable 2



As can be seen from the illustration the Cholesky approach imposes a triangular structure on the data, and confounds the factors accounting for the variance in variable 1 with those accounting for the covariance between variables 1 and 2. The causal model also imposes a particular structure on the

data in that the only way in which the aetiological factors effecting one measured variable can also predict variance in the other is via the causal relationship between the two measured variables. Thus the correlation between the two measured variables is entirely accounted for by the causal pathway between them. This suggests that the model of choice should be the general and specific factors model, which imposes no such structure and has no confounded factors, however in the bivariate case this model is unidentified. This is because although there are 10 data points in a binary variance-covariance matrix resulting in 20 data points when both MZ and DZ pairs are considered, there are many data points within these two matrices which are assumed under the model to be equal. For example, there are four different copies of the covariance between variable 1 and variable 2. Once these copies have been taken account, there are only 9 data points providing unique information (within-child variance of variables 1 and 2 and the covariance between variables 1 and 2, cross-twin covariance of both variables 1 and 2 for MZ and DZ pairs, and finally the cross-twin cross-measure covariance for both MZ and DZ pairs), and thus a Cholesky is only just identifiable and a full general and specific factors model is unidentifiable. For this reason, a general and specific factors model has to be reduced in the bivariate case. This can be done either by removing the C terms from the model leaving only 8 paths to be estimated or by constraining the paths from the shared factors to variables 1 and 2 to be equal which results in only 9 parameters being estimated. In the trivariate case the full general and specific factors model is identifiable.

For each of the final models from the bivariate Cholesky decomposition of the child-reported data the genetic correlation (r_g) was calculated according to the following equation:

$$r_g = \frac{A1 \times A2}{\sqrt{(A2^2 + a^2) \times (A1^2)}}$$

In addition to this, the proportion of the correlation between the two variables accounted for by the shared genetic factor was calculated according to a further equation:

$$\text{proportion of correlation accounted for by the shared genetic factor} = \frac{A1 \times A2}{(A1 \times A2) + (C1 \times C2) + (E1 \times E2)}$$

5.3.2: Group heritability analyses

An alternative method of genetic analysis is to estimate the role of genetic factors to extreme group membership. Probands are selected for being above a certain cut-off on a dimension. The heritability estimate for such a group is called a group heritability (h^2_g). This is estimated using a type of regression first described by DeFries and Fulker and thereafter known as DF regression (DeFries & Fulker 1985, 1988). In this methodology, the data from the twin pairs are all double entered. Pairs are then selected in which at least one twin scores above a certain cut-off, commonly one standard deviation above the mean. These subjects are referred to as the probands. In pairs in which both twins are probands the pair will be selected twice due the double entry, whereas pairs in which only one twin is a proband will only be selected once. Within this reduced sample of twin pairs containing a proband, the co-twins' scores (C) on the measure of interest are predicted using a regression analysis, with the proband's score (P) and the coefficient of genetic relatedness (R) between the twins being the independent variables. For monozygotic twins the coefficient of genetic relatedness is 1.0, for dizygotic twins it is 0.5. The regression equation can be written out as follows:

$$C = B_1P + B_2R + A$$

In this equation B_1 is the regression co-efficient that is a measure of the overall similarity of probands' and co-twins' scores. B_2 is the regression co-efficient that indicates how much of the similarity between co-twins and probands is due to the genetic relatedness of the twins. If the data are transformed prior to the regression analysis (such that each score is expressed as a deviation from the mean of the unselected population and then divided by the difference between the proband and control means) this co-efficient is a direct estimate of h^2_g . Finally, A is the regression constant. The standard errors for the h^2_g term provided by this regression procedure have to be corrected for the double-entered nature of the data (see Stevenson, Pennington, Gilger, DeFries, & Gillis 1993). This correction can be written out as follows:

$$\text{corrected SE} = \text{obtained SE} \times \sqrt{(N_D - K - 1)/(N_S - K - 1)}$$

where N_D is the number of double-entered twin pairs, N_S is the number of single entered twin pairs and K is the number of terms in the equation (2 in this case).

Group common environmentality (c^2_g), can be estimated by subtracting the value of h^2_g from the transformed MZ co-twin mean which gives an upper limit for the total genetic and common environmental influence. The standard errors for the c^2_g estimates were derived using the following formula (personal communication, Lee Thompson), in which SD_{DZ}^2 and SD_{MZ}^2 refer to the squared standard deviations (ie. variances) of the DZ and MZ co-twins' standardised scores respectively, and N_{DZ} and N_{MZ} refer to the number of single-entered DZ and MZ pairs respectively.

$$SE = \sqrt{[(4 \times SD_{DZ}^2)/(N_{DZ}) + (SD_{MZ}^2)/(N_{MZ})]}$$

In the bivariate extension of this type of analysis estimates the proportion of genetic factors that result in extreme scores in one variable that are shared with the factors that result in individual differences in another variable. The probands can be identified on either variable, and if one assumes that the two

variables are both on aetiological continua both methods should produce the same result. However due to the potential for different levels of reliability in different measures, results from choosing the probands on one measure may not be identical to those produced by selecting on the other measure (see Stevenson et al. 1993). There is currently no recognised way in which to estimate group common environmentality in the bivariate case.

Chapter 6: Results

This chapter is in three sections. The first of these presents the prevalence of depressive and anxious symptoms in the current sample, the construction of refined measures of depression and anxiety and the effects of age and sex on these symptom scores. The second section presents the results of the genetic analyses, and the final section presents the results relating to associations between life events, long-term experiences and depressive and anxious symptoms.

Section 6.1: Phenomenology of Depression and Anxiety

6.1.1: Prevalence rates

Sixty-seven percent of the same-sex twin pairs returned the questionnaires (395/589). Of the 194 pairs who did not return the questionnaires, 59 had moved away. This gives a corrected response rate of 75%. The proportion of individual children who scored above the cut-off of 17 on the CDI was 9.2%. The proportion above the cut-off of 37 on the STAIC-Trait was 9.1%. Four percent of the children scored above both of these cut-offs. The correlation between the CDI total score and the STAIC-Trait total score was 0.67. On the CBCL, the proportion of children who scored above the borderline clinical t-score cut-off of 67 was 5.8%, 8.5%, and 2.5% for the anxious/depressed, somatisation and withdrawn syndromes respectively. The proportion of children who scored above the cut-offs on both the STAIC-Trait, and the CDI, and also scored above the borderline cut-off on the anxious/depressed syndrome was 1.1%. The correlations between the anxious/depressed syndrome scores from the CBCL and the CDI and STAIC-Trait scores were .37 and .34 respectively. Agreement between being a case from child report (ie. above the cut-off on either the CDI or the STAIC-Trait) and being a case from parent report (ie. above the borderline clinical cut-off on the CBCL anxious/depressed syndrome) was very poor with a kappa value of 0.23. This finding reflects the typical low

agreement between parents and their children in reporting emotional symptoms.

Of the twin pairs in the first stage (N = 529) 22.3% were cases, 66.5% were controls, 4.3% were neither cases nor controls, and 6.8% had missing data. This latter groups largely consisted of families who returned the twin similarity questionnaire when it was sent, but did not return the CDI, STAIC and CBCL when they were subsequently sent out. Sixty-one case pairs were seen in the second stage, which was 51.7% of the identified case pairs. Twenty-nine control pairs were seen which was 8.2% of the available control sample. Thus there were 90 pairs of twins in the second stage of the study.

The Twin Similarity Questionnaire classified 223 pairs as MZ and 172 pairs as DZ. Of these, 192 were male pairs and 203 were female pairs. There were also 104 opposite sex DZ pairs. The age range was 8 to 16 years, with a mean of 11.61, and standard deviation of 2.82.

6.1.2: Creating refined measures of depression and anxiety

As the CDI and STAIC-Trait correlated so highly with one another, it was decided that a factor analysis should be undertaken using the variables from these two scales, with the aim of producing purer anxiety and depression measures. For this analysis the children were treated as individuals rather than as pairs, such that the factors took into account the data from all the children simultaneously. An oblique rotation with a delta of zero was used which allowed the factors to correlate. Factors with an eigenvalue of 1.00 or more were considered. There were 11 that met this criteria. Ten of these had two or more variables loading at a level of at least 0.40 onto them. The factor names and the variable loadings for the variables which loaded at least at the 0.40 level onto them are given in Table 6.1.2a. One exception given in this table is that the variable "worry about schoolwork" which loads 0.39 onto the schoolwork factor is given in the table as this aided interpretation of the factor.

Table 6.1.2a: Factor Analysis of the CDI and STAIC-Trait

Factor	Variable	Loading
Worry	things bother me	.49
	worry about things happening	.42
	worry about making mistakes	.53
	worry too much	.54
	unimportant thoughts bother me	.45
	worry about school	.49
	worry about things that may happen	.45
	feel troubled	.55
	worry what others think of me	.40
Bad	do not do as told	.67
	get into fights all the time	.60
	do everything wrong	.56
	bad all the time	.71
	bad things are my fault	.47
Sleep	trouble sleeping	.82
	hard to fall asleep	.82
Decisions	cannot make up mind	.71
	trouble deciding what to do	.64
	trouble making up mind	.79
Lonely	don't want to be with people	.62
	never have fun at school	.59
	have no friends	.56
	nothing is fun	.55
Self-esteem	look ugly	.72
	cannot be as good as others	.47
	do not like myself	.51
Schoolwork	doing schoolwork is a problem	.39
	schoolwork is worse than it used to be	.41
	worry about my parents	.49
Sad	feel sad	.51
	feel like crying (CDI)	.61
	feel like crying (STAIC-Trait)	.72
	get upset at home	.61
Physiological Anxiety	heart beats fast	.49
	hands get sweaty	.79
	funny feeling in stomach	.47
Stable	feel alone	.44
	not sure someone loves me	.77
	think about killing self	.49

The factor scores were saved for each child and a second-order analysis was conducted. This resulted in two fairly independent factors, one clearly representing depression, the other clearly representing anxiety. The correlation between these two second-order factors was only 0.27. The factor loadings are given in Table 6.1.2b. The loadings of 0.40 or more are in bold type.

Table 6.1.2b: Second Order Factor Analysis of the CDI and STAIC-Trait Factors

First Order Factor	Factor Loading on Depression	Factor Loading on Anxiety
Bad	.63	-.06
Self-esteem	.59	.07
Lonely	.58	.01
Sad	.41	.38
Stable	.52	-.10
Decisions	.29	.43
Physiological Anxiety	-.36	.79
Schoolwork	-.02	.48
Sleep	.18	.45
Worry	.33	.47

It should be noted that none of the five factors defining the depression second-order factor loaded onto the anxiety second-order factor at a level of 0.40 or more. The converse was also true. Of the 10 factors from the first stage of the analysis, only three loaded by more than 0.20 onto both factors. These three factors were “sad”, “worry” and “decide”. “Sad” loaded onto anxiety at a level of 0.38 and “worry” and “decide” loaded onto the depression factor at a level of 0.33 and 0.29 respectively, suggesting that these symptoms cannot be entirely separated. However, as noted above, the two second-order factors only correlated with one another at a level of 0.27, and thus represent more refined constructs of depression and anxiety than the total scale scores from the CDI and STAIC-Trait.

It was possible that due to inclusion of data from both members of each twin pair these factors were produced because the variables within them were aetiologically linked to one another. For this reason an identical procedure was carried out using only the first member of each pair, and this analysis produced a very similar final outcome to the original analysis. The correlation between the depression factors from the two analyses was .88, between the two anxiety factors was .83, and between the anxiety and depression factors from this second analysis was .21. This suggests that the second-order factors produced by these two analyses are very similar to one another in their content, and thus it is acceptable to use the factor scores created using the whole sample at once.

These factors represent more pure, refined measures of depression and anxiety, and as such are regarded as the more appropriate constructs for future analyses. The cut-off for cases on each of these factors was chosen to be one standard deviation above the mean. Using this cut-off 14.0% and 16.9% respectively of the children and adolescents were defined as depressed and anxious cases. These rates are somewhat higher than those for the cases defined using the cut-offs chosen for the CDI and STAIC-Trait (9.2% and 9.1% respectively) because the children tended to score lower in the whole sample than in the initial sample from which the CDI and STAIC cut-offs were calculated, so the means for the CDI and STAIC-Trait, and therefore of the depression and anxiety factors were lower in this sample than in the initial sample. Of the 84 children who were cases from the cut-off on the CDI, 94.4% were also cases on the depression factor, and these children accounted for 60.9% of all the cases on the depression factor. Considering the two anxiety measures, 81.1% of the children who were above the STAIC-Trait cut-off were rated as cases on the anxiety factor, but these children were only 43.7% of the whole case group for the anxiety factor. The parent-reported anxious-depressed factor from the CBCL correlated with the depression and anxiety factors by .37 and .24 respectively.

A factor analysis of the symptoms from the CBCL was undertaken to try to retrieve separate depression and anxiety factors from the parent-reported data.

At first only those symptoms included in the internalising syndrome (Achenbach 1991b) were entered into this analysis. As with the child-reported data, an oblique rotation was performed with a delta of zero to allow the factors to correlate. For two reasons this analysis did not produce a useful result. Firstly, there were several symptoms of anxiety and depression which were not part of the internalising syndrome and were therefore not being entered into this analysis (for example some of the fear items, and several of the socialisation items). In addition, three central symptoms did not load at a level of 0.4 or more onto any of the factors produced by this analysis ("unhappy, sad, or depressed", "nervous", and "anxious"). For this reason a second analysis was undertaken in which all the items which represented symptoms of either anxiety or depression were entered into the analysis. This analysis was once again conducted using an oblique rotation with a delta of zero. The factors were chosen as those with an eigenvalue of more than one. This resulted in an eight factor solution of which six were interpretable (ie. had two or more variables loading on them at a level of 0.4 or more, and which made conceptual sense). These six factors, and the variables that defined them are given in Table 6.1.2c. Two variables are included that load onto the relevant factor by less than 0.4, because these aided the interpretation of that factor.

These factors are not dissimilar to those created in the factor analysis of the CDI and the STAIC-Trait items. However, when these were saved as variables and subjected to a further factor analysis only one second-order factor was produced. When a two factor solution was forced, the grouping of the factors did not make conceptual sense. As can be seen from Table 6.1.2d the factor named nervous loads onto the second-order factor that otherwise represents depression, thus it was not possible to retrieve pure factors of depression and anxiety. This result is in line with the discussion by Achenbach (1991b) who found that parents were unable to distinguish between depression and anxiety in their children.

Table 6.1.2c: Factor Analysis of the Items Representing Depression and Anxiety from the CBCL

Factor	Variable	Loading
Social Anxiety	Anxious	.378
	Self-conscious	.721
	Shy	.838
Withdrawn	Withdrawn	.592
	Poor peer relationships	.755
	Likes to be alone	.590
	Not liked	.794
Nervous	Bites fingernails	.708
	Nervous	.593
	Twitches	.668
Sleep Anxiety/Fear	Sleep problems	.691
	Fears - general	.446
	Nightmares	.619
	Obsessions	.532
Sad	Unhappy, sad or depressed	.398
	Feels unloved	.731
	Feels persecuted	.655
	Feels worthless	.585
	Lonely	.579
	Cries	.415
Schoolwork	Fears school	.319
	Poor schoolwork	.853
	Poor concentration	.777

Table 6.1.2d: Second Order Factor Analysis of the CBCL Factors

First Order Factor	Factor Loading on Depression	Factor Loading on Anxiety
Nervous	.460	.124
Sad	.632	.110
Schoolwork Problems	.795	.223
Withdrawn	.586	.063
Sleep Anxiety/Fear	.164	.629
Social Anxiety	-.071	.847

6.1.3: Effects of age, sex and SES on prevalence

There were two stages to the analysis of the effects of age and sex on rates of depression and anxiety. The first of these were pairs of independent t-tests comparing the mean scores on each of the factors for boys and girls and for the children and adolescents. The age variable was re-coded into children (8-11 years, N = 254) and adolescents (12-16 years, N = 245) for use in these analyses.

Table 6.1.3a: Comparison of Mean Scores for Depression and Anxiety for Children and Adolescents, Males and Females

Factor	Group	Mean Score	t	df	p
Depression	Children	-0.11	-3.58	987	<.001
	Adolescents	0.11			
Anxiety	Children	0.10	3.12	987	<.005
	Adolescents	-0.10			
Depression	Males	-0.08	-2.46	974.43	<.05
	Females	0.08			
Anxiety	Males	-0.10	-2.93	987	<.005
	Females	0.10			

The non-integer degrees of freedom in this table is the result of correcting for variance differences between the groups. From this table it is clear that there are significant effects of both age and sex on depression and anxiety scores. For the depression factor the females and the adolescents scored higher, whereas for the anxiety factor the children and the females scored higher. Having ascertained that there were significant effects of both age and sex on mean levels of both depressive and anxious symptoms it was now of interest to ascertain whether there were any interaction effects. In order to investigate for possible interaction effects logit analyses were conducted, which calculate the effects of age, sex and their interaction on caseness (defined as a score of more than one standard deviation more than the mean) for each of the factors.

The results of these analyses are presented in Table 6.1.3b and Table 6.1.3c. The full model is not given, as the chi-square for this is necessarily zero.

Table 6.1.3b: Logit Analysis of Sex and Age effects on Depressive Symptoms

Terms Dropped	χ^2	df	p	$\Delta\chi^2$	Δdf	p
agegroup x sex	1.47	1	.225	1.47	1	ns
age-group x sex, age-group	3.99	2	.136	2.52	1	ns
age-group x sex, sex	8.87	2	.012	7.40	1	<.01

These results revealed a main effect of sex on depressive caseness, but no main effect of age-group, and no interaction effect. Looking at the prevalence rates for girls and boys, it was clear that more of the girls were scoring as cases than the boys on this factor (16.9% and 10.8% respectively). From the cross-tabulations of the data it also appeared that the older girls were more likely to rate themselves in such a way that they are classified as cases on this factor, but this did not come out as an interaction effect in the logit analysis. The percentage of cases for depression in the male adolescents, female adolescents, male children, and female children were 10.9%, 20.2%, 10.8%, and 13.5% respectively.

Table 6.1.3c: Logit Analysis of Sex and Age effects on Anxiety Symptoms

Terms Dropped	χ^2	df	p	$\Delta\chi^2$	Δdf	p
agegroup x sex	4.98	1	.026	4.98	1	<.05
age-group x sex, age-group	11.91	2	.006	6.96	1	<.01
age-group x sex, sex	6.62	2	.067	1.64	1	ns

This analysis revealed an interaction of age-group and sex on caseness on the anxiety factor, as well as a main effect of age. From the prevalence rates of the male adolescents, female adolescents, male children, and female children, it was clear that the male adolescents were less commonly reporting symptoms of case level (9.6%, 17.4%, 20.7%, 19.1% respectively).

One final factor that might have been related to rates of caseness on these two factors was SES. In order to test for such an association the SES ratings were re-coded into a binary variable. The two codings referred to fathers' work being manual or non-manual. Cross-tabulations were conducted with this variable and both the anxiety and depression factor caseness variables. Neither of the chi-squares associated with these cross-tabulations were significant ($\chi^2 = 1.91$, $df = 1$, $p = ns$; $\chi^2 = 1.02$, $df = 1$, $p = ns$ respectively).

In summary, there were effects of both age and sex on mean scores for both depression and anxiety. In addition to this there was a main effect of sex on depressive caseness with girls being more likely to score as cases on this factor than boys. Furthermore, there was an interaction effect of age and sex on depressive caseness that did not reach statistical significance, such that the adolescent girls were most likely to report high levels of depressive symptoms. This is in line with previous epidemiological research. The results for the anxiety factor show a main effect of age-group such that the adolescents scored less than the children, and an interaction effect of age and sex on caseness with adolescent boys being less likely to be rated as cases on this factor. SES was not associated with caseness on either of these factors.

Section 6.2: Genetic Analyses of Depression and Anxiety

In this section seven sets of analysis were undertaken. Firstly, univariate genetic analyses were conducted to estimate the contribution of additive genetic, common environment and non-shared environment factors to depression and anxiety scores across the full range of scores. Following this, bivariate genetic analyses are presented which reveal shared aetiological factors predictive of individual differences in both depression and anxiety as reported by children. In order to investigate further the relationship between depressive and anxious symptoms, models in which one type of symptom

predicts variance the other were fitted to the data. Third, having considered the heritability of depression and anxiety across the full range of scores, group heritability analyses were conducted to ascertain the role of genetic and environmental factors on extreme scores. The fourth analysis presented is the bivariate group heritability analyses which estimated the contribution of shared genetic factors to extreme group membership for depression and the mean score for an unselected group on anxiety and vice versa. The fifth analysis was a multivariate genetic model fitted to the child- and parent-reported data simultaneously. Following this are two sections looking at age and sex effects on the child-reported factors. These sections report on the univariate and bivariate analyses. In order to distinguish between aetiological factors and the factors of depression and anxiety identified in the previous section, these latter constructs will be referred to as dimensions.

6.2.1: Univariate genetic analyses

The genetic analyses were conducted using the structural equation modelling programme EQS. The parameter estimates for the full model and for the AE and CE models are given below. Where the C term could be dropped from the model without a significant decrement in fit, an ADE model was tested. Two sets of data are presented here, the child reported data and the parent-reported data.

6.2.1.1: Child reported data

For the child reported data, the refined depression and anxiety dimensions and also the CDI and STAIC-Trait total scores were analysed. This was because although the dimensions were regarded as the more satisfactory measures, which would be used in all further analyses, for the purposes of comparison with other available data it was useful to view the estimates for the original scales. Also, the comparisons between the models for the dimensions and for

the total scores showed the advantages of using more refined dimensions of depression and anxiety. The STAIC-State scores were not analysed in this way because this specifically measures transient emotions which are unlikely to have a consistent aetiology.

The most parsimonious and best-fitting model for the depression dimension was the AE model, whereas for the anxiety dimension it was the CE model. An ADE model was tested for the depression dimension, but this did not converge.

Table 6.2.1.1a: Univariate Genetic Analysis of Depression Dimension

	A ²	C ²	E ²	χ^2	df	p	CFI	AIC	$\Delta\chi^2$	Δdf	p
ACE	.41	.11	.48	2.65	3	.45	1.000	-3.347			
AE	.54	---	.46	3.20	4	.53	1.000	-4.801	0.55	1	ns
CE	---	.45	.55	9.85	4	.04	0.935	1.848	7.20	1	<.01

Table 6.2.1.1b: Univariate Genetic Analysis of Anxiety Dimension

	A ²	C ²	E ²	χ^2	df	p	CFI	AIC	$\Delta\chi^2$	Δdf	p
ACE	.10	.36	.54	3.51	3	.32	0.994	-2.486			
AE	.49	---	.51	10.40	4	.03	0.921	2.400	6.89	1	<.01
CE	---	.44	.56	3.90	4	.42	1.000	-4.105	0.41	1	ns

The results for the CDI and STAIC-Trait total scores are shown in Tables 6.2.1.1c and Table 6.2.1.1d. For the CDI, an ADE model also did not converge.

Table 6.2.1.1c: Univariate Genetic Analysis of CDI total score

	A ²	C ²	E ²	χ^2	df	p	CFI	AIC	$\Delta\chi^2$	Δdf	p
ACE	.48	.10	.42	0.92	3	.82	1.000	-5.077			
AE	.59	---	.41	1.49	4	.83	1.000	-6.506	.57	1	ns
CE	---	.47	.53	11.98	4	.02	0.926	3.983	11.06	1	<.001

Table 6.2.1.1d: Univariate Genetic Analysis of STAIC-TRAIT total score

	A ²	C ²	E ²	χ^2	df	p	CFI	AIC	$\Delta\chi^2$	Δdf	p
ACE	.14	.35	.51	0.68	3	.88	1.000	-5.324			
AE	.51	---	.49	7.19	4	.13	0.964	-0.084	6.51	1	<.02
CE	---	.45	.55	1.54	4	.82	1.000	-6.465	0.86	1	ns

As with the depression dimension, the model of best fit for the CDI score was the AE model, and as for the anxiety dimension, the model of STAIC-Trait was the CE model. This suggests that at the level of univariate genetic analyses there was little to be gained from refining the constructs of depression and anxiety. In both sets of analyses the non-significant term (C for depression and CDI scores and A for anxiety and STAIC-Trait scores) accounted for approximately 10% of the variance in individual differences.

The significant parameters in these univariate analyses are the same as those in the previously published child data, given in Table 6.2.1.1e.

Table 6.2.1.1e: Univariate Genetic Analyses of Depression and Anxiety in Children and Adolescents

Authors	Age-range	Sample	Measure	Individual parameters
Rende et al. 1993	9 - 18	707	CDI	$a^2 = .34$
		sibling and twin pairs	depression	$c^2 = .04$
Thapar & McGuffin 1994	11-16	100	MFQ	$a^2 = .70$
		twin pairs	depression	$c^2 = .00$
Thapar & McGuffin 1995	11-16	126	RCMAS	$a^2 = .00$
		twin pairs	anxiety	$c^2 = .55$

In conclusion, the data currently available including that of the present study suggests moderate to high heritability of child-reported depressive symptoms but little or no heritability of child-reported anxious symptoms.

6.2.1.2: Parent reported data

The parent-reported data consisted of the anxious/depressed syndrome scores from the CBCL. The univariate genetic analyses of the t-scores from this scale are given in Table 6.2.1.2a.

Table 6.2.1.2a: Univariate Genetic Analyses of
CBCL Anxiety/Depression Syndrome

	A ²	C ²	E ²	χ^2	df	p	CFI	AIC	$\Delta\chi^2$	Δdf	p
ACE	.49	.05	.46	4.44	3	.23	0.984	-1.561			
AE	.54	---	.46	4.50	4	.34	0.995	-3.197	0.06	1	ns
CE	---	.44	.56	14.13	4	.01	0.890	6.133	10.31	1	<.01

The model of best fit for the parent reported anxiety/depression syndrome was an AE model. Once again, an ADE model was fitted to the data, but this did not converge. This comparability with the models for the child-reported depression dimension, and the CDI total score suggests that the parent-report may be picking up more of the symptoms associated with child-reported depression than those associated with child-reported anxiety. This hypothesis was supported by the finding that the child-reported depression dimension correlated more highly than the child-reported anxiety dimension with the parent-reported anxious/depressed syndrome ($r = .37$ and $r = .24$ respectively).

It should be noted that there were no differences in variance between the MZ and DZ pairs for any of these variables, so sibling interaction models were not fitted to the data.

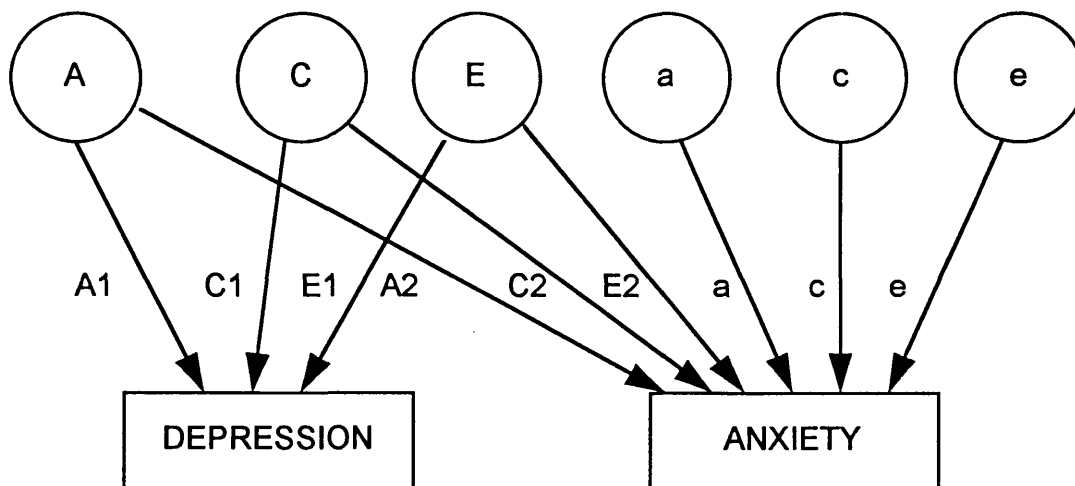
6.2.2: Multivariate genetic analyses of child-reported depression and anxiety

The next stage of the analysis was to conduct a multivariate genetic analysis of the depression and anxiety dimensions to identify factors that were shared between depression and anxiety and those that were specific to one or other state. As discussed earlier, in the bivariate case it is not possible to analyse a full shared and specific factors model, as this is under-identified. It was clear from the univariate results that to conduct this analysis without C terms was a nonsensical solution to the problem in this instance. Constraining the paths from the shared factors to the measured variables to be equal was a realistic possibility for these data, but this model may not always be that informative due to this constraint. Therefore as a first stage, a Cholesky decomposition was chosen as the appropriate analysis. This required an a priori decision as to whether it was the depression or the anxiety dimension that was to be governed by a set of specific factors over and above those that were shared with the other variable. As discussed in the literature review the available evidence suggests that in individuals and in families, where there is anxiety there is also likely to be depression, but that where there is depression there may not be anxiety. This can be interpreted in two ways.

Firstly, anxiety can be seen as sharing many factors with depression, but having some specific factors that are not shared with depression and that result in the situation of anxiety alone. An alternative explanation is to see depression as the more extreme state. If this were so, one would expect anxiety to accompany depression, it being a milder form of the same state, but one would also expect anxiety to occur alone, when those factors that are required to push the individual over the threshold for depression are not present. As this background can leave the reader unclear as to which state is more likely to require specific factors, Cholesky decompositions of both alternative possibilities were conducted. However, it should be noted that the second of the two arguments was regarded as the less valid as it makes assumptions about the relationship between depression and anxiety that may not be

accurate. For this reason the initial model was chosen to be that in which the specific factors were predicting anxiety, as illustrated in Figure 6.2.2a below. The variance-covariance matrices were fitted to the model, but as covariances are not readily interpretable the correlation matrices for the MZ and DZ twins are given in Table 6.2.2a. The model was fitted to the data for the depression and anxiety dimensions first, and this was then followed by an analysis using the total scores from the CDI and the STAIC-Trait. For each of the final models the genetic correlation (r_g) was calculated.

Figure 6.2.2a: Full Model for the Bivariate Genetic Analysis of the Depression and Anxiety Dimensions



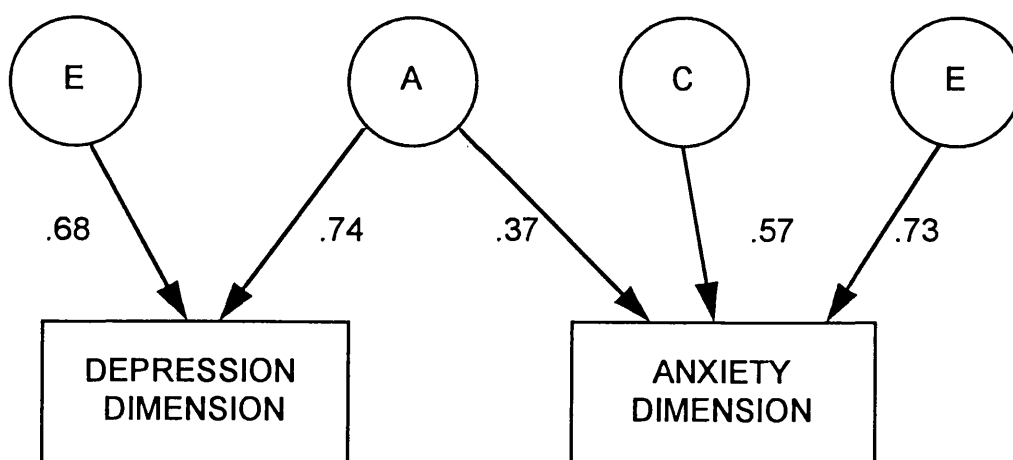
The full model did not converge. The correlation matrices suggested that the depression dimension did not require a C term so the path from the shared C term to depression was dropped. This did not converge either. Following this, the specific A term for anxiety was removed, but this resulted in linear dependency error messages which suggested that anxiety did not require both C terms, so the path from what had been the shared C term to anxiety was dropped. This model converged with a chi-square of 9.75 based on 14 degrees of freedom. The anxiety dimension did not require the path from the shared E term ($t = 0.87$, ns) so this was also dropped without a significant deterioration of fit ($\Delta\chi^2 = 0.78$, $\Delta df = 1$, $p = ns$). The final model with the parameter estimates and the fit of the model is given in Figure 6.2.2b.

Table 6.2.2a: Correlation matrices for Depression and Anxiety Dimensions, and for CDI and STAIC-Trait

Depression and Anxiety Dimensions						CDI and STAIC-Trait Total Scores				
Group	Variable	DT1	AT1	DT2	AT2	Variable	CT1	ST1	CT2	ST2
MZ	DT1	1.00				CT1	1.00			
	AT1	.25	1.00			ST1	.63	1.00		
	DT2	.54	.24	1.00		CT2	.57	.41	1.00	
	AT2	.20	.45	.22	1.00	ST2	.43	.47	.70	1.00
DZ	DT1	1.00				CT1	1.00			
	AT1	.35	1.00			ST1	.66	1.00		
	DT2	.28	.20	1.00		CT2	.34	.31	1.00	
	AT2	.16	.43	.35	1.00	ST2	.27	.42	.73	1.00

D = Depression score; A= Anxiety score; C = CDI score; S = STAIC-Trait;
T1 = Twin 1; T2 = Twin 2.

Figure 6.2.2b: Final Model from the Bivariate Genetic Analysis of the Depression and Anxiety Dimensions



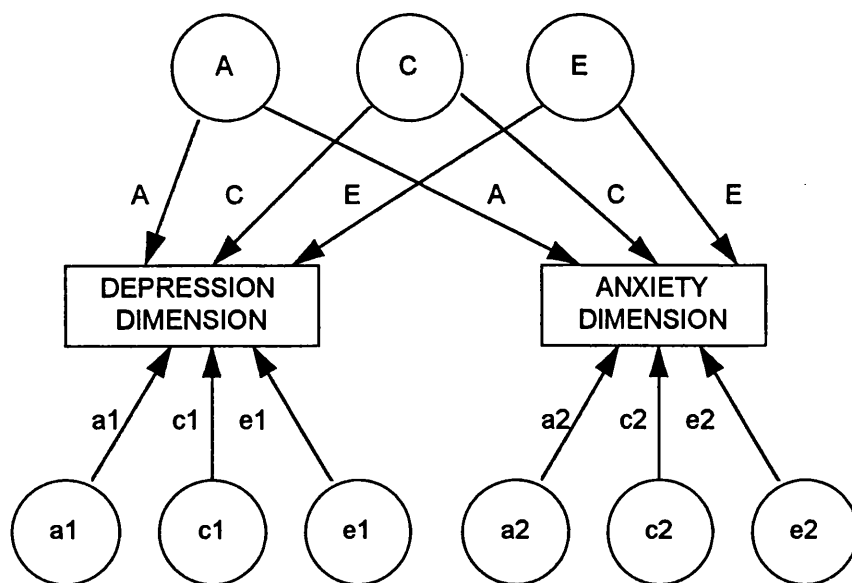
$\chi^2 = 10.53$, $df = 15$, $p = 0.79$, $AIC = -19.47$, $CFI = 1.000$

A second Cholesky decomposition in which the specific factors loaded onto depression rather than anxiety resulted in an identical final model. The specific A and C terms could be dropped without the model deteriorating at all. Thus, whichever original model was used, the final outcome was the same. The genetic correlation between depression and anxiety was 1.0 as there was no specific genetic factor in the model. Moreover, the correlation between depression and anxiety was entirely accounted for by this shared genetic factor. In addition to this shared genetic factor, the variance in anxiety required a further specific common environment factor. Furthermore, both variables required specific non-shared environment factors. This confirms the first of the two interpretations of the previous studies, and suggests that while depression and anxiety share some factors, anxiety requires factors additional to these, that are not shared with depression. This explains the common finding that anxiety can occur without concurrent depression, and without increased risk of depression in the relatives.

The results of these multivariate genetic analyses extend to children the findings in adult women of Kendler et al. (1987, 1992e) in showing that it is a shared genetic factor which entirely accounts for the co-occurrence of depression and anxiety. In order to validate the genetic factor as the true factor accounting for the covariance between depression and anxiety (rather than a shared common environment factor), a constrained general and specific factors model was fitted to the data. The full model is given in Figure 6.2.2c.

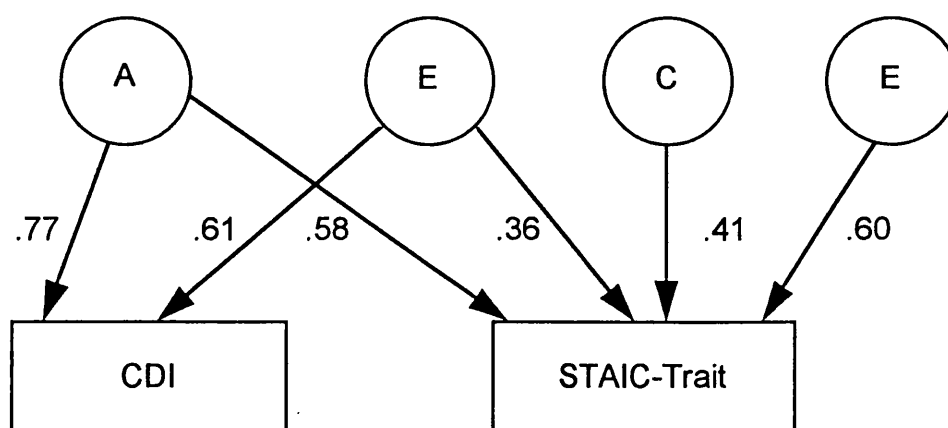
It was found that the specific A term for anxiety and the specific C term for depression had to be dropped for the model to converge. The solution revealed that the t value for the paths from the shared C term were only 1.31, and thus this factor was dropped from the model. The change in chi-square between these two models was 0.43 with a change in degrees of freedom of 1. Thus, the shared C term was not a significant factor in the aetiology of depression and anxiety. In addition to this, the shared specific environment term was also not required by the model. These findings confirm the earlier conclusion that it is shared genetic factors which account for the correlation between depression and anxiety.

Figure 6.2.2c: General and Specific Factors Model for Depression and Anxiety



A Cholesky decomposition of the child data using CDI and STAIC-Trait total scores (see Table 6.2.2a for correlation matrices) produced very similar results except that the shared specific environment factor could not be dropped from either variable. The parameter estimates and fit of the final model are given in Figure 6.2.2d.

Figure 6.2.2d: Final Model from the Bivariate Genetic Analysis of the CDI and STAIC-Trait



$$\chi^2 = 7.69, df = 14, p = 0.90, AIC = -20.31, CFI = 1.000$$

The major difference between the model for the factor scores and this one is that anxiety in this model is sharing the genetic factor with depression to a greater extent. As there is again no specific genetic factor, the genetic correlation is also 1.0, however only 67% of the correlation between the CDI and the STAIC-Trait is accounted for by this shared genetic factor $((.77 \times .58)/(.77 \times .58) + (.61 \times .36))$ as opposed to 100% of the correlation between the depression and anxiety dimension scores. This increased overlap in the factors predicting the CDI and the STAIC-Trait scores is due to the contamination of the STAIC-Trait scores by symptoms of depression and of the CDI scores by symptoms of anxiety. Thus it can be seen from this analysis that the shared aetiology of depressive and anxious symptomatology is more clearly revealed if the refined dimension scores are used. However, whichever set of data is considered, one thing remains constant. Genetic factors account for most, if not all of the correlation between self-reported depression and anxiety scores in children and adolescents.

The final approach to the bivariate model-fitting was to fit causal models to the data (Neale & Kendler 1995). Two models were tested. In the first model individual differences in anxiety accounted for variance in individual differences in depression (ie. anxiety caused depression) (AD). This model is illustrated in Figure 6.2.2e. The second model was the converse of this model, with depression predicting anxiety scores (DA). The fit of the final models is given in Table 6.2.2b. The C term specific to depression and the A term specific to anxiety were not needed in either of the final models and are therefore not presented in the table.

Figure 6.2.2e: Causal Model in which Anxiety Causes Depression

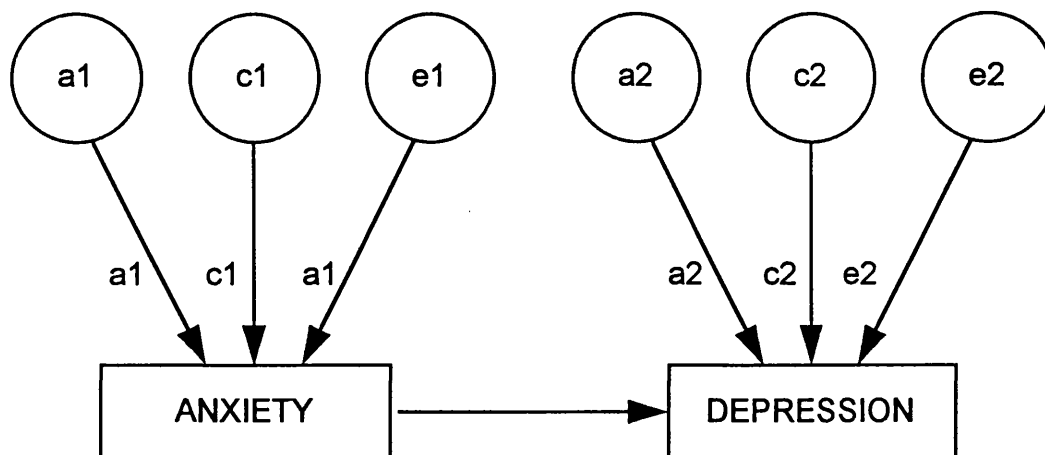


Table 6.2.2b: Final Solutions from Causal Models

Model	Depression		Anxiety		A→D	D→A	χ^2	df	p	AIC	CFI
	a_1^2	e_1^2	c_2^2	e_2^2							
AD	.44	.50	.44	.56	.06	---	23.98	15	.07	-6.12	0.960
DA	.53	.47	.37	.57	---	.06	21.10	15	.13	-8.90	0.973

Note: AD = Anxiety causes depression; DA = Depression causes anxiety.

As can be seen from the AIC values in the table above, the model in which depression accounts for variance in anxiety fitted the data slightly better than the model in which anxiety accounts for variance in depression. This is counter to what one would expect given the temporal relationship commonly seen between these two types of symptom, but the difference in fit is not great, and the interpretation of this finding must therefore be cautious. In comparing the fit of these models to that produced by the Cholesky decomposition of these two variables ($\chi^2 = 10.53$, $df = 15$, $p = 0.79$, $AIC = -19.47$, $CFI = 1.000$) it is clear that the causal models do not explain the data as well as the final model from the Cholesky which therefore remains the model of best fit for these data.

6.2.3: Group heritability analyses

Another aspect of the stage 1 data that warranted investigation was the heritability of extreme group membership. In this data set this refers to those who scored more than one standard deviation above the mean on each of the measures, in order that the figures can be compared across the measures.

In the table below are the estimates of h^2_g and c^2_g for the total scores from the CDI and the STAIC-Trait, for the depression and anxiety dimensions, and for the anxious/depressed syndrome from the CBCL. The number of double entered MZ and DZ proband pairs is also given. The standard errors for the h^2_g estimates have been corrected to take into account the double entered nature of the data.

Table 6.2.3a: Group Heritability Estimates for the Stage 1 Data

Measure	N (MZ)	N (DZ)	h^2_g	SE	c^2_g	SE
Depression Dimension	58	45	.46	.26	.03	.40
Anxiety Dimension	75	57	.01	.23	.40	.30
CDI Total Score	65	54	.24	.25	.27	.38
STAIC-Trait Total Score	74	60	.16	.17	.30	.29
CBCL Anxious/Depressed	72	51	.56	.26	.02	.37

Note: N = number of double-entered proband pairs

The only value of h^2_g which reached statistical significance in these analyses was that for the parent-reported anxious/depressed syndrome score from the CBCL. However, the size of the estimate for the child-reported depression is indicative of there being an influence of genetic factors on extreme group membership for this variable also. From this analysis, once again, it appears that the parents may be rating symptoms that correspond to child-reported depression rather than anxiety. It is interesting to note, that as with the bivariate analysis of the child-reported data, the depression and anxiety scores

show more distinct aetiologies, with the anxiety dimension having no genetic factors involved in the aetiology of extreme scores, but a large common environment factor is indicated as compared to that for depression. These results did not differ significantly when age and sex effects were controlled for suggesting that the same aetiological factors were involved for extreme group membership for both boys and girls of all ages. These results are consistent with the genetic analyses of individual differences in the normal range, suggesting these symptoms are on aetiological continua.

There has been one published group heritability analysis of depressive symptoms in childhood, and this used the CDI with a cut-off of 13 to identify the probands. For the purposes of comparison, an identical analysis was undertaken on the current data. The results from both of these data sets are given in Table 6.2.3b.

Table 6.2.3b: Group Heritability of CDI Scores with Cut-Off of 13

Study	h^2_g	SE	c^2_g	SE
Eley 1996	.23	.24	.29	.34
Rende et al. 1993	.23	.14	.44	.05

The h^2_g scores are remarkably similar, and suggest that the heritability of CDI scores at a level of more than or equal to a score of 13 may be moderately heritable. However, it must be noted that neither of these estimates differs significantly from zero, and are simply indicative of there being an influence of genetic factors on scores above 13 on the CDI. The group common environment estimates are rather different in the two studies, but not significantly so. They are both indicative of a contribution of common environment influences to extreme group membership on the CDI as defined as scores of more than 13.

6.2.4: Bivariate group heritability analyses

Having established the role of genetic factors on extreme scores univariately, it is now possible to consider the bivariate case. As discussed earlier, these analyses can be conducted by selecting the proband on either of the two measures involved in the analysis. Results from selecting probands on both measures for the depression and anxiety dimensions and for the CDI and STAIC-Trait total scores are given in Table 6.2.4a.

Table 6.2.4a: Bivariate Heritability Estimates for Depression and Anxiety Dimensions and for the CDI and STAIC-Trait

Proband Selection Measure	Co-Twin Prediction Measure	N (MZ)	N (DZ)	h^2_g	SE
Depression	Anxiety	58	45	-.02	.22
Anxiety	Depression	75	57	.07	.28
CDI	STAIC-Trait	64	51	.01	.24
STAIC-Trait	CDI	74	60	.19	.27

Note: N = number of double-entered proband pairs

There do not appear to be genetic factors that result in extreme group membership on the depression dimension and which also influence anxiety scores, or vice versa. The results for the CDI and STAIC-trait are less clear. The most likely explanation for the difference in the results when the CDI is taken as the proband measure, and when the STAIC-Trait is taken as the proband measure is that these two measures have differential reliabilities (Stevenson et al. 1993). This possibility is supported by the results from the two dimensions, which would have similar reliabilities and produce very similar estimates.

6.2.5: Multivariate genetic analyses of depression and anxiety: Child- and parent-report

This model-fitting analysis was carried out using the parent-reported anxious/depressed syndrome from the CBCL and the two child-reported dimensions of depression and anxiety. By this stage it was clear that these latter two variables provided more accurate representations of depression and anxiety than the total scores from the CDI and the STAIC-Trait so this analysis did not use these latter two variables. As there was no logical or theoretical reason by which to order the variables if a Cholesky decomposition was used, a general and specific factor model was fitted to the data in which there was one set of factors shared by all three variables, and three specific sets of factors. The initial model is given in Figure 6.2.5a. The correlation matrices for the MZ and DZ twins are given in Table 6.2.5a.

Figure 6.2.5a: General and Specific Factors Model, Child- and Parent-Reported Depression and Anxiety

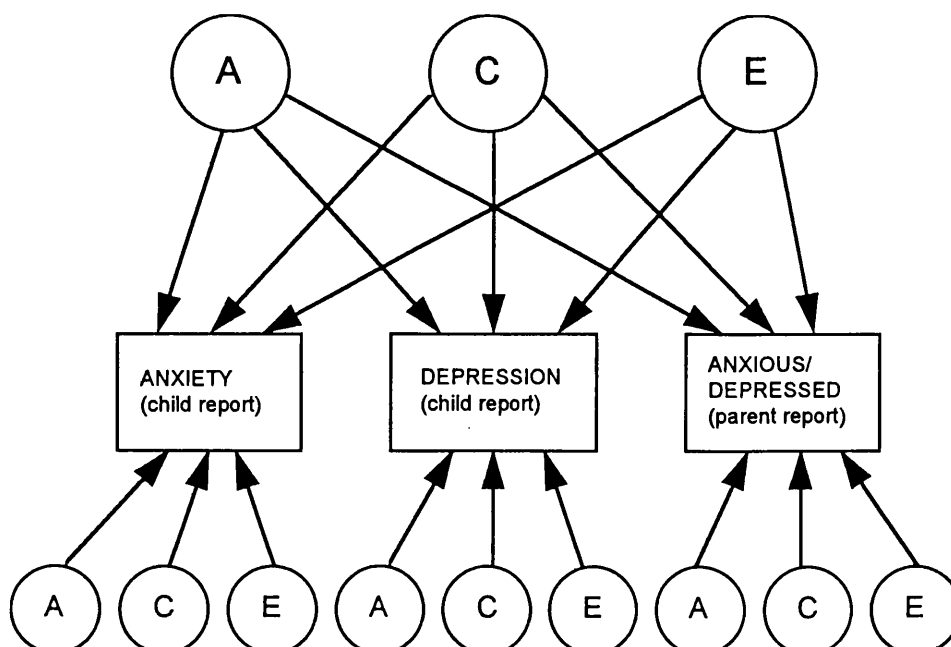


Table 6.2.5a: Correlation Matrices for Child- and Parent-Reported Depression and Anxiety Dimensions

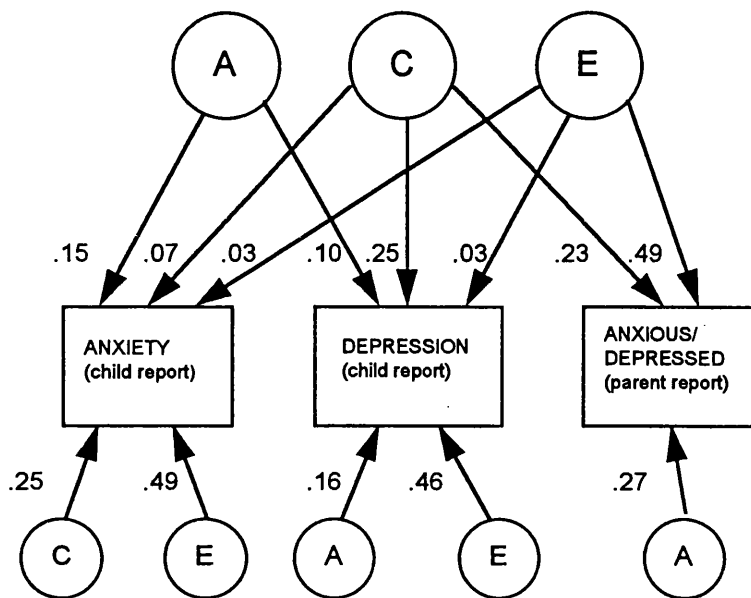
Group	Variable & Twin	AT1	DT1	A/DT1	AT2	DT2	A/DT2
MZ	AT1	1.00					
	DT1	.25	1.00				
	A/DT1	.28	.42	1.00			
	AT2	.45	.20	.15	1.00		
	DT2	.24	.54	.34	.22	1.00	
	A/DT2	.14	.29	.56	.28	.39	1.00
DZ	AT1	1.00					
	DT1	.35	1.00				
	A/DT1	.18	.37	1.00			
	AT2	.42	.17	.19	1.00		
	DT2	.20	.30	.28	.35	1.00	
	A/DT2	.10	.01	.25	.25	.32	1.00

A = Child-reported anxiety dimension; D = Child-reported depression dimension; A/D = Anxious/depressed syndrome reported by parents; T1 = Twin 1; T2 = Twin 2.

The full model failed to converge, so the univariate analyses and the correlations were inspected to identify which parameters should be dropped. The path from the specific A term to child-reported depression was dropped, followed by the specific A term from parent-reported anxious/depressed, followed by the specific C term from child-reported anxiety. None of these three increasingly reduced models converged. It therefore became necessary to identify parameters from the shared factors which could be dropped. In order to facilitate this process the cross-twin cross-measure correlations were considered, and it was decided that the most appropriate parameter to drop next was the path from the shared A term to the parent-reported anxious/depressed variable. This model converged with a chi-square of 43.97 and 28 degrees of freedom. From the t-values in the unstandardised solution it was clear that the specific E term was not required by child-reported anxiety, so this was dropped, resulting in a model with a chi-square value of 35.17 for 29

degrees of freedom, a non-significant worsening of fit. No other paths could be dropped without producing a significant deterioration of fit, so this was the final model. The path co-efficients (always to the left of the path) and the full fit of the model are given in Figure 6.2.5b.

Figure 6.2.5b: Final Model for Child- and Parent-Reported Depression and Anxiety



$$\chi^2 = 35.17, df = 29, p = 0.20, AIC = -22.83, CFI = .986$$

From this model two things are clear. First, once again it is seen that the correlation between the child-reported depression and anxiety dimensions is entirely due to genetic factors, but in addition to this, the correlation between these two dimensions and the parent-reported anxious/depressed syndrome is accounted for only by environmental factors. Second, as was to be expected from the earlier analyses, it is predominantly the child-reported dimension of depression that shares these factors with the parent-reported anxious/depressed syndrome. It is interesting to note that there are genetic factors specific to both the child-reported depression dimension and the parent reported anxious/depressed syndrome, but there are none that are shared by these two variables.

6.2.6: Effects of age and sex on the univariate genetic analyses of child-reported depression and anxiety

The following sections investigate the main effects of age-group and sex on the aetiologies of the depression and anxiety dimensions. It was found that when the sample was divided by age and by sex, the distribution of the depression dimension became skewed within sub-groups and this resulted in poor fits to the data. For this reason, for these analyses the natural log transformed depression dimension was used. The univariate results with the whole sample for this variable were virtually identical to those for the untransformed variable, and the bivariate analysis with the anxiety dimension also produced very similar results to that with the untransformed depression scores.

The first analysis addressed the issue of whether the aetiology of depressive and anxious symptoms for the children (8-11 years) was different from that for the adolescents (12-16). The sample sizes for the child MZ, child DZ, adolescent MZ and adolescent DZ groups were 108, 83, 113, and 86 pairs respectively. The correlation matrices for the depression and anxiety variables for these four groups are given in Table 6.2.6a.

Table 6.2.6a: Correlation Matrices for Transformed Depression and Anxiety Dimension Scores, divided by Age-Group and Zygosity

Group	Variable	Children				Variable	Adolescents			
		DT1	AT1	DT2	AT2		DT1	AT1	DT2	AT2
MZ	DT1	1.00				DT1	1.00			
	AT1	.10	1.00			AT1	.44	1.00		
	DT2	.42	.20	1.00		DT2	.60	.34	1.00	
	AT2	.16	.44	.17	1.00	AT2	.29	.43	.28	1.00
DZ	DT1	1.00				DT1	1.00			
	AT1	.31	1.00			AT1	.40	1.00		
	DT2	.26	.12	1.00		DT2	.38	.28	1.00	
	AT2	.20	.34	.36	1.00	AT2	.24	.53	.35	1.00

D = Natural log transformed depression score; A= Anxiety score; T1 = Twin 1; T2 = Twin 2.

In Table 6.2.6b below, the squared path co-efficients for the univariate analyses are given.

Table 6.2.6b: Univariate Genetic Analysis of Transformed Depression
Dimension: Main Effects of Age

Group	Model	A ²	C ²	E ²	χ^2	df	p	CFI	AIC	$\Delta\chi^2$	Δdf	p
Children	ACE	.34	.08	.57	1.12	3	.77	1.000	-4.88			
	AE	.43	---	.57	1.28	4	.87	1.000	-6.72	0.16	1	ns
	CE	---	.35	.65	3.07	4	.55	1.000	-4.93	1.95	1	ns
Adolescents	ACE	.28	.28	.44	3.91	3	.27	0.985	-2.09			
	AE	.58	---	.42	5.76	4	.22	0.971	-2.24	1.85	1	ns
	CE	---	.51	.49	5.93	4	.20	0.968	-2.07	2.02	1	ns

In these analyses, due to the reduced sample size, it was not possible to tell whether the less well fitting models represented a significant worsening of fit. For this reason, the full model is regarded as the model of best fit.

The next stage of the analysis was to model the children and adolescents simultaneously. There were two models, a free model and a constrained model. The free model allowed for different solutions for the two groups, the constrained (fixed) model forced equal solutions for both groups. In the free model solutions, the parameters are given for the children first and then the adolescents.

Table 6.2.6c: Free and Fixed Four Group Models
Main Effects of Age on Depression

	Model	A ²	C ²	E ²	χ^2	df	p	CFI	AIC	$\Delta\chi^2$	Δdf	p
Free	ACE - Ch	.34	.08	.57	5.03	6	.54	1.000	-6.97			
	ACE - Ad	.28	.28	.44								
Fixed	ACE	.34	.15	.51	16.55	9	.06	0.910	-1.45	11.52	3	<.01

Note: Ch = Children; Ad = Adolescents

For a change of degrees of freedom of 3, a change of χ^2 of 11.52 reveals a significant worsening of fit. Thus for the natural log transformed depression dimension from the child-reported data, the same model cannot be used for both the children and adolescents. This suggests that at around the age of twelve, where there is a change of prevalence of depression, this is due to a change in the aetiological factors involved. It has been demonstrated that it is age rather than puberty which is the crucial factor in predicting the changes in prevalence of depression in adolescence (Angold and Rutter 1992). This suggests that biological factors may not be as central to this change as has been thought, and that there may be additional common environment influences that become important for depressive symptoms at about the age of 12 years. As will be seen in later sections, adolescents experience higher levels of events and LTEs than children, and it may be these influences that are resulting in the increased role of common environment factors in the aetiology of depression in adolescents.

Analyses to consider the main effects of age on the aetiological models for the anxiety dimension were also conducted. Table 6.2.6d presents the solutions for the children and adolescents calculated separately. Table 6.2.6e contains the free and fixed models from the four-group analyses.

Table 6.2.6d: Models for Anxiety - Sample Divided by Age-Group

Group	Model	A ²	C ²	E ²	χ^2	df	p	CFI	AIC	$\Delta\chi^2$	Δ df	p
Children	ACE	.25	.20	.55	5.86	3	.12	0.911	-0.04			
	AE	.47	---	.53	6.78	4	.15	0.913	-1.22	0.92	1	ns
	CE	---	.39	.61	7.08	4	.13	0.904	-0.92	1.22	1	ns
Adolescents	AE	.51	---	.49	10.48	4	.03	0.869	2.48			
	CE	---	.48	.52	1.195	4	.88	1.000	-6.81			

It was found that the data from the older group would not converge with all three terms in the model. From the correlations it looked as if this was because an "A" term was not required, and this is confirmed by the chi-square, CFI, and

AIC values for the AE and CE models. Due to this lack of convergence for the ACE model for the older children, in the four-group analyses, the full free model would also not converge, so as illustrated in the table below, an ACECE model was fitted and allowed to be free. However, when the model was constrained to be equal for both groups, the full ACE model converged.

Table 6.2.6e: Free and Fixed Four Group Models
Main Effects of Age-Group on Anxiety

	Model	A ²	C ²	E ²	χ^2	df	p	CFI	AIC	$\Delta\chi^2$	Δdf	p
Free	ACE - Ch	.25	.20	.55	6.85	7	.44	1.000	-7.15			
	CE - Ad	---	.48	.52								
Fixed	ACE	.07	.38	.55	12.72	9	.18	0.954	-5.28	5.87	2	<.10

Note: Ch = Children; Ad = Adolescents

These results indicate that when treated separately the children fit a different model from the adolescents, although the fit just missed being significantly worsened by constraining the groups to be equal. This suggests that there is an effect of agegroup on the aetiology of anxious symptomatology, but that due to the relatively small sample sizes this does not quite reach statistical significance. Interestingly, it is the common environment term as in the depression dimension, that becomes of increased importance in the aetiology of anxiety in adolescents.

Similarly, main effects of sex on depressive and anxious symptomatology were investigated. The sample sizes for the male MZ, male DZ, female MZ, and female DZ groups were 96, 90, 122, and 79 respectively. The correlation matrices are presented in Table 2.6f. The results for the separate models for the boys and girls are given in Table 6.2.6g.

Table 6.2.6f: Correlation matrices for Depression and Anxiety Dimension Scores, divided by Sex and Zygosity

Group	Variable	Males				Variable	Females			
		DT1	AT1	DT2	AT2		DT1	AT1	DT2	AT2
MZ	DT1	1.00				DT1	1.00			
	AT1	.25	1.00			AT1	.23	1.00		
	DT2	.37	.26	1.00		DT2	.59	.23	1.00	
	AT2	.27	.47	.25	1.00	AT2	.14	.44	.16	1.00
DZ	DT1	1.00				DT1	1.00			
	AT1	.25	1.00			AT1	.45	1.00		
	DT2	.27	-.01	1.00		DT2	.38	.37	1.00	
	AT2	.08	.36	.21	1.00	AT2	.29	.46	.43	1.00

D = Natural log transformed depression score; A= Anxiety score; T1 = Twin 1; T2 = Twin 2.

Table 6.2.6g: Models for Depression - Sample Divided by Sex

Group	Model	A ²	C ²	E ²	χ^2	df	p	CFI	AIC	$\Delta\chi^2$	Δdf	p
Boys	ACE	.23	.14	.62	2.83	3	.42	1.000	-3.17			
	AE	.40	---	.60	3.31	4	.51	1.000	-4.69	0.48	1	ns
	CE	---	.32	.68	3.68	4	.45	1.000	-4.32	0.85	1	ns
Girls	ACE	.32	.25	.43	2.19	3	.53	1.000	-3.81			
	AE	.58	---	.42	3.62	4	.46	1.000	-4.38	1.43	1	ns
	CE	---	.52	.48	4.75	4	.31	0.988	-3.25	2.56	1	ns

As with the main effects of age of depression, the analyses dividing the sample by sex resulted in non-significant differences of fit between the three models in each group.

The next stage of the analysis was a four-group model, with the sexes free to differ, and then constrained to be equal. The results of this analysis are given in the following table.

Table 6.2.6h: Free and Fixed Four Group Models
Main Effects of Sex on Depression

	Model	A ²	C ²	E ²	χ^2	df	p	CFI	AIC	$\Delta\chi^2$	Δdf	p
Free	ACE - boys	.23	.14	.62	5.01	6	.54	1.000	-6.99			
	ACE - girls	.32	.25	.43								
Fixed	ACE	.32	.18	.50	12.69	9	.18	0.955	-5.31	7.68	3	<.10

A change in χ^2 of 7.68 for a change in degree of freedom of 3 is not a significant worsening of fit at the .05 level, suggesting that there are no differences in the aetiology of depression for girls and boys. However, both additive genetic and common environment factors appear to have more influence on depressive symptoms in girls than in boys, resulting in higher correlations in the female pairs (see Table 6.2.6f).

Sex effects were also investigated for the anxiety dimension.

Table 6.2.6i: Models for Anxiety - Sample Divided by Sex

	Model	A ²	C ²	E ²	χ^2	df	p	CFI	AIC	$\Delta\chi^2$	Δdf	p
Boys	ACE	.14	.30	.55	2.64	3	.45	1.000	-3.36			
	AE	.47	---	.53	4.73	4	.32	0.978	-3.27	2.09	1	ns
	CE	---	.41	.59	3.04	4	.55	1.000	-4.96	0.40	1	ns
Girls	ACE	.08	.38	.54	5.04	3	.17	0.952	-.096			
	AE	.50	---	.50	9.07	4	.06	0.881	1.07	4.03	1	<.05
	CE	---	.45	.55	5.19	4	.27	0.972	-2.81	0.15	1	ns

In these models it can be seen that the AE model results in a significant worsening of fit for the girls. However the free ACE model with both boys and girls was used in the four-group analysis allowing for direct comparison of this model with the fixed ACE model.

Table 6.2.6j: Free and Fixed Four Group Models
Main Effects of Sex on Anxiety

	Model	Group	A ²	C ²	E ²	χ^2	df	p	CFI	AIC	$\Delta\chi^2$	Δdf	p
Free	ACE	boys	.14	.30	.55	7.68	6	.26	0.978	-4.33			
		girls	.08	.38	.54								
Fixed	ACE		.11	.35	.55	7.98	9	.54	1.000	-10.02	0.30	3	ns

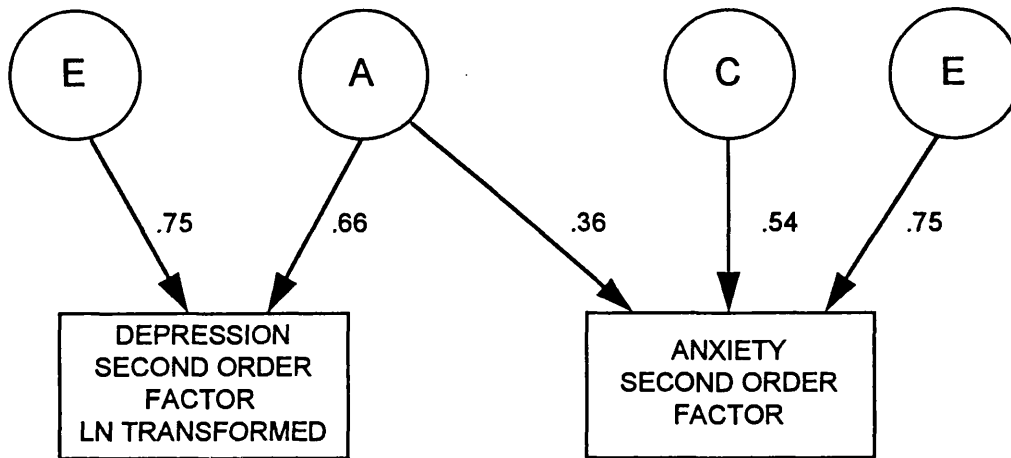
Constraining these models to be equal did not result in a significant worsening of the fit, indicating that there was no main effect of sex on the aetiology of anxiety.

In conclusion therefore, within this data set there was only a main effect of age on depressive symptoms that was significant at the .05 level. There were in addition to this, effects of age-group on anxiety and of sex on depression that were not quite statistically significant. These analyses suggest that as children reach adolescence, the higher level of challenges and experiences available have a direct impact on levels of internalising symptoms.

6.2.7: Effects of age and sex on the bivariate genetic analyses of depression and anxiety

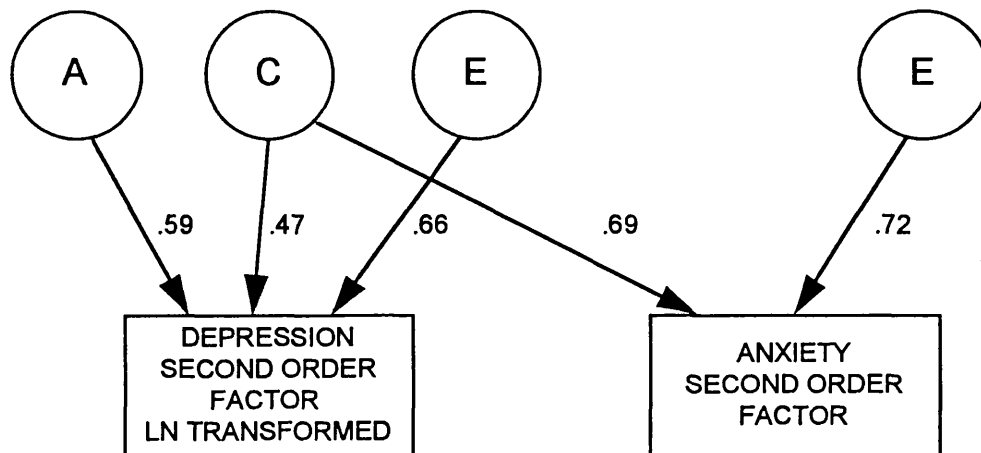
The next two issues to be investigated were whether there were main effects of age and sex on the shared aetiology of the depression dimension (natural log transformed) and the anxiety dimension. Firstly, Cholesky decompositions were conducted on these two variables with the data from the children and adolescents separately. The initial model had the specific set of factors on the anxiety variable (a, c, and e), as in the analyses of the whole sample (see Figure 6.2.2a). The final models from these two sets of analyses are given in Figures 6.2.7a and 6.2.7b.

Figure 6.2.7a: Final Model from the Cholesky Decomposition of the Transformed Depression Dimension and the Anxiety Dimension: Children only



$\chi^2 = 11.77$, $df = 15$, $p = 0.70$, AIC = -18.23, CFI = 1.000

Figure 6.2.7b: Final Model from the Cholesky Decomposition of the Transformed Depression Dimension and the Anxiety Dimension: Adolescents only



$\chi^2 = 14.06$, $df = 15$, $p = 0.52$, AIC = -15.94, CFI = 1.000

Both the free model in which the children and adolescents were not constrained to be equal, and the fixed model in which they were constrained to be equal, required the removal of the genetic factor specific to anxiety (a) from the full model in order to converge. The fits of these two solutions are given in the table below. The squared parameter estimates are given for the depression dimension first, then for the anxiety dimension. The factors in upper case are those that are shared, those in lower case are those that are specific to anxiety.

Table 6.2.7a: Main Effect of Age on the Cholesky Decomposition of Depression and Anxiety

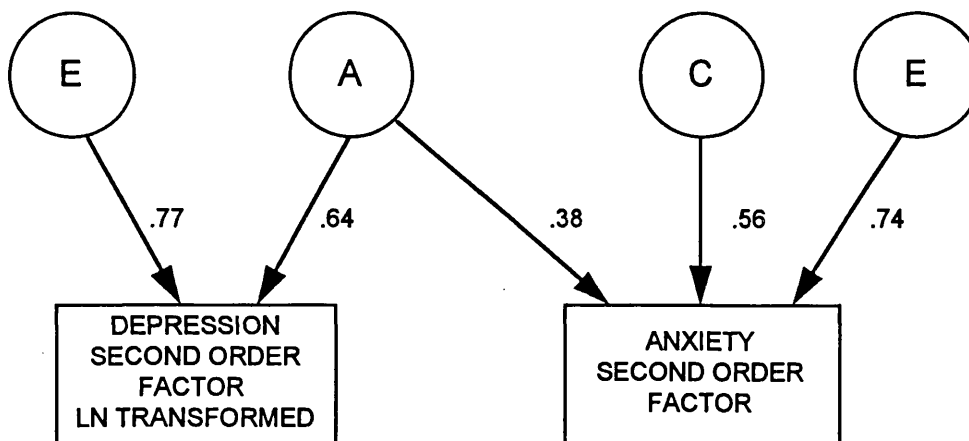
Group	Depression			Anxiety				
	A1 ²	C1 ²	E1 ²	A2 ²	C2 ²	E2 ²	c ²	e ²
Free Children	.37	.07	.56	.26	.04	.00	.16	.54
Adolescents	.31	.26	.43	.04	.16	.00	.29	.51
Fixed	.38	.12	.50	.12	.03	.00	.31	.54

	χ^2	df	p	CFI	AIC	$\Delta\chi^2$	Δdf	p
Free	20.78	24	.65	1.000	-27.22			
Fixed	42.63	32	.10	0.952	-21.37	21.85	8	<.01

The change in χ^2 of 20.81 is significant at the .01 level for a change in degrees of freedom of 8. This reveals a different aetiological relationship between depression and anxiety for children as compared to adolescents. The two main differences between the models for the children and adolescents are that the common environment influence becomes a significant parameter for the adolescents for both depression and anxiety, and the role of the shared additive genetic factor becomes less crucial for anxiety in the adolescents. These differences are not unexpected given the results from the univariate analyses, but in addition to what was revealed earlier, they suggest that it is common environment influences that are shared by depression and anxiety that become important in the adolescents.

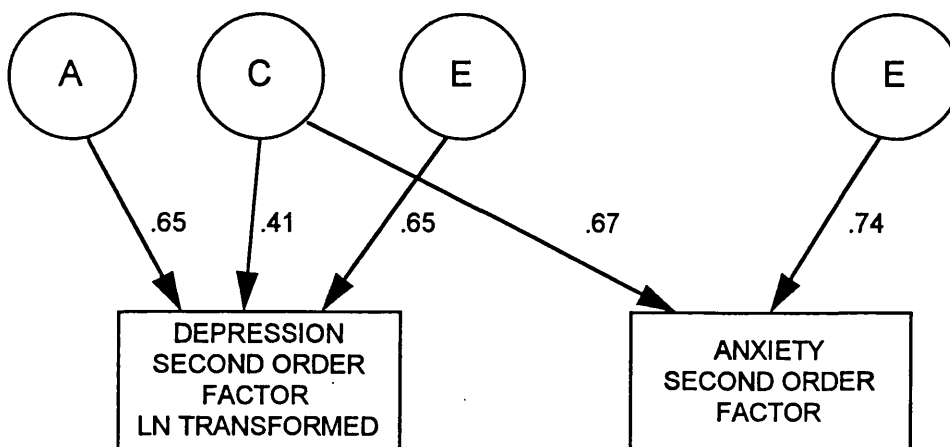
A similar analysis was conducted to consider main effects of sex on the shared aetiology of these two variables. The models of best fit and their fit data for the boys and for the girls are given below with their fit indices.

Figure 6.2.7c: Final Model from the Cholesky Decomposition of the Transformed Depression Dimension and the Anxiety Dimension: Boys only



$\chi^2 = 8.97$, $df = 15$, $p = 0.88$, $AIC = -21.03$, $CFI = 1.000$

Figure 6.2.7d: Final Model from the Cholesky Decomposition of the Transformed Depression Dimension and the Anxiety Dimension: Girls only



$\chi^2 = 18.09$, $df = 15$, $p = 0.26$, $AIC = -11.91$, $CFI = 0.977$

In order to calculate whether these the solutions for the boys and the girls were significantly different from one another, a four group analysis was conducted with the male MZ and DZ pairs and the female MZ and DZ pairs. The initial model was the same as that for the analysis considering the main effects of age, and as with this model both the free model and the fixed model required the removal of the genetic factor specific to anxiety (a) from the full model in order to converge. The fits of these two solutions are given in the table below.

Table 6.2.7b: Main Effect of Sex on the Cholesky Decomposition of Depression and Anxiety

Group	Depression			Anxiety				
	A1 ²	C1 ²	E1 ²	A2 ²	C2 ²	E2 ²	c ²	e ²
Free boys	.34	.07	.27	.27	.08	.00	.12	.53
girls	.41	.17	.20	.01	.23	.00	.21	.55
Fixed	.36	.15	.49	.13	.01	.00	.32	.53

	χ^2	df	p	CFI	AIC	$\Delta\chi^2$	Δdf	p
Free	24.75	24	.42	0.996	-23.25			
Fixed	34.15	32	.36	0.990	-29.85	9.40	8	ns

From this table it can be seen that constraining the models for the male and female children to be equal resulted in an increase in χ^2 of 9.40. This is not a significant worsening of fit for a change in degrees of freedom of 8, so the same model can be said to fit the data for the boys and the girls. However, it must be noted, that as with the models for the children and adolescents, there are differences here, with the influence of the shared common environment factor being greater for the girls than the boys. Interestingly, the two models parallel the models for the children and adolescents, in that the models for the children and the boys are rather similar, as are those for the adolescents and the girls. This suggests that there may be interaction effects of age and sex on the aetiology of depression and anxiety, but this sample was not large enough to investigate such a hypothesis.

In conclusion, these last two sections have found there to be differential roles for additive genetic and common environmental influences on depression and anxiety across the sexes and age-groups. It appears that common environmental influences which are shared for depression and anxiety play a more significant role in adolescents than in children, and in addition this may be the case for girls as compared to boys. As will be seen in the following section, life events and experiences are experienced at a higher rate by adolescents, and it may therefore be these influences that are resulting in the differences in prevalence of depression and anxiety seen for males and females and for children and adolescents.

Section 6.3: Associations Between Depression, Anxiety, Life Events and Long-Term Experiences

This section investigates which of the life event and long-term experience (LTE) variables are associated with proband status for either depression or anxiety on the child-reported dimension scores. The section is divided into five parts. Firstly the data from the current study is compared with that from Sandberg et al (1993). Then associations of life event variables with caseness for depression and anxiety are discussed. Thirdly, associations between LTEs and depressive and anxious caseness are presented. Following this, interactions between event and LTE variables are considered. Finally, confounding factors that might account for the associations found in the previous sections were investigated.

6.3.1: Baseline rates of life events and LTEs

As described earlier the method of life events ascertainment used in this study was an interview first described by Sandberg et al. (1993). Direct comparison of the baseline rates of events between these two data sets is difficult due to ascertainment of events from the 18 months before interview by Sandberg et

al., as compared to a period of one year in the current study. The period of one year was chosen here due to the potential unreliability of reporting of events that occurred more than 12 months before the date of the interview (Paykel 1983; Monck & Dobbs 1985). In order to facilitate direct comparisons between these two data sets, the figures from the Sandberg et al. (1993) study have been multiplied by 2/3. In addition to the total number of events and LTEs, the total number of negative life events (those scoring two or more on the variable "long-term negative impact") and negative LTEs (those scoring two or more on the variable "negative impact on the child") are also given. These figures are given separately for those children who were recruited onto the study as cases and those who were controls. The test used to ascertain whether there were significant mean differences in the scores for cases and control in both studies was an independent t-test, from which the significance levels (p) are given.

Table 6.3.1a: Baseline Rates of Life Events and LTEs
Comparison with Sandberg et al. (1993)

Variable	Eley 1996			Sandberg et al. 1993		
	12 month period			pro-rated 12 month period		
	Cases	Controls	p	Cases	Controls	p
No. of Life Events	4.7	3.7	.009	8.5	6.3	.003
No. of Negative Life Events	1.1	0.9	.271	2.9	1.4	.001
No. of LTEs	3.2	1.6	.001	4.4	2.5	.001
No. of Negative LTEs	2.1	1.0	.001	3.2	1.8	.001

As the cases in Sandberg et al. (1993) were a referred sample whereas those in the current study were extreme scorers within a normal population, it is not surprising that the cases from the present study showed lower levels of life events and LTEs than those from Sandberg et al. (1993). What was surprising however, was that the level of events was lower for the current study cases than for the controls from the previous study, and the current study controls had very low event scores. The differences here cannot simply be attributed to the difference of 6 months in the reporting time as this has been taken into account, so there must either be a difference in the level of events collected, or

in the true levels of events experienced by these two samples. It was thought possible that demographic differences in the sample might account for these differences. It was also of interest to see if demographic variables were associated with levels of LTEs, even though these were reported at a level that would have been predicted from the previous study. For this reason, the SES, sex and age distributions of the two samples were compared. In order to match the age division from the Sandberg et al. (1993) paper the children were divided those aged 8 to 10 years (younger group), and those aged 11 to 16 years (older group). Note that this divides the children at a different age from that which was chosen to divide the current sample into children and adolescents. For this reason the groups are referred to as the younger and older children in this context.

Table 6.3.1b: Percentage of Families from Each SES Group

SES	Eley 1996		Sandberg et al. 1993	
	Cases	Controls	Cases	Controls
I and II	60.7	57.6	26.0	32.0
IIINM and IIIM	25.0	32.2	49.0	46.0
IV and V	10.7	3.4	13.0	13.0
Unemployed	3.6	6.8	12.0	9.0

Table 6.3.1c: Percentage of Younger, Older, Male and Female Children

Group	Eley 1996		Sandberg et al. 1993	
	N	%	N	%
Younger (8-10 years)	32	36%	34	32%
Older (11-16 years)	58	64%	72	68%
Male	41	46%	65	61%
Female	49	54%	41	39%

As can be seen from this table the SES and sex distributions for the two samples were found to be rather different. It was thought that these differences

might be accounting for the different levels of events and LTEs reported in the two studies. In order to test this hypothesis the levels of life events and LTEs in the higher SES groups (I and II) were compared with those from the lower groups (IIINM to VI) using independent samples t-tests, as were the results for the boys and the girls. It was also of interest to see whether age-group was related to levels of events and LTEs even though the sample did not differ for this. The results of these analyses are presented in Tables 6.3.1d and 6.3.1e. For this analysis the age-group division was as in the rest of the study, those aged 8 to 11 were classified as the children, those aged 12 to 16 as the adolescents.

From the following table it was clear that there was no association between number of events and LTEs and SES. The higher levels of events and LTEs reported in the Sandberg et al. (1993) study could not therefore be attributed to SES differences between the samples.

Table 6.3.1d: Mean Number of Life Events and LTEs in Families of Higher and Lower SES

Variable	Higher	Lower	t	df	p
Life Events	4.03	4.00	.09	166	.93
Independent Life Events	3.19	3.08	.38	166	.71
Behaviour Related Life Events	0.84	0.92	-.34	166	.73
LTEs	2.13	2.10	.08	166	.94
Independent LTEs	1.64	1.56	.27	166	.78
Behaviour Related LTEs	0.49	0.54	-.33	166	.74

The non-integer degrees of freedom in the Table 6.3.1e are due to adjustments for non-equality of variance between the two groups.

Table 6.3.1e: Mean Number of Life Events and LTEs in
Children and Adolescents

Variable	Children	Adolescents	t	df	p
Life Events	3.40	4.64	-3.68	175.47	.001
Independent Life Events	3.11	3.29	-.66	180	.511
Beh. Rel. Life Events	0.29	1.35	-5.66	124.20	.001
LTEs	1.87	2.54	-2.30	176.30	.023
Independent LTEs	1.54	1.82	-1.21	176.82	.229
Beh. Rel. LTEs	0.33	0.72	-3.07	175.87	.002

Note: Beh. Rel. = Behaviour Related

Table 6.3.1f: Mean Number of Life Events and LTEs in
Male and Female Children

Variable	Male	Female	t	df	p
Life Events	3.60	4.48	-2.57	180	.011
Independent Life Events	2.94	3.43	-1.81	180	.072
Beh. Rel. Life Events	0.66	1.05	-1.82	180	.070
LTEs	2.27	2.21	.19	180	.850
Independent LTEs	1.76	1.64	.48	180	.634
Beh. Rel. LTEs	0.51	0.57	-.43	180	.668

Note: Beh. Rel. = Behaviour Related

From the previous two tables, two things are clear. Firstly, the older children are reporting more behaviour related events and LTEs, but not more independent events and LTEs. Secondly the girls are reporting more events than the boys, although some of these comparisons were not significant. The finding that age-group is related to levels of events and LTEs does not help explain the different levels reported in the two samples, because they did not differ enough on this variable. However, it is interesting to note that the older children are reporting more events over which they had some, if not all, control. Finally, the finding that the girls reported more events does not explain the

different levels of events in the two samples, because the current sample has the higher proportion of females, and if anything should therefore have found higher levels of events than the earlier study. The most plausible remaining possibility for the lower level of events in this study is that the interviewers were conservative over inclusion of events in that they had to be deemed to make a more significant impact on the child in this study than in the previous study in order to be rated.

6.3.2: Associations between caseness and life event data

The first hypothesis relating to the second stage data was that being a case for either depression or anxiety would be related to having experienced more severe negative events in the previous twelve months. There were two life event variables which were used to test the associations between severe negative life events and symptomatology. These were number of best estimated independent (of the behaviour of the child) negative life events per child and total independent long-term negative impact per child. Only independent events were considered as these were unlikely to be events that might have arisen from any symptoms present.

Two methods of analysis were used in order to test this hypothesis. The first of these used data from all of the children in the second stage. Cases and controls for anxiety and depression were identified using cut-offs of one standard deviation above the mean on the anxiety and depression factors respectively. Independent t-tests were conducted comparing mean scores of event variables for the cases and non-cases for both of these types of symptomatology. Differences identified between the cases and controls could be due to common environment factors, non-shared environment factors, or genetic factors. This analysis might be criticised for using a twin population sample in an independent t-tests analysis, as the subjects are not truly independent of one another. However, even though many events are shared within a family, their effects may well not be similar for two members of a twin

pair, as demonstrated by the high level of discordant pairs where only one child was a case on at least one of the measures as compared to concordant case pairs in which both members of the pair were a case for either depression or anxiety (N = 43 and N = 10 respectively).

The second method of analysis only used twin pairs that were discordant for either anxiety or depression using the cut-offs of one standard deviation above the mean to define cases of each type. Paired t-tests were then conducted comparing the probands' and their co-twins' event scores. Differences between members of matched pairs in this analysis could be only due to non-shared environmental influences or genetic factors, as the matching of the pairs controls for the common environment. Thus by comparing the results of independent and paired t-tests, certain influences can be inferred. Associations found to be significant in the analysis of the whole sample, but not in the analysis of the discordant pairs could only be due to shared factors. These could either be common environment factors or genetic influences. Associations that were found in both sets of analyses could be due either to non-shared environmental factors or non-shared genetic factors.

For both of these sets of analyses the effect size of the difference between the cases and the controls (or the probands and their co-twins) was calculated using the following formula:

$$\text{Effect Size} = \frac{\text{Mean of Case Group} - \text{Mean of Control Group}}{\text{Standard Deviation of Control Group}}$$

The effect sizes and the one-way significance values (p) are given in the tables of results. One-way p values were used because the hypotheses were unidirectional.

It is clear from the following table that independent negative impact events are not significantly associated with depressive or anxious symptomatology. This analysis considers the effects of events that are shared within families as well as those that are individual specific, whereas the next analysis of discordant

twin pairs controls for common environment influences. From this table it appears that depressive symptomatology may be associated with non-shared independent negative life events, but anxious symptomatology is not associated with such events.

Table 6.3.2a: Independent T-Tests of Negative Event Scores for Cases and Controls

Case Group	Variable	Effect Size	df	1-tailed p
Depressed	No. of Independent Negative Events	.072	178	.333
Depressed	Total Independent Long-Term Negative Impact	.180	178	.144
Anxious	No. of Independent Negative Events	.001	178	.496
Anxious	Total Independent Long-Term Negative Impact	.036	178	.413

Table 6.3.2b: Paired T-Tests of Negative Event Scores for Probands and their Co-Twins

Proband Group	Variable	Effect Size	df	1-tailed p
Depressed	No. of Independent Negative Events	.277	28	.055
Depressed	Total Independent Long-Term Negative Impact	.142	28	.153
Anxious	No. of Independent Negative Events	-.131	36	.127
Anxious	Total Independent Long-Term Negative Impact	.029	36	.384

These results suggest that the category of “independent negative events” may be too broad to be associated with either type of symptomatology. This leads to the second hypothesis which was that levels of loss events would be associated with depression scores but not anxiety scores, and that levels of danger events would be associated with anxiety but not depression scores. There were therefore two further life event variables which were expected to be associated with high depression scores. These were number of independent high loss (scoring two or more on this dimension) events per child, and total

independent loss per child. The number of independent high danger (scoring two or more on this dimension) events per child, and total independent danger per child were expected to be associated with anxiety. The danger variables were not expected to be associated with depression scores, and the loss scores were not expected to be associated with the anxiety scores. This hypothesis was tested by conducting independent t-tests with the whole sample, followed by the more refined analysis of the discordant pairs only.

Table 6.3.2c: Independent T-Tests of Loss and Danger Scores
for Cases and Controls

Case Group	Variable	Effect Size	df	1-tailed p
Depressed	No. of Independent Loss Events	.274	178	.048
Depressed	Total Independent Loss	.131	178	.200
Depressed	No. of Independent Danger Events	.288	93.46	.071
Depressed	Total Independent Danger	.220	92.54	.133
Anxious	No. of Independent Loss Events	.208	178	.100
Anxious	Total Independent Loss	.161	178	.151
Anxious	No. of Independent Danger Events	.288	178	.044
Anxious	Total Independent Danger	.397	114.39	.019

This table shows depression to be associated with loss and anxiety to be associated with danger. Three of the four associations which were predicted to be present from the hypothesis do reach significance. The four comparisons which were not expected to result in any significant associations do not do so. As such these results provide strong evidence in support of the second hypothesis. There is one unexpected result which is that the depressed cases reported more independent danger events than their non-depressed co-twins, but this difference did not reach statistical significance. This hypothesis was also considered by analysis of the results for the discordant pairs alone, and these are presented in Table 6.3.2d.

These results show no association between depression and loss when matched pairs are used. This suggests that such loss events that are

associated with depression are shared within twin pairs, making them similar for level of depressive symptomatology. However, the results for anxiety suggest as strong an association with danger as those from the independent t-tests suggesting that these events are individual specific. These results are somewhat surprising in view of the lack of a role for common environment in depressive symptoms and the significant role of common environment in anxiety symptoms found in the genetic analyses.

Table 6.3.2d: Paired T-Tests of Loss and Danger Scores for Probands and their Co-Twins

Proband Group	Variable	Effect Size	df	1-tailed p
Depressed	No. of Independent Loss Events	.101	28	.208
Depressed	Total Independent Loss	.113	28	.188
Depressed	No. of Independent Danger Events	.218	28	.092
Depressed	Total Independent Danger	-.024	28	.425
Anxious	No. of Independent Loss Events	.030	36	.406
Anxious	Total Independent Loss	.055	36	.297
Anxious	No. of Independent Danger Events	.352	36	.024
Anxious	Total Independent Danger	.454	36	.005

In conclusion, there is very little evidence to support the hypothesis that independent negative events are related to depression or anxiety in children and adolescents. However, there is some evidence for the specificity of loss events to depression, and there is strong evidence for the specificity of danger events to anxiety.

6.3.3: Associations between caseness and LTE Data

The next stage of the analysis was to examine the best estimated long-term experiences (LTE) data. As with the best estimated event data two methods of analysis were used. Firstly, independent t-tests were conducted to compare the

level of negative LTEs for cases and non-cases in the whole sample. Secondly paired t-tests were conducted to test for mean differences in level of negative LTEs between probands and their non-case co-twins.

The following table shows that while independent negative events were not associated with depressive and anxious symptoms, independent negative LTEs were associated with depressive and anxious symptoms. This association is particularly strong for depressive symptoms. The results from the analysis of the discordant pairs are presented in Table 6.3.3b.

Table 6.3.3a: Independent T-Tests of Negative LTE Scores for Cases and Controls

Case Group	Variable	Effect Size	df	1-tailed p
Depressed	No. of Independent Negative LTEs	.717	86.33	.001
Depressed	Total Independent Negative Impact	.653	87.19	.002
Anxious	No. of Independent Negative LTEs	.204	178	.089
Anxious	Total Independent Negative Impact	.315	178	.020

Table 6.3.3b: Paired T-Tests of LTE Scores for Depressed Probands and their Non-Depressed Co-Twins

Proband Group	Variable	Effect Size	df	1-tailed p
Depressed	No. of Independent Negative LTEs	.103	28	.245
Depressed	Total Independent Negative Impact	.112	28	.229
Anxious	No. of Independent Negative LTEs	.120	36	.128
Anxious	Total Independent Negative Impact	.131	36	.091

The lack of association between negative LTEs and depressive and anxious symptoms in this table suggests that the negative LTEs were all of a shared kind, and as such are not revealed in an analysis of discordant pairs. It is also possible that the small number of discordant pairs has reduced the power of the analysis such that these effects become non-significant, but considering the

previous analyses in which associations have remained significant even with the smaller number of discordant pairs, this does not seem likely.

The next stage of the analysis of the LTE data was to consider the roles of specific types of chronic experiences. Four types of LTE were considered to be likely to be associated with depressive and anxious symptomatology. These were friendship problems, schoolwork stresses, family relationship problems, and family structure problems. Friendship problems included factors such as social isolation, interaction problems, a lack of a confiding relationship with a peer, and bullying. Schoolwork stresses included diagnosed difficulties such as dyslexia and exams lasting more than one month (GCSEs). Family relationship problems could refer to any members of the family and did not have to include the respondent. The family structure was defined as being problematic if the children were members of a family that did not include the two biological parents, both living in the family home. The first three of these four situations are unlikely to be totally independent of the child's behaviour, but as they are interactional situations it is interesting to consider them regardless of independence from the behaviour of the child.

As with the earlier analyses of associations the initial analysis of these variables consisted of independent samples t-tests using the whole of the available sample. This was followed by paired t-tests of mean differences in the discordant pairs for the friendship and school-work variables between both anxious and depressed cases and their co-twins. The family variables were not analysed in this way because one would not expect any true within-pair variance in such variables.

Table 6.3.3c reveals associations between friendship problems and both depression and anxiety, although only the former reaches significance. In addition to these associations, depression is also strongly and significantly associated with family relationship problems, suggesting that the within-family negative LTEs identified as being associated with depression earlier may partly be characterised by internal familial relationship problems. Depression is also significantly associated with schoolwork stresses. However, anxiety is not

associated with either of these two factors, and neither depression nor anxiety are associated with family structure problems. As most of the families classified in this way were single-parent families, this is a positive, though unexpected finding.

Table 6.3.3c: Independent T-Tests of Friendship, School-work, Family Relationship and Family Structure Problems for Cases and Controls

Cases Group	Variable	Effect Size	df	1-tailed p
Depressed	No. of Friendship Problems	.887	71.51	.002
Depressed	No. of School-work Stresses	.326	95.83	.044
Depressed	No. of Family Relationship Problems	.887	86.10	.001
Depressed	No. Family Structure Problems	.129	178	.225
Anxious	No. of Friendship Problems	.227	119.39	.105
Anxious	No. of School-work Stresses	.008	178	.471
Anxious	No. of Family Relationship Problems	-.019	178	.449
Anxious	No. Family Structure Problems	.006	178	.485

The results for the schoolwork and friendship factors when considered within the discordant pairs only are presented below.

Table 6.3.3d: Paired T-Tests of Friendship, School-work, Family Relationship and Family Structure Problems for Probands and their Co-Twins

Probands Group	Variable	Effect Size	df	1-tailed p
Depressed	No. of Friendship Problems	1.854	28	.001
Depressed	No. of School-work Stresses	.180	28	.212
Anxious	No. of Friendship Problems	.172	36	.244
Anxious	No. of School-work Problems	.000	36	.500

These results show a very strong and significant association between depressive symptoms and non-shared friendship problems, but there is no

association between this type of LTE and anxious symptomatology. Schoolwork stresses are not significantly associated with either depressive or anxious symptoms in this analysis. This means that the schoolwork stresses that are associated with depressive symptomatology are shared within twin pairs, and certainly, as many of these schoolwork stresses are learning difficulties such as dyslexia, then a genetic explanation of this finding would perhaps be most appropriate. In order to test this hypothesis, only the MZ twin pairs were entered into a further analysis. This time an independent t-test of cases and controls for depression was conducted to look for mean differences in schoolwork stresses. An effect size of .807 was calculated ($df = 23.86$, 1-tailed $p = .021$). This effect size is double that when the DZ pairs were included, suggesting that this common factor is more strongly shared by MZ twins, and is therefore likely to be heritable. This effect would be even clearer if just the discordant MZ pairs were analysed, but this group was not large enough to allow for such an analysis. A second explanation of this finding that schoolwork problems are shared within-pairs is that as GCSEs were the other major contributor to this category of LTE, and as twins would tend to do these exams in the same year, this could be a common environment influence. Unfortunately the nature of the coding of this variable did not allow for testing for associations with schoolwork LTEs characterised by learning difficulties and those rating long exam periods separately.

In conclusion, independent negative LTEs have been shown to be associated with both depression and anxiety in children and adolescents. This association appears to relate to environmental influences shared within the pair. More specifically, friendship problems, schoolwork stresses, and family relationship problems are significantly associated with depression, but family structures that are non-nuclear were not found to be associated with higher levels of depressive or anxious symptoms. The effect of the friendship problems is particularly marked when only the discordant pairs are analysed, suggesting that such problems are typically not shared within the pair. Finally, the schoolwork stresses which appear to have an effect that tends to be shared within the twin pair have been demonstrated to be likely to be heritable.

6.3.4: Interaction effects of event and LTE scores on caseness

In the literature on life events, depression and anxiety, a recurrent theme has been to consider interactions between recent life events and chronic adversities. For example, it has been demonstrated that there is an additive interaction between poor friendships and recent stressful life events on caseness for anxiety or depression (Goodyer et al. 1990a). For this reason, the interaction between independent negative life events and friendship problems, school-work stresses and family problems were examined in a two stage analysis. At a first stage, the proportion of children who had experienced either an independent negative life event, the LTE under consideration, or both, and who were cases was established. These percentages are given in Table 6.3.4a.

Table 6.3.4a: Interaction Effects of Independent Negative Life Events and LTE Types on Caseness

Type of Proband	Term	N	% Cases
Depressed	Independent Negative Event only	48	22.9
	Friendship Problems only	10	50.0
	Independent Negative Event & Friendship Problems	11	81.8
Anxious	Independent Negative Event only	48	33.3
	Friendship Problems only	10	60.0
	Independent Negative Event & Friendship Problems	11	45.5
Depressed	Independent Negative Event only	45	26.7
	Schoolwork Stresses only	15	40.0
	Independent Negative Event & Schoolwork Stresses	14	57.1
Anxious	Independent Negative Event only	45	33.3
	Schoolwork Stresses only	15	33.3
	Independent Negative Event & Schoolwork Stresses	14	42.9
Depressed	Independent Negative Event only	42	26.2
	Family Problems only	28	67.9
	Independent Negative Event & Family Problems	17	52.9
Anxious	Independent Negative Event only	42	38.1
	Family Problems only	28	50.0
	Independent Negative Event & Family Problems	17	29.4

In addition to this, logit analyses were conducted to establish the significance of the main effects of the two terms, and the significance of their interaction on the likelihood of being a case for anxiety or depression. In these analyses, first the interaction between negative life events and the LTE variable was dropped from the model (eg. independent negative events x friendship problems). Then in addition to the interaction term, the negative events and the LTE variable were dropped one at a time. The results of these logit analysis are given in Table 6.3.4b. The p values given for the change in chi-square are one-tailed, as it was hypothesised that these factors would always if anything, increase rather than decrease the likelihood of a subject being a case.

Table 6.3.4b: Logit Analysis of Interaction Effects of Independent Negative Life Events and LTE Types on Caseness

Terms Dropped	Dependent Variable	χ^2	df	p	$\Delta\chi^2$	Δdf	1-tailed p
Ind. Neg. Ev. x Friend	Depression	3.50	1	.062	3.50	1	<.05
Ind. Neg. Ev. x Friend, Ind. Neg. Ev.	Depression	3.68	2	.158	0.18	1	ns
Ind. Neg. Ev. x Friend, Friend	Depression	14.80	2	.001	11.30	1	<.001
Ind. Neg. Ev. x Friend	Anxiety	0.17	1	.681	0.17	1	ns
Ind. Neg. Ev. x Friend, Ind. Neg. Ev.	Anxiety	0.74	2	.690	0.57	1	ns
Ind. Neg. Ev. x Friend, Friend	Anxiety	2.39	2	.302	2.22	1	ns
Ind. Neg. Ev. x School	Depression	1.27	1	.259	1.27	1	ns
Ind. Neg. Ev. x School, Ind. Neg. Ev.	Depression	1.30	2	.522	0.03	1	ns
Ind. Neg. Ev. x School, School	Depression	4.61	2	.010	3.34	1	<.05
Ind. Neg. Ev. x School	Anxiety	0.71	1	.400	0.71	1	ns
Ind. Neg. Ev. x School, Ind. Neg. Ev.	Anxiety	0.99	2	.611	0.28	1	ns
Ind. Neg. Ev. x School, School	Anxiety	0.71	2	.702	0.00	1	ns
Ind. Neg. Ev. x Family	Depression	1.16	1	.281	1.16	1	ns
Ind. Neg. Ev. x Family, Ind. Neg. Ev.	Depression	1.20	2	.549	0.04	1	ns
Ind. Neg. Ev. x Family, Family	Depression	22.80	2	.001	21.64	1	<.001
Ind. Neg. Ev. x Family	Anxiety	1.58	1	.209	1.58	1	ns
Ind. Neg. Ev. x Family, Ind. Neg. Ev.	Anxiety	1.91	2	.386	0.33	1	ns
Ind. Neg. Ev. x Family, Family	Anxiety	2.01	2	.367	0.43	1	ns

Note: Ind. Neg. Ev. = Independent Negative Life Event; Friend = Friendship Problem LTE; School = Schoolwork Problem LTE; Family = Family Relationship Problem LTE.

From these tables, the main effects of friendship problems, school-work stresses and family relationship problems are clear. In addition to this there is a significant effect of the interaction of negative life events and friendship problems on depressive symptoms. This acts in such a way as to make a child significantly more likely to respond to a negative life event with depression, if there are also friendship problems.

In conclusion therefore, there is only one interaction effect revealed in these analyses, and that is an interaction between independent negative life events and friendship problems on depression. However, friendship problems were not acting as a vulnerability factor, but as an independent predictor of depression. Thus this was an additive rather than multiplicative interaction. None of these LTE types were significantly associated with anxiety.

6.3.5: Confounding factors

The associations found in this chapter may be due to confounding factors which influence both of the associated variables thus leading to the relationship between them. In the independent t-test analyses, factors that could act in this way are age and sex of the child, SES of the family, and genetic factors. However, in the paired t-tests all but genetic factors are controlled for in that the sample consists of perfectly matched pairs. Clearly only variables which are themselves related to either depression or anxiety can act as confounding factors, so for this reason SES, which was not related to depression, anxiety, life events or LTEs was not considered further as a confounding factor. However, depressive caseness was associated with sex, so this factor may result in the associations seen earlier between depression, number of independent loss events, number of independent negative LTEs, total negative impact from independent LTEs, friendship problems, schoolwork problems and family relationship problems. As four of these variables were continuous and three were binary, two types of analysis were used to investigate this issue. In order to test for this possibility in those variables that were continuous,

independent t-tests were conducted to calculate the mean scores for boys and girls. The results of these tests are given in Table 6.3.5a. Friendship problems, schoolwork problems and family relationship problems were all binary variables, and thus cross-tabulations were conducted between these variables and sex, and chi-square values were calculated. The results from these analyses are given in Table 6.3.5b.

Table 6.3.5a: Testing for Associations Between Sex and the Event and LTE Measures Associated with Depression

Variable	Effect Size	df	p
Number of Independent Loss Events	-.075	179	.618
Number of Independent Negative LTEs	-.258	179	.078
Total Independent Negative Impact (LTEs)	-.279	179	.051

In this analysis a negative effect size reveals higher scores for the boys than the girls. Thus it can be seen that for all of these variables, the boys score more than the girls, but none of these associations quite reaches significance. In addition to this, sex cannot be viewed as a confounding factor because while the boys score more on these event and LTE measures, they score less on the depression measure than the girls. Thus, although there are associations with sex here, this variable cannot be acting as a confounding factor.

Table 6.3.5b: Testing for Associations Between Sex and LTE Type

LTE Type	χ^2	df	p
Friendship Problems	2.608	1	.106
Schoolwork Problems	1.250	1	.263
Family Relationship Problems	.752	1	.386

These results show that none of these types of LTE are more prevalent in either of the sexes, and as such, sex cannot be acting as a confounding factor in their relationships with depression.

Anxiety caseness was associated not only with age-group but also with an interaction effect between age-group and sex. Thus, the associations seen between anxiety and number of independent danger events, total independent danger from events, number of independent negative LTEs, and total negative impact from independent LTEs that were identified in the independent t-tests may be due to age-group or sex. However, the associations with the danger event variables were also seen in the paired t-tests of the discordant pairs, so age and sex cannot have been acting as confounding factors here. The relationship between the two LTE measures with age-group and sex was therefore tested using independent t-tests. The results for the association between negative LTEs and sex are the same as those presented in Table 6.3.5a. The results for the associations between age-group and the two measures of negative impact from LTEs are presented in Table 6.3.5c below.

Table 6.3.5c: Testing for Associations Between Age-Group and the Event and LTE Measures Associated with Anxiety

Variable	Effect Size	df	p
Number of Independent Negative LTEs	.279	179	.116
Total Independent Negative Impact (LTEs)	.263	179	.154

From this table it can be seen that there are no significant effects of age-group on the LTE variables that were found to be associated with anxiety. The higher level of LTEs in the boys revealed in Table 6.3.5a does not suggest that sex is a confounding factor for the relationships between anxiety and negative LTEs as the only effect of sex on anxiety was an interaction with age such that the older boys scored less than the other groups.

The final confounding factor considered was heritability which could only be a possibility for those event and LTE measures that were associated with depression and anxiety in the independent t-tests and not in the paired t-tests. In order to estimate the heritability of these events and LTEs, two types of analysis were used. For the event and LTE variables that were continuous,

correlations for the members of the MZ and DZ twin pairs were calculated. For those variables that were binary, probandwise concordance rates were calculated for the MZ twin pairs only and for the DZ twin pairs only. Note that the binary variables were only associated with depression. These two sets of results are presented in Tables 6.3.5d and 6.3.5e.

Table 6.3.5d: MZ and DZ Correlations for the Event and LTE Variables that were Associated with Depression and Anxiety

Variable	Factor of Association	rMZ	rDZ	h ²
No. of Independent Loss Events	Depression	.774	.785	-.022
No. of Independent Danger Events	Anxiety	.624	.377	.494
Total Independent Danger (Events)	Anxiety	.746	.550	.392
No. of Independent Negative LTEs	Depression and Anxiety	.847	.541	.612
Total Independent Negative Impact	Depression and Anxiety	.853	.687	.332

As these scores were calculated for those events deemed independent or likely to be independent of the child's behaviour it is slightly surprising that the danger events and negative LTEs appear to be heritable to some extent. However, independence from the child did not include any reference to whether the event was independent of the rest of the family or not. This leaves open the interpretation that there is a passive gene-environment correlation acting here, in that the danger events and negative LTEs may due to the behaviour of other family members who share genes with the child. It is also possible that the rating of independence of events and LTEs from the behaviour of the child was not accurate, but judging by the high inter-rater reliability for this variable, this seems unlikely.

The results in Table 6.5.3e suggest that while schoolwork problems are governed by genetic factors, friendship are only slightly heritable, and family relationship problems are not resulting from genetic factors.

Table 6.3.5e: MZ and DZ Probandwise Concordance Rates for the Binary
LTE Variables that were Associated with Depression

Variable	Probandwise Concordance	
	MZ	DZ
Friendship Problems	.308	.200
Schoolwork Problems	.800	.429
Family Relationship Problems	.875	.714

Two methods of analysis were chosen to estimate the contribution of shared genetic factors to pairs of associated variables, in which both factors appeared to be heritable to some extent. For those where the event or LTE measure was continuous a bivariate h^2_g was used. This estimates the extent to which the same genetic factors that influence caseness for anxiety or depression also influence the associated event or LTE measure. The method of analysis chosen for the binary event variables, was to select for the first twin in a double-entered file being a case for the depression factor and then to cross-tabulate zygosity with the LTE variable in question. The results of these analyses are given in Tables 6.3.5f and 6.3.5g.

Table 6.3.5f: Bivariate Group Heritability Estimates for Anxiety and
Depression and the Best Estimated Events and LTE Data

Proband Selection Measure	Co-twin Predicted Measure	N _{MZ}	N _{DZ}	h^2_g	SE
Depression Factor	No. of Ind. Loss Events	32	22	.37	.34
Depression Factor	No. of Ind. Negative LTEs	32	22	.56	.37
Depression Factor	Total Ind. Negative from LTEs	32	22	.51	.35
Anxiety Factor	No. of Ind. Danger Events	35	29	.22	.37
Anxiety Factor	Total Ind. Danger from Events	35	29	.07	.41
Anxiety Factor	No. of Ind. Negative LTEs	35	29	.19	.38
Anxiety Factor	Total Ind. Negative from LTEs	35	29	.24	.38

Note: N = number of double-entered proband pairs;
Ind. = Independent of the behaviour of the child.

This table shows that the genetic factors involved in becoming a proband on the depression dimension may be shared to a certain extent with the genetic factors influencing negative LTEs that are independent of the child. As suggested earlier the most plausible explanation of this finding is that this is a passive gene-environment correlation. There may also be genetic factors shared between depressive proband status and loss events, but as the latter did not appear to be heritable, the evidence for this is rather weak. The results for the event and LTE variables associated with proband status on the anxiety dimension are less suggestive of these pairs of variables sharing genetic factors.

Table 6.3.5g: Prevalence Rates of the LTEs in Co-Twins of Depressed MZ and DZ Probands

	Zygosity of twin pair			
	MZ twin pairs		DZ twin pairs	
	absent N (%)	present N (%)	absent N (%)	present N (%)
Long-Term Experience				
Schoolwork Problems	28 (46.67)	7 (11.67)	20 (33.33)	5 (8.33)
Friendship Problems	32 (53.33)	3 (5.00)	22 (36.67)	3 (5.00)
Family Problems	16 (26.67)	19 (31.67)	19 (31.67)	6 (10.00)

The results in Table 6.3.5g show that the co-twins of the MZ probands were no more likely to report schoolwork and friendship problems than the co-twins of the DZ probands. However, they were more likely to report family problems (31.67% vs. 10.00%) which is indicative of there being shared genetic influences on presence or absence of family relationship problems and caseness for depression. This seems a little counter-intuitive as the family relationship problems did not appear to be heritable from the concordance rates. However, as was seen earlier, even though genetic factors were not significant in the univariate analysis of anxiety, it was genetic factors alone which accounted for the co-occurrence of depression and anxiety. Thus it may be that genetic factors are accounting for the association between family relationship problems and depression, even though the former appear not to be

highly heritable. The family relationship problem LTEs were not divided into those independent of and those dependent on the child's behaviour, as it was of interest simply to look at the relationship between the presence or absence of such problems and caseness for depression or anxiety. For this reason there could be several interpretations of the shared genetic factors between depressive caseness and family relationship problems. The most direct possibility is that genetic factors in the child are responsible for both the depression and the family relationship problems, and that the association is therefore an active gene-environment correlation. However a less direct possibility is that the genetic factors which the child shares with other members of the family are responsible for depression in the child, and for the family relationship problems that may not even directly involve the child. Such a possibility would be another example of a passive gene-environment correlation.

In conclusion, this section has demonstrated that the associations between anxiety and depression and various measures of life events and LTEs are not due to sex or age. However, it does appear that there may be genetic factors that influence both high scores on the depression dimension and the report of loss events and negative LTEs that are independent of the child, and family relationship problems. Thus genes may be acting as confounding factors in the associations between depression and these variables.

Chapter 7: Discussion of Main Results and Conclusions

In this section the results relating to the hypotheses outlined in section 4.2 will be reviewed. Following this is a discussion of the limitations of the study. Finally, the implications of these results and suggestions for future research are presented.

Section 7.1: Producing Refined Measures of Depression and Anxiety

The first hypothesis in this study related to the finding that measures of self-reported depressive and anxious symptoms from children and adolescents tend to be very highly correlated (Norvell, Brophy, & Finch, 1985; Ollendick & Yule, 1990). This was hypothesised to be due in part to the high proportion of overlapping items on these measures. A recent confirmatory factor analysis of 9 self-report measures of depression and anxiety in children found that a two factor model fitted the data better than a one factor model, suggesting that it is possible to distinguish between these two types of symptom (Crowley & Emerson 1996). Thus it was predicted that while the CDI and STAIC-Trait total scores would be highly correlated, if the items measuring anxiety could be removed from the measure of depression and the items pertaining to depression removed from the measure of anxiety then purer, less correlated symptom scores could be created. Using a factor analysis such factors were identified, which only correlated by 0.27, as compared to a correlation of 0.67 between the CDI and STAIC-Trait total scores. This suggests that it is possible to distinguish more clearly between depressive and anxious symptoms from self-report by children and adolescents, and that self-report measures should in future be limited to those symptoms that are central to the condition of interest.

In clarifying these factors the clinical relevance of the data was not reduced from that of the original questionnaire total scores as a child could still score highly on both factors. However it was made possible for the child to score highly on just one measure, and thus it was possible to discriminate more clearly between children with depressive symptoms alone, children with anxious symptoms alone and children with mixed depressive and anxious symptoms.

The prevalence studies reviewed earlier found that adolescents tend to express higher levels of depression than children, and that girls tend to express higher levels of depressive symptoms than boys. This was also the case in the current study in that the adolescents and the girls were more depressed than the children and the boys. The literature on age-related changes in level of anxiety symptoms is less clear, but it does appear that girls tend to be more anxious than boys. In this data set, the girls were found to be more anxious than the boys, and there was also a significant effect of age-group, with the children being significantly more anxious than the adolescents.

Section 7.2: Genetic Analyses of Depressive and Anxious Symptoms

The second hypothesis related to the replication of the univariate genetic analyses of depressive and anxious symptoms. The data from this study are in line with other published data (Rende et al. 1993, Thapar & McGuffin 1994a, 1994b) in that the model of best fit for both measures of depressive symptoms (CDI total score and depression dimensions score) included additive genetic and non-shared environmental factors, whereas anxiety symptoms (STAIC-Trait score and anxiety dimension score) were best predicted by common environmental and non-shared environmental factors. This means that while genetic factors accounted for the within-pair similarity for depressive symptoms,

it was the common environment that accounted for within pair similarity for anxiety symptoms. As the symptoms of anxiety assessed in child report measures tend to reflect OAD rather than PD, it is interesting to note that the adult literature suggests that while PD is highly heritable, GAD appears not to be strongly governed by genetic factors (Torgersen 1990; Andrews, Stewart, Allen, & Henderson 1990; Kendler, Neale, Kessler, Heath, & Eaves 1992c).

In addressing the aetiology of anxiety and depression symptom scores at this level, there was little difference between the results from the dimensions and those from the total scale scores, suggesting that the refining of these measures did not alter the aetiological factors involved in individual differences in depressive and anxious symptoms. However, while the extremes analyses revealed substantial group heritability and negligible group common environmentality for the depression dimension, as compared to substantial group common environmentality but minimal group heritability for the anxiety dimension, extreme scores on the CDI and STAIC-Trait had less distinct aetiologies. Thus the use of these dimensions allowed for the identification of more distinct aetiologies when the extremes were considered. Furthermore, the factors involved in scoring at the extreme on either of these variables reflected those influencing individual differences in the normal range, suggesting that depressive and anxious symptoms as measured in this way are on aetiological continua as predicted in the third hypothesis. This is also in line with previous analyses of depression and fear symptoms in which the values of heritability of individual differences were not found to be significantly different from the values for group heritability (Rende, Plomin, Reiss, & Hetherington 1993; Stevenson, Batten, & Cherner 1992). This is particularly important when considering the generalizability of these aetiological results to the more sensitive and clinically relevant area of disorders.

The principle purpose of this study was to investigate the nature of the shared and specific aetiological factors involved in depressive and anxious symptoms in children and adolescents. The fourth hypothesis was that while a shared

genetic factors would account for the correlation between depression and anxiety, the environmental factors would be specific to each type of symptom. For the depression and anxiety dimensions this was found to be the case. The correlation between the two variables was entirely accounted for by a shared genetic factor, and the specific manifestation of the symptoms was predicted only by environmental influences, thus the genetic correlation was 1.0. For the depression dimension the environmental influences were all non-shared factors, whereas for the anxiety dimension, common environmental influences were also predictive of variance in addition to non-shared environmental influences. Crucially, the common environment factor did not account for covariance between these dimensions, such influences were specific to anxiety. In contrast, for the CDI and STAIC-Trait scores, although the genetic correlation was also 1.0, there was in addition to the shared genetic factor a specific environment factor shared by these two variables. This suggests that certain types of non-shared environmental influence predict variance in both depressive and anxious symptomatology as measured by the CDI and STAIC-Trait respectively. Thus while the shared genetic factor for the depression and anxiety dimensions accounted for 100% of the correlation between these scores, the genetic factor shared between the CDI and STAIC-Trait only accounted for 67% of the correlation between these variables. These results confirm the distinction drawn between the depression and anxiety dimensions and support the hypothesis that genetic factors would predict the covariance between depression and anxiety, but that it would be environmental influences that would result in the specific manifestation of the symptomatology. The finding of a shared genetic factor for the depression and anxiety dimensions remained when several different models were tested.

This shared genetic factor may seem surprising considering the lack of a significant genetic factor for anxiety in the univariate genetic analyses. However, in the full model from this analysis the genetic factor accounted for 10% of the variance. As discussed below this sample was not large enough to have the power to find a common environment term as small as this to be

significant, but the role of this genetic factor became significant in the bivariate analysis. It must be noted that there was some evidence for this finding of a shared genetic factor only applying to the children, and not to the adolescents. This will be discussed further below.

These results parallel in children the findings of Kendler's team (Kendler, Heath, Martin, & Eaves 1987; Kendler, Neale, Kessler, Heath, & Eaves 1992e; Roy, Neale, Pedersen, Mathe, & Kendler 1995) who identified shared genetic factors for depressive and anxious symptoms and disorders in adults, and non-shared environmental factors that were specific to each state. However, the current measures were symptom counts rather than diagnoses, and as such these results relate to dimensions of symptomatology rather than categorical disorders. The extension of these results to the disorder level in children and adolescents will be important, but for two reasons it is likely that these findings will hold for disorders. First, in the adult data the same model best fitted the data at both the symptom and disorder level (Kendler, Heath, Martin, & Eaves 1987; Kendler, Neale, Kessler, Heath, & Eaves 1992e). Second, these symptoms have been shown to be on etiological continua, with extreme group membership being governed by similar factors to those that predict variation in the normal range. Thus the aetiological processes resulting in the depressive and anxious symptoms and their co-occurrence are also likely to result in depressive and anxiety disorders and comorbidity of the two.

A further hypothesis regarding the explanation of the correlation between depressive and anxious symptoms tested in this data set was that one type of symptomatology caused the other. In such a model, either depression accounts for some of the variance in anxiety or vice versa. Both models were tested, and it was found that the model in which depression accounted for variance in anxiety fitted the data better. In the Neale and Kendler (1995) paper from which these models were taken, it was found that the model in which MD accounted for variance in GAD fitted the data better than the model in which GAD accounted for variance in MD. As there is considerable evidence to

suggest that the temporal relationship between these two is such that anxiety tends to precede depression, these are somewhat surprising findings. However, in the current data set, the final model from the Cholesky decomposition, in which the shared genetic factor entirely accounted for the correlation between the two types of symptom, fit the data significantly better than either of the two causal models. In Chapter 4 several models were offered to account for the comorbidity of depression and anxiety and the correlation between depressive and anxious symptoms. These results provide strong evidence for the hypothesis that the co-occurrence of these symptoms is due to shared aetiological factors, and more specifically to shared genetic factors.

Although there were no specific hypotheses regarding the effects of age and sex on the aetiology of these symptoms, the findings are discussed here as they form part of the interpretation of the associations between the measures of environmental influences and depressive and anxious symptomatology. The division of the sample by sex or age-group in order to investigate the aetiology of depressive and anxious symptoms in these sub-groups revealed no significant effects of sex, but some significant effects of age-group. The results for the children and adolescents reported here can only be regarded as preliminary due to the relatively small sample sizes resulting in low power to distinguish between alternative models. It is necessary to replicate these findings on a larger sample so that age-effects can be further investigated.

In the univariate genetic analyses only one significant sex or age-group effect was found, which was that for the depression scores the adolescents required a full ACE model whereas the children only required an AE model. However, for the anxiety factor there was an effect of age-group which although not significant also implicated an increased role for common environment in the adolescents as compared to the children. In addition to this the bivariate results revealed that while the correlation between depression and anxiety in the children was entirely due to a shared genetic factor, in the adolescents it was entirely due to a shared common environment factor. This suggests a role for

common environment influences in adolescents that impacts on both depressive and anxious symptomatology.

What may seem unclear from this is why adolescents are less anxious but more depressed if the effects of these common environmental influences are entirely shared. This finding is not easily resolved from the current data, but it must be re-iterated that sample sizes were small in these analyses and thus the power to detect specific factors over and above the shared factors was low. It is possible that additional common environmental influences specific to anxiety would be identified in a larger sample of adolescents.

Section 7.3: Environmental Factors, Depression and Anxiety

The results from the previously published bivariate genetic analyses of depression and anxiety data (Kendler, Heath, Martin, & Eaves 1987; Kendler, Neale, Kessler, Heath, & Eaves 1992e) led to the consideration of potential environmental influences that might result in the specific manifestation of depression as opposed to anxiety. Research into life events both in adult women (Brown & Harris 1978a) and in children (Goodyer et al. 1985, 1986, 1987; Loss et al. 1995) has shown that recent stressful life events and adverse situations are associated with depressive and anxious symptoms and disorders. In particular, the work of Finlay-Jones and Brown (1981) suggested specificity of certain types of life events, in that loss and danger events were found to be associated with depression and anxiety respectively.

In the current study the association of independent negative life events with depressive and anxious symptoms was investigated, as was the specificity of loss and danger events to depression and anxiety respectively. The results from these analyses suggested that independent negative events as a broad

category were not significantly associated with depression or anxiety. This may be because the cases were individuals who scored more than one standard deviation above the mean on a symptom count rather than being clinical cases. However there was some evidence for the specificity of loss events to depression and strong evidence for the specificity of danger events to anxiety. This confirmed the hypothesis that event types can be identified which are associated with only one type of symptomatology.

By comparing results from the independent sample t-tests and the matched pair t-tests, it was possible to identify whether the life event or LTE type being investigated was acting as a common environment or as a specific environment factor. From these analyses the effects of danger events on anxious symptomatology were shown to be individual specific, making members of a pair different from one another for proband status on anxiety. Thus this event category can be seen as an example of the specific environment factor that was revealed in the bivariate genetic analyses as predicting variance in anxiety scores alone.

In contrast, the effects of loss events on depression scores appeared to be shared within the pair. This result is surprising as the common environment was not a significant influence on depression scores univariately or in the bivariate analysis. However, as shown in Table 6.2.1.1a, the C term accounted for 11% of the variance in individual differences in depression scores in the full model. In addition, as loss events tended to refer to loss of a grandparent or family friend or to other shared losses, it is not surprising that this variable had the effect of making depression scores similar within a pair. Furthermore although the tests of associations between life event and LTE measures and depression and anxiety used proband and control group or proband and co-twin comparisons in order to infer common and specific environmental influences these influences were only inferred, and their associations were with proband status rather than with individual differences in scores. Finally, it must be noted that there was at best only moderate support for the hypothesis that

loss events were associated with depression scores, and the t-tests showed only a weak association, thus loss events would not be expected to account for a large proportion of the variance in depression scores.

As well as considering the influence of acute stressful life events on internalising symptoms, this study investigated the role of ongoing stressors or long-term experiences (LTEs) lasting four weeks or more. Independent negative LTEs acted in a non-specific way influencing levels of both depression and anxiety. These associations were not significant in the analysis of the discordant pairs suggesting that these experiences were shared within twin pairs and as such were common environmental influences. This at first seemed problematic in the light of the strong evidence for there being shared genetic rather than shared common environmental factors accounting for the correlation between depression and anxiety. However as discussed above, when the sample was broken down into children and adolescents, the covariance between the depression and anxiety scores from the adolescents required the inclusion of a shared common environment influence in the model. This result was particularly interesting in the light of the finding that adolescents report more LTEs. Taken together these results suggest that for adolescents the effects of the independent negative LTEs are not only shared within the twin pair, but also account for variance in both depression and anxiety and for covariance between the two.

Two types of LTE (schoolwork stresses and family relationship problems) were identified as being associated with depression when considering the whole sample, but not when the discordant pairs were analysed, suggesting that these factors were either governed by shared genes or were part of the common environment. As the schoolwork stresses variable included GCSEs, this as well as family relationship problems, which may be more common in families of adolescents, could be common environment factors that are contributing to the increase in depressive symptoms in adolescents. It is

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events, and schoolwork problems). Furthermore, bivariate analyses indicated that some of the associations between environmental influences and symptomatology may be due to shared genetic influences. Specifically, although family relationship problems were not found to be highly heritable, they were reported 3 times as often in the co-twins of MZ depressed probands than in the co-twins of DZ depressed probands. This suggests that family relationship problems are influenced by genetic factors shared with depression. These results must be regarded as highly exploratory as the sample sizes involved in these analyses were very small. However, it is interesting to note that a study by Bergeman, Plomin, Pederson, and McClearn (1991) found a shared genetic factor for perceived social support and depression in older adults. This is an area which warrants considerable future attention from behaviour genetics.

Having reviewed the main findings of this study, it is necessary to discuss the limitations of this project in order to assess the implications of these results.

Section 7.4: Limitations of the Study

As the limitations of behaviour genetics research using twins have been discussed in detail already these will not be re-considered here. Instead, the limitations specific to this project will be considered.

The primary limitation of this study is the sample size and resulting problems of power. Although at the first stage there were 395 same-sex pairs, this is not a large sample size when conducting model-fitting to behaviour genetic models. In particular, the sample sizes used when investigating age-group and sex effects were especially small (between 79 and 122 in each group). While for phenotypes which are highly familial these sample sizes are perfectly adequate, for less familial phenotypes such as internalising symptoms it

becomes harder to distinguish between common environment and additive genetic factors. This means that the results for the sub-groups cannot be interpreted with the same confidence as the results for the whole sample. With the sample size of 395 pairs, and familiarity of depressive and anxious symptoms at approximately 50%, this study had 80% power to detect A terms of 44% or more, and C terms of 36% or more (Neale & Cardon 1992).

At the second stage the sample size was 90 pairs in total, or 180 children and adolescents. In the independent samples t-tests the numbers for the case and control groups were 60 and 120 respectively for the depression dimension and 69 and 111 for the anxiety dimension respectively. A sample of 50 individuals per group is required to detect medium effect sizes (.50) at a power of 80%, and an α level of .10 (ie. 1-tailed p of .05) (Cohen 1992). However to detect small effect sizes (.20) there would need to be 310 individuals in each group. Due to time constraints a sample of this size was unfeasible in the current study, which therefore was only able to detect medium to large effect sizes. When the sample was reduced to those discordant for depression or anxiety the groups were only 29 and 37 pairs respectively. Although the power of paired samples t-tests is greater than that of independent samples t-tests, these sample sizes were such that effect sizes as large as 0.3 were not always significant. Furthermore, as there were multiple t-tests in this analysis it could be argued that a Bonferroni correction should have been undertaken or a MANOVA used for the analysis. However, as there were at most only 4 t-tests per hypothesis, a Bonferroni correction was not regarded as necessary. A MANOVA was not used as this is a cumbersome method of analysis.

An associated problem was that due to the small sample size there was not enough variance in the background factors assessed in the PACE (eg. early hospitalisation, early illness, loss of family member excluding those in the preceding 12 months, person:room ratio, parental unemployment) to conduct an analysis of these variables. As these factors were those that were most likely to act as vulnerability factors as described by Brown and Harris (1978b),

the role of such vulnerability factors in child and adolescent depression and anxiety could not be tested.

A second limitation of this study is that the sample is a volunteer register of twins and includes an over-representation of the middle classes as compared to the general population. This limits the generalisability of the results and emphasises the need for replication with a larger more representative sample.

A further limitation of these data is that they measure only symptom counts and the “probands” or “cases” were selected for being above a cut-off of one standard deviation above the mean on the dimensions of depression and anxiety. For this reason the associations between life event and LTE measures and proband status cannot be generalised to clinical cases, but refer rather to high scorers within the normal population. In addition, as the measures of symptoms were from self-report measures completed at home the data could have been contaminated by the twins completing their questionnaires together. If this were the case one would expect the correlation for the pairs to be similar for both depression and anxiety, and for both MZ and DZ pairs. This was not the case, and thus the data are regarded as a reasonably accurate reflection of individual symptomatology.

Finally, as this study was cross-sectional there can be no discussion of developmental trends in symptomatology or of true causality. In order to draw conclusions as to how symptoms of anxiety and depression develop throughout childhood and adolescence longitudinal data would be required. Furthermore, for the same reason there could not be a rigorous test of a causal relationship between depression and anxiety or between life events, LTEs and depressive and anxious symptoms. The associations found between certain types of life events and LTEs and proband status for depression and anxiety can only be interpreted as associations. No attempt was made to date the onset of the symptoms assessed in this study as this was found to be impractical. However, as the life events and LTE categories investigated were largely those that were

independent of the behaviour of the child, these results were compatible with the hypothesis that these environmental influences were acting in a causal manner.

Section 7.5: Implications of the Study

The results from this study suggest that while depressive and anxious symptomatology are correlated there is particular value in deriving relatively pure measures of each component. These allow a more incisive investigation both of the distinctive specific aetiologies of anxious and depressive symptoms, and of the aetiological factors they have in common. The principal implication of this study is that as the genetic factors involved in the aetiology of depressive and anxious symptoms in children and adolescents appear to be shared, the biological mechanisms are also likely to be shared.

One possible candidate that might be mediating the effects of the shared genetic factor is the personality construct "harm avoidance" (HA) (Cloninger 1986) which has been found not only to be related both to depression and anxiety in a variety of samples (Brown, Svrakic, Przybeck, & Cloninger, 1992; Mulder, Joyce, & Cloninger, 1994; Svrakic, Przybeck, & Cloninger, 1992), but also to be moderately heritable (Heath, Cloninger, & Martin, 1994). Furthermore, HA total score has been found to be predictive of treatment outcome in depressed subjects (Joyce, Mulder, & Cloninger, 1994a; Nelson & Cloninger, 1995). Cloninger (1986) reviewed several studies of metabolites of serotonin and concluded that there was substantial evidence to support his hypothesis that HA would be associated with high basal levels of serotonergic activity. As discussed earlier the evidence from biological studies can be interpreted as consistent with either increased or decreased activity in this system in depressed subjects (Rogeness, Javors, & Pliszka, 1992). In addition, recent evidence from molecular genetics suggests that there is an association between the serotonin transporter gene on chromosome 17 and depressive

disorders (Ogilvie et al. 1996). Furthermore, there is some evidence that both adults and children with anxiety disorders respond to imipramine (which is thought to act in part by inhibiting the reuptake of serotonin) (Strange 1992; Gittelman-Klein & Klein 1971; Deltito & Hahn; Ballenger, Carek, Steele, & Cornish-McTighe 1989). It seems plausible that serotonin functioning may be mediating the relationship between genetic factors on HA, depression and anxiety, but this is an area that requires clarification.

The second implication of these results is that while the genetic factors for depressive and anxious symptoms in children and adolescents are shared, the environmental influences are specific, and some of these have been identified. It may be that environmental influences such as friendship problems act as triggers to the underlying genetic influence resulting in the outcome of depression. Furthermore, as friendship problems and recent stressful life events were found to interact in their effects on depressive symptoms, both exerting an independent additive effect on outcome, they are clearly an area of environmental influence central to depressive symptoms. As such, friendship problems might be an area to target in aiming to reduce depressive symptomatology.

In conclusion, future research in this area should distinguish more clearly between self-reported symptoms of depression and anxiety in children. Furthermore, the genetic analyses conducted here would benefit from being replicated with data on depressive and anxious disorders. Finally, longitudinal data would allow one to test for developmental trends in symptomatology, and would also allow for more rigorous testing of a causal relationship between depression and anxiety, between life events, LTEs, depression and anxiety.

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Appendix 1: Stage 1 Measures

CDI

Name _____ Date of Birth _____ ID _____

Young people sometimes have different feelings and ideas. This form lists the feelings and ideas in groups of three. From each group, pick one sentence that describes best how you have been feeling in the last two weeks. After you have picked a sentence from the first group, go on to the next group.

There are no wrong or right answers, just pick the sentence that describes the way that you have been feeling recently. Put a tick next to the sentence that describes you best.

Remember, describe how you have been feeling in the last two weeks.

1. I am sad once in a while
..... I am sad many times
..... I am sad all the time
2. Nothing will ever work out for me
..... I am not sure if things will work out for me
..... Things will work out for me O.K.
3. I do most things O.K.
..... I do many things wrong
..... I do everything wrong
4. I have fun in many things
..... I have fun in some things
..... Nothing is fun at all
5. I am bad all the time
..... I am bad many times
..... I am bad once in a while
6. I think about bad things happening to me once in a while
..... I worry that bad things will happen to me
..... I am sure that terrible things will happen to me
7. I hate myself
..... I do not like myself
..... I like myself

PTO

Remember, describe how you have been feeling in the past two weeks.

8. All bad things are my fault
..... Many bad things are my fault
..... Bad things are not usually my fault
9. I do not think about killing myself
..... I think about killing myself but would not do it
..... I want to kill myself
10. I feel like crying every day
..... I feel like crying many days
..... I feel like crying once in a while
11. Things bother me all the time
..... Things bother me many times
..... Things bother me once in a while
12. I like being with people
..... I do not like being with people many times
..... I do not want to be with people at all
13. I cannot make up my mind about things
..... It is hard to make up my mind about things
..... I make up my mind about things easily
14. I look O.K.
..... There are some bad things about my looks
..... I look ugly
15. I have to push myself all the time to do my school work
..... I have to push myself many times to do my school work
..... Doing schoolwork is no big problem
16. I have trouble sleeping at night
..... I have trouble sleeping many nights
..... I sleep pretty well
17. I am tired once in a while
..... I am tired many times
..... I am tired all the time
18. Most days I do not feel like eating
..... Many days I do not feel like eating
..... I eat pretty well

PTO

Remember, describe how you have been feeling in the last two weeks.

19. I do not worry about aches and pains
..... I worry about aches and pains many times
..... I worry about aches and pains all the time
20. I do not feel alone
..... I feel alone many times
..... I feel alone all the time
21. I never have fun at school
..... I have fun at school only once in a while
..... I have fun at school many times
22. I have plenty of friends
..... I have some friends here but I wish I had more
..... I do not have many friends
23. My school work is all right
..... My school work is not as good as before
..... I do very badly in subjects I used to be good in
24. I can never be as good as other young people
..... I can be as good as other young people if I want to
..... I am just as good as other young people
25. Nobody really loves me
..... I am not sure if anybody really loves me
..... I am sure that somebody loves me
26. I usually do what I am told
..... I do not do what I am told most times
..... I never do what I am told
27. I get along with people
..... I get into fights many times
..... I get into fights all the time

THANK-YOU FOR FILLING IN THIS FORM

280

275

HOW-I-FEEL QUESTIONNAIRE
STAIC-STATE

NAME _____ DATE OF BIRTH _____ ID _____

A number of statements which boys and girls use to describe themselves are given below. Read each statement carefully and decide how you feel *right now*. Then put an X in the box in front of the word or phrase which best describes how you feel. There are no wrong or right answers. Do not spend too long on any one statement. Remember, find the word or phrase which best describes how you feel right now, *at this very moment*.

1. I feel ☐ very calm ☐ calm ☐ not calm
2. I feel ☐ very upset ☐ upset ☐ not upset
3. I feel ☐ very pleasant ☐ pleasant ☐ not pleasant
4. I feel ☐ very nervous ☐ nervous ☐ not nervous
5. I feel ☐ very jittery ☐ jittery ☐ not jittery
6. I feel ☐ very rested ☐ rested ☐ not rested
7. I feel ☐ very scared ☐ scared ☐ not scared
8. I feel ☐ very relaxed ☐ relaxed ☐ not relaxed
9. I feel ☐ very worried ☐ worried ☐ not worried
10. I feel ☐ very satisfied ☐ satisfied ☐ not satisfied
11. I feel ☐ very frightened ☐ frightened ☐ not frightened
12. I feel ☐ very happy ☐ happy ☐ not happy
13. I feel ☐ very sure ☐ sure ☐ not sure
14. I feel ☐ very good ☐ good ☐ not good
15. I feel ☐ very troubled ☐ troubled ☐ not troubled
16. I feel ☐ very bothered ☐ bothered ☐ not bothered
17. I feel ☐ very nice ☐ nice ☐ not nice
18. I feel ☐ very terrified ☐ terrified ☐ not terrified
19. I feel ☐ very mixed-up ☐ mixed-up ☐ not mixed-up
20. I feel ☐ very cheerful ☐ cheerful ☐ not cheerful

PLEASE TURN OVER

HOW-I-FEEL QUESTIONNAIRE
STAIC-TRAIT

Please read these instructions carefully they are different from the first page.

A number of statements which boys and girls use to describe themselves are given below. Read each statement and decide if it is *hardly-ever*, or *sometimes*, or *often* true for you normally. Then for each statement put an X in the box in front of the word that seems to describe you best. There are no right or wrong answers. Do not spend too much time on any one statement. Remember, choose the word which seems to describe how you **usually** feel.

1. I worry about making mistakes.....[] hardly-ever [] sometimes [] often
2. I feel like crying.....[] hardly-ever [] sometimes [] often
3. I feel unhappy.....[] hardly-ever [] sometimes [] often
4. I have trouble making up my mind.....[] hardly-ever [] sometimes [] often
5. It is difficult for me to face problems.....[] hardly-ever [] sometimes [] often
6. I worry too much.....[] hardly-ever [] sometimes [] often
7. I get upset at home.....[] hardly-ever [] sometimes [] often
8. I am shy.....[] hardly-ever [] sometimes [] often
9. I feel troubled.....[] hardly-ever [] sometimes [] often
10. Unimportant thoughts run through
my mind and bother me.....[] hardly-ever [] sometimes [] often
11. I worry about school.....[] hardly-ever [] sometimes [] often
12. I have trouble deciding what to do.....[] hardly-ever [] sometimes [] often
13. I notice my heart beats fast.....[] hardly-ever [] sometimes [] often
14. I am secretly afraid.....[] hardly-ever [] sometimes [] often
15. I worry about my parents.....[] hardly-ever [] sometimes [] often
16. My hands get sweaty.....[] hardly-ever [] sometimes [] often
17. I worry about things that may happen.....[] hardly-ever [] sometimes [] often
18. It is hard for me to fall asleep at night.....[] hardly-ever [] sometimes [] often
19. I get a funny feeling in my stomach.....[] hardly-ever [] sometimes [] often
20. I worry about what others think of me.....[] hardly-ever [] sometimes [] often

THANK-YOU FOR YOUR HELP

CHILD BEHAVIOR CHECKLIST FOR AGES 4-18

For Office Use Only
ID #

Please Print

CHILD'S FULL NAME FIRST MIDDLE LAST		PARENTS' USUAL TYPE OF WORK, even if not working now. (Please be specific—for example, auto mechanic, high school teacher, homemaker, laborer, lathe operator, shoe salesman, army sergeant.)	
SEX ☐ Boy ☐ Girl	AGE	FATHER'S TYPE OF WORK	
TODAY'S DATE Mo. Date Yr.		CHILD'S BIRTHDATE Mo. Date Yr.	MOTHER'S TYPE OF WORK
GRADE IN SCHOOL	Please fill out this form to reflect your view of the child's behavior even if other people might not agree. Feel free to print additional comments beside each item and in the spaces provided on page 2.		THIS FORM FILLED OUT BY: ☐ Mother (full name) ☐ Father (full name) ☐ Other—name & relationship to child:
NOT ATTENDING SCHOOL ☐			

I. Please list the sports your child most likes to take part in. For example: swimming, baseball, skating, skate boarding, bike riding, fishing, etc. ☐ None	Compared to others of the same age, about how much time does he/she spend in each?	Compared to others of the same age, how well does he/she do each one?
a. _____	Don't Know Less Than Average Average More Than Average	Don't Know Below Average Average Above Average
b. _____	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐
c. _____	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐
II. Please list your child's favorite hobbies, activities, and games, other than sports. For example: stamps, dolls, books, piano, crafts, cars, singing, etc. (Do not include listening to radio or TV.) ☐ None	Compared to others of the same age, about how much time does he/she spend in each?	Compared to others of the same age, how well does he/she do each one?
a. _____	Don't Know Less Than Average Average More Than Average	Don't Know Below Average Average Above Average
b. _____	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐
c. _____	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐
III. Please list any organizations, clubs, teams, or groups your child belongs to. ☐ None	Compared to others of the same age, how active is he/she in each?	
a. _____	Don't Know Less Active Average More Active	
b. _____	☐ ☐ ☐ ☐	
c. _____	☐ ☐ ☐ ☐	
IV. Please list any jobs or chores your child has. For example: paper route, babysitting, making bed, working in store, etc. (Include both paid and unpaid jobs and chores.) ☐ None	Compared to others of the same age, how well does he/she carry them out?	
a. _____	Don't Know Below Average Average Above Average	
b. _____	☐ ☐ ☐ ☐	
c. _____	☐ ☐ ☐ ☐	

203
278

Please Print

V. 1. About how many close friends does your child have? ☐ None ☐ 1 ☐ 2 or 3 ☐ 4 or more
(Do not include brothers & sisters)

2. About how many times a week does your child do things with any friends outside of regular school hours?
(Do not include brothers & sisters) ☐ Less than 1 ☐ 1 or 2 ☐ 3 or more

VI. Compared to others of his/her age, how well does your child:

	Worse	About Average	Better	
a. Get along with his/her brothers & sisters?	☐	☐	☐	☐ Has no brothers or sisters
b. Get along with other kids?	☐	☐	☐	
c. Behave with his/her parents?	☐	☐	☐	
d. Play and work alone?	☐	☐	☐	

VII. 1. For ages 6 and older—performance in academic subjects. ☐ Does not attend school because _____

Check a box for each subject that child takes

	Failing	Below Average	Average	Above Average
a. Reading, English, or Language Arts	☐	☐	☐	☐
b. History or Social Studies	☐	☐	☐	☐
c. Arithmetic or Math	☐	☐	☐	☐
d. Science	☐	☐	☐	☐
e. _____	☐	☐	☐	☐
f. _____	☐	☐	☐	☐
g. _____	☐	☐	☐	☐

Other academic subjects—for example: computer courses, foreign language, business. Do not include gym, shop, driver's ed., etc.

2. Does your child receive special remedial services or attend a special class or special school? ☐ No ☐ Yes—kind of services, class, or school: _____

3. Has your child repeated any grades? ☐ No ☐ Yes—grades and reasons: _____

4. Has your child had any academic or other problems in school? ☐ No ☐ Yes—please describe: _____

When did these problems start? _____

Have these problems ended? ☐ No ☐ Yes—when? _____

Does your child have any illness or disability (either physical or mental)? ☐ No ☐ Yes—please describe: _____

What concerns you most about your child? _____

Please describe the best things about your child: _____

Below is a list of items that describe children and youth. For each item that describes your child now or within the past 6 months, please circle the 2 if the item is *very true or often true* of your child. Circle the 1 if the item is *somewhat or sometimes true* of your child. If the item is *not true* of your child, circle the 0. Please answer all items as well as you can, even if some do not seem to apply to your child.

Please Print

0 = Not True (as far as you know) 1 = Somewhat or Sometimes True 2 = Very True or Often True

0 1 2	1.	Acts too young for his/her age	0 1 2	31.	Fears he/she might think or do something bad
0 1 2	2.	Allergy (describe): _____	0 1 2	32.	Feels he/she has to be perfect
		_____	0 1 2	33.	Feels or complains that no one loves him/her
0 1 2	3.	Argues a lot	0 1 2	34.	Feels others are out to get him/her
0 1 2	4.	Asthma	0 1 2	35.	Feels worthless or inferior
0 1 2	5.	Behaves like opposite sex	0 1 2	36.	Gets hurt a lot, accident-prone
0 1 2	6.	Bowel movements outside toilet	0 1 2	37.	Gets in many fights
0 1 2	7.	Bragging, boasting	0 1 2	38.	Gets teased a lot
0 1 2	8.	Can't concentrate, can't pay attention for long	0 1 2	39.	Hangs around with others who get in trouble
0 1 2	9.	Can't get his/her mind off certain thoughts; obsessions (describe): _____	0 1 2	40.	Hears sounds or voices that aren't there (describe): _____
0 1 2	10.	Can't sit still, restless, or hyperactive	0 1 2	41.	Impulsive or acts without thinking
0 1 2	11.	Clings to adults or too dependent	0 1 2	42.	Would rather be alone than with others
0 1 2	12.	Complains of loneliness	0 1 2	43.	Lying or cheating
0 1 2	13.	Confused or seems to be in a fog	0 1 2	44.	Bites fingernails
0 1 2	14.	Cries a lot	0 1 2	45.	Nervous, highstrung, or tense
0 1 2	15.	Cruel to animals	0 1 2	46.	Nervous movements or twitching (describe): _____
0 1 2	16.	Cruelty, bullying, or meanness to others			_____
0 1 2	17.	Day-dreams or gets lost in his/her thoughts	0 1 2	47.	Nightmares
0 1 2	18.	Deliberately harms self or attempts suicide	0 1 2	48.	Not liked by other kids
0 1 2	19.	Demands a lot of attention	0 1 2	49.	Constipated, doesn't move bowels
0 1 2	20.	Destroys his/her own things	0 1 2	50.	Too fearful or anxious
0 1 2	21.	Destroys things belonging to his/her family or others	0 1 2	51.	Feels dizzy
0 1 2	22.	Disobedient at home	0 1 2	52.	Feels too guilty
0 1 2	23.	Disobedient at school	0 1 2	53.	Overeating
0 1 2	24.	Doesn't eat well	0 1 2	54.	Overtired
0 1 2	25.	Doesn't get along with other kids	0 1 2	55.	Overweight
0 1 2	26.	Doesn't seem to feel guilty after misbehaving		56.	Physical problems without known medical cause:
0 1 2	27.	Easily jealous	0 1 2	a.	Aches or pains (not stomach or headaches)
0 1 2	28.	Eats or drinks things that are not food -- don't include sweets (describe): _____	0 1 2	b.	Headaches
		_____	0 1 2	c.	Nausea, feels sick
0 1 2	29.	Fears certain animals, situations, or places, other than school (describe): _____	0 1 2	d.	Problems with eyes (not if corrected by glasses) (describe): _____
		_____	0 1 2	e.	Rashes or other skin problems
0 1 2	30.	Fears going to school	0 1 2	f.	Stomachaches or cramps
		_____	0 1 2	g.	Vomiting, throwing up
		_____	0 1 2	h.	Other (describe): _____

Please Print

0 = Not True (as far as you know) 1 = Somewhat or Sometimes True 2 = Very True or Often True

0	1	2	57.	Physically attacks people	0	1	2	84.	Strange behavior (describe): _____
0	1	2	58.	Picks nose, skin, or other parts of body (describe): _____					_____
				_____	0	1	2	85.	Strange ideas (describe): _____
0	1	2	59.	Plays with own sex parts in public					_____
0	1	2	60.	Plays with own sex parts too much	0	1	2	86.	Stubborn, sullen, or irritable
0	1	2	61.	Poor school work	0	1	2	87.	Sudden changes in mood or feelings
0	1	2	62.	Poorly coordinated or clumsy	0	1	2	88.	Sulks a lot
0	1	2	63.	Prefers being with older kids	0	1	2	89.	Suspicious
0	1	2	64.	Prefers being with younger kids	0	1	2	90.	Swearing or obscene language
0	1	2	65.	Refuses to talk	0	1	2	91.	Talks about killing self
0	1	2	66.	Repeats certain acts over and over; compulsions (describe): _____	0	1	2	92.	Talks or walks in sleep (describe): _____
				_____					_____
0	1	2	67.	Runs away from home	0	1	2	93.	Talks too much
0	1	2	68.	Screams a lot	0	1	2	94.	Teases a lot
0	1	2	69.	Secretive, keeps things to self	0	1	2	95.	Temper tantrums or hot temper
0	1	2	70.	Sees things that aren't there (describe): _____	0	1	2	96.	Thinks about sex too much
				_____	0	1	2	97.	Threatens people
				_____	0	1	2	98.	Thumb-sucking
0	1	2	71.	Self-conscious or easily embarrassed	0	1	2	99.	Too concerned with neatness or cleanliness
0	1	2	72.	Sets fires	0	1	2	100.	Trouble sleeping (describe): _____
				_____					_____
0	1	2	73.	Sexual problems (describe): _____	0	1	2	101.	Truancy, skips school
				_____	0	1	2	102.	Underactive, slow moving, or lacks energy
				_____	0	1	2	103.	Unhappy, sad, or depressed
0	1	2	74.	Showing off or clowning	0	1	2	104.	Unusually loud
0	1	2	75.	Shy or timid	0	1	2	105.	Uses alcohol or drugs for nonmedical purposes (describe): _____
0	1	2	76.	Sleeps less than most kids	0	1	2	106.	Vandalism
0	1	2	77.	Sleeps more than most kids during day and/or night (describe): _____	0	1	2	107.	Wets self during the day
				_____	0	1	2	108.	Wets the bed
0	1	2	78.	Smears or plays with bowel movements	0	1	2	109.	Whining
0	1	2	79.	Speech problem (describe): _____	0	1	2	110.	Wishes to be of opposite sex
				_____	0	1	2	111.	Withdrawn, doesn't get involved with others
0	1	2	80.	Stares blankly	0	1	2	112.	Worries
0	1	2	81.	Steals at home				113.	Please write in any problems your child has that were not listed above:
0	1	2	82.	Steals outside the home	0	1	2	_____	_____
0	1	2	83.	Stores up things he/she doesn't need (describe): _____	0	1	2	_____	_____
				_____	0	1	2	_____	_____

PLEASE BE SURE YOU HAVE ANSWERED ALL ITEMS.

PAGE 4

TWIN SIMILARITY QUESTIONNAIRE

Please ring the answer that is correct for your twins. If questions 1-6 are difficult to answer because of the twins' age please enter N/A/ for not applicable.

- | | | | | | | |
|--|-----------|-------------------|------------|------------|---|----------|
| 1. Are the twins emotionally attached to each other? | N/A | Strongly | Somewhat | Not at all | | |
| 2. Do the twins have the same friends at the house? | N/A | Share all friends | Share some | Not shared | | |
| 3. Do the twins argue? | N/A | A lot | Sometimes | Not at all | | |
| 4. Do the twins try to be different from one another? | N/A | Yes | A little | Not at all | | |
| 5. Up to what age were the twins dressed alike? | Still are | 8 | 6 | 4 | 2 | Before 2 |
| 6. Has one of the twins ever told you that they should not be dressed the same any more? | N/A | Yes | No | | | |
7. To what extent are the twins similar at the moment for the following:
- | | | | |
|-------------------|------------|----------|---------|
| Height | Not at all | Somewhat | Exactly |
| Weight | Not at all | Somewhat | Exactly |
| Facial appearance | Not at all | Somewhat | Exactly |
| Hair colour | Not at all | Somewhat | Exactly |
| Eye colour | Not at all | Somewhat | Exactly |
| Complexion | Not at all | Somewhat | Exactly |
- | | | |
|--|----|-----|
| 8. Do they look as alike as peas in a pod? | NO | YES |
| 9. Do you ever confuse them? | NO | YES |
| 10. Are they sometimes confused by other people in the family? | NO | YES |
| 11. Is it hard for strangers to tell them apart? | NO | YES |

287
282

Appendix 2: Examples of Rated Life Events and LTEs

Life Events

Female, 13 years old: Left primary school

S had been at the same primary school since the age of 5 and had got on well with all of her class. Most of her class including her best friend were moving to the same senior school as her, as was her twin sister. However she knew when she left that her closest friends including her best friend were not to be in the same class as her in the senior school which had double-entry.

Negative Impact:

Short-term (0-3)	2	Long-term (0-3)	1
------------------	---	-----------------	---

Loss:

Loss of attachment figure (0-3)	2	Loss of an idea (0-3)	0
---------------------------------	---	-----------------------	---

Danger:

Risk of loss of person (0-3)	0	Physical jeopardy (0-3)	0
------------------------------	---	-------------------------	---

Trauma as witness (0-3)	0	Challenge (0-3)	0
-------------------------	---	-----------------	---

Independence:

Independence from **child** (0-1) 0

Independence from **family** (0-1) 0

Note: Independence: Probably or totally independent = 0; Probably or totally behaviour related = 1.

Male, 16 years old: Granddad had a stroke

S was not particularly close to his grandfather and has several closer male relatives. His grandfather suffered a stroke and can't now move in left hand and speaks with difficulty. The stroke was a month before the interview, and the grandfather was still in hospital at the time of the interview.

Negative Impact:

Short-term (0-3)	2	Long-term (0-3)	1
------------------	---	-----------------	---

Loss:

Loss of attachment figure (0-3)	0	Loss of an idea (0-3)	1
---------------------------------	---	-----------------------	---

Danger:

Risk of loss of person (0-3)	2	Physical jeopardy (0-3)	0
------------------------------	---	-------------------------	---

Trauma as witness (0-3)	0	Challenge (0-3)	0
-------------------------	---	-----------------	---

Independence:

Independence from **child** (0-1) 0

Independence from **family** (0-1) 0

Female, 8 years old: Brother had a biopsy

S has one younger brother who is two years old. A lump was found in his neck, and he had to have a biopsy. He was in hospital for a day and had a general anaesthetic. S knew these details but possibly did not understand them. The results of the test arrived within days and were fine.

Negative Impact:

Short-term (0-3)	1	Long-term (0-3)	0
------------------	---	-----------------	---

Loss:

Loss of attachment figure (0-3)	0	Loss of an idea (0-3)	0
---------------------------------	---	-----------------------	---

Danger:

Risk of loss of person (0-3)	1	Physical jeopardy (0-3)	0
------------------------------	---	-------------------------	---

Trauma as witness (0-3)	0	Challenge (0-3)	0
-------------------------	---	-----------------	---

Independence:

Independence from child (0-1)	0
-------------------------------	---

Independence from family (0-1)	0
--------------------------------	---

Male, 15 years old: Fight

S and his twin brother were walking some girls home. One boy had said he wanted a fight the day before but S said he wasn't interested. The next night this boy turned up with a gang of about 10 adolescents. S was hit over the head and a brick was thrown at him. Two other friends were also involved. S's twin brother was not badly hurt - he ran on ahead with the girls to get them home safely. S was later taken to hospital with concussion. There was no permanent damage.

Negative Impact:

Short-term (0-3)	3	Long-term (0-3)	1
------------------	---	-----------------	---

Loss:

Loss of attachment figure (0-3)	0	Loss of an idea (0-3)	1
---------------------------------	---	-----------------------	---

Danger:

Risk of loss of person (0-3)	0	Physical jeopardy (0-3)	2
------------------------------	---	-------------------------	---

Trauma as witness (0-3)	0	Challenge (0-3)	1
-------------------------	---	-----------------	---

Independence:

Independence from child (0-1)	0
-------------------------------	---

Independence from family (0-1)	0
--------------------------------	---

Long-Term Experiences

Male 9 years old: Friendship problems

The only "friends" S reported were 2 years older and were not close. He plays games with them in the playground but that is as far as it goes. He spoke about a lot of pushing and shoving and low key verbal bullying - both by him and to him. He said that the others usually started it but that he'd always fight back. He expressed a wish to have a proper friend who he could talk to about things that were bothering him. At present the only person he confides in is his twin brother, who has his own best friend.

Negative Impact:

Negative impact on child (0-3)	3	Negative impact on family (0-3)	0
--------------------------------	---	---------------------------------	---

Loss:

Loss of attachment figure (0-3)	0	Loss of an idea (0-3)	2
---------------------------------	---	-----------------------	---

Danger:

Risk of loss of person (0-3)	0	Physical jeopardy (0-3)	1
Trauma as witness (0-3)	0	Challenge (0-3)	1

Independence:

Independence from child (0-1)	1
Independence from family (0-1)	0

Female, 13 years old: Father away during the week

S's father was relocated within his company to a location three hours drive from their home. As the job market is insecure, he felt he must take the job, but the family were settled in their area and did not want to move. The father therefore lives in a caravan near work during the week and comes home only a week-ends. The family are quite close and miss the father.

Negative Impact:

Negative impact on child (0-3)	2	Negative impact on family (0-3)	2
--------------------------------	---	---------------------------------	---

Loss:

Loss of attachment figure (0-3)	2	Loss of an idea (0-3)	0
---------------------------------	---	-----------------------	---

Danger:

Risk of loss of person (0-3)	0	Physical jeopardy (0-3)	0
Trauma as witness (0-3)	0	Challenge (0-3)	0

Independence:

Independence from child (0-1)	0
Independence from family (0-1)	1

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Male, 8 years old: Family relationships problem

S and his twin brother clearly dislike each other. They fight constantly, and kick and punch each other frequently. The atmosphere between them was one of aggressiveness and dislike. The mother did not appear to be trying to reduce the tension between the boys in any coherent way.

Negative Impact:

Negative impact on child (0-3)	2	Negative impact on family (0-3)	2
--------------------------------	---	---------------------------------	---

Loss:

Loss of attachment figure (0-3)	0	Loss of an idea (0-3)	1
---------------------------------	---	-----------------------	---

Danger:

Risk of loss of person (0-3)	0	Physical jeopardy (0-3)	1
Trauma as witness (0-3)	0	Challenge (0-3)	0

Independence:

Independence from child (0-1)	1
Independence from family (0-1)	1

Female, 10 years old: Reading difficulties

S has problems with her reading. She does not get special needs teaching, but she gets lots of extra reading with volunteer mums who come in to help in the classroom. She also has problems with maths and is having similar extra help for this. These problems have been present throughout the last three years.

Negative Impact:

Negative impact on child (0-3)	1	Negative impact on family (0-3)	0
--------------------------------	---	---------------------------------	---

Loss:

Loss of attachment figure (0-3)	0	Loss of an idea (0-3)	1
---------------------------------	---	-----------------------	---

Danger:

Risk of loss of person (0-3)	0	Physical jeopardy (0-3)	0
Trauma as witness (0-3)	0	Challenge (0-3)	1

Independence:

Independence from child (0-1)	0
Independence from family (0-1)	1

CHILD BEHAVIOR CHECKLIST FOR AGES 4-18

For Office Use Only
ID #

Please Print

CHILD'S FULL NAME		FIRST	MIDDLE	LAST	PARENTS' USUAL TYPE OF WORK, even if not working now. (Please be specific—for example, auto mechanic, high school teacher, homemaker, laborer, lathe operator, shoe salesman, army sergeant.)
SEX	AGE	ETHNIC GROUP OR RACE		FATHER'S TYPE OF WORK	
TODAY'S DATE		CHILD'S BIRTHDATE		MOTHER'S TYPE OF WORK	
GRADE IN SCHOOL		Please fill out this form to reflect your view of the child's behavior even if other people might not agree. Feel free to print additional comments beside each item and in the spaces provided on page 2.		THIS FORM FILLED OUT BY:	
NOT ATTENDING SCHOOL				☐ Mother (full name) ☐ Father (full name) ☐ Other—name & relationship to child:	

I. Please list the sports your child most likes to take part in. For example: swimming, baseball, skating, skate boarding, bike riding, fishing, etc.	Compared to others of the same age, about how much time does he/she spend in each?	Compared to others of the same age, how well does he/she do each one?
☐ None	Don't Know Less Than Average Average More Than Average	Don't Know Below Average Average Above Average
a. _____	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐
b. _____	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐
c. _____	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐
II. Please list your child's favorite hobbies, activities, and games, other than sports. For example: stamps, dolls, books, piano, crafts, cars, singing, etc. (Do not include listening to radio or TV.)	Compared to others of the same age, about how much time does he/she spend in each?	Compared to others of the same age, how well does he/she do each one?
☐ None	Don't Know Less Than Average Average More Than Average	Don't Know Below Average Average Above Average
a. _____	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐
b. _____	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐
c. _____	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐
III. Please list any organizations, clubs, teams, or groups your child belongs to.	Compared to others of the same age, how active is he/she in each?	
☐ None	Don't Know Less Active Average More Active	
a. _____	☐ ☐ ☐ ☐	
b. _____	☐ ☐ ☐ ☐	
c. _____	☐ ☐ ☐ ☐	
IV. Please list any jobs or chores your child has. For example: paper route, babysitting, making bed, working in store, etc. (Include both paid and unpaid jobs and chores.)	Compared to others of the same age, how well does he/she carry them out?	
☐ None	Don't Know Below Average Average Above Average	
a. _____	☐ ☐ ☐ ☐	
b. _____	☐ ☐ ☐ ☐	
c. _____	☐ ☐ ☐ ☐	

203
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