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Sleep quality, insomnia and internalising difficulties in adolescents: insights from a twin study

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Abstract:

Objectives: There is a well-established association between poor sleep quality and internalising traits. This relationship has previously been studied using a twin design. However, when it comes to adolescence, there is a paucity of twin studies that have investigated this relationship, despite the importance of this developmental stage for both the development of poor sleep quality and internalising symptoms. Additionally, anxiety sensitivity, which is commonly associated with poor sleep quality, has not been studied in this context. Our objective was to estimate genetic and environmental influences on the relationships between insomnia, poor sleep quality and internalising symptoms in adolescence.

Methods: Insomnia, poor sleep quality, depression, anxiety and anxiety sensitivity traits were measured in a sample of 5,111 twin pairs from the Twins Early Development Study, born between 1994 and 1996 (mean age 16.32y (SD=0.68)).

Results: A moderate proportion of the variance for the different variables (.29-.42) was explained by genetic factors. Associations between sleep and internalising variables were moderate (r = .34 - .46) and there was a large genetic overlap between these variables (rA= 0.51 – 0.73).

Conclusion: This study adds novel information by showing that there are large genetic correlations between sleep disturbances and internalising symptoms in adolescence.

Keywords: adolescence, anxiety, depression, insomnia, internalising, sleep, twins.

Significance statement:

There is a paucity of information about the aetiology of the relationship between sleep and internalising traits in adolescents, despite this being an important period often characterised by changes in and the development of both sleep and internalising problems. This study included several measures of sleep and internalising symptoms and is the first study to investigate the relationship between sleep and anxiety sensitivity using a behavioural genetic approach. This large twin study allows us to examine genetic and environmental influences on these phenotypes and the extent of genetic and environmental overlap between variables. The results indicate large genetic overlap between sleep and internalising symptoms.

Introduction

Symptoms of sleep problems, depression and anxiety are of significant concern in adolescence as they are associated with poor outcomes.[1-4] For example, poor sleep quality and sleep problems are risk factors for ill health, poor cognitive functioning and accidents among other adverse consequences.[5-7] Anxiety and depression are associated with poor academic achievement, drug and alcohol consumption and suicidal ideation.[1,8]

Sleep and depression

There is a robust relationship between symptoms of insomnia and depression.[9,10] Other measures of sleep have also been linked with depression. For example, sleep quality is a broad concept which includes several measures such as sleep duration, sleep latency, sleep efficiency and sleep disturbances, among others.[11] Studies that have focused on the relationship between sleep quality and depression have reported a strong relationship in adolescents.[12,13]

Sleep and anxiety

As with depression, anxiety measures are also associated with insomnia symptoms and poor sleep quality.[9,14-16] Anxiety sensitivity can be defined as fear of the physical symptoms of anxiety.[17] This measure has also been linked to sleep problems,[18,19] and targeting anxiety sensitivity has been proposed to be an effective strategy for reducing insomnia symptoms.[20] Although anxiety sensitivity might be an important predictor of sleep disturbances,[18,21] and previous studies have shown that anxiety and anxiety sensitivity are strongly correlated but not completely overlapping,[22] there are no studies that have investigated genetic and environmental influences on the association between sleep and anxiety sensitivity as compared to anxiety.

Genetics of sleep quality, insomnia, depression and anxiety

Heritability typically explains around 30-40% of the variance in sleep quality[23-25]. There are also substantial genetic influences on insomnia symptoms, with heritability values around 20-50%.[26-29] Regarding depression and anxiety, approximately 30-50% of the variance is typically explained by genetic factors.[9,29-32] Studies examining the overlap between these variables have found that there is a substantial (sometimes complete) genetic overlap, with genetic correlations all above .5.[9,29,30,33]

Adolescence is a period of great change for sleep. During this stage of life, bedtime typically becomes later and it can be more difficult to wake early.[34] This shift in sleep timing can result in insufficient sleep or even symptoms of sleep disorders such as insomnia.[35,36] Poor sleep quality and sleep disorders are common during adolescence.[37,38]

Psychopathology begins early in life[39] and the move into adolescence appears to be a time of vulnerability for increased internalising symptoms.[40,41] For example, anxiety and depression levels can increase dramatically during this period.[42]

Despite well-established associations between poor sleep and internalising traits, and the importance of adolescence as a period of vulnerability for the development of these overlapping difficulties, there is a paucity of work aimed at understanding these associations from a behavioural genetic perspective at this stage of life. Behavioural genetic work addressing these questions has tended to focus on children[43,44] or adults,[30,33] or spans developmental stages[45]. Heritability is a population statistic, and estimates can vary depending on multiple factors, including the age of participants.[46] Thus, our main objective is to estimate genetic and environmental influences on the relationship between insomnia, poor sleep quality and internalising symptoms, employing a sample of adolescent twins, at which age both sleep problems and internalising disorders are common.. Our main hypothesis is that, as found to occur at other developmental stages, there is substantial genetic overlap between sleep disturbances and internalising symptoms. Understanding more about the pattern and aetiology of associations between these traits holds the promise of informing prevention techniques for the development of these common difficulties. The genetic and environmental influences on the associations between anxiety sensitivity and insomnia, and poor sleep quality, have not been examined previously. This is an important omission because anxiety and anxiety sensitivity could relate differently to insomnia and poor sleep quality. Our second aim was therefore to examine, for the first time, the aetiology of these associations.

Methods

Participants

The sample comprised 10,222 twins participating in the Twins Early Development Study (TEDS), which is a community-based, longitudinal study of twins born in England and Wales between 1994-1996.[47] This sample is reasonably representative of the general population in terms of ethnicity, parental education and employment status.[48] Zygosity was established either through a DNA test or a questionnaire assessing physical similarity. This questionnaire has an accuracy of over 95%.[49]

Analyses reported here focus on the data collection at age 16. At this wave, 10,874 families were contacted and invited to participate, and 5144 families (47.3%) provided data. Data from 33 families were excluded since there was no information on zygosity. Hence data from 5111 families were analysed (10,222 participants). The differences between participating and non-participating families have been reported elsewhere.[50] The sample was 44.8% male and 35.6% MZ (Table 1). Sensitivity analyses were conducted excluding an additional 249 families where twins had a severe medical disorder or there had been severe perinatal complications (low birth weight; short gestational age; maternal drinking during pregnancy; a long period of special care after birth; a long stay in hospital after birth). This resulted in similar results (estimates varied by up to 3%) so the full sample is reported here.

Measures

Sleep quality was measured using the Pittsburgh Sleep Quality Index (PSQI). The PSQI is a widely used questionnaire which assesses sleep quality referencing the previous month. It has 7 sub-scales: 1) subjective sleep quality; 2) sleep latency; 3) sleep duration; 4) habitual sleep efficiency; 5) sleep disturbances; 6) use of sleeping medication and 7) day time dysfunction. These seven sub-scales yield a global score ranging from 0-21, where higher scores represent poorer sleep quality.[51] For this study we focused on the global score.

The PSQI has shown adequate psychometric properties, high correlations with objective measures, and previous studies have also validated the single-factor scoring structure.[52-54] In our sample, the Cronbach's alpha for the global score was .70.

Insomnia was measured using the Insomnia Severity Index (ISI). The ISI is a 7-item questionnaire generating scores ranging from 0-28.[55] The ISI enquires about symptoms of insomnia in the previous month. This measure has demonstrated adequate psychometric properties, and a cut-off of 10 has been shown to provide specificity and sensitivity for detecting individuals with insomnia.[56] The Cronbach's alpha in our sample was .89.

Depression was measured using the Short Mood and Feelings Questionnaire (SMFQ). SMFQ has 13 items ranging from 0 (not true) to 2 (true) and these scores are summed to produce the total score which ranges from 0 to 26. Questions assess key symptoms of depression such as "I felt miserable or unhappy" and focus on the previous two weeks.[57] SMFQ has good psychometric properties.[58,59] Of note, this questionnaire does not contain sleep items. In this sample, Cronbach's alpha was .88.

Anxiety was measured using the emotional symptoms/anxiety domain of the Strengths and Difficulties Questionnaire (SDQ). The SDQ is a five-dimension questionnaire which measures the core domains of psychopathology in children and adolescents.[60] The questionnaire consists of 25 items (5 for each subscale). This questionnaire has shown good psychometric properties and validity.[61] For this study we only focused on the anxiety subscale (5 items). The Cronbach's alpha in this sample for the SDQ anxiety subscale was .69.

Anxiety Sensitivity was measured using the Children's Anxiety Sensitivity Index (CASI).[62] This measure has 18 items which measure fear of the physical symptoms of anxiety. The CASI has good internal consistency and validity.[62,63] In the current study, the scale had a Cronbach's alpha of .86.

Statistical analyses

Twin studies are a useful tool for research.[64] The classical twin design can be summarized as follows: the variance of one phenotype can be decomposed into genetic and environmental factors making use of the difference between MZ twins (who share

100% of their DNA) and DZ twins (who share on average 50% of their segregating DNA).[65] Genetic influences can be divided into those that are additive (A; the sum of allelic effects across all loci) and non-additive (D; the effects of genetic dominance). On the other hand, environmental contributions are shared (C; influences that make twin pairs raised in the same family similar to each other) and non-shared (E, effects that make family members less alike).[66]

It is not possible to estimate C and D simultaneously using only data from twins reared together. Therefore, the selection of C or D is made based on the pattern of correlations between MZ and DZ twins. An ACE model is selected when the DZ twin correlation is greater than half of the MZ twin correlation, and an ADE model is selected when the DZ twin correlation is less than half of the MZ correlation (i.e., non-additive genetic effects are implicated if the MZ twins are more than twice as similar as DZ twins[66,67]).

One univariate model (either ACE or ADE as indicated by the data) was fitted to each of the variables. Nested models (i.e., AE, CE, E) were also fitted to check if one (or two) components could be dropped without a significant decrease of model fit. The fit of the different models and submodels was checked using the likelihood-ratio chi-square test and the Akaike's information criterion (AIC).[68] Assumptions of twin models were checked in the saturated models in order to check for differences in means and variances between the different groups: MZ/DZ twins and twin1/twin2 (randomly selected within each pair).

We also fitted a multivariate correlated factor model. This model allows the estimation of genetic and environmental influences on both individual variance and also sources of covariance between the phenotypes. Put differently, the model allows us to estimate aetiological correlations which inform us of the extent to which the latent variables (A, C/D and E) correlate across two traits. These correlations (i.e., rA rC, rD, rE) can vary from -1 to 1, where 0 would mean no overlap, and 1 complete overlap. Using these statistics, we can also calculate bivariate heritability, which is the proportion of the phenotypic covariance explained by A. Equivalent bivariate shared environment and bivariate nonshared environment estimates can also be derived.

Descriptive analyses were performed using the statistical software SPSS v.22. Twin analyses were conducted using the package OpenMx in R.[69] Age and sex were used as covariates. All the variables were +1 log transformed to better meet the assumption of normality and reduce positive skew (variables ranged from 0.76 to 1.96 before transformation and from -0.67 to 0.22 after transformation).

Results

Descriptive statistics

Table 1 presents descriptive statistics. Females, as compared to males, reported poorer sleep quality (t[7520]= 9.77; p<.001; $\bar{x}_{female=4.96}$; $\bar{x}_{male=4.34}$; Cohen's d=0.23), higher levels of insomnia (t[7849]= 10.20; p<.001; $\bar{x}_{female=4.29}$; $\bar{x}_{male=3.33}$; Cohen's d=0.23) and greater levels of depression (t[10014]= 20.43; p<.001; $\bar{x}_{female=4.41}$; $\bar{x}_{male=2.69}$; Cohen's d=0.41), anxiety (t[10128]= 35.11; p<.001; $\bar{x}_{female=3.40}$; $\bar{x}_{male=1.94}$; Cohen's d=0.70) and anxiety sensitivity (t[10130]= 29.97; p<.001; $\bar{x}_{female=9.41}$; $\bar{x}_{male=6.13}$; Cohen's d=0.60). There were small but significant differences between MZ and DZ twins in symptoms of sleep quality, insomnia and depression. However, the effect sizes were small (lower than .07).

Univariate twin models

Table 2 shows all the univariate models. Intrapair correlations were higher for MZ (.41 to .43) than DZ (.16 to .27) twins, indicating genetic influences on these phenotypes. For the sleep variables, ADE models were indicated and therefore fitted. Nevertheless, the non-additive genetic component could be dropped for both sleep variables and the best fit was provided by an AE model. The heritability value was similar for insomnia, .41 (95% CI: .37- .44), and sleep quality, .42 (95% CI: .38- .46), with the rest of the variance attributable to non-shared environmental factors, as reported elsewhere.[70]

With regard to depression, ACE was the best fitting model, where 29% (95% CI: .20- .38) of the variance was due to genetic factors and 13% (95% CI: .06- .20) to common shared environment, similar to a previous report using these data.[50] An ADE model provided the best fit for anxiety. Additive genetic influences accounted for 23% (95% CI: .09- .37) of the variance and non-additive genetic influences 17% (95% CI: .02- .32). Finally, for anxiety sensitivity an AE model provided the best fit. Genetic influences accounted for 41% (95% CI: .38- .44) of the variance.

Multivariate twin model

Cross-twin cross-trait correlations are presented in Table 3. We ran both the ACE and ADE multivariate models. The fits were very similar (ACE_{BIC} =-310035.62; ADE_{BIC} =-310065.79), so we focus on the ACE model here because it is the more standard model to present. The full ACE model provided a significantly worse fit compared to the saturated model (an unconstrained model estimating all the observed parameters). However, this test of fit (the difference in -2LL) can be oversensitive to small deteriorations in model fit in large samples[70]. We were able to drop the C parameter from our model without a significant decrease in fit (see Table 4 for the fit statistics) – so present the AE model here (Figure 1). Table 5 (see also Figure 1) contains the results from the multivariate AE model. Moderate genetic correlations were found between anxiety and both, insomnia and sleep quality (r_A = .59, 95% CI: .53-.65 and r_A =.61, 95% CI: .55-.62 respectively). Slightly smaller genetic correlations were found between anxiety sensitivity and insomnia and sleep quality (r_A = .51, 95% CI: .45-.57 and r_A =.52, 95% CI: .47-.57 respectively). Similar genetic correlations were found between depression and insomnia (r_A =.73; 95% CI: .68- .74) and sleep quality (r_A =.73; 95% CI: .72-.77). The genetic correlation between depression and anxiety was 0.82 (95% CI: .79- 0.85). The genetic correlation between anxiety and anxiety sensitivity was .72 (95% CI: 0.68-0.77). We also found significant non-shared environmental correlations, but of smaller magnitude (ranging from .26 to .36) for all the associations except for those between sleep quality and insomnia, (r_E =.59; 95% CI: .56- .62), and depression and anxiety (r_E =.48; 95% CI: .45- .51), which were more substantial.

Discussion

Previous studies have not investigated the relationship between sleep disturbances and internalising traits in adolescents using a twin design. This study provided information about the magnitude of genetic and environmental influences on different measures of sleep and internalising symptoms, and their associations.

Genetic and environmental influences on poor sleep quality, insomnia, depression, anxiety and anxiety sensitivity

We found substantial genetic influence on all of the phenotypes. First, we found that 42% of the differences in sleep quality are explained by genetic factors, consistent with past reports on these data.[70] These results are similar to those reported from previous studies in young and middle-aged adults.[23,24,30,71] For insomnia we found a similar heritability estimate, and our results are also similar to those from studies of young and middle-aged adults.[26,29]

For all measures of internalising symptoms, higher correlations were found between MZ as compared to DZ twins. Our results showed that genetic influences accounted for a significant proportion of the variance in these phenotypes. However, in contrast to other studies,[9,30] for depression symptoms we found a significant influence of shared environment (explaining 13% of the variance) (see also[50]). For both measures of anxiety, substantial genetic influence was found. An ADE model provided the best fit for anxiety whereas for anxiety sensitivity the best fitting model was AE. These results are similar to those reported from other studies.[9,22]

Genetic and environmental overlap between sleep disturbances, depression and anxiety

Our results demonstrate that there is a large genetic overlap between both sleep variables (i.e., insomnia and sleep quality) and depression and anxiety. These results are consistent with previous studies conducted in samples of different ages (for example, in young and middle-aged adults).[9,30] Previous studies have also pointed to a significant genetic overlap between insomnia and depression and anxiety in adults.[29,33] In addition, Gehrman et al.[45] found a complete genetic overlap between insomnia symptoms and internalising disorders. Our results suggest that there is also a large genetic overlap between sleep problems and internalising symptoms at another point in the life span – namely adolescence.

Despite the large genetic overlap between insomnia and poor sleep quality with anxiety and depression, the genetic associations reported here were all lower than unity (and the CIs did not span 1.0). Therefore, our results suggest that, genetically speaking, sleep problems and internalising symptoms (in this study at least) are somewhat different from one another, although strongly correlated. This conclusion is also consistent with genome-wide association studies where moderate genetic correlations for common additive genetic variants have been reported between insomnia and depressive symptoms and anxiety disorders.[72,73] The current findings are in line with the conceptualisation of these associations from other perspectives. Indeed, insomnia used to be considered as a symptom of other disorders, or a difficulty that was secondary to co-occurring traits.[74] The current study reinforces the idea that, during adolescence insomnia (and also sleep quality) should be considered to be different from internalising difficulties, yet overlapping, entities with their own characteristics.[9]

Interestingly, the genetic correlations with other variables, differed slightly when comparing anxiety and anxiety sensitivity (they were slightly larger with the former as compared to the latter variable). In contrast, the environmental correlations were of a similar magnitude for both variables. This finding chimes well with previous studies that have shown that anxiety sensitivity and anxiety are strongly genetically correlated but do not completely overlap (something that we also found in this study).[22] The comparison of our results with those reported from other studies is difficult, since to the best of our knowledge no twin studies have investigated the relationship between sleep problems and anxiety sensitivity, despite phenotypic associations having been regularly flagged.

Large genetic correlations have been reported between anxiety/anxiety sensitivity and depression in previous studies.[22] In this study, we also found a large genetic overlap between depression and anxiety, but a smaller overlap with anxiety sensitivity. Although not the focus of this article, it is noteworthy that adolescent anxiety and depression symptoms are influenced to a large extent by the same set of genes, a finding that chimes well with previous work in this area.[9,75]

Sleep problems occurring during adolescence have been associated with the subsequent develop of emotional problems — and the converse relationship has also been reported. [76,77] Several potential mechanisms appear to underlie the relationship between sleep disturbances and internalising symptoms. They include common genetic factors (something that has previously been reported in populations with different age ranges, [9,33,45] and now also in adolescence). Psychological factors such as worry and rumination may also underlie the relationship between sleep and internalising symptoms. For example, a model proposed by Harvey [78] proposes that the tendency to worry and ruminate during the day may extend to the pre-sleep period, which can have negative consequences for initiating sleep.

Altogether, a plethora of factors may play a role in the association between sleep disturbances and internalising difficulties and there are bidirectional relationships between them. The deterioration or improvement of one trait can impact upon the other. Our results show that sleep disturbances and internalising symptoms share common etiological underpinnings in adolescence – information that may be useful for the early identification and prediction of both difficulties.

Strengths and limitations

This study has several strengths, such as the use of a large sample of twins, providing ample power to study genetic and environmental overlaps between variables. Furthermore, there were several measures of internalising symptoms, which allowed us to study whether there were different associations between different internalising symptoms and sleep variables. There were also two different measures of sleep. One focused on the most common sleep problem (i.e., insomnia) and a second focused on sleep quality more generally.

Despite these strengths, our results must be considered in light of several limitations. First, we used self-report measures, which was necessary because of the large sample size. Conducting a large-scale study with objective measures such as polysomnography would involve greater resources than were available. Second, the sample comprised a non-clinical population. This offers the advantage of the results being generalizable to the whole population. Nonetheless, it also means that further research is needed to examine whether the aetiology of associations between sleep problems and internalising symptoms differ in clinical populations. Finally, our design is cross-sectional, so we cannot establish directionality between the phenotypes. Previous work suggests bidirectional links between the variables,[79] and future research should address the longitudinal and causal links between sleep problems and internalising symptoms in adolescents using designs such as cross-lagged models or mendelian randomization.

Conclusions

This study investigated, for the first time, the relationship between sleep problems and internalising symptoms in a sample of adolescents using a behavioural genetic approach. Also, for the first time, the links between sleep and anxiety sensitivity were examined in a twin study. The results revealed a large genetic overlap between sleep problems and internalising symptoms. Although the genetic overlap was large in all cases, we found possible differences between the two measures of anxiety. While these results add novel information about these complex associations, future research, including longitudinal studies will be needed to study the complex link between sleep problems and internalising psychopathology.

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Declarations: AMG is an advisor for a project sponsored by Johnson's Baby. She has written a book, Nodding Off (Bloomsbury Sigma, 2018), and has a second book, The Sleepy Pebble and Other Stories forthcoming (Nobrow, 2019). She is a regular contributor to BBC Focus magazine and has contributed to other outlets (such as The Conversation, The Guardian and Balance Magazine). She occasionally receives sample products related to sleep (e.g. blue light blocking glasses) and has given a paid talk to a business. **AR** has done some consultant writing for the National Childbirth Trust.

List of abbreviations

MZ: Monozygotic

DZ: Dizygotic

TEDS: Twins Early Development Study

PSQI: Pittsburgh Sleep Quality Index

ISI: Insomnia Severity Index

SMFQ: Short Mood and Feelings Questionnaire

SDQ: Strengths and Difficulties Questionnaire

CASI: Children's Anxiety Sensitivity Index

AIC: Akaike's information criterion

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Figure Legend

Figure 1: Multivariate AE model

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Sleep quality, insomnia and internalising difficulties in adolescents: insights from a twin study

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Abstract:

Objectives: There is a well-established association between poor sleep quality and internalising traits. This relationship has previously been studied using a twin design. However, when it comes to adolescence, there is a paucity of twin studies that have investigated this relationship, despite the importance of this developmental stage for both the development of poor sleep quality and internalising symptoms. Additionally, anxiety sensitivity, which is commonly associated with poor sleep quality, has not been studied in this context. Our objective was to estimate genetic and environmental influences on the relationships between insomnia, poor sleep quality and internalising symptoms in adolescence.

Methods: Insomnia, poor sleep quality, depression, anxiety and anxiety sensitivity traits were measured in a sample of 5,111 twin pairs from the Twins Early Development Study, born between 1994 and 1996 (mean age 16.32y (SD=0.68)).

Results: A moderate proportion of the variance for the different variables (.29-.42) was explained by genetic factors. Associations between sleep and internalising variables were moderate (r = .34 - .46) and there was a large genetic overlap between these variables (rA= 0.51 – 0.73).

Conclusion: This study adds novel information by showing that there are large genetic correlations between sleep disturbances and internalising symptoms in adolescence.

Keywords: adolescence, anxiety, depression, insomnia, internalising, sleep, twins.

Significance statement:

There is a paucity of information about the aetiology of the relationship between sleep and internalising traits in adolescents, despite this being an important period often characterised by changes in and the development of both sleep and internalising problems. This study included several measures of sleep and internalising symptoms and is the first study to investigate the relationship between sleep and anxiety sensitivity using a behavioural genetic approach. This large twin study allows us to examine genetic and environmental influences on these phenotypes and the extent of genetic and environmental overlap between variables. The results indicate large genetic overlap between sleep and internalising symptoms.

Introduction

Symptoms of sleep problems, depression and anxiety are of significant concern in adolescence as they are associated with poor outcomes.[1-4] For example, poor sleep quality and sleep problems are risk factors for ill health, poor cognitive functioning and accidents among other adverse consequences.[5-7] Anxiety and depression are associated with poor academic achievement, drug and alcohol consumption and suicidal ideation.[1,8]

Sleep and depression

There is a robust relationship between symptoms of insomnia and depression.[9,10] Other measures of sleep have also been linked with depression. For example, sleep quality is a broad concept which includes several measures such as sleep duration, sleep latency, sleep efficiency and sleep disturbances, among others.[11] Studies that have focused on the relationship between sleep quality and depression have reported a strong relationship in adolescents.[12,13]

Sleep and anxiety

As with depression, anxiety measures are also associated with insomnia symptoms and poor sleep quality.[9,14-16] Anxiety sensitivity can be defined as fear of the physical symptoms of anxiety.[17] This measure has also been linked to sleep problems,[18,19] and targeting anxiety sensitivity has been proposed to be an effective strategy for reducing insomnia symptoms.[20] Although anxiety sensitivity might be an important predictor of sleep disturbances,[18,21] and previous studies have shown that anxiety and anxiety sensitivity are strongly correlated but not completely overlapping,[22] there are no studies that have investigated genetic and environmental influences on the association between sleep and anxiety sensitivity as compared to anxiety.

Genetics of sleep quality, insomnia, depression and anxiety

Heritability typically explains around 30-40% of the variance in sleep quality[23-25]. There are also substantial genetic influences on insomnia symptoms, with heritability values around 20-50%.[26-29] Regarding depression and anxiety, approximately 30-50% of the variance is typically explained by genetic factors.[9,29-32] Studies examining the overlap between these variables have found that there is a substantial (sometimes complete) genetic overlap, with genetic correlations all above .5.[9,29,30,33]

Adolescence is a period of great change for sleep. During this stage of life, bedtime typically becomes later and it can be more difficult to wake early.[34] This shift in sleep timing can result in insufficient sleep or even symptoms of sleep disorders such as insomnia.[35,36] Poor sleep quality and sleep disorders are common during adolescence.[37,38]

Psychopathology begins early in life[39] and the move into adolescence appears to be a time of vulnerability for increased internalising symptoms.[40,41] For example, anxiety and depression levels can increase dramatically during this period.[42]

Despite well-established associations between poor sleep and internalising traits, and the importance of adolescence as a period of vulnerability for the development of these overlapping difficulties, there is a paucity of work aimed at understanding these associations from a behavioural genetic perspective at this stage of life. Behavioural genetic work addressing these questions has tended to focus on children[43,44] or adults,[30,33] or spans developmental stages[45]. Heritability is a population statistic, and estimates can vary depending on multiple factors, including the age of participants.[46] Thus, our main objective is to estimate genetic and environmental influences on the relationship between insomnia, poor sleep quality and internalising symptoms, employing a sample of adolescent twins, at which age both sleep problems and internalising disorders are common.. Our main hypothesis is that, as found to occur at other developmental stages, there is substantial genetic overlap between sleep disturbances and internalising symptoms. Understanding more about the pattern and aetiology of associations between these traits holds the promise of informing prevention techniques for the development of these common difficulties. The genetic and environmental influences on the associations between anxiety sensitivity and insomnia, and poor sleep quality, have not been examined previously. This is an important omission because anxiety and anxiety sensitivity could relate differently to insomnia and poor sleep quality. Our second aim was therefore to examine, for the first time, the aetiology of these associations.

Methods

Participants

The sample comprised 10,222 twins participating in the Twins Early Development Study (TEDS), which is a community-based, longitudinal study of twins born in England and Wales between 1994-1996.[47] This sample is reasonably representative of the general population in terms of ethnicity, parental education and employment status.[48] Zygosity was established either through a DNA test or a questionnaire assessing physical similarity. This questionnaire has an accuracy of over 95%.[49]

Analyses reported here focus on the data collection at age 16. At this wave, 10,874 families were contacted and invited to participate, and 5144 families (47.3%) provided data. Data from 33 families were excluded since there was no information on zygosity. Hence data from 5111 families were analysed (10,222 participants). The differences between participating and non-participating families have been reported elsewhere.[50] The sample was 44.8% male and 35.6% MZ (Table 1). Sensitivity analyses were conducted excluding an additional 249 families where twins had a severe medical disorder or there had been severe perinatal complications (low birth weight; short gestational age; maternal drinking during pregnancy; a long period of special care after birth; a long stay in hospital after birth). This resulted in similar results (estimates varied by up to 3%) so the full sample is reported here.

Measures

Sleep quality was measured using the Pittsburgh Sleep Quality Index (PSQI). The PSQI is a widely used questionnaire which assesses sleep quality referencing the previous month. It has 7 sub-scales: 1) subjective sleep quality; 2) sleep latency; 3) sleep duration; 4) habitual sleep efficiency; 5) sleep disturbances; 6) use of sleeping medication and 7) day time dysfunction. These seven sub-scales yield a global score ranging from 0-21, where higher scores represent poorer sleep quality.[51] For this study we focused on the global score.

The PSQI has shown adequate psychometric properties, high correlations with objective measures, and previous studies have also validated the single-factor scoring structure.[52-54] In our sample, the Cronbach's alpha for the global score was .70.

Insomnia was measured using the Insomnia Severity Index (ISI). The ISI is a 7-item questionnaire generating scores ranging from 0-28.[55] The ISI enquires about symptoms of insomnia in the previous month. This measure has demonstrated adequate psychometric properties, and a cut-off of 10 has been shown to provide specificity and sensitivity for detecting individuals with insomnia.[56] The Cronbach's alpha in our sample was .89.

Depression was measured using the Short Mood and Feelings Questionnaire (SMFQ). SMFQ has 13 items ranging from 0 (not true) to 2 (true) and these scores are summed to produce the total score which ranges from 0 to 26. Questions assess key symptoms of depression such as "I felt miserable or unhappy" and focus on the previous two weeks.[57] SMFQ has good psychometric properties.[58,59] Of note, this questionnaire does not contain sleep items. In this sample, Cronbach's alpha was .88.

Anxiety was measured using the emotional symptoms/anxiety domain of the Strengths and Difficulties Questionnaire (SDQ). The SDQ is a five-dimension questionnaire which measures the core domains of psychopathology in children and adolescents.[60] The questionnaire consists of 25 items (5 for each subscale). This questionnaire has shown good psychometric properties and validity.[61] For this study we only focused on the anxiety subscale (5 items). The Cronbach's alpha in this sample for the SDQ anxiety subscale was .69.

Anxiety Sensitivity was measured using the Children's Anxiety Sensitivity Index (CASI).[62] This measure has 18 items which measure fear of the physical symptoms of anxiety. The CASI has good internal consistency and validity.[62,63] In the current study, the scale had a Cronbach's alpha of .86.

Statistical analyses

Twin studies are a useful tool for research.[64] The classical twin design can be summarized as follows: the variance of one phenotype can be decomposed into genetic and environmental factors making use of the difference between MZ twins (who share

100% of their DNA) and DZ twins (who share on average 50% of their segregating DNA).[65] Genetic influences can be divided into those that are additive (A; the sum of allelic effects across all loci) and non-additive (D; the effects of genetic dominance). On the other hand, environmental contributions are shared (C; influences that make twin pairs raised in the same family similar to each other) and non-shared (E, effects that make family members less alike).[66]

It is not possible to estimate C and D simultaneously using only data from twins reared together. Therefore, the selection of C or D is made based on the pattern of correlations between MZ and DZ twins. An ACE model is selected when the DZ twin correlation is greater than half of the MZ twin correlation, and an ADE model is selected when the DZ twin correlation is less than half of the MZ correlation (i.e., non-additive genetic effects are implicated if the MZ twins are more than twice as similar as DZ twins[66,67]).

One univariate model (either ACE or ADE as indicated by the data) was fitted to each of the variables. Nested models (i.e., AE, CE, E) were also fitted to check if one (or two) components could be dropped without a significant decrease of model fit. The fit of the different models and submodels was checked using the likelihood-ratio chi-square test and the Akaike's information criterion (AIC).[68] Assumptions of twin models were checked in the saturated models in order to check for differences in means and variances between the different groups: MZ/DZ twins and twin1/twin2 (randomly selected within each pair).

We also fitted a multivariate correlated factor model. This model allows the estimation of genetic and environmental influences on both individual variance and also sources of covariance between the phenotypes. Put differently, the model allows us to estimate aetiological correlations which inform us of the extent to which the latent variables (A, C/D and E) correlate across two traits. These correlations (i.e., rA rC, rD, rE) can vary from -1 to 1, where 0 would mean no overlap, and 1 complete overlap. Using these statistics, we can also calculate bivariate heritability, which is the proportion of the phenotypic covariance explained by A. Equivalent bivariate shared environment and bivariate nonshared environment estimates can also be derived.

Descriptive analyses were performed using the statistical software SPSS v.22. Twin analyses were conducted using the package OpenMx in R.[69] Age and sex were used as covariates. All the variables were +1 log transformed to better meet the assumption of normality and reduce positive skew (variables ranged from 0.76 to 1.96 before transformation and from -0.67 to 0.22 after transformation).

Results

Descriptive statistics

Table 1 presents descriptive statistics. Females, as compared to males, reported poorer sleep quality (t[7520]= 9.77; p<.001; $\bar{x}_{female=4.96}$; $\bar{x}_{male=4.34}$; Cohen's d=0.23), higher levels of insomnia (t[7849]= 10.20; p<.001; $\bar{x}_{female=4.29}$; $\bar{x}_{male=3.33}$; Cohen's d=0.23) and greater levels of depression (t[10014]= 20.43; p<.001; $\bar{x}_{female=4.41}$; $\bar{x}_{male=2.69}$; Cohen's d=0.41), anxiety (t[10128]= 35.11; p<.001; $\bar{x}_{female=3.40}$; $\bar{x}_{male=1.94}$; Cohen's d=0.70) and anxiety sensitivity (t[10130]= 29.97; p<.001; $\bar{x}_{female=9.41}$; $\bar{x}_{male=6.13}$; Cohen's d=0.60). There were small but significant differences between MZ and DZ twins in symptoms of sleep quality, insomnia and depression. However, the effect sizes were small (lower than .07).

Univariate twin models

Table 2 shows all the univariate models. Intrapair correlations were higher for MZ (.41 to .43) than DZ (.16 to .27) twins, indicating genetic influences on these phenotypes. For the sleep variables, ADE models were indicated and therefore fitted. Nevertheless, the non-additive genetic component could be dropped for both sleep variables and the best fit was provided by an AE model. The heritability value was similar for insomnia, .41 (95% CI: .37- .44), and sleep quality, .42 (95% CI: .38- .46), with the rest of the variance attributable to non-shared environmental factors, as reported elsewhere.[70]

With regard to depression, ACE was the best fitting model, where 29% (95% CI: .20- .38) of the variance was due to genetic factors and 13% (95% CI: .06- .20) to common shared environment, similar to a previous report using these data.[50] An ADE model provided the best fit for anxiety. Additive genetic influences accounted for 23% (95% CI: .09- .37) of the variance and non-additive genetic influences 17% (95% CI: .02- .32). Finally, for anxiety sensitivity an AE model provided the best fit. Genetic influences accounted for 41% (95% CI: .38- .44) of the variance.

Multivariate twin model

Cross-twin cross-trait correlations are presented in Table 3. We ran both the ACE and ADE multivariate models. The fits were very similar (ACE_{BIC} =-310035.62; ADE_{BIC} =-310065.79), so we focus on the ACE model here because it is the more standard model to present. The full ACE model provided a significantly worse fit compared to the saturated model (an unconstrained model estimating all the observed parameters). However, this test of fit (the difference in -2LL) can be oversensitive to small deteriorations in model fit in large samples[70]. We were able to drop the C parameter from our model without a significant decrease in fit (see Table 4 for the fit statistics) – so present the AE model here (Figure 1). Table 5 (see also Figure 1) contains the results from the multivariate AE model. Moderate genetic correlations were found between anxiety and both, insomnia and sleep quality (r_A = .59, 95% CI: .53-.65 and r_A =.61, 95% CI: .55-.62 respectively). Slightly smaller genetic correlations were found between anxiety sensitivity and insomnia and sleep quality (r_A = .51, 95% CI: .45-.57 and r_A =.52, 95% CI: .47-.57 respectively). Similar genetic correlations were found between depression and insomnia (r_A =.73; 95% CI: .68- .74) and sleep quality (r_A =.73; 95% CI: .72-.77). The genetic correlation between depression and anxiety was 0.82 (95% CI: .79- 0.85). The genetic correlation between anxiety and anxiety sensitivity was .72 (95% CI: 0.68-0.77). We also found significant non-shared environmental correlations, but of smaller magnitude (ranging from .26 to .36) for all the associations except for those between sleep quality and insomnia, (r_E =.59; 95% CI: .56- .62), and depression and anxiety (r_E =.48; 95% CI: .45- .51), which were more substantial.

Discussion

Previous studies have not investigated the relationship between sleep disturbances and internalising traits in adolescents using a twin design. This study provided information about the magnitude of genetic and environmental influences on different measures of sleep and internalising symptoms, and their associations.

Genetic and environmental influences on poor sleep quality, insomnia, depression, anxiety and anxiety sensitivity

We found substantial genetic influence on all of the phenotypes. First, we found that 42% of the differences in sleep quality are explained by genetic factors, consistent with past reports on these data.[70] These results are similar to those reported from previous studies in young and middle-aged adults.[23,24,30,71] For insomnia we found a similar heritability estimate, and our results are also similar to those from studies of young and middle-aged adults.[26,29]

For all measures of internalising symptoms, higher correlations were found between MZ as compared to DZ twins. Our results showed that genetic influences accounted for a significant proportion of the variance in these phenotypes. However, in contrast to other studies,[9,30] for depression symptoms we found a significant influence of shared environment (explaining 13% of the variance) (see also[50]). For both measures of anxiety, substantial genetic influence was found. An ADE model provided the best fit for anxiety whereas for anxiety sensitivity the best fitting model was AE. These results are similar to those reported from other studies.[9,22]

Genetic and environmental overlap between sleep disturbances, depression and anxiety

Our results demonstrate that there is a large genetic overlap between both sleep variables (i.e., insomnia and sleep quality) and depression and anxiety. These results are consistent with previous studies conducted in samples of different ages (for example, in young and middle-aged adults).[9,30] Previous studies have also pointed to a significant genetic overlap between insomnia and depression and anxiety in adults.[29,33] In addition, Gehrman et al.[45] found a complete genetic overlap between insomnia symptoms and internalising disorders. Our results suggest that there is also a large genetic overlap between sleep problems and internalising symptoms at another point in the life span – namely adolescence.

Despite the large genetic overlap between insomnia and poor sleep quality with anxiety and depression, the genetic associations reported here were all lower than unity (and the CIs did not span 1.0). Therefore, our results suggest that, genetically speaking, sleep problems and internalising symptoms (in this study at least) are somewhat different from one another, although strongly correlated. This conclusion is also consistent with genome-wide association studies where moderate genetic correlations for common additive genetic variants have been reported between insomnia and depressive symptoms and anxiety disorders.[72,73] The current findings are in line with the conceptualisation of these associations from other perspectives. Indeed, insomnia used to be considered as a symptom of other disorders, or a difficulty that was secondary to co-occurring traits.[74] The current study reinforces the idea that, during adolescence insomnia (and also sleep quality) should be considered to be different from internalising difficulties, yet overlapping, entities with their own characteristics.[9]

Interestingly, the genetic correlations with other variables, differed slightly when comparing anxiety and anxiety sensitivity (they were slightly larger with the former as compared to the latter variable). In contrast, the environmental correlations were of a similar magnitude for both variables. This finding chimes well with previous studies that have shown that anxiety sensitivity and anxiety are strongly genetically correlated but do not completely overlap (something that we also found in this study).[22] The comparison of our results with those reported from other studies is difficult, since to the best of our knowledge no twin studies have investigated the relationship between sleep problems and anxiety sensitivity, despite phenotypic associations having been regularly flagged.

Large genetic correlations have been reported between anxiety/anxiety sensitivity and depression in previous studies.[22] In this study, we also found a large genetic overlap between depression and anxiety, but a smaller overlap with anxiety sensitivity. Although not the focus of this article, it is noteworthy that adolescent anxiety and depression symptoms are influenced to a large extent by the same set of genes, a finding that chimes well with previous work in this area.[9,75]

Sleep problems occurring during adolescence have been associated with the subsequent develop of emotional problems — and the converse relationship has also been reported.[76,77] Several potential mechanisms appear to underlie the relationship between sleep disturbances and internalising symptoms. They include common genetic factors (something that has previously been reported in populations with different age ranges,[9,33,45] and now also in adolescence). Psychological factors such as worry and rumination may also underlie the relationship between sleep and internalising symptoms. For example, a model proposed by Harvey[78] proposes that the tendency to worry and ruminate during the day may extend to the pre-sleep period, which can have negative consequences for initiating sleep.

Altogether, a plethora of factors may play a role in the association between sleep disturbances and internalising difficulties and there are bidirectional relationships between them. The deterioration or improvement of one trait can impact upon the other. Our results show that sleep disturbances and internalising symptoms share common etiological underpinnings in adolescence – information that may be useful for the early identification and prediction of both difficulties.

Strengths and limitations

This study has several strengths, such as the use of a large sample of twins, providing ample power to study genetic and environmental overlaps between variables. Furthermore, there were several measures of internalising symptoms, which allowed us to study whether there were different associations between different internalising symptoms and sleep variables. There were also two different measures of sleep. One focused on the most common sleep problem (i.e., insomnia) and a second focused on sleep quality more generally.

Despite these strengths, our results must be considered in light of several limitations. First, we used self-report measures, which was necessary because of the large sample size. Conducting a large-scale study with objective measures such as polysomnography would involve greater resources than were available. Second, the sample comprised a non-clinical population. This offers the advantage of the results being generalizable to the whole population. Nonetheless, it also means that further research is needed to examine whether the aetiology of associations between sleep problems and internalising symptoms differ in clinical populations. Finally, our design is cross-sectional, so we cannot establish directionality between the phenotypes. Previous work suggests bidirectional links between the variables,[79] and future research should address the longitudinal and causal links between sleep problems and internalising symptoms in adolescents using designs such as cross-lagged models or mendelian randomization.

Conclusions

This study investigated, for the first time, the relationship between sleep problems and internalising symptoms in a sample of adolescents using a behavioural genetic approach. Also, for the first time, the links between sleep and anxiety sensitivity were examined in a twin study. The results revealed a large genetic overlap between sleep problems and internalising symptoms. Although the genetic overlap was large in all cases, we found possible differences between the two measures of anxiety. While these results add novel information about these complex associations, future research, including longitudinal studies will be needed to study the complex link between sleep problems and internalising psychopathology.

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Declarations: AMG is an advisor for a project sponsored by Johnson's Baby. She has written a book, Nodding Off (Bloomsbury Sigma, 2018), and has a second book, The Sleepy Pebble and Other Stories forthcoming (Nobrow, 2019). She is a regular contributor to BBC Focus magazine and has contributed to other outlets (such as The Conversation, The Guardian and Balance Magazine). She occasionally receives sample products related to sleep (e.g. blue light blocking glasses) and has given a paid talk to a business. **AR** has done some consultant writing for the National Childbirth Trust.

List of abbreviations

MZ: Monozygotic

DZ: Dizygotic

TEDS: Twins Early Development Study

PSQI: Pittsburgh Sleep Quality Index

ISI: Insomnia Severity Index

SMFQ: Short Mood and Feelings Questionnaire

SDQ: Strengths and Difficulties Questionnaire

CASI: Children's Anxiety Sensitivity Index

AIC: Akaike's information criterion

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Figure Legend

Figure 1: Multivariate AE model

Table 1 Descriptive statistics

	Male	Female	MZ	DZ	Total sample
Total N (%)	4576 (44.8)	5646 (55.2)	3636 (35.6)	6586 (64.4)	10222 (100)
Age mean (SD)	16.30 (0.69)	16.34 (0.67)	16.35 (0.66)	16.30 (0.69)	16.32 (0.68)
Mean PSQI (SD) †† (N=7572)	4.34 (2.66)	4.96 (2.84)	4.55 (2.71)	4.74 (2.81)	4.67 (2.78)
Mean ISI (SD) †† (N=7853)	3.33 (3.87)	4.29 (4.44)	3.66 (4.11)	3.95 (4.27)	3.85 (4.22)
Mean SMFQ (SD) †† (N=10142)	2.69 (3.54)	4.41 (4.92)	3.48 (4.40)	3.72 (4.46)	3.64 (4.44)
Mean $SDQ_{anxiety}$ (SD)† (N=10130)	1.94 (1.86)	3.40 (2.31)	2.73 (2.26)	2.76 (2.24)	2.75 (2.24)
Mean CASI (SD) † (N=10140)	6.13 (4.85)	9.41 (6.18)	7.98 (5.87)	7.93 (5.86)	7.95 (5.86)

Note: 7148 participants had data for all the variables. ISI: Insomnia Severity Index; PSQI: Pittsburgh Sleep Quality Index; SMFQ: Short Mood and Feelings Questionnaire; SDQ: Strengths and Difficulties Questionnaire; CASI: Children's Anxiety Sensitivity Index

††Significant differences (p<.05) between MZ-DZ and Male-Female.

† Significant differences (p<.05) between Male-Female.

Table 2: Univariate analyses

	Model	Model for comparison	A (95% CI)	C/D (95% CI)	E (95% CI)	df	-2LL	AIC	DiffLL	Diffdf	P	rMZ	rDZ
Sleep quality												0.43 (0.38,0.47)	0.19 (0.15,0.23)
	ADE		0.34 (0.18,0.45)	0.10 (0,0.27)	0.57 (0.53,0.61)	7566	11510.74	-3621.26					
	AE	ADE	**0.42 (0.38,0.46)**	*	**0.58 (0.54,0.62)**	**7567**	**11511.91**	**-3622.09**	**1.17**	**1**	**0.28**		
	E	AE	*	*	1 (1,1)	7568	11847.70	-3288.30	335.79	1	<0.001		
Insomnia												0.42 (0.38,0.46)	0.17 (0.14,0.21)
	ADE		0.26 (0.11,0.42)	0.16 (0,0.33)	0.58 (0.53,0.62)	7847	18909.28	3215.28					
	AE	ADE	**0.41 (0.37,0.44)**	*	**0.59 (0.56,0.63**	**7848**	**18912.79**	**3216.79**	**3.51**	**1**	**0.06**		
	E	AE	*	*	1 (1,1)	7849	19253.94	3555.94	341.15	1	<0.001		
Depression												0.42 (0.38,0.46)	0.27 (0.24,0.30)
	ACE		**0.29 (0.20,0.38)**	**0.13 (0.06,0.20)**	**0.58 (0.55,0.62)**	**10136**	**25157.21**	**4885.21**					
	AE	ACE	0.45 (0.41,0.47)	*	0.55 (0.53,0.59)	10137	25169.06	4895.05	11.84	1	<0.001		
	CE	ACE	*	0.33 (0.30,0.35)	0.67 (0.65,0.70)	10137	25192.53	4918.53	35.32	1	<0.001		
	E	AE	*	*	1 (1,1)	10138	25755.64	5479.64	589.59	1	<0.001		
Anxiety												0.41 (0.37,0.45)	0.16 (0.13,0.19)
	ADE		**0.23 (0.09,0.37)**	**0.17 (0.02,0.32)**	**0.59 (0.56,0.63)**	**10124**	**18994.53**	**-1253.47**					
	AE	ADE	0.39 (0.35,0.42)	*	0.61 (0.58,0.65)	10125	18999.51	-1250.49	4.98	1	0.03		
	E	AE	*	*	1 (1,1)	10126	19403.67	-848.32	404.16	1	<0.001		
Anxiety Sensitivity												0.41 (0.37, 0.45)	0.22 (0.19, 0.25)
	ACE		0.35 (0.25,0.43)	0.05 (0,0.12)	0.60 (0.57,0.64)	10134	21548.43	1280.93					
	AE	ACE	**0.41 (0.38,0.44)**	*	**0.59 (0.56,0.62)**	**10135**	**21550.69**	**1280.69**	**1.76**	**1**	**0.18**		
	CE	ACE	*	0.29 (0.26,0.32)	0.71 (0.69,0.74)	10135	21596.40	1326.41	47.48	1	<0.001		
	E	AE	*	*	1 (1,1)	10136	22036.98	1764.98	486.29	1	<0.001		

Note: A, additive genetic influence; C, shared environmental influence; D, dominant genetic influence E, non-shared environmental influence; -2LL, negative 2 log-likelihood; AIC, Akaike's information criterion; CI, confidence interval; df, degrees of freedom; P-value, significance value of the likelihood-ratio chi-square test; rDZ, dizygotic correlations; rMZ, monozygotic correlations. Bold text indicates best fitting models

Table 3: cross-twin cross-trait correlations

Measure	MZ Estimate	95% CI	DZ Estimate	95% CI
Cross-trait cross-twin correlation from the multivariate AE model				
Sleep quality-Insomnia	0.34	(0.32,0.36)	0.17	(0.15,0.18)
Sleep quality-Depression	0.31	(0.29,0.32)	0.16	(0.15,0.16)
Sleep quality-Anxiety	0.24	(0.21,0.26)	0.12	(0.11,0.13)
Sleep quality-Anxiety Sensitivity	0.21	(0.19,0.24)	0.11	(0.09,0.12)
Insomnia-Depression	0.31	(0.28,0.32)	0.15	(0.14,0.16)
Insomnia-Anxiety	0.23	(0.20,0.25)	0.11	(0.10,0.13)
Insomnia-Anxiety Sensitivity	0.21	(0.18,0.23)	0.10	(0.09,0.12)
Depression-Anxiety	0.33	(0.31,0.34)	0.17	(0.15,0.18)
Depression-Anxiety Sensitivity	0.29	(0.27,0.31)	0.15	(0.14,0.15)
Anxiety-Anxiety-Sensitivity	0.28	(0.26,0.31)	0.14	(0.13,0.15)

Note: A, additive genetic influence; E, non-shared environmental influence; DZ, dizygotic; MZ, monozygotic

Table 4: Model fit statistics

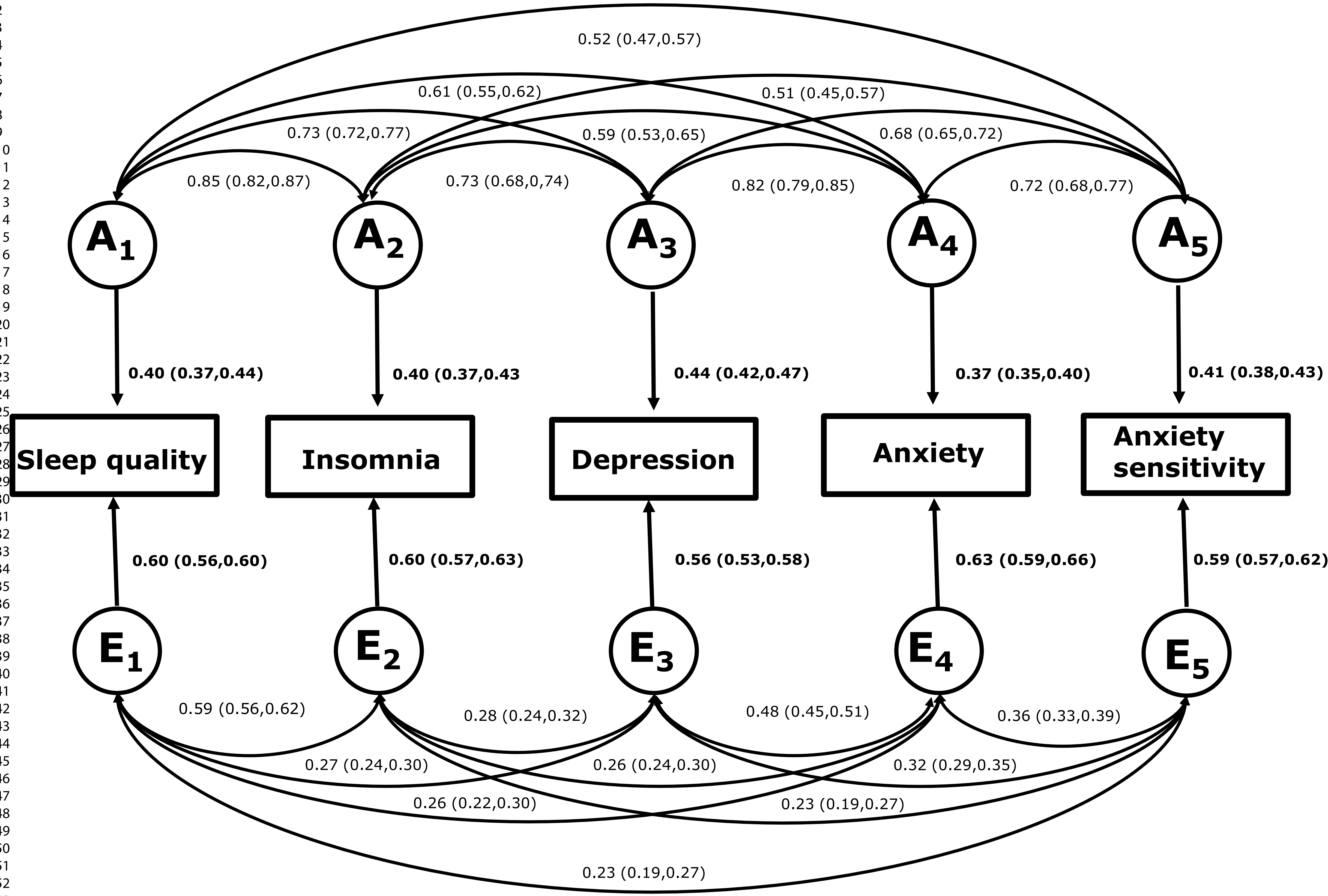
Model	-2LL	df	Parameters	AIC	diffLL	Diffdf	*p*
SATURATED	80702.18	45699	138	-10695.82			
ACE	80861.07	45777	60	-10692.93	158.89	78	<0.001
AE	80880.39	45792	45	-10703.61	19.32	15	0.20
CE	81063.43	45792	45	-10520.57	202.36	15	<0.001
E	82206.23	45807	30	-9407.77	1325.84	15	<0.001

-2LL= fits statistic; A= additive genetic influences; AIC= akaike information criterion; C common environmental influences; df= degrees of freedom; E= unique environmental influences; P= significance value of the likelihood ration chi-square test;

Table 5: Multivariate AE model

	Sleep Quality	Insomnia	Depression	Anxiety	Anxiety Sensitivity
Additive genetic and nonshared environmental overlap between phenotypes					
Sleep Quality					
Insomnia	rA=0.85 (0.82,0.87) rE=0.59 (0.56,0.62) rPH=0.69 (0.68,0.71)				
Depression	rA=0.73 (0.72,0.77) rE=0.27 (0.24,0.30) rPH=0.46 (0.44,0.48)	rA=0.73 (0.68,0,74) rE=0.28 (0.24,0.32) rPH=0.47 (0.45,0.48)			
Anxiety	rA=0.61 (0.55,0.62) rE=0.26 (0.22,0.30) rPH=0.39 (0.38,0.41)	rA=0.59 (0.53,0.65) rE=0.26 (0.24,0.30) rPH=0.39 (0.37,0.41)	rA=0.82 (0.79,0.85) rE=0.48 (0.45,0.51) rPH=0.62 (0.61,0.63)		
Anxiety Sensitivity	rA=0.52 (0.47,0.57) rE=0.23 (0.19,0.27) rPH=0.35 (0.33,0.37)	rA=0.51 (0.45,0.57) rE=0.23 (0.19,0.27) rPH=0.34 (0.32,0.35)	rA=0.68 (0.65,0.72) rE=0.32 (0.29,0.35) rPH=0.47 (0.46,0.49)	rA=0.72 (0.68,0.77) rE=0.36 (0.33,0.39) rPH=0.50 (0.49,0.52)	
Additive genetic and nonshared environmental on the phenotypes and their association					
Sleep Quality	**A=0.40 (0.37,0.44)** **E=0.60 (0.56,0.60)**				
Insomnia	A=0.49 (0.44,0.53) E=0.51 (0.47,0.52)	**A=0.40 (0.37,0.43)** **E=0.60 (0.57,0.63)**			
Depression	A=0.66 (0.63,0.71) E=0.34 (0.30,0.37)	A=0.66 (0.64,0.70) E=0.34 (0.30,0.40)	**A=0.44 (0.42,0.47)** **E=0.56 (0.53,0.58)**		
Anxiety	A=0.60 (0.54,0.66) E=0.40 (0.34,0.46)	A=0.59 (0.53,0.65) E=0.41 (0.35,0.43)	A=0.54 (0.50,0.58) E=0.46 (0.43,0.50)	**A=0.37 (0.35,0.40)** **E=0.63 (0.59,0.66)**	
Anxiety Sensitivity	A=0.61 (0.54,0.67) E=0.39 (0.32,0.41)	A=0.60 (0.53,0.67) E=0.40 (0.34,0.47)	A=0.61 (0.58,0.65) E=0.39 (0.35,0.40)	A=0.56 (0.52,0.60) E=0.44 (0.39,0.44)	**A=0.41 (0.38,0.43)** **E=0.59 (0.57,0.62)**

Bold figures in the lower part of the table represent within-trait standardized components of the variance and figures below the diagonal represent the standardized components of the covariance; A, additive genetic influence; E, non-shared environmental influence; rA= additive genetic correlation; rE non-shared environmental correlation; rPH phenotypic correlation from the model


0.52 (0.47,0.57)
0.61 (0.55,0.62)
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0.73 (0.72,0.77)
0.59 (0.53,0.65)
0.68 (0.65,0.72)
0.85 (0.82,0.87)
0.73 (0.68,0,74)
0.82 (0.79,0.85)
0.72 (0.68,0.77)
A1
A2
A3
A4
A5
0.40 (0.37,0.44)
0.40 (0.37,0.43
0.44 (0.42,0.47)
0.37 (0.35,0.40)
0.41 (0.38,0.43)
Sleep quality
Insomnia
Depression
Anxiety
Anxiety sensitivity
0.60 (0.56,0.60)
0.60 (0.57,0.63)
0.56 (0.53,0.58)
0.63 (0.59,0.66)
0.59 (0.57,0.62)
E1
E2
E3
E4
E5
0.59 (0.56,0.62)
0.28 (0.24,0.32)
0.48 (0.45,0.51)
0.36 (0.33,0.39)
0.27 (0.24,0.30)
0.26 (0.24,0.30)
0.32 (0.29,0.35)
0.26 (0.22,0.30)
0.23 (0.19,0.27)
0.23 (0.19,0.27)