

**Genetic and Environmental Influences on
Insomnia Symptoms and Associated Cognition
and Arousal in Young Adults**

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DECLARATION

I, Melanie Nicole Schneider, hereby declare that this thesis and the work presented in it is entirely my own. Where I have consulted the work of others, this is always clearly stated.

Signed: _____

Date: _____

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STATEMENT OF AUTHORSHIP

The data for this PhD thesis has mainly come from wave 5 of the G1219 sample (some wave 4 data is also included), a data set which has been jointly collected by a team of researchers at Goldsmiths and the Institute of Psychiatry. While I was studying for my MSc at Goldsmiths in 2012, I was involved in the data collection for wave 5, carrying out minor tasks such as helping with the mail-out and entering the information from the questionnaires into the data set. I was also involved in the coding of some of the variables and in checking the coding of variables from other team members. In addition, I became the data manager for G1219 soon after I had started my PhD. I kept the participant contact data up to date, reorganised the data set, corresponded with the participants themselves, and was also the main contact person for questions from the participants. I was also in charge of the Facebook contact website for G1219. In addition to this, I was involved in drafting a newsletter to keep the participants informed and organised the mail-out of the newsletter itself.

ABSTRACT

Current, influential theories of insomnia emphasise the role of cognitive and arousal factors in the development and maintenance of insomnia. Even though we know that insomnia is heritable, genetic influences have not been given enough attention in these models of insomnia. This thesis investigates the extent to which genes and the environment influence these cognitive and arousal variables (and their subscales) and their associations with insomnia symptoms. Furthermore, the theory that insomnia can be subtyped into insomnia with short sleep duration and insomnia with normal sleep duration (being distinguishable by for example differences in arousal) has not yet been tested.

Data came from 862 individuals (aged 22 to 32, mean age 25, 34% males) of Wave 5 of the G1219 twin/sibling sample. The five studies reported in the current thesis investigated: 1) Mindfulness 2) Pre-sleep arousal 3) Dysfunctional beliefs about sleep (DBAS) and their associations with insomnia symptoms; 4) Non-shared environmental factors associated with DBAS; and 5) Self-reports of insomnia with short versus normal sleep duration.

Mindfulness, pre-sleep arousal and DBAS (and their subscales) were all found to be associated with insomnia symptoms. Mindfulness was found to be familial, while DBAS had no familial influence. Pre-sleep arousal showed moderate, significant genetic influence. No genetic or shared environmental influence was found for the associations between mindfulness and symptoms of insomnia, depression and anxiety, nor was any found for the association between DBAS and insomnia symptoms. Genetic influences were important in the relationship between pre-sleep arousal and insomnia symptoms. Furthermore, for DBAS, drug use was a non-shared environmental influence un-confounded by genetic factors. The theory of subtypes of insomnia (short versus normal sleep duration) could not be confirmed. The findings provide novel insight into the concept and aetiology of insomnia, by integrating the behavioural genetics perspective into the current theories of insomnia.

TABLE OF CONTENTS

DECLARATION	2
ACKNOWLEDGEMENTS.....	3
ACKNOWLEDGEMENTS FOR G1219 SAMPLE	4
STATEMENT OF AUTHORSHIP	5
ABSTRACT.....	6
LIST OF TABLES.....	16
LIST OF FIGURES	18
LIST OF PUBLICATIONS ARISING FROM THIS THESIS.....	20
LIST OF PUBLICATIONS RELATED TO THIS THESIS	21
LIST OF ABBREVIATIONS.....	22
<u>CHAPTER 1: Introduction</u>	26
1.1 What is sleep?	26
1.1.1 Definition of sleep.....	26
1.1.2 Sleep stages.....	26
1.1.3 The function of sleep	27
1.2 What is insomnia?.....	28
1.2.1 Definition and prevalence of insomnia	28
1.2.2 Classification and clinical diagnosis of insomnia	30
1.2.3 Subtypes of insomnia	33
1.2.3.1 Duration	33
1.2.3.2 Sleep length.....	33
1.2.3.3 Paradoxical insomnia: A subtype unrelated to ‘normal’ insomnia	35

1.2.4	<i>Symptoms versus diagnosis</i>	35
1.2.5	<i>Differential diagnosis</i>	37
1.3	What do we know about insomnia from a theoretical point of view?	41
1.3.1	<i>Theories most relevant to this thesis – Cognitive models of insomnia</i>	42
1.3.1.1	The 3P model of insomnia	42
1.3.1.2	The hybrid cognitive-behavioural model	43
1.3.1.3	The microanalytic model of insomnia	45
1.3.1.4	The cognitive model of insomnia	46
1.3.2	<i>Occurrence of the analysed traits in cognitive theories</i>	51
1.3.3	<i>Interaction of the analysed traits in cognitive theories</i>	52
1.3.4	<i>Overview of other main theories of insomnia</i>	53
1.4	Risk factors, comorbidities and associated negative factors.....	56
1.4.1	<i>General risk factors</i>	56
1.4.2	<i>Gender differences</i>	58
1.4.3	<i>Insomnia and the brain</i>	58
1.4.4	<i>Comorbidities and associated negative factors</i>	59
1.4.5	<i>Costs of insomnia</i>	60
1.5	How can insomnia be measured?.....	62
1.5.1	<i>Subjective measures</i>	62
1.5.1.1	Self-report questionnaires for insomnia.....	62
1.5.1.1.1	<i>Insomnia Severity Index (ISI)</i>	62
1.5.1.1.2	<i>Insomnia Symptom Questionnaire (ISQ)</i>	63
1.5.1.2	Sleep diaries	63
1.5.1.3	Structured interviews	64
1.5.2	<i>Objective measures</i>	64
1.5.2.1	Polysomnography	64
1.5.2.2	Actigraphy.....	68
1.6	How can insomnia be treated?	70
1.6.1	<i>Psychotherapeutic treatment of insomnia</i>	70
1.6.2	<i>Pharmacological treatment of insomnia</i>	74
1.6.3	<i>Self-medication of insomnia</i>	75
1.6.4	<i>New and alternative forms of treatment</i>	76
1.6.4.1	Light therapy.....	76

1.7 The heritability of insomnia.....	77
1.7.1 <i>Studies of genetic influence</i>	77
1.7.2 <i>Genes involved</i>	79
1.7.3 <i>Epigenetic studies</i>	80
1.8 What can you learn about insomnia from this thesis? – Rationale and research questions	82
CHAPTER 2: Methods	86
2.1 Overview.....	86
2.2 Path diagrams.....	86
2.3 The twin method	88
2.3.1 <i>Assumptions and associated limitations</i>	88
2.3.1.1 Equal environments assumption	88
2.3.1.2 Sibling interaction.....	89
2.3.1.3 Assortative mating	90
2.3.1.4 Gene-environment correlation and interaction	91
2.3.1.5 Generalisability	91
2.3.2 <i>Univariate analysis</i>	92
2.3.2.1 The ACE model	92
2.3.2.2 The ADE model	97
2.3.3 <i>Structural equation modelling</i>	98
2.3.4 <i>Model fitting</i>	99
2.3.5 <i>Multivariate analysis</i>	100
2.3.5.1 The correlated factors model	102
2.3.5.2 The independent pathway model	105
2.3.5.3 The common pathway model.....	105
2.3.5.4 Models including three measured variables.....	106
2.4 The G1219 sample	107
2.4.1 <i>History of data collection for G1219: Waves 1, 2 and 3</i>	107
2.4.2 <i>Relevance to the current analyses: Waves 4 and 5</i>	108
2.4.3 <i>Ethical approval</i>	109
2.4.4 <i>Data preparation</i>	109
2.5 Sensitivity analyses.....	110

<u>CHAPTER 3: Mindfulness and associations with symptoms of insomnia, anxiety and depression in early adulthood: a twin and sibling study</u>	111
3.1 Introduction.....	111
3.1.1 <i>Conceptualisation of mindfulness</i>	111
3.1.2 <i>Mindfulness sub-scales and other traits</i>	112
3.1.3 <i>Heritability of mindfulness</i>	113
3.1.4 <i>Aims of the current study</i>	114
3.2 Method.....	115
3.2.1 <i>Sample</i>	115
3.2.2 <i>Mindfulness</i>	116
3.2.3 <i>Insomnia symptoms</i>	117
3.2.4 <i>Depression symptoms</i>	117
3.2.5 <i>Anxiety symptoms</i>	118
3.2.6 <i>Data preparation</i>	118
3.2.7 <i>Analysis</i>	118
3.3 Results.....	120
3.3.1 <i>Descriptive statistics</i>	120
3.3.2 <i>Phenotypic correlations and MZ, DZ and sibling correlations</i>	123
3.3.3 <i>Univariate genetic model fitting</i>	127
3.3.4 <i>Multivariate model fitting</i>	131
3.4 Discussion.....	133
3.4.1 <i>Associations between variables</i>	134
3.4.2 <i>Familial influences</i>	135
3.4.4 <i>Limitations</i>	138
3.4.5 <i>Conclusion</i>	139

<u>CHAPTER 4: Associations Between Pre-Sleep Arousal and Insomnia Symptoms in Early Adulthood: A Twin and Sibling Study</u>	140
4.1 Introduction.....	140
4.1.1 <i>Pre-sleep arousal and insomnia symptoms</i>	140
4.1.2 <i>Heritability of pre-sleep arousal</i>	142
4.1.3 <i>Aims of the current study</i>	142

4.2 Method	143
4.2.1 <i>Sample</i>	143
4.2.2 <i>Pre-sleep arousal</i>	143
4.2.3 <i>Insomnia symptoms</i>	144
4.3 Analysis	144
4.3.1 <i>Data preparation</i>	144
4.3.2 <i>Preliminary analyses</i>	144
4.3.3 <i>Regression analyses</i>	145
4.3.4 <i>Twin/sibling analyses</i>	145
4.4 Results	146
4.4.1 <i>Descriptive statistics</i>	146
4.4.2 <i>Phenotypic correlations</i>	147
4.4.3 <i>MZ, DZ and sibling correlations</i>	148
4.4.4 <i>Regression analyses</i>	149
4.5 Discussion	156
4.5.1 <i>Association between variables</i>	157
4.5.2 <i>Familial influences</i>	157
4.5.3 <i>Limitations</i>	159
4.5.4 <i>Conclusion</i>	160

CHAPTER 5: Dysfunctional Beliefs about Sleep and Insomnia Symptoms in Early

<u>Adulthood: A Twin and Sibling Study</u>	161
5.1 Introduction and theoretical background	161
5.1.1 <i>The concept of dysfunctional beliefs about sleep</i>	161
5.1.2 <i>The association of dysfunctional beliefs about sleep and insomnia</i>	163
5.1.3 <i>The role of dysfunctional beliefs about sleep in the treatment of insomnia</i>	164
5.1.4 <i>Heritability of dysfunctional beliefs about sleep</i>	167
5.1.5 <i>Aims of the current study</i>	167
5.2 Method	168
5.2.1 <i>Sample</i>	168
5.2.2 <i>Dysfunctional beliefs about sleep</i>	168
5.2.3 <i>Insomnia symptoms</i>	169

5.3 Analyses.....	170
5.3.1 Data preparation and preliminary analyses.....	170
5.3.2 Univariate twin and sibling analyses.....	170
5.3.3 Multivariate twin and sibling analyses.....	171
5.4 Results.....	172
5.4.1 Descriptive statistics.....	172
5.4.2 Phenotypic analysis.....	173
5.4.3 MZ, DZ and sibling correlations.....	174
5.4.4 Twin analysis.....	176
5.5 Discussion.....	182
5.5.1 Associations between variables.....	182
5.5.2 Factors influencing dysfunctional beliefs about sleep.....	182
5.5.3 Factors influencing the association between overall dysfunctional beliefs about sleep and insomnia symptoms.....	183
5.5.4 Limitations.....	184
5.5.5 Conclusion.....	185

CHAPTER 6: Non-shared Environmental Factors Associated with Dysfunctional

<u>Beliefs about Sleep in Early Adulthood: A Monozygotic Twin Differences Study.....</u>	<u>186</u>
6.1 Introduction.....	186
6.1.1 Previously conducted study.....	186
6.1.2 Background.....	186
6.1.3 Selection of candidate ‘environmental’ factors.....	187
6.1.4 Aims of the current study.....	189
6.2 Method.....	189
6.2.1 Sample.....	189
6.2.2 Measures.....	190
6.2.2.1 Dysfunctional beliefs about sleep (DBAS).....	190
6.2.2.2 Relationship (status, satisfaction, and cohesion).....	190
6.2.2.3 Education.....	191
6.2.2.4 Employment.....	191
6.2.2.5 General health.....	192
6.2.2.6 Smoking status.....	193
6.2.2.7 Alcohol use.....	193

6.2.2.8 Drug use.....	193
6.2.2.9 Life events.....	194
6.3 Analyses.....	194
6.3.1 <i>Data preparation and preliminary analyses</i>	194
6.3.2 <i>MZ differences analysis</i>	194
6.3.3 <i>Sensitivity analyses</i>	196
6.4 Results.....	196
6.4.1 <i>Descriptive statistics</i>	196
6.4.2 <i>MZ differences analyses</i>	196
6.5 Discussion.....	199
6.5.1 <i>Factors influencing dysfunctional beliefs about sleep</i>	200
6.5.2 <i>The link between drug use and dysfunctional beliefs about sleep</i>	201
6.5.3 <i>Limitations</i>	202
6.5.4 <i>Conclusion</i>	203

CHAPTER 7: Self-reports of insomnia with short versus normal sleep duration:

comparing the subtypes in terms of heritability, associated phenotypes and persistence

<u>over time</u>	205
7.1 Introduction.....	205
7.1.1 <i>Background</i>	205
7.1.2 <i>Predictions of the theory to be tested in the current study</i>	207
7.2 Method.....	208
7.2.1 <i>Sample</i>	208
7.2.2 <i>Definition of sleep length for the insomnia SSD and insomnia NSD group</i>	209
7.2.3 <i>Subjective sleep duration</i>	209
7.2.4 <i>Insomnia and insomnia symptoms</i>	209
7.2.5 <i>Cognitive and somatic pre-sleep arousal</i>	210
7.2.6 <i>Life events</i>	210
7.2.7 <i>Anxiety symptoms</i>	211
7.3 Analysis.....	211
7.3.1 <i>Data preparation</i>	211
7.3.2 <i>Twin analysis</i>	212
7.3.3 <i>Regression analysis</i>	212
7.3.4 <i>Sensitivity analyses</i>	212

7.4 Results.....	212
7.4.1 Descriptive statistics	212
7.4.2 Twin analyses/MZ and DZ correlations	214
7.4.3 Phenotypic analyses.....	215
7.4.4 Persistence over time	218
7.5 Discussion.....	219
7.5.1 Hypothesis 1: Insomnia is more heritable for those with SSD versus those with NSD	220
7.5.2 Hypothesis 2: There are differences between insomnia SSD and NSD in associated traits	220
7.5.3 Hypothesis 3: There are differences between insomnia SSD and NSD in persistence over time	221
7.5.4 Limitations	221
7.5.5 Conclusion	222
<u>CHAPTER 8: Discussion.....</u>	<u>223</u>
8.1 Goals of this PhD thesis.....	223
8.2 The current findings within the context of cognitive theories and the treatment of insomnia.....	224
8.2.1 The current findings within the context of the cognitive theories.....	224
8.2.2 The results of this thesis within the context of the metacognitive model of insomnia.....	225
8.2.3 The relevance of the results to the treatment of insomnia	227
8.3 Future directions	229
8.3.1 Re-evaluation of the results	229
8.3.2 Adding an objective measure of sleep.....	230
8.3.3 Testing the theory of subtypes of insomnia (SSD versus NSD).....	230
8.3.4 Adding treatment intervention	230
8.3.5 Adding sleep hygiene	231
8.3.6 Re-evaluation of mindfulness, ideas for a new measure.....	231
8.4 General limitations.....	234
8.4.1 Self-report measures	234
8.4.2 Age	236
8.4.3 Twin sample	237

8.4.4 <i>Non-clinical sample</i>	237
8.4.5 <i>Sample size</i>	238
8.4.6 <i>Cross-sectional data</i>	238
8.4.7 <i>Additional factors</i>	239
8.5 Conclusion	240
REFERENCES	242
APPENDIX A: Comparison of the correlated factors solution and the independent pathway model for three variables.....	284
APPENDIX B: Items included from the FFMQ.....	285
APPENDIX C: Comparison of the ISI and the ISQ	286
APPENDIX D: The correlated factors solution for overall mindfulness and symptoms of insomnia, depression and anxiety.....	287
APPENDIX E: Items included in the PSAS.....	289
APPENDIX F: The independent pathway model for cognitive pre-sleep arousal, somatic pre-sleep arousal and symptoms of insomnia.....	290
APPENDIX G: Items included in the DBAS-10	291
APPENDIX H: Fit statistics of additional multivariate analyses	292
APPENDIX I: Items included in the measure of relationship satisfaction and relationship cohesion	293
APPENDIX J: Items included in the measure of negative life events.....	294
APPENDIX K: Additional regression analyses.....	295

LIST OF TABLES

Table 3.1	Means (SD) of raw scores for overall mindfulness, mindfulness subscales and symptoms of insomnia, depression and anxiety	122
Table 3.2	Phenotypic correlations for overall mindfulness, subscales of mindfulness, symptoms of insomnia, depression and anxiety	124
Table 3.3	Phenotypic correlations for each subscale of mindfulness with symptoms of insomnia, depression and anxiety after partialling out all other subscales	125
Table 3.4	Twin/sibling correlations for the subscales of mindfulness	126
Table 3.5	Twin/sibling correlations (within-trait and between-traits) for overall mindfulness, insomnia symptoms, depression and anxiety	127
Table 3.6	Fit statistics of all univariate genetic model fitting analyses	129
Table 3.7	Estimates for A, C and E for the univariate genetic model fitting analyses	130
Table 3.8	Fit statistics for the multivariate genetic model fitting analyses	131
Table 4.1	Means (SD) of raw scores for overall pre-sleep arousal, cognitive arousal, somatic pre-sleep arousal and symptoms of insomnia	147
Table 4.2	Phenotypic correlations for overall pre-sleep arousal, cognitive pre-sleep arousal, somatic pre-sleep arousal and symptoms of insomnia	148
Table 4.3	Twin/sibling correlations for overall pre-sleep arousal, cognitive arousal, somatic pre-sleep arousal and insomnia symptoms	149
Table 4.4	Fit statistics of all univariate genetic model fitting analyses	151
Table 4.5	Estimates for A, C and E for the univariate genetic model fitting analyses	152
Table 4.6	Fit statistics for the multivariate genetic model fitting analyses	152
Table 5.1	Means (SD) of raw scores for overall dysfunctional beliefs about sleep, its subscales, and symptoms of insomnia	173

Table 5.2	Phenotypic correlations for overall dysfunctional beliefs about sleep, its subscales, and symptoms of insomnia	174
Table 5.3	Twin/sibling correlations for overall dysfunctional beliefs about sleep, its subscales, and symptoms of insomnia	175
Table 5.4	Fit statistics of all univariate genetic model fitting analyses	177
Table 5.5	Estimates for A, C and E for all univariate genetic model fitting analyses	178
Table 5.6	Fit statistics for the multivariate genetic model fitting analyses	179
Table 6.1	Regression analyses predicting a) Absolute DBAS Scores and b) MZ Differences, controlling for genetic influence and shared environmental influence on the environmental measures	199
Table 7.1	Means (SD) of raw scores for cognitive pre-sleep arousal, somatic pre-sleep arousal, life events and anxiety symptoms	213
Table 7.2	MZ and DZ correlations for insomnia SSD and insomnia NSD	214

LIST OF FIGURES

Figure 1.1	The integrative model of the interaction between sleep-interfering and sleep-interpreting processes (Lundh & Broman, 2000)	44
Figure 1.2	Microanalytic model of insomnia (Morin, 1993)	45
Figure 1.3	Harvey's (2002) cognitive model of insomnia	47
Figure 1.4	Two-level model of sleep-related arousal, presented in the metacognitive model of insomnia by Ong and colleagues (2012)	49
Figure 2.1	Conventions for the elements used in path diagrams	87
Figure 2.2	The variance of a trait in any twin/sibling	93
Figure 2.3	The covariance for any trait for MZ twin pairs (reared together)	94
Figure 2.4	The covariance for any trait for DZ twin pairs (reared together)	95
Figure 2.5	Correlated factors solution	104
Figure 2.6	Independent pathway model	105
Figure 2.7	Common pathway model	106
Figure 3.1	Path diagram of the independent pathway model, including overall mindfulness, symptoms of insomnia, depression and anxiety	133
Figure 4.1	Path diagram of the bivariate analysis, including overall pre-sleep arousal and insomnia symptoms	153
Figure 4.2	Path diagram of the correlated factors solution, including cognitive pre-sleep arousal and insomnia symptoms	155
Figure 4.3	Relative contributions of A, C and E to the overall phenotypic correlations	156
Figure 5.1	Path diagram of the bivariate analysis, including overall dysfunctional beliefs about sleep (overall DBAS) and insomnia symptoms	179

Figure 5.2	Path diagram of the correlated factors solution, including <i>beliefs about immediate consequences</i> (DBAS factor I), <i>beliefs about long-term consequences</i> (DBAS factor II), <i>beliefs about control</i> (DBAS factor III) and insomnia symptoms	181
Figure 6.1	Histogram of distribution of MZ differences for the overall DBAS score	197
Figure 7.1	Mean differences in cognitive pre-sleep arousal between the no insomnia, insomnia SSD and insomnia NSD group	215
Figure 7.2	Mean differences in somatic pre-sleep arousal between the no insomnia, insomnia SSD and insomnia NSD group	216
Figure 7.3	Mean differences in life events between the no insomnia, insomnia SSD and insomnia NSD group	217
Figure 7.4	Mean differences in anxiety symptoms between the no insomnia, insomnia SSD and insomnia NSD group	218

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- Denis, D., French, C., **Schneider, M. N.** & Gregory, A. M. (2017). Sleep-related variables in those who have and have not experienced sleep paralysis. Manuscript submitted for publication.

LIST OF ABBREVIATIONS

Δdf	Change in degrees of freedom
$\Delta\chi^2$	Change in chi-square
β	Standardised beta coefficient
-2LL	Minus twice the Log-Likelihood
χ^2	Chi-square goodness-of-fit statistic
95% CI	95% Confidence Interval
A	Additive genetic influence
a^2	Additive genetic influence
ACT	Acceptance and Commitment Therapy
AIC	Akaike Information Criterion
AIS	Athens Insomnia Scale
APA	American Psychiatric Association
B	Unstandardised beta coefficient
C	Shared (common) environmental influence
c^2	Shared environmental influence
CBT	Cognitive Behavioral Therapy
CBT-I	Cognitive Behavioral Therapy for Insomnia
COMB	Combination of pharmacotherapy and CBT
CovDZ	Covariance between DZ twin 1 and DZ twin 2
CovMZ	Covariance between MZ twin 1 and MZ twin 2
D	Non-additive genetic (dominance) influence
d^2	Non-additive genetic (dominance) influence
DBAS	Dysfunctional beliefs about sleep
DBAS	Beliefs about immediate negative consequences of insomnia

factor I	
DBAS	Beliefs about long-term consequences
factor II	
DBAS	Beliefs about the need for control over insomnia
factor III	
<i>df</i>	Degrees of freedom
DNA	Deoxyribonucleic Acid
DSM-5	Diagnostic and Statistical Manual of Mental Disorders 5th edition
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders 5th edition
DZ	Dizygotic
E	Non-shared environmental influence
e^2	Non-shared environmental influence
EEG	Electroencephalography
EMG	Electromyography
EOG	Electro-Oculography
FFMQ	Five Facet Mindfulness Scale
FIRST	Ford Insomnia Response to Stress Test
G1219	Genesis 12-19 years sample
GWAS	Genome Wide Association Studies
ICD-10	International Classification of Mental and Behavioural Disorders (10th edition)
ICD-11	International Classification of Mental and Behavioural Disorders (11th edition)
ICSD-3	International Classification of Sleep Disorders (3rd edition)
ISI	Insomnia Severity Index
ISQ	Insomnia Symptoms Questionnaire
MBCT	Mindfulness-Based Cognitive Therapy

MBSR	Mindfulness-Based Stress Reduction
MBTI	Mindfulness-Based Therapy for Insomnia
MZ	Monozygotic
N	Number of participants
NREM	Non-rapid eye movement sleep
NHS	National Health Service
NSD	Normal sleep duration
r	Correlation coefficient
R	A language and environment for statistical computing and graphics
rA	Additive genetic correlation
rC	Shared environmental correlation
RCADS	Revised Children Anxiety and Depression Scale
rE	Non-shared environmental correlation
rDZ	Dizygotic twins' correlation
rMZ	Monozygotic twins' correlation
RNA	Ribonucleic acid
OCT	Over the counter
<i>p</i>	p-value
PCT	Pharmacotherapy
PLA	Placebo group
PSAS	Pre-sleep Arousal Scale
PSG	Polysomnography
PSQI	Pittsburgh Sleep Quality Index
REM	Rapid eye movement sleep
SCI	Sleep Condition Indicator
SD	Standard Deviation

SE	Standard Error
Sib	Siblings
SHI	Sleep Hygiene Index
SOL	Sleep onset latency
SPSS	Statistical Package for the Social Sciences
SSD	Short sleep duration
STATA	A general-purpose statistical software package created in 1985 by StataCorp
<i>t</i>	t-statistic
WASO	Wake time after sleep onset
WHO	World Health Organisation

CHAPTER 1: Introduction

1.1 What is sleep?

1.1.1 Definition of sleep

Sleep is a distinct brain state involving partial or full unconsciousness which occurs periodically (usually every night) and is reversible. It is characterised by reduced sensitivity to stimuli, inactivity, reduced metabolism and by a lack of muscle tone (VandenBos, 2007; Carskadon & Dement, 2005). It can be differentiated from other forms of unconsciousness (for example, as a result of drug use or head injury) by unique patterns that are shown by brain imaging or electroencephalography which illustrate the different stages of sleep (VandenBos, 2007).

1.1.2 Sleep stages

During the night we periodically move through different stages of sleep. These can be measured using polysomnography (see **1.5.2.1 Polysomnography** for more details). We differentiate between rapid eye movement sleep (REM) and non-rapid eye movement sleep (NREM, including the stages N1, N2 and N3). The main characteristic of rapid-eye-movement (REM) sleep is, as the name implies, a rapid movement of the eyeballs. The other sleep stages are also non-REM sleep as this was found to be such a crucial feature (Carskadon & Dement, 2005; Espie, 1991). The EEG pattern during REM sleep looks quite similar to wakefulness or the transient stage between sleep and wakefulness (stage 1) but the electromyograph shows that there is no muscle tone (Espie, 1991; Espie, 2006; Peigneux, Urbain & Schmitz, 2012).

Stage N1 is the lightest form of sleep. It is a transitional stage between sleep and wakefulness when the muscles start to relax and eye movement slows down. The EEG waves are slower at this stage as well, disappearing of alpha waves and displaying theta

waves, getting slower in frequency and greater in amplitude compared to during sleep onset (Espie, 2006; Peigneux et al., 2012). Stage N2 is a light form of sleep, characterised by mixed frequencies in the EEG, highlighted by sleep spindles (rapid bursts of high-frequency waves) and K-complexes (rapid decline followed by a sharp rise in the wave) in the EEG data. Stage N3 represent deep sleep and is also called slow wave sleep because the EEG now shows lower frequencies of higher waves now (Carskadon & Dement, 2005; Espie, 2006; Peigneux et al., 2012). Measuring the sleep stages gives us an indication of the structure, quality and quantity of the sleep of the individual from an objective point of view, which can help us to better understand possible sleep disturbances (Espie, 2006).

1.1.3 The function of sleep

Even though there is a long history of sleep research, we are still not sure why we all have to sleep and a whole series of competing hypotheses exists (Krueger, Frank, Wisor, & Roy, 2016). The key theories of the function of sleep include the idea that we need to sleep for the following reasons: memory processing and learning, emotion regulation, protection, preservation, restoration and for ‘cleaning’ the brain. It is unlikely that there is just one reason why we need to sleep, it is much more likely that it is a combination of reasons. Sleep is a state in which learned information is processed and stored. It also correlates with structural reorganization of the brain and brain plasticity (Dinkelmann & Born, 2010). During sleep recent emotional experiences are processed, our affective neural systems are modulated and REM sleep plays a role in emotional-memory processing (Walker & van Der Helm, 2009). Sleep may also have an adaptive function when viewed from an evolutionary perspective because staying indoors and sleeping when it is dark outside reduces the risk of being harmed - for example, by a predator (Meddis, 1983). Periods of sleep also help us to conserve energy

which is, for example, evident in a reduction of metabolic rate during sleep (Jung et al., 2011; White, Weil, & Zvillich, 1985). It helps the restoration of the body by promoting healing and also helps the immune system (Ingiosi, Opp, & Krueger, 2013).

Furthermore, during sleep, the brain is cleared of metabolic waste products much faster than during wake-times (Eugene & Masiak, 2015; Herculano-Houzel, 2013). There are various other theories of the function of sleep which are not mentioned here. It should be mentioned that some researchers consider that these theories compete with one another while others accept that there is more than one reason why we sleep (Krueger et al., 2016). In summary, it can be said that it is not yet clear what the main function of sleep actually is. However, what we do know is that sleep disturbances (particularly when they occur frequently as in insomnia) can have serious consequences for our physical and mental health (see Roth et al. 2011; Roth & Roehrs, 2003; Taylor et al., 2014, for a more detailed outline of the consequences of insomnia see **1.4.4**

Comorbidities and associated negative factors).

1.2 What is insomnia?

1.2.1 Definition and prevalence of insomnia

The key variable of interest for this PhD thesis is insomnia symptoms. When conducting research, it is of the highest importance to clearly characterise the phenotype of interest (Perlis, Corbitt, & Kloss, 2014). Insomnia is characterised by difficulties initiating sleep, maintaining sleep and/or early awakenings, resulting in an impairment in daytime functioning (Morin & Benca, 2012). According to the Diagnostic and Statistical Manual of Mental Disorders DSM-5 (APA, 2013), to meet criteria for diagnosis, the symptoms need to be present for at least 3 nights a week. There are three classifications of insomnia: acute insomnia (duration of symptoms < 1 month), sub-

chronic insomnia (1 - 3 months) and chronic insomnia (duration > 3 months) (APA, 2013). It is important to mention that this thesis focuses on insomnia *symptoms* found within the general population and not on insomnia *diagnosis*. In some cases (see **Chapter 7: Self-reports of insomnia with short versus normal sleep duration**), the term ‘insomnia’ is used but only when participants actually met the diagnostic criteria of the DSM-IV (APA, 2010), respectively the Research Diagnostic Criteria for insomnia (Edinger et al., 2004), as identified by a self-measure – the Insomnia Symptoms Questionnaire (ISQ, Okun et al., 2009 – which was based on the DSM version at the time).

Insomnia is one of the most common health problems (Hublin & Partinen, 2002; Leger & Bayon, 2010; Ohayon, 2002). Prevalence rates vary but it has been estimated that approximately one-third of our society experience insomnia symptoms at any given time (Morin, LeBlanc, Daley, Grégoire, & Mérette, 2006; Ohayon, 2002). Worldwide, between 9% and 15% of the general adult population suffer from insomnia and experience the consequences of insomnia during the day and are therefore in substantial distress (Ohayon, 2002). Depending on the diagnostic criteria used, 10% to 30% of children and 3% to 12% of adolescents also experience insomnia (Roberts, Roberts, & Chan, 2008). It can be criticised that no common consensus exists about which criteria should be applied to define insomnia, which is one of the reasons why estimates vary across the different studies.

In a more recent study, the America Insomnia Survey, it was found that up to 30% of the adult population in the US experience insomnia symptoms, and 10% of the individual experience insomnia that affects their daytime functioning (Kessler et al., 2011; Shahly et al., 2012). The survey also showed that among employed (or self-employed) individuals, 20% of them experienced chronic insomnia symptoms of a

duration of 12 months or more (Shahly et al., 2012). However, it should be mentioned that the sample of this survey was limited to the US population while the earlier review by Ohayon (2002) included data from various countries world wide, which may be one possible explanation why estimates are higher in this review.

In another recent review, it was pointed out that estimates of the prevalence of insomnia (summarised here to lie between 2% and 4% for primary insomnia as diagnosed by DSM-IV which is referring to ‘insomnia disorder’ in the DSM-5) in some studies and between 30% to 48% for insomnia symptoms experienced in the general population in others) vary largely because of the differences in how insomnia is defined according to the different diagnostic manuals currently in use (Grewal & Doghramji, 2017).

1.2.2 Classification and clinical diagnosis of insomnia

Currently there are three main manuals in use for classifying or diagnosing insomnia, the International Classification of Sleep Disorders (ICSD-3, American Academy of Sleep Medicine, 2015), the Diagnostic and Statistic Manual of Mental Disorders from the American Psychiatric Association (DSM-5; APA, 2013) and the International Classification of Mental and Behavioural Disorders from the World Health Organization (ICD-10; WHO, 1992).

The DSM-5 and the ICSD-3 largely overlap in terms of diagnostic criteria. They both include the following symptoms: difficulty initiating and/or maintaining sleep and/or early-morning awakenings and (in children) bedtime resistance/struggles. They also agree on the frequency (at least three nights per week), duration (lasting at least three months) and opportunity (having adequate opportunity for sleep). Both classification systems include fatigue, cognitive impairment (attention, concentration or memory), mood disturbance, impaired social, interpersonal, occupational or academic

functioning, and behavioural problems (for example, aggression). The differences here are that the DSM-5 includes negative impact on the caregiver and the functioning of the family, while the ICSD-3 also refers to daytime sleepiness, reduced motivation or energy, proneness to accidents and errors and dissatisfaction with sleep (or concerns about sleep). Dissatisfaction with sleep quality or quantity is also mentioned in the DSM-5. The ICSD-3 and the DSM-5 both allow for comorbidities to be added to the insomnia diagnosis (American Academy of Sleep Medicine, 2015; APA, 2013).

The DSM-5 and the ICSD-3 both provide rough guidelines as to when latency to fall asleep, awakenings during the night and early awakenings can be considered clinically significant (American Academy of Sleep Medicine, 2015; APA, 2013). Adults who struggle for more than 30 minutes to fall asleep or who are awake for more than 30 minutes during the night meet the criteria of “difficulty initiating sleep” or “difficulty maintaining sleep” respectively. The 30-minute-rule also applies to the “waking up earlier than desired” diagnostic criterion (American Academy of Sleep Medicine, 2015; Hood, Carney, & Harris, 2011).

In contrast to the other two diagnostic manuals (DSM-5 and the ICSD-3), the ICD-10 has a more basic structure of classification for insomnia, comprising only four diagnostic criteria:

- 1) Complaining about a disruption in sleep, problems with sleep disruption during the night, poor sleep quality or not feeling refreshed in the morning;
- 2) A sleep disturbance that occurs at least three times a week for at least one month;
- 3) The sleep problems cause distress or impair everyday functioning; and

- 4) Other organic causes, including somatic disorders and effects caused by psychotropic substances or medications can be excluded.

This does not allow for the duration or intensity of the insomnia disorder to be specified (such as, for example, in the DSM-5 where episodic, persistent and recurrent can be added to the insomnia diagnosis), nor does it take into account other sleep disorders as a differential diagnosis (WHO, 1992).

With the different classification systems available, the question arises as to which one to use. The American Insomnia Survey included diagnostic criteria in line with both the ICD-10 and the DSM-IV when assessing insomnia (10,094 participants were included). It was found that the prevalence rates vary greatly depending on which criteria are utilised (22% for the DSM; 4% for the ICD-10, 15% for the ICSD-2) (Roth et al., 2011). It was argued that the ICD-10 criteria might give a narrower diagnosis of insomnia and include the more severe cases but it was recommended that the DSM criteria should be applied as some cases may be missed by the ICD-10 criteria (Roth et al., 2011). Even though it can be criticised that not the most recent versions of the DSM and the ICSD were used (although they were in fact the most recent versions at the time), an important point has been made here about the ICD-10. In the ICD-11, which will be published shortly, it is likely that there will be a further sub-division of insomnia into the following subtypes: chronic insomnia, short-term insomnia and disorders of initiating and maintaining sleep (WHO, 2016).

Preferences for using either the ICD or DSM diagnostic system vary across different countries but, in general, the ICD-10 was used more commonly within a clinical context (for diagnosis and training), while the DSM-IV was more frequently used for research in the past (Mezzich, 2002). With the newest version of the DSM, the DSM-5 and the newest version of the ICSD, the ICSD-3, more concordance has been

achieved between the two classification systems and both are frequently used within a research context (Wilson & Attarian, 2017). Discussing the differences between the various diagnostic systems and considering the differences in prevalence rates between the various epidemiological studies, it has become clear how important it is to outline how insomnia is defined when conducting research in this area.

1.2.3 Subtypes of insomnia

1.2.3.1 Duration

The ICSD-3 only distinguishes between three subtypes of insomnia: chronic insomnia disorder, short-term insomnia disorder (also called acute insomnia) and ‘other’ insomnia disorder. The ‘other insomnia disorder’ can be used when not all the criteria have been met and can also be used as a preliminary diagnosis until enough information about the patient is available to decide on whether he/she has a short-term or chronic insomnia disorder (American Academy of Sleep Medicine, 2015). Short-term insomnia may be related to a stressor (for example, grief) and may improve over time or when the stressor is removed (American Academy of Sleep Medicine, 2015). The DSM-5 allows specification of whether the insomnia is episodic (meaning more than one month, but less than three months), persistent (more than three months) or recurrent (two or more occurrences within one year). The ICD-10 only classifies ‘nonorganic insomnia’ and no distinctions are made in terms of duration (such as short-term or chronic) but this is likely to change in the ICD-11 (WHO, 2016).

1.2.3.2 Sleep length

Previous research and theory suggests that insomnia with objective short sleep duration (SSD, typically < 6h of sleep per night; Vgontzas, Fernandez-Mendoza, Liao,

Edward & Bixler, 2013; American Academy of Sleep Medicine, 2014) differs importantly from insomnia with normal sleep duration (Vgontzas et al., 2013; NSD, ≥ 6 h of sleep per night). For example, it was shown that those individuals with SSD insomnia have an increased risk of cardiometabolic morbidity and mortality as compared to those individuals with NSD insomnia. More recently, SSD insomnia (defined in that study as 5-6 hours of sleep) was also found to be associated with hypercholesterolemia (Lin, Tsai, & Yeh, 2016). This theory is discussed in the ICSD-3 (American Academy of Sleep Medicine, 2015), and has also gained support from another recent study (Fernandez-Mendoza et al., 2016). Considering a sample of adolescents, insomnia symptoms with SSD (in that study defined as ≤ 7 hours of sleep) were found to be associated with rumination, depression, social isolation and problems with mood regulation, while NSD insomnia symptoms were found to be related to aggressive and rule-breaking behaviours (and, to a lesser extent, to rumination). One criticism that could be made here is that normal sleep length for the majority of the general population is about 7 hours (American Academy of Sleep Medicine, 2015; Markov & Goldman, 2006) but has been defined as SSD in this study. And, in general, there seems to be no consensus in the time period that should be used to define sleep length as being either normal or short. The definition of short sleep time varies from study to study. Sometimes a median split is used which will inevitably lead to differences in the definition of what is short or long sleep as it depends on the sample (Fernandez-Mendoza et al., 2016; Lin et al., 2016; Vgontzas et al., 2013). This theory is discussed in more detail in **Chapter 4: Self-reports of insomnia with short versus normal sleep duration.**

1.2.3.3 Paradoxical insomnia: A subtype unrelated to ‘normal’ insomnia

The term ‘paradoxical insomnia’ (also called ‘sleep-state misperception’) is outdated. It was part of the primary insomnia classification and a distinctive subtype as outlined in the ICSD-2 but is no longer included in the ICSD-3 (American Academy of Sleep Medicine, 2015). However, it is still mentioned under chronic insomnia (American Academy of Sleep Medicine, 2015). This may be related to the issue that people with insomnia generally have a tendency to underestimate their sleep length and their complaint is subjectively measurable rather than objectively measurable (American Academy of Sleep Medicine, 2015; Feige et al., 2008). Therefore, in current clinical practice, insomnia patients are typically assessed using subjective measures (American Academy of Sleep Medicine, 2015, APA, 2013).

1.2.4 Symptoms versus diagnosis

In the past, there was a discussion about the terms ‘primary’ and ‘secondary’ insomnia, and the extent to which insomnia was just a symptom of another (secondary) disorder rather than being regarded as a ‘stand-alone’ (primary) disorder in itself. Insomnia was often considered to be a symptom of anxiety disorders, depression or substance use/abuse (Ford & Kamerow, 1989; see Harvey, 2001) which meant that insomnia was trivialised and the main treatment focused on the other (‘primary’) disorder (Kupfer, 1999). Harvey (2002) highlighted evidence showing that insomnia is more than just the symptom of another disorder. This issue is also highlighted in the ICD-10 where it is stated that insomnia is often a symptom or part of the diagnostic criteria of another disorder and should therefore only be diagnosed if the insomnia symptoms actually dominate the clinical picture (WHO, 1992).

Even though insomnia can be a symptom of physical and mental disorders, this does not mean that it cannot be an entity on its own. According to Harvey (2002), it is

not useful to describe insomnia as ‘secondary’ as it often develops first. Plenty of research has shown that sleep problems precede or predict, for example, depression (Baglioni et al., 2011; Breslau, Roth, Rosenthal, & Andreski, 1997; Eaton, Baldawi, & Melton, 1995). It can be helpful to treat insomnia even without treating the comorbid disorder. Recently, it was found that treating insomnia also improves a comorbid depression or anxiety disorder (Bélanger et al., 2016). More specifically, after treating insomnia, 66% of the group with comorbid depression or anxiety disorder no longer met the diagnostic criteria for those illnesses. Furthermore, when only the insomnia is targeted, comorbid depression or anxiety does not impair the effectiveness of the treatment for the sleep problem (Bélanger et al., 2016). This is only to some extent in line with previous findings that showed that cancer patients treated with cognitive behavioural therapy for insomnia (CBT-I) because of their insomnia also improved in fatigue, but only 6% of all participants improved in anxiety symptoms as well and about 9% of all participants also showed a remission in depression as a results of CBT-I. One criticism that could be made here is that the study by Bélanger and colleagues (2016) only focused on a particular population and had a relatively small sample size (n = 113) out of which only 20 showed comorbid fatigue, depression and anxiety at the same time. Therefore, it may not be possible to generalise these results to the general population (Fleming, Randell, Harvey, & Espie, 2014).

Early research has also shown that insomnia can occur without any comorbidity (see, for example, Weissman, Greenwald, Nino-Murcia, & Dement, 1997). Harvey (2002) argues that in clinical practice, usually only one disorder is the focus of treatment. This means that if insomnia is diagnosed as the ‘primary’ disorder, it is treated while the other disorder is neglected. However, if insomnia was considered to be just a symptom of another disorder, then the treatment focuses mainly on the other

disorder. It has been suggested that it might be helpful to consider the two disorders as comorbid and treat both of them, rather than just focusing on one. This is also underlined in a comment about comorbidity of insomnia disorder in the DSM-5 where it states that the relationship between medical disorders (such as coronary heart disease or arthritis) as well as mental disorders (such as depression or anxiety) and insomnia is not just one-directional but bidirectional and possibly changes over time. Therefore, the term ‘comorbid insomnia’ should be used (APA, 2013). In the most recent version of the DSM, primary insomnia is no longer included (see, DSM-5, APA, 2013). It should be mentioned here that the terms ‘primary’ and ‘secondary’ insomnia are still being used by some researchers to date (see, for example, Chiu, Chang, Hsieh, & Tsai, 2016). However, the terms are used in the sense of ‘with (secondary) or without (primary) a comorbidity’ – they do not imply any particular order of occurrence of the insomnia. In a review of studies considering CBT-I and for comorbid insomnia (comorbid with depression, substance use disorders, post-traumatic stress disorder and anxiety) it was suggested that CBT-I may be useful, even if insomnia is not the primary mental health issue (Taylor & Pruiksma, 2014). However, the results were not conclusive and more research in this area is needed (Taylor & Pruiksma, 2014). It should be mentioned that some difficulties were encountered when conducting this meta-analysis because of the different types of analyses, the inconsistencies in reporting means, standard deviations and interaction effects across the various studies included (Taylor & Pruiksma, 2014).

1.2.5 Differential diagnosis

According to the DSM-5, insomnia can be diagnosed as a stand-alone disorder or may be comorbid with a sleep disorder (like sleep apnoea), a medical disorder (for example, diabetes) or any other psychological disorder (such as depression). For a differential diagnosis, variations in normal sleep should be taken into account (for

example, some people do not need as much sleep as others but this is no reason for concern) (Taylor, Gehrman, Dautovich, Lichstein, & McCrae, 2014). The individual's personal situation should also be taken into account. If insomnia only occurs for a short period as a result of life events or problems related to the sleep schedule but still causes distress, a diagnosis of 'other specified' or 'unspecified' insomnia disorder should be given (APA, 2013). There are other disorders that also cause symptoms similar to those in insomnia which should be differentiated: advanced or delayed sleep phase syndrome and circadian rhythm sleep-wake disorders (including shift work type), restless legs syndrome, breathing-related sleep disorders (featuring, for example, long pauses in breathing which disturb normal sleep), narcolepsy, parasomnias and substance or medication induced sleep disorder (insomnia symptoms are caused by a substance or medication, for example caffeine-induced sleep disorder) (APA, 2013; WHO, 1992; Roth & Roehrs, 2003). It is important to be aware of these other disorders in order to make sure their symptoms are not mistaken for insomnia when conducting research in this area.

According to the ICD-10, nonorganic insomnia should be distinguished from 'nonorganic disorder of the sleep-wake schedule', sleep terrors, sleepwalking or nightmares which represent a separate diagnosis (WHO, 1992).

Shift-work sleep disorder is caused by a disturbance of the circadian rhythm as a result of an irregular shift-work pattern (WHO, 1992). In a similar way, sleep disturbances can also be caused by jetlag (American Academy of Sleep Medicine, 2015). There are two processes for regulating the wake- and sleep-times: the circadian rhythm and sleep homeostasis (see two process model of sleep regulation for a detailed outline, Borbély, 1982). The circadian rhythm is usually somewhat longer than 24 hours and zeitgeber (environmental cues such as light/darkness, etc.) synchronise the

biological clock to the 24-hour rhythm (Berson, Dunn, & Takao, 2002; Guardiola-Lemaitre & Quera-Salva, 2011). Sleep homeostasis is related to the need to sleep, meaning that the longer one is awake the greater is the need to sleep again, while the more sleep that one has had, the lower the sleep propensity (Borbély, 1982).

In advanced sleep phase disorder (often occurring in elderly individuals), the individual falls asleep too early and therefore wakes up too early in the morning (this has to do mainly with having a slightly shorter circadian rhythm, and environmental factors may be involved as well, such as life-style changes). This is similar to delayed sleep phase disorder, in which the individual struggles to fall asleep in the evening and then has difficulties getting up at the socially desired time in the morning (this is related to a slightly longer circadian rhythm and environmental factors may be involved as well, for example, staying up late on purpose to have more leisure time) (ICSD Diagnostic Classification Steering Committee, 1990). Advanced or delayed sleep phase disorder and insomnia are sometimes difficult to differentiate. They can overlap, not just in terms of early awakenings or problems falling asleep at night; but they might also include negative cognitions associated with sleep or arousal as the individual may get frustrated because of the sleep problems (American Academy of Sleep Medicine, 2015). However, they differ from insomnia, as an individual with advanced or delayed sleep phase disorder would not have any sleep complaints if he/she was able to stick to his/her own circadian rhythm (American Academy of Sleep Medicine, 2015).

In restless legs syndrome and periodic limb movement syndrome, involuntary movements of the legs (or arms or legs respectively) during sleep causes a disturbance of sleep (APA, 2013). For sleep related breathing disorders, it is problems breathing during the night (pauses in breathing as well as snoring) that can cause a disturbance in sleep rather than insomnia (APA, 2013).

Narcolepsy is another sleep disorder that should be differentiated from insomnia. Symptoms include excessive daytime sleepiness (this includes falling asleep involuntarily), sleep paralysis (an inability to move after waking up), cataplexy (a sudden loss of muscle tone while being fully conscious which is often triggered by intense emotions) and/or sleep-related hallucinations (APA, 2013). The ICSD-3 also states that falling asleep unintentionally is not a common feature of insomnia disorder, but typical for sleep disorders such as narcolepsy or sleep apnoea (American Academy of Sleep Medicine, 2015). However, insomnia can also lead to brief 'lapses', which are moments of non-responsivity or micro-sleep (Roth & Roehrs, 2003).

Parasomnias include involuntary behaviours during sleep (for example, sleepwalking) that can disturb the sleep and cause awakenings (APA, 2013). Insomnia-like symptoms can also be caused by alcohol or illicit drug or medication abuse (APA, 2013).

The ICSD-3 also distinguishes between insomnia and insufficient sleep syndrome which is caused by voluntarily delaying sleep because of social activities, busy daytime schedules or in order to enjoy more leisure time (also called 'social jet lag', American Academy of Sleep Medicine, 2015).

In practice, if not thoroughly assessed, the sleep disorders outlined above may be mistaken for insomnia. The sleep disorders outlined above may result in nightly awakenings, low sleep quality, unrestful sleep, problems falling asleep or waking up too early in the morning, which may be misinterpreted by a layperson as insomnia symptoms. For example, parasomnias or restless legs syndrome may cause nightly awakenings, or sleep disordered breathing can result in low sleep quality and unrestful sleep. Delayed sleep phase disorder may cause problems falling asleep at night and advanced sleep phase disorder may cause the early morning awakenings – there are

numerous examples (Taylor et al., 2014). As the treatment for all of these disorders can to some extent differ from the treatment for insomnia, it is important to exclude these differential diagnoses (APA, 2013; Taylor et al., 2014). Therefore, the individual with the sleep problem needs to be questioned carefully. It should be easy to obtain information about the person's shift work and it is usually also possible to identify advanced and delayed sleep phases simply by asking the patient the right questions. However, restless legs syndrome, periodic limb movement disorder, sleep related breathing disorders, narcolepsy and parasomnias can be more difficult to exclude. It can be helpful to ask the patient's bed partner or to assess the person in a sleep laboratory to make sure that the right diagnosis is made (Taylor et al., 2014).

It is worth mentioning a further disorder here that should be considered as being different from the insomnia discussed in this thesis. Fatal familial insomnia is a completely different disorder which is unrelated to the insomnia discussed here. It is a rare disorder of genetic origin which is characterised by motor disturbances, dysautonomia (a disorder of autonomic nervous system function) and an inability to sleep which leads to rapid death (Lugaresi et al., 1986; Lugaresi, Tobler, Gambetti, & Montagna, 1998). The usual age for the onset of this disease is 50 (although cases of early onset have been discovered – Harder et al. 2004). This disorder should be differentiated from the insomnia as discussed in this PhD thesis and will therefore not be discussed further.

1.3 What do we know about insomnia from a theoretical point of view?

Various theories of insomnia have been developed in order to attempt to understand the mechanisms and the aetiology of insomnia (Marques, Allen Gomes,

Clemente, Santos, & Castelo-Branco, 2015). In the light of the vast number of theories of insomnia that have derived from the different areas of research, it is only possible to present a selection of the ones that are most relevant to the topic of this PhD thesis. The main focus of this thesis is on the cognitive theories of insomnia and, in particular, on the most recent model by Ong and colleagues (2012) – the metacognitive model of insomnia. Only some of the main cognitive models will be discussed in more detail while other theories will just be briefly mentioned and/or excluded from this review altogether.

It is important to note that some of the theories mentioned here are discussed using different names in the various literature. For example, the integrative model of the interaction between sleep-interfering and sleep-interpreting processes by Lundh & Broman, 2000 is also called hybrid cognitive-behavioral model (Marques et al., 2015). This model will be referred to as hybrid cognitive-behavioral model from here on. The micro-analytic model of insomnia by Morin (1993) was also called integrative model of insomnia in the original publication but also sometimes referred to as cognitive-behavioural model of insomnia (see Ong et al., 2012). This model will be referred to as micro-analytic model of insomnia from here on.

1.3.1 Theories most relevant to this thesis – Cognitive models of insomnia

1.3.1.1 The 3P model of insomnia

Starting with the theories most relevant to the topics discussed in this thesis, one of the most important early models of insomnia, which was the basis for many other models of insomnia, is the ‘3P model of insomnia’ (Spielman & Glovinsky, 1991; Spielman, Caruso, & Glovinsky, 1987). In this theory the factors involved in the various possible stages of insomnia (acute, short-term and chronic) are discussed. The three Ps refer to: Predisposing factors (such as hyperarousal), precipitating factors

(psychological and medical factors and life events) that may trigger insomnia, and perpetuating factors which maintain insomnia (certain thoughts and beliefs and unhelpful adopted behaviors). The 3P model of insomnia is an attempt to explain how the different stages of insomnia may be developed. This model has stimulated research and has led to the development of many related theories, often including similar elements, but setting different foci. For example, more recently the role of the cortisol awakening response was discussed as being a possible measure of a biological process that is related to the predisposition, precipitation and perpetuation of insomnia (Elder, Wetherell, Barclay, & Ellis, 2014). Self-reported worry (a trait-like characteristic related to predisposition as discussed in the '3P model') was associated with a greater display of cortisol awakening response in healthy individuals (Spielman et al., 1987; Spielman & Glovinsky, 1991; Zoccola, Dickerson, & Yim, 2011). Cortisol is released when stress is experienced, which also affects the cortisol awakening response (Izawa, Saito, Shiotsuki, Sugaya, & Nomura, 2012). Life events which cause stress or stress itself can be considered to be a precipitating factor, according to the 3P model (Elder et al., 2014). An example of how the cortisol awakening response can be related to a perpetuating factor of insomnia is maladaptive behaviours, such as drinking coffee (Spielman et al., 1987; Spielman & Glovinsky, 1991). Caffeine intake (measured in coffee consumption per week) is related to the cortisol awakening response (Harris, Ursin, Murison, & Eriksen, 2007). It can be criticised that this study only focused on nursing staff. It can therefore be questioned if the findings apply to the general population.

1.3.1.2 The hybrid cognitive-behavioural model

Another interesting theory is the hybrid cognitive-behavioural model (also called integrative model of the interaction between sleep-interfering and sleep-interpreting

processes, Lundh & Broman, 2000; Marques et al., 2015 – see **Figure 1.1**). It suggests that, in the case of insomnia, sleep-interfering and sleep-interpreting processes interact. Various factors can contribute to predispose individuals to sleep-interfering processes. These include behavioural and cognitive strategies (including, for example, rumination), conflicts in interpersonal relationships, increased levels of arousability and stimulus-arousal association (to what extent arousal is caused by new stimuli) (Lundh & Broman, 2000).

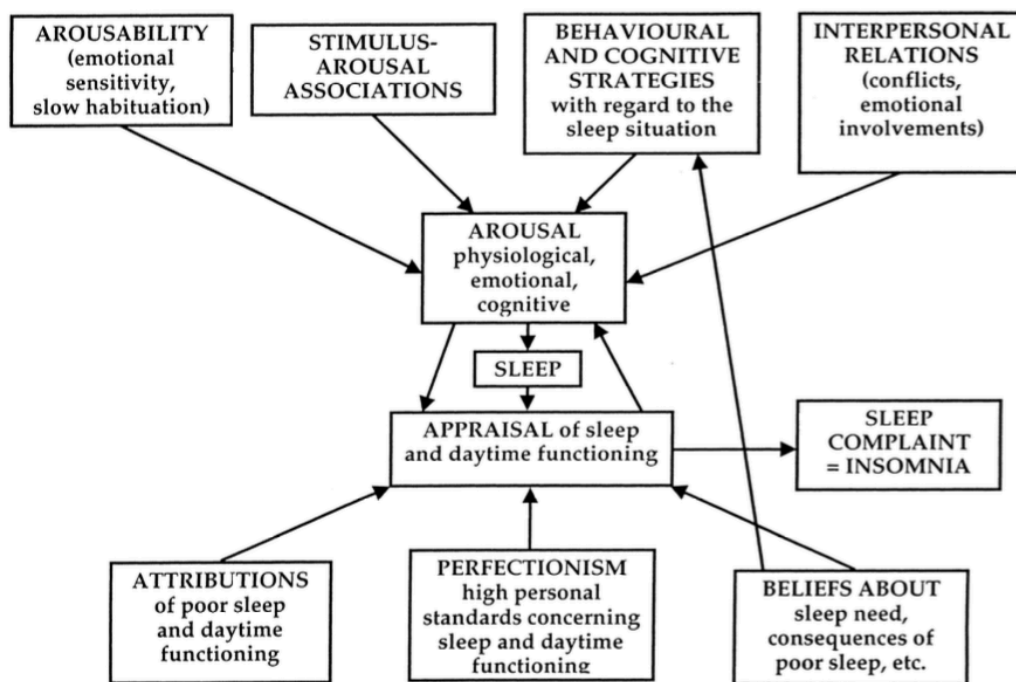


Figure 1.1 The integrative model of the interaction between sleep-interfering and sleep-interpreting processes. Reprinted from “Insomnia as an interaction between sleep-interfering and sleep-interpreting processes” by L. G. Lundh and J. E Broman, 2000, *Journal of Psychosomatic Research*, 49(5), p. 308.

In contrast to the sleep-interfering processes, the sleep-interpreting processes include: perfectionistic expectations about sleep and daytime functioning, dysfunctional beliefs about sleep and false attributions about the consequences of insomnia. This theory stimulated the idea of including the mindfulness approach as a possible element in the treatment of insomnia (Lundh, 2011; Lundh & Broman, 2000).

1.3.1.3 The microanalytic model of insomnia

The microanalytic model is another well-studied theory (Marques et al., 2015; Morin, 1993; also called integrative model of insomnia in the original publication and called cognitive-behavioural model by Ong et al., 2012). It considers how insomnia is maintained as a vicious cycle of sleep disruption, feeding into arousal, negative cognitions, maladaptive behaviours – all of which again cause disturbance of sleep (Morin, 1993; Ellis, Gehrman, Espie, Riemann, & Perlis, 2012). This theory considers hyperarousal to be a central element in the development and maintenance of insomnia, as arousal (cognitive, emotional and somatic arousal) which is a crucial factor in regulating wakefulness and sleep (Morin, 1993) – see **Figure 1.2**.

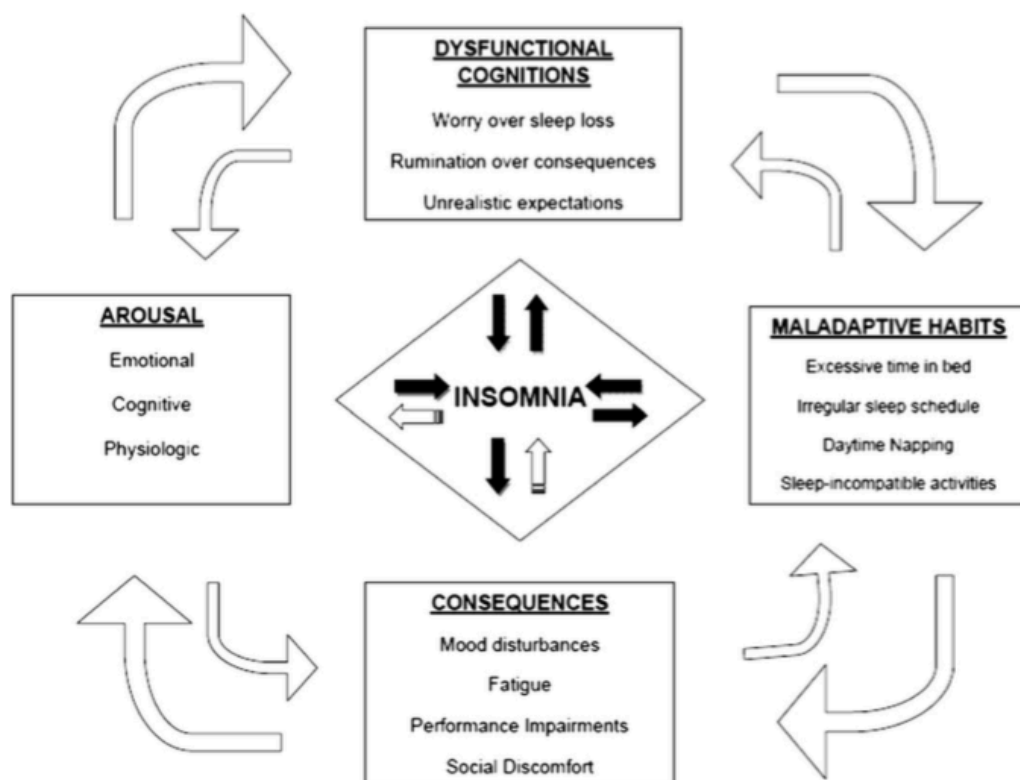


Figure 1.2 Microanalytic model of insomnia (also called Cognitive-Behavioral Model of insomnia) (Morin, 1993). Reprinted from “Improving sleep with mindfulness and acceptance: A metacognitive model of insomnia” by J. C. Ong, C. S. Ulmer and R. Manber, 2012, *Behaviour Research and Therapy*, 50, p. 652.

Arousal may be affected by various influences such as negative daytime events. In turn, arousal and sleeplessness may lead to rumination and worries over sleep, which again results in sleep disturbance and daytime consequences such as fatigue. Insomnia symptoms and its negative consequences during the day then lead to maladaptive behaviours (for example, spending excessive time in bed, trying to fall asleep), as the individual tries to cope with the sleeping problem. The various factors interact rather than influence each other in just one direction only (Morin, 1993).

1.3.1.4 The cognitive model of insomnia

Another theory that builds on the ideas behind the '3P model' is Harvey's (2002) cognitive model of insomnia (see **Figure 1.3 overleaf**) which attempts to explain the factors involved in maintaining insomnia. This theory states that increased negative cognitive activation leads to somatic arousal, which is one of the factors that cause a distorted perception of sleep deficits in the night and distorted daytime functioning (two characteristics of insomnia).

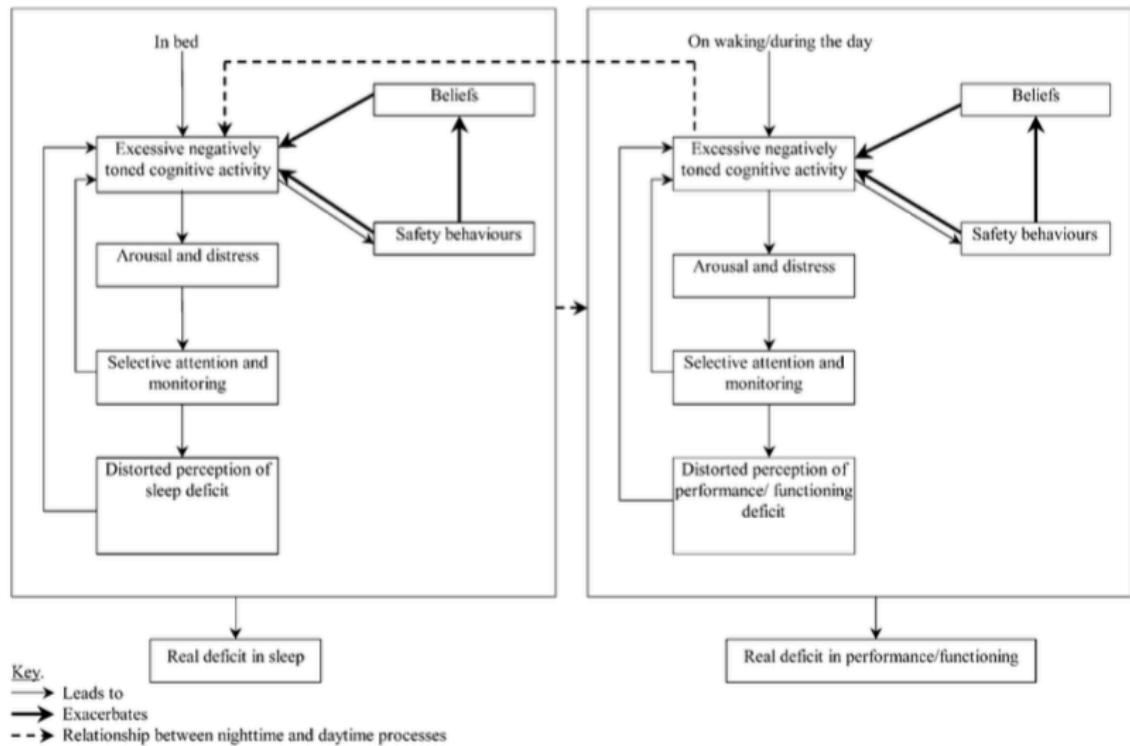


Figure 1.3 Harvey’s cognitive model of insomnia. Reprinted from “Improving sleep with mindfulness and acceptance: A metacognitive model of insomnia” by J. C. Ong, C. S. Ulmer and R. Manber, 2012, *Behaviour Research and Therapy*, 50, p. 653.

Somatic arousal refers to physical arousal and includes symptoms such as increased heart rate, while cognitive activation relates to the psychological part that includes for example, not being able to ‘shut off’ thoughts, etc. (Nicassio, Mendlowitz, Fussell, & Petras, 1985). Furthermore, dysfunctional beliefs about sleep exacerbate negative cognitions (for example, excessive worry), which in turn leads to safety behaviours (for example, spending an excessive amount of time in bed). Safety behaviours again reinforce dysfunctional beliefs about sleep and exacerbate negative cognitions. A recent literature review has shown that there is plenty of support for the cognitive model of insomnia as proposed by Harvey (2002; Hiller, Johnston, Dohnt, Lovato, & Gradisar, 2015). The model ‘3P model’ by (Spielman et al., 1987) and Harvey’s cognitive model were also the basis for understanding insomnia through cognitive modelling as outlined by Espie (2007).

1.3.1.5 The metacognitive model of insomnia

One of the most recent and most comprehensive cognitive theories is the metacognitive model of insomnia (Ong et al., 2012). It builds on the previous cognitive theories, as well as on the hybrid cognitive-behavioural model (also described as the integrative model of the interaction between sleep-interfering and sleep-interpreting processes) by Lundh and Broman (2000) (Marques et al., 2015). This theory also aimed to illuminate how mindfulness-based therapies help to enhance cognitive flexibility, equanimity (a stance in which the individual is no longer overly attached to the outcome of sleep), balanced appraisal and commitment to values (all metacognitive processes) to lower secondary distress, reduce sleep-related arousal and, in this way, to also improve insomnia (Ong et al., 2012). By re-conceptualising cognitive arousal, another level was added, dividing it into primary arousal and secondary arousal. Primary arousal is influenced by expectations about sleep, consequences of insomnia during the day and by an increase in mental activity while in bed (Ong et al., 2012). Secondary arousal, on the other hand, comprises cognitive bias, rigidity of thought, attachment to negative thoughts, and absorption in terms of interpretative value – this refers to a metacognitive level which perpetuates insomnia (Ong et al., 2012) (see **Figure 1.4** overleaf for illustration).

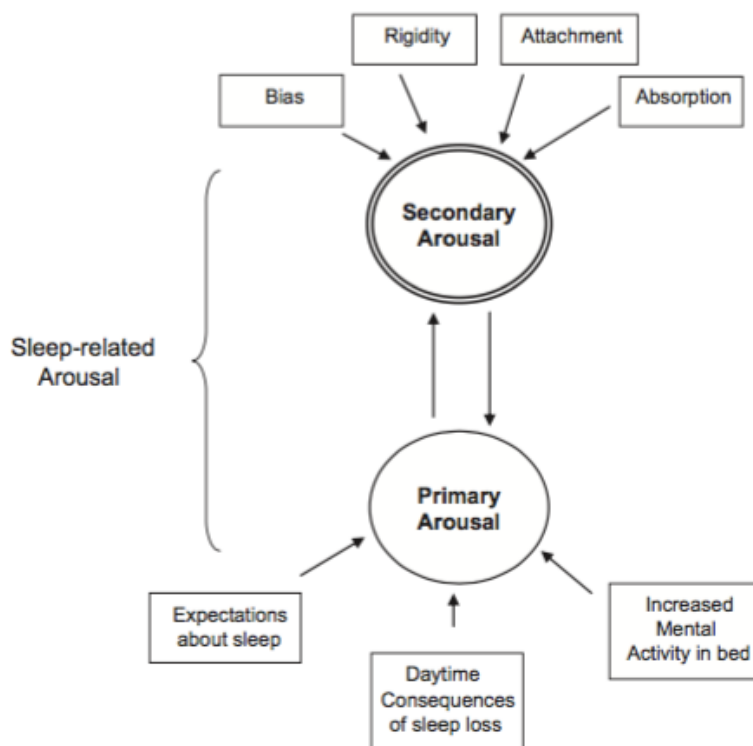


Figure 1.4 Two-level model of sleep-related arousal, presented in the metacognitive model of insomnia by Ong and colleagues (2012). Reprinted from “Improving sleep with mindfulness and acceptance: A metacognitive model of insomnia” by J. C. Ong, C. S. Ulmer and R. Manber, 2012, *Behaviour Research and Therapy*, 50, p. 653.

Note: Primary arousal = cognitive processes relate to the inability to sleep; Secondary arousal = (meta-level) addressing how the individual relates to thoughts about sleep.

The idea is that metacognitive awareness is the first step in allowing a shift in the relationship with the negative cognitions, rather than attempting to change the thoughts themselves, hence trying to adopt a new metacognitive stance (Ong et al., 2012). The metacognitive stance incorporates the main principles of acceptance and mindfulness, in which balance is achieved. This means that the individual neither avoids nor is overly attracted to emotions and thoughts related to sleep (Ong et al., 2012). For example, the person does not avoid the thought of going to bed because he/she does not expect to not be able to fall asleep anyway, and neither is staying in bed for an excessive time after awakening trying harder to fall asleep in spite of not being able to fall asleep again. Furthermore, with this approach, flexibility is practiced, which means to let go of the

rigidity of thoughts about sleep and to realise that thoughts are not facts. For example, by regarding every night as a new opportunity to sleep well again (adopting a beginner's mind) (Ong et al., 2012). Also, it is attempted to achieve equanimity, which describes a stance in which the individual is no longer overly attached to the outcome of sleep, thus facilitating de-arousal. Finally, increasing commitment to their own values again is another way in which metacognitive processes can help to improve insomnia (Ong et al., 2012). This means not losing focus on other important aspects or needs in life. For example, by not sleeping in after a bad night's sleep but going to the gym as planned to keep oneself physically fit (Ong et al., 2012). In this way, an over-emphasis on the topic 'sleep' can be avoided and long-term goals (for example, staying physically fit) are not given up over short-term goals (for example catching up on more sleep). For a more detailed outline of all aspects in which metacognitive processes help to improve insomnia, see Ong and colleagues (2012).

This theory was supported by the findings of a longitudinal study that certain cognitive processes (including selective attention, worry, dysfunctional beliefs about sleep, somatic arousal, monitoring and maladaptive safety behaviours) were associated with the persistence of insomnia, and distinguishes those individuals with insomnia from good sleepers (Norell-Clarke, Jansson-Fröjmark, Tillfors, Harvey, & Linton, 2014). It can be criticised that attrition was high (53%) in this study and that responders were significantly older than non-responders. Furthermore, it was not possible to determine if the participants had experienced one long episode of insomnia or various shorter episodes during the time-span considered in this study (data was collected at three time points, spanning 18 months overall) (Norell-Clarke et al., 2014).

1.3.2 Occurrence of the analysed traits in cognitive theories

The numerous cognitive models of insomnia include traits similar to those analysed within this PhD thesis. For example, please refer to the **Figures 1.1, 1.2 and 1.3** above for a comparison of a selection of the different cognitive models of insomnia: the hybrid cognitive-behavioural model (also called integrative model of the interaction between sleep-interfering and sleep-interpreting processes, Lundh & Broman, 2000; Marques et al., 2015), the microanalytic model (Marques et al., 2015; Morin, 1993; also called integrative model of insomnia in the original publication and called cognitive-behavioural model by Ong et al., 2012) of insomnia and the cognitive model of insomnia (Harvey, 2002).

This illustrates the claim that cognitive pre-sleep arousal, somatic pre-sleep arousal and dysfunctional beliefs about sleep all play a role in insomnia and that there are other factors which may also be important in those theories. Mindfulness is not included directly in these three theories but it is implicit here. Indeed, meta-cognitive processes can be interpreted as a form of mindfulness and acceptance in terms of how an individual think about thinking (Ong et al., 2012). This is also related to sleep-interpreting processes in the model by Lundh & Broman (2000, see **Figure 1.1** above).

Similarly, the attitudes about sleep and the interpretative value of dysfunctional cognitions can be interpreted as overlapping with metacognitive processes or as being related to mindfulness (Ong et al., 2012; see **Figure 1.4** above).

Furthermore, the selective attention and monitoring discussed in Harvey's (2002) cognitive model of insomnia also refers to facets of mindfulness (Baer et al., 2006; **Figure 1.3** above), that relate to the mindfulness subscales 'acting with awareness' and 'observing'.

One element mentioned in these theories that was not included in this thesis, as no data was collected on this trait for G1219, is maladaptive behaviours. It will therefore not be discussed here in detail but will be mentioned in various sections of this discussion, whenever relevant. Maladaptive behaviours predict the severity of insomnia – the stronger the need to adopt safety behaviours, the more severe the insomnia experienced. They are also associated with dysfunctional beliefs about sleep – the more frequent the safety behaviours, the more dysfunctional beliefs about sleep (Hood et al., 2011).

It can be summarized that all these cognitive models include elements similar to the traits mindfulness, cognitive pre-sleep arousal, somatic pre-sleep arousal and dysfunctional beliefs about sleep. Although they seem to play a crucial role in the development and maintenance of insomnia, very little is known about their aetiology and origin it was decided to analyse these from a behavioural genetic perspective for this PhD thesis.

1.3.3 Interaction of the analysed traits in cognitive theories

According to previous literature about cognitive models of insomnia, it is likely that the variables analysed within this PhD thesis interact with and influence each other rather than being linked in a one-directional way (see Harvey 2002, Morin, 1993; Ong et al., 2012). The cognitive models vary in how they describe the way in which the traits that have been discussed interact. In the hybrid cognitive-behavioural model, cognitive, physiological and emotional arousal influence sleep directly but they are not directly influenced by beliefs about sleep (Lundh & Broman, 2000). In contrast to this model, the microanalytic model states that arousal (including emotional, cognitive and physiological arousal) interacts with dysfunctional cognitions and vice versa and both also mutually influence insomnia (Morin, 1993). In Harvey's (2002) cognitive model of

insomnia, it is stated that the direction of influence of the various factors shows less interaction with each other. Beliefs are only influenced by safety behaviours and have a one-way association with negative cognitions which influence arousal and distress and are themselves also influenced by selective attention and distorted perception. For an illustration of this explanation, see **Figures 1.1, 1.2 and 1.3** above. All these models include additional factors that influence insomnia, which are discussed in detail elsewhere (see, Harvey, 2002; Lundh & Broman, 2000; Morin, 1993). In summary, it can be said that, even though these cognitive theories vary, they all consider cognitive pre-sleep arousal, somatic pre-sleep arousal and dysfunctional beliefs about sleep to be in some way important factors in the development and maintenance of insomnia and they also indirectly include aspects that are (to some extent) indirectly related to mindfulness. The role of mindfulness in insomnia symptoms may be indirect (as discussed by Ong et al., 2012). However, the underlying mechanisms of the association between these traits and insomnia symptoms are unclear. Therefore, the relationship between these elements and insomnia symptoms are considered phenotypically in the analyses included in this PhD thesis. Furthermore, some light is shed on the extent to which genetic and environmental influences are involved in these associations to broaden our knowledge about the roots of insomnia.

1.3.4 Overview of other main theories of insomnia

In addition to the theories discussed above, other approaches have been taken in order to consider insomnia from a theoretical point of view, taking into account various points of view including medical/pharmacological, neurological, circadian, psychiatric/psychological and behavioural/cognitive perspectives (Roth & Roehrs, 2003).

One of the first theories relating to insomnia was the internalising of conflicts model (Kales, Caldwell, Preston, Healey, & Kales, 1976). It attempted to define the type of personality that would be typical of patients with primary insomnia, stating that internalising emotions, conflicts and problems (for example, in the form of depression) is a characteristic of individuals with insomnia. This leads to an increase in emotions (for example, fear of sleeplessness) which again promotes physiological arousal, making the person less likely to be able to fall asleep (Borkovec, 1982; see also Marques et al., 2015). Finding personality traits associated with insomnia is still the subject of current research. For example, most recently a study of insomnia in shift workers showed that neuroticism predicts insomnia (the higher the score in neuroticism, the higher the insomnia symptoms score), while morningness was found to be negatively associated with insomnia symptoms (Larsgård & Saksvik-Lehouillier, 2016). This study can be criticised because the response rates in time 1 and time 2 were low (only 30% of the contacted individuals at time 1 and less than 30% of the contacted individual at time 2 responded) and there were only 86 participants remaining for the final analyses. Furthermore, different types of shift work were all analysed together (Larsgård & Saksvik-Lehouillier, 2016). The findings are in line with the theory of Harvey, Gehrman and Espie (2014) that individuals who are high in neuroticism are more likely to exhibit high stress-reactivity and more negative emotions, suggesting that when experiencing the first disruptions in sleep, this is learned to be associated with the sleep environment and with sleep itself (Harvey et al., 2014).

In another study, it was outlined that carrying the s/s homozygous variant for the serotonin transporter polymorphism 5HTTLPR (two s-allele), which is involved in the serotonin regulation in the synapse, is associated with a genetic vulnerability to increased stress reactivity (this also taps into the concept of neuroticism) (Karg,

Burmeister, Shedden & Sen, 2011). This is thought to be related to disrupted sleep and is relevant to the onset of insomnia and to how ‘easily’ someone can be conditioned to develop insomnia (Deuschle et al., 2010). This theory builds a bridge from genetics to neurobiological and to the psychological perspective (Harvey et al., 2014). However, it should be pointed out that research has moved away from looking at single genetic variants (such as that a certain serotonin transporter polymorphism 5HTTLPR may be involved here) as being the big cause of complex traits (Plomin, DeFries, Knopik, & Neiderheiser, 2013). Even when considering the whole genome to identify genetic patterns involved in insomnia, findings are still very limited. A more detailed discussion can be found under **1.7.2 Genes involved**. The finding, that 5HTTLPR is involved in the serotonin regulation in the synapse, is in line with the idea of the stimulus control model (Bootzin, 1973; see also Marques et al., 2015). This suggests that insomnia arises from an erroneous conditioning of stimuli that are supposed to induce sleep and stimuli that cause arousal (for example, lying in bed causes arousal, but sitting on the sofa watching TV induces sleep).

The psychobiological inhibition model (Espie et al., 2006), suggests that there is an attention-intention-effort pathway involved in the development of insomnia. In a nutshell, the model states that falling asleep is a passive or unintentional process that can be distracted by actively directing one’s attention to it (scanning mode), instructing oneself to fall asleep (planning mode) and trying harder to sleep (performing mode) (Espie et al., 2006). This leads to maladaptive behaviours (such as alcohol use) which again reduce the chances of a good night’s sleep. The theory underlines the role that homeostatic and circadian processes play in sleep and states that the body/brain must be ready for sleep. It also argues that the inability to de-arouse is the main problem with insomnia (Espie et al., 2006).

Another model that should be mentioned is the hyperarousal model as proposed by Riemann and colleagues (2010). Reviewing studies considering EEG, autonomous, neuroimaging, neuroendocrine and neuro-immunological measures of participants with insomnia, it was found that there is an increase of arousal at night as well as during the day (Riemann et al., 2010). In conjunction with earlier theories of neurobiological mechanisms involved in the regulation of the wake-sleep rhythm (see, Lu et al., 2006; Morruzi & Magoun, 1995; Saper et al., 2005), it was argued that these findings support the idea of a genetic predisposition to hyperarousal. This genetic predisposition makes the individual more vulnerable to experiencing insomnia symptoms and stressors can trigger the vicious cycle of developing insomnia. The hyperarousal model is an interesting attempt to incorporate different perspectives. A more detailed discussion of this theory can be found elsewhere (see, Riemann et al., 2010).

1.4 Risk factors, comorbidities and associated negative factors

1.4.1 General risk factors

The most common risk factors that were found to be associated with insomnia are gender, age, shift work and medical and psychiatric diseases (Roth et al., 2011; Roth & Roehrs, 2003). Having a disability or a severe disease such as cancer was also found to be associated with an increased likelihood of developing insomnia (Roth et al., 2011; Savard & Savard, 2013). Another study found that there is an association between age and the probability of experiencing insomnia but it also stated that the impairment caused by sleep problems actually declines with age. This leads to the assumption that sleep problems may be better tolerated with increasing age (Roth et al., 2011), which is also an interesting point to keep in mind when considering the prevalence rates of insomnia at different ages. Even though the study by Roth and colleagues (2011)

mentioned here was based on a large sample size, it can be criticised for just focusing on the north American population and just on individuals who were members of a large commercial health plan.

There is some inconsistency as to what extent people with insomnia differ from normal sleepers in terms of physically (or objectively) measurable parameters of arousal, such as heart rate variability, cortisol levels or metabolic indices (Bonnet & Arand, 1998; Nofzinger et al., 2004; Nofzinger et al., 2006). For example, the long-held claim that heart rate variability is impaired in individuals with insomnia could not be confirmed in a recent review (Dodds, Miller, Kyle, Marshall, & Gordon, in press).

Alcohol, caffeine and stimulant (drug) use/abuse are also a risk factor for developing insomnia (American Academy of Sleep Medicine, 2015, Ohayon, 2002). Furthermore, various medications can also cause insomnia symptoms (for example, endocrine drugs such as Tamoxifen or antiviral drugs such as Didanosine) (Taylor et al., 2014). Therefore, it is important to check which medications are being taken by the patient with insomnia symptoms (for a detailed review, see, Taylor et al., 2014). However, it should be kept in mind that side effects can differ from individual to individual and it is possible that multiple factors are involved at the same time. Furthermore, the sleep environment itself can also play a role in the development of insomnia. Uncomfortable surroundings, for example too much noise or too much light can also cause sleep disturbances which can subsequently lead to insomnia symptoms (Ohayon, 2002). This is a point that may be under-estimated by the patient but may become evident in comments such as ‘I do not mind sleeping in bright daylight, I never close the curtains’ and then the next moment, the patient is once again complaining about his/her insomnia symptoms.

1.4.2 Gender differences

Insomnia does occur in males and females of all ages but women are slightly more likely to experience insomnia than men, and insomnia is also more common in older rather than younger individuals (APA, 2013; Lichstein, Durrence, Taylor, Bush, & Riedel, 2003; Ohayon, 2002). However, these findings are inconsistent because there is not always a clear association between age and insomnia (see, for example, Weyerer & Dilling, 1991). For adolescents, the prevalence of an insomnia disorder is also higher in females but only after puberty (American Academy of Sleep Medicine, 2015; Roberts et al., 2008). Here again, estimates for prevalence rates vary.

1.4.3 Insomnia and the brain

There is mixed evidence as to whether individuals with insomnia have a brain structure different from that of normal sleepers (Riemann et al., 2007; Winkelmann et al., 2010). However, brain lesions caused by multiple sclerosis, brain trauma or stroke can all cause insomnia symptoms but these are usually accompanied by a variety of other neurological symptoms rather than just appearing on their own (American Academy of Sleep Medicine, 2015). Furthermore, some neurobiological studies on the sleep-wake regulation have shown that the ascending reticular activation system (ARAS) may play a crucial role in cortical arousal and the regulation of sleep and wakefulness (Moruzzi & Magoun, 1995). And it has been suggested that there might be something like a 'key-switch' in the hypothalamus which is related to switching off arousal during sleep (Lu, Sherman, Devor, & Saper, 2006; Saper, Scammell, & Lu, 2005). It has been speculated that this switch plays a role in insomnia (Riemann et al., 2010). However, it can be criticised that some of the reviewed PSG studies showed only a very small difference between those individuals with insomnia and good sleepers in terms of the objective measures of sleep, compared to subjectively reported sleep

(Riemann et. al, 2010). For more information about insomnia and related neurological structures, see also **1.3.4 Overview of the main theories of insomnia**.

1.4.4 Comorbidities and associated negative factors

Insomnia is associated with a wide range of medical and psychiatric diseases, as well as chronic pain, disabilities, and poor health in general (for more details, see also, Roth et al. 2011; Roth & Roehrs, 2003; Taylor et al., 2014). Some of these consequences have already been discussed under **1.2.4 Symptoms versus diagnosis**.

The most common comorbid mental health problem associated with insomnia is depression (Roth & Roers, 2003). The prevalence of psychiatric disorders in individuals with chronic insomnia lies between 40% and 50%, with affective disorders and anxiety being most frequently diagnosed (Ohayon & Roth, 2003). Insomnia and burnout were also found to be linked, having an aversive effect on one another (Armon, 2009). Burnout predicted a change in insomnia over time and vice versa, even when the participant was experiencing, for example, low work pressure (Armon, 2009). However, it should be mentioned here that the effect of burnout on insomnia, as measured at the second time point, was only minimal (the β weight of the effect of burnout on insomnia at time 2 was < 0.10 in the regression model).

As discussed under **1.2.4 Symptoms versus diagnosis**, a direction of causation is difficult to establish. However, some findings indicate that insomnia more frequently precedes than follows depressive and anxiety disorders and longitudinal studies have shown that individuals with insomnia were more likely to experience depression (see, for example, Ohayon & Roth, 2003; Roth & Roehrs, 2003).

Insomnia has also been found to be linked with an increased likelihood of suicide and accidental, fatal drug overdose (for a review see Winsper & Tang, 2014). For example, depressed patients differ in their sleep, depending on whether or not they

are suicidal, and insomnia was found to be linked to suicidality in depressed participants (Agargun et al., 2007; Chellappa & Araujo, 2007; Li, Lam, Yu, Zhang, & Wing, 2010; McCall et al., 2013). It should be pointed out that there were some inconsistencies in these findings. In one of the previously mentioned studies (Li et al., 2010), the link between suicidality and insomnia was no longer significant when controlling for depression or nightmares. It was also shown that the link between insomnia and suicidality was mediated by nightmares and dysfunctional beliefs about sleep (McCall et al., 2013).

A review of the literature shows that transient (also called short-term) insomnia is related to increased sleepiness and impaired psychomotor functioning (including slower reaction-times and problems with attention and vigilance), while chronic insomnia is not always associated with these problems (Roth & Roehrs, 2003). The review also shows that quality of life and memory functioning were found to be impaired, while the findings that insomnia is a risk factor for drug use were not consistent (Drummond et al., 2013; Roth & Roehrs, 2003). Fatigue is the most common complaint among patients with chronic insomnia (Roth & Roehrs, 2003). It can be criticised that this review was carried out some time ago. However, it does flag up some interesting points. For more physical risks and consequences associated with insomnia, see also the point mentioned under **1.2.3.2 Sleep length**.

1.4.5 Costs of insomnia

Sleep problems are a significant problem in our society and also present a financial burden as they generate both direct costs (for example, treatment costs) and indirect costs (for example, car accidents caused by sleepiness) and put a strain on our health care system (Daley, Morin, LeBlanc, Grégoire, & Savard, 2009). For example, the costs associated with reduced work efficiency in the United States due to insomnia

are estimated to be around 63 billion dollars (Kessler et al., 2011). Insomnia was also found to be linked to workplace injuries, costly workplace accidents and also to errors that add to the costs of a company (Kessler et al., 2011; Shahly et al., 2012; Uehli et al., 2014). It was estimated that workplace accidents and errors associated with insomnia added up to a combined cost of about 31.1 billion dollars a year (Shahly et al., 2012). A recent field experiment showed that this link can to some extent be explained by a worker's decreased safety behaviours if he/she is suffering from insomnia (Kao, Spitzmueller, Cigularov, & Wu, 2016). It can be criticised that this study used a cross-sectional design. Therefore, causality cannot be inferred and the sample was limited solely to the construction industry (Kao, Spitzmueller, Cigularov, & Wu, 2016). Using a wait list control (random assignment), the findings show that CBT-I not only improves insomnia and well-being directly but also indirectly enhances work-related outcomes (Barnes, Miller, & Bostock, 2017). This suggests that it may be beneficial for organizations to offer cost effective CBT-I to those employees who are experiencing insomnia (Barnes et al., 2017). It could be criticised that this study could have been improved by including a placebo treatment group in order to rule out a placebo effect, which has been done in the past. (see, for example, Espie et al., 2012). As a placebo treatment, for example, Imagery Relief Therapy can be used, i.e. training to visualise objects and at the same time thinking about their evening routine. This would be provided on the same application platform, with a similar design and functionality as for CBT, but with no active therapeutic elements (Espie et al., 2012). However, even when a placebo treatment group had been included, CBT-I has been shown to be effective (Espie et al., 2012).

1.5 How can insomnia be measured?

Since there were different definitions of insomnia in the past (across the various diagnostic manuals and across research), an attempt was made to standardise definitions and approaches for assessing insomnia (Bloom et al., 2009; Buysse, Ancoli-Israel, Edinger, Lichstein, & Morin, 2006; Edinger et al., 2004). This was attempted, for example, by outlining research diagnostic criteria for insomnia (Edinger et al., 2004). However, a certain degree of heterogeneity remains, as is demonstrated in the variety of measures that have been used to date and the differences in diagnostic criteria discussed (see below).

1.5.1 Subjective measures

1.5.1.1 Self-report questionnaires for insomnia

Various self-measure questionnaires to assess insomnia or insomnia symptoms or sleep disturbance are currently used in research and clinical practice. Common measures of insomnia symptoms include the Athens Insomnia Scale, the Insomnia Severity Index, the Insomnia Symptoms Questionnaire and the Sleep Condition Indicator. Furthermore, the Pittsburgh Sleep Quality Index and the Ford Insomnia Response to Stress Test are frequently used in conjunction with measures of insomnia. Only the Insomnia Severity Index and the Insomnia Symptoms Questionnaire are relevant to this thesis and will be discussed here.

1.5.1.1.1 Insomnia Severity Index (ISI)

The ISI is mainly based on the diagnostic criteria of the DSM-IV and the ICSD (Bastien, Vallières, & Morin, 2001). It focuses on the insomnia symptoms experienced and the distress and negative consequences caused by insomnia. It includes seven items targeting problems with falling asleep and maintaining sleep, satisfaction with quality of

sleep, issues with daytime functioning and distress and impairment caused by insomnia (Bastien et al., 2001; Morin, Belleville, Bélanger, & Ivers, 2011). It is available as a self-report measure, or it can be used by a clinician. There is also a version which can be completed by a significant other (meaning bedpartner) (Bastien et al., 2001). A recent meta-analysis comparing the PSQI, AIS and ISI found that all three had comparable psychometric properties (Chiu et al., 2016). It should be pointed out here that one limitation of this meta-analysis was that when the data was combined, the different diagnostic criteria used across the studies may have caused an inaccuracy in the estimates judging the psychometric properties of the self-report-questionnaires (Chiu et al., 2016).

1.5.1.1.2 Insomnia Symptom Questionnaire (ISQ)

The ISQ is similar to the ISI as it is based on the diagnostic criteria for insomnia of the DSM-IV as well, but is usually coded as a dichotomous variable in terms of whether or not the diagnostic criteria for insomnia are met (Okun et al., 2009). The ISQ is the measure (in a 6-item version) used in the analyses in this thesis and is therefore discussed in more detail in the third chapter (see **3.2.3 Insomnia symptoms**).

1.5.1.2 Sleep diaries

Sleep diaries are a further option for adding extra information when assessing insomnia subjectively. However, they are usually not used on their own to measure insomnia symptoms. Various versions of sleep diaries exist and an attempt was made to find a common consensus in terms of which elements should be included (see Carney et al., 2012, for the consensus sleep diary). The idea is that the participant fills out the sleep diary every morning after waking up (preferably not longer than 30 minutes after awakening) and then gives a retrospective report on the previous night's sleep guided by

answering standardised questions. For example, “What time did you go to bed?”; “What time did you fall asleep?”, etc. (Carney et al., 2012; Taylor et al., 2014). However, sleep diaries are usually used for two weeks only. A longer period of time would be required to provide enough information to diagnose insomnia (APA, 2013).

1.5.1.3 Structured interviews

Conducting a structured interview with the participants is another option for assessing insomnia. It is more common within a clinical setting than in a research context and it is a time-consuming method that requires training (Chiu et al., 2016; Taylor et al., 2014). A validation of the different structured clinical interviews is still needed (Taylor et al., 2014). One available option is the Insomnia Interview Schedule (ISS; for further details, see Morin, 1993). This can be helpful for making a diagnosis according to the current diagnostic guidelines (American Academy of Sleep Medicine, 2015; APA, 2013; WHO, 1992).

1.5.2 *Objective measures*

Various options for measuring sleep or insomnia symptoms exist but this review will just focus on the two most common and best evaluated objective methods: polysomnography and actigraphy. However, it should be mentioned here that insomnia is mainly a subjective complaint (see, for example, American Academy of Sleep Medicine, 2015; APA, 2013; Krystal, Edinger, Wohlgemuth, & Marsh, 2002).

1.5.2.1 Polysomnography

Polysomnography (PSG) is the gold standard for measuring sleep problems objectively but it is costly and time consuming (Gehrman et al., 2011). With PSG various measures (EEG, electro-oculograph, electromyograph and visual monitoring, also other biological signals such as heart rate may be included) are recorded

simultaneously over the course of a whole night (Hertenstein et al., 2015; Kolk, Hanewald, Schagen, & van Wijk, 2003). Usually, several nights are recorded and the data from the first night might be disregarded as the patient may have trouble sleeping because of the ‘first night effect’ (meaning having to get used to the new environment and the idea of having their sleep assessed, etc.) (Normand, St-Hilaire, & Bastien, 2016). Adaptions in technology now also allow PSG to be used in the home of the participants (home PSG, Blackwell et al., 2016). However, recent findings indicate that even when using ‘home PSG’, sleep is worse on those nights with the PSG measure compared to those nights where it is not used (assessed by actigraphy and subjective measure) (Blackwell et al., 2016). In order to determine the sleep architecture of the participant (or patient), the data is usually analysed according to standardised rules, to examine which sleep stage the participant was in at what time and for how long. This also includes sleep-onset latency (SOL) and wake time after sleep onset (WASO) (Gehrman et al., 2011, Kolk et al., 2003).

Sometimes a discrepancy is found between the objective measures and the reported subjective complaint of the individual. For example, polysomnographic measures might indicate problems with sleep continuity and patients seem to remain in stage 1 sleep for longer, spending less time in sleep stages 3 and 4 (deeper sleep) but they do not always reflect the severity of the patient’s subjective complaint (American Academy of Sleep Medicine, 2015; APA, 2013, Krystal et al., 2002; Normand et al., 2016).

In some PSG studies, it was not possible to detect any objective indications at all for disturbed sleep even though the participants had experienced insomnia subjectively (Gehrman et al., 2011). It is possible that this is related to the complexity of the EEG data and that the methods of analysis need to be further improved in order to better

understand sleep architecture (Gehrman et al., 2011). Another possible explanation is that the individual may sleep better when taken out of their usual environment in order to have their sleep assessed in a sleep-laboratory (Gehrman et al., 2011).

There is a general tendency in individuals with insomnia to over-estimate their wake-time and under-estimate their sleep duration as measured by polysomnography. This may in part also be explained by the increased activity in the beta frequency range observed in insomnia patients during sleep (determined by EEG) which has been shown in computer-based spectral analysis methods that allow a more detailed examination of the sleep architecture (Gehrman et al., 2011; Perlis, Merica, Smith, & Giles, 2001; Perlis, Smith, Andrews, Orff, & Giles, 2001). This EEG pattern is usually associated with mental activity during wake-time, supporting the idea that insomnia might be a mixed wake-sleep state which is misinterpreted by the individual as being awake (Perlis et al., 2001). According to the results, insomnia seems to be characterised by hyperarousal in the central nervous system (Perlis et al., 2001). It should be pointed out here that this study assumes that arousal in the central nervous system can be considered separately from somatic arousal, which is controversial (Perlis et al., 2001).

Furthermore, a study comparing participants with insomnia with a group of participants with good sleep in their subjective and objective (PSG) measures of sleep, showed that on the basis of the subjective measure, more participants with insomnia (compared to good sleepers) over-estimated their objective wake-times. Arousal was increased in participants with insomnia (mainly during REM sleep phases) and further analysis showed that the time spent in REM-sleep contributed significantly to subjective wake time, meaning that objectively measured REM sleep might be partly perceived and recalled as being awake in patients with insomnia (Feige et al., 2008). It can be criticised that the subjective measure was not used for all participants with insomnia and

the good sleeper control group (Feige et al., 2008). The findings suggest that REM sleep-related processes may play a role in the subjectively experienced sleep disturbance and the overestimation of wake times in insomnia patients (Feige et al., 2008).

But there is also some evidence that individuals with insomnia do in fact sleep objectively worse. A meta-analysis reviewing polysomnographic data of individuals with primary insomnia compared to good sleepers showed that sleep continuity was disrupted (6 more awakenings per night). This was associated with a reduction of rapid-eye-movement sleep as well as slow wave sleep (11min less 'deep sleep') (Baglioni et al., 2014). Furthermore, individuals reporting insomnia had less total sleep time (23 minutes), more wake time after sleep onset (22 minutes) and a lower sleep efficiency (Baglioni et al., 2014). One of the limitations of this meta-analysis was that some of the included studies have taken only one night into consideration while others have taken an average over several nights. This means that confounding first-night-effects (i.e. sleeping worse on the first night of PSG measure) were not controlled for in all of the studies (Baglioni et al., 2014).

Most recently, the issue was raised again that objective, quantitative measures such as those obtained from PSG should be included in our definition and diagnosis of insomnia (Edinger, 2016; Pillai, Roth, & Drake, 2016). A study by Edinger (2016) examined wake time after sleep onset (WASO) and sleep-onset latency (SOL) in individuals with a diagnosis of insomnia (according to the DSM-5 criteria) and included a follow-up after one year. It was found that most of the participants showed a 'remission' from insomnia (according to the DSM-5 criteria) but 66% of these participants still reported more than half an hour of WASO or SOL during the night and a daytime impairment similar to the group of participants who had no remission from

insomnia. This supports the argument to add a quantitative cut-off (for WASO or SOL) to the diagnosis of insomnia (Pillai et al., 2016). It can be criticised that no objective measure of sleep was used in this study and therefore the estimates for WASO or SOL may not be representative. Even though the DSM-5 and ICSD-3 do provide some rough guidelines for WASO and SOL which could be considered as disruption of sleep (20-30 minutes), they do not form part of the diagnostic criteria for insomnia (Edinger, 2016; APA, 2013; American Academy of Sleep Medicine, 2015). It has also been pointed out that other sleep disorders (for example, obstructive sleep apnoea) do already include specific PSG measures within their diagnostic criteria, but PSG measures are not included for insomnia symptoms even though they might be useful (American Academy of Sleep Medicine, 2015; Edinger, 2016). However, a good argument against the inclusion of PSG measures for the diagnostic criteria of insomnia is that insomnia seems to be a mainly subjective complaint (see arguments outlined above).

1.5.2.2 Actigraphy

Another cheaper way of measuring sleep objectively that provides an additional measure used in context with the assessment of insomnia is actigraphy (Natale, Plazzi, & Martoni, 2009). An actigraph is a small device that is worn around the wrist to monitor wake and sleep times (Larouche, Lorrain, Côté, & Bélisle, 2015). A sleep log diary is often used in conjunction with the actigraphic measure as this makes it easier to interpret the data. A big advantage of actigraphy is that sleep can be monitored in the participant's normal environment over a period of several days (typically one week or longer) without the person having to get used to sleeping in a sleep lab. It also seems to disturb the sleep less compared to home PSG, which has recently been used more and more frequently (Blackwell et al., 2016). Furthermore, sleep and wake times are not just monitored during the night but also during the day (including napping times).

Actigraphy is still used in recent research to measure sleep parameters and to provide additional information in the assessment of insomnia (see, for example, Larouche et al., 2015).

1.5.3 Insomnia assessed within a clinical context: Patient history

The handbook of insomnia suggests that, in clinical practice, a patient's sleep history should be taken whenever a patient reports insomnia symptoms (Taylor et al., 2014). This should include any medical factors that may affect sleep (for example, osteoarthritis, as this causes pain), any psychological disorders which may possibly be associated with insomnia (for example, depression) and also general anxiety levels and mood. If any mental illness is reported, then it should be assessed to what extent this correlates with insomnia. In the case of depression for example, it is important to establish whether or not insomnia persists in the non-depressive phases of life. The patient should also be questioned about any events prior to the onset of insomnia (if there are any) or about any other possible factors that may have triggered insomnia (for example, a change in medication). A sleep history should be taken, including sleep times, bed times, time taken to fall asleep, number of awakenings during the night (and possible reasons for the interruption in sleep, such as a snoring bedpartner), difficulties initiating sleep again after waking up, napping routines, onset of insomnia, number of nights per week affected, early awakenings, sleep hygiene, the severity of insomnia symptoms over time (constant in form or rather fluctuating) and daytime functioning. This might help to identify the factors that cause and/or maintain the sleep problems. Any information about the chronotype and the daily routine of the patient may also be helpful. If patients have a different sleep schedule on the days that they do not work and if they sleep better on those days than during the time when they are working, then this

is an indication that their sleep problems may be due to a circadian rhythm problem rather than as a result of insomnia (Taylor et al., 2014).

1.6 How can insomnia be treated?

1.6.1 Psychotherapeutic treatment of insomnia

A wide range of psychotherapeutic treatment methods for insomnia exist, including: sleep restriction therapy, sleep hygiene, stimulus control therapy, relaxation techniques, paradoxical intention, sleep compression, cognitive restructuring, cognitive therapy, cognitive behavioural therapy, intensive sleep retaining, behavioural experiments, brief behaviour treatment and mindfulness-based therapy, as well as interventions to reduce misperceptions of sleep, dysfunctional beliefs about sleep and maladaptive safety behaviours (Perlis, 2011). This review will focus mainly on the therapies involving a cognitive component (hence cognitive behavioural therapy) and mindfulness-based therapy, as these are the areas most relevant for the analyses conducted in this thesis. A detailed description and discussion of all methods mentioned above can be found elsewhere (see, for example, Espie 1991; Perlis, 2011).

Cognitive therapy targets dysfunctional beliefs directly by applying behavioural experiments to help the participants to challenge their beliefs and, in this way, to implement cognitive restructuring (for example, by staying up all night to challenge the worry about daytime functioning following a poor night's sleep). Behaviour therapy is mainly directed at altering behaviour, applying sleep restriction and helping the participants to control stimuli (for example, by removing the TV from the bedroom). Cognitive behavioural therapy (CBT) combines the two approaches and attempts to alter behaviour and to restructure cognitions (Eidelman et al., 2016).

A recent review of the behavioural and psychological treatments commonly used to treat insomnia (including sleep hygiene education, stimulus control, sleep restriction, relaxation training, brief behavioural treatment, cognitive therapy and cognitive behavioural therapy) showed that CBT-I had the best outcomes (Brasure et al., 2016). This again confirms the results of an earlier meta-analysis which showed that CBT is effective for treating insomnia (Okajima, Komada, & Inoue, 2011). Stimulus control and multicomponent behavioural therapy may also improve sleep to some extent. The other single-component interventions showed only limited evidence for improvement in sleep (Brasure et al., 2016). It can be criticised that this review did not control for publication bias and, because of the large number of comparisons that were included, the ability to pool data was limited. A meta-analysis also showed that CBT-I was effective for treating insomnia with other comorbid physiological or psychological disorders (for example, chronic pain or depression), even when the other disorder ‘overshadowed’ the insomnia (Grandner & Perlis, 2015). It can be criticised that this meta-analysis included all forms of CBT-I without differentiating between them, even though some of the included studies considered the different elements separately (for example, whether or not sleep restriction was included in CBT-I) (Grandner & Perlis, 2015).

CBT-I has further been recommended by the practice guidelines of the American College of Physicians as the first choice of treatment for chronic insomnia in adults, even before considering medication as forms of treatment (Qaseem, Kansagara, Forcica, Cooke, & Denberg, 2016). It can be criticised that the sample size of most of the randomised controlled trials included in this review were small. It should be mentioned that in general a large placebo effect was observed for the studies considering pharmacological treatment of insomnia (Qaseem et al., 2016).

By focusing exclusively on CBT delivered via the internet, a recent meta-analysis confirmed that it is indeed effective for treating insomnia. On average, sleep efficiency improved by 7%, sleep time increased, insomnia symptoms improved, and so did the depression symptoms (Seyffert et al., 2016). The internet-delivered CBT did not differ significantly from the person-delivered version in outcome and the effects lasted over time (between 4 weeks and 48 weeks following treatment) (Seyffert et al., 2016). It should be mentioned that even though an overall improvement in insomnia symptoms was found, not all measures of sleep were found to improve significantly. For example, the number of awakenings after sleep onset was not improved. Furthermore, it can be criticised that some of the studies that were included had a relatively high attrition rates (up to 25% in the insomnia group). However, the drop-out in the control group (in-person delivery of CBT) was similarly high (20%).

Some evidence has shown that sleep restriction therapy (delivered as a single-component treatment rather than in the full CBT-I package) may actually have negative effects on the patient, rather than improving their insomnia symptoms (Kyle et al., 2014). Sleep restriction therapy was associated with increased daytime sleepiness, reduced overall sleep time (objectively measured) and impaired vigilance (objectively measured). One limitation of this study is that the sample size was relatively small (16 participants), but it does flag up an important issue that should be investigated further (Kyle et al., 2014).

Mindfulness-based approaches are also used to treat insomnia (Hofmann, Sawyer, Witt, & Oh, 2010; Hubbling, Reilly-Spong, Kreitzer, & Gross, 2014). Mindfulness-Based Therapy for Insomnia (MBTI) combines elements of the Mindfulness-Based Stress Reduction Program (MBSR) and Mindfulness-Based Cognitive Therapy (MBCT) with components of behavioural therapy (sleep hygiene,

sleep restriction and stimulus control) (Ong & Manber, 2011). MBSR and MBCT are described in detail elsewhere (see, Kabat-Zinn, 1990; Kabat-Zinn, 2013). MBTI is usually delivered as a group therapy (6 to 8 participants) and it is a person-centered approach that encourages the participants to reflect on the feelings and thoughts that arise during the meditation exercises and behavioural components. The idea is to facilitate mindfulness. This means that each night should be considered as a new night (beginner's mind) and that the patients should understand that sleep cannot be forced (non-striving) but that they should let go of the idea of an ideal sleep and not regard waking up during the night as negative but rather they should accept what cannot be changed (for example, getting out of bed if they aren't tired). They should try to simply trust in their body and its ability to regulate sleep and exercise patience (Ong & Manber, 2011; Ong & Sholtes, 2010).

There is already some evidence indicating that mindfulness-based approaches are effective for treating insomnia (see, for example, Carlson & Garland, 2005; Ong, Shapiro, & Manber, 2008; Ong, Shapiro, & Manber, 2009). A small study (only 12 participants), using pre- and post-intervention measures for sleep, has recently confirmed that mindfulness-based therapy is a useful approach for treating insomnia, showing a significant improvement in the subjective and also in objective measures of sleep (obtained by actigraphy), in addition to enhanced coping strategies (Larouche et al., 2015). A pre-test post-test design was adopted and no control or comparison group was used. Because of the small sample size and the design of the study, it can be questioned how meaningful the findings are. Randomised controlled trials are needed to further evaluate the effectiveness of mindfulness-based approaches for the treatment of insomnia in comparison to other forms of treatment (Ong et al., 2008). Such a study is currently being conducted by Morin and colleagues (see, Morin et al., 2016).

1.6.2 Pharmacological treatment of insomnia

Between 1993 and 2007, the frequency of medication being prescribed for treating insomnia increased drastically, with nonbenzodiazepine sedative hypnotics being prescribed 30-times more often (Moloney et al., 2011). It can be criticised that this study did not include the lower income groups of people who use emergency services for their primary health care. According to a review of sleep medication prescribed to treat insomnia in the US (1999 until 2010), the most common medications were ‘Z-medications’ (eszopiclone, zaleplon and zolpidem), Trazodone, Benzodiazepines, Quetiapine and Doxepin – listed in order from the most frequently prescribed to the least frequently prescribed (Bertisch, Herzig, Winkelman, & Buettner, 2014). Both reviews mentioned here were based on the US population. It can be criticised that, it may not be possible to generalise the findings because the approaches and the amount of sleep medicine prescribed in the US may differ from that prescribed in other countries.

The recommendations for medicine to be prescribed to treat insomnia vary. Whilst the handbook of insomnia, which is frequently used for guidance within a clinical context, lists benzodiazepine receptor agonists, non-benzodiazepine hypnotics, zaleplon, zolpidem, melatonin receptor agonists, antidepressants and other new medications (Suvorexant – Orexin; Tasimelton) as pharmaceutical treatment options, the ICSD-3 only recommends prescribing benzodiazepine receptor agonists for the treatment of insomnia, without mentioning the other options (American Academy of Sleep Medicine, 2015; Taylor et al., 2014).

One sedating tricyclic drug that has been approved more recently for treating insomnia is doxepin (3 mg and 6 mg) (Yeung, Chung, Yung, & Ng, 2015). In a recent review including randomised placebo-controlled trials (including a total of 1983

participants), it was found that a low dose of doxepin could be safely used and effectively increased sleep duration and helped to maintain sleep but it did not aid sleep initiation (Yeung et al., 2015). It can be criticised that all studies included in this review were industry sponsored.

Based on a review of the research, the recent guidelines by the American College of Physicians for the treatment of chronic insomnia disorder suggest that CBT-I should be offered to patients first. In addition, one of the following medications may be prescribed, but only if CBT-I has not been successful: Eszopiclone, Zolpidem, Suvorexant and Doxepin (Ramelton rather than Suvorexant was recommended for older adults) (Qaseem et al., 2016). Note that product names may vary from country to country.

More research is needed to compare the different pharmacological and psychological therapies used to treat insomnia as well as a combination of the two. Currently, a randomised controlled trial is being conducted that considers sequential psychological and pharmacological therapies for insomnia (primary, as well as comorbid) and results are expected to be published soon (Morin et al., 2016).

For the choice of sleep medication, it should further be considered when the insomnia symptoms are most prevalent during the night (problems falling asleep, maintaining sleep or early awakenings) (Schweitzer & Feren, 2017). Furthermore, it is also important to bear in mind that the pharmacological treatment of insomnia does come with certain risks. Some medications have been found to be not safe to use, and side effects may be caused (Schweitzer & Feren, 2017).

1.6.3 Self-medication of insomnia

When someone is struggling with sleeping problems, one unhealthy coping strategy can be to self-medicate using alcohol (or illicit drugs) in order to induce sleep

at night and/or caffeine (or other drugs) to fight sleepiness during the day (American Academy of Sleep Medicine, 2015; APA, 2013). This can potentially lead to substance use disorder (APA, 2013).

Over the counter (OTC) medicines present another form of self-medication for insomnia (Culpepper & Wingertzahn, 2015). A recent review (including studies considering H₁ antagonists or antihistamines, melatonin, valerian and valerian/hops) showed that there is not yet enough clinical evidence to support the view that OTC medicines are effective in improving the symptoms of insomnia. Furthermore, it was not even possible to confirm that OTC medicines are safe to use (Culpepper & Wingertzahn, 2015). It can be criticised that studies of OTC medicines used for occasional sleep disturbance in otherwise healthy individuals have also been included here (rather than only studies of individuals experiencing insomnia symptoms or who were diagnosed with insomnia).

1.6.4 New and alternative forms of treatment

Different types of treatments for insomnia keep appearing in the literature. These include acupuncture, Tai Chi and other less common or less evaluated types of treatment (see, for example, Lee & Lim, 2016; Raman, Zhang, Minichiello, D'Ambrosio, & Wang, 2013; Sarris & Byrne, 2011). Evidence supporting these alternative forms of treatment is very limited. However, one example of a less frequently used form of therapy to treat insomnia that is worth mentioning is light therapy.

1.6.4.1 Light therapy

An alternative form of treatment for insomnia that is supported by various studies is light therapy (Berson et al., 2002; Guardiola-Lemaitre & Quera-Salva, 2011;

van Maanen, Meijer, van der Heijden, & Oort, 2016). There is no consensus about the exact guidelines that should be applied in terms of timing and light intensity but the basic idea is that light is a zeitgeber for the circadian rhythm and it can help to regulate it (Berson et al., 2002; Guardiola-Lemaitre & Quera-Salva, 2011). For example, light exposure in the early morning (4 am, when the body temperature is at its lowest) helps to shift the biological clock to an earlier timing (this may help the participant to fall asleep more easily earlier in the evening). In a recent meta-analysis, light therapy was shown to be effective for treating both insomnia and other sleep disorders and higher light intensity seemed to be particularly helpful for treating insomnia (van Maanen et al., 2016). It can be criticised that not all of the included studies focused on insomnia or sleep disorders as defined in the common diagnostic manuals (DSM, ICD or ICSD) and that there were large discrepancies in relation to the diagnostic criteria applied. Furthermore, publication bias was found for some of the outcome measures even though an attempt has been made to include unpublished studies.

1.7 The heritability of insomnia

1.7.1 Studies of genetic influence

The findings of a small number of published family history studies or familial aggregation studies show that a family history of insomnia predisposes for developing insomnia (Dauvilliers & Morin, 2013; Gehrman et al., 2011). These results are in line with the findings of the twin studies, suggesting that insomnia is heritable to a modest degree as described above (see also Gehrman et al., 2011).

The ICSD-3 does not acknowledge that there are familial patterns associated with insomnia but only mentions that the prevalence of insomnia is higher between MZ twins than between DZ twins and between first degree-relatives (compared to the

general population; Zhang et al., 2010). However, plenty of research evidence does suggest that insomnia is heritable (see Gehrman, Byrne, Gillespie, & Martin, 2011 for a review of the genetics of insomnia). The exact estimates of heritability for insomnia vary across previous studies (for example, Drake, Friedman, & Wright Jr, 2011, $A = .43$ for males and $A = .55$ for females; Gehrman et al., 2011, $A = .30$; Wing et al., 2012, $A = .48$) as heritability is a population statistic and estimates may vary in the different samples considered (Plomin et al., 2013). For adults, the heritability of insomnia-related measures consistently falls into a range between .25 and .45 (Gehrman et al., 2011; some exceptions exist giving higher estimates (see, for example, Drake et al., 2011). For the G1219 sample, which was used for the various analyses in this thesis, the heritability of insomnia was estimated to be .29 (95% confidence interval = .13 - .43) for wave 4 and .31 (95% confidence interval = .08 - .49) for wave 5 (Gregory et al., 2016). Compared to other traits (such as depression), relatively few studies exist that estimate the genetic and environmental influence on insomnia as this is a new area of research (Gehrman et al., 2011). We need to consider these previous findings in order to check if the current findings are in line with them or if they deviate (for example, if the sample was not representative). This is particularly important because the genetic and environmental influences for other key variables (mindfulness, pre-sleep arousal and dysfunctional beliefs about sleep) have been estimated for the first time in an adult sample in the current analyses and therefore no point of reference exists for them.

Decomposing the genetic and environmental influence on a trait is key in understanding the aetiology of the trait and deepens our understanding of the concept by illuminating its roots. (Carlin, Gurrin, Sterne, Morley, & Dwyer, T., 2005). Estimating the heritability of insomnia can be considered as a first important step, providing direction and the foundation for new research. For example, if insomnia was found to be highly

heritable (which was not the case), it would have made sense to invest in locating the associated genes. As it was not found to be highly heritable, this might stimulate future research to focus more on detecting the potential environmental factors that influence insomnia.

1.7.2 Genes involved

The rare subtype of fatal familial insomnia was found to be a single-gene disorder, whereas, in the case of the other types of insomnia, the picture is more complex (Dauvilliers & Morin, 2013). Issues such as the discrepancy between subjective and objective measures, short sleep versus long sleep duration, comorbid versus primary, transient versus chronic insomnia, etc. make it more difficult to identify the genes involved in insomnia (Dauvilliers & Morin, 2013). A range of candidate gene studies, linkage studies and genome-wide association studies (GWAS) have attempted to identify genes (or genetic patterns) associated with insomnia with some success but still need replication. These results are discussed elsewhere (for a review of findings see Dauvilliers & Morin, 2013; Gehrman et al., 2011).

A most recent GWAS study, which is worth mentioning, considered self-reported insomnia symptoms, sleep duration and excessive daytime sleepiness in a sample of 112,586 adults (UK Biobank) (Lane et al., 2017). Specific genes that are significantly associated with insomnia symptoms were discovered (MEIS1, TMEM132E, CYCL1, WDR27 – for males, TGFBI – for females). Also some loci associated with sleep duration (PAX-8), daytime sleepiness (near AR/OPHN1), as well as for a composite trait, including sleep duration, insomnia symptoms, excessive daytime sleepiness, and chronotype were located (near INADL and HCRTR2) (Lane et al., 2017). The same study also found a genetic correlation for longer sleep duration and

schizophrenia ($rA = .29$), and increased daytime sleepiness and BMI ($rA = .20$). These are exciting new findings that need to be replicated.

Identifying the genes associated with insomnia will open up new opportunities and interesting areas of research for the future. The first attempts have been made to use gene editing in humans to treat diseases (for example, lung cancer or HIV). However, there is still a long way to go before disorders such as insomnia can be treated using this method (Cyranoski, 2016; Tebas et al., 2014). But identifying genes associated with insomnia may, at some point in the future, also help us to detect who might be at risk of developing this disorder and will allow us to help those individuals by using targeted prevention and potentially help us develop new treatment methods (Palagini, Biber, & Riemann, 2014; Dauvilliers & Morin, 2013; Gehrman et al., 2011). Again, it should be pointed out that research has moved away from looking at single genetic variants as being the big cause of complex traits (Plomin et al., 2013) and even when considering the whole genome to identify genetic patterns involved in insomnia, findings are still limited. There is still a large discrepancy between the influence the genes we identify have on the overall variance of a trait and the estimated heritability of the trait (for a detail explanation of the missing heritability problem, see, for example, Manolio et al., 2009).

1.7.3 Epigenetic studies

The evidence for epigenetic mechanisms related to insomnia has been discussed by some researchers (see, for example, Palagini et al., 2014). Epigenetics is a term that refers to the idea that gene expression (meaning that genes produce protein if they are instructed to do so by the DNA via an RNA messenger) does not happen in isolation but can to some extent be influenced by the environment or external factors. Information can be passed on from one cell to another, ‘switching’ gene expression on or off

(Plomin et al., 2013). This can happen through cellular or molecular changes, such as histone modification or DNA methylation, which regulate gene expression and can 'silence' genes without changing the DNA sequence itself, even though these changes can remain for a considerable period of time (Plomin et al., 2013). Explaining this at a very basic level, histone modification refers to the enzymatic modification of histone proteins which change their interaction with the DNA. This is how gene expression is influenced here (in terms of up or down regulation) (Strachan & Read, 2011). In DNA methylation groups of methyl connect to the DNA and, in this way, can stop this part of the DNA from being active (for example, by repressing the transcription of genes when this takes place in a gene promoter region) (Strachan & Read, 2011). The exact biochemical process of how histone modification or DNA methylation works is discussed elsewhere (see, for example, Plomin et al., 2013 or, for a more detailed explanation, see Strachan & Read, 2011).

The idea that epigenetic mechanisms play a role in insomnia has been discussed recently (Palagini et al., 2014). For example, we know that DNA methylation and histone modification are epigenetic processes that have been found to be associated with stress-related changes in the hippocampus (see, for example, Hunter, McCarthy, Milne, Pfaff, & McEwen, 2009). It has been argued that there is a certain degree of genetic influence on reacting with disturbed sleep when stressful life events occur and also a reduced volume of the hippocampus has been found to be associated with insomnia (Palagini et al., 2014). However, it should be mentioned that the findings are not consistent. Various processes that are involved in sleep were found to be affected by epigenetic mechanisms as well, which lead to the idea that epigenetic mechanisms may be involved in developing and maintaining insomnia (for a detailed discussion, see, Palagini et al., 2014). This discussion underlines that environmental factors (in spite of

a possible genetic predisposition) may play a role in the development and recovery of insomnia (Perlis et al., 2014). However, it can be criticised that no evidence of epigenetic mechanisms being directly involved in insomnia has yet been found and that the arguments outlined by Palagini and colleagues (2014) do include some speculation. Furthermore, some of the epigenetic research is based on animal models and future research will show to what extent these findings can be extrapolated to humans (Perlis et al., 2014). However, the hypothesis that epigenetic mechanisms are involved in developing and maintaining insomnia is interesting and should be further investigated in future research.

1.8 What can you learn about insomnia from this thesis? – Rationale and research questions

The rationale behind this PhD thesis is to gain a better understanding of the concept and aetiology of insomnia symptoms by illuminating the key elements involved in the development and maintenance of insomnia symptoms and by testing current theory. In considering the various cognitive (and arousal) theories of insomnia, it has been shown that that mindfulness, pre-sleep arousal and dysfunctional beliefs about sleep all play a crucial role in insomnia symptoms. These theories are supported by a wide variety of research findings. Behavioural genetic studies further indicate that that insomnia is heritable to a certain extent. However, at the present time, the cognitive theories of insomnia (and findings) and genetic research are largely considered separately. The missing piece of the puzzle is how to bring those two areas together. This is the underlying idea behind this PhD thesis which is entitled ‘Genetic and Environmental Influences on Insomnia Symptoms and Associated Cognition and Arousal in Young Adults’.

In order to gain a better understanding of the concept of insomnia, the underlying mechanisms described in the cognitive (and arousal) theories of insomnia will be considered from a behavioural genetics perspective by taking various steps. Firstly, each of the main elements (mindfulness, pre-sleep arousal and dysfunctional beliefs about sleep) that play a crucial role in the cognitive models of insomnia and particularly in the meta-cognitive model of insomnia are examined closely. This is done by assessing the genetic and environmental influence on each of them separately in order to understand the root of these traits. This has never been done before and is therefore important because it deepens our understanding of the aetiology of those key traits and broadens our knowledge of why these traits develop. In addition, the genetic and environmental influences on insomnia symptoms will also be estimated. The association of each of these elements with insomnia symptoms will be considered phenotypically and the genetic and environmental influence on these associations will also be investigated, which will help us to illuminate the mechanisms involved. We do know that these traits are important in the development and maintenance of insomnia symptoms but we do not know yet how these associations work. These associations have never been investigated from a behavioural genetics perspective. To add a further level of detail, an additional aim of this thesis is to consider the subscales of those variables (mindfulness, pre-sleep arousal and dysfunctional beliefs about sleep) and their association with insomnia. This will help us to dissect the relationship of these elements with insomnia symptoms at a deeper level. Once again, this has never been done before. Furthermore, possible environmental factors involved in dysfunctional beliefs about sleep are also explored. In order to gain an even broader insight into the concept of insomnia, non-behavioural genetics analyses were added, focusing on similar variables, to illuminate the concept of insomnia from various angles, testing the theory that there are two distinct types of

insomnia – one with short sleep length and one with normal sleep length (insomnia SSD versus insomnia NSD; Vgontzas et al., 2013). In summary, five empirical studies were conducted, using a twin and sibling sample of young adults to consider:

- 1) Mindfulness (its subscales) and its association with symptoms of insomnia, anxiety and depression;
- 2) Associations between pre-sleep arousal (its subscales) and insomnia symptoms;
- 3) Dysfunctional beliefs about sleep (its subscales) and insomnia symptoms;
- 4) Non-shared environmental factors associated with dysfunctional beliefs about sleep;
- 5) Self-reports of insomnia with short versus normal sleep duration: comparing the subtypes in terms of heritability, associated phenotypes and persistence over time

Please note that, in the first study which considers mindfulness and its association with insomnia symptoms, the depression and anxiety variables were added. These variables were not considered in the other studies. They were only added because a study of genetic and environmental influences on mindfulness and its association with depression and anxiety in adolescence had recently been published (see, Waszczuk et al., 2015) and it was attempted to re-evaluate the results in an adult sample. Another reason for just adding them to this study only was that a lot of mindfulness-based treatment for insomnia is based on the mindfulness-based treatment for depression and anxiety. However, conceptually, the measures used for anxiety and depression symptoms overlap too much with the measure for pre-sleep arousal and/or dysfunctional beliefs about sleep to be included in the same studies (these are the key variables that have been investigated in the other chapters). Therefore, symptoms of anxiety and depression have not been added for any of the other studies conducted.

The final chapter of this PhD thesis aims to put the current findings (of studies one to five) into context, alongside the current cognitive (and arousal) theories about insomnia which have been very influential but have so far largely neglected the aetiological influence of genetics on insomnia. The role that pre-sleep arousal and dysfunctional beliefs about sleep play and how mindfulness fits in with all of this will be discussed in detail in the final chapter of this thesis. In this way, it is hoped that light can be shed on the mechanisms underlying the aetiology of insomnia symptoms, which could help us to gain an insight into the developmental processes involved and to deepen our understanding of the concept of insomnia symptoms. This will help us to gain a better understanding of the current cognitive models.

If a high genetic overlap between these traits and insomnia symptoms is found, this may indicate that they are part of the same genetic cluster (as indicated in previous research, for example, for sleep disturbances and depression disorders; Middeldorp, Cath, Van Dyck, & Boomsma, 2005). This could provide us with some clues about possible candidate genes that can be considered in future studies. Furthermore, if we know that these traits are highly (genetic and/or environmental) correlated then the development of one (or more) these traits might give us a hint that there is a good chance of developing the insomnia symptoms. In the future, this could potentially help us to identify who is at risk of developing insomnia symptoms.

CHAPTER 2: Methods

2.1 Overview

This methods chapter aims to provide an overview of the methodology which is relevant to the empirical chapters. The chapter begins by explaining the basics of path diagrams, as these are used throughout the PhD thesis. Following this, the main principles behind the twin method will be illustrated and the main assumptions, univariate analysis, structural equation modelling, model fitting, multivariate analysis and the ADE model will be outlined. In addition, detailed information about the G1219 sample is provided, as this sample was the basis for all the analyses conducted for this PhD thesis. Finally, details concerning the main variable (insomnia symptoms) will be provided.

2.2 Path diagrams

The method of using path coefficients was first described in detail by Wright (1934). Path diagrams are still widely used today as a common method of illustrating the models presented in twin studies (see, for example, Gregory et al., 2016; Spirtes, Richardson, Meek, Scheines, & Glymour, 1998). They can help us to understand the algebra behind the model by outlining the analysed relationships in a visual way and by illustrating the resemblance between twins and/or the relationships between the various factors involved (including the variances and covariances in a model). There are certain conventions as to how the elements in a path diagram should be interpreted – see **Figure 2.1** overleaf (Rijsdijk, 2015).

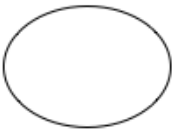



<p>a) Latent variable</p> 	<p>Circle or ellipsis = refers to a latent variable. This is a parameter which is estimated in a model. For example, the variance components to be estimated. (A = genetic influence; C = shared environment; E = non-shared environment)</p>
<p>b) Observed variable</p> 	<p>Rectangle = refers to an observed variable. This is a measured parameter (i.e. something fed into the model to work with). For example, insomnia symptoms as measured in the current sample.</p>
<p>c) Causal Path</p> 	<p>One-sided, straight arrow = represents a causal pathway (or partial regression coefficient), meaning that one element leads to the other.</p>
<p>d) Correlation (Covariance) Path</p> 	<p>Double-headed arrow = indicates a correlation or a (standardised) covariance between two elements in the model. This element is, for example, used to illustrate the genetic correlation between two traits.</p>

Figure 2.1 Conventions for the elements used in path diagrams

In addition, there are a number of path tracing rules to follow when interpreting a path diagram (Rijsdijk, 2015):

- 1) The covariance between two traits (or two twins) is represented by the sum of the paths which connect the two elements in the path diagram.
- 2) For a chain of paths, a numerical value can be calculated by multiplying the coefficients of each path traced.
- 3) It is not possible to trace through the same variable twice when following a chain of paths.
- 4) In relation to the one-headed arrows: the tracing can go backward and then forward, but not vice versa (meaning forward and then backward).
- 5) For every chain of paths that is traced, there can only be one bi-directional path

(double-headed arrow). Bi-directional paths' from an independent variable to itself are traced unless there is another double-headed arrow (for example, indicating a correlation).

For an illustration of how path tracing works, see the example explained under **2.3.2.1 The ACE model.**

2.3 The twin method

2.3.1 Assumptions and associated limitations

2.3.1.1 Equal environments assumption

The twin method is based on a series of assumptions. The first assumption is that the environment for MZ twins is just the same as it is for DZ twins if they are reared together. If MZ twins were treated more equally than the DZ twin pairs (for example, by dressing them alike), then this would possibly increase the MZ correlations and increase the difference to the DZ correlations. This would result in an inflated estimate of genetic influence on the trait being considered (Plomin et al., 2013). MZ twins were found to share the same bedroom more frequently than DZ twins of the same sex (Loehlin & Nichols, 1976). This may potentially affect their sleep during childhood and it is not clear as to what extent this effect may carry over into adulthood. However, for most phenotypes that have been investigated, it appears that the equal environment assumption is valid (see, for example, Bouchard Jr & Propping, 1993; Derks, Dolan, & Boomsma, 2006). A more recent review of literature, evaluating whether or not the equal environments assumption is applicable, argued that the evidence is mixed but that the bias caused in case of a violation was found to be only modest most of the time (Felson, 2014). It was concluded that twin studies are no more flawed than other studies and may actually be less flawed (Felson, 2014). Furthermore, some evidence indicates

that twins do not differ from non-twins in terms of insomnia experienced (Kendler et al., 1995). In addition to this, a recent study comparing MZ twin pairs, DZ twin pairs and non-twin pairs found no mean level differences for sibling relationship quality and no substantial differences in the way the three types of siblings behaved towards each other (Mark, Pike, Latham, & Oliver, 2017). It should also be mentioned here, that all analyses conducted for this thesis controlled for non-independence of observations.

2.3.1.2 Sibling interaction

A further point that should be taken into consideration is that siblings or twins actually form part of each other's environment and therefore interaction is inevitable. Therefore, a trait in one twin may influence the trait in the other twin. For example, if twins/siblings share the same bedroom and one has sleeping problems, this is likely to negatively affect the sleep of the other twin/sibling (Plomin et al., 2013).

A further limitation may be related to the approach of including siblings (non-twins) in the twin analyses to add participants to the DZ group (in order to increase power). DZ twins are the same age whereas siblings are not. This may lead to greater differences in their experience and their development compared to DZ twins, which could lead to a bias in the results. However, siblings were modelled as a separate group (additional to MZ twins and DZ twins) for all analyses and the assumptions (whether or not the groups can be equated in means and variances) were checked thoroughly. Therefore, this limitation should be irrelevant for the current findings. It should be pointed out that the inclusion of siblings can also be considered to be a strength as it increases the sample size and should therefore increase statistical power (for more details see **Chapter 2: Methods, 2.3.3 Structural equation modelling**)

2.3.1.3 Assortative mating

The second assumption is that mating is random, not selective (or assortative). If this is the case, then DZ twins should, on average, share about 50% of their segregating genes, which is one of the fundamental principles on which the twin design is based (see also, Falconer's formula outlined under **2.3.2.1 The ACE model**). Segregating genes are the genes that make us different from each other as individuals, as opposed to the genes that make us similar as a human species (Plomin et al., 2013). If this is not the case and we were to choose partners who were similar to us, then this would result in a greater variance in traits within the general population, because extremes would not be averaged out. This would also mean that DZ twins are more likely to turn out to be similar, increasing the correlation between them (as it would be more likely that they would inherit the same genes if the parents were genetically similar), while MZ twins should not be affected as they share 100% of their segregating genes (Rijsdijk, 2015). Therefore, the difference between MZ correlations and DZ correlations would be reduced and the genetic influence would be underestimated. If the opposite was the case and the saying 'opposites attract' was true, this would result in a lower variance in traits within the general population, as traits would 'balance out' (Evans & Martin, 2000). For example, if tall individuals always mated with shorter ones, then the result would be that the offspring would be of average height (Plomin et al., 2013; Rijsdijk, 2015). Research indicates that we are prone to choosing a partner who is similar to ourselves. For example, assortative mating for psychiatric disorders has been found. This means that individuals with a psychiatric disorder are more likely to choose a partner who is also suffering from a psychiatric disorder (Maes et al., 1998).

2.3.1.4 Gene-environment correlation and interaction

Further assumptions are that there are no gene-environment interactions or gene-environment correlations (Evans & Martin, 2000). However, it is possible that genes and environment do not act independently but that they can also interact with one another, producing effects that are greater than each in itself (Plomin et al., 2013). Gene-environment interaction means that an individual can have a certain genetic predisposition which makes him/her more likely to be affected by certain environments (Plomin et al., 2013). For example, it was found that individuals who carry the s/s homozygous variant for the serotonin transporter polymorphism 5HTTLPR (two s-allele), were more likely to experience depression after stressful life events as compared to others (long alleles in 5-HTTLPR) (Caspi et al., 2003).

Gene-environment correlation can occur in three different forms: passive, evocative or active. Taking musical ability (which is heritable) as an example, if a child is musically gifted, he or she may have parents who are also musical and would therefore provide an environment in which the child's musical ability could thrive (passive gene-environment correlation). The musical ability of the child may also be recognised at school where he/she may evoke a positive reaction from others and be further encouraged to develop this ability (evocative gene-environment correlation). The child may also actively choose environments that allow for the development of the musical ability, for example by joining a band (active gene-environment correlation) (Plomin et al., 2013; Evans & Martin, 2000). These examples illustrate how genes can play a role in our environment.

2.3.1.5 Generalisability

Finally, it is assumed that the findings obtained from twin samples can be generalised to the general population, assuming that twins are not different from non-

twins (Plomin et al., 2013; Rijdsdijk, 2015). However, it is known that twins differ from non-twins in a range of factors such as birth weight or complications at birth (Evens & Martin, 2000). Furthermore, MZ twins were found to be more likely to share the same room than DZ twins of the same gender, it is likely that twins in general share a bedroom more often compared to non-twins (Loehlin & Nichols, 1976). Furthermore, an early study showed that twins and singletons differ in terms of problem behaviours and emotional problems (Gau, Silberg, Erickson, & Hewitt, 1992).

2.3.2 Univariate analysis

2.3.2.1 The ACE model

If all the assumptions outlined above are correct, then we can say that any difference between MZ twins must be due to non-shared environment (as they share 100% of their segregating genes and 100% of their environment). Non-shared environment does include error as well. DZ twins share 100% of their environment but only 50% of their segregating genes. Therefore, any difference between DZ twins could be due to genes and/or non-shared environment (Plomin et al., 2013). In all the current analyses siblings were added. However, in order to keep the following explanation simple, the role of siblings will not be discussed below, but at some later point (see

2.3.3 Structural equation modelling). In twin analysis, intra-class correlations between MZ twin pairs and DZ twin pairs for a trait are compared in order to estimate the relative contribution of additive genetic (A), shared environmental (C) (or non-additive genetic influence: D, dominance - when the effects of the alleles are not equal; see **2.3.2.2 The ADE model** for further explanation) and non-shared environmental influence (E) on the trait under investigation. Intra-class correlations are different from the regular Pearson's correlations as they are based on the whole group (all MZ twin pairs or DZ twin pairs or pooled), rather than on the single pairs independently (Rijdsdijk

& Sham, 2002). In summary, if we compare the difference in similarity in a trait between the MZ group and the DZ group, the relative contribution of genetic and environmental influences on that trait can be estimated. How this works exactly is illustrated below, using path diagrams.

According to Wright's rules of path tracing (1934), the variance (which is the covariance of a trait with itself) is the sum of all legitimate paths' in the chain as outlined below (Rijsdijk, 2015). By following the dotted arrows in the path diagram, the expected variance can be calculated using the formula below. To describe the variance of any measured trait (irrespective of whether it is an MZ twin or DZ twin) the chain of paths would be traced as follows: starting at the measured variable, we go up the 'a' path, multiply by one and go down again. Then we trace up the 'c' path, multiply by one and go down again, Finally, the chain of paths is completed by going up the 'e' path, multiplying by one and then going back to the measured variable again (see **Figure 2.2**).

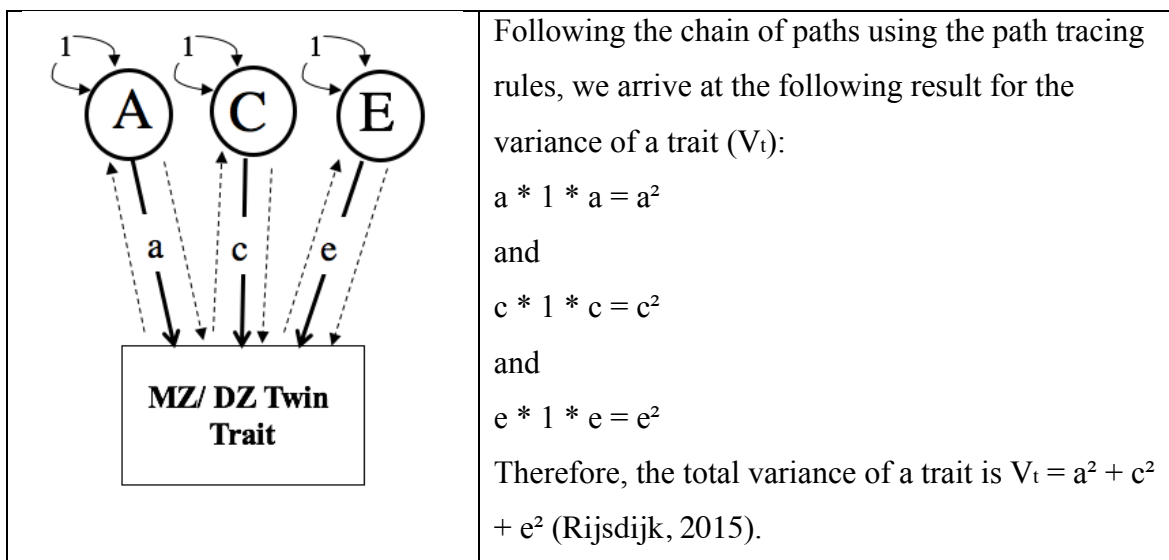


Figure 2.2 The variance of a trait in any twin/sibling (applies to both twins/siblings of a twin/sibling pair)

Note: a = path coefficient for genetic influence; c = path coefficient for shared environmental influence; e = path coefficient for non-shared environmental influence; A = estimate of additive genetic influence; C = estimate for shared environmental influence; E = non-shared environmental influence

The covariance between twin one and twin two for the same trait for MZ twins is the sum of all legitimate paths' in the chain as outlined below (Rijsdijk, 2015).

Following the dotted lines in **Figure 2.3**: We trace from twin 1 (measured trait) up the 'a' path of the first twin and move across the double-headed arrow, which has the value 1 assigned to it (as MZ twins share 100% of the segregating genes). Then we trace down the 'a' path of the second twin (to the measured trait in the second twin). We also need to add a second chain of paths, going up the 'c' path of the first twin, moving across the double-headed arrow which has the value 1 assigned to it (as MZ twins share 100% of their environment), then going down the 'c' path of the second twin (to the measured trait of the second twin).

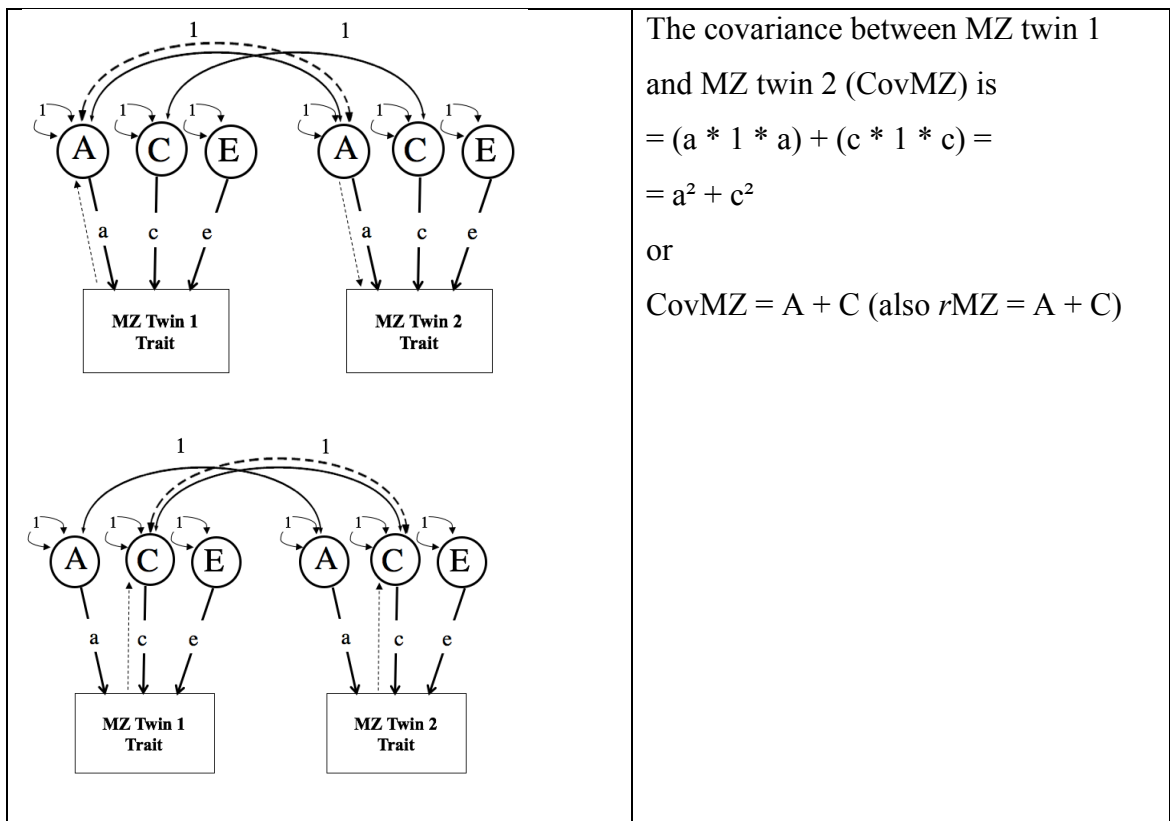


Figure 2.3 The covariance for any trait for MZ twin pairs (reared together)

Note: a = path coefficient for genetic influence; c = path coefficient for shared environmental influence; e = path coefficient for non-shared environmental influence; A = estimate of additive genetic influence; C = estimate for shared environmental influence; E = non-shared environmental influence

The covariance between twin one and twin two for the same trait for DZ twins is the sum of all legitimate paths' in the chain as outlined below (see **Figure 2.4**) (Rijsdijk, 2015). Following the dotted lines in **Figure 2.4**: We trace from twin 1 (measured trait) up the 'a' path of the first twin, move across the double-headed arrow which has the value .5 assigned to it (as DZ twins share on average 50% of the segregating genes), then go down the 'a' path of the second twin (to the measured trait in the second twin). We also need to add a second chain of paths, going up the 'c' path of the first twin, moving across the double-headed arrow which has the value 1 assigned to it (as DZ twins share 100% of their environment), then going down the 'c' path of the second twin (to measured trait of the second twin).

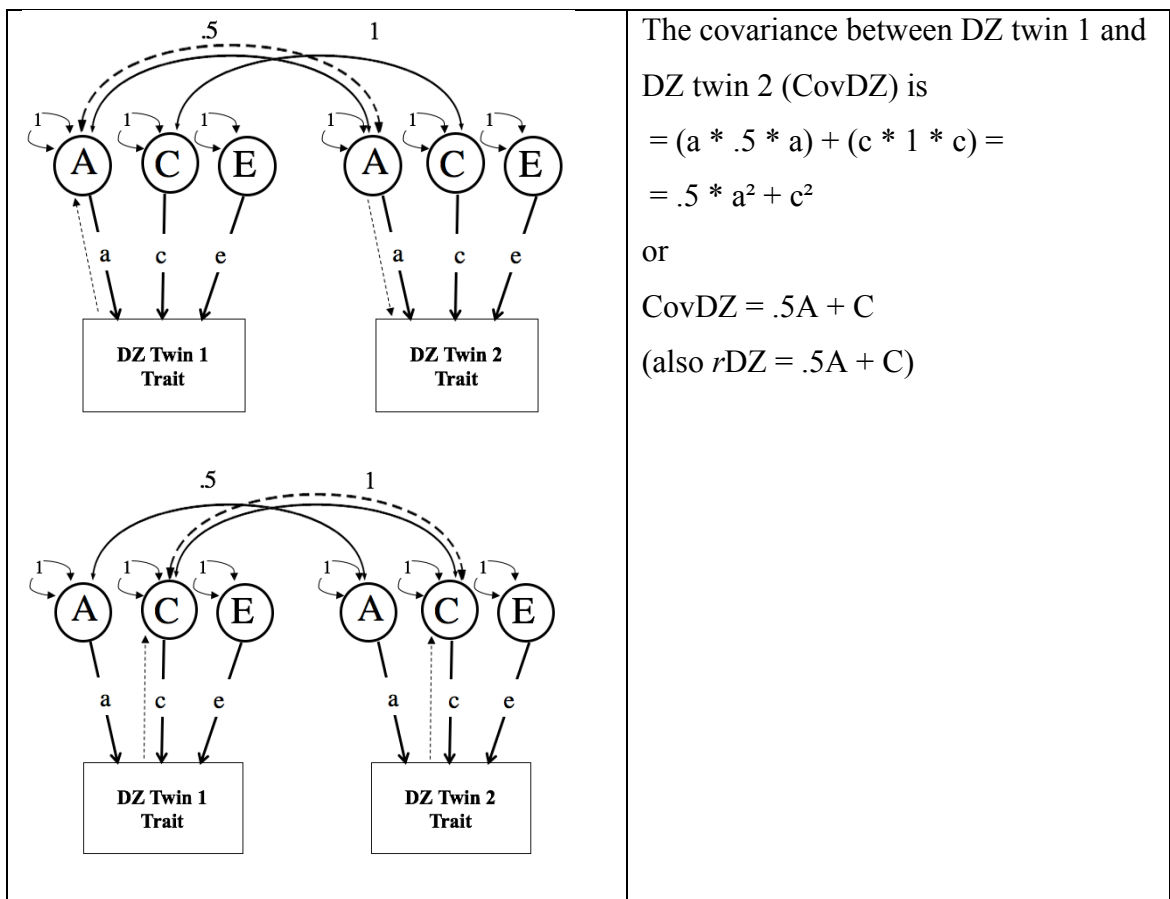


Figure 2.4 The covariance for any trait for DZ twin pairs (reared together)

Note: a = path coefficient (unstandardised) for genetic influence; c = path coefficient for shared environmental influence; e = path coefficient for non-shared environmental influence; A = estimate of additive genetic influence; C = estimate for shared environmental influence; E = non-shared environmental influence

In order to obtain the covariance between MZ twins, as well as when considering DZ twins, we do not need to trace the ‘e’ path. Only genes and shared environment contribute to the similarity between twins, while non-shared environment includes all those factors that make them different from each other. Therefore, this path does not need to be traced.

The path coefficients can be standardised by dividing their value by the square-root of the (overall, unstandardised) variance. Once they are then multiplied by themselves (a^2 , c^2 or e^2) they are also referred to as A, C and E (as they describe the path for the estimate). Note also that a correlation is a standardised covariance (Rijsdijk, 2015).

In summary, the variance of a trait is $V_t = a^2 + c^2 + e^2$, the covariance within MZ twin pairs for a trait is $r_{MZ} = a^2 + c^2$ and the covariance within DZ twin pairs for a trait is $r_{DZ} = .5 * a^2 + c^2$. If we combine all this information into one formula, we know that:

$$a^2 = 2(r_{MZ} - r_{DZ})$$

$$c^2 = r_{MZ} - a^2$$

$$e^2 = 1 - r_{MZ}$$

This means that if we have data that provides information about V_t , r_{MZ} and r_{DZ} for a trait, then we have enough information to estimate a^2 , c^2 and e^2 for that trait – this is also known as Falconer’s formula or equation (Rijsdijk & Sham, 2002). As we have three parameters to be estimated (a^2 , c^2 and e^2) and three predictive statistics (V_t , r_{MZ} and r_{DZ}), the model is described as a ‘just identified’ one. Theoretically, the total variance of a trait is $V_t = a^2 + c^2 + d^2 + e^2$, which also includes the non-additive genetic influence (d^2). However, in order to make the above explanation simpler, d^2 has been omitted. Furthermore, it is only possible to estimate three parameters using the formula (as we only have three predictive statistics, otherwise the model would not be identified

– a model is ‘identified’ if we estimate as many parameters as we have predictive statistics). Therefore, we can either estimate a^2 , c^2 and e^2 (called ACE model) or a^2 , d^2 and e^2 (called ADE model) in a univariate model like the one outlined above (Rijsdijk & Sham, 2002; Purcell, 2013). For more information about the ADE model, see below.

2.3.2.2 The ADE model

In one of the chapters, an additional model (the ADE model) was run but was not presented as it did not add any useful information (D was not significant in the model - 95% confidence interval overlapping 0). This model is therefore discussed only briefly here. This model was run in **Chapter 4: Associations between pre-sleep arousal and insomnia symptoms in early adulthood: a twin and sibling study**, because the difference between the MZ correlations and the DZ correlations was relatively large. We can explain the difference between the genetic influences in the following way: while we assume for ‘A’ that genetic influences add up, ‘D’ refers to dominance or non-additive genetic influence. Non-additive genetic influence occurs when alleles (variants of genes) at the same locus interact (in contrast to epistasis which refers to alleles interacting at different loci) (Rijsdijk, 2015). Dominance does not play a role in the similarity of MZ twins, as they are genetically identical. For DZ twins, the chances of inheriting the same allele for a DZ twin pair are one in four for each gene (which has two allele), as only one allele is inherited from each parent and two DZ twins are considered (Plomin et al., 2013). Therefore, DZ twins correlate .25 for D – hence the algebra behind the ACE model can easily be adapted to test the ADE model (by changing the value of 1 for C in the ACE model to .25 for D to represent the ADE model). However, in the performed analysis, D was not significant. Therefore, this model did not add any useful information and was not reported.

2.3.3 Structural equation modelling

The Falconer's formula outlined above gives us a rough idea of the magnitude of genetic, shared and non-shared environmental influences explaining the variance in a trait when analysing twin data. Whereas simple algebra can be calculated by hand, structural equation modelling is more advanced in that it allows us to obtain more exact estimates and also 95% confidence intervals which provide information about the precision of the estimates.

Structural equation modelling also provides more flexibility as it allows us to form the model according to certain requirements, which makes it more exact. For example, in the analyses presented in this PhD thesis, siblings were included as a separate group to be modelled in addition to the MZ and the DZ twins, rather than just adding them to the DZ twin group. This allowed for the assumptions to be checked and tested whether or not the two groups could be equated without a significant decrease in model fit. The details about the sibling group are provided in the tables of the descriptive statistics and in the tables for the twin/sibling correlations for each of the studies conducted. However, as it was possible to equate the sibling group to the other groups for all analyses, this group will not, from this point on, be discussed separately and will only be referred to as the DZ twin group in all result sections, explanations and discussions.

An additional advantage of structural equation modelling is that it allows for different models to be compared. For example, it is possible to drop parameters (or add constraints) and then to check whether or not the fit becomes significantly worse. If this is the case, then we know that the model is better with that parameter included in it – hence, the parameter must have played a role to some extent (Rijsdijk, 2015). When different models are compared, the one that best describes the data is chosen. This gives

a more detailed insight than just considering the rough estimates obtained using the Falconer's formula.

2.3.4 Model fitting

The twin analyses conducted within this PhD thesis were all run in OpenMX, a twin model fitting package in 'R' (Boker et al., 2011). This software starts by fitting a saturated model to the twin/sibling data. A saturated model describes the data perfectly by including a maximum number of free parameters to describe the means, variances and covariances/correlations for an observed trait (or various observed traits) (Rijsdijk, 2015). It provides a baseline for fit comparison. Furthermore, the twin model assumptions are tested in the saturated model by checking whether or not means and variances can be equated within the twin/sibling pairs and across the different zygosity groups (Rijsdijk, 2015). In addition, it is possible to test whether means and variances can be equated between the twin allocated as '1' and the twin allocated as '2' according to their birth-order. For the G1219 sample the twins were entered in a random order, but this assumption was still tested. In the next step, a genetic model is fitted (dropping parameters, or adding constraints) and compared to the saturated model. Model fitting is basically a process of optimisation which means that the parameters are manipulated (changing the parameters in an intelligent way, trying out different values) to find out which estimates produce the best fit for the observed values (sample-dependent) and the expected values (model-dependent) (Purcell, 2013). In the genetic model, parameters can be dropped until the most parsimonious model (which still fits the data well) is achieved. Parsimony refers to the idea of a 'simpler' model, which means that fewer parameters are estimated wherever possible (Sober, 1981; Vandekerckhove, Matzke, & Wagenmakers, 2014). In general, according to the law of parsimony or 'Ockham's razor' ("entities should not be multiplied beyond necessity" Neale, 2015, p. 9), more

parsimonious models should be preferred over less parsimonious ones, unless this results in a decreased model fit (Neale, Heath, Hewitt, Eaves, & Fulker, 1989). This is based on the idea that the simpler the theory, the more likely it is that it can be applied and the less difficult it is to test – hence the more parsimonious the model, the more likely it is to be accurate (Neale et al., 1989). If the fit does not get significantly worse, this indicates that the nested model still fits the data well (with the parameters dropped). It should be noted that E can never be dropped as it includes measurement error (Purcell, 2013).

The goodness of fit is indicated by the difference in twice the negative log likelihood (-2LL), which is tested in OpenMX by applying a chi-squared test. A p-value > .05 indicates that the fit for the nested model got worse and therefore it would be less ideal for describing the data (Rijsdijk & Sham, 2002). The idea is to choose the most parsimonious model which still describes the data well (meaning that it does not get significantly worse in fit in comparison to other models which include more parameters or fewer constraints) (Purcell, 2013).

A further indicator for the model fit is the Akaike Information Criterion (AIC). It is calculated by the chi-squares minus two times the degrees of freedom (Neale et al., 1989; Tabachnick & Fidell, 2007).

$$AIC = \chi^2 - 2(df)$$

(Tabachnick & Fidell, 2007, p.719)

A negative AIC is an indication of a good model fit, and the lower the AIC, the better the goodness of fit (Neale et al., 1989).

2.3.5 Multivariate analysis

Multivariate genetic analysis allows consideration of various traits at the same time, making it possible to illuminate the role that genetic and environmental factors

play on their associations. Instead of just estimating the correlations between twins or sibling pairs for one trait (as in univariate analysis), within-twin/sibling-cross-trait and cross-twin/sibling-cross-trait covariances are added to the model to illuminate the genetic, shared environmental and non-shared environmental factors involved in the association between the considered variables. This is done in addition to estimating the influence of A, C and E on each trait separately, as in univariate analyses (Rijsdijk & Sham, 2002). Common aetiological influences can be inferred from the within-twin/sibling-cross-trait covariances, while the cross-twin/sibling-cross-trait covariances indicate whether or not these influences are familial (meaning because of an overlap in A and/or C). By considering the ratio between the MZ cross-twin-cross-trait covariance and the DZ/sibling-cross-twin-cross-trait covariance, it can be differentiated if these common familial factors are due to genetic or shared environmental influences (Rijsdijk & Sham, 2002).

For the multivariate analysis referred to in various chapters (see **Chapters 3, 4 and 5**), three models were compared: the correlated factors solution, the independent pathway and the common pathway model. These models are outlined in the following examples using four variables for illustration. They make similar assumptions but they vary in terms of the model constraints which are added (Rijsdijk & Sham, 2002). As the three models are nested, it is possible to compare them (see also, **Chapters 3, 4 and 5**). Models are nested within each other if they make similar assumptions, but just constraints are added or parameters are dropped (for a more detailed explanation see **2.3.5.3 The common pathway model**). If a model fit does not get significantly worse, then the more parsimonious model can be chosen. A further indicator that can help with the decision as to which model to choose is the AIC (see, explanation above). Note that

other models do exist but are not mentioned here as they are not relevant to the analyses conducted within this PhD thesis.

The decision which variables to include in a multivariate analysis in the first place is usually based on theoretical knowledge and on the phenotypic correlations. It should be mentioned here that there is a general consensus that very small or non-significant associations should not be decomposed at all but there is no consensus as to where the exact cut-off point should be for associations that are worth decomposing. Consequently, no cut-off point has been provided for the analyses conducted in this PhD thesis. However, only significant phenotypic correlations were considered for multivariate analysis. Note also that, conceptually, it does not make sense to include an overall score in the same multivariate as the subscales because this is just the sum of the subscales.

2.3.5.1 The correlated factors model

For the correlated factors solution, it is assumed that each trait has genetic, shared-environmental and non-shared environmental influences. These influences are allowed to correlate with the same influences on the other traits in the model (see **Figure 2.5** on the next pages, Loehlin, 1996). Note that the correlated factor solution and the Cholesky decomposition are mathematically equivalent (Rijsdijk, 2015). This is not relevant to the analyses conducted within this PhD and is therefore not discussed here in detail. However, the Cholesky model makes additional assumptions about the causal directions of effects and should therefore only be used if the analysis is based on a specific hypothesis or theory that justifies these causal directions (Loehlin, 1996). As causality cannot be established reliably from cross-sectional data, this model is better used with longitudinal data (Loehlin, 1996).

The path diagram below illustrates that the correlated factors solution allows us

to draw conclusions about the extent to which the genetic factors influencing variables W, X, Y and Z correlate with each other. If a high genetic correlation is found for all variables, this means that there is overlap between genes influencing one trait and the others (see **Figure 2.5.a**, Loehlin, 1996; Rijdsdijk & Sham, 2002). This kind of analysis can, for example, also reveal that there is a genetic overlap between two traits but not between other traits – allowing us to differentiate between the various associations.

The correlated factors solution also shows the extent to which there is an overlap in shared environment. This examines whether or not the shared environmental factors on one trait correlate with those that influence another trait (see **Figure 2.5.b**; Loehlin, 1996; Rijdsdijk & Sham, 2002). Genetic and shared environmental factors are influences that contribute to the similarity between twins. There is a wide range of possible shared environmental factors, for example, parental education or neighbourhood – although these are only ‘shared environmental influences’ if they increase similarity within individuals within a family (Plomin et al., 2013).

The model also reveals the extent to which the non-shared environmental factors of one trait correlate with the other traits (see **Figure 2.5.c**, Loehlin, 1996; Rijdsdijk & Sham, 2002). This refers to the overlap in non-genetic factors which makes twins dissimilar. For example, if there was a high correlation of non-shared environmental factors between the variables X, Y and Z, but not with W, this would mean that the environmental factors that cause a difference between twins in variables X overlap with the ones that cause a difference between twins in variables Y and Z while for variable W other factors were involved causing dissimilarities. Examples of non-shared environmental influences could include peer influence, accidents or independent life events in general (such as the death of the spouse), although specific non-shared environmental influences depend on the effect they have (Plomin et al., 2013).

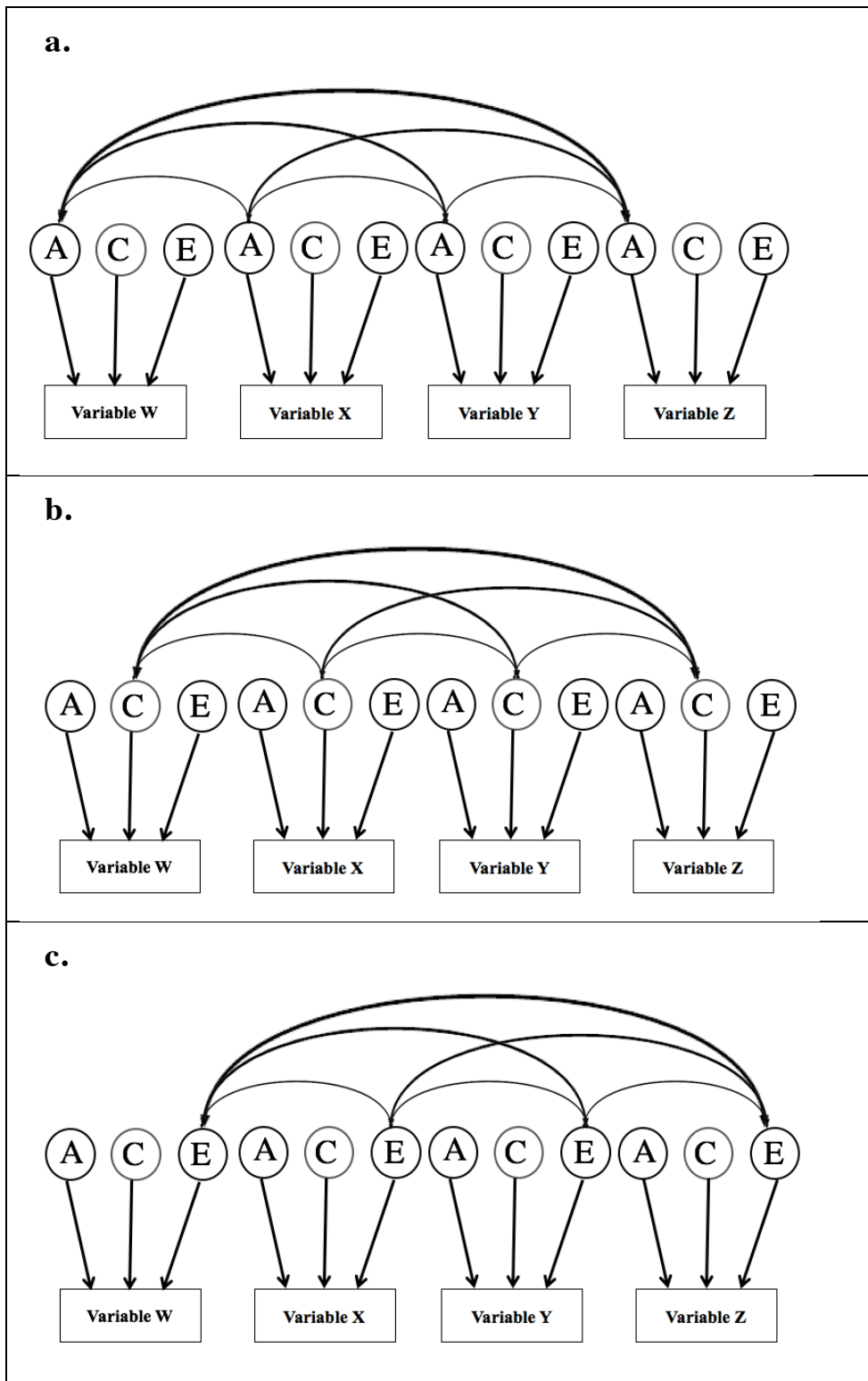


Figure 2.5 Correlated factors solution

Note: A = additive genetic influence; C = shared environmental influence; E = non-shared environmental influence; part a. shows the genetic correlations; part b. shows the shared-environmental correlations; part c. shows the non-shared environmental correlations

2.3.5.2 The independent pathway model

The independent pathway model assumes that common genetic factors, common shared environmental factors and common non-shared environmental factors influence traits directly. *Specific* genetic, shared environmental and non-shared environmental factors are also allowed to contribute to the variance of each phenotype individually (see **Figure 2.6**) (Markon & Krueger, 2004). The independent pathway model is nested in the correlated factor solution (if more than three variables are analysed) and it is the more parsimonious model (Markon & Krueger, 2004).

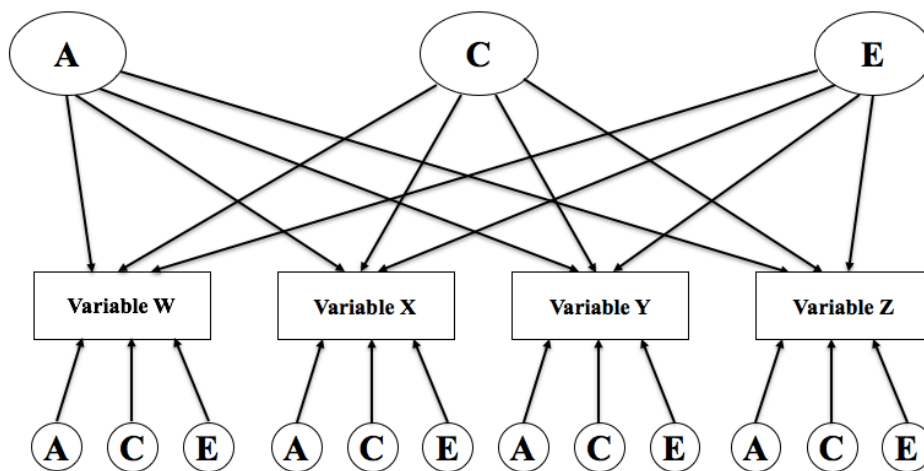


Figure 2.6 Independent pathway model

Note: A = additive genetic influence; C = shared environmental influence; E = non-shared environmental influence

2.3.5.3 The common pathway model

The common pathway model assumes a genetic, shared environmental and a non-shared environmental influence on the variables via a higher order latent (estimated) factor (Rijsdijk & Sham, 2002). Specific genetic, shared environmental and non-shared environmental factors that contribute to the variance of each phenotype independently are also specified (see **Figure 2.7** overleaf) (Markon & Krueger, 2004). The common pathway model is nested in the two previously discussed models, makes similar assumptions but estimates fewer parameters. Therefore, it is even more

parsimonious than the independent pathways model. An easy way to demonstrate that the common pathway model is more parsimonious than the independent pathway model, which again is more parsimonious than the correlated factor solution, is to count the paths for each model (illustrated as arrows). The common pathway model with four variables includes 19 paths while the independent pathway model has 24, and the correlated factor solution has 30 paths. If we add the number of variables to the total number of paths counted (as the mean for each of the four variables is also estimated), then we get the total number of estimated parameters for the model.

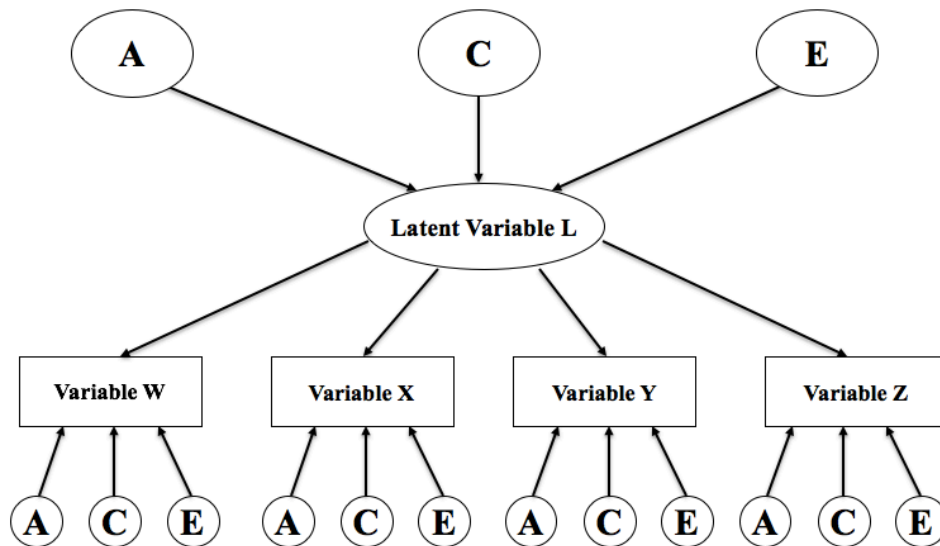


Figure 2.7 Common pathway model

Note: A = additive genetic influence; C = shared environmental influence; E = non-shared environmental influence

2.3.5.4 Models including three measured variables

If three variables are included, then the same number of parameters are estimated for both the correlated factors solution and the independent pathway model (21 parameters in total: the mean for each variable plus all the paths', see **Appendix A** for illustration). In this case, the independent pathway model is not nested in the correlated factor solution (neither is it more parsimonious). Two models can only be compared in

fit if one model is nested in the other. This means that the set of parameters of the first model is a subset of parameters of the second (nested) model (Rijsdijk and Sham, 2002; see also, chapter four).

2.4 The G1219 sample

2.4.1 History of data collection for G1219: Waves 1, 2 and 3

The participants for the Genesis 12-19 sample (G1219) were recruited from two different sources – via the families of the GENESiS study (Sham et al., 2000) and via the UK Office for National Statistics. Of the 40,000 adults from the GENESiS study, approximately 9,000 indicated that they had children. Those adults were invited to participate if their children were between 12 and 19 years old. This resulted in responses from 1,241 families with 1,747 adolescent children (aged 12 - 19 with a mean age 15), including 445 sibling pairs (McAdams et al., 2012). The twins were mainly recruited through the UK Office of National Statistics by randomly selecting twin pairs born between 1985 and 1988 and then contacting their parents (2,947 families in total). Of the total number of parents contacted, 1,381 families and just as many twin pairs agreed to participate (McAdams et al., 2012). Over five consecutive waves, data was collected from the twin and sibling pairs, as well as from their parents (but not for all the waves). The original aim was to investigate how genes and environment interplay in depression in adolescence but measures of various other traits were added across the waves (McAdams et al., 2012).

The data collection for wave one started in 1999 and 1,890 families with 3,640 adolescents (aged 12 to 19, with a mean age of 14 and with 48% males) took part. In 2001/02, the second wave of data collection was conducted but only twin and sibling pairs (not their parents) were asked to complete the battery of questionnaires. There was

some attrition which meant that 73% of the original sample took part, resulting in a total of 2,651 participants (1,372 families). The age range was 12 to 21 (mean age 15 years) and 44% of the participants were male (McAdams et al., 2012). In 2003/04, the third wave of data was collected. This included twins, siblings and their parents (parents reported their own emotions and behaviour, as well as that of their children). Again there was some attrition and, in comparison to wave two, 67% participated in the study. In comparison to wave one, 48% participated in the third wave. This meant that 1,778 twins and siblings from 913 families actually took part. They were aged between 14 and 23 (with a mean age of 17) and 40% of them were males. For wave 2 and 3, zygosity was assessed by using a questionnaire which asked the mothers of the twins about physical similarities (Cohen et al., 1975). Where there was doubt, a genetic test was undertaken to obtain zygosity (26 cases) (McAdams et al., 2012).

2.4.2 Relevance to the current analyses: Waves 4 and 5

The data from waves 4 and 5 of the G1219 longitudinal twin and sibling study was the focus of the analyses in this PhD thesis, as sleep-related measures were only added for those two waves. Wave 4 data was collected in 2007 and 88% of the participants of the previous wave agreed to take part. In comparison to wave one, 42% participated in the fourth wave. This meant that a total of 1,556 individuals from 896 families participated. The sample included 39% of males with an age range of 18 - 27 and a mean age of 20. (Denis et al., 2015; McAdams et al., 2012).

The most recent data collection wave took place in 2012/13. Wave 5 was the only wave in which the key variables central to this PhD topic were measured (mindfulness, pre-sleep arousal and dysfunctional beliefs about sleep). This is the reason why wave 5 data was used for all of studies in this PhD thesis. For one study it was also possible to use wave 4 (see **Chapter 7: Self-reports of insomnia with short**

versus normal sleep duration: comparing the subtypes in terms of heritability and associated phenotypes) because all the variables relevant to the analysis were collected in wave 4 as well. Tests showed that there was no selective attrition in the key variables between those waves (for more information, see **Chapter 7, 7.4.4 Persistence over time**). In comparison to the previous wave, 55% participated in wave five (23% in comparison to wave one). Wave 5 included data from 862 individuals, consisting of 223 monozygotic (MZ) twins, 404 dizygotic (DZ) twins and 218 siblings (Denis et al., 2015). Participants were aged between 22 and 32 (with a mean age of 25) and 34% of them were male (Denis et al., 2015).

2.4.3 Ethical approval

For all data collection waves, ethical approval was either gained from Goldsmiths College, University of London (for waves 4 and 5) or from the Research Ethics Committees of the Institute of Psychiatry (South London and Maudsley NHS Trust, for waves 1 to 4). Informed consent was obtained from all participants (either directly if ≥ 16 years of age, or via the parents if < 16 years of age).

2.4.4 Data preparation

SPSS (IBM, 2013; version 22) was used for data cleaning and transformation of various variables and deleting outliers ± 3 SD away from the mean, as is standard (if required; Gregory et al. 2016). The variables which were skewed or showed kurtosis were transformed where necessary. Furthermore, sex and age were regressed out in preparation for the genetic model fitting with OpenMX (Boker et al., 2011), as is standard for twin/sibling analyses (Bolhuis et al., 2014; Gregory et al., 2011). Age and sex should be regressed out because if we do not correct for these influences this would result in an over-estimation of the intraclass twin correlations (McGue & Bouchard,

1984). Age is the same in both MZ and DZ twin pairs and could make them more alike if age was an important factor influencing the trait under investigation (i.e. artificially inflating both MZ and DZ intraclass correlations). Sex needs to be regressed out because it is perfectly correlated in MZ but not in DZ twin pairs. Therefore, this could artificially inflate the MZ twin intraclass correlation in comparison to the DZ intraclass correlation (McGue & Bouchard, 1984). It should also be mentioned that cases where the zygosity information is missing ($N = 14$) were excluded from all analyses.

2.5 Sensitivity analyses

Sensitivity analyses were performed for all analyses run in SPSS (IBM, 2013), STATA (StataCorp, 2015) and OpenMX (Boker et al., 2011). This means that all analyses were re-run on raw data (without transforming the variables, deleting outliers or regressing out age and sex), verifying whether or not different results were obtained. Wherever the sensitivity analyses showed similar results, only the results from the prepared data were presented.

CHAPTER 3: Mindfulness and associations with symptoms of insomnia, anxiety and depression in early adulthood: a twin and sibling study

3.1 Introduction

Mindfulness, or meta-cognition, is the central element of the meta-cognitive theory of insomnia (Ong et al., 2013) (see **1.3.1 Theories most relevant to this thesis – Cognitive models of insomnia** for a detailed discussion). The rationale of this study is to gain a better understanding of the concept and the aetiology insomnia, by considering the roots of mindfulness and its association with insomnia symptoms from a behavioural genetics perspective. By understanding the mechanisms underlying the aetiology of insomnia symptoms and gaining an insight in the elements involved at a deeper level (by considering the subscales of insomnia) it may further be possible to improve insomnia treatment in the future. Furthermore, in spite the great research interest in mindfulness over the last two decades (Ie, Ngnoumen, & Langer, 2014; Kabat-Zinn, 2003), there is still much to learn. We need to further understand the reasons why some people are more mindful than others. Here, a behavioural genetic approach is adopted to shed light on these individual differences.

3.1.1 Conceptualisation of mindfulness

When conducting research involving mindfulness, it is crucial to explain how mindfulness is conceptualised for the present study. Mindfulness is generally defined as being present in the moment and being aware of inner as well as outer experiences while adopting a non-judging perspective (Kabat-Zinn, 1994). Mindfulness can be conceptualised in various ways: as a state, trait, or a skill that is learned (Sauer et al., 2013). To allow for a detailed insight into the concept of state mindfulness, five elements

are focused on in the current analyses: ‘nonreactivity to inner experience’, ‘observing’, ‘acting with awareness’, ‘describing’ and ‘nonjudging of inner experience’.

‘Nonreactivity to inner experience’ refers to the extent to which one is able to notice emotions and thoughts but then to be able to let them go without having to react to them. For example, one may notice that he/ she is sad without having to cry. ‘Observing’ reflects the extent to which someone is able to observe, notice or attend to the world around them as well as their inner experience, including their sensations, perceptions, thoughts and feelings. The ‘acting with awareness’ component examines the extent to which one is present in the moment, the here and now, and is paying attention to what they are doing or experiencing. The facet ‘describing’ refers to the ability to label or describe any experience of the inner world (for example feelings, thoughts, beliefs and expectations). Finally, ‘nonjudging of inner experience’ reflects the extent to which someone is able to accept feelings and thoughts, avoiding making a judgement about their inner experience (Baer, Smith, Hopkins, Krietemeyer and Toney, 2006). This is in line with Baer and colleagues view (2006) of mindfulness as having various facets which are useful to be explored.

3.1.2 Mindfulness sub-scales and other traits

Before exploring the association of mindfulness (and its subscales) with insomnia symptoms, depression and anxiety, it is useful to consider what we already know about the association mindfulness and related traits in this area. Greater mindfulness has been associated with better sleep quality (Howell, Digdon, Buro & Sheptycki, 2008), greater well-being (Brown & Ryan, 2003) and with lower levels of depressive and anxiety symptoms (Cash & Whittingham, 2010; Waszczuk et al., 2015). Furthermore, mindfulness-based approaches are used to treat insomnia, depression and anxiety (Hofmann et al., 2010; Hubbling et al., 2014; Ong et al., 2012; Vøllestad, Sivertsen, &

Nielsen, 2011). Metacognitive processes such as mindfulness were further discussed to be crucial in the development and maintenance of insomnia and have taken a central role in cognitive theories of insomnia (for a detailed discussion see **1.3.1 Theories most relevant to this thesis – Cognitive models of insomnia**). Despite these associations, it is important to consider mindfulness subscales when examining co-occurrence with other traits because certain mindfulness subscales may be particularly strongly associated with certain psychiatric difficulties. For example, self-reported ability to adopt a nonjudging attitude has been shown to predict lower levels of depression and anxiety symptoms (Cash & Whittingham, 2010). Furthermore, a greater ability to act with awareness was found to predict lower levels of depression symptoms but did not predict anxiety symptoms (Cash & Whittingham, 2010). It should be mentioned that this study used cross-sectional data. Therefore, causality cannot be inferred. Furthermore, a non-clinical sample was used. In a different study, four of the five subscales of mindfulness (‘nonreactivity to inner experience’, ‘describing’, ‘acting with awareness’ and ‘nonjudging of inner experience’, but not ‘observing’) were found to be associated with sleep quality (Caldwell, Harrison, Adams, Quin & Greeson, 2010) – with greater mindfulness being related to better sleep quality. It can be criticised that this study focused exclusively on college students. No study has yet examined the role that the subscales of mindfulness play in insomnia symptoms (at the time that this chapter was written).

3.1.3 Heritability of mindfulness

Little is known about the heritability of mindfulness. To date, only one twin study has explored the genetic and environmental influences on ‘trait’ mindfulness in adolescents. This study focused exclusively on the attentional aspect of mindfulness, finding that ‘trait’ mindfulness in adolescence was moderately heritable (additive

genetic influence, $A = .32$) and was influenced by non-shared environmental factors ($E = .66$), with no significant influence of shared environmental factors ($C = .02$; Waszczuk et al., 2015). However, it can be criticised that only a shortened version of the measure Mindfulness Attention and Awareness Scale (5 items only) was used, giving a rather limited insight into the concept of mindfulness (Waszczuk et al., 2015; Bergomi et al., 2013).

Twin studies can go beyond telling us about the heritability of a trait and can also help to elucidate the reasons why it overlaps with other traits (see Plomin et al., 2013). Only one study has addressed the reason for overlap between mindfulness and other variables (namely depressive symptoms and anxiety sensitivity) and this work was conducted in the aforementioned adolescent sample (Waszczuk et al., 2015). It was found that mindfulness, symptoms of depression, and anxiety sensitivity shared moderate genetic and to a lesser extent non-shared environmental correlations. Furthermore, genetic influences accounted for more than half of the phenotypic association between the three traits. The results are yet to be evaluated in an adult sample. Therefore, the variables depression and anxiety symptoms were added in the current study. Furthermore, the genetic and environmental influences on the association between mindfulness and insomnia symptoms are yet to be explored.

3.1.4 Aims of the current study

Given the links between mindfulness, sleep and good mental health, it is important to understand more about what makes people differ in terms of this trait. Understanding more about the aetiology of the overlap between mindfulness and symptoms of insomnia (and depression and anxiety) will also help us to further understand these interesting links with the ultimate aim of using this information to

facilitate prevention efforts and treatment. Very little is known about the heritability of mindfulness. The current study is novel in that it estimates genetic and environmental influences on mindfulness and its subscales for the first time (in early adulthood). Furthermore, the genetic and environmental influences on the association between overall mindfulness and symptoms of insomnia, depression and anxiety and their association will be estimated for the first time. Therefore, aims were formulated rather than hypotheses, which would point into a certain direction:

- 1) The magnitude of associations between mindfulness (including focusing on the subscales) and symptoms of insomnia, depression and anxiety.
- 2) Genetic and environmental influences on mindfulness (including focusing on the subscales) and the association with symptoms of insomnia, depression and anxiety.

3.2 Method

3.2.1 *Sample*

Data from wave 5 of the Genesis 12-19 (G1219) longitudinal twin/sibling study (Denis et al., 2015) was the focus of this study as this is the only wave in which mindfulness has been measured. Wave 5 included data from 223 monozygotic (MZ) twins, 404 dizygotic (DZ) twins and 218 siblings (see Denis et al., 2015). Participants were aged between 22 and 32 (mean age 25 years) and, out of a total of 862 individuals, 34.3% were male. For a more detailed description of the sample, see **Chapter 2: Methods, 2.4 The G1219 sample**.

3.2.2 Mindfulness

Mindfulness was assessed by the Five Facet Mindfulness Questionnaire (FFMQ, Baer et al., 2006). The FFMQ comprises five subscales ('nonreactivity to inner experience', 'observing', 'acting with awareness', 'describing' and 'nonjudging of inner experience'). The original version of the measure contains 39 items, but for the current study, it was shortened to 21 items (see **Appendix B**: Items included from the FFMQ). The four items with the highest factor loading for each subscale were selected (Baer et al., 2006). The 'nonreactivity to inner experience' subscale had three items with the same factor loading so five items were included for this scale (Baer et al., 2006). Each item of the FFMQ was coded 1-5, ranging from "never or very rarely true", to "always or almost always true", as recommended in the original publication of the FFMQ (Baer et al., 2006). Items were summed for the subscales and for overall mindfulness (the latter therefore had a theoretical range from 21 to 105). Cronbach's alphas for the current sample were 'nonreactivity to inner experience' = .87; 'observing' = .80; 'acting with awareness' = .84; 'describing' = .86; 'nonjudging of inner experience' = .88; and overall mindfulness = .81.

Usually, higher scores on the FFMQ indicate greater mindfulness. For ease of interpretation and to allow the decomposition of positive associations in the multivariate genetic models, all mindfulness scores were reverse coded so that higher scores indicate less mindfulness. The question "How much experience do you have with meditation?" was added to the battery. This allowed us to control for meditation experience in our analyses, which is known to influence the mindfulness score (see, for example, Baer et al., 2006; Walach, Buchheld, Büttenmüller, Kleinknecht & Schmidt, 2006). This way it was possible to look at individual differences in this trait regardless of training.

3.2.3 Insomnia symptoms

Insomnia symptoms were measured using the Insomnia Symptoms Questionnaire (ISQ, Okun et al., 2009), using a 6-item version. The first data collection for insomnia symptoms (wave 4) was in process already before the ISQ was published, while collaborating with one of the co-authors (Dan Buysse). In the final published version of the ISQ a few items were added which are here summarised under item 6 (Okun et al., 2009). The ISQ was designed to be coded as a dichotomous variable but was coded as a continuous variable for the purpose of the current study (after corresponding with one of the authors of the original measure, Dan Buysse). Each item was coded 0 - 4 based on frequency response ('never/don't know' = 0; 'rarely' = 1; 'sometimes' = 2; 'frequently' = 3; 'always' = 4). The total scale score was calculated by taking the sum of all the responses, ranging from 0 to 24, with higher scores indicating more severe insomnia symptoms. The items of the ISQ (Okun et al., 2009) overlap largely with the items of the ISI (Morin et al., 2011), which is coded as a continuous variable (see **Appendix C** for a list of items included in the ISQ and the ISI). The ISQ was coded as a continuous measure in a previous study using the G1219 sample (Gregory et al. 2016), as well as in other studies (see, for example, Sánchez-Ortuño & Edinger, 2010). Furthermore, Cronbach's alpha for the ISQ in the current sample was .87 and the ISQ score was highly correlated with the global score of the Pittsburgh Sleep Quality Index (PSQI; $r = .73, p < .01$; Buysse et al., 1989), confirming the validity of the continuous scoring of the measure.

3.2.4 Depression symptoms

Depression symptoms were measured by the mood and feelings questionnaire (MFQ; Angold et al., 1995) which assesses depression symptoms experienced over the past 2 weeks via self-measurement. The measure includes 13 items which are coded as

0 = 'not true', 1 = 'sometimes' and 2 = 'true'. Items were summed to produce a total score. Items include "I felt miserable or unhappy" or "I cried a lot". The scores have a theoretical range from 0 to 26. Cronbach's alpha for the current sample was .90 (see Gregory et al., submitted).

3.2.5 Anxiety symptoms

Symptoms of anxiety were measured by an age-adapted version of the Revised Children Anxiety and Depression Scale (RCADS, Chorpita, Yim, Moffitt, Umemoto & Francis, 2000; Willis, 2007), comprising 36 items for assessing symptoms of anxiety as described by the DSM-IV (APA, 2000). For example, items such as "I would feel afraid of being on my own at home" or "I feel worried when I think someone is angry with me" were included (Chorpita et al., 2000; Willis, 2007). The total score was calculated by coding each item (never = 0, sometimes = 1, often = 2, always = 3) and then taking the sum (Gregory et al., 2011). The scores have a theoretical range from 0 to 108. Cronbach's alpha for the current sample was .94. This age-adapted version of the RCADS has been used in previous research (see for example Gregory et al., 2011).

3.2.6 Data preparation

The data was prepared (see **2.4.4 Data preparation** for more details). The variable depression symptoms was slightly skewed (skew = 1.42, SE = .08, kurtosis = 1.67, SE = .17) and therefore it was log₁₀-transformed, which has been done in previous publications including this variable (see, Gregory et al., 2016). This procedure successfully reduced the skewness (skew = -.15, SE = .08; kurtosis = -.79, SE = .17).

3.2.7 Analysis

Descriptive statistics were run on untransformed variables in SPSS (version 22; IBM, 2013). Phenotypic correlations (focusing on one twin only to control for non-

independence of observations) examined associations between the variables and partial correlations were used to explore the independent role of each subscale in the association between mindfulness and symptoms of insomnia, depression and anxiety. The partial correlations allowed us to consider the associations between each mindfulness subscale and insomnia, depression and anxiety symptoms without being confounded by the relationship with the other subscales. For example, when assessing the association between ‘acting with awareness’ and symptoms of insomnia, depression and anxiety, the analysis controlled for the effects of all the other mindfulness subscales. In this manner it was possible to assess whether certain mindfulness subscales were more important than others in driving associations. The resulting partial correlations were compared in magnitude using JavaScript (Lee & Preacher, 2013; Steiger, 1980). For all phenotypic analyses, the focus was on the transformed data of one twin/sibling from each pair to control for non-independence of observations, using SPSS (version 22; IBM, 2013).

Twin analyses were used to investigate the aetiology of mindfulness and its relationship with anxiety, depression and insomnia. See **Chapter 2: Methods, 2.3. The twin method** for a detailed explanation of the analyses. All twin/sibling analyses were performed, using R with a package for genetic model fitting called OpenMX which uses maximum likelihood estimation to compare model fits (Boker et al. 2011; McAdams, Gregory, & Eley, 2013). For more background about the structural equating modelling and model fitting applied in OpenMX, see **Chapter 2: Methods, 2.3.3 Structural equation modelling and 2.3.4 Model fitting**.

A univariate analysis was run for each variable, applying maximum-likelihood model fitting analysis to estimate the relative contribution of genetic, shared and non-shared environmental influence (Neale & Cardon, 2013). For a detailed explanation of

univariate analysis, see **Chapter 2: Methods, 2.3.2 Univariate Analysis**.

Multivariate analyses, including overall mindfulness, insomnia symptoms depression symptoms and anxiety symptoms, were run to examine the contribution of A, C and E on the associations between traits. For a detailed explanation of multivariate analysis, see **Chapter 2: Methods, 2.3.5 Multivariate analysis**. Three models were compared: the correlated factors solution, the independent pathway and the common pathway model. For an explanation of the three models fitted, see **Chapter 2: Methods, 2.3.5.1 The correlated factor model, 2.3.5.2 The independent pathway model and 2.3.5.3 The common pathway model**.

Sensitivity analyses were performed as outlined under **2.5 Sensitivity analyses**. Additional sensitivity analysis was performed by excluding all cases with meditation experience ($N = 246$) and re-running all twin analyses. The results were similar. Therefore, the results from the complete sample will be presented here to maximise statistical power.

3.3 Results

3.3.1 Descriptive statistics

Descriptive statistics for each variable are summarised in **Table 3.1** (please see table on the following pages). There were significant sex differences for overall mindfulness ($t(847) = 3.01, p < .01, d = .21$), males were more mindful than females. For insomnia symptoms, significant sex differences were found as well ($t(625) = -3.28, p < .01, d = .25$), males reported fewer insomnia symptoms than females. For depression symptoms, significant sex differences were found ($t(681) = -2.63, p < .01, d = .19$), males reported fewer depression symptoms than females. Also, for symptoms of anxiety, significant sex

differences were found as well ($t(662) = -7.23, p < .01, d = .52$), males reported fewer symptoms of anxiety than females.

Table 3.1 Means (SD) of raw scores for overall mindfulness, mindfulness subscales and symptoms of insomnia, depression and anxiety

	Means (SD)		
	Total	Males	Females
Overall Mindf.	35.70 (10.37)	34.23 (10.90)*	36.46 (10.01)*
‘Nonreactivity’	9.40 (4.54)	8.00 (4.39)	10.12 (4.45)
‘Observing’	9.53 (3.59)	9.42 (3.54)	9.59 (3.61)
‘Acting with Awareness’	5.27 (3.21)	5.37 (3.27)	5.21 (3.18)
‘Describing’	6.69 (3.66)	6.70 (3.79)	6.69 (3.60)
‘Nonjudging’	4.83 (3.73)	4.79 (3.68)	4.85 (3.76)
Insomnia symptoms	6.48 (5.22)	5.65 (4.89)*	6.92 (5.33)*
Depression symptoms	5.31 (5.30)	4.68 (4.73)*	5.64 (5.55)*
Anxiety symptoms	22.13 (14.81)	17.31 (13.19)*	24.65 (14.99)*
	MZ	DZ	Siblings
Overall Mindf.	35.88 (10.47)	36.19 (10.74)	34.67 (9.68)
‘Nonreactivity’	9.77 (4.72)	9.44 (4.57)	8.96 (4.35)
‘Observing’	9.47 (3.75)	9.49 (3.67)	9.60 (3.29)
‘Acting with Awareness’	5.07 (3.15)	5.30 (3.39)	5.42 (2.95)
‘Describing’	6.85 (3.88)	6.93 (3.60)	6.16 (3.60)
‘Nonjudging’	4.74 (3.77)	5.04 (3.91)	4.54 (3.30)
Insomnia symptoms	6.09 (4.97)	6.68 (5.38)	6.61 (5.19)
Depression symptoms	5.34 (5.44)	5.73 (5.73)	4.54 (4.21)
Anxiety symptoms	23.93 (15.03)	22.32 (15.32)	20.11 (13.32)

Note: *sex differences were found. Mindfulness scores are reverse coded. Overall Mindf. = overall score of mindfulness (FFMQ); ‘Nonreactivity’ = subscale of mindfulness (FFMQ), higher scores indication stronger reaction to inner experience; ‘Observing’ = subscale of mindfulness (FFMQ), higher scores indicating lower ability to observe, notice, attend to sensations, perceptions, thoughts and feelings; ‘Acting with A.’ = subscale of mindfulness (FFMQ), higher scores indicating acting less aware; ‘Describing’ = subscale of mindfulness (FFMQ), higher scores indicating lower ability to describe or label feelings, thoughts, beliefs, expectations, etc.; ‘Nonjudging’ = subscale of mindfulness (FFMQ), higher score indicating more judging of inner experience; Insomnia symptoms = insomnia symptoms (ISQ), higher scores indicating more insomnia symptoms; Depression symptoms = symptoms of depression (MFQ), higher scores indicating more symptoms of depression; Anxiety symptoms = symptoms of anxiety (RCADS), higher scores indicating more anxiety symptoms.

3.3.2 Phenotypic correlations and MZ, DZ and sibling correlations

The phenotypic correlations are displayed in **Table 3.2** (please see table overleaf). Less mindfulness was associated with more insomnia symptoms, higher depression and more anxiety symptoms ($r = .22$ to $.48$, $p < .01$). When considering mindfulness subscales, ‘nonjudging’ was the subscale most highly correlated with insomnia symptoms ($r = .34$, $p < .01$), depression symptoms ($r = .54$, $p < .01$) and anxiety symptoms ($r = .55$, $p < .01$).

Table 3.2 Phenotypic correlations for overall mindfulness, subscales of mindfulness, symptoms of insomnia, depression and anxiety

	Overall mindf.	‘Nonreact.’	‘Observ.’	‘Acting w. a.’	‘Describ.’	‘Nonjud.’	Insomnia symp.	Depression symp.	Anxiety symp.
Overall mindfulness	1								
‘Nonreactivity’	.62**	1							
‘Observing’	.32**	.16**	1						
‘Acting with a.’	.54**	.08	-.10*	1					
‘Describing’	.63**	.17**	.11*	.28**	1				
‘Nonjudging’	.54**	.12*	-.17**	.40**	.24**	1			
Insomnia symptoms	.22**	.01	-.13**	.31**	.17**	.34**	1		
Depression symptoms	.48**	.25**	-.08	.42**	.26**	.54**	.49**	1	
Anxiety symptoms	.46**	.29**	-.16**	.37**	.26**	.55**	.46**	.62**	1

Note: * $p < .05$; ** $p < .01$. Correlations were calculated on transformed data, using twin 1 only to control for non-independence of observations. Overall mindfulness = overall score of mindfulness (FFMQ), reverse coded, higher score indicating lower mindfulness; ‘Nonreactivity’ = subscale of mindfulness, reverse coded, higher scores indicating stronger reaction to inner experience; ‘Observing’ = subscale of mindfulness, reverse coded, higher scores indicating lower ability to observe, notice, attend to sensations, perceptions, thoughts and feelings; ‘Acting with a.’ = subscale of mindfulness, reverse coded, higher scores indicating acting less aware; ‘Describing’ = subscale of mindfulness, reverse coded, higher scores indicating lower ability to describe or label feelings, thoughts, beliefs, expectations, etc.; ‘Nonjudging’ = subscale of mindfulness, reverse coded, higher score indicating more judging of inner experience; Insomnia symptoms = insomnia symptoms (ISQ), higher scores indicating more insomnia symptoms; Depression symptoms = symptoms of depression (MFQ), higher scores indicating more symptoms of depression; Anxiety symptoms = symptoms of anxiety (RCADS), higher scores indicating more symptoms of anxiety.

Further examining these associations, partial correlations were explored. However, none of the subscales was found to drive the association between overall mindfulness and symptoms of insomnia, depression and anxiety (see **Table 3.3**). After partialling out the other subscales, the ‘nonjudging of inner experience’ subscale still showed the highest correlation with insomnia symptoms, $r = .23, p < .01$ (note however that the correlation between ‘acting with awareness’ and insomnia symptoms, $r = .18, p < .01$ was not significantly lower). The ‘nonjudging of inner experience’ subscale (as compared to the other mindfulness subscales) also correlated most strongly with depression symptoms ($r = .43, p < .01$) and anxiety symptoms ($r = .44, p < .01$). The subscales ‘describing’ and ‘observing’ were not significantly correlated with insomnia and depression; and ‘describing’ was not significantly correlated with anxiety symptoms, after controlling for the other subscales.

Table 3.3 Phenotypic correlations for each subscale of mindfulness with symptoms of insomnia, depression and anxiety after partialling out all other subscales

	‘Nonreact.’	‘Observ.’	‘Acting w. a.’	‘Describing’	‘Nonjudging’
Insomnia symptoms	-.04	-.07	.18**	.06	.23**
Depression symptoms	.21**	-.03	.23**	.07	.43**
Anxiety symptoms	.29**	-.15**	.19**	.07	.44**

Note: * $p < .05$; ** $p < .01$. ‘Nonreactivity’ = subscale of mindfulness, reverse coded, higher scores indication stronger reaction to inner experience; ‘Observing’ = subscale of mindfulness, reverse coded, higher scores indicating lower ability to observe, notice, attend to sensations, perceptions, thoughts and feelings; ‘Acting with a.’ = subscale of mindfulness, reverse coded, higher scores indicating acting less aware; ‘Describing’ = subscale of mindfulness, reverse coded, higher scores indicating lower ability to describe or label feelings, thoughts, beliefs, expectations, etc.; ‘Nonjudging’ = subscale of mindfulness, reverse coded, higher score indicating more judging of inner experience; Insomnia symptoms = insomnia symptoms (ISQ), higher scores indicating more insomnia symptoms; Depression symptoms = symptoms of depression (MFQ), higher scores indicating more symptoms of depression; Anxiety symptoms = symptoms of anxiety (RCADS), higher scores indicating more symptoms of anxiety.

The MZ, DZ and sibling within-trait correlations are presented in **Table 3.4** and **Table 3.5** and cross-trait correlations for all of the variables are presented in **Table 3.5** (please see table overleaf). The MZ correlations for overall mindfulness (and all subscales, except for ‘nonreactivity’), symptoms of insomnia, depression and anxiety were larger (although not significantly, as indicated by overlapping confidence intervals) than the DZ correlations, indicating possible genetic influence. As the MZ correlations are substantially less than 1 for all of the traits, the importance of non-shared environmental influence (E; including error) is highlighted.

Table 3.4 Twin/sibling correlations for the subscales of mindfulness

	Correlations		
	MZ	DZ	Sibling
‘Nonreactivity’	.11 (-.10 - .31)	.14 (-.03 - .29)	.14 (-.10 - .36)
‘Observing’	.25 (.04 - .44)	.01 (-.15 - .17)	-.03 (-.28 - .22)
‘Acting with awareness’	.19 (-.02 - .38)	.16 (.01 - .31)	.18 (-.05 - .39)
‘Describing’	.40 (.21 - .56)	.07 (-.09 - .23)	-.08 (-.30 - .15)
‘Nonjudging’	.22 (.01 - .41)	.08 (-.08 - .24)	-.01 (-.27 - .26)

Note: The 95% confidence intervals are presented in brackets. MZ = monozygotic twins; DZ = dizygotic twins; Sibling = sibling pairs; the MZ, DZ and Sibling correlations are based on the transformed data, outliers deleted with age and sex and obtained from OpenMX. ‘Nonreactivity’ = subscale of mindfulness (FFMQ), reverse coded, higher scores indication stronger reaction to inner experience; ‘Observing’ = subscale of mindfulness (FFMQ), reverse coded, higher scores indicating lower ability to observe, notice, attend to sensations, perceptions, thoughts and feelings; ‘Acting with awareness.’ = subscale of mindfulness (FFMQ), reverse coded, higher scores indicating acting less aware; ‘Describing’ = subscale of mindfulness (FFMQ), reverse coded, higher scores indicating lower ability to describe or label feelings, thoughts, beliefs, expectations, etc.; ‘Nonjudging’ = subscale of mindfulness (FFMQ), reverse coded, higher score indicating more judging of inner experience.

Table 3.5 Twin/sibling correlations (within-trait and between-traits) for overall mindfulness, insomnia symptoms, depression and anxiety

	Correlations		
	MZ	DZ	Sibling
<i>Within-trait</i>			
Overall mindfulness	.27 (.07 - .44)	.20 (.05 - .34)	.14 (-.14 - .38)
Insomnia symptoms	.37 (.19 - .53)	.21 (.05 - .36)	.12 (-.13 - .34)
Depression symptoms	.36 (.17 - .52)	.20 (.05 - .33)	-.03 (-.27 - .21)
Anxiety symptoms	.41 (.24 - .54)	.21 (.07 - .34)	.35 (-.01 - .56)
<i>Cross-traits-cross-twins</i>			
Overall mindfulness – Insomnia symptoms	.09 (-.05 - .22)	.07 (-.04 - .18)	.18 (-.01 - .34)
Overall mindfulness – Depression symptoms	.23 (.08 - .35)	.08 (-.04 - .19)	.09 (-.11 - .28)
Overall mindfulness – Anxiety symptoms	.16 (.01 - .28)	.09 (-.02 - .20)	.24 (-.01 - .42)
Insomnia symptoms – Depression symptoms	.32 (.18 - .45)	.10 (-.02 - .21)	.05 (-.14 - .24)
Insomnia symptoms – Anxiety symptoms	.32 (.18 - .44)	.09 (-.02 - .20)	.17 (-.05 - .35)
Depression symptoms – Anxiety symptoms	.31 (.16 - .43)	.11 (-.01 - .22)	.18 (-.08 - .37)

Note: The 95% confidence intervals are presented in brackets. MZ = monozygotic twins; DZ = dizygotic twins; Sibling = sibling pairs; Overall mindf. = overall score of mindfulness (FFMQ), reverse coded, higher score indicating lower mindfulness; Insomnia symptoms = insomnia symptoms (ISQ), higher scores indicating more insomnia symptoms; Depression symptoms = symptoms of depression (MFQ), higher scores indicating more symptoms of depression; Anxiety symptoms = symptoms of anxiety (RCADS), higher scores indicating more anxiety symptoms

3.3.3 Univariate genetic model fitting

Univariate analyses were run on all variables for completeness; even for ‘nonreactivity to inner experience’ for which the DZ correlations were very slightly

higher than the MZ correlations and so genetic influence would not be assumed. The fit statistics and the results of the full ACE models are presented in **Table 3.6** (please refer to table overleaf).

Table 3.6 Fit statistics of all univariate genetic model fitting analyses

<i>Variable/</i> Model	ep	-2LL	df	AIC	Δ -2LL	Δ df	<i>p</i>
<i>Overall mindfulness</i>							
Saturated	15	6165.79	818	4519.77	-	-	-
ACE	4	6166.07	829	4508.07	10.29	11	.50
E	2	6181.56	831	4519.56	15.48	2	< .01
<i>'Nonreactivity'</i>							
Saturated	15	4835.75	821	3193.75	-	-	-
ACE	4	4845.43	832	3181.43	9.68	11	.56
E	2	4850.46	834	3182.46	14.71	2	.08
<i>'Observing'</i>							
Saturated	15	4505.53	823	2859.54	-	-	-
ACE	4	4516.76	834	2848.76	11.22	11	.32
E	2	4520.42	836	2848.42	3.66	2	.16
<i>'Acting with awareness'</i>							
Saturated	15	4244.63	819	2609.63	-	-	-
ACE	4	4260.19	830	2600.19	15.56	11	.16
E	2	4269.73	832	2605.73	9.54	2	.01
<i>'Describing'</i>							
Saturated	15	4524.38	824	2876.38	-	-	-
ACE	4	4533.24	835	2863.24	8.86	11	.63
E	2	4544.54	837	2870.54	11.30	2	< .01
<i>'Nonjudging of inner experience'</i>							
Saturated	15	4503.57	820	2869.86	-	-	-
ACE	4	4522.29	831	2860.29	18.72	11	.07
E	2	4526.87	833	2860.87	4.58	2	.10
<i>Insomnia symptoms</i>							
Saturated	15	5033.03	819	3395.03	-	-	-
ACE	4	5041.81	830	3381.81	8.78	11	.64
E	2	5059.69	832	3395.69	17.88	2	< .01
<i>Depression symptoms</i>							
Saturated	15	724.47	829	-933.53	-	-	-
ACE	4	736.00	840	-944.00	11.53	11	.40
E	2	752.27	842	-931.73	16.27	2	< .01
<i>Anxiety symptoms</i>							
Saturated	15	6632.89	820	4992.89	-	-	-
ACE	4	6653.79	831	4991.79	20.89	11	.03
E	2	6682.30	833	5016.30	28.51	2	< .01

Note: All analyses focus on transformed variables, regressed out age and sex. ep = estimated parameters; -2LL = $-2 \times (\log \text{likelihood})$; df = degrees of freedom; $\Delta\chi^2$ and Δdf = change in chi-square statistic and corresponding degrees of freedom (computed as the difference in likelihood and df between each model and the saturated model); AIC = Akaike's Information Criterion statistic (calculated as $\chi^2 - 2df$). The fit of the ACE model is relative to saturated model, the fit of the E model relative to ACE model.

The estimates of genetic (A), shared environmental (C) and non-shared environmental influence (E), with 95% confidence intervals, are presented in **Table 3.7**. Full ACE models are presented for the univariate analyses throughout. Overall mindfulness was mainly influenced by E (.72; 95% CI = .06 - .88). When A and C were both dropped from the model, it led to a significant decline in fit ($\chi^2 = 6181.56$, $df = 831$, $p < .01$, $AIC = 4519.56$), suggesting that familial influences also play a role in the aetiology of mindfulness. For the subscales, non-shared environment appeared to be most important and familiarity was indicated for the subscales ‘acting with awareness’ and ‘describing’ but not for ‘observing’ and ‘nonjudging of inner experience’. Similarly, non-shared environmental influence was key for symptoms of insomnia, depression and anxiety, which were all found to also show familiarity.

Table 3.7 Estimates for A, C and E for the univariate genetic model fitting analyses

Variable	Parameter Estimates		
	A (CI)	C (CI)	E (CI)
Overall mindfulness	.17 (0 - .45)	.11 (0 - .32)	.72 (.06 - .88)
‘Nonreactivity’	0 (0 - .28)	.13 (0 - .24)	.87 (.72 - .98)
‘Observing’	.16 (0 - .31)	0 (0 - .16)	.84 (.69 - 1)
‘Acting with awareness’	.09 (0 - .40)	.12 (0 - .28)	.79 (.60 - .93)
‘Describing’	.28 (.06 - .42)	0 (0 - .13)	.72 (.58 - .88)
‘Nonjudging’	.18 (0 - .33)	0 (0 - .21)	.82 (.67 - .99)
Insomnia symptoms	.36 (0 - .50)	0 (0 - .30)	.64 (.50 - .84)
Depression symptoms	.33 (.01 - .48)	0 (0 - .20)	.67 (.52 - .83)
Anxiety symptoms	.36 (0 - .53)	.04 (0 - .33)	.60 (.47 - .77)

Note: All analyses focus on transformed variables, regressed out age and sex. A = additive genetic, C = shared environmental; E = non-shared environmental. The 95% confidence intervals are presented in brackets.

3.3.4 Multivariate model fitting

Fit statistics for multivariate analyses are presented in **Table 3.8**. The fit of the correlated factors solution ($\chi^2 = 17616.00$, $df = 3312$, $p = .07$, $AIC = 10992.00$) and the independent pathway model ($\chi^2 = 17623.34$, $df = 3318$, $p = .06$, $AIC = 10987.34$) were similar, while the common pathway model had a significantly worse fit ($\chi^2 = 17650.15$, $df = 3324$, $p < .01$, $AIC = 11002.15$). The independent pathway model had a slightly better fit (lower AIC) and was more parsimonious. Therefore, results from the independent pathway model are presented, see **Figure 3.1**. Given the similar fit of the correlated factors solution, this has been presented additionally in **Appendix D**.

Table 3.8 Fit statistics for the multivariate genetic model fitting analyses

	ep	-2LL	df	AIC	Δ -2LL	Δ df	p
<i>Model: Overall mindfulness, symptoms of insomnia, depression and anxiety</i>							
Saturated	132	17496.51	3214	11068.51	-	-	-
ACE Correlated Factors Solution	34	17616.00	3312	10992.00	119.49	98	.07
ACE Independent Pathway	28	17623.34	3318	10987.34	126.84	104	.06
ACE Common Pathway	23	17650.15	3324	11002.15	153.64	110	< .01

Note: All analyses focus on transformed variables, regressing out age and sex. ep = estimated parameters; -2LL = $-2 * (\log \text{likelihood})$; df = degrees of freedom; $\Delta\chi^2$ = change in chi-square statistic; Δdf = change in degrees of freedom; AIC = Akaike's Information Criterion statistic; Saturated = full model, A = additive genetic, C = shared environmental; E = non-shared environmental. The fit statistics of the ACE correlated factors model, the ACE independent pathway model and the ACE common pathway model are relative to the saturated model. *Model - Phenotypes: overall mindfulness (reverse coded, FFMQ), insomnia symptoms (ISQ), symptoms of depression (MFQ), anxiety (RCADS)*

From **Figure 3.1** (please see figure on the next pages), we can see that overall mindfulness had no significant common genetic or shared environmental influence, only common non-shared environmental influence with symptoms of insomnia, depression

and anxiety. It was also influenced by specific non-shared environment. Insomnia symptoms had a significant common genetic influence with depression symptoms and a non-significant common influence with anxiety symptoms and significant common non-shared environmental influence with symptoms of depression and anxiety. It was also influenced by specific non-shared environment and there was some non-significant shared-environmental influence indicated. Depression symptoms had only non-significant common genetic and shared environmental influence, but significant common non-shared environmental influence with anxiety symptoms. Furthermore, significant specific non-shared environmental influence and some non-significant specific genetic and specific shared-environmental influence was found for anxiety symptoms.

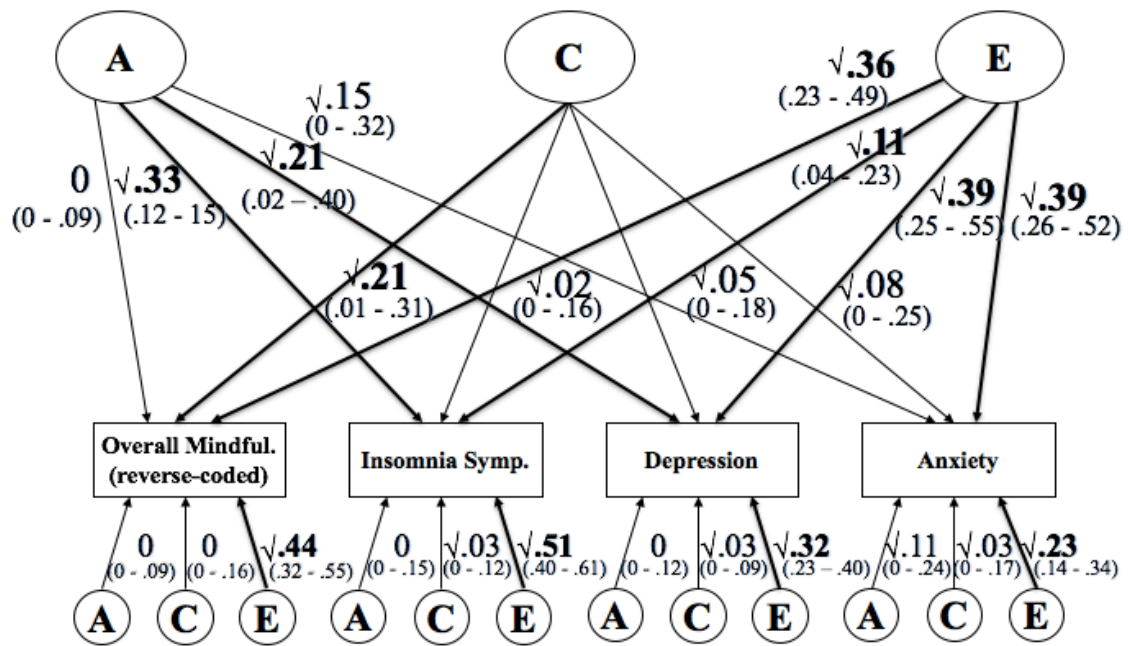


Figure 3.1 Path diagram of the independent pathway model, including overall mindfulness, symptoms of insomnia, depression and anxiety

Note: Significant paths and estimates are presented in bold, see brackets for 95% confidence intervals. A = additive genetic; C = shared environmental; E = non-shared environmental; Overall Mindful. = overall score of mindfulness (FFMQ), reverse coded, higher score indicating lower mindfulness; Insomnia Symptom = insomnia symptoms (ISQ), higher scores indicating more insomnia symptoms; Depression Symptoms = symptoms of depression (MFQ), higher scores indicating more symptoms of depression; Anxiety Symptoms = symptoms of anxiety (RCADS), higher scores indicating more symptoms of anxiety

3.4 Discussion

The rationale of this study was to gain a better understanding of the concept and the aetiology insomnia, by considering the roots of mindfulness (its subscales) and its associations with insomnia symptoms from a behavioural genetics perspective. To achieve this, the association between mindfulness (its subscales) and symptoms of insomnia, depression and anxiety were considered phenotypically. In addition, the genetic and environmental influences on mindfulness (its subscales) and symptoms of insomnia, depression and anxiety were estimated. Furthermore, the genetic and environmental influences on the association between these four variables were estimated.

3.4.1 Associations between variables

Lower mindfulness was associated with greater symptoms of insomnia, depression and anxiety. This is in line with research by Waszczuk and colleagues (2015) – although the magnitude of the associations reported here were slightly higher than those in the aforementioned study (which focused on slightly different phenotypes).

Of the mindfulness subscales, ‘nonjudging of inner experience’ had the strongest association with symptoms of insomnia, depression and anxiety (although the associations with ‘acting with awareness’ were of a similar magnitude for the association with insomnia symptoms). These findings are in line with previous research that focused on the subscales of mindfulness and sleep quality (Caldwell et al., 2010), depression and anxiety symptoms, which found that four of the five subscales of mindfulness (‘nonreactivity to inner experience’, ‘describing’, ‘acting with awareness’ and ‘nonjudging of inner experience’, but not ‘observing’) were found to be associated with sleep quality – with greater mindfulness related to better sleep quality (Cash & Whittingham, 2010). Baer and colleagues (2006) also found that of the five subscales ‘nonjudging of inner experience’ had the highest (negative) correlation and ‘act with awareness’ had the second highest correlation with psychological symptoms. The current phenotypic analysis also showed that ‘observing’ was not associated with insomnia symptoms, which is in line with a study that focused on mindfulness and sleep quality (Caldwell et al., 2010). ‘Observing’ was further found to have a small non-significant negative association with depression and a small significant association with anxiety. Interestingly, when evaluating the FFMQ, Baer and colleagues (2006) have previously pointed out that, when considering the association between the mindfulness subscales and other constructs, ‘observing’ was the only subscale that showed

correlations in an unexpected direction. A possible explanation for this was that the items of the ‘observing’ subscale may not adequately capture this aspect of mindfulness (Baer et al., 2006). Furthermore, Cash and Whittingham (2010) found that the observing subscale did not predict depression, anxiety and stress symptoms, while ‘non-judging of inner experience’ did.

While none of the subscales appeared to drive the association between overall mindfulness and symptoms of insomnia, depression and anxiety, it may be worth further investigating the trends generated here. Indeed, finding that certain subscales are more strongly associated with symptoms of insomnia, depression and anxiety than others could potentially be useful for generating ideas for improving mindfulness-based treatment. For example, treatment could specifically focus on the importance of certain skills (such as the ability to avoid judgement about inner experiences such as thoughts and feelings).

3.4.2 Familial influences

In this study, it was found that overall mindfulness as well as the subscales ‘acting with awareness’ and ‘describing’ (in addition to symptoms of insomnia, depression and anxiety) were familial. This means that some influence had come from factors common to family members (i.e., genetic and/or common environmental influences) - it was not possible to detangle these two influences, due to the small sample size. It was important to investigate the genetic and environmental influences on mindfulness and its subscales as this gives us insight in the aetiology of these traits, which are central in the development of insomnia, according to the meta-cognitive model of insomnia (Ong et al., 2013). The findings reported here are largely consistent with the only previous twin study which found genetic influence on the attentional aspect of mindfulness (Waszczuk et al., 2015). Therefore, the result that ‘acting with

awareness' was indicated to be familial also fits in well with the previous findings on attentional mindfulness. The discrepancy in the magnitude of parameter estimates between studies (for example, there was greater genetic influence and no shared environmental influence in the previous study) may arise from having used a different measure and conceptualisation of mindfulness. Here, the focus was on mindfulness including attentional as well as emotional/interpretational aspects. Furthermore, the subscales of mindfulness were included as well, whereas the other report focused exclusively on the attentional aspects of mindfulness and only used a shortened version of the measure Mindfulness Attention and Awareness Scale (5 items only), giving a rather limited insight into the concept of mindfulness (Waszczuk et al., 2015; Bergomi et al., 2013). Furthermore, heritability is a population statistic, which means that estimates may vary in different samples and, while the current study focused on adults, the previous study analysed data from adolescents. Sleep, sleep disturbances and the prevalence of insomnia vary across the different ages (Roth et al., 2011; Roth & Roehrs, 2003). Young adulthood is an interesting age to consider in the context with sleep because it is a time after the adaption of the circadian rhythm has happened (i.e. during adolescence) and the interaction between sleep homeostasis and the circadian system is in balance again, which means returning to a 'normal' sleep pattern (Crowley, 2016). Young adulthood is also the time of life when sleep duration is usually considered to be normal, whereas we speak of extended amount of sleep required during childhood and reduced amount of sleep required during late adulthood (Crowley, 2016).

No common genetic influences for overall mindfulness and insomnia, depression and anxiety symptoms was found. It was important to investigate the genetic and environmental influences on these traits as this gives us deeper insight in the structure of the association suggested by the meta-cognitive model of insomnia and

helps us understand the mechanism underlying the association of this key element with insomnia symptoms.

The current findings differ from the findings by Waszczuk et al. (2015) which highlighted a moderate genetic overlap for mindfulness with anxiety sensitivity and depression. However, it would have been difficult to find common genetic influences for overall mindfulness and insomnia, depression and anxiety symptoms in the current sample as the genetic influence on overall mindfulness was not significant here. In addition to the explanations provided above, it is important to note that measures also differed for depression and that the previous study focused on anxiety sensitivity (while the current study focused on anxiety).

Although it was not the focus of this study, a common genetic influence for symptoms of insomnia, depression and anxiety (not significant) was found which is consistent with our previous work using G1219 data on this and similar topics (see for example, Gregory et al., 2006; Gregory, et al., 2011; Gregory et al., 2016). According to the “generalist genes hypothesis”, we would expect that mindfulness, symptoms of insomnia, depression and anxiety share common genetic influences as co-variation between traits is often explained by additive genetic influences – with environmental influences explaining differences (Eley, 1997). The findings indicate that mindfulness may not be part of the same genetic cluster which is influencing symptoms of insomnia, depression and anxiety.

3.4.3 Non-shared environmental influences - Future directions

Despite some evidence of familiarity for mindfulness and associations with insomnia, depression and anxiety, the largest influence was that of the non-shared environment. Future research should attempt to specify non-shared environmental factors that play a role for mindfulness. While meditation experience is an obvious

candidate, with more meditation experience associated with greater mindfulness (see for example Walach et al., 2006; Baer et al., 2006) – this was controlled for in the current study by running a sensitivity analysis, so cannot explain the results reported here. Other candidates include certain life events, cultural influence and peer relationships (Waszczuk et al., 2015).

3.4.4 Limitations

The current study has some limitations which include the use of self-report measures, non-clinical data and the sample size. For a more detailed discussion of these limitations, see **Chapter 8: Discussion, 8.4 General limitations**.

It should be pointed out that self-report measure is considered to be the optimal approach to assessing mindfulness and insomnia symptoms and this was necessary given the scope of the study. Nevertheless, future work should aim to incorporate additional information (for example, symptoms rated by other reporters, objective measures of sleep, etc.). Furthermore, it should be pointed out here that a shortened version of the mindfulness measure was used here (see **Chapter 3, 3.2.2 Mindfulness**). This has not been evaluated previously, but it did show a good Cronbach's alpha of .81.

There are further limitations relating to the method applied (twin design). These limitations are discussed in detail in the methods chapter (see **Chapter 2: Methods, 2.3.2 Assumptions and associated limitations**). Based on the limitations, it is recommended that estimates should be considered as approximations rather than absolute values (Plomin et al., 2013).

However, the current findings were largely in line with previous findings (for example the same subscales of mindfulness were found to be associated with insomnia as in a non-twin sample, see Caldwell et al., 2010) and when comparing twins and their

related non-twins, similar levels of symptoms of insomnia and depression were found (Kendler, Martin, Heath & Eaves, 1995).

3.4.5 Conclusion

It can be summarised that the link between mindfulness and symptoms of insomnia, depression and anxiety was confirmed. This supports the idea that mindfulness is an important element in the development and maintenance of insomnia as suggested in the meta-cognitive model (Ong et al., 2013). ‘Nonjudging of inner experience’ and ‘act with awareness’ were the mindfulness subscales most strongly (negatively) associated with symptoms of insomnia which shows us that these may be factors particularly useful to target in insomnia treatment. It further gives us a deeper insight in the meta-cognitive model of insomnia, as it dissects which facet of mindfulness is particularly relevant in the association with insomnia symptoms. Mindfulness and its subscales was not as heritable as we expected it to be, but did show familial influence. This give us insight in the roots of mindfulness and its subscales, and why individuals vary in this trait. Furthermore, it broadens our knowledge of the cognitive theories of insomnia as it sheds light on the aetiology of one of their central elements. Genetic influence was not important for explaining the association of mindfulness and symptoms of insomnia, depression and anxiety. This helps us to understand the underlying mechanisms of the development and maintenance of insomnia by illuminating how the association between mindfulness and insomnia symptoms works. The findings further suggest that overall mindfulness and insomnia symptoms may not be part of the same genetic cluster; instead this association was mainly found to be influenced by common non-shared environmental factors.

CHAPTER 4: Associations Between Pre-Sleep Arousal and Insomnia Symptoms in Early Adulthood: A Twin and Sibling Study

4.1 Introduction

The rationale behind this study is to gain insight in the aetiology of pre-sleep arousal and its subscales by considering the genetic and environmental influences on these traits, which helps us to understand why variation in these traits occur. Furthermore, it is attempted to shed light on the mechanisms involved in the development and maintenance of insomnia. This is done by considering the genetic and environmental influences on the association of pre-sleep arousal (and its subscales) with insomnia symptoms to understand how these associations work. This is inspired by the cognitive theories, which have never been investigated from a behavioural genetics perspective.

4.1.1 Pre-sleep arousal and insomnia symptoms

According to earlier literature, pre-sleep arousal plays a crucial role in insomnia. For example, Espie (2002) argued in the ‘psychobiological inhibition model of insomnia’, that the inability to de-arouse is the main problem associated with insomnia. Furthermore, Harvey (2002), in the cognitive model of insomnia, has stated that increased negative cognitive activation leads to somatic arousal, which is one of the factors that cause a distorted perception of sleep deficits during the night and distorted daytime functioning (two characteristics of insomnia). For a more detailed discussion of the role of pre-sleep arousal in cognitive theories see **1.3.2 Occurrence of the analysed traits in cognitive theories**.

That pre-sleep arousal plays a crucial role in insomnia is also supported by research findings. Cognitive and somatic arousal are often differentiated when

discussing treatment for insomnia (see, for example, Cincotta, Gehrman, Gooneratne & Baime, 2011; Schwartz & Carney, 2012). In one study, insomnia was treated by reducing cognitive arousal and, in turn, somatic arousal, which resulted in improved insomnia symptoms (Cincotta et al., 2011). It should be mentioned here that the sample size for this study was small ($N = 17$) and that no control group was included. Interestingly, whilst subjective sleep improved, no objective evidence of an improvement in sleep was found. Somatic arousal refers to physical arousal, including symptoms such as increased heart rate, while cognitive arousal relates to the psychological part including, for example, not being able to 'shut off' thoughts (Nicassio et al., 1985). It can therefore be concluded that the extent to which a person is easy or difficult to arouse seems to be an important factor in the development and maintenance of insomnia (Espie, 2007). Furthermore, cognitive and somatic aspects of pre-sleep arousal seem to differ in the role they play in insomnia (see for example Gregory, Willis, Wiggs, Harvey, & STEPS Team, 2008; Norell-Clarke et al., 2014). In addition, it was shown that it is important to target pre-sleep arousal when treating insomnia (see for example Ong et al., 2012; Ong et al., 2014). Previous research has also found that cognitive and somatic pre-sleep arousal are independent predictors of sleep disturbances (Gregory et al., 2008; Nicassio et al., 1985) and the results also indicate that cognitive pre-sleep arousal is associated to a greater extent with sleep disturbances than with somatic pre-sleep arousal. However, this previous study focused on children (not young adults) and the sleep disturbances were not formally diagnosed. Furthermore, there were some discrepancies between the sleep disturbances reported by the parents compared to the sleep disturbances reported by the children (Gregory et al., 2008).

4.1.2 Heritability of pre-sleep arousal

The genetic and environmental influences on overall pre-sleep arousal as well as its subscales (cognitive and somatic pre-sleep arousal) in adults are yet to be explored. Furthermore, sleep researchers have recently become interested in why certain risks are associated with insomnia. For example, research has shown that insomnia symptoms and sleep reactivity (as measured by the Ford Insomnia Response to Stress; Drake et al., 2004) share some genetic influences (Drake et al., 2011). Sleep reactivity describes the extent to which sleep disruption is caused by various challenges (for example, an important meeting the next day) and is distinct from pre-sleep arousal. Here, we are dealing with the arousal itself, measuring two sub-scales – somatic and cognitive arousal, which gives us a more detailed conceptualisation of arousal (Nicassio et al., 1985). To gain a better understanding of the aetiology of insomnia and to better understand why pre-sleep arousal (respectively the cognitive and somatic aspects of pre-sleep arousal) is associated with insomnia symptoms, it would be useful to explore the genetic and environmental influences on pre-sleep arousal and insomnia symptoms.

4.1.3 Aims of the current study

No previous study has yet considered the genetic and environmental influences on pre-sleep arousal (and its subscales) and its association with insomnia symptoms. As research in this area is very limited, aims were formulated rather than hypotheses:

- 1) Consider the magnitude of the associations between overall pre-sleep arousal, its cognitive and somatic arousal subscales and insomnia symptoms. In line with previous work, we expect insomnia symptoms to be associated more strongly with *cognitive* rather than *somatic* pre-sleep arousal.

- 2) Estimate the relative contribution of genetic and environmental influences on the variance of: a) overall pre-sleep arousal b) cognitive pre-sleep arousal c) somatic pre-sleep arousal and d) insomnia symptoms.
- 3) Estimate genetic and environmental influences on the associations between overall pre-sleep arousal and insomnia symptoms and cognitive pre-sleep arousal, somatic pre-sleep arousal and insomnia symptoms.

4.2 Method

4.2.1 *Sample*

Data from Wave 5 of the Genesis 12-19 (G1219) longitudinal twin/sibling study was the focus of this study as this is the only wave by which pre-sleep arousal has been measured. Wave 5 included data from 223 monozygotic (MZ) twins, 404 dizygotic (DZ) twins and 218 siblings (Denis et al., 2015). The participants were aged between 22 and 32 years (mean age 25 years) and 34.3% of them were male (Denis et al., 2015). For a more detailed description of the sample, see **Chapter 2: Methods, 2.4 The G1219 sample**.

4.2.2 *Pre-sleep arousal*

Pre-sleep arousal was measured using the pre-sleep arousal scale (PSAS, Nicassio et al., 1985). Each item was coded from 1 ('not at all') to 5 ('extremely'), based on the participants' responses. For the somatic arousal subscale, items 1 to 8 were added, and the scores have a theoretical range from 8 to 40 (actual range 8 to 33 in the current sample). The cognitive pre-sleep arousal subscale was calculated by summing the responses for items 9 to 16, and the scores have a theoretical range from 8 to 40 (actual range 8 to 40 in the current sample). The total score is the sum of all responses, theoretical range from 16 to 80 (actual range 16 to 69 in this sample), with higher scores

indicating more overall pre-sleep arousal. The Cronbach's alpha in the current sample was .78 for somatic arousal, .91 for cognitive pre-sleep arousal and .91 for the overall score. See **Appendix E** for a list of items included in the PSAS.

4.2.3 Insomnia symptoms

Insomnia symptoms were measured by the Insomnia Symptoms Questionnaire (ISQ, Okun et al., 2009), using a 6-item version. The total scale score is the sum of these responses, ranging from 0 to 24, with higher scores meaning more severe insomnia symptoms. For a more detailed explanation of the insomnia symptoms measure, see **Chapter 3, 3.2.3 Insomnia symptoms**.

4.3 Analysis

4.3.1 Data preparation

The data was prepared (see **2.4.4 Data preparation** for more details). The variable somatic pre-sleep arousal was skewed (skewness = 1.82, std. error = .08; kurtosis = 4.16, std. error = .17) and therefore it was log10-transformed, which successfully reduced the skewness (skewness = 1.03, std. error = .08; kurtosis = .63, std. error = .17).

4.3.2 Preliminary analyses

SPSS (IBM, 2013; version 22) was used for a preliminary analysis which included descriptive and inferential statistics. Pearson's correlations for overall pre-sleep arousal, the cognitive and somatic pre-sleep arousal subscales and insomnia symptoms were also considered (phenotypic correlations), focusing on twin 1 only to control for non-independence of observations. This was helpful to get a first idea of the role each variable plays in association with insomnia symptoms.

4.3.3 Regression analyses

A regression analysis was run (controlling for non-independence of observations) in Stata (StataCorp, 2015; version SE 14.0) to examine whether or not cognitive and somatic arousal are independent predictors of insomnia symptoms, as was found in previous research (see Gregory et al., 2008; Nicassio et al., 1985). It was further considered whether or not cognitive pre-sleep arousal was associated to a greater extent with sleep disturbances rather than with somatic pre-sleep arousal. The covariates age and sex were added to the regression models.

4.3.4 Twin/sibling analyses

Twin and sibling correlations (within traits) as well as cross-twin-cross-trait correlations, were considered. This allowed a rough estimation of the relative contributions of genetic and environmental influences on pre-sleep arousal (and its cognitive and somatic arousal subscales) and insomnia symptoms.

A univariate analysis was run for each variable (using OpenMX version 1, R version 3.0.3; Boker et al., 2011), applying maximum-likelihood model fitting analysis to estimate the relative contribution of genetic, shared and non-shared environmental influence (Neale & Cardon, 2013). For a detailed explanation of univariate analysis, see **Chapter 2: Methods, 2.3.2 Univariate Analysis.**

A bivariate analysis was run to consider the association between overall pre-sleep arousal and insomnia symptoms. A trivariate analysis was used to consider genetic and environmental factors in the association between cognitive pre-sleep arousal, somatic pre-sleep arousal and insomnia symptoms. To examine the extent to which genetic and environmental factors explain the association between cognitive pre-sleep arousal, somatic pre-sleep arousal and insomnia symptoms, the correlated factors solution was selected as an appropriate model (for a detailed explanation of the model

see **Chapter 2: Methods, 2.3.5.1 The correlated factor model**). The independent pathway model and common pathway model were also run and compared in fit (for a detailed explanation of the models see **Chapter 2: Methods, 2.3.5.2 The independent pathway model and 2.3.5.3 The common pathway model**). The best fitting model(s) will be presented. For a detailed explanation of multivariate analysis, see **Chapter 2: Methods, 2.3.5 Multivariate analysis**.

4.4 Results

4.4.1 Descriptive statistics

Descriptive statistics for each variable are summarised in **Table 4.1** (see table overleaf). For overall pre-sleep arousal, significant sex differences were found ($t(651) = -2.42, p = .02, d = .17$), males reported less overall pre-sleep arousal than females. For somatic pre-sleep arousal, significant sex differences were found ($t(655) = -3.33, p < .01, d = .23$), males reported less somatic pre-sleep arousal than females. For insomnia symptoms, significant sex differences were found as well ($t(625) = -3.28, p < .01, d = .25$), males reported fewer insomnia symptoms than females.

Table 4.1 Means (SD) of raw scores for overall pre-sleep arousal, cognitive arousal, somatic pre-sleep arousal and symptoms of insomnia

	Means (SD)		
	Total	Males	Females
Overall pre-sleep arousal	28.39 (9.64)	27.32 (8.96)*	28.94 (9.94)*
Cognitive pre-sleep arousal	17.09 (6.76)	16.60 (6.32)	17.34 (6.98)
Somatic pre-sleep arousal	11.30 (3.84)	10.72 (3.54)*	11.60 (3.96)*
Insomnia symptoms	6.48 (5.22)	5.65 (4.89)*	6.92 (5.33)*
	MZ	DZ	Siblings
Overall pre-sleep arousal	28.29 (9.08)	28.78 (10.42)	27.98 (8.91)
Cognitive pre-sleep arousal	16.96 (6.42)	17.31 (7.28)	16.97 (6.25)
Somatic pre-sleep arousal	11.33 (3.70)	11.47 (4.05)	11.01 (3.67)
Insomnia symptoms	6.09 (4.97)	6.68 (5.38)	6.61 (5.19)

Note: * sex differences were found. Means and SD were obtained from SPSS and are based on the raw data (untransformed, including outliers, etc.); MZ = monozygotic twin; DZ = dizygotic twins; siblings = non-twin sibling pairs; Overall pre-sleep arousal = overall pre-sleep arousal (PSAS), higher score indicating higher overall pre-sleep arousal; Cognitive pre-sleep arousal = cognitive pre-sleep arousal (PSAS subscale), higher score indicating higher cognitive pre-sleep arousal; Somatic pre-sleep arousal = somatic pre-sleep arousal (PSAS subscale), higher score indicating higher somatic pre-sleep arousal; Insomnia symptoms = insomnia symptoms (ISQ), higher scores indicating more insomnia symptoms

4.4.2 Phenotypic correlations

The phenotypic correlations for all variables are displayed in **Table 4.2** (please see table overleaf). Higher overall pre-sleep arousal was associated with more insomnia symptoms ($r = .61, p < .01$). Higher cognitive pre-sleep arousal and higher somatic pre-sleep arousal was also associated with more insomnia symptoms ($r = .62, p < .01$ $r = .44, p < .01$). Cognitive and somatic pre-sleep arousal were also found to be highly correlated ($r = .60, p < .01$). The correlation between cognitive pre-sleep arousal and insomnia symptoms was significantly larger than the correlation between somatic pre-

sleep arousal and insomnia symptoms ($p < .01$; see Steiger, 1980 for the calculation that was performed to compare the magnitude of the correlations). These associations were further examined in a regression analysis (see information overleaf).

Table 4.2 Phenotypic correlations for overall pre-sleep arousal, cognitive pre-sleep arousal, somatic pre-sleep arousal and symptoms of insomnia

	Overall pre-sleep arousal	Cognitive pre-sleep arousal	Somatic pre-sleep arousal	Insomnia symptoms
Overall pre-sleep arousal	1			
Cognitive pre-sleep arousal	.95**	1		
Somatic pre-sleep arousal	.81**	.60**	1	
Insomnia symptoms	.61**	.62**	.44**	1

Note: * $p < .05$; ** $p < .01$. Correlations were calculated on age and sex regressed variables, and after outliers (± 3 SD away from the mean) and data was transformed if necessary, using twin 1 only to control for non-independence of observations. Overall pre-sleep arousal = overall pre-sleep arousal (PSAS), higher score indicating higher overall pre-sleep arousal; Cognitive pre-sleep arousal = cognitive pre-sleep arousal (PSAS subscale), higher score indicating higher cognitive pre-sleep arousal; Somatic pre-sleep arousal = somatic pre-sleep arousal (PSAS subscale), higher score indicating higher somatic pre-sleep arousal; Insomnia Symptoms = insomnia symptoms (ISQ), higher scores indicating more insomnia symptoms.

4.4.3 MZ, DZ and sibling correlations

The MZ, DZ and sibling within-trait and cross-trait-cross-twin correlations for all variables are presented in **Table 4.3** (please refer to table overleaf). The MZ correlations for all variables were greater (although not significantly as indicated by overlapping confidence intervals) than the DZ correlations, indicating possible genetic influence. The MZ correlations are substantially less than 1 for all of the traits, which highlights the importance of non-shared environmental influence (E; including error).

Table 4.3 Twin/sibling correlations for overall pre-sleep arousal, cognitive arousal, somatic pre-sleep arousal and insomnia symptoms

	Correlations		
	MZ	DZ	Sibling
<i>Within-trait</i>			
Overall pre-sleep arousal	.42 (.24 - .57)	.26 (.10 - .40)	.13 (-.10 - .34)
Cognitive pre-sleep arousal	.30 (.10 - .47)	.25 (.09 - .39)	.11 (-.11 - .33)
Somatic pre-sleep arousal	.44 (.28 - .58)	.20 (.03 - .35)	.11 (-.12 - .32)
Insomnia symptoms	.37 (.19 - .53)	.21 (.05 - .36)	.12 (-.13 - .34)
<i>Cross-traits-cross-twins</i>			
Cogn. pre-sleep arousal - Som. pre-sleep arousal	.41 (.27 - .52)	.09 (-.03 - .21)	.13 (-.12 - .32)
Cogn. pre-sleep arousal - Insomnia symptoms	.33 (.18 - .46)	.18 (.05 - .29)	.19 (-.04 - .38)
Som. pre-sleep arousal - Insomnia symptoms	.38 (.26 - .48)	.08 (-.05 - .20)	.09 (-.12 - .28)

Note: The 95% confidence intervals are presented in brackets. MZ = monozygotic twins; DZ = dizygotic twins; Sibling = sibling pairs; Overall pre-sleep arousal = overall pre-sleep arousal (PSAS), higher score indicating higher overall pre-sleep arousal; Cogn. pre-sleep arousal = cognitive pre-sleep arousal (PSAS subscale), higher score indicating higher cognitive pre-sleep arousal; Som. pre-sleep arousal = somatic pre-sleep arousal (PSAS subscale), higher score indicating higher somatic pre-sleep arousal; Insomnia symptoms = insomnia symptoms (ISQ), higher scores indicating more insomnia symptoms.

4.4.4 Regression analyses

In the stepwise regression, the overall model was significant $F(2,546) = 141.46$, $p < .01$, and predicted 38% (adjusted R squared = .38) of the variance of insomnia symptoms. Sex was a significant factor ($B(SE) = .77(.30)$; $\beta = .07$; $t = 2.59$; $p = .01$), whilst age was non-significant ($B(SE) = .10(.08)$; $\beta = .04$; $t = 1.27$; $p = .21$). Both cognitive ($B(SE) = .39(.03)$; $\beta = .50$; $t = 14.46$; $p < .01$) and somatic pre-sleep arousal

($B(SE) = .68(.17)$; $\beta = .14$; $t = 3.97$; $p < .01$) were significant predictors for insomnia symptoms.

4.4.5 Twin/sibling analyses

The fit statistics of the univariate models are presented in **Table 4.4** and the results (estimates for A, C and E with 95% confidence intervals) are shown in **Table 4.5** (please refer to tables on the next pages). For somatic pre-sleep arousal, the difference between the MZ correlations and the DZ was substantial (somatic pre-sleep arousal: $r_{MZ} = .44$, $r_{DZ} = .20$). This suggests possible non-additive genetic effects, namely dominance (D). Therefore, the ADE model was also tested for this variable, but D was not significant in the model (95% confidence interval overlapping 0). Therefore, the ADE model has not been presented. Overall pre-sleep arousal and somatic pre-sleep arousal showed significant genetic influence (overall pre-sleep arousal: $A = .47$, 95% confidence interval = $.19 - .60$; somatic pre-sleep arousal: $A = .49$, 95% confidence interval = $.24 - .61$), no shared environmental influence, but non-shared environmental influence (overall pre-sleep arousal: $E = .53$, 95% confidence interval = $.40 - .70$; somatic pre-sleep arousal: $E = .51$, 95% confidence interval = $.39 - .67$). When the ACE model and the E model were compared for these variables, the fit declined significantly in both cases ($\chi^2 = 6054.39$, $df = 834$, $p < .01$, $AIC = 43836.39$ for overall pre-sleep arousal and $\chi^2 = 2536.12$, $df = 835$, $p < .01$, $AIC = 866.12$ for somatic pre-sleep arousal), indicating familial influence, once again confirming the results. For cognitive pre-sleep arousal and insomnia symptoms, non-shared environment appeared to be most important (cognitive pre-sleep arousal: $E = .74$, 95% confidence interval = $.56 - .90$; insomnia symptoms: $E = .61$, 95% confidence interval = $.47 - .80$) and familiarity was indicated in both cases as the fit of E model declined significantly when compared to

the ACE model ($\chi^2 = 5559.70$, $df = 838$, $p < .01$, $AIC = 3883.70$ for cognitive pre-sleep arousal and $\chi^2 = 5135.58$, $df = 837$, $p < .01$, $AIC = 3461.58$ for insomnia symptoms).

Table 4.4 Fit statistics of all univariate genetic model fitting analyses

<i>Variable/</i>	ep	-2LL	df	AIC	Δ -2LL	Δ df	<i>p</i>
<i>Model</i>							
<i>Overall pre-sleep arousal</i>							
Saturated	15	6006.78	821	4364.78	-	-	-
ACE	4	6028.64	832	4364.64	21.85	11	.03
E	2	6054.39	834	4386.39	25.75	2	< .01
<i>Cognitive pre-sleep arousal</i>							
Saturated	15	5529.05	825	3879.05	-	-	-
ACE	4	5547.11	836	3875.13	18.08	11	.08
E	2	5559.70	838	3883.70	12.57	2	< .01
<i>Somatic pre-sleep arousal</i>							
Saturated	15	2497.20	822	853.20	-	-	-
ACE	4	2505.77	833	839.77	8.56	11	.66
E	2	2536.12	835	866.12	30.35	2	< .01
<i>Insomnia Symptoms</i>							
Saturated	15	5096.90	824	3448.90	-	-	-
ACE	4	5112.43	835	3442.43	15.53	11	.16
E	2	5135.58	837	3461.58	23.15	2	< .01

Note: All analyses focus on the transformed data, outliers deleted with age and sex regressed out. ep = estimated parameters; -2LL = -2*(log likelihood); df = degrees of freedom; $\Delta\chi^2$ = change in chi-square statistic; Δdf = change in degrees of freedom; AIC = Akaike's Information Criterion statistic; Saturated = full model, A = additive genetic, C = shared environmental; E = non-shared environmental. The fit of the ACE model is relative to saturated model, the fit of the E model relative to ACE model.

Table 4.5 Estimates for A, C and E for the univariate genetic model fitting analyses

Variable	<i>Parameter Estimates</i>		
	A (CI)	C (CI)	E (CI)
Overall pre-sleep arousal	.47 (.19 - .60)	0 (0 - .17)	.53(.40 - .70)
Cognitive pre-sleep arousal	.13 (0 - .44)	.13 (0 - .31)	.74 (.56 - .90)
Somatic pre-sleep arousal	.49 (.24 - .61)	0 (0 - .15)	.51(.39 - .67)
Insomnia Symptoms	.36 (0 - .53)	.03 (0 - .32)	.61 (.47 - .80)

Note: All analyses focus on the transformed data, outliers deleted with age and sex regressed out. A = additive genetic, C = shared environmental; E = non-shared environmental. The fit of the ACE model is relative to saturated model, the fit of the E model relative to ACE model. The 95% confidence intervals are presented in brackets.

Fit statistics for the bivariate and trivariate analyses are presented in **Table 4.6**.

Table 4.6 Fit statistics for the multivariate genetic model fitting analyses

	ep	-2LL	df	AIC	Δ -2LL	Δ df	p
<i>Model: Overall pre-sleep arousal and symptoms of insomnia</i>							
Saturated	42	10739.18	1633	7473.18	-	-	-
ACE	11	10781.59	1664	7453.59	42.41	31	0.08
<i>Model: Cognitive pre-sleep arousal, somatic pre-sleep arousal and symptoms of insomnia</i>							
Saturated	81	12357.87	2435	7487.87	-	-	-
ACE Correlated Factors Solution	21	12427.52	2495	7437.52	69.65	60	0.18
ACE Independent Pathway	21	12427.52	2495	7437.52	69.65	60	0.18
ACE Common Pathway	18	12437.32	2499	7439.32	9.80	4	0.04

Note: All analyses focus on the transformed data, outliers deleted with age and sex regressed out. ep = estimated parameters; -2LL = -2*(log likelihood); df = degrees of freedom; $\Delta\chi^2$ = change in chi-square statistic; Δdf = change in degrees of freedom; AIC = Akaike's Information Criterion statistic; Saturated = full model; A = additive genetic, C = shared environmental; E = non-shared environmental. The fit statistics of the ACE correlated factors model, the ACE independent pathway model are relative to the saturated model. The fit statistic of the ACE common pathway model is relative to the ACE model correlated factors model.

The results of the bivariate analyses including overall pre-sleep arousal and insomnia symptoms are presented in **Figure 4.1**. There was a very high, significant correlation for the genetic influences on overall pre-sleep arousal and insomnia symptoms ($r_A = .88$, 95% confidence interval = .61 - 1), a high but not significant correlation for the shared environmental factors on both traits ($r_C = 1$, 95% confidence interval = -1 - 1), and a moderate, significant overlap in the non-shared environmental influences ($r_E = .42$, 95% confidence interval = .27 - .55) for the two traits.

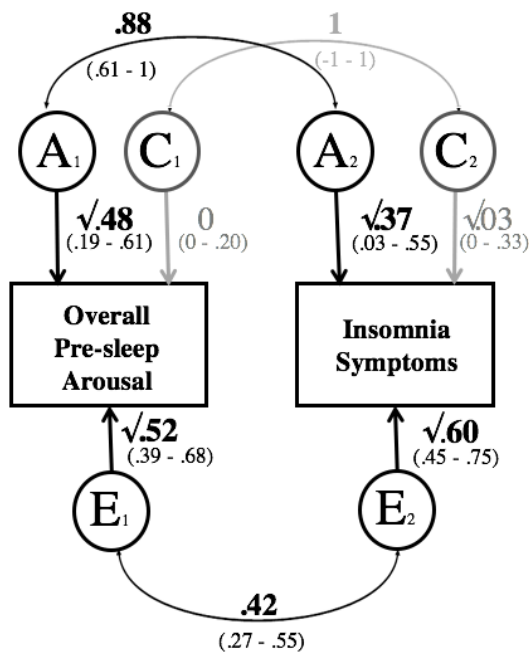


Figure 4.1 Path diagram of the bivariate analysis, including overall pre-sleep arousal and insomnia symptoms

Note: A = additive genetic, C = shared environmental; E = non-shared environmental. Significant paths are shown in black, see brackets for 95% confidence intervals. Paths with confidence intervals spanning 0 are depicted in grey. $r_{Ph} = .61$ (95%CI = .55 - .66). Overall pre-sleep arousal = overall pre-sleep arousal (PSAS), higher score indicating higher overall pre-sleep arousal; Somatic pre-sleep arousal = somatic pre-sleep arousal (PSAS subscale), higher score indicating higher somatic pre-sleep arousal; Insomnia Symptoms = insomnia symptoms (ISQ), higher scores indicating more insomnia symptoms.

For the trivariate analyses including cognitive pre-sleep arousal, somatic pre-sleep arousal and insomnia symptoms, the fit of the correlated factors solution and the independent pathway model ($\chi^2 = 12427.52$, $df = 2495$, $p = .18$, $AIC = 7437.52$) were the same. This was expected because the two models have the same number of estimated parameters. Two models can only be compared in fit if one model is nested in the other; meaning that the set of parameters of the first model is a subset of parameters of the second (nested) model (Rijsdijk and Sham, 2002). For a more detailed explanation see **Chapter 2, 2.3.5.4 Models including three measured variables**.

When comparing the common pathway model to the correlated factors model, the fit became significantly worse ($\chi^2 = 12437.32$, $df = 2499$, $p = .04$, $AIC = 7439.32$). Therefore, the correlated factor solution and the independent pathway model were the two best fitting models. As this is the first study about genetic and environmental influences on cognitive pre-sleep arousal, somatic pre-sleep arousal and insomnia symptoms, both models will be presented. The correlated factor solution is presented in the main text (see **Figure 4.2a, 4.2.b, 4.2c** and **4.3** on the following pages) and the independent pathways model is shown additionally, in the appendix (see **Appendix F, Figure F.4**).

From **Figure 4.2a**, we can see that the genetic influences on cognitive pre-sleep arousal, somatic pre-sleep arousal and insomnia symptoms were all highly and significantly correlated (ranging from .93 to 1). The shared environmental influences between the three traits were indicated to be high (1 respectively -1), but not significant (95% confidence intervals all -1 to 1) – see **Figure 4.2b**. As **Figure 4.2c** shows, the non-shared environmental influence between cognitive pre-sleep arousal, somatic pre-sleep arousal and insomnia symptoms was moderately correlated (ranging from .22 to .41).

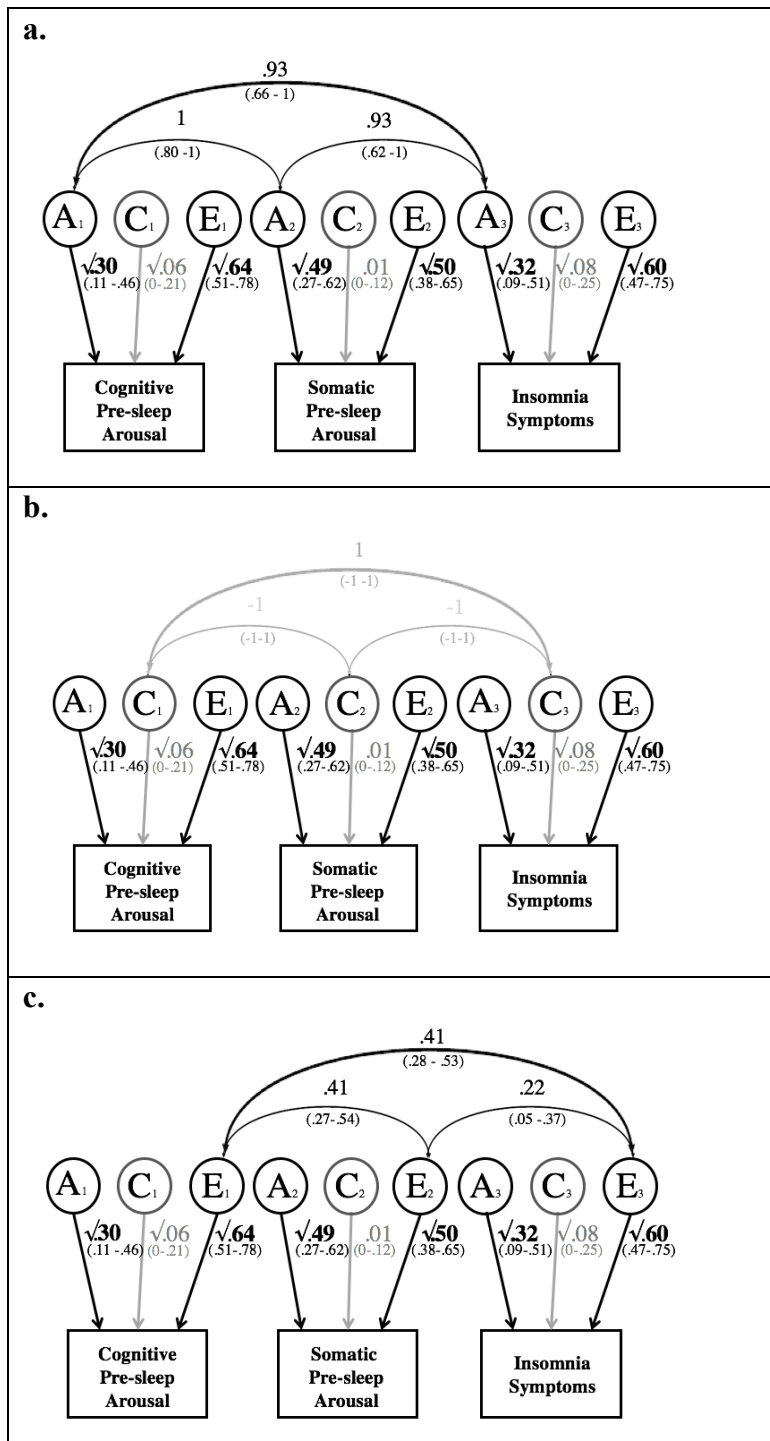
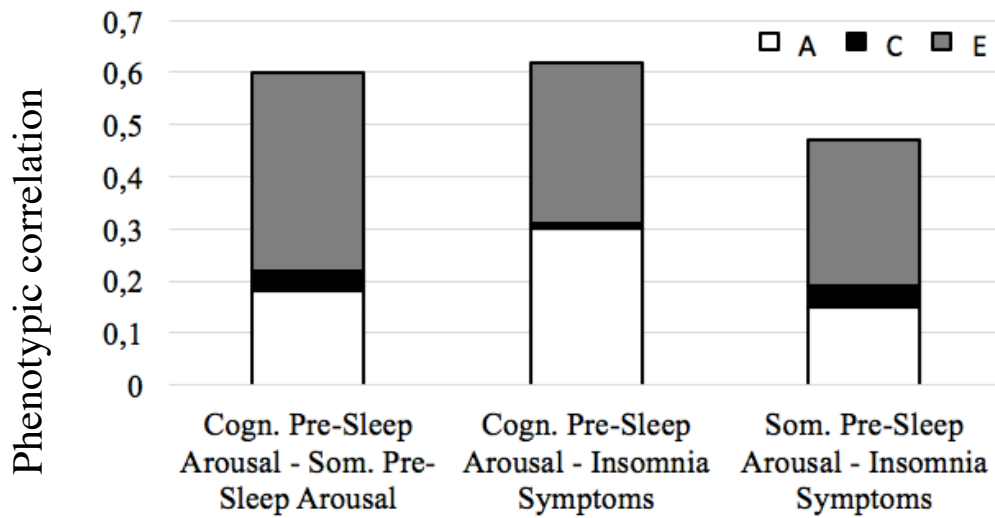


Figure 4.2 Path diagram of the correlated factors solution, including cognitive pre-sleep arousal and insomnia symptoms

Note: A = additive genetic, C = shared environmental; E = non-shared environmental. Significant paths are shown in black. Paths with confidence intervals spanning 0 are depicted in grey. Cognitive pre-sleep arousal = cognitive pre-sleep arousal (PSAS subscale), higher score indicating higher cognitive pre-sleep arousal; Somatic pre-sleep arousal = somatic pre-sleep arousal (PSAS subscale), higher score indicating higher somatic pre-sleep arousal; Insomnia Symptoms = insomnia symptoms (ISQ), higher scores indicating more insomnia symptoms; part a. shows the genetic correlations; part b. shows the shared-environmental correlations; part c. shows the non-shared environmental correlations

For an alternative illustration of the results, the relative contribution of A, C and E to the phenotypic correlations is displayed in **Figure 4.3**.



Correlations between phenotypes

Figure 4.3 Relative contributions of A, C and E to the overall phenotypic correlations

Note: A = additive genetic, C = shared environmental, E = non-shared environmental. Cogn. Pre-sleep Arousal = Cognitive Pre-Sleep Arousal (PSAS subscale), higher score indicating higher cognitive pre-sleep arousal; Som. Pre-Sleep Arousal = somatic pre-sleep arousal (PSAS subscale), higher score indicating higher somatic pre-sleep arousal; Insomnia Symptoms = insomnia symptoms (ISQ), higher scores indicating more insomnia symptoms

4.5 Discussion

The first aim of the current study was to consider the magnitude of the associations between overall pre-sleep arousal, its cognitive and somatic arousal subscales and insomnia symptoms. We examined whether and to what extent cognitive pre-sleep arousal is associated with insomnia symptoms rather than with somatic pre-sleep arousal, and whether cognitive and somatic pre-sleep arousal are independent factors for predicting insomnia symptoms. A further aim was to estimate the relative contribution of genetic and environmental influences on overall pre-sleep arousal, cognitive pre-sleep arousal, somatic pre-sleep arousal and insomnia symptoms. Furthermore, we aimed to estimate the genetic and environmental influences on the

associations between overall pre-sleep arousal and insomnia symptoms and cognitive pre-sleep arousal, somatic pre-sleep arousal and insomnia symptoms.

4.5.1 Association between variables

Pre-sleep arousal and cognitive and somatic pre-sleep arousal were found to be associated with insomnia symptoms, which is in line with the current theories of insomnia (see, for example, Espie 2002; Harvey, 2002; Spielman et al., 1987). The correlation between cognitive pre-sleep arousal and insomnia symptoms was significantly greater than that between somatic pre-sleep arousal and insomnia symptoms. The regression analysis further showed that both cognitive and somatic pre-sleep arousal were significant, independent predictors of insomnia symptoms (with cognitive arousal being a slightly stronger predictor than somatic arousal) which is in line with previous findings (Gregory et al., 2008; Nicassio et al., 1985).

4.5.2 Familial influences

This was the first study to estimate the heritability of pre-sleep arousal and its subscales. The twin analyses revealed that overall pre-sleep arousal and somatic pre-sleep arousal showed a significant and surprisingly high genetic influence and no shared environmental influence, but non-shared environmental influence. This is worth further investigation in future research.

For cognitive pre-sleep arousal and insomnia symptoms, non-shared environment appeared to be most important, and familiarity was indicated. To discover a substantial genetic influence for somatic pre-sleep arousal, but not for cognitive arousal is interesting. This gives us an insight into the concepts of somatic pre-sleep arousal and cognitive pre-sleep arousal and this helps us to gain a better understanding

of overall pre-sleep arousal, by decomposing the influences on the two subscales that make up overall pre-sleep arousal.

Furthermore, there was a very high, significant association for the genetic influences in overall pre-sleep arousal and insomnia symptoms, a high but not significant correlation for the shared environmental factors in both traits and a moderate yet significant overlap in the non-shared environmental influences for both traits. The high, but not significant estimate for the overlap in C can be explained by the small and non-significant estimates of C for each of the variables.

Having considered cognitive pre-sleep arousal, somatic pre-sleep arousal and insomnia symptoms in a trivariate analysis, high and significant genetic correlations were again found for all three traits. The shared environmental influences between the three traits were also indicated to be high but not significant (95% confidence intervals all -1 to 1), which again can be explained by the small and non-significant estimates of C for each of the variables. The non-shared environmental influence between cognitive pre-sleep arousal, somatic pre-sleep arousal and insomnia symptoms were moderately correlated. As cognitive pre-sleep arousal, somatic pre-sleep arousal and insomnia symptoms showed a high genetic correlation, the findings indicate that they may perhaps be part of the same genetic cluster (as indicated in previous research, for example, for sleep disturbances and depression disorders; Middeldorp et al., 2005). This also means that developing cognitive and/or somatic pre-sleep arousal may hint at an increased vulnerability to develop insomnia symptoms.

The high, significant association of the genetic influences on overall pre-sleep arousal (respectively cognitive and somatic pre-sleep arousal) and insomnia symptoms is also an interesting finding as this helps us to gain a better understanding of the aetiology of insomnia and the role that pre-sleep arousal plays in insomnia. The findings

are in line with current theories (see Espie, 2002; Harvey, 2002; Spielman et al., 1987) and support the idea of pre-sleep arousal being a predisposing and maintaining factor for insomnia (even though we must bear in mind that the current findings cannot establish the direction of effects). The large overlap of genetic influences between pre-sleep arousal and insomnia symptoms demonstrates again how closely linked pre-sleep arousal and insomnia are. This can help us to understand why targeting pre-sleep arousal is effective in the treatment of insomnia (see, for example, Ong et al., 2012; Ong et al., 2014).

4.5.3 Limitations

There are limitations which relate to the assumptions made by the twin design. These are discussed in detail in the methods chapter (see **Chapter 2: Methods, 2.3.1 Assumptions and associated limitations**).

Further limitations relate to the sample size and the use of self-report measures. For a more detailed discussion see **Chapter 8: Discussion, 8.4 General limitations**. Because of these limitations, further work using larger samples and including objective measures would be of value. However, there was significant genetic influence on overall pre-sleep arousal and somatic pre-sleep arousal. It should also be pointed out here that the current findings are largely in line with previous findings. For example, cognitive and somatic pre-sleep arousal were indicated to be independent factors for predicting insomnia symptoms and the magnitude of the association with insomnia symptoms was greater for cognitive as opposed to somatic pre-sleep arousal (Gregory et al., 2008; Nicassio et al., 1985). Similar estimates for the heritability of insomnia have been previously reported for the G1219 sample (Gregory et al., submitted) and in other previous findings (for example Gehrman et al., 2011, Wing et al., 2012). As heritability is a population statistic, the estimates may vary in different samples.

4.5.4 Conclusion

The current findings are novel and exciting as they help us to gain a better understanding of pre-sleep arousal, the concept of insomnia and the role that pre-sleep arousal plays in the aetiology of insomnia. Furthermore, this is a first step towards gaining a better understanding of the mechanisms underlying the link between pre-sleep arousal and insomnia symptoms, shedding light on the principles discussed in the cognitive therapies of insomnia. The results indicate that developing cognitive and/or somatic pre-sleep arousal may hint at an increased vulnerability for developing insomnia symptoms. Even though we are confident of our findings, the results need to be validated in a larger sample. Further research into the cognitive and somatic arousal within the context of insomnia would be useful as it could potentially help to prevent insomnia and improve the treatment of insomnia in the future as we gradually begin to understand the concept of insomnia in greater depth.

CHAPTER 5: Dysfunctional Beliefs about Sleep and Insomnia

Symptoms in Early Adulthood: A Twin and Sibling Study

5.1 Introduction and theoretical background

The rationale behind this study is to gain insight into the aetiology of dysfunctional beliefs about sleep and its subscales, by considering the genetic and environmental influences involved. Furthermore, it is attempted to provide a better understanding of the concept and aetiology of insomnia symptoms by illuminating the association between dysfunctional beliefs about sleep (its subscales) and insomnia symptoms from a behavioral genetics perspective to shed light on the underlying mechanisms involved in the development and maintenance of insomnia.

5.1.1 The concept of dysfunctional beliefs about sleep

Dysfunctional beliefs about sleep play a crucial role in cognitive theories of insomnia. They can be described as intrusive thoughts, excessive expectations or mistaken beliefs about sleep. For example, it would be dysfunctional to believe that we need 8 hours of sleep *every* night to be able to function the following day or to worry excessively about the possible consequences of loss of sleep (for example, that one's health will be affected by loss of sleep). Such beliefs can lead to a sleep disturbance (Espie, Inglis, Harvey, & Tessier, 2000; Harvey, 2002; Morin, Blais, & Savard, 2002).

Considering the cognitive theories can help us understand the mechanisms underlying the association between dysfunctional beliefs about sleep and insomnia and help us explain the role dysfunctional beliefs about sleep play in the treatment of insomnia. For example, Harvey (2002) stated in the cognitive model of insomnia that dysfunctional beliefs about sleep exacerbate negative cognitions (for example, excessive worry), which in turn leads to safety behaviours (for example, spending an

excessive amount of time in bed). Safety behaviours again reinforce dysfunctional beliefs about sleep and exacerbate negative cognitions. According to this theory, dysfunctional beliefs about sleep are one of the factors that maintain and exacerbate insomnia. A recent literature review has shown that there is plenty of support for the cognitive model of insomnia as proposed by Harvey (2002; Hiller et al., 2015). Various studies provide support for each factor that is claimed to play a role in maintaining insomnia, including dysfunctional beliefs about sleep (Hiller et al., 2015).

Prior to the ‘Cognitive Model of Insomnia’, the ‘3P model of insomnia’ (Spielman et al., 1987) discussed predisposing, precipitating and perpetuating factors of insomnia. This model claimed that dysfunctional beliefs about sleep are a crucial factor in maintaining insomnia. More recently, this topic has been picked up in the metacognitive model of insomnia (Ong et al., 2012) which notes that changing how we ‘think about the way we think’ may be helpful when targeting dysfunctional beliefs about sleep in the treatment of insomnia. As dysfunctional beliefs about sleep play an important role in the current theories of insomnia, their association with insomnia should be further investigated. For a more detailed discussion of the role of dysfunctional beliefs about sleep in cognitive theories, see **1.3.2 Occurrence of the analysed traits in cognitive theories.**

To enable detailed insight into the concept of dysfunctional beliefs about sleep, in addition to focusing on a global score for dysfunctional beliefs, the current study will focus on three subscales. Firstly, beliefs about the immediate negative consequences of insomnia (referred to as *beliefs about immediate consequences* from here on). For example, that we need 8 hours of sleep in order to function the next day. Secondly, beliefs about the long-term negative consequences of insomnia (referred to as *beliefs about long-term consequences* from here on), including beliefs like chronic insomnia

having serious consequences for our physical health. Thirdly, beliefs about the need for control over insomnia (referred to as *beliefs about control* from here on). For example, when having trouble falling asleep, that it is important to stay in bed and try harder (Espie, et al., 2000; Morin et al., 1993). The use of the subscales has previously been found to be a fruitful line of enquiry. For example, one study compared ‘good sleepers’, ‘normal sleepers’, ‘poor sleepers’ and participants with insomnia in terms of different aspects of dysfunctional beliefs about sleep. It was found that all four groups differed significantly in their *beliefs about long-term consequences* (Espie, et al., 2000). Interestingly, there were no significant differences between ‘good sleepers’ and ‘normal sleepers’ or ‘poor sleepers’ and participants with insomnia in terms of their *beliefs about immediate consequences*. Since there is limited research on the different aspects of dysfunctional beliefs about sleep, it is important to examine the role they play in the association with insomnia symptoms in more detail.

5.1.2 *The association of dysfunctional beliefs about sleep and insomnia*

Previous research has shown that dysfunctional beliefs about sleep and insomnia are associated. For example, when considering factors involved in developing and maintaining insomnia in a clinical sample and a healthy control group, insomnia was best predicted by dysfunctional beliefs about sleep and sleep quality (Palagini et al., 2015). In a long-term, follow up study (over 6 years) which used a clinical sample, dysfunctional beliefs about sleep (as well as stress related sleep vulnerability) were found to be a good predictor of insomnia (Yang, Hung, & Lee, 2014). In line with previous research (see, for example, Carney et al., 2010), dysfunctional beliefs about sleep and sleep reactivity were found to be significantly higher in those participants with insomnia, compared to the good sleepers (Palagini et al., 2015). Sleep reactivity refers to the idea of how prone someone is to experiencing sleep disturbances as a

consequence of stress. This means the higher the sleep reactivity, the easier it is for that person's sleep to be disturbed. Sleep reactivity was further found to be predicted by dysfunctional beliefs about sleep in the insomnia group. However, it can be criticised that because of the cross-sectional design of the study, the direction of effects could not be established and the relationships between dysfunctional beliefs about sleep, sleep reactivity and insomnia may be complex, rather than going in just one direction only (Palagini et al., 2015). Previous research has shown that dysfunctional beliefs about sleep and insomnia are associated but the mechanisms underlying this association are complex. This is worth to further investigate.

5.1.3 The role of dysfunctional beliefs about sleep in the treatment of insomnia

The crucial role that dysfunctional beliefs about sleep play in insomnia is underlined in research that considers the treatment of insomnia. A meta-analysis of randomised controlled studies has shown that cognitive-behavioural therapy is effective in treating insomnia (Okajima et al., 2011). However, this meta-analysis can be criticised for not differentiating between CBT-I delivered as group-therapy or on a one-on-one basis. Furthermore, age groups were not differentiated either (for example, young adults and mid-aged compared to older adults). One of the central aims of CBT-I (cognitive-behavioural therapy for insomnia) is to correct dysfunctional beliefs about sleep (Sivertsen, Vedaa, & Nordgreen, 2013). In a recent study, using a randomised controlled trial, the authors compared cognitive therapy, behaviour therapy and cognitive-behavioural therapy (CBT) as treatments of insomnia (Eidelman et al., & Harvey, 2016; for a detailed explanation of the different forms of therapy, see **Chapter 1: Introduction, 1.6.1 Psychotherapeutic treatment of insomnia**). Irrespective of the therapy method applied, it was found that the greater the change in dysfunctional beliefs about sleep during treatment, the greater the improvement in insomnia symptoms

(Eidelman et al., 2016). This was the case both directly after treatment and in the 6-month and 12-month follow-up. Dysfunctional beliefs about sleep were also found to be improved, but to a lesser extent, by behaviour therapy. Interestingly, behaviour therapy does not target dysfunctional beliefs about sleep directly as an element of therapy (Eidelman et al., 2016). Another meta-analysis of randomised controlled trials of CBT for insomnia further showed that dysfunctional beliefs about sleep could be reduced and insomnia could be improved significantly when CBT was administered in the form of self-help (Ho et al., 2015). Self-help therapy can include written material, audio-visual material and telephone consultation. It can be criticised that relatively few studies (20 in total) have been included in this meta-analysis and the included studies often excluded participants with comorbidities (Ho et al., 2015).

In a longitudinal study that considered factors associated with the persistence and remission of insomnia, it was possible to distinguish those participants with insomnia from those participants with normal sleep, based on their cognitive processes (Norell-Clarke et al., 2014). Dysfunctional beliefs about sleep (in addition to worry, somatic arousal, safety behaviours, selective attention, and monitoring) were a significant predictor of sleep status. Specifically, dysfunctional beliefs about sleep were associated with a greater likelihood of reporting persistent insomnia than with a normal sleep pattern (Norell-Clarke et al., 2014). As dysfunctional beliefs about sleep and insomnia remission were measured at the same time, a causal link could not be established. It is possible that a third factor was involved, simultaneously influencing the severity of insomnia and dysfunctional beliefs about sleep (for example, the link could be via pre-sleep arousal, which is influenced by dysfunctional beliefs about sleep, and this in turn has an effect on insomnia) (Norell-Clarke et al., 2014). It can be criticised that the

response rate for this study was not very high (47%) and selective attrition occurred (older participants were more likely to respond).

An earlier study, using a randomised controlled trial in a sample of older adults (N = 78; mean age = 64.7), compared cognitive-behavioural therapy (CBT), pharmacotherapy (PCT), a combination of the two (COMB) and a placebo group (PLA; Morin et al., 2002). It was found that dysfunctional beliefs about sleep improved with CBT and COMB but not with PCT or PLA. A greater improvement in dysfunctional beliefs about sleep was associated with greater sleep improvement following treatment. Furthermore, fewer dysfunctional beliefs about sleep after treatment were associated with a better outcome over time (in the 3-month, 12-month and 24-month follow-up; Morin et al., 2002). It has been speculated that the main reason why CBT-I is so effective might be that it corrects dysfunctional beliefs about sleep (Okajima et al., 2011). The changes in dysfunctional beliefs about sleep were less strongly associated with the *objective* (polysomnography) than with the *subjective* (sleep diary) measures of sleep (Morin et al., 2002). It should also be noted that insomnia is often described as a ‘*subjective* complaint’ and in current clinical practice insomnia patients are typically assessed using *subjective* measures rather than *objective* ones (American Academy of Sleep Medicine, 2014; American Psychiatric Association, 2013; World Health Organization, 1992).

However, in a study using a small clinical sample (64 participants with chronic insomnia), dysfunctional beliefs about sleep and insomnia were shown to be linked but reducing dysfunctional beliefs about sleep was not found to mediate an improvement in insomnia (Okajima, Nakajima, Ochi, & Inoue, 2014). One limitation of this study is that the participants were recruited from the same sleep disorder clinic. Therefore, the sample may not have been representative of the wider clinical population. It is possible

that other variables are involved in this link too. For example, Ong and colleagues (2012) proposed in the metacognitive model of insomnia that dysfunctional cognitions, arousal and maladaptive behaviours are all interacting factors and this interplay has influence on insomnia, rather than there being a simple one-directional link between dysfunctional beliefs about sleep and insomnia. In summary, plenty of previous research has shown that dysfunctional beliefs about sleep play a crucial role in the treatment of insomnia, as well as in the theory of insomnia. Therefore, this relationship is worth further investigating.

5.1.4 Heritability of dysfunctional beliefs about sleep

In spite of the extensive research interest in dysfunctional beliefs about sleep, no research has explored genetic and environmental influences on individual differences for this variable yet. Furthermore, even though the link between dysfunctional beliefs about sleep and insomnia symptoms is well established (see, for example, Morin et al., 2002; Norell-Clarke et al., 2014; Palagini et al., 2015) and dysfunctional beliefs about sleep play a crucial role in the current theories and the treatment of insomnia (see, for example, Eidelman et al., 2016; Harvey, 2002; Ong et al., 2012), the role that genetic and environmental influences play in this association has yet to be explored.

5.1.5 Aims of the current study

In summary, dysfunctional beliefs about sleep are an important element in the development of insomnia and are therefore discussed in the cognitive theories of insomnia. They are known to be associated with insomnia and they are a crucial aspect to target in the treatment of insomnia. However, no previous study has yet considered the roots of dysfunctional beliefs about sleep (and its subscales) and the mechanisms underlying their association with insomnia symptoms. As this study is the first to

attempt to investigate these points, aims were formulated rather than hypotheses. The aims of this study were:

- 1) Estimate the relative contribution of genetic and environmental influences on
 - a) overall dysfunctional beliefs about sleep, b) *beliefs about immediate consequences*, c) *beliefs about long-term consequences*, d) *beliefs about control* and e) insomnia symptoms.
- 2) Examine the magnitude of the association between overall dysfunctional beliefs about sleep, different aspects of dysfunctional beliefs about sleep and insomnia symptoms.
- 3) Explore the relative contribution of genetic and environmental influences on the association between dysfunctional beliefs about sleep (as well as its subscales) and insomnia symptoms.

5.2 Method

5.2.1 Sample

Data from Wave 5 of the G1219 longitudinal twin/sibling study was the focus of this study as this is the only wave at which dysfunctional beliefs about sleep have been measured. Wave 5 included data from 223 monozygotic (MZ) twins, 404 dizygotic (DZ) twins and 218 siblings (Denis et al., 2015). The participants were aged between 22 and 32 years (mean age 25 years) and 34.3% of them were male (Denis et al., 2015).

For a more detailed description of the sample, see **Chapter 2: Methods, 2.4 The G1219 sample**.

5.2.2 Dysfunctional beliefs about sleep

In the present study the DBAS-10 was utilised. It is a shortened version of the dysfunctional beliefs and attitudes about sleep scale (DBAS; Morin et al., 1993),

developed by Espie et al. (2000). It comprises only 10 items (Espie et al., 2000) and three subscales. Namely, *beliefs about immediate negative consequences* of insomnia (DBAS factor I), *beliefs about long-term negative consequences* of insomnia (DBAS factor II), and *beliefs about the need for control* over insomnia (DBAS factor III). The items included in the DBAS-10 were shown to be sensitive to recovery (Espie et al., 2000; Edinger & Wohlgemuth, 2001). This means that the DBAS-10 was able to detect differences before and after treatment. This version of the DBAS is now widely used (see, for example, Ellis, Hampson, & Cropley, 2007; Norell-Clarke et al., 2014). See **Appendix G** for the items included in each of the subscales. Each item was coded from 1 ('strongly disagree') to 10 ('strongly agree'), based on the participants' responses. For the subscale *beliefs about immediate consequences* (DBAS factor I), items 1 to 5 were added, giving a theoretical range from 5 to 50. For *beliefs about long-term consequences* (DBAS factor II), items 6 to 8 were added, resulting in a theoretical range from 3 to 30. For *beliefs about control* (DBAS factor III), items 9 and 10 were added, therefore the theoretical range was from 2 to 20. The total scale score is the sum of all responses (theoretical range from 10 to 100), with higher scores indicating more dysfunctional beliefs about sleep. In the current sample, the Cronbach's alpha for the overall DBAS is .78, the DBAS factor I is .78, the DBAS factor II is .69 (in line with the approach taken by Espie et al., 2000, the Cronbach's alpha for the DBAS factor III was not calculated for the current sample, because it only consisted of two items).

5.2.3 *Insomnia symptoms*

Insomnia symptoms were measured by the Insomnia Symptoms Questionnaire (ISQ, Okun et al., 2009), using a 6-item version. The total scale score is the sum of these responses, ranging from 0 to 24, with higher scores meaning more severe

insomnia symptoms. For a more detailed explanation of the insomnia symptoms measure, see **Chapter 3, 3.2.3 Insomnia symptoms**.

5.3 Analyses

5.3.1 Data preparation and preliminary analyses

The data was prepared (see **2.4.4 Data preparation** for more details). None of the variables required transformation. SPSS (IBM, 2013; version 22) was used for a preliminary analysis, which included descriptive and inferential statistics. Pearson's correlations between the overall DBAS, as well as its subscales (DBAS factor I, DBAS factor II and DBAS factor III) and insomnia symptoms were also considered (phenotypic correlations), focusing on twin one only to control for non-independence of observations. This was helpful to get a first idea of the role each variable plays in association with insomnia symptoms.

5.3.2 Univariate twin and sibling analyses

A univariate analysis was run for each variable (using OpenMX version 1, R version 3.0.3; Boker et al., 2011), applying maximum-likelihood model fitting analysis to estimate the relative contribution of genetic, shared and non-shared environmental influence (Neale & Cardon, 2013). For a detailed explanation of univariate analysis, see **Chapter 2: Methods, 2.3.2 Univariate Analysis**.

Furthermore, the ACE model and E model were compared. If, by dropping A and C at the same time, the fit for the E model gets worse (compared to the ACE model), it can be concluded that familial influences (either A and/or C) must have played a role (Waszczuk et al., 2016).

5.3.3 *Multivariate twin and sibling analyses*

The phenotypic correlations show a small to moderate yet significant association between the phenotypes considered, therefore further analyses were performed. A bivariate analysis was run to examine the relationship between the genetic and environmental factors that affect overall dysfunctional beliefs about sleep and insomnia symptoms. A multivariate analysis explored this association in more detail by examining the relationship between the genetic and environmental factors that influence the three subscales of dysfunctional beliefs about sleep and insomnia symptoms. For a detailed explanation of multivariate analysis, see **Chapter 2: Methods, 2.3.5 Multivariate analysis**. It was planned to test different multivariate models (the correlated factors model, independent pathway model and common pathway model) and present the model which represented the best fit. For a detailed explanation of the model see **Chapter 2: Methods, 2.3.5.1 The correlated factor model, 2.3.5.2 The independent pathway model and 2.3.5.3 The common pathway model**. The correlated factors model allows us to consider the correlation of the non-shared environment separately, while the independent pathway model and the common pathway model take into account a combination of genetic, shared and non-shared environmental influences. Based on the results of the univariate analyses (see **5.4 Results**), we deviated from the original plan and present the correlated factors model only. For completion, the fit statistics of the independent pathway model and common pathway model are presented in **Appendix H**, but should not be interpreted further. Sensitivity analyses were performed for analyses as outlined under **2.5 Sensitivity analyses**.

5.4 Results

5.4.1 Descriptive statistics

Descriptive statistics for each variable are summarised in **Table 5.1** (please refer to table overleaf). For overall dysfunctional belief about sleep, significant sex differences were found ($t(850) = -4.04, p < .01, d = .29$), males reported fewer insomnia symptoms than females. There was also a significant difference between males and females in terms of the *beliefs about immediate consequences* (DBAS factor I; $t(850) = -6.20, p < .01, d = .45$), with males showing on average lower scores than females. For insomnia symptoms, significant sex differences were found as well ($t(625) = -3.28, p = .01, d = .25$), males reported fewer insomnia symptoms than females.

Table 5.1 Means (SD) of raw scores for overall dysfunctional beliefs about sleep, its subscales, and symptoms of insomnia

	Means (SD)		
	Total	Males	Females
Overall DBAS	50.26 (15.24)	47.30 (15.45)*	51.78 (14.93)*
DBAS factor I	31.24 (9.36)	28.51 (9.31)*	32.66 (9.07)*
DBAS factor II	9.50 (6.07)	9.57 (6.18)	9.46 (6.02)
DBAS factor III	9.51 (4.41)	9.21 (4.31)	9.67 (4.46)
Insomnia symptoms	6.48 (5.22)	5.65 (4.89)*	6.92 (5.33)*
	MZ	DZ	Siblings
Overall DBAS	49.52 (15.34)	50.49 (15.99)	50.40 (13.78)
DBAS factor I	30.75 (9.18)	30.91 (9.92)	32.07 (8.41)
DBAS factor II	8.86 (5.69)	9.98 (6.56)	9.26 (5.52)
DBAS factor III	9.91 (4.48)	9.58 (4.46)	9.06 (4.26)
Insomnia symptoms	6.09 (4.97)	6.68 (5.38)	6.61 (5.19)

Note: * sex differences were found. Means and SD are based on the raw data (untransformed, including outliers, etc.); MZ = monozygotic twin; DZ = dizygotic twins; siblings = non-twin sibling pairs; Overall DBAS = overall dysfunctional beliefs about sleep (DBAS); DBAS factor I = beliefs about the immediate negative consequences of insomnia (DBAS subscales); DBAS factor II = beliefs about the long-term negative consequences of insomnia (DBAS subscale); DBAS factor III = beliefs about the need for control over insomnia (DBAS subscale) – higher scores indicating more dysfunctional beliefs about sleep; Insomnia symptoms = insomnia symptoms (ISQ), higher scores indicating more insomnia symptoms.

5.4.2 Phenotypic analysis

The phenotypic correlations are displayed in **Table 5.2** (please refer to table overleaf). Higher overall dysfunctional beliefs about sleep were associated with more insomnia symptoms

($r = .37, p < .01$). Higher scores in *beliefs about immediate consequences* (DBAS factor I), *beliefs about long-term consequences* (DBAS factor II) and *beliefs about control* (DBAS factor III) scores were also associated with more insomnia symptoms (DBAS

factor I: $r = .18, p < .01$; DBAS factor II: $r = .44, p < .01$; DBAS factor III: $r = .44, p < .01$).

Table 5.2 Phenotypic correlations for overall dysfunctional beliefs about sleep, its subscales, and symptoms of insomnia

	Overall DBAS	DBAS Factor I	DBAS Factor II	DBAS Factor III	Insomnia Symptoms
Overall DBAS	1				
DBAS factor I	.84**	1			
DBAS factor II	.75**	.37**	1		
DBAS factor III	.67**	.31**	.49**	1	
Insomnia symptoms	.37**	.18**	.44**	.34**	1

Note: * $p < .05$; ** $p < .01$. Correlations were calculated on data with outliers deleted and age and sex was regressed out in SPSS, using twin 1 only to control for non-independence of observations. Overall DBAS = overall dysfunctional beliefs about sleep (DBAS); DBAS factor I = beliefs about the immediate negative consequences of insomnia (DBAS subscale); DBAS factor II = beliefs about the long-term negative consequences of insomnia (DBAS subscale); DBAS factor III = beliefs about the need for control over insomnia (DBAS subscale) – higher scores indicating more dysfunctional beliefs about sleep; Insomnia Symptoms = insomnia symptoms (ISQ), higher scores indicating more insomnia symptoms.

5.4.3 MZ, DZ and sibling correlations

The MZ, DZ and sibling within-trait and cross-trait-cross-twin correlations for all variables are presented in **Table 5.3** (see table overleaf). The MZ and the DZ correlations for the overall DBAS, DBAS factor I, DBAS factor II and DBAS factor III were similar, hinting at the possibility that there is little or no genetic influence at work here. For insomnia symptoms, the difference between the MZ and DZ correlation was larger (although not significantly, as indicated by overlapping confidence intervals),

indicating a possible genetic influence. As the MZ correlations are substantially less than 1 for all of the traits, the importance of non-shared environmental influence (E; including error) is highlighted.

Table 5.3 Twin/sibling correlations for overall dysfunctional beliefs about sleep, its subscales, and symptoms of insomnia

	Correlations		
	MZ	DZ	Sibling
<i>Within-trait</i>			
Overall DBAS	.15 (-.04 - .34)	.17 (0 -.32)	-.03 (-.26 - .20)
DBAS factor I	.23 (.03 - .38)	.20 (.03 - .35)	-.16 (-.37 - .07)
DBAS factor II	.05 (-.15 - .24)	.18 (.01 - .34)	.11 (-.14 - .34)
DBAS factor III	.16 (-.05 - .36)	.07 (-.10 - .23)	.10 (-.15 - .33)
Insomnia symptoms	.37 (.19 - .53)	.21 (.05 - .36)	.12 (-.13 - .34)
<i>Cross-traits-cross-twins</i>			
Overall DBAS - Insomnia symptoms	.14 (-.01 - .27)	.11 (-.01 - .22)	-.08 (-.28 - .13)
DBAS factor I - Insomnia symptoms	.09 (-.05 - .22)	.04 (-.07 - .14)	-.16 (-.33 - .04)
DBAS factor II - Insomnia symptoms	.09 (-.08 - .23)	.16 (.04 - .27)	0 (-.21 - .21)
DBAS factor III - Insomnia symptoms	.18 (.04 - .31)	.08 (-.04 - .19)	0 (-.18 - .18)
DBAS factor I - DBAS factor II	.02 (-.14 - .17)	.07 (-.04 - .18)	-.17 (-.36 - .10)
DBAS factor I - DBAS factor III	.04 (-.10 - .18)	-.01 (.13 - .10)	-.06 (-.25 - .15)
DBAS factor II - DBAS factor III	.11 (-.07 - .26)	.04 (-.08 - .16)	-.02 (-.24 - .20)

Note: The 95% confidence intervals are presented in brackets. MZ = monozygotic twins; DZ = dizygotic twins; Sibling = sibling pairs; Overall DBAS = overall dysfunctional beliefs about sleep (DBAS); DBAS factor I = beliefs about the immediate negative consequences of insomnia (DBAS subscale); DBAS factor II = beliefs about the long-term negative consequences of insomnia (DBAS subscale); DBAS factor III = beliefs about the need for control over insomnia (DBAS subscale) – higher scores indicating more dysfunctional beliefs about sleep; Insomnia symptoms = insomnia symptoms (ISQ), higher scores indicating more insomnia symptoms.

5.4.4 Twin analysis

Univariate analyses were run on all variables; the fit statistics and the results of the full ACE models are presented in **Table 5.4** and the estimates of A, C and E with 95% confidence intervals are shown in **Table 5.5** (see tables following on the next pages). Overall dysfunctional beliefs about sleep, *beliefs about long-term consequences* (DBAS factor II) and *beliefs about control* (DBAS factor III) showed no significant genetic influence (overall DBAS: A = .09, 95% CI = 0 - .31; DBAS factor II: A = 0, 95% CI = 0 - .32; DBAS factor III: A = .17, 95% CI = 0 - .32) and no significant shared environmental influence (overall DBAS: C = .05, 95% CI = 0 - .22; DBAS factor II: C = .13, 95% CI = 0 - .24; DBAS factor III: C = 0, 95% CI = 0 - .21), and mainly non-shared environmental influence (overall DBAS: E = .86, 95% CI = .69 - .99; DBAS factor II: E = .87, 95% CI = .68 - .99; DBAS factor III: E = .83, 95% CI = .68 - .99). For the *beliefs about immediate consequences* (DBAS factor I) some significant genetic influence was indicated (A = .19; 95% CI = .01 - .38), no shared environmental influence was evident (C = 0, 95% CI = 0 - .22) and the main influence came from non-shared environment (E = .81, 95% CI = .65 - .98). When the ACE model and the E model were compared for these four variables, the fit did not decline significantly in any of the cases (overall DBAS: $\chi^2 = 6953.24$, $df = 839$, $p = .12$, AIC = 5275.92; DBAS factor I: $\chi^2 = 6106.98$, $df = 839$, $p = .07$, AIC = 4428.98; DBAS factor II: $\chi^2 = 5314.09$, $df = 832$, $p = .11$, AIC = 3650.09; DBAS factor III: $\chi^2 = 4882.15$, $df = 839$, $p = .11$, AIC = 3204.15), indicating no familial influence, once again confirming the results. For insomnia symptoms, non-shared environment appeared to be most important and familiarity was found, indicated by a decline in fit for the E model ($\chi^2 = 5135.58$, $df = 837$, $p < .01$, AIC = 3461.58).

Table 5.4 Fit statistics of all univariate genetic model fitting analyses

<i>Variable/</i>	ep	-2LL	Df	AIC	Δ -2LL	Δ df	<i>p</i>
Model							
<i>Overall DBAS</i>							
Saturated	15	6933.43	826	5281.43	-	-	-
ACE	4	6949.72	837	5275.72	16.29	11	.13
E	2	6953.24	839	5275.92	4.20	2	.12
<i>Beliefs about immediate consequences (DBAS Factor I)</i>							
Saturated	15	6083.25	826	4431.25	-	-	-
ACE	4	6101.63	837	4427.63	18.38	11	.07
E	2	6106.98	839	4428.98	5.35	2	.07
<i>Beliefs about long-term consequences (DBAS Factor II)</i>							
Saturated	15	5275.74	819	3637.74	-	-	-
ACE	4	5309.73	830	3649.73	33.99	11	< .01
E	2	5314.09	832	3650.09	4.36	2	.11
<i>Beliefs about control (DBAS Factor III)</i>							
Saturated	15	4873.04	826	3221.04	-	-	-
ACE	4	4877.81	837	3203.81	4.77	11	.94
E	2	4882.15	839	3204.15	4.34	2	.11
<i>Insomnia symptoms</i>							
Saturated	15	5096.90	824	3448.90	-	-	-
ACE	4	5112.43	835	3442.43	15.53	11	.16
E	2	5135.58	837	3461.58	23.15	2	< .01

Note: All analyses focus on transformed data, outliers deleted with age and sex regressed out. ep = estimated parameters; -2LL = $-2 \times (\log \text{likelihood})$; df = degrees of freedom; $\Delta\chi^2$ = change in chi-square statistic; Δdf = change in degrees of freedom; AIC = Akaike's Information Criterion statistic; Saturated = full model. The fit of the ACE model is relative to saturated model, the fit of the E model relative to ACE model.

Table 5.5 Estimates for A, C and E for all univariate genetic model fitting analyses

Variable	Parameter Estimates		
	A (CI)	C (CI)	E (CI)
Overall DBAS	.09 (0 - .31)	.05 (0 - .22)	.86(.69 - .99)
DBAS factor I	.19 (.01 - .38)	0 (0 - .22)	.81 (.65 - .98)
DBAS factor II	0 (0 - .32)	.13 (0 - .24)	.87 (.68 - .99)
DBAS factor III	.17 (0 - .32)	0 (0 - .21)	.83 (.68 - .99)
Insomnia symptoms	.36 (0 - .53)	.03 (0 - .32)	.61 (.47 - .80)

Note: All analyses focus on transformed data, outliers deleted with age and sex regressed out. The 95% confidence intervals are presented in brackets. Overall DBAS = overall dysfunctional beliefs about sleep (DBAS); DBAS factor I = beliefs about the immediate negative consequences of insomnia (DBAS subscale); DBAS factor II = beliefs about the long-term negative consequences of insomnia (DBAS subscale); DBAS factor III = beliefs about the need for control over insomnia (DBAS subscale) – higher scores indicating more dysfunctional beliefs about sleep; Insomnia symptoms = insomnia symptoms (ISQ) – higher scores indicating more insomnia symptoms.

Fit statistics for the bivariate and the multivariate analyses are presented in **Table 5.6** (see table overleaf). The results of the bivariate analyses including overall dysfunctional beliefs about sleep and insomnia symptoms are shown in **Figure 5.1** (see figure on the following page). The genetic and shared environmental correlation between dysfunctional beliefs about sleep and insomnia symptoms were not significant ($r_A = .74$, 95% CI = -1 - 1; $r_C = -.17$, 95% CI = -1 - 1), and a moderate yet significant overlap in the non-shared environmental influences ($r_E = .32$, 95% CI = .17 - .47) for the two traits was evident.

Table 5.6 Fit statistics for the multivariate genetic model fitting analyses

	ep	-2LL	df	AIC	Δ -2LL	Δ df	<i>p</i>
<i>Model 1: Overall DBAS and symptoms of insomnia</i>							
Saturated	42	11904.61	1638	8628.61	-	-	-
ACE	11	11941.04	1669	8603.04	36.43	31	0.23
<i>Model 2: DBAS Factor I, DBAS Factor II, DBAS Factor III and symptoms of insomnia</i>							
Saturated	132	20732.85	3223	14286.85	-	-	-
ACE Correlated	34	20865.04	3321	14223.04	132.19	98	0.01
Factors Solution							

Note: All analyses focus on transformed data, outliers deleted with age and sex regressed out. ep = estimated parameters; -2LL = -2*(log likelihood); df = degrees of freedom; $\Delta\chi^2$ = change in chi-square statistic; Δdf = change in degrees of freedom; AIC = Akaike's Information Criterion statistic; Saturated = full model, A = additive genetic, C = shared environmental; E = non-shared environmental. The fit statistics of the ACE respectively the correlated factors solution is relative to the saturated model.

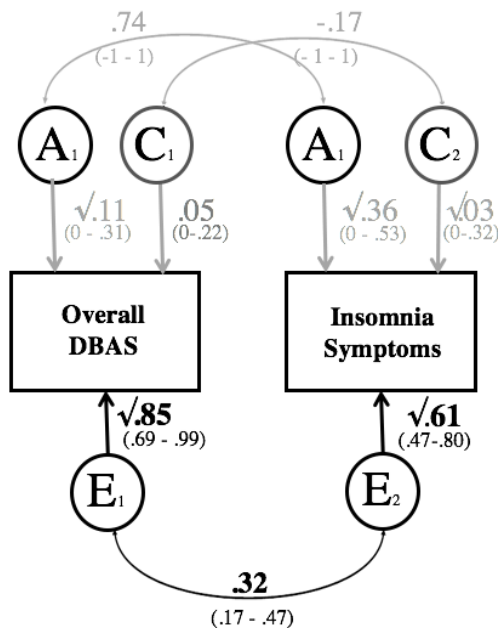


Figure 5.1 Path diagram of the bivariate analysis, including overall dysfunctional beliefs about sleep (overall DBAS) and insomnia symptoms

Note: A = additive genetic, C = shared environmental; E = non-shared environmental. Significant paths are shown in black, see brackets for 95% confidence intervals. Paths with confidence intervals spanning 0 are depicted in grey. $r_{Ph} = .37$ (95%CI = $.31 - .43$). Overall DBAS = overall dysfunctional beliefs about sleep (DBAS), higher score indicating more dysfunctional beliefs about sleep; Insomnia Symptoms = insomnia symptoms (ISQ), higher score indicating more insomnia symptoms.

The results of the multivariate analyses including *beliefs about immediate consequences* (DBAS factor I), *beliefs about long-term consequences* (DBAS factor II), *beliefs about control* (DBAS factor III) and insomnia symptoms are displayed in **Figure 5.2** (see figure overleaf). For completeness, the fit statistics for the correlated factors solution, the independent pathway model and the common pathway model are shown in **Appendix H**. No significant overlap for genetic or shared environmental factors was indicated, see **Figure 5.2a and 5.2b** (see figure overleaf). Furthermore, the overall DBAS, DBAS factor II and DBAS factor III were not found to be familial in the previously run univariate analyses. As **Figure 5.2c** shows (see figure overleaf), the non-shared environmental influence between the subscales of the DBAS and insomnia symptoms were all significantly, moderately correlated (r_E ranging from .24 to .46), except for *beliefs about immediate consequences* (DBAS factor I) and insomnia symptoms ($r_E = .17$, 95% CI = 0 - .33).

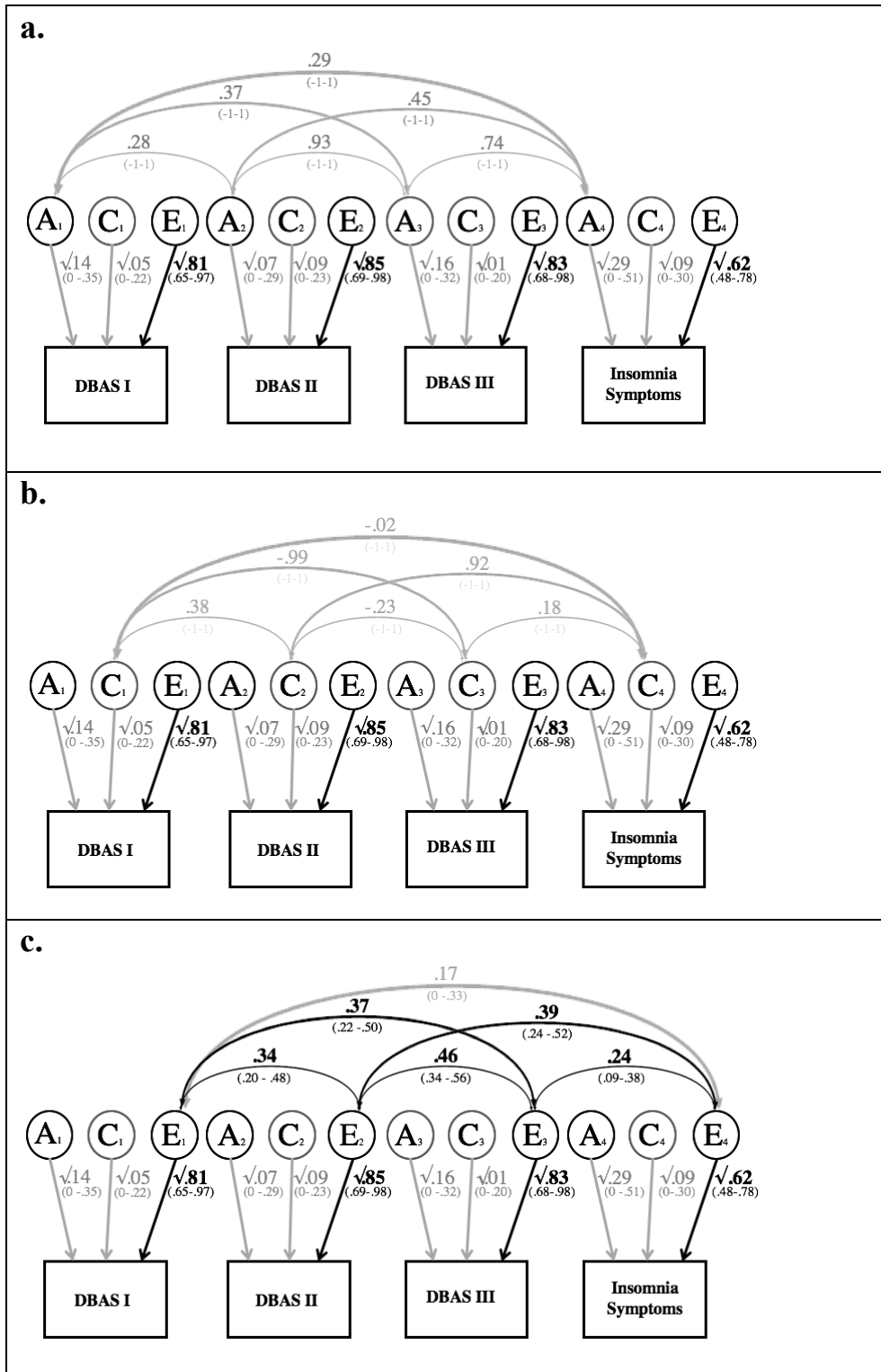


Figure 5.2 Path diagram of the correlated factors solution, including *beliefs about immediate consequences* (DBAS factor I), *beliefs about long-term consequences* (DBAS factor II), *beliefs about control* (DBAS factor III) and insomnia symptoms

Note: A = additive genetic, C = shared environmental; E = non-shared environmental. Significant paths are shown in black. Paths with confidence intervals spanning 0 are depicted in grey; part a. shows the genetic correlations; part b. shows the shared-environmental correlations; part c. shows the non-shared environmental correlations

5.5 Discussion

The rationale behind this study was to gain insight into the aetiology of dysfunctional beliefs about sleep and its subscales, by considering the genetic and environmental influences involved. Furthermore, it was attempted to gain a better understanding of the concept and aetiology of insomnia symptoms by illuminating the association between dysfunctional beliefs about sleep (its subscales) and insomnia symptoms from a behavioral genetics perspective to shed light on the underlying mechanisms involved in the development and maintenance of insomnia.

5.5.1 Associations between variables

Dysfunctional beliefs about sleep and its subscales were all associated with insomnia symptoms. However, the association between the subscale *beliefs about immediate consequences* and insomnia symptoms was only weak, but significant. This finding could help to improve insomnia treatment in the future, as it may be useful to focus on the subscales *beliefs about long-term consequences* and *beliefs about control* which showed stronger associations with insomnia symptoms.

5.5.2 Factors influencing dysfunctional beliefs about sleep

This was the first study to estimate the heritability of dysfunctional belief about sleep and its subscales. The twin analyses revealed that overall dysfunctional beliefs about sleep showed neither a significant genetic influence (except for *beliefs about immediate consequences*) nor shared environmental influence but was mainly influenced by the non-shared environment (including error). The results held up in the sensitivity analysis for all variables except for *beliefs about immediate consequences*. When re-running the analysis on the raw data (outliers still included, age and sex not regressed out yet), the genetic influence was not significant (95% CI spanning zero) but

when A and C were dropped at the same time, the fit actually got worse. Considering the results together with the results of the sensitivity analysis for the *beliefs about immediate consequences*, it seems likely that some familial influence was at work here, whilst no familial influence was indicated for overall dysfunctional beliefs about sleep, *beliefs about long-term consequences* and *beliefs about control*, but the results should be interpreted with caution. However, even though most traits have some genetic influence (Polderman et al., 2015), there are some findings which indicate very small (i.e. almost no) genetic influence on interpersonal variables. For example, interpersonal cognition was found to have a genetic influence of only .03 (Gregory et al., 2007). Interpersonal cognition refers to expectations and perceptions of others, as well as beliefs about oneself (Gregory et al., 2007).

5.5.3 Factors influencing the association between overall dysfunctional beliefs about sleep and insomnia symptoms

The results of the correlated factor solution showed that neither the correlations between the genetic influences nor the correlations between the shared environmental influences were significant in the multivariate model. This actually makes sense as we did not find any genetic or shared environmental influence either in the univariate analyses for overall dysfunctional beliefs about sleep and its subscales (except for *beliefs about immediate consequences*) or for these separate variables in the multivariate. All non-shared environmental correlations were significant except for *beliefs about immediate consequences* and insomnia symptoms, which was also the association with the lowest correlation in the phenotypic analysis (see **Table 5.2**). The results held up in the sensitivity analysis. It can be concluded that for the association of the DBAS subscales and insomnia symptoms, the non-shared environmental influences overlapped to some extent.

5.5.4 Limitations

The twin design has some limitations which are discussed in detail in the methods chapter (see **Chapter 2: Methods, 2.3.1 Assumptions and associated limitations**). Whilst the results from twin studies are used to draw conclusions about individual differences in the general population, it is possible that twins may not be representative of the wider non-twin population (Plomin et al., 2013).

Further limitations include the relatively small sample size, which meant that some of the confidence intervals were wide and slight inconsistencies occurred in the sensitivity analysis (described below). However, we did find a significant genetic estimate for overall and somatic pre-sleep arousal in the previous chapter, when using the same sample (see **CHAPTER 4: Associations between pre-sleep arousal and insomnia symptoms in early adulthood: a twin and sibling study**). Therefore, the small sample size may not explain the lack of genetic or shared environmental influence indicated for dysfunctional beliefs about sleep in the current study. For additional, general limitations see **Chapter 8: Discussion, 8.4 General limitations**.

It should also be mentioned that the subscale *beliefs about control* (DBAS factor III) only included two items so no Cronbach's alpha was calculated. However, the DBAS-10 has been evaluated previously and the subscales were found to be valid and useful (Espie et al., 2000). This variable was further moderately associated with insomnia symptoms ($r = .34, p < .01$). Therefore, we decided to include it in the analyses. Despite these limitations, the current findings were largely in line with previous findings - for example, with regard to the estimate for heritability for insomnia (Gregory et al., 2016; Wing et al., 2012; Gehrman et al., 2011). Heritability is a population statistic. Therefore, estimates may vary in different samples (Plomin et al., 2013).

5.5.5 Conclusion

This was the first study to examine dysfunctional beliefs about sleep and its subscales in a twin study. The current findings give us a novel insight into the concept of dysfunctional beliefs about sleep, its subscales and the association between dysfunctional beliefs about sleep and insomnia symptoms. This helps to deepen our understanding of the cognitive theories of insomnia, by dissecting one of its crucial elements and illuminating the factors involved in its association with insomnia symptoms. The findings may also help to improve insomnia treatment in the future. These results now need to be validated in a larger sample. The current findings are novel, exciting and raise new questions such as ‘Which are the environmental factors involved in influencing dysfunctional beliefs about sleep?’. This will be explored in the next chapter.

CHAPTER 6: Non-shared Environmental Factors Associated with Dysfunctional Beliefs about Sleep in Early Adulthood: A Monozygotic Twin Differences Study

6.1 Introduction

6.1.1 Previously conducted study

In the previous chapter ‘Dysfunctional Beliefs about Sleep and Insomnia Symptoms in Early Adulthood: A Twin and Sibling Study’, one of the main findings was that no genetic or shared environmental factors were indicated as having an influence on dysfunctional beliefs about sleep. Instead, non-shared environmental influences accounted for 86% of the variance (for a more detailed discussion of dysfunctional beliefs about sleep see **Chapter 5, 5.1 Introduction and theoretical background**). As a result of this previous finding, it was decided to conduct further analyses to attempt to identify these specific non-shared environmental influences. The findings will help us to gain insight in the mechanisms involved in developing insomnia by considering environmental factors which influence dysfunctional beliefs about sleep which in turn is a factor that plays a crucial role in the development of insomnia (as we know from the cognitive theories of insomnia). In this way the underlying mechanism is dissected.

6.1.2 Background

The present study is exploratory in nature. Currently, we do not know much about the environmental factors influencing dysfunctional beliefs about sleep as research in this area is limited. However, previous literature illustrates that there are certain environmental factors which are associated with insomnia or sleep quality in general. Since dysfunctional beliefs about sleep and insomnia symptoms and sleep

quality are associated (for example, Carney et al., 2010; Hiller et al., 2015; Palagini et al., 2015; Yang et al., 2014; see previous chapter for a detailed discussion), these environmental factors might also be related to dysfunctional beliefs about sleep.

6.1.3 Selection of candidate 'environmental' factors

In this study, data previously collected for the G1219 study is used (at wave 5, the only time point at which information about dysfunctional beliefs about sleep has been collected). Variables considered to be associated with sleep were included in the testing battery and are investigated here as possible non-shared environmental influences on dysfunctional beliefs about sleep. These variables happen to also being associated with insomnia, which makes them even more suitable for being possible candidate environmental influences on dysfunctional beliefs about sleep.

Relationship status, relationship satisfaction, highest level of education, employment status and general health have all previously been found to be associated with insomnia and sleep quality (Arber, Bote, & Meadows, 2009; Barclay & Gregory, 2013; Healey, Kales, Monroe, Bixler, Chamberlin, & Soldatos, 1981; Janson, Lindberg, Gislason, Elmasry, & Boman, 2001; Ohayon, 2002; Troxel, Buysse, & Matthews, 2009; Troxel, Robles, Hall, & Buysse, 2007).

Smoking status and alcohol dependence have also been found to be associated with insomnia symptoms (Janson et al., 2001). However, it can be criticised that this study focused only on males. Furthermore, alcohol use has been found to be related to sleep disturbance (see, for example, Kenney, LaBrie, Hummer, & Pham, 2012; Sivertsen, Skogen, Jakobsen, Hysing, 2015; Valerio, Kim, & Sexton-Radek, 2016). For example, sleep quality was found to be lower in nights after alcohol use (Lydon et al., 2016). The study by Lydon and colleagues (2016) could have been improved by

including a more precise measure for alcohol use (highest amount recorded here was 5 or more drinks). Previous studies have also found that drug use/misuse is associated with various sleep-related parameters, such as sleep quality, sleep duration, sleep deficit and insomnia (see, for example, Ogeil, Phillips, Rajaratnam, & Broadbear, 2015; Sivertsen et al., 2015). It can be criticised that the study by Ogeil and colleagues (2015) mainly focused on marijuana and did not include hard drugs such as cocaine or heroin.

Negative life events were shown to be related to insomnia and sleep quality (Barclay, Eley, Rijdsdijk, & Gregory, 2011; Bernert, Merrill, Braithwaite, Van Orden, & Joiner, 2007; Vahtera et al., 2007) and the number of stressful life events experienced was associated with the onset of insomnia (Healey et al., 1981). Life events are commonly divided into dependent and independent life events. Dependent life events refer to events that the individual has to some extent influence on (for example, getting divorced), whilst independent life events are beyond their control (for example, the death of a close relative) (Brown & Harris, 1978). The distinction between dependent and independent life events has been included in our analyses from this sample previously (Barclay et al. 2011). In particular dependent negative life events appear to have the strongest association with sleep quality which was found to be explained to some extent by a gene-environment correlation (Barclay et al. 2011). However, it is possible that life events also act as non-shared environmental factors un-confounded by genetic influence influencing dysfunctional beliefs about sleep. Therefore, both dependent and independent life events are included in the analyses. Based on the previous literature as discussed above, all these variables are useful to consider as potential environmental influences un-confounded by genetic factors in the analyses for the current study.

6.1.4 Aims of the current study

In summary, the current study is exploratory in nature and aims to specify general ‘environmental’ factors which influence dysfunctional beliefs about sleep for the first time. Therefore, no hypotheses were formulated and an overall aim was provided instead. We acknowledge that these candidate ‘environmental’ influences themselves may in part also be influenced by genes and/or shared environment. By adopting a MZ differences design, we attempt to identify those factors that can be considered to have a non-shared environmental influence un-confounded by genetic factors influencing dysfunctional beliefs about sleep. Based on the previous literature the following candidate ‘environmental’ factors were included in the analyses: relationship status, relationship satisfaction, relationship cohesion, highest level of education, employment status, general health, smoking status, alcohol use, drug use, dependent life events and independent life events.

6.2 Method

6.2.1 Sample

Data from Wave 5 of the Genesis 12-19 (G1219) longitudinal twin/sibling study was the focus of this study as this is the only wave at which dysfunctional beliefs about sleep have been measured. Wave 5 included data from 223 monozygotic (MZ) twins, 404 dizygotic (DZ) twins and 218 siblings (Denis et al., 2015). The participants were aged between 22 and 32 years (mean age 25 years) and 34.3% of them were male (Denis et al., 2015). For the 88 MZ twin pairs who both completed the overall DBAS (dysfunctional beliefs about sleep scale), which were the main focus in the analyses conducted, the age range was 23 to 27 (mean age = 24.66, SD = 1.27), 74% of the MZ

twin pairs were female. For a more detailed description of the sample, see **Chapter 2: Methods, 2.4 The G1219 sample**.

6.2.2 Measures

6.2.2.1 Dysfunctional beliefs about sleep (DBAS)

The DBAS-10 comprises ten items tapping into dysfunctional beliefs about sleep (Espie et al., 2000). The total scale score is the sum of all responses (theoretical range from 10 to 100), with higher scores indicating more dysfunctional beliefs about sleep. For a more detailed discussion of the DBAS see **Chapter 5, 5.2.2 Dysfunctional beliefs about sleep**.

6.2.2.2 Relationship (status, satisfaction, and cohesion)

Relationship status was assessed by asking the question “Are you...? (single, living with a partner, married, legally separated/divorced or ‘other’)” (Spanier, 1976). For the response ‘other’, it was possible for the participants to add their own text. Combining the additional information added under ‘other’ resulted in the following categories: married, living together, engaged, in a serious relationship, ‘just casual’ and single. Thirty-five per cent (302 cases) of the participants of the overall sample were single, 12% married (102 cases), 23% were living together (195 cases), 7% were engaged (59 cases), 19% were in a serious relationship (164 cases), and 4% were ‘just casual’ (31 cases).

Looking just at the MZ sub-sample, the ‘just casual’-group was too small to be analysed (4 cases) and was therefore excluded from all analyses (using a cut-off of minimum 5 cases for the MZ sub-sample). Of the remaining categories, the MZ sub-sample had the following distribution: 38% (65 cases) were single, 10% of the participants were married (17 cases), 20% were living together (34 cases, excluding the married couples), 9% were engaged (15 cases), and 24% were in a serious relationship

(41 cases). For the total sample, this means that 37% (65 cases) were single and 63% (111 cases) in some kind of relationship.

The Dyadic Adjustment Scale (Spanier, 1976) was used to measure relationship satisfaction and cohesion (see **Appendix I** for a list of items included in the two scales). Responses were given on a 5-point Likert scale ranging from ‘all the time’ (coded as 1) to ‘rarely/never’ (coded as 5) for relationship status and from ‘daily’ (coded as 1) to ‘never’ (coded as 5) for relationship cohesion. The scores of each of the items were summed. The higher scores indicated less relationship satisfaction and cohesion. This measure has previously been reported to show good levels of reliability (see for example Busby, Christensen, Crane, & Larson, 1995, relationship satisfaction Cronbach’s alpha = .85, cohesion Cronbach’s alpha = .80). However, in the current sample, the Cronbach’s alpha for relationship satisfaction was only .40, while the Cronbach’s alpha for relationship cohesion was .73.

6.2.2.3 Education

The highest level of education was assessed using just one item, namely asking the participants to “Please write how many of each of these qualifications you have achieved...”. The variable was coded as a continuous variable as follows: None = 0, GCSEs (other grades) = 1; GCSEs (A* - C) = 2; GNVQ/NVQ = 3; AS Level = 4; A Levels = 5; City and Guilds or BTEC = 6; National Cert/Diploma (e.g. HND) = 7; Degree (e.g. BA, BSc) = 8; and Postgraduate Degree (e.g. MA, MSc, PhD) = 9. Consequently, higher scores indicate a higher level of education.

6.2.2.4 Employment

Employment was determined by asking the question “At the moment are you...?”. The possible answers were ‘studying at college’, ‘studying at university’,

‘full-time parent’, ‘on government benefit’, ‘working full-time’, ‘working part-time’ or ‘other’ (free text could be added here). The ‘full-time parent’ (7 cases in the overall sample, but only 2 in the MZ sub-sample), ‘unemployed’ (5 cases in the overall sample, but none in the MZ sub-sample) and ‘on government benefit’ (6 cases in the overall sample, but none in the MZ sub-sample) categories were too small (less than 5 cases in the MZ sub-sample) to be considered in the analyses. A similar approach was also adopted in previous studies using this variable for the G1219 sample (Barclay et al., 2012; Barclay et al., 2013). The remaining categories were summarised as follows: ‘studying’ (66 cases; 8% of the total sample), ‘working’ (695 cases; 88% of the total sample) and ‘working and studying’ (27 cases; 3% of the total sample). For the MZ twins, this resulted in the categories: ‘studying’ (14 cases; 8% of the MZ twins), ‘working’ (147 cases; 87% of the MZ twins) and ‘working and studying’ (8 cases; 5% of the MZ twins).

6.2.2.5 General health

The participants indicated the state of their general health by responding to a single question (“In general, how good would you say your health is now?”). Responses were given on a 5-point Likert scale, ranging from poor (5) to excellent (1), where the higher scores indicated poorer health (see Ware Jr & Sherbourne, 1992). This approach was adopted in previous research and found to be reliable (see for example Troxel et al., 2009).

6.2.2.6 Smoking status

Whether or not the participants smoked was established by asking the question: “Do you smoke?”. Possible answers were ‘yes’, ‘used to, given up’ and ‘never’ (Currie, Samdal, Boyce, & Smith, 2001). In the overall sample 15% (130 cases) replied ‘yes’, 12% (103 cases) ‘used to, given up’ and 72% (620 cases) ‘never’, while in the MZ twins 9% (16 cases) responded ‘yes’, 14% (24 cases) ‘used to, given up’ and 77% (135 cases) ‘never’.

6.2.2.7 Alcohol use

Alcohol use was established by asking the following question: “Do you drink?” (Currie et al., 2001). A simple yes/no answer was required here. Of the overall sample 94% of the participants (799 cases) indicated that they drank and 6% of the participants (55 cases) indicated that they did not drink. For the MZ twins 93% of the participants (163 cases) actually consumed alcohol whilst 7% of them (13 cases) drank no alcohol at all. See **6.3.3 Sensitivity analysis** for additional alcohol related variables that were not included in the results.

6.2.2.8 Drug use

Illicit drug use was established by responding to one statement, taken from the Youth Self-Report (Achenbach, 1991): “I use drugs (other than alcohol and nicotine) for non-medical purposes”. The possible answers were ‘not true’ (784 cases; 92% of the total sample), ‘somewhat true’ (42 cases; 5% of the total sample) and ‘very true’ (28 cases; 3% of the total sample). After considering the frequencies of scores for this measure in the MZ twins produced the following categories: 94% participants replied ‘not true’ (165 cases), 3% said ‘somewhat true’ (5 cases), and 3% responded ‘very true’ (6 cases).

6.2.2.9 Life events

Life events were measured using items from the Coddington Stressful Life Events Scale (Coddington, 1984) and the List of Threatening Experiences (Brugha, Bebbington, Tennant, & Hurry, 1985). See **Appendix J** for a list of the items that were included. The participants were asked to respond with a ‘yes’ or ‘no’ to a list of negative life events to indicate whether or not they had experienced a particular negative life event during the past year. The higher scores indicate more negative life events. Thirteen of the items were coded as dependent negative life events (i.e. events influenced to some extent by the participant’s behaviour), eight items were coded as independent life events (i.e. events which were not really a consequence of the participants’ behaviour). The scores are the sum of all dependent life events, respectively independent life events. This approach has been taken in previous studies (see, for example, Silberg, Rutter, Neale, & Eaves, 2001), including studies that used the G1219 sample (see, for example, Barclay et al., 2012; Barclay et al., 2013).

6.3 Analyses

6.3.1 Data preparation and preliminary analyses

The data was prepared (see **2.4.4 Data preparation** for more details). SPSS (IBM, 2013; version 22) was used for a preliminary analysis which included descriptive and inferential statistics.

6.3.2 MZ differences analysis

The idea behind the MZ differences analysis design is that we know that MZ twins share 100% of their genes, as well as 100% of their shared environment (Plomin et al., 2013). Hence any discrepancy between MZ twins must be due to non-shared environmental influence (which includes measurement error). This means that, when

using MZ differences scores, we are controlling for genetic and shared environmental influences, which allows us to identify non-shared environmental components, unconfounded by genetic factors, which influence the outcome variable (Barclay et al., 2013; Vitaro, Brendgen, & Arseneault, 2009). MZ differences scores were calculated for each variable by subtracting the score of twin 2 from that of twin 1 (the co-twin). Note that for the current sample, twins were entered in random order to control for birth order effects.

Two series of regression analyses were run in STATA (StataCorp, 2015; version SE 14.0), controlling for the non-independence of observations and the effects of sex and age. The first series investigated the extent to which various factors contributed to the overall DBAS score, considering the full sample. This gives us an idea about ‘environmental’ factors that generally influence dysfunctional beliefs about sleep (which could be influenced by genetic and/or shared environment as well).

The second series of regression analyses used MZ differences scores to examine whether any of the MZ differences in candidate non-shared environmental influences could predict the differences between the MZs for the overall DBAS score (in the 88 full MZ pairs). This provides information about which factors have a non-shared environmental influence, unconfounded by genetic factors, influencing dysfunctional beliefs about sleep. All regression analyses controlled for age and sex.

The regressions were run separately instead of using one model including all variables in order to avoid the problem of multicollinearity, which had occurred. Bonferroni correction was applied, multiplying the p-value by the number of analyses run (11 analyses), to correct for multiple testing.

6.3.3 Sensitivity analyses

Sensitivity analyses were performed for all analyses as outlined under **2.5 Sensitivity analyses**. For additional sensitivity analyses, the categorical variables drug use and smoking status were re-coded into simple yes/no answers to check whether or not different results were obtained. Additional variables for alcohol use were also considered ('How often?', 'Number of drinks?') but the results were in line with the results presented for variable alcohol use and did not add to the findings and have therefore not been included in the main text (see **Appendix K** for the additional analyses conducted).

6.4 Results

6.4.1 Descriptive statistics

The key variable dysfunctional beliefs about sleep had a mean of 50.26 (SD = 15.25) for the overall sample and a mean of 50.14 (SD = 15.83) for the MZ twins. The theoretical range was 10 - 100, with higher scores indicating more dysfunctional beliefs about sleep. For overall dysfunctional belief about sleep significant sex differences were found ($t(850) = -4.04, p < .01, d = .29$), males reported fewer overall dysfunctional belief about sleep than females.

6.4.2 MZ differences analyses

As discussed previously, significant difference between males and females was found for the overall DBAS but not when considering the MZ sub-sample, which was the main focus of the analysis (for the MZ sub-sample $t(174) = -1.09$). Therefore, the regression analysis was run on all MZs and not on males and females separately, as elsewhere (Barclay et al., 2012). The distribution of the MZ differences of the DBAS score is presented in **Figure 6.1** (see figure overleaf). As twins within each pair were

entered into the dataset in a random order, the calculation of the MZ differences scores produces a mean difference score approximating zero. The deviation away from the mean of zero in the current sample illustrates that there are MZ differences in dysfunctional beliefs about sleep.

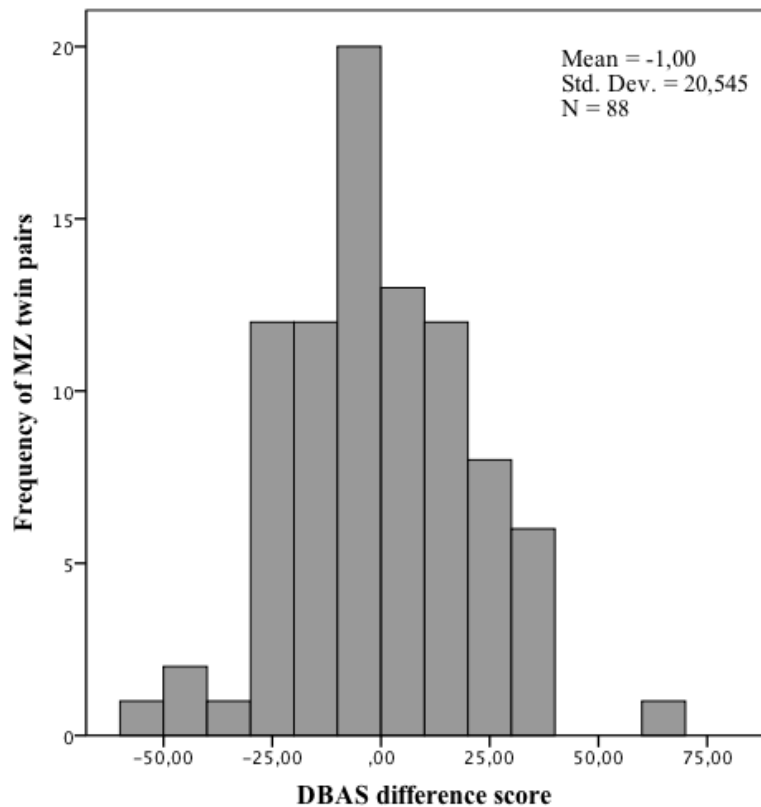


Figure 6.1 Histogram of distribution of MZ differences for the overall DBAS score

Note: DBAS difference scores = difference in the overall dysfunctional beliefs about sleep (DBAS) score between twin 1 and twin 2 for the MZ twins, scores further away from 0 (the mean) indicating greater difference in dysfunctional beliefs about sleep.

The results of the first series of univariate linear regressions are presented in part **a)** of **Table 6.1** (see table overleaf). This shows the extent to which the measured variables in the full sample predict absolute dysfunctional beliefs about sleep. Relationship satisfaction, general health, dependent and independent life events were all correlates of overall dysfunctional beliefs about sleep. However, the variable

independent life events did not remain significant after controlling for multiple comparisons.

Part **b)** of **Table 6.1** shows the results of the MZ differences analyses (see table overleaf). Various univariate linear regressions were run on the MZ sub-sample, using the MZ differences scores to control for genetic and shared environmental influences, revealing associations with a non-shared environmental component which is unconfounded by genetic influence. Drug use was the only variable that was found to have a non-shared environmental component unconfounded by genetic influence in the association with dysfunctional beliefs about sleep, after controlling for multiple comparisons.

Table 6.1 Regression analyses predicting a) Absolute DBAS scores and b) MZ differences, controlling for genetic influence and shared environmental influence on the environmental measures

	a) Absolute DBAS score analysis			b) MZ differences analysis		
	R ²	β	<i>t</i>	R ²	β	<i>t</i>
Relationship status	.02	-.12	-.23	.04	1.32	.56
Relationship satisfaction	.04	-2.14	-3.34**	.04	-3.48	-.81
Relationship cohesion	.02	-.72	-.98	.02	-.25	-.07
Education	.02	.54	.87	.04	-2.77	-.91
Employment	.02	-.64	-1.14	.04	-.58	-.34
General health	.05	2.60	4.88**	.07	4.19	1.69
Smoking status	.02	-1.03	-1.92	.02	-.56	-.18
Alcohol use	.02	-.30	-.62	.04	-.49	-.30
Drug use	.02	.19	.32	.08	-4.83	-3.20**
Dependent life events	.06	2.99	6.26**	.04	-2.57	-.95
Independent life events	.02	1.21	2.24*	.04	.86	.32

Note: * $p < .05$; ** $p < .01$. Significant values are displayed in **bold**. Values shown in grey did not remain significant after controlling for multiple testing. Analyses under a) are focusing on the full sample. Analyses under b) are focusing on the MZ twins only.

6.5 Discussion

In the previous chapter, non-shared environment was found to be key in explaining the variance in dysfunctional beliefs about sleep (for more details see **Chapter 5**). The literature about environmental factors that influence dysfunctional beliefs about sleep is limited. The aim of the current study was therefore to find those

factors that influence dysfunctional beliefs about sleep. It was then attempted to identify which of these factors can be considered to have a non-shared environmental component, un-confounded by genetic factors, influencing dysfunctional beliefs about sleep, by adopting a MZ differences design. In this way, a deeper insight into the mechanisms involved in the development of insomnia symptoms was gained, by attempting to find the roots of dysfunctional beliefs about sleep, which is, according to the cognitive theories, a crucial element associated with insomnia (see Harvey 2002, Morin, 1993; Ong et al., 2012).

6.5.1 Factors influencing dysfunctional beliefs about sleep

In the absolute measure analysis relationship satisfaction, general health and dependent life events were all associated with dysfunctional beliefs about sleep, showing that these were general ‘environmental’ influences on dysfunctional beliefs about sleep. Importantly, these were no longer significant in the MZ differences analyses, suggesting that the association between those variables and dysfunctional beliefs about sleep was to some extent also influenced by genes and/or shared environment and not just a non-shared environmental influence un-confounded by genetic influence (Barclay et al., 2013).

In MZ differences analysis, only drug use was significant (and remained significant when correcting for multiple comparisons). This means that drug use was a non-shared environment influence un-confounded by genetic factors, which had an influence on dysfunctional beliefs about sleep, with no genetic or shared environmental influences being directly involved.

It is interesting that, in the current study, the difference in drug use was associated with difference in dysfunctional beliefs about sleep between MZ twins; but there was no association between the phenotypes in the full sample. One possible

explanation is that, in the absolute measure analysis, our analyses included differences *between* families (therefore introducing between family variance), whilst in the MZ differences analysis, we examined differences *within* families. Decreasing variance increases statistical power (Scherbaum & Ferrerter, 2009). Therefore, the effects of drug use might have been washed out in the absolute measure analysis. However, when using the MZ sub-sample instead of the full sample, sample size was also decreased, which also lowers power again at the same time (Scherbaum & Ferrerter, 2009). This means that the results do make sense but they need to be interpreted with caution. It is true that illicit drug use might have quite a strong impact on the individual (for example on their sleep, see Sivertsen et al., 2015), so it also makes sense that this might cause MZ differences in dysfunctional beliefs about sleep. It may be that the more drugs the individual uses, the more dysfunctional beliefs he/she has. However, we did not quantify drug use for the current sample but this would be an interesting point to investigate further in future research. It would also be interesting to know which drugs were used by the participants to better understand how they might have been affected, but this was not asked so is a further topic for future investigation.

6.5.2 The link between drug use and dysfunctional beliefs about sleep

Research on the association between dysfunctional beliefs about sleep and drug use is limited. There are various possible mechanisms underlying this link. It is possible that the link between dysfunctional beliefs about sleep and drug use is direct or via a third variable. One idea is that dysfunctional beliefs about sleep and drug use are linked via another sleep-related variable. For example, previous studies have found that drug use/misuse is associated with sleep disturbances including poorer sleep quality, shorter sleep duration, sleep deficit and insomnia (see, for example, Ogeil et al., 2015; Sivertsen et al., 2015). Dysfunctional beliefs about sleep were also found to be

associated with sleep variables and insomnia (see, for example, Ho Park, An, Sook Jang, & Chung, 2012; Morin et al., 2002). It can be criticised that the study by Ho Park and colleagues (2012) used a cross sectional design and did not control for possible gender effects. When controlling for insomnia symptoms results remained robust, but it is possible that one or various sleep-related parameters mediate or moderate the association between dysfunctional beliefs about sleep and drug use. In case of a mediation effect, this would mean that it is possible that drug use may only affect sleep duration and sleep quality, which in turn may lead (indirectly) to the development of dysfunctional beliefs about sleep. This would mean that sleep duration and sleep quality would explain the relationship between drug use and dysfunctional beliefs about sleep. However, it should be kept in mind, that this kind of relationship is less likely to be one-directional. Another possibility would be a moderation effect, which means that the strength of association between drug use and dysfunctional beliefs about sleep is moderated (or affected) by sleep parameter variables, such as sleep duration or sleep quality.

6.5.3 Limitations

The twin design has some limitations, and it is possible that twins may not be representative of the wider non-twin population (Plomin et al., 2013). These limitations relating to the twin method are discussed in detail in the methods chapter (see **Chapter 2: Methods, 2.3.1 Assumptions and associated limitations**).

Further additional limitations, for example, the sample size and the use of self-report measure are discussed in detail under **Chapter 8: Discussion, 8.4 General limitations**. The relatively small sample size may have explained the low Cronbach's alpha of .40 reported for relationship satisfaction (only 63% of the participants in the total sample were in a relationship). However, relationship cohesion produced a

satisfactory Cronbach's alpha of .73 while it also focused exclusively on a sub-sample of participants in a relationship.

Another issue to consider is that non-shared environmental candidates such as drug use are also genetically influenced to some extent (see, for example, van den Bree, Johnson, Neale, & Pickens, 1998; Barclay, Eley, Buysse, Rijdsdijk, & Gregory, 2010). While accepting that most if not all of the candidate influences included in this study are likely to be influenced by genes and/or shared environment, here it was considered whether they can also identify as non-shared environmental component, un-confounded by genetic factors, influencing dysfunctional beliefs about sleep.

Additionally, it should be kept in mind that drug use had a low prevalence in the sample. In the whole sample, 92% had not used any drugs. Therefore, the results should be interpreted with caution. It can further be questioned how robust the reporting of drug use was, as the use of the drug itself may have influenced the ability to report it.

Despite these limitations, the current findings were largely in line with previous findings. For example, previous studies using the same sample but from an earlier wave (wave 4), showed that dependent life events and general health were among the factors that influenced other sleep-related variables (absolute measures analysis), namely, sleep quality and chronotype (Barclay et al., 2012, Barclay et al., 2013). Drug use was further found to have a non-shared environmental component un-confounded by genetic factors influencing chronotype (this variable was not considered in the study of sleep quality), in the MZ differences analysis in the previous study (Barclay et al., 2013).

6.5.4 Conclusion

The current findings give us a novel insight into the concept of dysfunctional beliefs about sleep as this is the first study that attempts to identify environmental factors un-confounded by genetic influence. Relationship satisfaction, general health,

dependent life events, were found to be associated with dysfunctional beliefs about sleep. Drug use was identified to have a non-shared environmental component unconfounded by genetic factors influencing dysfunctional beliefs about sleep. The exact mechanisms underlying the link between drug use and dysfunctional beliefs about sleep are not clear yet. It would be interesting to explore this further in the future. These results now need to be validated in a larger sample. The results also help us to better understand the cognitive models of insomnia by providing a deeper insight into the mechanisms involved in the development of insomnia symptoms, attempting to find the roots of dysfunctional beliefs about sleep, which is a crucial element associated with insomnia.

CHAPTER 7: Self-reports of insomnia with short versus normal sleep duration: comparing the subtypes in terms of heritability, associated phenotypes and persistence over time

7.1 Introduction

In order to gain a deep insight into the concept of insomnia symptoms the current study adds a further analytical level by testing a current theory about the existence of two subtypes of insomnia. The theory of interest, states that insomnia with objective short sleep length and insomnia with objective normal sleep length can be differentiated as two distinct subtypes of insomnia (Vgontzas et al., 2013).

7.1.1 Background

Previous research and theory suggests that insomnia with objective short sleep duration (SSD, typically referring to < 6h of sleep per night) differs importantly from insomnia with normal sleep duration (NSD, typically referring to \geq 6h of sleep per night) (Vgontzas et al., 2013; American Academy of Sleep Medicine, 2014). This theory has been well-cited (Carroll, Irwin, Merkin, & Seeman, 2015; Irwin, 2015), has been discussed in the ICSD-3 (American Academy of Sleep Medicine, 2015) and has also gained support from previous investigation (see, for example, Fernandez-Mendoza et al., 2015; Sivertsen, Harvey, Lundervold, & Hysing, 2014). Despite this, certain aspects of the theory are yet to be tested.

The following assumptions are made by the theory. The theory states that there is a biological vulnerability to insomnia SSD, in contrast to a mainly psychological vulnerability to insomnia NSD, which may cause a difference in heritability for the two subtypes of insomnia (Vgontzas et al., 2013). The theory also states that there are

differences between the two insomnia subtypes in terms of associations with certain psychological factors. This means that while both subtypes are associated with cognitive arousal, insomnia SSD is assumed to be associated with physiological hyperarousal and stress, while insomnia NSD is associated with a lack of physiological hyperarousal and an anxious-ruminative profile (Vgontzas et al., 2013). Furthermore, the theory claims that there are differences in persistence over time between the two subtypes of insomnia, with insomnia SSD being more likely to persist, while insomnia NSD is more likely to remit (Vgontzas et al., 2013).

Previous research has found support for this theory. For example, it has been suggested that those individuals with insomnia SSD are at an increased risk of cardiometabolic morbidity and mortality and are more likely to have impaired neurocognitive functioning as compared to those individuals with insomnia NSD (Fernandez-Mendoza et al., 2017b; Lin, Tsai, & Yeh, 2016). Furthermore, it was found that insomnia with short sleep duration (but not normal sleep duration) predicted depression and anxiety disorders (Fernandez-Mendoza et al., 2016; Fernandez-Mendoza et al., 2015; van Mill, Vogelzangs, van Someren, Hoogendijk, & Penninx, 2014). Insomnia with short sleep duration was further found to be associated with increased rates of inflammation (Fernandez-Mendoza et al., 2017a; Irwin, 2015). However, it is important to note that different cut-off values have been used in previous research for defining short and normal sleep time in context with insomnia (Fernandez-Mendoza et al., 2014; Irwin, 2015; van Mill, Vogelzangs, van Someren, Hoogendijk, & Penninx, 2014). It can be criticised that the cut-off seems to be set rather arbitrarily in some of the previous studies, even though the theory by Vgontzas and colleagues (2013) is mentioned which suggests a cut off of ≥ 6 h for normal sleep (see, for example, Fernandez-Mendoza et al., 2017a; Fernandez-Mendoza et al., 2014). This resulted in

different cut-offs for defining normal and short sleep duration, even when some of the same researchers were involved in the study (see, for example, Fernandez-Mendoza et al., 2017a; Fernandez-Mendoza et al., 2017b; Fernandez-Mendoza et al., 2016).

While the theory clearly focuses on *objectively* defined sleep length, there is some evidence that differences between insomnia SSD and insomnia NSD are indicated even when sleep length is assessed subjectively (Chandola, Ferrie, Perski, Akbaraly, & Marmot, 2010). This is noteworthy because, in current clinical practice, insomnia patients are typically assessed using subjective measures (American Academy of Sleep Medicine, 2015; APA, 2013; WHO, 1992). This being the case, it makes sense to also assess whether differences between the two insomnia subtypes are found when using subjective reports.

7.1.2 Predictions of the theory to be tested in the current study

Given widespread interest in this theory and the need to understand more about the distinctions between these subtypes when they are assessed using subjective measures, the aim of this study was to assess three predictions, which can be made from the theory:

- 1) Difference in heritability: The theory states that there is a biological vulnerability for insomnia SSD, in contrast to a mainly psychological vulnerability for insomnia NSD (Vgontzas et al., 2013). The hypothesis that *insomnia symptoms are more heritable for those with SSD versus NSD* will therefore be tested.
- 2) Difference in associated traits: The theory states that both subtypes are associated with cognitive arousal. Insomnia SSD is assumed to be associated with physiological hyperarousal and stress, while insomnia NSD is associated with a lack of physiological hyperarousal and an anxious-

ruminative profile (Vgontzas et al., 2013). It is hypothesised that *there will be no significant mean difference in cognitive pre-sleep arousal between the insomnia SSD group and the insomnia NSD group but that somatic arousal will be significantly higher in insomnia SSD compared to NSD. Furthermore, life events (as an indicator of stress) will be significantly lower in SSD compared to NSD and anxiety symptoms will be significantly lower in insomnia SSD compared to NSD. Also, the insomnia SSD and insomnia NSD groups should show higher cognitive pre-sleep arousal, somatic pre-sleep arousal, and more life events and anxiety symptoms than the no insomnia group.*

- 3) Difference in persistence over time: The theory states that insomnia SSD is more likely to persist, while insomnia NSD is more likely to remit (Vgontzas et al., 2013). It is hypothesised that *a significantly higher proportion of those with insomnia SSD at Time 1 will have insomnia at Time 2 as compared to those with insomnia NSD at Time 1.*

7.2 Method

7.2.1 Sample

Data from wave 4 (which, from here on, will be called Time 1 for ease of presentation) and 5 (which, from here on, will be called Time 2) of the G1219 longitudinal twin study was the focus of this study as they were the only waves in which sleep has been assessed (McAdams et al., 2012). At wave 4 a total of 1,556 individuals from 896 families took part. The sample was 61% female with an age range of 18 - 27, and a mean age of 20 (McAdams et al., 2012). Data from wave 5 was also used for this study and comprised 862 individuals in total. It included data from 223 monozygotic

(MZ) twins, 404 dizygotic (DZ) twins and 218 siblings (see Denis et al., 2015).

Participants were aged between 22 and 32 (with a mean age of 25) and 34.3% of them were male. For a more detailed description of the sample, see **Chapter 2: Methods, 2.4 The G1219 sample**.

7.2.2 Definition of sleep length for the insomnia SSD and insomnia NSD group

For all analyses, short sleep duration (SSD) was defined as < 6 hours per night, while normal sleep duration (NSD) was defined as \geq 6 hours of sleep per night, as specified in the theory of focus (Vgontzas et al., 2013). For the twin analyses, splitting the sample in this way resulted in only a very few full twin pairs experiencing short sleep duration (i.e. insomnia SSD: N = 5, of which 2 are MZs and 3 are DZs, and 0 sibling pairs). For this reason, it was not possible to run the twin analyses.

7.2.3 Subjective sleep duration

Subjective sleep duration was assessed using the Pittsburgh Sleep Quality Index (PSQI; Buysse et al., 1989), as has been done in previous research (Carroll et al., 2015). Participants were asked the following question: “During the past month, how many hours of *actual* sleep did you get at night? (This may be different than the number of hours you spend in bed.)”.

7.2.4 Insomnia and insomnia symptoms

In the previous chapters, insomnia symptoms were measured using the Insomnia Symptoms Questionnaire (ISQ, Okun et al., 2009) and coded as a continuous variable. The continuous variable insomnia symptoms was needed for the twin analysis. In order to be able to split the participants into the following groups: no insomnia, insomnia SSD and insomnia NSD, the ISQ measure was also coded as a dichotomous variable, as outlined in the original publication (ISQ, Okun et al., 2009). If the participants replied

positively (i.e. ‘sometimes’, ‘frequently’ or ‘always’) to one or more of the first 5 items and positively (i.e. ‘moderate’, ‘quite a bit’ or ‘extreme’) to the last item (which was a necessary criterion to be met in addition), then the score was coded as meeting the diagnostic criteria for insomnia (coded as ‘1’). Not meeting the diagnostic criteria was coded as ‘0’. For a more detailed explanation of the insomnia symptoms measure, see **Chapter 3, 3.2.3 Insomnia symptoms**. For a list of items included in the measure see **Appendix C**.

7.2.5 Cognitive and somatic pre-sleep arousal

Pre-sleep arousal was measured using the pre-sleep arousal scale (PSAS, Nicassio et al., 1985). For the somatic arousal subscale, the scores have a theoretical range from 8 to 40. For cognitive pre-sleep arousal subscale, the scores also have a theoretical range from 8 to 40. Higher scores indicate more pre-sleep arousal. See **Chapter 4, 4.2.2 Pre-sleep arousal** for a more detailed discussion of the measure. As pre-sleep arousal was only measured in the most recent wave of data collection, it was only possible to include wave 5 data for those two variables.

7.2.6 Life events

Life events were measured using items from the Coddington Stressful Life Events Scale (Coddington, 1984). The participants were asked to respond with a ‘yes’ or ‘no’ to a list of negative life events to indicate whether or not they had experienced a particular negative life event during the past year. The scores are the sum of all life events. The higher scores indicate more negative life events. The theoretical range of all life events (including dependent and independent ones) is 0 to 21. See **Appendix J** for a list of the items that were included and see **Chapter 6, 6.2.2.9 Life events** for a more detailed discussion of the measure. Life events were assessed in wave 4 and wave 5. As

the number of participants was higher for wave 4 than it was for wave 5, wave 4 data was included for the analysis of this variable to maximise power.

7.2.7 Anxiety symptoms

Symptoms of anxiety were measured by an age-adapted version of the Revised Children Anxiety and Depression Scale (RCADS; Chorpita et al., 2000; Willis, 2007). This scale comprises 36 items for assessing symptoms of anxiety as described by the DSM-IV (APA, 2000). The scores have a theoretical range from 0 to 108. See **Chapter 3, 3.2.5 Anxiety symptoms** for a more detailed discussion of the measure. Anxiety symptoms were also assessed in wave 4. As the number of participants was higher for wave 4 than it was for wave 5, wave 4 data was included for the analysis of this variable to maximise power.

7.3 Analysis

7.3.1 Data preparation

The data was prepared (see **2.4.4 Data preparation** for more details). The variable somatic pre-sleep arousal (wave 5) was skewed (skewness = 1.82, std. error = .08; kurtosis = 4.16, std. error = .17) and was therefore log-transformed, which successfully reduced the skewness (skewness = 1.03, std. error = .08; kurtosis = .63, std. error = .17). The variable life events (wave 4) was also skewed (skewness = 1.67, std. error = .06; kurtosis = 3.71, std. error = .13), log-transformation successfully reduced the skewness (skewness = .18, std. error = .06; kurtosis = -.85, std. error = .13).

Splitting the insomnia symptoms variable into insomnia symptoms SSD and insomnia symptoms NSD resulted in the loss of some of the complete twin/sibling pairs, in some cases, as one twin had a sleep duration of 6 hours or less (SSD), while the other had a sleep duration of more than 6 hours (NSD) – this caused them to end up in

different groups. There were no complete sibling pairs were in the insomnia symptoms SSD group. Therefore, siblings were excluded from the twin analyses.

7.3.2 Twin analysis

Due to the very small number of twins for insomnia SSD, a formal twin analysis (using OpenMX; Boker et al., 2011) could not be performed. Furthermore, it would not be sensible to draw larger conclusions based on the comparison of MZ and DZ correlations for insomnia SSD as very few participants were included in this group.

7.3.3 Regression analysis

The mean differences for the insomnia SSD, insomnia NSD and no insomnia groups were compared for the following variables: cognitive pre-sleep arousal (wave 5), somatic pre-sleep arousal (wave 5), life events (wave 4) and anxiety symptoms (wave 4). All regressions were run in Stata/MP version 14.0 (StataCorp, 2015), controlling for non-independence of observations, age and sex.

7.3.4 Sensitivity analyses

Sensitivity analyses were performed as outlined under **2.5 Sensitivity analyses**. As additional sensitivity analyses, the mean differences for the insomnia SSD, insomnia NSD and no insomnia group were compared for the variables life events (as assessed in wave 5) and anxiety symptoms (as assessed in wave 5). Again, similar results were obtained (unreported).

7.4 Results

7.4.1 Descriptive statistics

Descriptive statistics for each variable are summarised in **Table 7.1** (see table overleaf). For somatic pre-sleep arousal (wave 5), significant sex differences were

found ($t(655) = -3.33, p < .01, d = .23$). Males reported less somatic pre-sleep arousal than females. The variable life events (wave 4) also showed significant sex differences ($t(1123) = 2.84, p < .01, d = .15$). Males reported more life events than females. There was also a significant sex difference for anxiety symptoms (wave 4) $t(1439) = -9.11, p < .01, d = .26$. Males showed fewer anxiety symptoms than females. Splitting the sample by sex would have resulted in very small groups for some of the analyses. To maximise power and to be consistent across all the analyses, all of the following analyses were run on the full sample (not splitting the sample by sex).

Table 7.1 Means (SD) of raw scores for cognitive pre-sleep arousal, somatic pre-sleep arousal, life events and anxiety symptoms

	Means (SD)		
	Total	Males	Females
Cognitive pre-sleep arousal	17.09 (6.76)	16.60 (6.32)	17.34 (6.98)
Somatic pre-sleep arousal	11.30 (3.84)	10.72 (3.54)*	11.60 (3.96)*
Life events	1.85 (1.98)	2.04 (2.14)*	1.73 (1.87)*
Anxiety symptoms	25.06 (14.88)	21.00 (12.77)*	24.65 (14.99)*
	No insomnia	Insomnia SSD	Insomnia NSD
Cognitive pre-sleep arousal	15.96 (5.94)	25.90 (7.98)	23.65 (7.27)
Somatic pre-sleep arousal	10.70 (3.19)	16.38 (7.19)	14.71 (4.74)
Life events	1.68 (1.87)	3.54 (2.57)	2.87 (2.30)
Anxiety symptoms	23.06 (13.20)	36.70 (18.24)	38.65 (18.59)

Note: * sex differences were found. Means and SD were obtained from SPSS and are based on the raw data (untransformed, including outliers, etc.); Cognitive pre-sleep arousal (wave 5) = cognitive pre-sleep arousal (PSAS subscale), higher score indicating higher cognitive pre-sleep arousal; Somatic pre-sleep arousal (wave 5) = somatic pre-sleep arousal (PSAS subscale), higher score indicating higher somatic pre-sleep arousal; Life events (wave 4) = Life events (List of Threatening Experiences), higher score indicating more life events experienced; Anxiety symptoms = symptoms of anxiety (RCADS), higher scores indicating more anxiety symptoms.

Using the 6-hour cut-off for the SSD group resulted in the following groups: participants without insomnia (Time 1: 1323 cases, 87%; Time 2: 732 cases 86%), participants with insomnia SSD (Time 1: 38 cases, 3%; Time 2: 21 cases, 2%), and participants with insomnia NSD (Time 1: 159 cases, 10%; Time 2: 102 cases, 12%).

7.4.2 Twin analyses/MZ and DZ correlations

The MZ and DZ correlations for all variables are presented in **Table 7.2**. At Time 1, the MZ correlation for insomnia symptoms SSD was 1 ($N = 2, p < .01$) and the DZ correlation was .10 ($N = 3, p < .01$), while for insomnia symptoms NSD the MZ correlation was .40 ($N = 163, p < .01$) and the DZ correlation was .24 ($N = 279, p < .01$). As the twin analysis scripts (OpenMX) did not run stable, results were obtained from SPSS. The number of cases included for each of the correlations is also presented in the table in order to illustrate the problems with running the twin analysis. The MZ correlations for both variables were greater than the DZ correlations, indicating possible genetic influence. However, it would not be sensible to draw larger conclusions for insomnia SSD as this group was very small.

Table 7.2 MZ and DZ correlations for insomnia SSD and insomnia NSD

	Correlations	
	MZ	DZ
<i>Wave 4</i>		
Insomnia SSD	1** (N = 2)	.10** (N = 3)
Insomnia NSD	.40** (N = 163)	.24** (N = 279)

Note: * $p < .05$; ** $p < .01$. MZ = monozygotic twins; DZ = dizygotic twins. Correlations were obtained from SPSS. Insomnia SSD = Participants meeting the insomnia criteria and having a sleep duration < 6 hours per night; Insomnia NSD = Participants meeting the insomnia criteria and having a sleep duration \geq 6 hours per night.

7.4.3 Phenotypic analyses

The results of the regressions and the mean scores of participants with no insomnia, insomnia SSD and insomnia NSD for all variables included in the analyses are shown in **Figures 7.1 to 7.4**. Note that for ease of presentation in the figure, all mean scores were converted to z-scores.

There was no significant mean difference between insomnia SSD and insomnia NSD for cognitive pre-sleep arousal but both insomnia SSD and insomnia NSD were significantly higher in cognitive pre-sleep arousal (wave 5) than in the no insomnia group ($F(2, 549) = 80.42, p < .01; R^2 = .19$; Scheffe's post-hoc no insomnia vs. insomnia SSD $p < .01$; no insomnia vs. insomnia NSD $p < .01$; insomnia SSD vs. insomnia NSD $p = .420$).

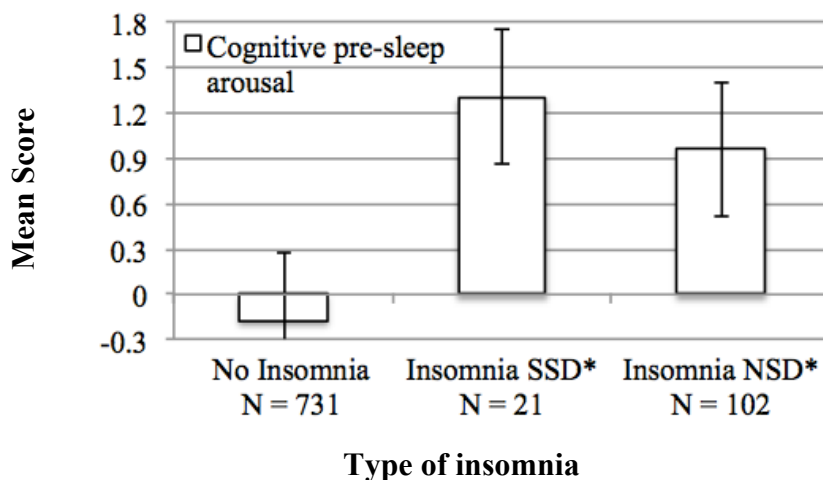


Figure 7.1 Mean differences in cognitive pre-sleep arousal between the no insomnia, insomnia SSD and insomnia NSD group

Note: * Significant mean difference; variables were transformed, outliers +/- 3 SD away from the mean deleted; standardised values (z-scores) are presented here; No insomnia = group of participants, who did not experience insomnia; Insomnia SSD = group of participants, who did have insomnia with a sleep duration of < 6h; Insomnia NSD = group of participants, who did have insomnia with a sleep duration of >= 6h; Cognitive pre-sleep arousal (wave 5) = cognitive pre-sleep arousal (PSAS subscale), higher score indicating higher cognitive pre-sleep arousal

There was no significant mean difference between insomnia SSD and insomnia NSD for somatic pre-sleep arousal (wave 5), but both insomnia SSD and insomnia NSD were significantly higher in somatic pre-sleep arousal than in the no insomnia group ($F(2, 550) = 61.46, p < .01; R^2 = .15$; Scheffe's post-hoc no insomnia vs. insomnia SSD $p = .01$; no insomnia vs. insomnia NSD $p < .01$; insomnia SSD vs. insomnia NSD $p = .99$) – see **Figure 7.2**.

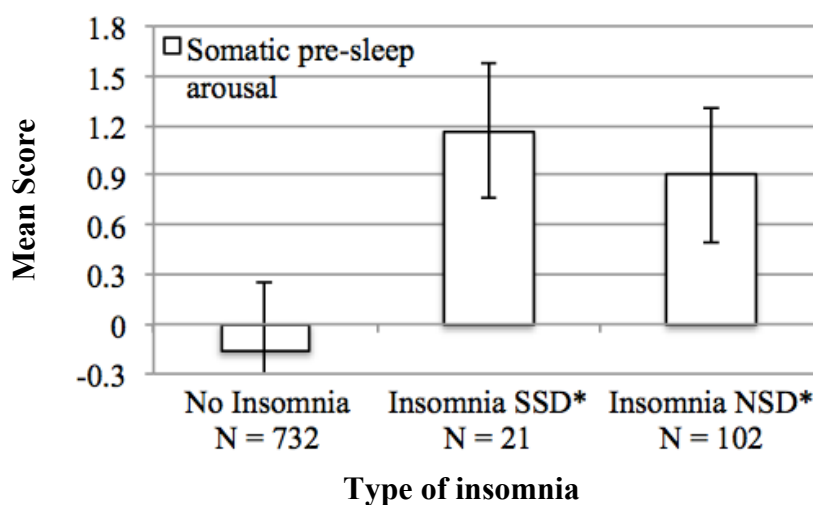


Figure 7.2 Mean differences in somatic pre-sleep arousal between the no insomnia, insomnia SSD and insomnia NSD group

Note: * Significant mean difference; variables were transformed, outliers +/- 3 SD away from the mean deleted; standardised values (z-scores) are presented here; No insomnia = group of participants, who did not experience insomnia; Insomnia SSD = group of participants, who did have insomnia with a sleep duration of < 6h; Insomnia NSD = group of participants, who did have insomnia with a sleep duration of >= 6h; Somatic pre-sleep arousal (wave 5) = somatic pre-sleep arousal (PSAS subscale), higher score indicating higher somatic pre-sleep arousal

There was no significant mean difference between insomnia SSD and insomnia NSD for life events (wave 4). However, both insomnia SSD and insomnia NSD reported significantly more life events than the no insomnia group ($F(2, 882) = 32.21, p < .01; R^2 = .05$; Scheffe's post-hoc no insomnia vs. insomnia SSD $p < .01$; no insomnia vs. insomnia NSD $p < .01$; insomnia SSD vs. insomnia NSD $p = .50$) – see **Figure 7.3** overleaf.

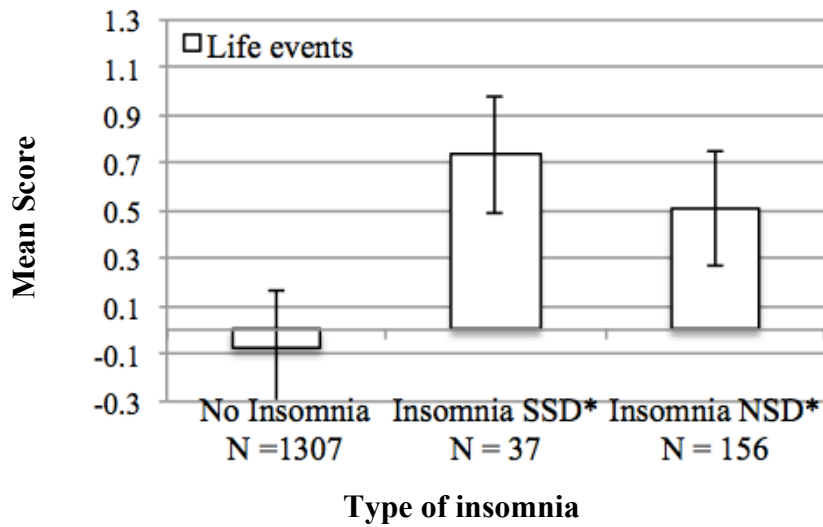


Figure 7.3 Mean differences in life events between the no insomnia, insomnia SSD and insomnia NSD group

Note: * Significant mean difference; variables were transformed, outliers +/- 3 SD away from the mean deleted; standardised values (z-scores) are presented here; No insomnia = group of participants, who did not experience insomnia; Insomnia SSD = group of participants, who did have insomnia with a sleep duration of < 6h; Insomnia NSD = group of participants, who did have insomnia with a sleep duration of >= 6h; Life events (wave 4) = Life events (List of Threatening Experiences), higher score indicating more life events experienced

There was no significant mean difference between insomnia SSD and insomnia NSD for anxiety symptoms (wave 4) but both insomnia SSD and insomnia NSD were significantly higher in anxiety symptoms than the no insomnia group ($F(2, 884) = 91.00, p < .01; R^2 = .10$; Scheffe's post-hoc no insomnia vs. insomnia SSD $p < .01$; no insomnia vs. insomnia NSD $p < .01$; insomnia SSD vs. insomnia NSD $p = .83$) – see **Figure 7.4** overleaf.

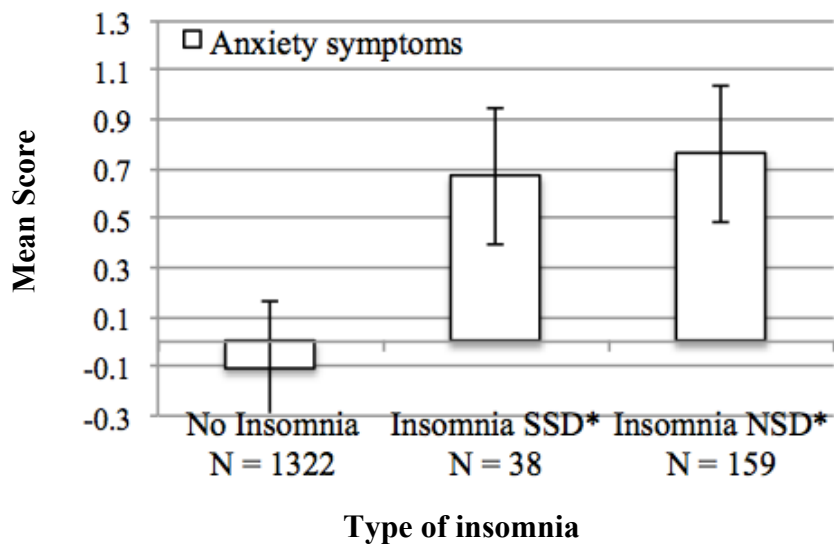


Figure 7.4 Mean differences in anxiety symptoms between the no insomnia, insomnia SSD and insomnia NSD group

Note: * Significant mean difference; variables were transformed, outliers +/- 3 SD away from the mean deleted; standardised values (z-scores) are presented here; No insomnia = group of participants, who did not experience insomnia; Insomnia SSD = group of participants, who did have insomnia with a sleep duration of < 6h; Insomnia NSD = group of participants, who did have insomnia with a sleep duration of >= 6h; Anxiety symptoms = symptoms of anxiety (RCADS), higher scores indicating more anxiety symptoms.

One point to note is that, when controlling for multiple testing, applying Bonferroni correction (multiply the p-value by the number of tests undertaken), the results of the regression analyses all remained significant. Similar results were obtained in the sensitivity analysis.

7.4.4 Persistence over time

Only 17 participants with insomnia SSD at Time 1 also participated at Time 2. Of these, 5 participants (29%) were considered to have insomnia at Time 2. Eighty-seven participants with insomnia NSD at Time 1 also participated at Time 2. Of these 19 (22%) were considered to have insomnia at Time 2.

There was high attrition between waves 4 and 5 (45% dropped out). However, selective attrition for the key variables was tested (unreported) and there did not appear

to be selective attrition in any of the key variables assessed at Time 1 (e.g. insomnia symptoms, life events, etc.). No formal analysis was run, because of the small sample size and the high attrition rate between the two waves considered.

7.5 Discussion

The rationale behind this study was to gain a deep insight into the concept of insomnia symptoms by adding a further analytical level, testing a current theory about the existence of two subtypes of insomnia. The theory of interest states that insomnia with objective short sleep length and insomnia with objective normal sleep length can be differentiated as two distinct subtypes of insomnia (Vgontzas et al., 2013). It was therefore attempted to test the hypotheses which can be derived from the theory (Vgontzas et al., 2013). No previous study has yet attempted to test all aspects of the theory at once. While the theory clearly focuses on *objectively* defined sleep length, the aim was to examine whether differences between the two insomnia subtypes could be found when using *subjective* reports. The theory was tested based on three assumptions that were made, which allowed testable hypotheses to be formulated. The first assumption is that insomnia symptoms are more heritable for those individuals with SSD compared to those individuals with NSD. The second assumption is that a difference between insomnia SSD and insomnia NSD can be found in relation to associated traits (somatic pre-sleep arousal, life events and anxiety symptoms). The third assumption is that there is a difference between insomnia SSD and NSD in persistence over time.

7.5.1 Hypothesis 1: Insomnia is more heritable for those with SSD versus those with NSD

It was not possible to run any univariate analyses as errors occurred when running the script because of the very small sample size. Furthermore, comparing the difference between the MZ twins and the DZ twins correlations for insomnia SSD to the one for insomnia NSD, it would not be sensible to draw larger conclusions as very few full twin pairs were included in the insomnia SSD group. Further research is needed in order to run the twin analyses in a larger sample so that this claim can be tested thoroughly.

7.5.2 Hypothesis 2: There are differences between insomnia SSD and NSD in associated traits

According to the theory, it was hypothesised that *there will be no significant mean difference in cognitive pre-sleep arousal between the SSD group and the NSD group but somatic arousal will be significantly higher in insomnia with SSD compared to insomnia with NSD, life events (as an indicator of stress) will be significantly lower in SSD compared to NSD and anxiety symptoms will be significantly lower in insomnia with SSD compared to NSD*. For cognitive pre-sleep arousal, the mean scores of insomnia SSD and insomnia NSD were similar but were significantly higher than for the no insomnia participants, which is in line with the theory (Vgontzas et al., 2013). Contrary to the expectations, no significant differences were found in the mean scores between insomnia SSD and insomnia NSD for somatic arousal, life events and anxiety symptoms. However, the scores were higher for both insomnia groups in comparison to the no insomnia group.

7.5.3 Hypothesis 3: *There are differences between insomnia SSD and NSD in persistence over time*

The final hypothesis to be tested was that *a higher proportion of those individuals with insomnia SSD at Time 1 will have insomnia at Time 2 as compared to those individuals with insomnia NSD at Time 1*. It was not possible to formally test this hypothesis as the sample size was too small and the attrition rate between Time 1 and 2 was relatively high.

7.5.4 Limitations

The results of this study need to be considered along with the limitations. The general limitations are discussed under **Chapter 8: Discussion, 8.4 General limitations**. Focusing on a larger sample would have allowed to formally test for heritability differences and to test for differences in persistence over time between the two subtypes of insomnia. Nevertheless, the lack of power is not able to explain the non-significant phenotypic results, as the effect sizes were very small. Note that significant differences between the two insomnia groups were found, compared to the no insomnia group. Furthermore, a *subjective* rather than an *objective* measure of sleep length was used in the current study. This made it possible to examine whether simply asking about sleep length (when this has not yet been measured objectively) may be informative during case conceptualization. It is perhaps unsurprising that certain differences were not possible to be identified when using this approach, as it is known that people with insomnia struggle to estimate their sleep length correctly (Vgontzas et al., 2013; Silva et al., 2007), but this approach has been used in previous research (Carroll et al., 2015). It should also be mentioned that in chronic insomnia, there is a tendency to underestimate sleep length and general sleep misperception is mentioned as a feature of insomnia NSD (Buysse et al., 2006; Vgontzas et al., 2013)

7.5.5 Conclusion

In summary, it can be said that the current findings are only preliminary and cannot provide sufficient support for the theory that insomnia subtypes (insomnia SSD versus insomnia NSD) exist. As the sample size was too small, it was not possible to thoroughly test all of the hypotheses. As far as the one hypothesis that could be tested is concerned, no substantial support was found for the theory as no mean differences in somatic pre-sleep arousal, life events and anxiety symptoms could be found between those individuals with insomnia SSD and those with NSD when using *subjective* measures. It is interesting to note that, for the ICSD-3 it was decided not to include insomnia SSD, as not sufficient evidence was found to support this construct (American Academy of Sleep Medicine, 2015). However, some later findings have since confirmed the existence of the two subtypes since and the theory has been quoted frequently (see, for example Fernandez-Mendoza et al., 2015; Lian et al., 2015; Carroll et al., 2015; Irwin, 2015). Further research on larger samples, including *subjective* as well as *objective* measures of sleep length and additionally more detailed measures of associated phenotypes is needed to confirm and extend the current findings. If it can be confirmed that two subtypes of insomnia exist, one with SSD and the other with NSD and that differences between these subtypes can only be found when using an *objective* measure for sleep length, this could call into question the common practice of diagnosing insomnia, which currently relies on *subjective* measures of sleep length. Furthermore, if support for this theory is found in the future, this could potentially help to optimize insomnia treatment since Vgontzas and colleagues (2013) claim that the two subtypes may vary in their response to different types of treatment.

CHAPTER 8: Discussion

8.1 Goals of this PhD thesis

The rationale of this PhD thesis was to gain a better understanding of the concept and aetiology of insomnia symptoms by illuminating the key elements involved in the development and maintenance of insomnia symptoms and by testing current theory. We know from the cognitive (and arousal) models of insomnia that mindfulness, pre-sleep arousal and dysfunctional beliefs about sleep may all play a role in insomnia symptoms in one way or the other. However, why these traits develop was not yet clear, nor was the underlying mechanisms of their association with insomnia symptoms. This is an important topic of investigation as it helps to deepen our understanding of the concept of insomnia and the roots of its development. It was therefore attempted to examine the principles outlined in the cognitive theories using a behavioural genetics framework to examine the traits involved and their association with insomnia symptoms. To achieve this, the genetic and environmental influence on each of these elements was assessed separately and the genetic and environmental influence on their association with insomnia was estimated. To add a further level of detail, the genetic and environmental influences on the subscales of those variables and their association with insomnia symptoms were also estimated, which helped us to dissect the relationship of those variables with insomnia in more detail. As one of these key elements (dysfunctional beliefs about sleep) did not show any genetic influence, environmental influences on this variable were investigated, which added another layer of insight. As a final step towards enriching our understanding of models of insomnia, a further theory was tested directly. Evidence for a model of insomnia which distinguishes between subtypes based

on sleep duration (i.e. insomnia with short sleep duration and insomnia with normal sleep duration) was considered.

8.2 The current findings within the context of cognitive theories and the treatment of insomnia

8.2.1 The current findings within the context of the cognitive theories

The discussion of the cognitive models of insomnia has shown that mindfulness, pre-sleep arousal and dysfunctional beliefs about sleep play an important role in insomnia (see **1.3.1 Theories most relevant to this thesis – Cognitive models of insomnia** for a detailed discussion). Expanding on the cognitive theories, it can be said that mindfulness was found to be familial, pre-sleep arousal showed moderate, significant genetic influence and dysfunctional beliefs had no familial influence. These elements were further decomposed by estimating genetic and environmental influence on their subscales, thus deepening our knowledge of the concept of insomnia by developing the cognitive theories further. Another level of understanding was added by considering the environmental influences on dysfunctional beliefs about sleep, which was found to have no familial influence. Drug use was the only variable to have a non-shared environmental influence un-confounded by genetic factors.

The mechanisms underling the development and maintenance of insomnia symptoms were illuminated by considering the association of the key traits (and their subscales) with insomnia symptoms phenotypically. Mindfulness, pre-sleep arousal and dysfunctional beliefs about sleep (and their subscales) were all found to be associated with insomnia symptoms. In order to gain an even deeper insight into the aetiology of insomnia symptoms, the genetic and environmental influences on these associations were considered. No common genetic influence for overall mindfulness and insomnia

symptoms was evident. Neither was any genetic overlap found between overall dysfunctional beliefs about sleep and insomnia symptoms or the subscales of dysfunctional beliefs about sleep (*beliefs about immediate consequences*, *beliefs about long-term consequences* and *beliefs about control*) and insomnia symptoms. However, cognitive and somatic pre-sleep arousal overlapped highly and significantly with insomnia symptoms in genetic influence. The current findings add another layer to the cognitive theories by drilling down into the details of the associations of the key elements associated with insomnia symptoms.

8.2.2 The results of this thesis within the context of the metacognitive model of insomnia

In the metacognitive model of insomnia, Ong and colleagues (2012) reviewed some of the cognitive (and behavioural) models and added metacognitive processes to pre-sleep arousal and the cognitive aspects that had already been included. Ong and colleagues attempted to identify the way in which metacognition (or mindfulness and acceptance) could enhance the regulation of emotions and reduce the distress caused by insomnia. For a more detailed outline of all aspects in which metacognitive processes help to improve insomnia, see Ong and colleagues (2012). It should be noted here that this theory of how mindful-based approaches work to improve insomnia still needs to be tested thoroughly. However, the current findings shed light on various aspects of this theory. Going back to the first study conducted, ‘nonjudging’ and ‘acting with awareness’ were the only mindfulness subscales associated with insomnia symptoms after controlling for the effect of the other subscales (‘nonreactivity’, ‘observing’ and ‘describing’). This is noteworthy because ‘acting with awareness’ relates to the step that has to be taken before a change in metacognitive stance is possible (as described in the Ong and colleagues model, 2012). It is therefore a very important aspect of

mindfulness. In fact, this is so important that some of the mindfulness research focusses exclusively on this aspect (see, for example, Waszczuk et al., 2015). Hence, it is not surprising that this aspect is key and that it is associated with insomnia symptoms. ‘Nonjudging’ may be considered to be related to equanimity in terms of being less attached to the negative thoughts and emotions and also as being part of ‘balance’ – i.e. allowing thoughts just to be thoughts without avoiding them or being overly drawn to them. This is also related to other cognitive theories, suggesting that people with insomnia may interact with their thoughts in a counter-productive way. For example, excessive worrying and telling oneself not to think in certain way can act as a sleep-interfering process as discussed in the hybrid cognitive-behavioural model (Lundh & Broman, 2000). For a detailed discussion of the hybrid cognitive-behavioural model see

1.3.1 Theories most relevant to this thesis – Cognitive models of insomnia.

Furthermore, the finding of the second study, i.e. that cognitive pre-sleep arousal is more strongly associated with insomnia symptoms than somatic pre-sleep arousal, is in line with previous literature (Gregory et al., 2008; Nicassio et al., 1985) and gives rise to the idea that mental arousal might be a particularly good target for the treatment of insomnia. This is also in line with Ong and colleagues’ theory (2012) and the principle of primary and secondary arousal as it underscores the idea that dealing differently with our thoughts might be a good angle to adopt in order to change other aspects of arousal. This finding also works well within the context of Harvey’s cognitive model of insomnia (2002) which emphasises that it is the cognitive arousal which reinforces the somatic arousal and that this would, therefore, be a useful point to address in the treatment of insomnia. Therefore, the current findings do, to some extent, support the hybrid cognitive-behavioural model (Lundh & Broman, 2000), the metacognitive model (Ong et al., 2012), and the cognitive model (Harvey, 2002). In the future, it may be

possible to combine the various cognitive models into one and thus extend the new model by adding genetic and environmental influences to the cognitive variables. However, the current findings should be re-evaluated first.

8.2.3 The relevance of the results to the treatment of insomnia

In terms of the development of the treatment of insomnia, different approaches have been adopted over time. As already discussed in detail in **Chapter 1: Introduction, 1.6.1 Psychotherapeutic treatment of insomnia**, assuming that the main problem with insomnia is increased arousal, early treatments adopted a behavioural approach, using relaxation techniques, behavioural intention, stimulus control or biofeedback to reduce arousal (Ong et al., 2012). The second wave of treatment approaches (CBT-I) included addressing cognitive arousal, i. e. targeting sleep-related cognitions by adding a cognitive therapy component (see, Espie, 2002; Lundh & Broman, 2000; for the distinction between cognitive and behavioural therapy, see **Chapter 5**). The more recent third wave of treatments for insomnia includes aspects of metacognition by adding elements of mindfulness-based cognitive therapy (MBCT), mindfulness-based stress reduction (MBSR) and acceptance and commitment therapy (ACT) to the previous approaches, effectively treating insomnia (see, for example, Dalrymple, Fioentino, Politi, & Posner, 2010; Garland, Zhou, Gonzalez, & Rodriguez, 2016; Gong et al., 2016; Hofmann et al., 2010; Khusid, Vythilingam, 2016; Ong, 2017). For a more detailed discussion, see, **1.6.1 Psychotherapeutic treatment of insomnia**. The findings of this PhD thesis could help to refine those third wave approaches. For example, the results of the first study showed that certain aspects of mindfulness seem to be more strongly related to insomnia than others. ‘Nonjudging of inner experiences’ and ‘acting with awareness’ may be particularly useful in treating insomnia and should therefore be further investigated. To exercise and note one’s own thoughts and to

challenge them may be particularly helpful for improving ‘Nonjudging of inner experiences’. For example, noting the thought “Of course I am not able to sleep now. I am incapable of doing the simplest task!” and then challenging it by saying to oneself “This is just a thought; this is not reality!” (Perlis, 2011). It may also be particularly helpful to include mindfulness exercises that practice focusing on the here and now during the day, as well as at bedtime in order to practice ‘acting with awareness’. For example, mindful eating or mindful walking during the day and simple exercises such as focusing on one’s breathing or performing a body scan (i.e. mentally scanning through the body from head to toe, noticing how it feels without sticking to any of the areas) (for more details, see Kabat-Zinn, 1994; Kabat-Zinn, 2003, Kabat-Zinn, 2013). This could give rise to new, more specific mindfulness-based approaches for treating insomnia. Cognitive pre-sleep arousal also showed a particularly strong association with insomnia symptoms and therefore may also be very useful to focus on even more intensely in the treatment of insomnia. Adopting a mindfulness and acceptance approach or a metacognitive stance towards cognitive arousal, i.e. noticing it without judging or being attached to it or attempting to force a change in cognition, may help to improve this aspect (Ong et al., 2012).

The theory that two subtypes of insomnia exist, i.e. one with short sleep duration and the other with normal sleep duration, was not supported when using subjective measures. However, due to the small sample size, it was not possible to formally test for differences in heritability, or differences in persistence over time. If we had found support for this theory, this could potentially have helped to further optimize insomnia treatment, as Vgontzas and colleagues (2013) claimed that the two subtypes may respond different to different types of treatment. They suggested that insomnia SSD may be best treated by focusing on decreasing physiological arousal and attempting to

increase sleep duration using pharmacological treatment, while insomnia NSD may be better treated by focusing on decreasing cognitive arousal and sleep misperception using CBT-I (Vgontzas et al., 2013).

8.3 Future directions

8.3.1 *Re-evaluation of the results*

Many of the findings of this PhD are novel. The genetic and environmental influences on overall mindfulness and its subscales (in an adult sample), overall pre-sleep arousal and its subscales cognitive and somatic pre-sleep arousal, as well as dysfunctional beliefs about sleep (and its subscales *beliefs about immediate consequences*, *beliefs about long-term consequences* and *beliefs about control*), have, for the first time, been estimated in an adult sample. In addition, the genetic and environmental influences on the association of these variables with insomnia symptoms and the environmental factors that influence dysfunctional beliefs about sleep were examined for the first time. Therefore, future research should re-evaluate the current results in different (and preferably larger) twin samples. Furthermore, it would be very interesting to consider all of these variables together in one large model – which would be possible in a much larger sample. To consider all variables together in one large model would be interesting because it would allow us to consider all associations of the key variables at once. If power was sufficient, this would give us more exact estimates. Furthermore, it would be possible to test in a common pathway model if there is a higher order latent variable via which the genetic, shared environmental and a non-shared environmental factors influence all these key variables. This latent variable would be in addition to the specific genetic, shared environmental and non-shared environmental factors that contribute to the variance of each phenotype independently.

If the common pathway model was the best fitting model, then this would tell us something about the structure of the association between all of the elements which are considered to be crucial in the development and maintenance of insomnia, as outlined in the meta-cognitive model of insomnia. In this way, a direct bridge would be built between the cognitive theories and behavioural genetics findings.

8.3.2 Adding an objective measure of sleep

One idea for being able to explore new and interesting research questions would be to add an objective measure of sleep. One suggestion for future work would be to invite back those participants who meet the criteria for insomnia (according to the ISQ) so that their sleep can be assessed using an objective measure. Depending on the funding available, this could either be done in a sleep laboratory using a PSG or in their own homes using actigraphy (as the research team already owns actigraphs).

8.3.3 Testing the theory of subtypes of insomnia (SSD versus NSD)

Adding an objective level to the existing data would also allow to assess the theory that two separate subtypes of insomnia (insomnia SSD and insomnia NSD) exist as independent subtypes on a new level. No previous study has yet considered testing the theory on an objective and a subjective level at the same time. This could enhance our knowledge of the concept of insomnia and would also help us to evaluate whether or not it would be useful to apply an objective measure in the context of diagnosing insomnia and whether or not it may be useful to include the two subtypes of insomnia in future diagnosis.

8.3.4 Adding treatment intervention

Members of the G1219 team have been working on a project examining genetic, environmental, demographic and clinical predictors of treatment outcome using the

SLEEPIO program (Denis et al., 2017). For future work, members of the team plan to include a CBT-I in a twin study to examine this question further. In addition, it would also be possible to test to what extent any improvement in insomnia symptoms were driven by an improvement in the variables crucial to insomnia, as assessed in this PhD thesis: overall mindfulness (and its subscales), overall pre-sleep arousal (and its subscales), overall dysfunctional beliefs about sleep (and its subscales), and in addition, maladaptive behaviours. Even though previous research has considered how some of those elements are improved when insomnia is treated (see, for example, Eidelman et al., 2016), a comprehensive study including all those elements would be interesting from the point of view of gaining a more holistic understanding.

8.3.5 Adding sleep hygiene

If more data on the G1219 is collected, it would be useful to include a measure of sleep hygiene such as the Sleep Hygiene Index (SHI; Mastin, Bryson, & Corwyn, 2006), as this is another element mentioned in the cognitive models of insomnia that was not assessed in wave 5 of the G1219 study (see, Espie, 2007; Harvey, 2002; Harvey, 2005; Lundh & Broman, 2000; Ong et al., 2012). This would be another interesting area of research that could help provide a better understanding of the concept of insomnia symptoms in the G1219 sample in the future.

8.3.6 Re-evaluation of mindfulness, ideas for a new measure

The FFMQ (Baer et al., 2006) that was used in the research conducted within the framework of this PhD is currently considered to be the most useful questionnaire for measuring mindfulness in a detailed way. However, it should be kept in mind that we have used an abbreviated version of the questionnaire. Furthermore, as already mentioned before (see **Chapter 3**), current research and theory leads to differing

opinions in terms of the understanding of the concept of mindfulness and how it should be measured. In spite of having reviewed a great deal of mindfulness literature at the beginning of this PhD, no clear picture emerged of what mindfulness actually is – the concept remained ambiguous. Reviewing literature related to the topic mindfulness from a Buddhist perspective (see, for example, Gutoski, 2011; Hesse, 1922; Rinpoche, 2008) helped to enhance the understanding of the topic by adding a philosophical level. The reviewed literature gives rise to the idea that the discrepancy in the concept and measures of mindfulness may be rooted in the issue that different ‘signs of mindfulness’ are measured rather than mindfulness itself. To illustrate this point, mindfulness is described (from a Buddhist perspective) as a deeper level of thinking that provides us with more profound thoughts and feelings and allows us to have some control over our mind and our emotions (Gyatsho & Alt, 2016). This change of thinking will inevitably lead to a shift of perspective when reflecting on our own behaviour, thoughts and value system which will in turn lead to a change in experience (for the ‘inner world’ as well as for the ‘world outside’) (Rinpoche, 2008). Considering the complexity and depth of the concept from this point of view, it seems challenging to be captured by a self-measure questionnaire. However, this does not mean that mindfulness, as it is conceptualised within Western research literature, is not valid or useful. It just represents a different approach which attempts to integrate a complex concept into a format that can be applied in research. It would be useful to try to broaden our knowledge by conducting even more research in this area. To acknowledge the complexity of this topic, it may be better to refer to it as ‘signs of mindfulness’ in context with assessment. Instead of avoiding the topic because of its complexity, effort should be made to further improve the existing measures, such as the FFMQ (Bear et al., 2006).

For example, Rinpoche (2008) mentions that empathy and kindness towards ourselves and others are part of being mindful. This is only partially captured by the subscale ‘non-judging’. It does not, for example, cover whether or not the inner dialogue is positive and empathic or rather more negative. This idea is supported by recent literature which confirms the association between positive effects and sleep but was mainly based on cross-sectional studies (Ong, Kim, Young, & Steptoe, 2016). It was pointed out that limited research in this area has been conducted on clinical populations and one criticism was that some of the studies included had methodological weaknesses (Ong et al., 2016).

Another important concept to consider in relation to mindfulness is that of ‘not grabbing’ or ‘non-striving’, in contrast to ‘being grateful’ for what we have or for what is happening (Rinpoche, 2008). This is related to the ‘nonreactivity’ subscale or to a general acceptance in a broader sense but it also shows some differences. It basically describes the inner attitude that things could be better. For example, we could achieve more, be better looking or have more money, etc. This attitude or feeling is completely independent of what we actually have. For example, a model could feel that he/she could be prettier or a rich person could feel that he/she needs more money – there are numerous examples of ‘grabbing’ or ‘striving’. If we apply this to the concept of insomnia, this would be reflected in thoughts such as “I woke up several times tonight, but I should be able to sleep better. Everyone else sleeps better than me. I should try harder.”, etc. Alternative thoughts of gratefulness would be reflected in thought patterns such as “Thankfully, I was able to sleep for a couple of hours. Even though I woke up several times, I was able to fall asleep again”.

Also, the realisation that everything is constantly changing and nothing stays the same forever seems to be a crucial idea that is related to mindfulness (Rinpoche, 2008;

Gutoski, 2011). This is also reflected in the fact that we hold on to the present and is evident in thoughts such as “I have insomnia right now and it is probably chronic. I will never be cured. I will always have insomnia...”. This is also reflected in the concept of equanimity in the metacognitive model which underlines the importance of adopting a beginners’ mind and to consider every night as a new night and detaching oneself from the sleep outcome (Ong et al., 2012).

Furthermore, the general focus on the self seems to be over-emphasised in individuals who are less mindful (Gutoski, 2011; Rinpoche, 2008). Therefore, this concept may also be usefully incorporated into the measure of ‘signs of mindfulness’. This would be reflected in thoughts such as “I am the only person who has insomnia.” or “Why am I sleeping so badly, while everyone else sleeps well?”.

The topic of how mindfulness could be better conceptualised and be better measured is substantial enough to fill another PhD thesis. Further research is needed to evaluate whether or not the elements suggested here (‘empathy/kindness’, ‘non-striving’, ‘acceptance of change’ and ‘letting go of the self/ego’) would be a useful addition to the ‘signs of mindfulness’ measure.

8.4 General limitations

8.4.1 Self-report measures

Some criticism has been levelled in relation to the use of self-measures (see, for example, Haeffel & Howard, 2010). For example, it could be questioned to what extent mindfulness can be measured by self-report (Grossman, 2011; Sauer et al., 2013). However, with the amount of data collected, it would have been difficult to try to get a more ‘objective measure’ of mindfulness (e.g. rating of behaviour by an experienced meditator) or to have used other methods such as interview methods, which may possibly have been able to assess mindfulness in a more exact way (Grossman, 2011;

Sauer et al., 2013). It should also be mentioned here that being mindful may in itself enhance the ability to self-reflect. This means that an experienced meditator who is very mindful may estimate his/her mindfulness to be lower than a rather inexperienced/‘mindless’ person would (Grossman, 2011; Sauer et al., 2013). Being aware of this issue, all analyses conducted here (which include the mindfulness measure) have controlled for meditation experience. Furthermore, to date, questionnaire-based measures are still the standard for measuring mindfulness (Grossman, 2011). Also, some researchers have argued that the FFMQ is the most comprehensive measure for measuring mindfulness within the general population as it covers various facets of mindfulness (Baer et al., 2006; Bergomi, Tschacher, & Kupper, 2013).

In relation to measuring insomnia symptoms, it should be pointed out that insomnia is a subjective complaint rather an objective one (see discussion below). Some researchers may still argue that sleep or insomnia symptoms were assessed by using self-report measures and not by also using an objective measure such as PSG in addition. For example, individuals with insomnia generally have a tendency to underestimate their sleep length (American Academy of Sleep Medicine, 2015; Feige et al., 2008). However, various studies have shown that subjective reports are very valuable in the context of insomnia, particularly when considering associated cognitive traits. For example, a study that compared different treatments for insomnia showed that changes in dysfunctional beliefs about sleep were less strongly associated with the *objective* (polysomnography) and more strongly associated with the *subjective* (sleep diary) measures of sleep (Morin et al., 2002). In a different study which used a clinical sample, dysfunctional beliefs about sleep were also found to improve following mindfulness-based cognitive therapy (MBCT) to treat chronic insomnia (Larouche et

al., 2015). Again, while no improvement in the *objective* sleep measure was found, a *subjective* improvement in sleep and insomnia symptoms was reported and was maintained in the 3-month follow-up (Larouche et al., 2015). It should be emphasised again that insomnia is often described as a ‘*subjective* complaint’ and, in current clinical practice, insomnia patients are typically assessed using *subjective* measures rather than *objective* ones (American Academy of Sleep Medicine, 2014; APA, 2013; WHO, 1992). The discrepancy between *subjective* and *objective* measures of sleep is not exclusive to insomnia symptoms; it can also be found in other disorders. For example, when measuring sleep duration in overweight individuals, the total sleep time measured by actigraphy differed by more than an hour from the *subjective* sleep time for one-third of the participants (O’Brien, Hart, & Wing, 2016).

Despite the criticism of self-report measures discussed, this approach of data collection was necessary, given the scope of the study (assessing numerous variables in a sample of many hundreds of participants) and is also currently considered to be the optimal approach to assessing certain phenotypes (e.g. insomnia symptoms). It should also be mentioned that all the self-report measures chosen for the analyses have frequently been used in previous studies and have been thoroughly evaluated (see **Chapter 1: Introduction** and the **methods sections of Chapters 3 to 7**). As the self-report measures could have artificially inflated the associations, future work should attempt to incorporate additional information (e.g. symptoms rated by other reporters, objective measures of sleep, etc.).

8.4.2 Age

The current findings are based on a sample of young adults (wave 5 of G1219 which includes individuals aged between 22 and 32 years, with a mean age of 25) and therefore only apply to this particular age group as heritability is a population statistic

(Plomin et al., 2013).

Age is a risk factor for insomnia as it is more common in older individuals (in terms of an increased prevalence in older adults) than in younger ones (APA, 2013; Lichstein et al., 2003; Ohayon, 2002). However, there is some inconsistency in these findings because some studies have found that the prevalence rate between the different age groups remains quite stable (see, for example, Chevalier et al., 1999). Furthermore, sleep changes over the course of a lifetime, which means that sleep duration decreases and subjective quality and sleep becomes more fragmented over the years (Blackwell et al., 2014; Chee, 2016; Lo, Groeger, Cheng, Dijk, & Chee, 2016; Sivertsen et al., 2015). Therefore, future research should consider other age groups as well.

8.4.3 Twin sample

The twin design has some limitations (Plomin et al., 2013), which are discussed in detail in **Chapter 2: Methods, 2.3.1 Assumptions and associated limitations**.

8.4.4 Non-clinical sample

The current findings are based on a population-based sample and not on a clinical sample and they focus on insomnia symptoms rather than on the clinical diagnosis of insomnia (except for the last study conducted, see **Chapter 7**). This makes the findings applicable to the general population. Insomnia symptoms are highly prevalent in the general population (see, for example, Ohayon, 2002; Roth et al., 2011), therefore research in this area is needed. The term ‘insomnia symptom’ was used rather than just referring to insomnia in order to underline the fact that the sample was a non-clinical one. The term ‘Insomnia’ was used only when participants actually met the diagnostic criteria of the DSM-IV (APA, 2000) as identified by the self-measure – the Insomnia Severity Questionnaire (ISQ, Okun et al., 2009 – which was based on the

DSM version at the time). Future research should re-evaluate the results in a clinical sample. It would also be informative to use a mindfulness treatment intervention (see also description under **8.4.4 Adding treatment intervention**) when considering a clinical sample.

8.4.5 Sample size

A further limitation relates to the sample size. Wave 5 of the G1219 sample was relatively small for a twin study. This meant that some of the confidence intervals were wide so further work using large samples would be of value. However, the results presented here were largely in line with previous research (see **discussion sections of the empirical Chapters 3 to 7**). Furthermore, using methods such as comparing the ACE model to the E model allowed us to draw conclusions about familial influence on the traits analysed when it could not be determined whether the influence was due to additive genetic or shared-environmental factors.

8.4.6 Cross-sectional data

Except for the last study, all analyses focused exclusively on wave 5 of the G1219 sample. The reason for this is that the key variables (mindfulness, pre-sleep arousal and dysfunctional beliefs about sleep) were only assessed during that wave. The conclusions that can be drawn from cross-sectional data are limited in terms of direction of effects or causality. In order to establish causality, longitudinal-data and/or treatment intervention (for example, by using a wait list control) would be needed in order to allow to conclude to what extent an improvement in one or more of the parameters would result in an improvement in insomnia symptoms (see description under **8.4.4 Adding treatment intervention**). According to the counterfactual model of causal effects, to guarantee that there really is a causal order in the factors considered (which

need to be measurable), the best approach is to conduct an experiment and measure the baseline and the outcome after the manipulation (such as treatment intervention, ideally with random allocation to the groups) has happened (for a more detailed discussion see Höfler, 2005). It should be pointed out that measuring ‘real life’ (also including confounding variables) in research does not always provide us with the perfect conditions and that we have to work within the constraints that are provided in the given situations (Hill, 1965).

According to the cognitive theories as discussed earlier, we also have to keep in mind that the various factors are likely to interact and influence each other rather than being linked in a one-directional way (see, Harvey, 2002; Morin, 1993; Ong et al., 2012). Therefore, it would be less likely to find a straightforward, one-directional causality between the different traits considered in the model anyway.

8.4.7 Additional factors

Additional factors likely to be important in insomnia symptoms (see, for example, **Figure 1.1** in the Introduction Chapter). The list of other possible candidates that could influence insomnia is long and includes, for example, stress and factors associated with mental health in general (see, for example, Dewa et al., 2017; Elder et al., 2014; Ohayon, 2002; Roth et al., 2011; Roth & Roehrs, 2003). Nevertheless, the current results do add to our understanding of the key elements involved in developing and maintaining insomnia. In order to establish direction of effects and possible causal links, longitudinal-data of a treatment intervention (preferably conducted with a wait list control) would be needed to allow for conclusions to be drawn about which parameters are related to an improvement in insomnia symptoms. This type of study has been conducted in the past but research typically focuses on single elements rather than attempting to obtain a more holistic picture. For example, irrespective of the therapy

method applied, it was found that the greater the change in dysfunctional beliefs about sleep during treatment, the greater the improvement in insomnia symptoms (Eidelman et al., 2016).

8.5 Conclusion

This PhD thesis represents one of the very first pieces of work aimed at advancing our knowledge about cognitive models of insomnia by examining key variables in a genetically sensitive design. The G1219 sample provided the opportunity to conduct a series of original studies that investigated the concept and aetiology of insomnia by illuminating the genetic and environmental influences on the key traits that play an important role in developing and maintaining insomnia (including overall mindfulness, overall pre-sleep arousal and overall dysfunctional beliefs about sleep) and their subscales, as well as their association with insomnia symptoms. In addition, the work conducted in this thesis aimed to test the theory about short versus normal sleep length insomnia using a subjective measure of insomnia but could not be confirmed. The findings show that nature and nurture play an important role in influencing insomnia, once more underlying the importance of behavioural genetics research. The findings also demonstrate how valuable it is to illuminate current theory from different angles and to integrate new approaches in order to gain a deeper understanding of the concept of insomnia. Future research would benefit from using an objective measure of sleep, considering other age groups, exploring additional factors likely to be important in insomnia symptoms and using longitudinal data to advance our knowledge of insomnia even further. Researchers should also feel inspired to test the theory by Vgontzas and colleagues (2013) in a systematic and comprehensive way (by using a strict cut-off for defining insomnia with short sleep length).

Working on this PhD thesis has brought forward a whole range of interesting and novel findings. The results make a valuable contribution to the field of sleep research by providing insight into the roots of insomnia symptoms and the mechanisms underlying the development and maintenance of insomnia symptoms. The findings have helped to broaden our understanding of the concept and the current cognitive theories of insomnia. They will stimulate further research and will hopefully help to improve the diagnosis and treatment of insomnia in the future.

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APPENDIX A: Comparison of the correlated factors solution and the independent pathway model for three variables

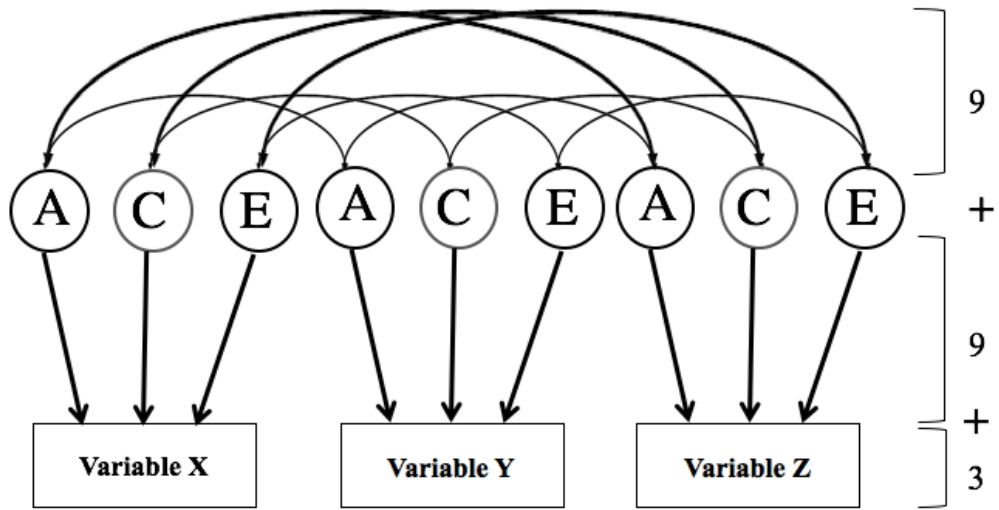


Figure A.1 Correlated factors solution, three variables

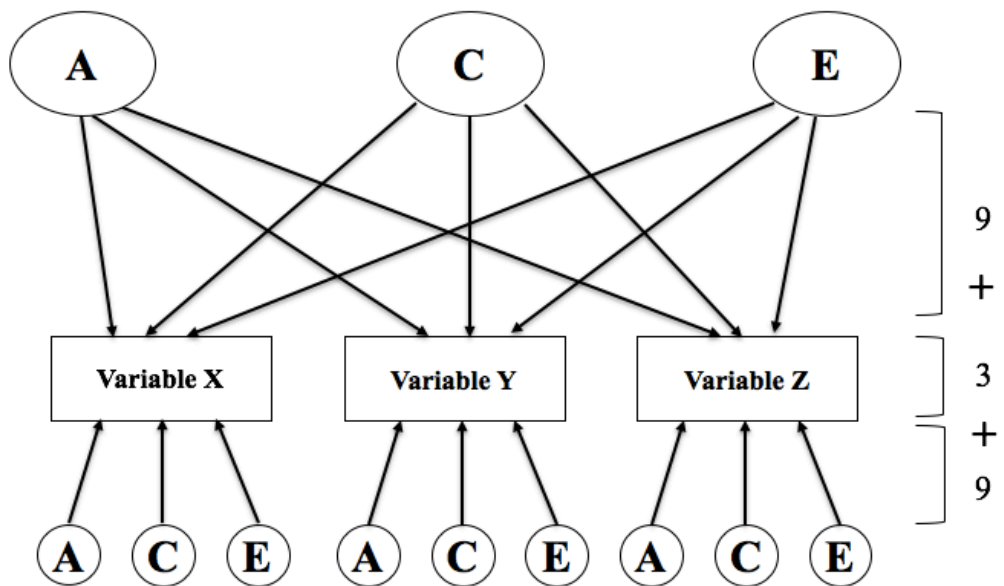


Figure A.2 Independent pathway model, three variables

APPENDIX B: Items included from the FFMQ

Table B.1 Items included from the FFMQ (Baer et al., 2006, pp. 34-35) to measure the five sub-scales of mindfulness

<i>Sub-scale</i>	<i>Items included</i>
'Nonreactivity'	<ol style="list-style-type: none"> 1. "I perceive my feelings and emotions without having to react to them" 2. "I watch my feelings without getting lost in them" 3. "Usually when I have distressing thoughts or images, I am able just to notice them without reacting" 4. "Usually when I have distressing thoughts or images, I "step back" and am aware of the thought or image without getting taken over by it" 5. "Usually when I have distressing thoughts or images, I just notice them and let them go"
'Observing'	<ol style="list-style-type: none"> 6. "When I'm walking, I deliberately notice the sensations of my body moving" 7. "When I take a shower or a bath, I stay alert to the sensations of water on my body" 8. "I pay attention to sensations, such as the wind in my hair or sun on my face" 9. "I pay attention to sounds, such as clocks ticking, birds chirping, or cars passing"
'Acting with awareness'	<ol style="list-style-type: none"> 10. "I find it difficult to stay focused on what's happening in the present" 11. "It seems I am "running on automatic" without much awareness of what I'm doing" 12. "I rush through activities without being really attentive to them" 13. "I find myself doing things without paying attention"
'Describing'	<ol style="list-style-type: none"> 14. "I'm good at finding the words to describe my feelings" 15. "I can easily put my beliefs, opinions, and expectations into words" 16. "It's hard for me to find the words to describe what I'm thinking" 17. "I have trouble thinking of the right words to express how I feel about things"
'Nonjudging of inner experience'	<ol style="list-style-type: none"> 18. "I believe some of my thoughts are abnormal or bad and I shouldn't think that way" 19. "I make judgments about whether my thoughts are good or bad" 20. "I tell myself I shouldn't be thinking the way I'm thinking" 21. "I think some of my emotions are bad or inappropriate and I shouldn't feel them"

Note: The original version of the FFMQ (Baer et al., 2006) contains 39 items, for the current study it was shortened to 21 items. The four items with the highest factor loading for each subscale were selected. Sub-scale 'nonreactivity to inner experience' had 3 items with the same factor loading, therefore five items were included for this scale.

APPENDIX C: Comparison of the ISI and the ISQ

Table C.1 Comparison of the ISI (Morin et al., 2011) and the ISQ (Okun et al., 2009)

	ISI (Morin et al., 2011, Bastien et al., 2001, p. 299)	ISQ (Okun et al., 2009, p. 50)
Items	1. "Difficulty falling asleep"	1. "Difficulty falling asleep"
	2. "Difficulty staying asleep"	2. "Difficulty staying asleep"
	3. "Problems waking up too early"	3. "Frequent awakenings from sleep"
	4. "How satisfied/dissatisfied are you about your current sleep pattern?"	4. "Feeling that your sleep is not sound"
	5. "How noticeable to others do you think your sleep problem is in terms of impairing the quality of your life?"	5. "Feeling that your sleep is unrefreshing"
	6. "How worried/distressed are you about your current sleep problem?"	6. "Have your sleep difficulties interfered with your daily life?"
	7. "To what extent do you consider your sleep problem to interfere with your daily functioning currently?"	

Note: In the published version of the ISQ, eight additional items relating to the effect on daily life are also included, which are summarised under item 6 here.

APPENDIX D: The correlated factors solution for overall mindfulness and symptoms of insomnia, depression and anxiety

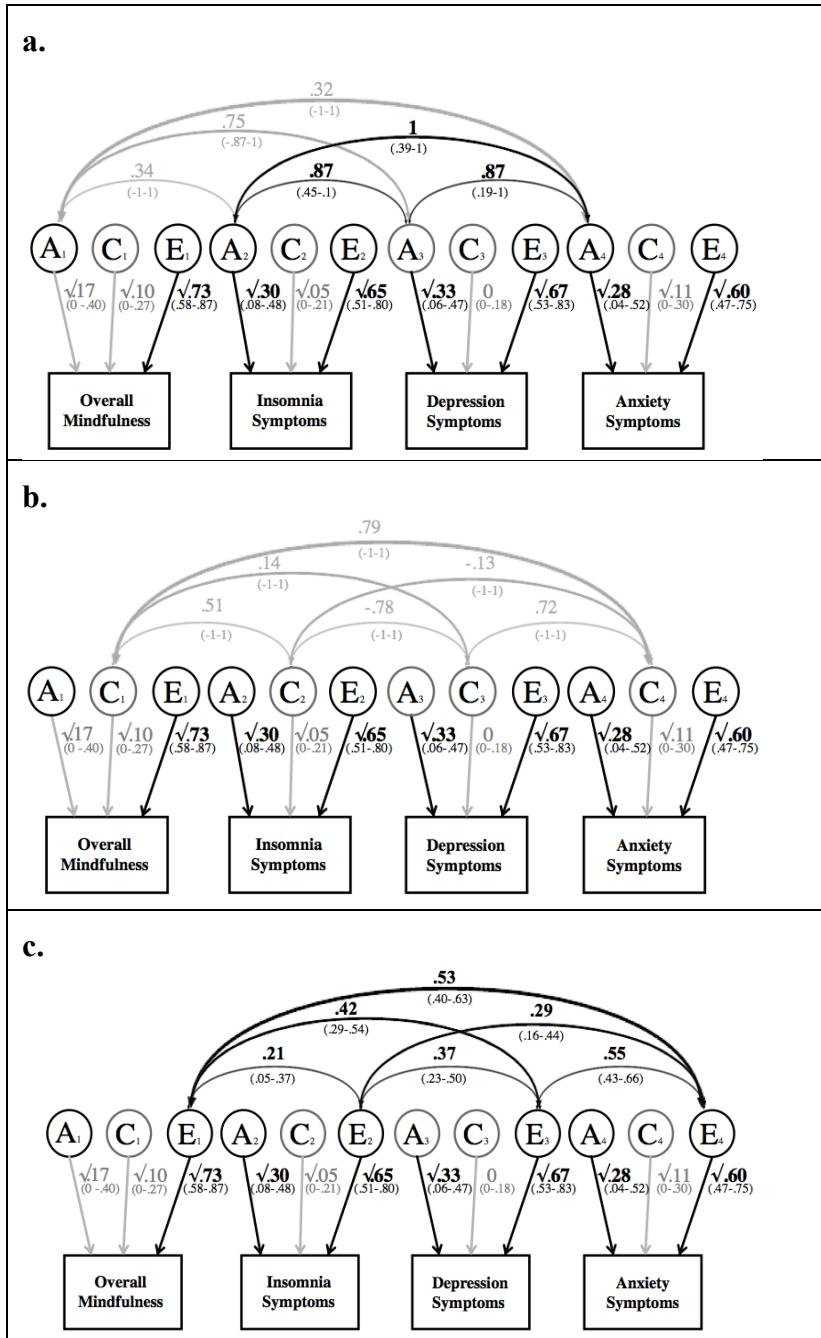
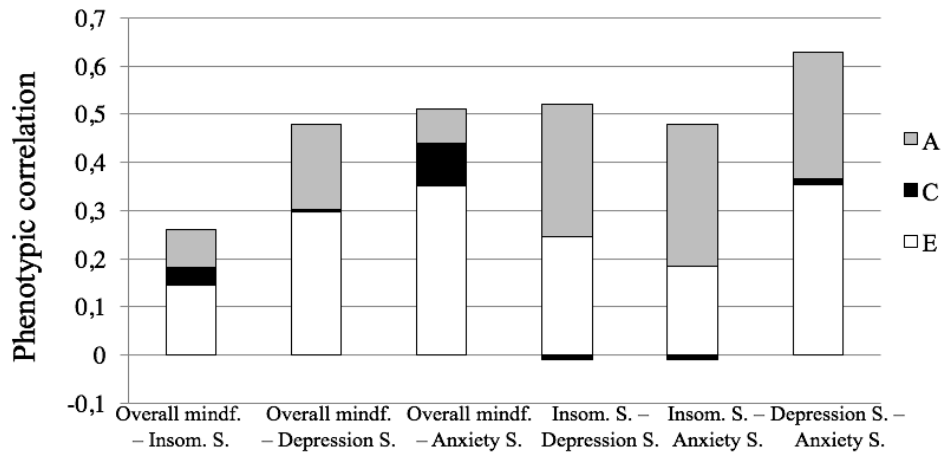


Figure D.1 Path diagram of the correlated factors solution, including overall mindfulness, insomnia symptoms, depression and correlations

Note: A = additive genetic, C = shared environmental; E = non-shared environmental. Significant paths are shown in black. Paths with confidence intervals spanning 0 are depicted in grey. Overall mindfulness = overall score of mindfulness (FFMQ), reverse coded, higher score indicating lower mindfulness; Insomnia Symptoms = insomnia symptoms (ISQ), higher scores indicating more insomnia symptoms; Depression Symptoms = symptoms of depression (MFQ), higher scores indicating more symptoms of depression; Anxiety Symptoms = symptoms of anxiety (RCADS), higher scores indicating more symptoms of anxiety; part a. shows the genetic correlations; part b. shows the shared-environmental correlations; part c. shows the non-shared environmental correlations



Correlation between phenotypes

Figure D.2 Relative contributions of A, C and E to the overall phenotypic correlations

Note: Overall mindf. = overall score of mindfulness, (FFMQ), reverse coded, higher score indicating lower mindfulness; Insom. S. = insomnia symptoms (ISQ), higher scores indicating more insomnia symptoms; Depress. S. = symptoms of depression (MFQ), higher scores indicating more symptoms of depression; Anxiety S. = symptoms of anxiety (RCADS), higher scores indicating more symptoms of anxiety

APPENDIX E: Items included in the PSAS

Table E.1 List of items included in the PSAS (Nicassio et al., 1985, p. 266)

Items included in Somatic Pre-sleep Arousal

1. "Heart racing, pounding or beating irregularly"
 2. "A jittery, nervous feeling in your body"
 3. "Shortness of breath or labored breathing"
 4. "A tight, tense feeling in your muscles"
 5. "Cold feeling in your hands, feet or body in general"
 6. "Have stomach upset (knot or nervous feeling in stomach, heartburn, nausea, gas etc.)"
 7. "Perspiration in palms of your hands or other parts of your body"
 8. "Dry feeling in mouth or throat"
-

Items included in Cognitive Pre-sleep Arousal

9. "Worry about falling asleep"
 10. "Review or ponder events of the day"
 11. "Depressing or anxious thoughts"
 12. "Worry about problems other than sleep"
 13. "Being mentally alert, active"
 14. "Can't shut off thoughts"
 15. "Thoughts keep running through your head"
 16. "Being distracted by sounds, noise in the environment (e.g. ticking of clock, house noises, traffic)"
-

APPENDIX F: The independent pathway model for cognitive pre-sleep arousal, somatic pre-sleep arousal and symptoms of insomnia

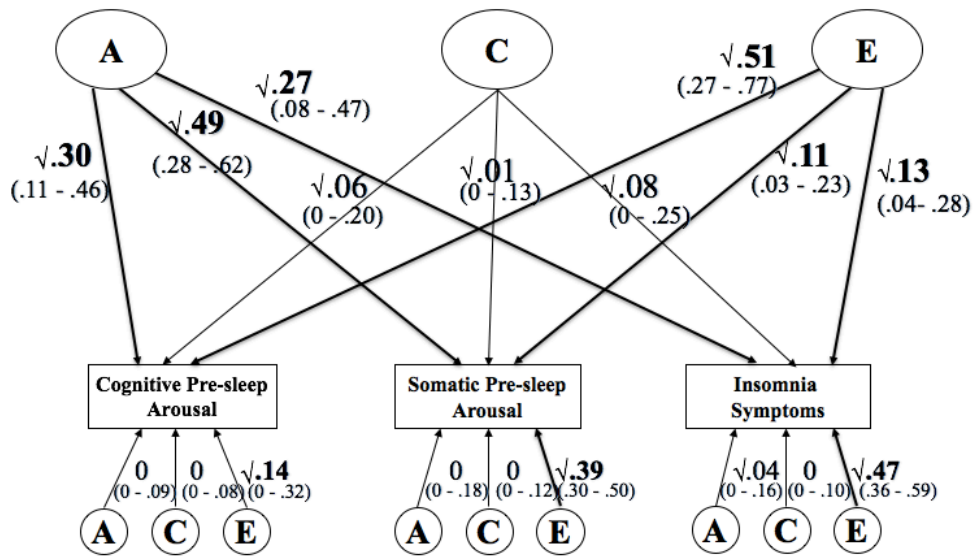


Figure F.1 Path diagram of the independent pathway model, including cognitive pre-sleep arousal, somatic pre-sleep arousal and symptoms of insomnia

Note: Significant paths and estimates are presented in bold, see brackets for 95% confidence intervals. A = additive genetic influence; C = shared environmental influence; E = non-shared environmental influence; Cognitive pre-sleep arousal = cognitive pre-sleep arousal (PSAS subscale), higher score indicating higher cognitive pre-sleep arousal; Somatic pre-sleep arousal = somatic pre-sleep arousal (PSAS subscale), higher score indicating higher somatic pre-sleep arousal; Insomnia Symptoms = insomnia symptoms (ISQ), higher scores indicating more insomnia symptoms

APPENDIX G: Items included in the DBAS-10

Table G.1 Items included in the DBAS-10 (Morin et al., 1993; Espie et al., 2000, p.145)

DBAS factor I – *Beliefs about the immediate negative consequences*

1. (Item 1) “I need 8 hours of sleep to feel refreshed and function well during the day.”
2. (Item 2) “When I don't get the proper amount of sleep on a given night, I need to catch up on the next day by napping or on the next night by sleeping longer.”
3. (Item 10) “After a poor night’s sleep, I know that it will interfere with my daily activities on the next day.”
4. (Item 12) “When I feel irritable, depressed, or anxious during the day, it is mostly because I did not sleep well the night before.”
5. (Item 21) “When I feel tired, have no energy, or just seem not to function well during the day, it is generally because I did not sleep well the night before.”

DBAS factor II – *Beliefs about the long-term negative consequences*

6. (Item 5) “I am concerned that chronic insomnia may have serious consequences on my physical health.”
7. (Item 8) “I am worried that I may lose control over my abilities to sleep.”
8. (Item 17)”When I sleep poorly on one night, I know it will disturb my sleep schedule for the whole week.”

DBAS factor III – *Beliefs about the need for control*

9. (Item 7) “When I have trouble falling asleep or getting back to sleep after night-time awakening, I should stay in bed and try harder.”
10. (Item 22) “I get overwhelmed by my thoughts at night and often feel I have no control over this racing mind”

APPENDIX H: Fit statistics of additional multivariate analyses

Table H.1 Full table of fit statistics for all multivariate genetic model fitting analyses

	ep	-2LL	df	AIC	Δ -2LL	Δ df	<i>p</i>
<i>Model 1: Overall DBAS and symptoms of insomnia</i>							
Saturated	42	11904.61	1638	8628.61	-	-	-
ACE	11	11941.04	1669	8603.04	36.43	31	0.23
<i>Model 2: DBAS factor I, DBAS factor II, DBAS factor III and insomnia symptoms</i>							
Saturated	132	20732.85	3223	14286.85	-	-	-
Correlated Factors Solution	34	20865.04	3321	14223.04	132.19	98	0.01
Independent Pathway	28	20871.19	3327	14217.19	6.15	6	0.41
Common Pathway	23	20883.69	3333	14217.69	12.51	6	0.05

Note: All analyses focus on transformed data, outliers deleted with age and sex regressed out. ep = estimated parameters; -2LL = $-2 \times (\log \text{likelihood})$; df = degrees of freedom; $\Delta\chi^2$ = change in chi-square statistic; Δdf = change in degrees of freedom; AIC = Akaike's Information Criterion statistic; Saturated = full model, A = additive genetic, C = shared environmental; E = non-shared environmental. Model 1: The fit statistics of the ACE model is relative to the saturated model. Model 2: The fit statistics of the correlated factors solution is relative to the saturated model. The fit statistics of the independent pathway model is relative to the correlated factors solution. ACE common pathway model is relative to the independent pathway model. Phenotypes: Overall DBAS = overall dysfunctional beliefs about sleep; *DBAS factor I* = beliefs about the immediate negative consequences of insomnia (DBAS subscale); *DBAS factor II* = beliefs about the long-term negative consequences of insomnia (DBAS subscale); *DBAS factor III* = beliefs about the need for control over insomnia (DBAS subscale) – higher scores indicating more dysfunctional beliefs about sleep. Please note that the fit of the independent pathway model and the common pathway model cannot be interpreted as valid results, because the univariate analyses of the overall DBAS, beliefs about immediate consequences, beliefs about long-term consequences and beliefs about control did not indicate familiarity.

APPENDIX I: Items included in the measure of relationship satisfaction and relationship cohesion

Table I.1 Items included in the measure of relationship satisfaction and relationship cohesion (Spanier, 1976, p.14-15)

Relationship satisfaction

1. "How happy are you in your relationship?"
2. "You think that, in general, things between you and your partner are going well?"
3. "You and your partner get on each other's nerves?"
4. "You and your partner have an argument?"
5. "You regret you started the relationship?"
6. "You and your partner discuss or consider divorce, separation, or ending your relationship?"

Relationship cohesion

7. "Have a stimulating exchange of ideas"
 8. "Laugh together"
 9. "Calmly discuss something"
 10. "Work together on a project"
 11. "Do you and your partner engage in any outside interests together?"
-

APPENDIX J: Items included in the measure of negative life events

Table J.1 Items included in the measure of negative life events (Coddington, 1984; Brugha et al., 1985, p.194)

Dependent negative life events

1. "Separation due to marital difficulties"
2. "Serious problem with a close friend, neighbor or relative"
3. "Problems with police or court appearance"
4. "Unemployed or seeking work for more than one month"
5. "Suspension/expulsion from college or university"
6. "Have become involved in drugs"
7. "Had a major financial crisis"
8. "Break up of a steady relationship"
9. "Failed end of year exams"
10. "Start of a new problem between you and your parents"
11. "Been sacked from job"
12. "Been invited by a friend to break the law"
13. "Have failed to achieve something you really want"

Independent negative life events

1. "Been in hospital with a serious illness or injury"
 2. "A parent hospitalized for a serious illness or injury"
 3. "Death of a second degree relative (e.g. grandparent)"
 4. "A sibling hospitalized for a serious illness or injury"
 5. "Death of a parent"
 6. "Had something valuable lost or stolen"
 7. "Death of a sibling"
 8. "Death of a close friend"
 9. "Death of a child or spouse"
 10. "A child or spouse hospitalized for a serious illness or injury"
-

APPENDIX K: Additional regression analyses

Table K.1 Additional regression analyses predicting a) Absolute DBAS score (full sample) and b) MZ differences, controlling for genetic influence and shared environmental influence on the environmental measures – run for sensitivity analyses

	a) Absolute DBAS score analysis			b) MZ differences analysis		
	R ²	β	<i>t</i>	R ²	β	<i>t</i>
Alcohol (How often?)	.02	-.13	-.25	.05	-2.74	-.96
Alcohol (no. of drinks)	.02	.58	.96	.04	-1.51	-.55
Drug use (yes/no only)	.02	.41	.76	.08	-6.56	-3.41**
Smoking status (yes/no only)	.02	-.94	-1.76	.06	5.49	1.81

Note: * $p < .05$; ** $p < .01$. Significant values are displayed in **bold**. Multiply p-value by 11, to control for multiple testing using Bonferroni correction.