Comorbid sleep problems and dysregulation profile from childhood to adolescence – longitudinal course, concurrent development and reciprocal relationship

Dissertation

zur Erlangung des humanwissenschaftlichen Doktorgrades

in der Medizin

der Georg-August-Universität Göttingen

vorgelegt von

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Goettingen, 2019

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Statement of Originality

I hereby declare that this thesis ‘‘Comorbid sleep problems and dysregulation profile from childhood to adolescence – longitudinal course, concurrent development and reciprocal relationship’’ was independently written and with no other sources and aids than quoted in the text, references and acknowledgements.

Goettingen, 31.03.2019

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Chapter 1 – Introduction

Co-occurrence of different psychopathologies over time reflects a great clinical problem. For example, during child development sleep problems are extensively associated with impairments in self-regulation of emotional and behavioral difficulties (Cortese, Faraone, Konofal, & Lecendreux, 2009; Ivanenko, Crabtree, & Gozal, 2005; O'Brien et al., 2011; Peterman, Carper, & Kendall, 2015). However, so far little is known about the mutual influence between sleep and self-regulation across early childhood to adolescence. Studying their patterns of co-occurrence and interaction may improve our understanding of the nature and development of these problems. Further, such information may serve for a better design of evidence-based screening, prevention and intervention programs in clinical practice.

1.1 Sleep Problems

1.1.1 Sleep Problems in Childhood and Adolescence

Sleep problems in childhood and adolescence are common (Honaker & Meltzer, 2016; Meltzer & McLaughlin Crabtree, 2015; Meltzer & Mindell, 2006; Owens, 2005). Estimates of the prevalence of sleep problems vary depending upon differences in definitions (i.e., insomnia vs. general sleep problems) and methods (i.e., subjective vs. objective) of assessment (O'Callaghan et al., 2010), which could take a wide range from 5%-46% in the community samples (e.g., Fricke-Oerkermann et al., 2007; Johnson, Roth, Schultz, & Breslau, 2006; Owens, 2005; Spruyt, O'Brien, Cluydts, Verleye, & Ferri, 2005) and females were generally more disturbed than males (Krishnan & Collop, 2006; Zhang & Wing, 2006). The prevalence are even

higher in clinical referred population, such as attention-deficit hyperactivity disorder (25%-73.3%, see Corkum, Tannock, & Moldofsky, 1998; Sung, Hiscock, Sciberras, & Efron, 2008 for examples) and autism (44%-83%, see Gail Williams, Sears, & Allard, 2004). Despite classification of sleep issues may vary according the systems applied, such as the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5, American Psychiatric Association, 2013) or the 3rd edition of the International Classification of Sleep Disorders (ICSD-3, American Academy of Sleep Medicine, 2014), behavioral sleep problems are generally well distinguished from physical sleep problems. The former usually takes the form of dyssomnias (such as insomnia and hypersomnia) or parasomnias (such as sleep walking, nightmares, and night terrors), while the latter may manifest as breathing or movement-related problems. In the current cumulative dissertation, the focus is on general behavioral sleep problems in children and adolescents. This measurement of overall sleep functioning can be measured with the sleep composite from the Child Behavior Checklist which covers six aspects of behavioral sleep problems: trouble getting to sleeping, nightmares, overtired without good reason, sleeps less than most kids, talks or walks in sleep, and sleeps more than most kids during day and/or night.

Sleep problems not only affect children and adolescents' academic, neurocognitive and behavioral performance, but can also have a negative impact on family functioning and the well-being of family members (Curcio, Ferrara, & De Gennaro, 2006; Kheirandish & Gozal, 2006; Martin, Hiscock, Hardy, Davey, & Wake, 2007; Meltzer & Mindell, 2007; Mitchell & Kelly, 2006). Moreover, Sleep problems are often accompanied by psychiatric disturbances like anxiety (Peterman et al., 2015), depression (Gregory et al., 2005), autism (Cohen, Conduit, Lockley, Rajaratnam, &

Cornish, 2014), attention-deficit/hyperactivity disorder (Cortese et al., 2009) and tic disorders (Ghosh et al., 2014; Kirov, Kinkelbur, Banaschewski, & Rothenberger, 2007).

1.1.2 Long-term Development of Sleep Problems

Compared to the large number of studies reporting prevalence of sleep disturbances at different stages of childhood and adolescence (e.g., Fricke-Oerkermann et al., 2007; Gaultney, 2010; Ohayon, Roberts, Zulley, Smirne, & Priest, 2000; Spruyt et al., 2005), investigations on the long-term development of sleep issues are scarce. Furthermore, the majority of current research was dominated by studies with short time frames which reported sleep variations on descriptive levels. Such designs can provide only limited information in terms of the developmental course.

Only a handful studies have explored general sleep problems during childhood and adolescence as a long-term developmental course. Gregory and O'Connor followed 490 children (46.3% girls) from ages 4 to 15 years. Using repeated measures analyses, they found a decrease in the average level of sleep problems (Gregory & O'Connor, 2002). Friedman and colleagues examined the longitudinal development of seven specific sleep problems (e.g., nightmares, talks or walks) among 916 twins (50.8% girls) from ages 4 to 16 years. By adopting latent growth curve analyses, they found that most reported sleep problems declined over time (Friedman, Corley, Hewitt, & Wright, 2009). The above-mentioned studies could be regarded as first efforts on modelling the development of general and specific sleep problems related to a time/age-course. However, limited by the variable-centered approach they applied and focused on the average course, they were not able to give

full information on the heterogeneity of the sample and thus they could not detect individuals with different developmental patterns (onset and progression).

Very few studies with population samples have investigated subgroups of children and adolescents with distinct developmental course of sleep problems. Among 1492 children, Touchette et al. detected four subgroups of sleep duration (i.e., short persistent, short increasing, 10-hour persistent and 11-hour persistent) in early childhood from 2.5 to 6 years (Touchette et al., 2007). On the same topic, Magee et al. found four subgroups of sleep duration (i.e., typical sleepers, initially short sleepers, poor sleepers and persistent short sleepers) following 2926 children from age 0 to 1 years to age 6 to 7 years (Magee, Gordon, & Caputi, 2014). Similarly, Seegers et al. identified three distinct developmental courses (i.e., short sleepers, 10.5-hour sleepers and 11-hour sleepers) by examining the time spent in bed among 1916 preadolescents from age 10 to 13 years (Seegers et al., 2011). These studies explored developmental subgroups of specific sleep problems in terms of sleep duration and time in bed. However, to our knowledge, no studies have launched the investigation into general sleep problems.

1.2 Dysregulation Profile

1.2.1 The Broad Syndrome of Dysregulation Profile

Self-regulation as a concept is thought to be divided into three components: affective, behavioral, and cognitive (Althoff, Verhulst, Rettew, Hudziak, & van der Ende, 2010). Consequently, impaired self-regulation could possibly be visible in any of these domains, namely impairment in the ability to regulate mood (depression) or worry (anxiety), to regulate behavior (disruptive behaviors), or to regulate cognitions

(attention deficit hyperactivity disorder). Concurrent impairments in regulating emotion, cognition and behavior are defined by the term ‘dysregulation profile’ and can be measured using the Anxious/Depressed, Attention Problems and Aggressive Behavior subscales of the Child Behavior Checklist (Althoff et al., 2010; Ayer et al., 2009). Severe dysregulation affects 1%-5% of the general population (Althoff et al., 2010; Holtmann et al., 2007; Hudziak, Althoff, Derks, Faraone, & Boomsma, 2005) and more than 20% of clinical samples (Brotman et al., 2006).

The dysregulation profile is best conceptualized as a broad dysregulation syndrome, which overarches emotion, attention and aggression problems as specific issues (Deutz, Geeraerts, van Baar, Dekovic, & Prinzie, 2016; Geeraerts et al., 2015). Such a combination of problems has been shown to be heritable and stable throughout childhood, probably due to genetic factors (Althoff, Rettew, Faraone, Boomsma, & Hudziak, 2006; Boomsma et al., 2006; Hudziak et al., 2005). The dysregulation profile represents a useful index for identifying children and adolescents at risk for psychiatric problems in early adulthood (Bellani, Negri, & Brambilla, 2012) and vast evidence has shown that it is related to various negative outcomes, such as psychosocial impairment, substance use, suicidal thoughts and behavior, and a range of psychiatric disorders in young adulthood, including personality disorders, mood disorders, and anxiety disorders (Althoff et al., 2010; Ayer et al., 2009; De Caluwe, Decuyper, & De Clercq, 2013; Deutz et al., 2017; Halperin, Rucklidge, Powers, Miller, & Newcorn, 2011; Holtmann et al., 2011; Jucksch et al., 2011; Meyer et al., 2009).

1.2.2 Long-term Development of Dysregulation Problems

As an emerging topic, the dysregulation profile has drawn an expanding body of research. However, our knowledge concerning the development of dysregulation profile during childhood and adolescence is still limited. To date, previous longitudinal studies on dysregulation profile mostly focused on testing it as an antecedent and a vulnerability of later problems rather than presenting its developmental characteristics in terms of a time/age related course. Examination of the dysregulation profile development during childhood and adolescence initially took the form of correlation or mean level tests. For example, Boomsma et al. assessed the developmental stability of dysregulation profile in a large population-based twin sample of 8013 pairs and found correlations between were .66 and .77 across ages 7, 10, and 12 years (Boomsma et al., 2006). Similar results were found in those studies that reported a decrease of dysregulation profile scores from childhood to adolescence (Halperin et al., 2011; Nobile et al., 2016) which supports the view that children's ability to self-regulate typically increases with development (Gestsdottir & Lerner, 2008; Raffaelli, Crockett, & Shen, 2005). Only recently, some efforts were made to explore the normative developmental course of the dysregulation profile. Deutz et al. mapped the dysregulation profile from ages 4 to 17 years in a population-based sample of 668 children using cohort-sequential latent growth modeling. They operationalized dysregulation profile as a latent variable underlying anxiety/depression, aggressive behavior, and attention problems and found a nonlinear developmental course with a peak in early adolescence (Deutz et al., 2017). Despite these findings could indicate inter-individual stability and a decreasing within-person course of dysregulation during childhood and adolescence, it could not distinguish individuals with different

development patterns (i.e., onset level and progression speed), although these information, revealing heterogeneity in the population, are critical for personalized screening and prevention.

1.3 Relations between Sleep Problems and Dysregulation Profile

1.3.1 Sleep Problems and Dysregulation Profile as Specific Problems

Sleep problems were associated with both emotional and behavioral difficulties in childhood and adolescence (Gregory & O'Connor, 2002). Such linkage covers all three components of the concept of dysregulation: impairment in regulating mood (depression) or worry (anxiety), cognitions (attention problems) and behavior (aggressive behaviors).

When emotional dysregulation was measured as separated symptoms of depression and anxiety, robust associations in childhood and adolescence have been reported (sleep and depression see Ivanenko et al., 2005; Lovato & Gradisar, 2014 for review; sleep and anxiety see Peterman et al., 2015; Willis & Gregory, 2015 for review). It also holds the same when depression and anxiety were combined as a single construct of emotional problems (Johnson, Chilcoat, & Breslau, 2000). Efforts were made to verify sleep problems both as cause and effect of emotional difficulties. On the one hand, insufficient sleep interferes one's ability to regulate emotions (i.e., the ability to control or modulate one's emotions) and alters one's understanding, expressing, and modifying of emotions (Kahn, Sheppes, & Sadeh, 2013; Walker & van Der Helm, 2009). On the other hand, problematic emotional state results in sleep disruptions, such as difficulty falling asleep and bedtime ruminations (Bos et al., 2009; Vandekerckhove et al., 2011). It still remains unclear what is the reciprocal

relationship among sleep problems and emotional regulatory difficulties and therefore calls for more longitudinal investigations on this topic in children and adolescents (Leahy & Gradisar, 2012).

Numerous evidences have unmasked the link between sleep problems and behavioral difficulties. The relationship between sleep problems and attention-related difficulties has been a widespread research interest (see Cortese et al., 2009; Sadeh, Pergamin, & Bar-Haim, 2006 for review). Sleep disorders may affect children on their daytime functioning, including the regulation of attention (O'Callaghan et al., 2010). Sleep problems in early childhood have been found to be a predictor of subsequent attention problems which may persist into adolescence and even adulthood (Gregory & O'Connor, 2002; Gregory, Van der Ende, Willis, & Verhulst, 2008; Simola, Liukkonen, Pitkaranta, Pirinen, & Aronen, 2014). For those children diagnosed with attention-deficit/hyperactivity disorder, many studies have reported their sleep issues as a common problem compared with controls (Cortese et al., 2009; Owens, 2008; Sadeh et al., 2006). Underlying mechanisms might be that sleep deprivation or disruption affects neurobehavioral functioning in children, and thus contributes to the origination and/or deterioration of symptoms of ADHD.

Relatively less attention has been paid to the link between sleep problems with aggression, although there are clues these problems might be linked together. Despite many people have experienced disturbed sleep accompanied by greater irritability and short-temperedness, usually it will not result in physical outbursts of aggression. However, the case might be different in a vulnerable population such as psychiatric patients who often experience serious sleep problems (Kamphuis, Meerlo, Koolhaas, & Lancel, 2012). The relationship between sleep problems and aggression may be mediated by the negative effect of sleep loss on prefrontal cortical functioning

which contributes to impaired control over emotions, including loss of the regulation of aggressive impulses to context-appropriate behavior (Kamphuis et al., 2012).In a review of existing literature on the relation between poor sleep and aggression, irritability, and hostility, Kamphuis et al have suggested poor sleep as a causal factor in aggression and violence (Kamphuis et al., 2012). Such view was supported by several studies in childhood and adolescence. Children with sleep disturbances (e.g. breathing problems) had increased aggressive behavior and conduct problems (Chervin, Dillon, Archbold, & Ruzicka, 2003; O'Brien et al., 2011) and treatment of children's sleep disorder resulted in reduced aggression (Pakyurek, Gutkovich, & Weintraub, 2002).

1.3.2 Sleep Problems and Dysregulation Profile as a Broad Syndrome

It is also important to extend the above-mentioned content of emotional and behavioral self-regulatory impairments to the broader syndrome of dysregulation profile in order to capture the integrated risk. Such a combination of problems is a multi-dimensional construct which is heritable, stable and appears to exist over and above emotion, attention and aggression problems as specific issues (Althoff et al., 2006; Boomsma et al., 2006; Deutz et al., 2016; Geeraerts et al., 2015; Hudziak et al., 2005). Problems with sleep, self-regulation of emotion and behavior in childhood are both common problems during childhood and adolescence (Boomsma et al., 2006; Deutz et al., 2017; Fricke-Oerkermann et al., 2007; Gregory & Sadeh, 2016) and have each been independently associated with adverse outcomes, such as poor academic performance and social-emotional issues (Blair, Calkins, & Kopp, 2010; Campbell, Spieker, Burchinal, Poe, & Network, 2006; Quach, Hiscock, & Wake, 2012). Moreover, both dysregulation profile as well as sleep problems seem to have

clinical impact on other childhood psychopathologies (Alfano & Gamble, 2009; Althoff et al., 2010; De Caluwe et al., 2013; Holtmann et al., 2011). Emerging research has revealed the presence of concurrence in the symptoms of sleep difficulties and inability to self-regulate in emotional, cognitive, and behavioral domains, we know little about the longitudinal relationships among these problems across the important developmental stage from early childhood to adolescence. Their concurrent courses and mutual influence in a longitudinal perspective are worth investigating in order to improve theoretical knowledge and derive practical considerations, especially considering the enduring impact the dysregulation profile has on the development of children and adolescents. Moreover, in-depth investigation of sleep versus dysregulation mutuality and temporal associations may shed light on the research question of temporal sequencing, which is an important step in determining the causality over and beyond their independent stability and co-occurrence (Alvaro, Roberts, & Harris, 2013; Gruber, 2014; Hansen, Skirbekk, Oerbeck, Wentzel-Larsen, & Kristensen, 2014). Such information can inform clinicians and relevant personnel about the focus and timing of interventions that would be optimal for each of the two domains when they co-exist in children.

Chapter 2 – The Cumulative Dissertation

2.1 Aims of the Cumulative Dissertation

According to the rationale given so far, the present cumulative dissertation aimed to investigate the longitudinal relationship between comorbid difficulties of sleep and self-regulation during the key developmental stage from early childhood to adolescence. Benefiting from the Western Australian Pregnancy Cohort (Raine) Study (Newnham, Evans, Michael, Stanley, & Landau, 1993), we were able to conduct the investigation in a large community sample of 1993 children from age 5 to age 17 over a span of 13 years. The following research questions were particular of our interests: a) whether there were longitudinal associations between sleep problems and dysregulation profile. If so, b) how did their associations present overtime and what was the extent of their concurrence. Finally, c) what was their reciprocal relationship and whether temporal precedence, i.e., direction of impact, could be determined. Our investigation was accordingly divided into three successive studies each designed in order to answer one of these above-mentioned questions. To be noted, in all studies in the present cumulative dissertation, sleep problems took the form of general behavioral sleep problems (composed of different kinds of sleep problems) as opposed to physical sleep problems as such breathing or movement-related sleep disorders.

In the first study, we aimed to explore the longitudinal associations between difficulties of sleep and self-regulation from childhood to adolescence. Since little is known about the developmental course of sleep problems, we firstly applied latent growth curve modeling (LGM) to examine the overall pattern of sleep problems. By

such means, an average developmental course was modeled for the general population. When significant variances around growth factors of the average course were observed, it is suggested that there were inter-individual differences (heterogeneity) in the general population. Therefore, growth mixture modeling (GMM) was further adopted to detect subgroups of individuals following different developmental courses of sleep problems, which can provide critical information for the screening of high-risk individual. Considering the long recognized links between sleep problems and emotional/behavioral problems in childhood and adolescence (Gregory & O'Connor, 2002), the content of dysregulation profile in this study manifested as self-regulatory difficulties in separate domains as emotional problems in terms of anxiety/depression and behavioral problems in terms of attention problems and aggressive behavior. We examined whether early childhood (baseline) emotional and behavioral problems could serve as predictors of developmental course of sleep problems and in turn whether developmental course of sleep problems were predictive of emotional and behavioral problems later in adolescence (as an outcome variable). In addition, we also explored the potential moderating role of gender on the relationship between sleep problems and emotional and behavioral difficulties.

In the second study, we aimed to reveal the mutual relations among difficulties of sleep and self-regulation across childhood and adolescence. In this study self-regulatory difficulties were not only presented as dimensions relating to anxiety/depression, attention deficiency and aggressive behaviors, but also jointly as a broad syndrome of the dysregulation profile in order to capture the integrated risk. The development and maintenance of sleep problems and regulation difficulties both as a broad syndrome of dysregulation profile and affective, behavioral and cognitive

functional impairments as single specific problems were examined firstly as single and independent disturbances using growth mixture modeling (GMM). And on this basis, joint models will be built pairing sleep problems and regulation difficulties and each yield two sets of probabilities. The joint probabilities could reflect the distribution of population with different combinations of sleep problems and concurrent regulation difficulties. The conditional probabilities could reflect the probability of an individual with sleep problems conditional on their regulation difficulties, and vice versa. This information is useful for understanding the co-occurrence and mutual association in the development of sleep problems and difficulties of dysregulation.

In the third study, we aimed to explore the reciprocal relationship between general sleep problems and dysregulation profile as a broad syndrome in childhood and adolescence. In this study, dysregulation profile took the form of an underlying latent variable comprised of three components of difficulties with self-regulation, namely anxious/depressed (emotional dysregulation), attention problems (attention dysregulation), and aggressive behavior (behavioral dysregulation). Therefore, the longitudinal measurement invariance of dysregulation profile was firstly examined to guarantee that the latent construct stayed the same at each time point, so that any observed changes over time reflected true changes in the level of dysregulation profile, rather than changes referent of latent structure. Subsequently, the reciprocal relationship between general sleep problems and dysregulation profile was examined by a series of autoregressive cross-lagged models. These analytic approaches allow us to reveal the longitudinal influences/impacts among constructs while controlling for their concurrent associations and the stability within each construct over time. Such information could provide evidence of temporal precedence of the cross-domain difficulties of sleep and self-regulation in childhood and adolescence, and may shed

light on potential causality and thus inform the focus and timing of clinical interventions that would be optimal for each of the two domains.

2.2 The Raine Study

Data from this cumulative dissertation were based on the large-scale, longitudinal, population-based cohort sample of the Western Australian Pregnancy Cohort (Raine) Study. Raine Study is one of the largest successful prospective cohorts of pregnancy, childhood, adolescence and now early adulthood to be carried out anywhere in the world. The cohort was established between 1989 and 1991 to determine how events during pregnancy and childhood influence health in later life (www.rainestudy.org.au). Pregnant women were recruited from the public antenatal clinic at King Edward Memorial Hospital (KEMH) and surrounding private clinics between May 1989 and November 1991 were invited to participate (Newnham et al., 1993). Eligibility criteria for participation were between 16 and 20 weeks pregnant, having sufficient proficiency in English to give informed consent, an expectation to deliver at KEMH and an intention to reside in Western Australia to make future follow-ups of their child feasible. A total of 2900 women (‘Generation 1’) were enrolled into the study. There were 2868 live births (49.3% girls) – the index participants of ‘Generation 2’ – including 60 sets of twins (n = 120) and two sets of triplets (n = 6), from 2826 mothers. The cohort has been regularly followed up since birth. Initial assessment was at 18 weeks gestation, and subsequent assessments were undertaken at 34 weeks, at birth and at ages 1, 2, 3, 5, 8, 10, 14, 17, 18, 20 and 22 years. Currently assessment of participants at age 27 years is under way (Straker et al., 2017). Early assessments were questionnaires and clinical/physical assessments provided by parents of their child (index participant). For the 14- and 17-year follow-

ups, index participants also provided self-report information to complement parental reporting and continued to perform clinical/physical assessments. From the 18-year follow-up onwards, index participants provided self-report information along with performing clinical/physical assessments. Written parental consent was obtained at recruitment and at each follow-up until the age of 18. Assent was obtained from participants at age 14 to 17, and written consent from participants from age 18. Data collection was conducted in accordance with Australian National Health and Medical Research Council (NHMRC) Guidelines for Ethical Conduct and was approved by the ethics committees of KEMH, Princess Margaret Hospital for Children and the University of Western Australia.

Data collection covered a wide range of health and behavior variables with over 85,000 phenotypic, behavioral and environmental variables are available for each participant, along with an extensive genetics database (Straker et al., 2015). The cumulative dissertation had a primary focus on the 5, 8, 10, 14 and 17-year follow-ups, as these follow-ups contained detailed data on sleep problems and difficulties with self-regulation in emotional (anxiety/depression) and behavioral (attention deficiency and aggressive behaviors) domains all measured with the Child Behavior Checklist (CBCL, Achenbach, 1991); i. e. the only informant were the parents. Available data on sleep problems were as follows: 2,116 participants at age 5 (73.8% retention); 2,037 participants at age 8 (71.0% retention); 1,994 participants at age 10 (69.5% retention); 1,774 participants at age 14 (61.9% retention); and 1,380 participants at age 17 (48.1% retention); corresponding data on difficulties with self-regulation measured by anxiety/depression, attention deficiency and aggressive behaviors were available for 2,170 participants at age 5 (75.7% retention); 2,075 participants at age 8 (72.4% retention); 2,017 participants at age 10 (70.3%

retention); 1,784 participants at age 14 (62.2% retention); and 1,355 participants at age 17 (47.2% retention). For the sake of data validity, only samples with enough measurement points (for the first study, at least three out of the four measurement points and for the second and third study, at least four out of the five measurement points) were included in the main analysis. This data management resulted in reduced samples, the effective sample size for study 1 was 1993 (48.6% girls; 69.5% retention) and the effective sample size for study 2 and 3 was 1625 (56.7% retention).

2.3 Methods

2.2.1 Latent Growth Curve Model

Latent growth curve model (LGM) is a conventional growth model which analyzes longitudinal data by relating observed outcome variables to time or to a time-related variable such as age (Bollen & Curran, 2006; Duncan & Duncan, 2004). As a variable-centered approach, LGM focuses on describing the relationships among variables and how dependent and independent variables are related. LGM assumes that all individuals are from a single population and therefore share a common/homogeneous developmental course/trajectory. Such a general and averaged growth curves for all individuals were described by a set of growth parameters named as latent growth factors. The average initial level was described by the intercept parameters, the average growth over time was reflected by the slope parameters (which could be linear, quadratic, etc.), and individual variation around the mean growth curve was captured by the estimation of the latent growth factor variances.

The adequacy of fit of growth models (with data) could be assessed within the structural equation modeling (SEM) framework. It is possible to judge the fit of a hypothesized model relative to a saturated baseline model allowing for the estimation of standalone indices of overall fit for a given model. Frequently used methods include the chi-square test and fit indices such as the root mean squared error of approximation (RMSEA; Steiger, 1980), comparative fit index (CFI; Bentler, 1990)), and Tucker-Lewis index (TLI; Tucker & Lewis, 1973), among many others (Curran, Obeidat, & Losardo, 2010).

However, as all variable-centered approach methods, LGM assumes that a single estimate of growth parameters can adequately describe all individuals(Laursen & Hoff, 2006). In this way, these methods precluded the possibility of examining individual differences in the onset and progression of psychopathologies, which is of great clinical relevance.

2.2.2 Growth Mixture Model

Growth mixture model (GMM) is based on conventional growth models (such as LGM) and relaxes its assumption and allows for differences in growth parameters across unobserved subpopulations. As a person-centered approach, GMM focuses on the relationships among individuals and captures the heterogeneity in the population by classifying individuals into several distinct and meaningful subgroups (i.e., latent classes) based on their response patterns so that individuals within a subgroup are more similar than individuals between subgroups(Jung & Wickrama, 2008). For each latent class, its own developmental course/trajectory with a set of growth factors in terms of intercept (initial level) and slope (average growth), with unique estimations of variances were separately estimated.

Assuming there are multiple heterogeneous subgroups in the population, an important question that stands is the determination of appropriate number of latent classes. A series of nested models should be estimated and compared, starting from the model with only one latent class (in this case would be LGM) to model with several (usually five to eight depending on the status of data convergence) latent classes. Evaluation of the best-fitting models took into account several criteria (Muthén, 2004; Nylund, Asparouhov, & Muthén, 2007). The Bayesian Information Criterion (BIC; Schwarz, 1978) and the adjusted BIC (aBIC; Sclove, 1987) were calculated from the maximized likelihood with a correction for number of parameters estimated in the model which consider the balance between model fit and parsimony. Models with smaller information criteria (i.e., closer to 0) indicated better fitting models. The Lo–Mendell–Rubin likelihood ratio test (LMR-LRT; Lo, Mendell, & Rubin, 2001) and bootstrap likelihood ratio test (BLRT; McLachlan, 2004) were used to compare the k and the k-1 latent class model (i.e., the model of interest vs. the model with one fewer class). Models with p value smaller than .05 indicated a statistically significant improvement in model fit with the inclusion of one more latent class. The entropy index (Celeux & Soromenho, 1996) was used to quantify the certainty of classifying individuals into latent classes. High values of entropy (> .80) indicate that individuals are classified with confidence and different latent classes were adequately separated (Ram & Grimm, 2009). Moreover, large enough group size, theoretical rationality and interpretability were also important consideration of the validity of latent classes.

2.2.3 Joint Trajectory Model

As an extension to GMM, joint trajectory models were used to examine the concurrent developmental trajectories of distinct but related behaviors (Nagin & Tremblay, 2001). Separate developmental trajectories should be estimated for each problem as the starting point for the joint models. Key outputs of a joint model are the joint probabilities and the conditional probabilities. The former reflects the probability of individuals following different combinations of trajectories (i.e., latent classes of studied problems), while the latter reflects the probability of individuals following each trajectory of one problem conditional on their trajectories of the other, and vice versa. These information are helpful in understanding the important issue of comorbidity and heterotypic continuity in developmental psychopathology (Nagin & Tremblay, 2001).

2.2.4 Autoregressive Cross-lagged Model

In the great deal of interest in the developmental sciences in finding reciprocal relations between psychopathologies, the autoregressive cross-lagged (ARCL) model serves as an useful tool for identifying the relations between variables across time (Selig & Little, 2012). The core of ARCL model is that scores at time *t* are sufficiently explained by score deviation at previous time *t-1* (Curran & Bollen, 2001). The ARCL model generates two sets of parameters, autoregressive effects and cross-lagged effects. Autoregressive effects describe the effect of a construct on itself measured at a later time point (i.e., within variable effects). Therefore, larger autoregressive coefficients would indicate little inter-individual variance in the construct and stronger longitudinal stability. Correspondingly, cross-lagged effects describe the influences from one construct on another measured at a later time point (i.e., between variable

effects). With these parameters, the ARCL model allows for the exploration of longitudinal influences among constructs while controlling for their concurrent associations and the stability within each construct over time. This information could assist our understanding of the temporal precedence of psychopathologies, an important step towards determining potential causality over their co-occurrence.

To find the best fitting ARCL model, nested models with different inclusion of autoregressive and cross-lagged effects should be estimated and compared. These nested models include the base model in which only autoregressive paths between adjacent time points were included, step up to autoregressive paths between distant time points, cross-lagged paths between adjacent time points, early cross-lagged effects and finally with all remaining potential cross-lagged paths. Model comparison takes into consideration multiple selection criteria under the framework of SEM, such as RMSEA (Steiger, 1980), CFI (Bentler, 1990) and TLI (Tucker & Lewis, 1973). Moreover, all the non-significant paths should be removed for the consideration of model parsimony.

Chapter 3 – Original manuscripts

This chapter contains two published articles and one submitted manuscript.

The first study mapped the longitudinal developmental course of sleep problems from childhood to adolescence and detected subgroups of individuals with distinct developmental patterns. Cross-sectional self-regulatory difficulties in emotion, attention and aggression domains were examined both as early childhood predictors of developmental course of sleep problems and in turn as later outcomes.

Wang, B., Isensee, C., Becker, A., Wong, J., Eastwood, P. R., Huang, R. C., ... & Rothenberger, A. (2016). Developmental trajectories of sleep problems from childhood to adolescence both predict and are predicted by emotional and behavioral problems. Frontiers in psychology, 7, 1874. doi: 10.3389/fpsyg.2016.01874

The second study revealed the mutual relations among difficulties of sleep and self-regulation across childhood and adolescence by building their joint developmental model. In this study, self-regulatory difficulties were not only presented as dimensions relating to anxiety/depression, attention deficiency and aggressive behaviors, but also jointly as a broad syndrome of the dysregulation profile in order to capture the integrated risk.

Wang, B., Eastwood, P. R., Becker, A., Isensee, C., Wong, J. W., Huang, R. C., ... Rothenberger, A. & Zepf, F. D. (2018). Concurrent developmental course of sleep problems and emotional/behavioral problems in childhood and adolescence as reflected by the dysregulation profile. Sleep. doi: 10.1093/sleep/zsy243.

The third study explored the reciprocal relationship between general sleep problems and dysregulation profile as a broad syndrome in childhood and adolescence by .examining a series of autoregressive cross-lagged models. The findings revealed the longitudinal influences/impacts among sleep and dysregulation while controlling for their concurrent associations and the inner stability.

Wang, B., Runions, K., Eastwood, P. R., Poustka L., Becker, A., Wong, J., ... & Rothenberger, A. (submitted). Causality and mutuality of predictors in children along a 13-year period: dysregulation profile impacts on sleep problem.

3.1 Original Article 1

Wang, B., Isensee, C., Becker, A., Wong, J., Eastwood, P. R., Huang, R. C., ... & Rothenberger, A. (2016). Developmental trajectories of sleep problems from childhood to adolescence both predict and are predicted by emotional and behavioral problems. Frontiers in psychology, 7, 1874. doi: 10.3389/fpsyg.2016.01874

frontiers in Psychology

ORIGINAL RESEARCH
published: 01 December 2016
doi: 10.3389/fpsyg.2016.01874

Developmental Trajectories of Sleep Problems from Childhood to Adolescence Both Predict and Are Predicted by Emotional and Behavioral Problems

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OPEN ACCESS

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Specialty section:
This article was submitted to Psychopathology, a section of the journal Frontiers in Psychology

Received: *03 September 2016*
Accepted: *14 November 2016*
Published: *01 December 2016*

Citation:
Wang B, Isensee C, Becker A, Wong J, Eastwood PR, Huang R-C, Runions KC, Stewart RM, Meyer T, Brüni LG, Zepf FD and Rothenberger A (2016) Developmental Trajectories of Sleep Problems from Childhood to Adolescence Both Predict and Are Predicted by Emotional and Behavioral Problems. Front. Psychol. 7:1874. doi: 10.3389/fpsyg.2016.01874

Although the prevalence rates of sleep disorders at different stages of childhood and adolescence have been well established, little is known about the developmental course of general sleep problems. This also holds true for the bidirectional relationship between sleep problems and emotional as well as behavioral difficulties. This longitudinal study investigated the general pattern and the latent trajectory classes of general sleep problems from a large community sample aged 5–14 years. In addition, this study examined the predictive value of emotional/behavioral difficulties (i.e., anxiety/depression, attention problems, and aggressive behavior) on sleep problems latent trajectory classes, and vice-versa. Participants (N = 1993) were drawn from a birth cohort of Western Australian children born between 1989 and 1991 who were followed until 14 years of age. Sleep problems were assessed at ages 5, 8, 10, and 14, respectively, whereas anxiety/depression, attention problems, and aggressive behavior were assessed at ages 5 and 17 years. Latent growth curve modeling revealed a decline in an overall pattern of sleep problems during the observed 10-year period. Anxiety/depression was the only baseline factor that predicted the longitudinal course of sleep problems from ages 5 to 14 years, with anxious and depressed participants showing faster decreasing patterns of sleep problems over time than those without anxiety or depression. Growth mixture modeling identified two classes of sleep problem trajectories: *Normal Sleepers* (89.4%) and *Troubled Sleepers* (10.6%). Gender was randomly distributed between these groups. Childhood attention problems, aggressive behavior, and the interaction between gender and anxiety/depression were significantly predictive of membership in the group of *Troubled Sleepers*. Group membership in *Troubled Sleepers* was associated with higher probability of having attention problems and aggressive behavior in mid-adolescence. Boys and girls with behavioral difficulties,

and girls with emotional difficulties were at increased risk of having sleep problems during later childhood and adolescence. Developmental trajectories of sleep problems were also predictive of behavioral difficulties in later life. Findings from this study provide empirical evidence for the heterogeneity of sleep problems and their development, and emphasize the importance of understanding sleep problems and their relationship to children and adolescents' mental health.

Keywords: sleep problems, childhood and adolescence, latent trajectory classes, anxiety/depression, attention problems, aggressive behavior, CBCL, Raine study

INTRODUCTION

Sleep problems in children and adolescents are common (Kahn et al., 1989; Owens et al., 2000b; Goodnight et al., 2007). Estimates of the prevalence of sleep problems vary depending upon differences in definitions and methods of assessment (O'Callaghan et al., 2010). Furthermore, these disturbances can take many forms, including dyssomnias (such as insomnia) and parasomnias (such as sleep walking). Moreover, the classification of such disorders varies, depending on the system being followed – the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5, American Psychiatric Association, 2013) or the third edition of the International Classification of Sleep Disorders (ICSD-III, American Academy of Sleep Medicine, 2014). Sleep problems often co-occur with a wide range of psychiatric and neurodevelopmental problems like autism (Allik et al., 2006; Richdale and Schreck, 2009; Cohen et al., 2014; Brand et al., 2015a), epilepsy (Pereira et al., 2012; Carotenuto et al., 2014), and tic disorders (Kirov et al., 2007; Ghosh et al., 2014).

Sleep problems not only affect children and adolescents' psychological functioning as well as their academic, neurocognitive, and behavioral performance, but can also have a negative impact on family functioning and the well-being of family members (Curcio et al., 2006; Kheirandish and Gozal, 2006; Mitchell and Kelly, 2006; Martin et al., 2007; Meltzer and Mindell, 2007; Bell and Belsky, 2008; Kalak et al., 2014; Brand et al., 2015b). However, many parents tend to overlook or ignore sleep problems, or possibly underestimate the importance of healthy sleep habits for good daily psychological functioning of their children (Stein et al., 2001). Disturbed sleep during childhood seems to be an invisible phenomenon to many parents, and often fails to receive attention until it interferes with the child's well-being (Smaldone et al., 2007). A greater understanding of the nature and development of sleep problems and their relationship to children's mental health may provide critical information for researchers and clinicians in the early screening, prevention, and treatment of sleep problems in childhood and adolescence.

Developmental Course of Sleep Problems

Although much has been learned about the prevalence rates of sleep disorders at different stages of childhood and adolescence (Ohayon et al., 2000; Ipsiroglu et al., 2002; Spruyt et al., 2005; Roberts et al., 2011; Schlarb et al., 2015), our knowledge concerning the individual development of sleep problems is still rather limited. According to a recent review of the latest science in sleep problems (Gregory and Sadeh, 2016), there is a critical need to clarify the nature and impact of such problems on child development.

To date, longitudinal studies on sleep problems during childhood and adolescence are dominated by designs with short time frames, typically using just a few years (Gregory and O'Connor, 2002). For example, Laberge et al. (2001) analyzed data on sleep problems from a randomly stratified, proportional sample of 1146 children (48.7% girls), with a particular focus on mothers' annual report of children's sleep patterns, sleep habits and sleep disturbances over a course of 4 years. They detected that the proportion of children with difficulties in initiating sleep declined significantly from ages 10 to 13 years. However, such studies focused on the percentage of participants with sleep problems can provide only limited information on the developmental time-course of sleep problems.

To our knowledge, very few studies have examined the development of sleep problems during childhood and adolescence in terms of a longitudinal course covering a longer time period. Gregory and O'Connor (2002) investigated the sleep problems among 490 children (46.3% girls) from ages 4 to 15 years. A decrease in the average level of sleep problems (50% decline) was found from preschool to mid-adolescence, with modest stability ($r = 0.29$). Developmental changes in sleep problems were assessed using repeated measures analyses, whilst inter-participant stability across this particular time period was assessed with bivariate correlations. Such correlational approaches tell us little about the developmental course of sleep problems; developmental trajectory analyses are required. Friedman et al. (2009) modeled the longitudinal trajectories of seven specific sleep problems frequently observed in childhood (i.e., nightmares, talks or walks, wets bed, sleeps less, sleeps more, trouble sleeping, and overtired) among 916 twins (50.8% girls) from age 4 to 16. Using latent growth curve analyses, they detected that most reported sleep problems declined over time. These studies presented the first attempt to document the average course of sleep problems (general or specific) in a community sample. However, the variable-centered approach applied in these studies precluded the possibility of examining heterogeneity in the development of sleep problems, which can provide critical information for the screening of high-risked individuals, as well as for the design of pertinent treatment approaches. Hence, person-centered trajectory analyses are required to better clarify the development of sleep problems.

Using such person-centered approaches, several studies have detected distinct subgroups of sleep problem development amongst normative child and adolescent samples. Touchette et al. (2007) investigated sleep duration among 1492 children in early childhood (2.5–6 years). Four developmental sleep duration patterns were identified: short persistent (<10h/night; 6.0%), short increasing (4.8%), 10-h persistent (50.3%), and 11-h persistent (38.9%). Similarly, Magee et al. (2014) found four distinct subgroups using growth mixture modeling (GMM): typical sleepers (40.6%), initially short sleepers (45.2%), poor sleepers (2.5%), and persistent short sleepers (11.6%) when examining the sleep duration patterns from age 0 to 1 years to age 6–7 years among 2926 children (42.7% girls). Seegers et al. (2011) examined the time spent in bed from age 10 to 13 among 1916 preadolescents (47.2%) girls and identified three distinct developmental course of time-in-bed: short sleepers (14.5%), 10.5-h sleepers (68.2%), and 11-h sleepers (17.3%). These studies identified distinct developmental courses of several normative aspects of sleep (e.g., sleep duration, time in bed) – in general about 10–15% of children were characterized as having a short sleep duration. However, to our knowledge, no studies have investigated longitudinal trajectories of general sleep problems.

Specifically, there is a need for research that examines developmental trajectories spanning childhood through adolescence. Puberty brings maturational changes to neural architecture involved in sleep as well as (in many cultures) new norms and expectations regarding sleep patterns (Dahl and Lewin, 2002; Soffer-Dudek et al., 2011). These changes (related to neural system's reorganization) have been posited to results in increased fatigue in adolescence (Soffer-Dudek et al., 2011). Thus, sleep trajectories beginning in early childhood and spanning late adolescence are worth investigating.

Predictors and Predictive Value of Sleep Problems

Sleep problems have been linked to both emotional (e.g., anxiety and depression) and behavioral (e.g., attention and conduct) difficulties in childhood and adolescence (Gregory and O'Connor, 2002). Improved understanding of the co-occurrence and longitudinal associations between these difficulties could potentially facilitate the development evidence-based prevention and intervention programs (Gregory and Sadeh, 2016).

The relationship between sleep and emotional problems has been examined in studies that have separated symptoms of anxiety and depression and in studies that have combined anxiety and depression into a single construct (Gregory and Sadeh, 2012). For instance, one study showed that troubled sleeping was associated with parent-reported anxiety/depression measures in children at ages 6 and 11 years (Johnson et al., 2000). Another study reported that sleep problems at age 4 were predictive of anxiety/depression in mid-adolescence (Gregory and O'Connor, 2002). Furthermore, robust associations between sleep problems and anxiety, as well as sleep problems and depression have been detected in children and adolescents (Ivanenko et al., 2005; Lovato and Gradisar, 2014; Peterman et al., 2015; see Willis and Gregory, 2015 for review). It is likely that the nature of any relationships between these psychopathologies are both *complex* and *bidirectional*. For example, it remains to be established whether sleep problems serve as a precursor to emotional difficulties (Alvaro et al., 2013; Lovato and Gradisar, 2014), or whether emotional difficulties may contribute to the development of sleep problems. Longitudinal studies have shown mixed results. Some studies have suggested that both disorders contribute similarly to the development of sleep problems (e.g., Kaneita et al., 2009; Meijer et al., 2010). However, others have suggested that the observed cause-effect associations were distinct (Ohayon and Roth, 2003; Johnson et al., 2006). Therefore, the etiological relationship between sleep and emotion remains unclear. A dearth of longitudinal, experimental, and more methodologically rigorous research limits our capacity to interpret the current literature (Peterman et al., 2015). Additional studies (in particular longitudinal ones) are required to further delineate the association between sleep and emotional problems in children and adolescents (Leahy and Gradisar, 2012).

Although most research has focused on sleep problems in association with emotional difficulties, there is emerging evidence that sleep problems may also be linked to subsequent behavioral difficulties (Gregory et al., 2008). The links between sleep and attention deficit hyperactivity disorder (ADHD) have been extensively studied (see Sadeh et al., 2006; Owens, 2008; Cortese et al., 2009; Tsai et al., 2016 for review). In this context, the topic of ADHD and related symptoms and behaviors has received considerable scientific and clinical attention (Gregory and Sadeh, 2012). In non-clinical samples, sleep disorders may affect children, and may potentially have an effect on daytime functioning of the child, including the regulation of attention (O'Callaghan et al., 2010). Longitudinal studies have suggested that sleep and attention problems are positively related. Sleep problems in early childhood are an indicator of subsequent attention problems that may persist into adolescence and adulthood (Gregory and O'Connor, 2002; Gregory et al., 2008; O'Callaghan et al., 2010; Simola et al., 2014).

Other behavioral problems such as aggression have received less attention, although there are indications that such problems may also be linked to sleep problems (Gregory and Sadeh, 2012). Several studies have suggested that poor sleep may be a causal factor in aggression and violence (see Kamphuis et al., 2012 for a review). For example, children at high-risk for sleep disorders (e.g., breathing problems, periodic leg movements during sleep) have significantly increased parent-reported aggression (Chervin et al., 2003). Children rated as having a conduct problem by a parent or teacher showed more disordered-breathing during sleep, and sleepiness predicted their behavior problems (O'Brien et al., 2011). Persistent sleep problems also appear to confer increased risk of aggressive symptoms (Pakyurek et al., 2002; Simola et al., 2014). In addition, parent-rated sleep problems in childhood are correlated with higher scores on an aggressive behavior scale later in life (Gregory et al., 2008).

Few studies have examined longitudinal relationships between sleep and behavioral problems (Gregory and Sadeh, 2012). In one

such study, Pieters et al. (2015) showed that, in the short term (i.e., within a year), sleep problems appear to predict externalizing problems in early adolescence. Longer-term evidence is rarer and in the only study to date Wong et al. (2009) have suggested that early childhood sleep problems (at ages 3–8 years) predict trajectories of externalizing problems, with such problems particularly linked to sleep problems for boys.

Finally, as most research on gender differences in sleep has been conducted in adults, the literature regarding the role of gender on sleep problems in childhood and adolescence is scarce and has shown mixed results (see Krishnan and Collop, 2006; Galland et al., 2012; Mong and Cusmano, 2016 for review). Some studies have indicated that gender has no or relatively little influence on sleep (Voderholzer et al., 2003; Chaput and Tremblay, 2007; Dollman et al., 2007). In contrast, other studies have suggested the presence of gender differences with regards to sleep patterns and insomnia prevalence, the latter showing a considerable female preponderance (Hysing et al., 2013). For example, nightmares were reported more frequently by girls (Liu et al., 2000), and an increase in a variety of sleep problems (insomnia, daytime tiredness, and insufficient sleep) has been associated with the pubertal development period in girls, but not in boys (Knutson, 2005). Therefore, specific attention should be paid to the role of gender when examining sleep problems in minors.

The Present Study

The present study aimed to investigate the overall pattern and the latent trajectory classes of general sleep problems from ages 5 to 14 years among a large community sample, using latent growth curve modeling and GMM. These analytic approaches allow examination of the overall course of sleep problems during childhood to adolescence, as well as examination of subgroups with distinct developmental patterns. The purported bidirectional nature of any relationships between sleep problems and emotional (anxiety and depression) and behavioral (attention problems and aggressive behavior) difficulties were examined by testing whether baseline emotional and behavioral problems could serve as predictors of sleep trajectory classes. Moreover, the predictive value of sleep trajectory classes on anxiety/depression, attention problems, and aggressive behavior later in life (i.e., at age 17) was analyzed. Based on extant research (Gregory and O'Connor, 2002), we expected a general decline in sleep problems over the 10-year period of the trajectories (from ages 5 to 14 years).

Further, we expected to find at least two subgroups with a distinct trajectory of sleep problems, i.e., one group including the majority of children and adolescents reporting none or few sleep problems, and another group of children and adolescents reporting persistent sleep problems during childhood and adolescence. As associations between sleep problems and emotional and behavioral difficulties have been well established (O'Callaghan et al., 2010; Kamphuis et al., 2012; Lovato and Gradisar, 2014), we expected that anxiety/depression, attention problems, and aggressive behaviors would predict the development of sleep problems, and vice-versa.

With respect to the role of gender, we did not have a specific hypothesis concerning the gender differences in sleep problems due to minimal prior research in this area (Galland et al., 2012), therefore an explorative approach was implemented for this particular research question. However, as girls tend to report more emotional difficulties (see Hyde et al., 2008; McLean and Anderson, 2009 for review), and boys tend to report more behavioral difficulties (see Archer, 2004; Rucklidge, 2010 for review), we also explored the potential moderating role of gender on the relationship between sleep problems and emotional and behavioral difficulties.

MATERIALS AND METHODS

Participants and Procedures

Participants were from the Western Australian Pregnancy Cohort (Raine) Study. The methodology and recruitment for this study are described in detail elsewhere (Newnham et al., 1993). In brief, 2900 women between 16 and 20 weeks gestation (mean 18 weeks) were recruited from the public antenatal clinic at King Edward Memorial Hospital (KEMH) in Perth, Western Australia and surrounding private clinics between May 1989 and November 1991. Data collection occurred in accordance with Australian National Health and Medical Research Council (NHMRC) Guidelines for Ethical Conduct and was approved by the ethics committees of KEMH, Princess Margaret Hospital for Children and the University of Western Australia. Written parental consent was obtained at recruitment and at each follow-up until the age of 18. Assent was obtained from participants at age 14–17, and written consent from participants from age 18. Eligible women were required to have sufficient English-language skills to give informed consent, an expectation to deliver at KEMH, and an intention to reside in Western Australia to enable future follow-ups of their child.

Of the 2900 women enrolled, 2804 delivered live babies. There were 64 multiple births, and as such, the initial cohort consisted of 2868 children (49.3% girls). These children were assessed at birth, and were followed up at ages 1, 2, 5, 8, 10, 14, 17, 20, and 22 years of age using questionnaires and physical assessments. This study focused on the 5, 8, 10, and 14-year follow-ups, as detailed sleep problems data were collected at these assessments with adequate retention rate.

Data on sleep problems were available for 2116 participants at age 5 (73.8% retention); 2037 participants at age 8 (71.0% retention); 1994 participants at age 10 (69.5% retention); and 1774 participants at age 14 (61.9% retention). In order to better capture the developmental patterns, we focused on participants who had data on sleep problems for at least three out of the four measurement points. The effective sample size was 1993 (48.6% girls; 69.5% retention).

Measures

Sleep Problems

Six items from the parent-report of Child Behavior Checklist (CBCL, Achenbach, 1991a) comprised of a 'sleep problem scale' and were used to measure child and adolescent sleep problems.

Although not a standardized CBCL scale, the CBCL sleep composite has been shown to be strongly correlated with the validated Children's Sleep Habits Questionnaire (CSHQ, Owens et al., 2000c) and also with clinical diagnoses of sleep disorders. The sleep composite shows similar external correlations with youths' social problems and psychopathology symptoms as the CSHQ score (Becker et al., 2015). It has been widely used in previous research as a measure of overall sleep functioning (Stoléru et al., 1997; Gregory and O'Connor, 2002; Alfano et al., 2006; Beebe et al., 2007; Gregory et al., 2008; Storch et al., 2009; Troxel et al., 2013). The specific sleep-content items are "trouble sleeping," "nightmares," "overtired without good reason," "sleeps less than most kids," "talks or walks in sleep," and "sleeps more than most kids during day and/or night." Each item is rated on a 3-point scale (0 = not true, 1 = somewhat or sometimes true, 2 = very true or often true). A sum score of the 6-items scale was used to represent the level of children and adolescents' sleep problems (range 0–12), with higher scores indicating higher levels of sleep problems. Cronbach's alpha of the four measurement points ranged between 0.55 and 0.61

Emotional and Behavioral Problems at Baseline (Age 5)

The Anxious/Depressed, Attention Problems, and Aggressive Behavior scales were examined using the parent-report of CBCL (Achenbach, 1991a). None of these scales included sleep problems. The Anxious/Depressed scale consists of 14 items, sample items of the subscale included "feels or complains that no one loves him/her" and "too fearful or anxious." The Attention Problems scale consists of 11 items, sample items of the subscale included "daydreams or gets lost in his/her thoughts" and "can't sit still, restless, or hyperactive." The Aggressive Behavior scale consists of 20 items, sample items of the subscale included "cruelty, bullying, or meanness to others" and "destroys things belonging to his/her family or others." Responses were rated on a 3-point scale (0 = not true, 1 = somewhat or sometimes true, 2 = very true or often true). A sum score of all the items of the subscale was used to represent the level of children and adolescents' emotional and behavioral problems (range 0–28, 22, 40 for the Anxious/Depressed, Attention Problems, and Aggressive Behavior scale, respectively), with higher scores indicating higher levels of emotional or behavioral problems. Cronbach's alpha was 0.97, 0.96, and 0.98 for the Anxious/Depressed, Attention Problems, and Aggressive Behavior scale, respectively.

Emotional and Behavioral Problems at Age 17

The Anxious/Depressed, Attention Problems, and Aggressive Behavior scales were obtained using the Youth Self-Report (YSR, Achenbach, 1991b). Items are scored in the same way as for the parent-report CBCL. Responses were rated on a 3-point scale (0 = not true, 1 = somewhat or sometimes true, 2 = very true or often true). The sum score of all the items of the subscale was used to represent the level of children and adolescents' emotional and behavioral problems (range 0–28, 22, 40 for the Anxious/Depressed, Attention Problems, and Aggressive Behavior scale, respectively), with higher scores indicating higher levels of emotional or behavioral problems. Cronbach's alpha was 0.90, 0.85, and 0.92 for the Anxious/Depressed, Attention Problems, and Aggressive Behavior scale, respectively.

Statistical Analyses

After presenting children and adolescents' sleep problems and emotional/behavioral difficulties in a descriptive manner, the data analysis proceeded in five consecutive steps. In step 1, we applied latent growth curve modeling (LGM) to examine the overall pattern of sleep problems. Four measurements of sleep problem data assessed from childhood (age 5 years) to adolescence (age 14 years) were used as outcome variables to estimate latent growth factors that represent the average initial level (i.e., intercept) and the average growth (i.e., slopes) of sleep problems. Individual differences were modeled using random effects around these latent growth factors. A series of unconditional LGMs including different growth factors (e.g., intercept-only, linear slope, quadratic slope) were estimated to identify the model that best fit the average sleep problems longitudinal course. Because the χ^2 is sensitive to sample size, we assessed fit primarily with the comparative fit index (CFI), root-mean-square error of approximation (RMSEA), and standardized root-mean-square residual (SRMR) using criteria of CFI $\geq$ 0.95, RMSEA $\leq$ 0.06, and SRMR $\leq$ 0.08 as indicators of good fit (Hu and Bentler, 1999).

In step 2, baseline emotional and behavioral predictors (i.e., anxiety/depression, attention problems, and aggressive behavior) were added to the best fitting model identified at step 1 to get a conditional LGM, which simultaneously examined the effects of baseline emotional and behavioral predictors on the course of sleep problems. The latent growth factors (e.g., intercept and slope) were regressed on the baseline predictors. The interaction effects between baseline predictors and gender on sleep problems latent growth factors were also explored.

In step 3, we used GMM to estimate latent trajectory classes in sleep problems. GMM captures the heterogeneity in unobserved subpopulations by allowing for the differences in growth parameters, and identifies a finite number of subgroups of individuals following different developmental courses (Jung and Wickrama, 2008). GMM results in separate growth model for each latent class, which differs in terms of intercept (initial level), slope (average growth), and with their unique estimates of variances and covariate influences.

A series of models were fitted, beginning with a one trajectory model and moving to a five trajectory model. Each model was fitted using at least 1000 random perturbations of starting values to ensure replication of the best likelihood and to avoid local maxima. Evaluation of the best fitting models took into account several criteria (Nylund et al., 2007). Firstly, Bayesian Information Criterion (BIC) and adjusted BIC (aBIC) were examined with lower (i.e., closer to 0) value indicating better balance between model fit and parsimony. Secondly, Lo–Mendell–Rubin likelihood ratio test (LMR-LRT) and bootstrap likelihood ratio test (BLRT) were used to compare the k and the k−1 trajectory models. A significant p-value (<0.05) in LMR-LRT and BLRT indicated a statistically significant

improvement in model fit with the inclusion of one more trajectory. Thirdly, we examined the entropy index that ranges from 0 to 1 while entropy closer to one indicates better classification.

In step 4, participants were assigned to their most likely trajectory latent class based on their highest posterior probability. Gender-specific group membership was compared. We conducted multinomial logistic regression with baseline emotional and behavioral predictors (i.e., anxiety/depression, attention problems, and aggressive behavior) as independent variables to examine their usefulness in predicting sleep problems trajectory group membership. The interaction between gender and each predictor variable was also examined. Odds ratios with 95% confidence intervals were estimated and reported.

In step 5, to test the predictive value of sleep problems trajectory classes on emotional and behavioral problems later in adolescence, we examined level of later anxiety/depression, attention problems, and aggressive behavior conditional on the latent trajectory class membership. Mean scores of anxiety/depression, attention problems, and aggressive behavior at age 17 years were compared between sleep problem trajectory classes using independent sample *t*-test.

Latent growth curve modelings and growth mixture modelings were performed using Mplus version 7.3 (Muthén and Muthén, 1998-2015). Other analyses were carried out using SPSS version 23. Missing data on the outcome variables were handled through full information maximum likelihood (FIML) estimation in Mplus as a standard procedure under the assumption of missing at random (Muthén and Muthén, 1998-2015). Individuals with missing values on predictors were excluded from multinomial logistic regression and comparison of means.

RESULTS

Descriptive Statistics

Table 1 presents descriptive statistics and bivariate correlations for all study variables. Results from Little's MCAR test showed that missing data on all variables were missing completely at random ($p = 0.317$). Means of children and adolescents' sleep problems experienced a significant decrease over time ($t = 11.855$, $df = 1576$, $p < 0.001$). Almost all study variables were significantly inter-correlated (except for anxiety/depression at age 5 and attention problems at age 17). Correlations between sleep problems measured in the four waves showed that the magnitude of associations between adjacent assessments ($rs = 0.50$–0.53, $p < 0.01$) was greater than that between non-adjacent ones ($rs = 0.38$–0.43, $p < 0.01$). Cross-sectional relationships between sleep problems and baseline emotional/behavioral predictors ($rs = 0.41$–0.46, $p < 0.01$) were also higher than their relationships over time ($rs = 0.23$–0.34, $p < 0.01$). The longitudinal relationships between sleep problems (at age 5, 8. 10, and 14) and later emotional/behavioral (at age 17) was trivial ($rs = 0.09$–0.16, $p < 0.01$).

Longitudinal Course of Sleep Problems from Age 5 to 14

Unconditional Latent Growth Curve Models

A model including a linear slope (CFI = 0.85, RMSEA = 0.13, and SRMR = 0.08) fit the data better than an intercept-only model (CFI = 0.98, RMSEA = 0.07, and SRMR = 0.03). The addition of a quadratic slope also improved the model fit (CFI = 0.99, RMSEA = 0.06, and SRMR = 0.01). Thus, a model including both linear and quadratic slopes was selected for the subsequent analyses. A significant negative linear slope ($s = -0.56$, $p < 0.01$) and a non-significant quadratic slope ($q = 0.04$, $p = 0.76$) indicated a stable decreasing trend over time (**Figure 1A**). Significant variances were observed around the intercept and both slope factors, suggesting inter-individual differences in sleep problems at initial level as well as in the development of sleep problems. This significant variance suggested that GMM might provide insight into the heterogeneity in the development of sleep problems.

Baseline Predictors of Longitudinal Course of Sleep Problems

Results from the conditional LGM are presented in **Table 2**. Significant effects were observed on the intercept factor for all baseline emotional and behavioral predictors. Children and adolescents with higher levels of anxiety/depression, attention problems, and aggressive behavior at baseline were concurrently reported with higher levels of sleep problems. Gender was not significantly related to the initial level of sleep problems.

Only emotional difficulties at age 5 were predictive of the linear and quadratic slope factors. Anxious and depressed children showed a faster decreasing pattern of sleep problems over time, characterized by a steeper and a subsequent more marked decline. Conversely, gender and baseline differences in behavioral vulnerabilities (i.e., attention problems and aggressive behavior) did not predict the longitudinal course of sleep problems from age 5 to 14.

With respect to the moderating role of gender, no significant interaction effect between gender and anxiety/depression, attention problems, or aggressive behavior was found (effect not presented). Associations between emotional and behavioral predictors and the development of sleep problems were similarly affecting boys and girls.

Latent Trajectory Classes of Sleep Problems from Age 5 to 14

Unconditional Growth Mixture Models

Unconditional GMMs with 1–5 trajectory classes were estimated including both linear and quadratic slopes. **Table 3** shows the model selection criteria used to decide on the best class solution for sleep problems trajectories. The BIC and aBIC both consistently declined for 1- through 5-class solution, although with a decelerated decreasing rate with the addition of classes. However, the model complexity also increased with the number of latent classes. Both the LMR-LRT and BLRT suggested that the 2-class solution significantly improved the model fit as compared to the 1-class solution, whereas the 3-class solution did not fit

TABLE 1 | Descriptive statistics and bivariate correlations between all study variables.

	N	*M*	*SD*	1	2	3	4	5	6	7	8	9	10
(1) Sleep problems at 5	1857	1.30	1.49	1									
(2) Sleep problems at 8	1861	1.21	1.55	0.52**	1								
(3) Sleep problems at 10	1902	1.01	1.40	0.42**	0.53**	1							
(4) Sleep problems at 14	1705	0.85	1.34	0.38**	0.43**	0.50**	1						
(5) Anxiety/depression at 5	1873	2.78	2.93	0.46**	0.30**	0.25**	0.24**	1					
(6) Attention problems at 5	1860	2.88	2.79	0.41**	0.30**	0.27**	0.23**	0.49**	1				
(7) Aggressive behavior at 5	1789	8.08	6.21	0.43**	0.34**	0.30**	0.29**	0.53**	0.58**	1			
(8) Anxiety/depression at 17	1182	5.04	5.20	0.11**	0.10**	0.09**	0.14**	0.11**	0.06*	0.10	1		
(9) Attention problems at 17	1182	5.00	3.13	0.11**	0.10**	0.11**	0.16**	0.05	0.13**	0.13**	0.60**	1	
(10) Aggressive behavior at 17	1182	7.91	5.11	0.13**	0.15**	0.12**	0.12**	0.10**	0.11**	0.23**	0.46**	0.60**	1

*The total sample size was 1993. *p < 0.05, **p < 0.01.*

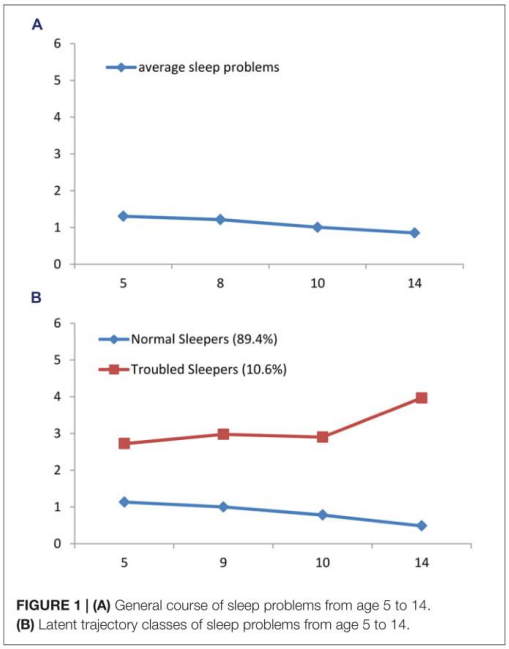

FIGURE 1 | (A) General course of sleep problems from age 5 to 14. **(B)** Latent trajectory classes of sleep problems from age 5 to 14.

the data better than the 2-class solution. Moreover, the 3-class solution yielded two classes showing a highly similar trend. In addition, the 2-class solution achieved a slightly higher entropy (0.92) than the 3-class solution (0.91), although they both showed adequate classification accuracy. Therefore, the 2-class solution was chosen.

The quadratic slope emerged to be significant only for one trajectory class. After fixing the non-significant quadratic slope, the new 2-class solution achieved a better model fit (BIC = 23740.00; aBIC = 23689.16), therefore this more parsimonious model is presented. Latent trajectory classes of sleep problems are shown in **Figure 1B**.

TABLE 2 | Unstandardized parameter estimates for predictors of sleep problems latent growth factors.

Predictors	Intercept	Linear slope	Quadratic slope
	Estimate (*SE*)	Estimate (*SE*)	Estimate (*SE*)
Gender	0.10 (010)	0.12 (0.45)	−0.16 (0.46)
Anxiety/depression at 5	0.15 (0.02)**	−0.35 (0.10)**	0.23 (0.09)**
Attention problems at 5	0.10 (0.02)**	−0.14 (0.10)	0.10 (0.10)
Aggressive behavior at 5	0.04 (0.01)**	0.04 (0.05)	−0.04 (0.05)

Gender was dummy-coded as boys = 0 and girls = 1.
***p < 0.01.*

The trajectory with the majority of adolescents (89.4%) was labeled *Normal Sleepers* (n = 1782). This class included adolescents with a lower initial level of sleep problems ($i = 1.16$, $p < 0.01$), which tended to decrease over time, as indicated by the significant negative linear slope ($s = -0.75$, $p < 0.01$). The second class was the *Troubled Sleepers* ($n = 211$), which consisted of adolescents who followed a persistent higher sleep problems trajectory (10.6 %). This class was described by a higher initial level of sleep problems ($i = 2.73$, $p < 0.01$), and a curvilinear trend as indicated by a non-significant negative linear slope ($s = -0.48$, $p = 0.59$) and a significant positive quadratic slope ($q = 2.08$, $p = 0.02$).

A contingency analysis was performed to determine whether boys and girls were similarly distributed in the sleep problems latent trajectory classes. Results of chi-square test showed a random gender distribution between *Normal Sleepers* and *Troubled Sleepers* ($\chi^2 = 0.92$, $p = 0.34$).

Baseline Predictors of Sleep Problems Latent Trajectory Classes

Results from multivariate binomial logistic regression showing the effects of baseline emotional and behavioral predictors as well as their interaction with gender on sleep problems trajectory classes are presented in **Table 4**. Only baseline behavioral predictors were able to differentiate the sleep problems between the two trajectory classes. Specifically, children and adolescents with attention problems and aggressive behavior at age 5 years were more likely to follow the *Troubled Sleepers* trajectory class

TABLE 3 | Model selection criteria to determine trajectory classes of sleep problems.

Model	Log likelihood	BIC	aBIC	LMR-LRT	BLRT	Entropy
1-class	−12188.88	24476.32	24435.02	–	–	
2-class	−11808.13	23745.41	23691.40	<0.001	<0.001	0.92
3-class	−11589.41	23338.36	23271.64	0.06	1.00	0.91
4-class	−11466.47	23122.68	23043.25	0.07	0.08	0.94
5-class	−11348.76	22917.65	22825.52	0.24	1.00	0.93

BIC, Bayesian Information Criterion; aBIC, Sample size adjusted BIC; LMR, Lo–Mendell–Rubin test; BLRT, Bootstrap likelihood ratio test.

TABLE 4 | Multivariate binomial logistic regression of baseline predictors on sleep problems trajectory classes.

Predictors	*Normal Sleepers* vs. *Troubled Sleepers*			
	OR	Lower 95% CI	Upper 95% CI	Sig.
Gender	2.76	1.72	6.62	0.97
Anxiety/depression at 5	2.72	2.53	2.95	0.96
Attention problems at 5	3.00	2.75	3.30	0.03
Aggressive behavior at 5	2.94	2.82	3.07	0.00
Gender*Anxiety/depression at 5	3.24	2.85	3.74	0.01
Gender*Attention problems at 5	2.50	2.23	2.84	0.19
Gender*Aggressive behavior at 5	2.65	2.50	2.82	0.43

Gender was dummy-coded as boys = 0 and girls = 1.

as compared to those without behavioral difficulties. Moreover, the interaction between gender and anxiety/depression was significantly predictive of sleep problems class membership, suggesting girls with emotional problems were at elevated risk of being *Troubled Sleepers*.

Sleep Problems Latent Trajectory Classes and Later Emotional/Behavioral Problems

We examined the level of emotional and behavioral difficulties later in life among sleep problem trajectory classes. A reduced sample ($n = 1182$) was used in this step due to missing data on emotional and behavioral problems at age 17. Means of anxiety/depression, attention problems, and aggressive behavior at age 17 in the reduced sample were compared. Results from independent sample *t*-test showed that there were significant differences at the level of attention problems ($M_{\text{Normal}} = 4.93$, $M_{\text{Troubled}} = 5.73$, $p < 0.05$) and aggressive behavior ($M_{\text{Normal}} = 7.79$, $M_{\text{Troubled}} = 9.04$, $p < 0.05$) between *Normal Sleepers* and *Troubled Sleepers* at age 17. No significant differences were observed for later anxiety and depression ($M_{\text{Normal}} = 4.96$, $M_{\text{Troubled}} = 5.81$, $p = 0.14$) between the trajectory groups. Missingness analyses indicated that the participants ($n = 811$) who dropped out reported significantly higher sleep problems at age 13 ($p < 0.05$) and attention problems at age 5 ($p < 0.05$) compared with the reduced sample.

DISCUSSION

Viewed as a whole, sleep problems decreased stably across the childhood and adolescence period. This finding is consistent with the work of Gregory and O'Connor (2002) in a similar aged community sample (5–14 years vs. 4–15 years) of 400 Americans, despite the current study being developed and designed in a different cultural background (Australian) and using a different statistical method (LGM vs. repeated measures analyses). Both of the studies suggest that sleep problems show a gradual declining trend during childhood and adolescence in the general population. However, this group trend does not elucidate the implicit heterogeneity of these data. Indeed, this normative picture is complicated by our finding of heterogeneity in the development of sleep problems, which showed that one in 10 young people experience chronic sleep problems into adolescence.

Hence, our second major finding from GMM identified two distinct trajectory classes of sleep problems from childhood to adolescence. The majority of children and adolescents (89.4%) reported few sleep problems, which is modeled by the latent growth curve analyses and also is reflected by the overall trajectory. However, this general course obscured the small group of children and adolescents (10.6%) who were troubled with higher levels of sleep problems over the 10-year period. Notably, this group of troubled sleepers was characterized with high, but stable sleep problems from age 5 to 10 and a sudden statistically significant rise in sleep problems from age 10 to 14 years probably due to the pubertal developmental phase. In consideration of the high prevalence of sleep disturbance in the adult population (10–40% of insomnia, e.g., Ohayon, 2002; Morphy et al., 2007) and corresponding predictive value of adolescence sleep (e.g., Dregan and Armstrong, 2010), such reported sleep problems might continue into adulthood and thus reflect a persistent disturbance. However, given the lack of later-time-point data, such an assumption should remain speculative, but should be a focus of examination in future studies.

In summary, these findings provide empirical support for the existence of two distinct subgroups of children and adolescents with different levels of sleep problems over time. The presence of *Troubled Sleepers* echoes previous literature on the continuation/persistence of sleep problems (e.g., Fricke-Oerkermann et al., 2007; Luo et al., 2013).

These results may help to reconcile a paradox within the sleep literature. On the one hand, studies on the longitudinal course of general sleep problems (Gregory and O'Connor, 2002; Umlauf et al., 2011) suggest that sleep problems decrease from early childhood through adolescence. On the other hand, sleep problems amongst adolescents are considered to be especially prevalent (e.g., Pieters et al., 2015) and receive special attention (e.g., Gradisar et al., 2011). Although our mixture modeling could visualize a subgroup with declining trajectory to reflect the cessation/remission of sleep problems (the 5-class solution), we did not report it due to insufficient statistical support. As was already proved by previous studies using sleep electroencephalography and actigraphy (Hatzinger et al., 2013, 2014; Perkinson-Gloor et al., 2015), the present findings reveal that during childhood and adolescence, the long term development of sleep problems is dominated by its stability. Heterogeneous trajectory classes of sleep problems mainly differed in the level (quantity-wise), rather than the shape of developmental course (quality-wise). If the stable nature of the trajectory class of the persistent troubled sleepers can be replicated and predictors are found, we might be able to identify this group of children and adolescents from early assessments on and find ways of prevention or early intervention of sleep problems.

In this study, early *emotional and behavioral problems* were used as predictors of the general course and distinct trajectory subgroups of sleep problems. When the average course of sleep problems in the general population was considered, anxiety/depression, attention problems, and aggressive behavior (together also known as the Dysregulation Profile, see Deutz et al., 2016) at baseline all predicted higher initial levels of sleep. Furthermore, children with early attention problems or aggressive behavior, and girls with early anxiety and depression were more likely to be *Troubled Sleepers* compared to their counterparts.

These results suggest that both emotional and behavioral problems should be considered as potent risk factors of sleep problems. Also, these findings suggest that behavioral problems share a close link with the initial level, rather than the change of sleep problems over time. This suggests that accounts of the relationship of these emotional and behavioral problems and sleep should focus on the earlier years of life, prior to the fifth year. The interaction between emotional problems and gender, being predictive of group membership in *Troubled Sleepers*, may stem from girls' greater vulnerabilities for anxiety and depression (see Hyde et al., 2008; McLean and Anderson, 2009 for review) and calls for further investigation into this complex relationship.

Trajectory group membership of *sleep problems* were used as predictors of later emotional and behavioral problems. Results showed that *Troubled Sleepers* reported significantly higher levels of attention problems and aggressive behavior at age 17 years when compared to *Normal Sleepers*, while they had similar levels of anxiety and depression. These results are partly consistent with findings from previous research (e.g., Gregory and O'Connor, 2002; Umlauf et al., 2011; Pieters et al., 2015) that sleep problems are predictive of later behavioral/emotional problems. Our findings extend these findings in important ways. For example, Gregory and O'Connor (2002) used sleep problems as single measurement at age 4 years while we used sleep problems as group membership of trajectory classes from ages 5 to 14 years. Pieters et al. (2015) examined change in relative levels via panel analyses over a single year, whereas we were able to examine over a decade of data. However, we still know little about how sleep problems are implicated in different modes of aggression. Our data, in conjunction with research indicating the impact of fatigue on impulsivity amongst adolescents (e.g., Abe et al., 2010), would suggest that future research focuses on the role of sleep disturbance in impulsively enacted aggression and violence, including cyber-aggression (Runions, 2013).

Our findings are indicative of the *bidirectional relationship between sleep problems and behavioral problems*. In contrast, only a one-way relationship was found between sleep and emotional problems, that early anxiety and depression were predictive of higher initial level of general course of sleep problems. According to the recent findings from Mulraney et al. (2016), sleep problems and emotional problems were predictors of one another in a 6-month interval but not in a 12-month interval, such a relationship might weaken or vanish in long term development.

With respect to the role of gender in sleep problems, our findings suggest that there is no or little gender difference, either in the prevalence, initial level, general course or distinct trajectory classes of sleep problems. These findings support previous studies (Voderholzer et al., 2003; Chaput and Tremblay, 2007; Dollman et al., 2007) and extend our knowledge to individual-level. The only exception was the finding that girls with emotional problems were more likely to be *Troubled Sleepers*. The underlying mechanism of such an interaction effect is unclear, however, may be an important direction for future research.

Findings from this study have *implications for the screening and treatment of sleep problems*. The stable nature of sleep problems suggests that children with sleep problems at early time point have a great chance/risk to maintain or aggravate the symptoms throughout childhood and adolescence. Thus, early screening (i.e., in kindergarten) could present a particularly important time for early intervention to improve future sleep behaviors. Such early intervention might be particularly important given the bidirectional relationship between sleep and behavioral problems. Indeed, the presence of attention problems and aggressive behavior may be suggestive of increased later sleep problems and vice-versa. It would be useful for clinicians therefore to not only assess sleep problems but also behavioral problems and vice-versa to evaluate the integrated risk. In addition, the data from our study suggests that special attention should to be paid to girls with emotional problems since they tend to show more sleep problems in childhood and adolescence.

It is important to consider *strengths and limitations of this study*. The adoption of a large sample size and longitudinal design enabled us to model the general pattern of sleep problems during childhood and adolescence and replicate the work of Gregory and O'Connor (2002). Furthermore, the utilization of GMM, a person-centered approach, allowed us to identify distinct trajectory classes in sleep problems, which is hidden in general population analyses. To our knowledge, this is the first study to empirically investigate subgroups with a different course of general sleep problems and thus find subgroup-specific predictors for better assessment and treatment.

Despite these strengths, some limitations must be considered. First, sleep problems were measured using six items derived from CBCL to assess the general sleep problems (composed of different kinds of sleep problems) and thus might not generalize to specific categorical and isolated disorders of sleep, like insomnia, hypersomnia, and parasomnia. These disorders have certainly different pathological backgrounds, implications, and trajectories. However, even when adding an exploratory factor analysis, we could not derive valid factors related to these three categories. Therefore, we suggest future study to apply more specific (or even objective) sleep assessments in longitudinal designs, to investigate the unique feature of these disorders. Second, data regarding sleep problems and early emotional/behavioral problems were based exclusively on parent-reports and there is potential for rater bias (Owens et al., 2000a; Gregory et al., 2006), although the consistency of prediction to self-reported emotional and behavioral problems at age 17 may mitigate this concern. Furthermore, since parents typically have less knowledge of internalizing problems in their adolescents, self-reports may be more appropriate than parent-reports in assessing older children. Third, although the CBCL sleep composite is a valid and reliable parameter, formal diagnoses of sleep disorder or mental health status (e.g., diagnoses of anxiety/depression disorder or other psychiatric abnormalities) would have strengthened our evaluation. Fourth, given the focus on emotional and behavioral problems, we did not examine other predictors that might influence the development of sleep problems, such as family/parental factors (Adam et al., 2007; Cousins et al., 2007; Brand et al., 2009; Kalak et al., 2012; Bajoghli et al., 2013). It would be of particular value if future research could additionally examine the predictive value of other risk factors. Finally, despite the longitudinal methodology, this is an observational study, which at best can only show associations, not causation, between trajectories and risk factors and outcomes.

CONCLUSION

In summary, this study revealed a lessening overall pattern of sleep problems from childhood to adolescence. Within this general decline, two distinct trajectory classes of sleep problems were identified: *Normal Sleepers* with the great majority of children and adolescents reporting lower level sleep problems over time, and *Troubled Sleepers*, a small group of children and adolescents reporting persistently higher level of sleep problems throughout the period investigated. Children and adolescents with attention problems, aggressive behavior, and girls with anxiety/depression at age 5 years were more likely to be *Troubled Sleepers* compared with *Normal Sleepers*. Those subjects in the *Troubled Sleepers* trajectory group had higher levels of attention problems and aggressive behavior at age 17 years. This study provided evidence for the stable nature of sleep problems during childhood and adolescence and partly supported the bidirectional model between sleep and emotional/behavioral problems.

AUTHOR CONTRIBUTIONS

BW and AR conceived and designed the study; FZ was responsible for data acquisition; BW performed the statistical analysis, interpreted the data, drafted and revised the manuscript; CI, AB, and AR contributed to interpretation of the data, drafting and revising the paper; JW, PE, R-CH, KR, RS, TM, LB, and FZ helped to drafted and revised the manuscript. All authors read and approved the final manuscript and agree to be accountable for all aspects of the work specifically to responding to questions related to the accuracy or integrity of any part of the work. FZ and AR are joint senior author. FZ is responsible for the group's correspondence with Raine Study.

ACKNOWLEDGMENTS

We would like to acknowledge the Raine Study participants and the Raine Study Team for study co-ordination and data collection. We acknowledge the University of Western Australia (UWA), Curtin University, the Raine Medical Research Foundation, the UWA Faculty of Medicine, Dentistry and Health Sciences, the Telethon Kids Institute, the Women's and Infant's Research Foundation (King Edward Memorial Hospital), and Edith Cowan University for providing funding for the Core Management of the Raine Study.

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Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

3.2 Original Article 2

Wang, B., Eastwood, P. R., Becker, A., Isensee, C., Wong, J. W., Huang, R. C., ... Rothenberger, A. & Zepf, F. D. (2018). Concurrent developmental course of sleep problems and emotional/behavioral problems in childhood and adolescence as reflected by the dysregulation profile. Sleep. doi: 10.1093/sleep/zsy243.

SLEEPJ, 2018, 1–12

doi: 10.1093/sleep/zsy243
Advance Access Publication Date: 6 December 2018
Original Article

ORIGINAL ARTICLE

Concurrent developmental course of sleep problems and emotional/behavioral problems in childhood and adolescence as reflected by the dysregulation profile

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Abstract

Objectives: Longitudinal data on the course and relationship of concurrent psychopathology in youth are scarce but are of need for better practical patient care and prevention. This study explores the course of (and relationships over time) between sleep problems and concurrent dimensional difficulties relating to anxiety/depression, attention deficiency, and aggressive behaviors in childhood and adolescence. The latter three may jointly form a broad syndrome, the dysregulation profile.

Methods: Young people from the Raine Study, a large community cohort sample ($N = 1625$) were followed from age 5 to 17 years. Developmental courses of sleep problems and its concurrent regulatory difficulties were estimated separately and jointly.

Results: The majority of adolescents reported low levels of problems and which appeared to be stable over time, while a small group (rates between 7.8% and 10.1%) reported enduring problematic developmental courses. Sleep problems and regulatory difficulties shared a strong association in their development over time (individual's probabilities of having the same courses, i.e. low-low and high-high, were between 89.8% and 92.3%). Furthermore, having persistent sleep problems over time was associated with an increased risk of having regulatory difficulties by approximately 10 times, and vice versa.

Conclusion: Findings from this study provide empirical evidence for a strong mutual association in the development of sleep problems and difficulties of dysregulation with emotion, cognition, and aggression. It may be suggested that a positive screening of one such psychopathological dimension should lead to a careful assessment, not only to reduce the problem in question but also to prevent the youth from further problems.

Statement of Significance

Little is known about the mutual relations among sleep and self-regulation across childhood and adolescence. This study explores the development of, and longitudinal relationships between sleep problems and regulation difficulties as a broad syndrome of dysregulation profile and impairments in affective, behavioral and cognitive functions as single specific problems. Findings from this study provide empirical evidence for the existence of subgroups with distinct development course, unmasks heterogeneity which is hidden in general trends of sleep problems and dysregulation. Therefore, early screening of individuals at high risk could inform timely intervention and pertinent treatment. Strong associations in the development of sleep problems and regulation difficulties were revealed, that persistence in one problem greatly increased the risk of the other. Such mutual associations emphasize the importance of understanding their integrated risk.

Key words: sleep problems; childhood and adolescence; joint courses/trajectories; dysregulation profile; anxiety/depression; attention problems; aggressive behavior; Raine Study

Submitted: 19 July, 2018; **Revised:** 4 October, 2018

Introduction

Mutuality

In clinical practice, co-occurrence of different psychopathologies and their interaction over time reflects a great problem, but such longitudinal data are scarce in youth. For example, problems with sleep and self-regulation of emotion and behavior in childhood have each been independently associated with poorer academic and social-emotional outcomes [1–3]. However, so far little is known about the mutual influence between sleep and self-regulation across early childhood [4]. When examining the relationship between sleep and various aspects of health and psychological functioning [5], emerging research supports the notion that sleep problems are associated with both emotional (e.g. anxiety and depression) and behavioral (e.g. attention and conduct) difficulties in children and adolescents [6].

Although sleep problems play a role both as common symptoms of and risk factors for a range of psychiatric disorders, inadequate attention has been paid to the complex, mutual relationships involved in the early regulation of sleep, emotion, and behavior [7, 8]. Studying the co-occurring difficulties and patterns of occurrence may shed light on the understanding of the development for such problems, and aid researchers and clinicians in the early identification, prevention, and treatment of psychiatric disorders. The need to better understand the interplay among sleep problems, emotional, attentional, and behavioral regulation in young children has been highlighted by others [7, 9, 10]. However, studies to date have produced inconsistent findings, and the directionality and persistence of these relations across time remain unclear [6, 11]. The majority of investigations on the relationship between sleep and self-regulations during childhood and adolescence have been cross-sectional or correlational in nature [12–14]. Such studies provide limited information about the developmental changes at specific ages (e.g. puberty). Longitudinal studies on these issues, have been dominated by single-direction designs [15–18] and thus have not been able to examine any mutual associations between problematic sleep and self-regulation (i.e. the effects of sleep on self-regulation and the effects of self-regulation on sleep). A few recent studies have applied both longitudinal and bidirectional design to explore the co-occurrence of these difficulties. Williams and colleagues followed 4109 children in Australia from infancy to 8–9 years of age at five time points and examined the longitudinal and reciprocal relations among behavioral sleep problems, emotional and attentional self-regulation [4]. They found a persistent negative effect of sleep problems on emotional regulation, which in turn contributed to ongoing sleep problems and poorer attentional regulation over time. Their findings suggest that sleep behaviors could be an important target for interventions aimed at improving children's self-regulatory capacities. Foley and Weinraub used a normative sample of 1057 children across four waves from 4.5 to 10.5 years old and studied the transactional relationships between sleep problems, anxious-depressed symptoms, and social functioning [19]. They found that preschool sleep problems directly predicted anxious-depressed symptoms 2 years later, and indirect effects continued into preadolescence. These studies represent the first attempts to document the long-term mutual associations between sleep problems and self-regulation.

Heterogeneity

The above-mentioned studies, however, could only provide limited insight in clinical practice due to the methodological approaches they applied. Those traditionally and commonly used statistical methods, such as regression analysis, factor analysis, and structural equation modeling, take variable-centered/ oriented approaches to data analysis which focus on the relationship among variables in the overall sample, such as relating independent with dependent variables [20]. An important assumption underlying those variable-centered methods is that the variable/outcome relationship, with respect to how the predictors operate on the outcomes, is the same across all members of the population [21]. Consequently, all individuals were taken as a homogeneous group with their characteristics or developmental pathways averaged to a general level. But this is rarely the case either in clinical or public health practice; individual differences widely exist in the onset and progression of mental health problems. Identifying those with the most impairing difficulties or highest risk is of great clinical relevance and serves as the prerequisites for effective future treatment.

Methods that take unobserved heterogeneity (individuals with different patterns of characteristics or developmental courses/trajectories) into account often are referred to as person-centered/oriented. Examples of such methods include cluster analysis, latent class analysis, and growth mixture modeling. Person-centered methods capture relationships among individuals with the goal to group individuals into categories, each one of which contains individuals who are similar to each other and different from individuals in other categories [20]. Although heterogeneity in the population is unobserved, it is inferred from the data and can be taken into account by using latent classes. A categorical latent variable can be used to represent the latent classes of which each corresponds to a subpopulation that has its own patterns (in terms of distinct set of parameter values). The importance of revealing such heterogeneity in population cannot be overstated. It can provide critical information for the screening of individuals at high risk, as well as for the design of pertinent treatment approaches.

Dysregulation profile

It is also important to extend the above-mentioned content of emotional and behavioral self-regulation to the broader syndrome of the well-established dysregulation profile. Children with both emotional and behavioral problems show dysregulation across three components of self-regulation: affective, behavioral, and cognitive functions. Impairment to regulate mood (depression, bipolar disorder) or worry/cognition (anxiety), to regulate behavior (disruptive behaviors, substance use), or to regulate cognition (Attention deficit hyperactivity disorder, ADHD) would be possible outcomes of deficiency in such ability [22]. This phenotype of severe dysregulation can be measured using the Child Behavior Checklist Dysregulation Profile [23]. The dysregulation profile is best conceptualized as a broad dysregulation syndrome, which overarches anxiety/depression, aggression, and attention problems (AP) as specific problems [24, 25], but the dysregulation profile is still a (multi-) dimensional construct. Such a combination of problems has been shown to be heritable [26, 27] and to be stable throughout childhood

due to genetic factors [28, 29]. Furthermore, the dysregulation profile is related to various adjustment problems later in life, including a range of psychological disorders, suicidality, and substance abuse [22, 30–32]. Both dysregulation profile as well as sleep problems seem to have cross-sectional clinical impact on/and predictive value for childhood psychopathologies. Hence, in a practically important longitudinal perspective it would be worth to investigate their concurrent courses and their mutual influence in order to improve theoretical knowledge and derive practical considerations.

The present study

To address this, the present study followed a community sample of Australian children for 13 years. By examining the longitudinal course of their sleep problems, emotional/behavioral problems as reflected by the dysregulation profile from childhood to adolescence. This study aimed to reveal the development and maintenance of deficiency in self-regulation not only as joint difficulties or comorbidities (as the dysregulation profile) but also single and independent disturbances (as anxiety/depression, AP, and aggressive behavior [AB]). We examined (1) whether groups with distinct developmental courses of sleep problems and deficiency in self-regulation, respectively, could be identified in childhood and adolescence and (2) whether the developmental course of sleep problems was related to the courses of its concurrent self-regulatory difficulties.

Methods

Participants and procedures

Participants were from the Western Australian Pregnancy Cohort (Raine) Study. The methodology and recruitment for this study have been described in detail elsewhere [33]. In brief, 2900 women between 16 and 20 weeks gestation (mean 18 weeks) were recruited from the public antenatal clinic at King Edward Memorial Hospital (KEMH) in Perth, Western Australia and surrounding private clinics between May 1989 and November 1991. Eligible women were required to have sufficient English-language skills to give informed consent, an expectation to deliver at KEMH, and an intention to reside in Western Australia to enable future follow-ups of their child. Of the 2900 women enrolled, 2804 delivered live birth babies. Due to 64 multiple births, the initial cohort included 2868 children. These children were assessed at birth and were followed up at ages 1, 2, 5, 8, 10, 14, 17, 20, and 22 years of age using questionnaires and physical assessments. The study described in this paper had a primary focus on the 5, 8, 10, 14, and 17-year follow-ups, as these follow-ups contained detailed data on sleep problems and difficulties of dysregulation profile, emotional/behavioral problems.

Data on sleep problems were available for 2116 participants at age 5 (73.8% retention); 2037 participants at age 8 (71.0% retention); 1994 participants at age 10 (69.5% retention); 1774 participants at age 14 (61.9% retention); and 1380 participants at age 17 (48.1% retention); dysregulation profile as well as emotional/behavioral problems data were available for 2170 participants at age 5 (75.7% retention); 2075 participants at age 8 (72.4% retention); 2017 participants at age 10 (70.3% retention); 1784 participants at age 14 (62.2% retention); and 1355 participants at age 17 (47.2% retention). In order to better capture the longitudinal nature of developmental patterns, we focused on participants who had data on at least four out of the five measurement points for all studied variables. The effective sample size was 1625 (56.7% retention). Excluded participants (n = 1243) reported significantly higher sleep problems and anxious/depressed (AD) age 14, dysregulation profile and AB at age 5, 8, and 14, and AP at all time points. Data collection occurred in accordance with Australian National Health and Medical Research Council Guidelines for Ethical Conduct and was approved by the ethics committees of KEMH and Princess Margaret Hospital for Children. Written parental consent was obtained at recruitment and at each follow-up.

Measures

Sleep problems

The "sleep problem scale" was derived from six items from the Child Behavior Checklist for ages 4 to 18 (CBCL/4–18) [34] and was used to measure children and adolescents' sleep problems. Although not a standard CBCL scale, the CBCL sleep composite is shown to be strongly correlated with validated sleep measures such as the Children's Sleep Habits Questionnaire (CSHQ) [35] and with clinical sleep disorder diagnoses. Additionally, it has shown similar external correlations with social problems and psychopathology symptoms as the CSHQ score [36]. The CBCL sleep composite has been widely used in previous research as a measure of overall sleep functioning [17, 37–42]. The six specific sleep-related items are: "trouble getting to sleeping," "nightmares," "overtired without good reason," "sleeps less than most kids," "talks or walks in sleep," and "sleeps more than most kids during day and/or night." Each item is rated on 3-point scale (0 = not true, 1 = somewhat or sometimes true, 2 = very true or often true). The sum score of the six-items scale was used to represent the level of children and adolescents' sleep problems (range 0–12).

Emotional problems

An AD scale was derived from the parent-report of CBCL to measure children and adolescents' emotional problems [34]. The AD scale were proved to significantly discriminate individuals with or without anxiety and depression disorders [43, 44]. It has been widely used as a measure of emotional problems for general population in many societies (see meta-analyses [45, 46]). The AD scale consists of 14 items, sample items of the subscale included "feels or complains that no one loves him/her" and "too fearful or anxious." Responses were rated on a 3-point scale (0 = not true, 1 = somewhat or sometimes true, 2 = very true or often true). A sum score of all the items of the subscale was used to represent the level of children and adolescents' emotional problems (range 0–28), with higher scores indicating higher levels of emotional or behavioral problems. Raw scores were converted to gender and age standard T-scores (M = 50 and SD = 10). A minimum T-score of 50 was assigned to scores that fell at midpoint percentiles of ≤50 on the syndrome scales to permit comparison of standardized scores across scales [47].

Attention problems

One measure of children and adolescents' behavioral problems was AP scale derived from the parent-report of CBCL [34].

A number of studies have supported strong relations between the AP syndrome and a DSM diagnosis of ADHD [48, 49]. It could serve as a rapid and useful screening instrument of ADHD and has been widely used cross-culturally (see meta-analyses [45, 46]). The AP scale consists of 11 items, sample items of the subscale included "daydreams or gets lost in his/her thoughts" and "can't sit still, restless, or hyperactive." Responses were rated on a 3-point scale (0 = not true, 1 = somewhat or sometimes true, 2 = very true or often true). A sum score of all the items of the subscale was used to represent the level of children and adolescents' AP (range 0–22), with higher scores indicating higher levels of emotional or behavioral problems. Raw scores were converted to gender and age standard T-scores (M = 50 and SD = 10). A minimum T-score of 50 is assigned to scores that fall at midpoint percentiles of ≤50 on the syndrome scales to permit comparison of standardized scores across scales [47].

Aggressive behavior

Another measure of children and adolescents' behavioral problems was an AB scale derived using the parent-report of CBCL [34]. The AB syndrome was strongly related to Conduct Disorder and Oppositional Defiant Disorder [50] and could effectively discriminate children with ODD/CD from children without ODD/CD [51]. The AB scale has been widely used in many cultures (see meta-analyses [45, 46]). The AB scale consists of 20 items, sample items of the subscale included "cruelty, bullying, or meanness to others" and "destroys things belonging to his/her family or others." Responses were rated on a 3-point scale (0 = not true, 1 = somewhat or sometimes true, 2 = very true or often true). A sum score of all the items of the subscale was used to represent the level of children and adolescents' AB (range 0–40), with higher scores indicating higher levels of emotional or behavioral problems. Raw scores were converted to gender and age standard T-scores (M = 50 and SD = 10). A minimum T-score of 50 is assigned to scores that fall at midpoint percentiles of ≤50 on the syndrome scales to permit comparison of standardized scores across scales [47].

Dysregulation profile

The Anxiety/Depression-Attention-Aggression (AAA) scale was used to measure children and adolescents' levels of deficiency in self-regulation. Scores of the AAA scale can help distinguish children and adolescents with different levels of deficits in emotional regulation and serves as a measure of dysregulatory syndrome [23, 47, 52]. The AAA scale was calculated from the ratings on items from three CBCL syndrome scales AD, AP, and AB. However, it has been shown to be distinct from each of its components (i.e. anxiety/depression, AP, and aggression) either alone or in tandem [26, 27, 29] and reflective of a single syndrome, rather than of comorbid attention, behavior, and mood problems [23]. T-scores of AD, AP, and AB scales were summed to form the AAA score (range 150–300).

Statistical analysis

Statistical analyses were performed between sleep problems and its concurrent psychopathologies separately (i.e. sleep & dysregulation, sleep & anxiety/depression, sleep & AP, sleep & aggression). Relationships between the psychopathologies were not calculated since their measurements were inner correlated (e.g. dysregulation was calculated by summing the scores of anxiety/depression, AP, and aggression). After examining children and adolescents' sleep problems and difficulties of the dysregulation profile (=AAA scales), emotional/behavioral problems in a descriptive manner, the statistical analysis was performed in two steps. In step 1, models for the developmental trajectories were separately estimated for sleep problems and the dysregulation profile, anxiety/depression, AP, and ABs. Growth Mixture Modeling (GMM) was used to estimate the trajectories in Mplus version 7.3 [53]. GMM is based on conventional growth modeling. Conventional growth modeling is used to analyze longitudinal data by relating an observed outcome variable to time or to a time-related variable such as age. As a variable-centered approach, conventional growth modeling estimate a mean growth curve under the assumption that all individuals in the sample come from a single population with common population parameters (e.g. slopes, intercepts, and error variances). Individual variation around the mean growth curve is captured by the estimation of the growth factor variances. GMM, in contrast, estimates a mean growth curve for each latent class which corresponds to a heterogeneous subpopulation. Individual variation around these growth curves is captured by the estimation of growth factor variances for each latent class [20, 54]. By such means, GMM captures the heterogeneity in unobserved subpopulations by identifying a number of latent classes each with distinct developmental course. Every latent class has its own growth parameters in terms of intercept (representing its initial level), and slope (representing its average growth), with unique estimates of variances and covariate influences. In the current study, five measurements of children and adolescents' sleep problems and difficulties in psychopathology assessed from childhood (age 5) to adolescence (age 17) were used as outcome variables to identify latent trajectories. Missing data on the outcome variables were handled through full information maximum likelihood estimation in Mplus as a standard procedure under the assumption of missing at random [53].

A series of models, including both linear and quadratic slopes, were fitted, beginning with a one-trajectory model and moving to a five-trajectory model. Each model was fitted using at least 1000 random perturbations of starting values to ensure replication of the best likelihood and to avoid local maxima. Evaluation of the best-fitting models took into account several criteria. First, we compared those models with relative fit information criteria which is commonly used. The Bayesian Information Criterion (BIC) [55] and the adjusted BIC (aBIC) [56] were calculated from the maximized likelihood with a correction for number of parameters estimated in the model and consider the balance between model fit and parsimony. Lower information criteria (in terms of absolute value) indicated better fitting models [57, 58]. Second, the Lo–Mendell–Rubin likelihood ratio test (LMR-LRT) [59] and bootstrap likelihood ratio test (BLRT) [60] were used to quantify the specific comparisons between the model of interest and a model with one fewer class and a p value smaller than 0.05 indicating that the additional class significantly improves fit over a model with fewer classes [59]. Among these criteria, we predominately relied on the BLRT and BIC due to their superiority as shown in previous simulation study [57]. Third, the entropy index was calculated for models with more than one class, to quantify the uncertainty of classification

of subjects into latent classes. Entropy values range from 0 to 1, with 0 corresponding to randomness and 1 to a perfect classification [61]. High values of entropy (>.80) indicate that individuals are classified with confidence (i.e. the model is generally pretty sure that persons belong to a particular class) and there is adequate separation between the latent classes [58]. Given the practical goal of identifying individuals' likely group membership, we suggest that models with higher entropy are favored when selecting among models with similar relative fit indices [62]. Fourth, we set minimum requirements on the group size (proportionally >1.0% and numerically $n > 25$) in the consideration of class validity and usefulness since a latent class that includes a very small proportion of subjects would have little applicability in clinical practice [63]. In addition, consistency of the identified classes with prior theoretical and empirical work was also critical to ensure the sensibility, distinctiveness, and interpretability of the optimal model.

In step 2, the joint trajectories of sleep problems and dysregulation profile, sleep problems and anxiety/depression, sleep problems and AP, and sleep problems and ABs were estimated separately. The best-fitting trajectory models that were found in step 1 were used as the starting point for the joint models. Joint trajectory models yielded two main sets of results, named as joint and conditional probabilities [64]. The joint probabilities reflect the probability of adolescents following different combinations of sleep problems and concurrent psychopathology trajectories. The conditional probabilities reflect the probability of adolescents following each trajectory of sleep problems conditional on their trajectories of psychopathology, and vice versa. Both joint and conditional probabilities are useful for understanding the developmental trajectories of two distinct but related behaviors [64]. All GMMs were performed using Mplus version 7.3 [53]. Other analyses were carried out using SPSS version 23.

Results

Descriptive statistics

Tables 1–4 present descriptive statistics for all study variables. Mean scores of sleep problems (t_{sleep} = 9.806, df = 1206, $p < 0.001$, Cohen's d = 0.565), dysregulation ($t_{dysregulation}$ = 13.344, df = 1215, $p < 0.001$, Cohen's d = 0.766), emotional/behavioral problems ($t_{anxiety/depression}$ = 7.487, df = 1215, $p < 0.001$, Cohen's d = 0.430; $t_{attention}$ = 10.862, df = 1215, $p < 0.001$, Cohen's d = 0.623; $t_{aggression}$ = 13.617, df = 1215, $p < 0.001$, Cohen's d = 0.781) showed decreasing trends over five assessments. The large standard deviations found in sleep problems over time indicated there were considerable inter-individual differences in the population. Correlations within and between sleep problems and dysregulation profile or emotional/behavioral problems measured in the five follow-ups showed that they were significantly inter-correlated ($p < 0.01$). The magnitude of associations between scores of dysregulation profile (rs = 0.384–0.692), AP (rs = 0.377–0.671) and ABs (rs = 0.364–0.687) were greater than those between sleep problems (rs = 0.307–0.522) and anxiety/ depression (rs=0.253–0.563). Cross-sectional relationships

Table 1. Descriptive statistics and bivariate correlations between sleep problems and dysregulation profile

	N	M	SD	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)
(1) Sleep problems at 5	1557	1.29	1.48	1	0.512**	0.407**	0.373**	0.307**	0.521**	0.384**	0.327**	0.327**	0.245**
(2) Sleep problems at 8	1573	1.20	1.53		1	0.522**	0.436**	0.335**	0.391**	0.507**	0.371**	0.323**	0.304**
(3) Sleep problems at 10	1599	1.01	1.40			1	0.512**	0.346**	0.328**	0.380**	0.485**	0.363**	0.228**
(4) Sleep problems at 14	1562	0.82	1.31				1	0.470**	0.306**	0.340**	0.371**	0.517**	0.315**
(5) Sleep problems at 17	1275	0.83	1.34					1	0.282**	0.294**	0.306**	0.360**	0.560**
(6) Dysregulation profile at 5	1583	162.27	15.86						1	0.687**	0.582**	0.487**	0.384**
(7) Dysregulation profile at 8	1589	162.30	17.10							1	0.692**	0.598**	0.496**
(8) Dysregulation profile at 10	1610	160.17	16.02								1	0.671**	0.525**
(9) Dysregulation profile at 14	1569	159.16	14.18									1	0.619**
(10) Dysregulation profile at 17	1258	156.19	11.81										1

The total sample size was 1625.
**$p < 0.01$.

Table 2. Descriptive statistics and bivariate correlations between sleep problems and anxiety/depression

	N	M	SD	(1)	(2)	(3)	(4)	(5)	(11)	(12)	(13)	(14)	(15)
(1) Sleep problems at 5	1557	1.29	1.48	1	0.512**	0.407**	0.373**	0.307**	0.452**	0.347**	0.269**	0.273**	0.223**
(2) Sleep problems at 8	1573	1.20	1.53		1	0.522**	0.436**	0.335**	0.325**	0.462**	0.335**	0.289**	0.247**
(3) Sleep problems at 10	1599	1.01	1.40			1	0.512**	0.346**	0.245**	0.329**	0.448**	0.281**	0.186**
(4) Sleep problems at 14	1562	0.82	1.31				1	0.470**	0.233**	0.309**	0.315**	0.458**	0.276**
(5) Sleep problems at 17	1275	0.83	1.34					1	0.216**	0.254**	0.268**	0.305**	0.501**
(11) Anxiety/ depression at 5	1583	53.37	5.49						1	0.550**	0.414**	0.273**	0.253**
(12) Anxiety/ depression at 8	1589	54.18	6.41							1	0.563**	0.418**	0.359**
(13) Anxiety/ depression at 10	1610	53.51	6.04								1	0.501**	0.393**
(14) Anxiety/ depression at 14	1569	52.68	5.21									1	0.551**
(15) Anxiety/ depression at 17	1258	52.05	4.47										1

The total sample size was 1625.
**$p < 0.01$.

Table 3. Descriptive statistics and bivariate correlations between sleep problems and attention problems

	N	M	SD	(1)	(2)	(3)	(4)	(5)	(16)	(17)	(18)	(19)	(20)
(1) Sleep problems at 5	1557	1.29	1.48	1	0.512**	0.407**	0.373**	0.307**	0.423**	0.290**	0.260**	0.254**	0.205**
(2) Sleep problems at 8	1573	1.20	1.53		1	0.522**	0.436**	0.335**	0.328**	0.412**	0.298**	0.276**	0.272**
(3) Sleep problems at 10	1599	1.01	1.40			1	0.512**	0.346**	0.294**	0.310**	0.413**	0.339**	0.210**
(4) Sleep problems at 14	1562	0.82	1.31				1	0.470**	0.252**	0.245**	0.300**	0.417**	0.258**
(5) Sleep problems at 17	1275	0.83	1.34					1	0.225**	0.202**	0.217**	0.265**	0.450**
(16) Attention problems at 5	1583	54.14	6.34						1	0.650**	0.565**	0.483**	0.377**
(17) Attention problems at 8	1589	54.23	6.74							1	0.660**	0.581**	0.466**
(18) Attention problems at 10	1610	53.56	6.69								1	0.671**	0.490**
(19) Attention problems at 14	1569	53.03	5.55									1	0.588**
(20) Attention problems at 17	1258	52.11	4.60										1

The total sample size was 1625.
**$p < 0.01$.

Table 4. Descriptive statistics and bivariate correlations between sleep problems and aggressive behavior

	N	M	SD	(1)	(2)	(3)	(4)	(5)	(21)	(22)	(23)	(24)	(25)
(1) Sleep problems at 5	1557	1.29	1.48	1	0.512**	0.407**	0.373**	0.307**	0.444**	0.348**	0.307**	0.286**	0.194**
(2) Sleep problems at 8	1573	1.20	1.53		1	0.522**	0.436**	0.335**	0.337**	0.426**	0.316**	0.247**	0.247**
(3) Sleep problems at 10	1599	1.01	1.40			1	0.512**	0.346**	0.286**	0.337**	0.378**	0.289**	0.181**
(4) Sleep problems at 14	1562	0.82	1.31				1	0.470**	0.284**	0.321**	0.333**	0.421**	0.266**
(5) Sleep problems at 17	1275	0.83	1.34					1	0.262**	0.292**	0.285**	0.316**	0.454**
(21) Aggressive behaviors at 5	1583	54.76	6.99						1	0.687**	0.590**	0.502**	0.365**
(22) Aggressive behaviors at 8	1589	53.89	6.83							1	0.684**	0.603**	0.480**
(23) Aggressive behaviors at 10	1610	53.11	6.12								1	0.665**	0.508**
(24) Aggressive behaviors at 14	1569	53.44	6.28									1	0.587**
(25) Aggressive behaviors at 17	1258	52.03	4.92										1

The total sample size was 1625.
**$p < 0.01$.

between sleep problems and dysregulation profile (*rs* = 0.485–0.560), anxiety/ depression (*rs* = 0.448–0.501), AP (*rs* = 0.412–0.450), and ABs (*rs* = 0.378–0.454) were also higher than their relationships overtime (*rs* = 0.181–0.384).

Latent courses/trajectories of sleep problems and dysregulation profile, emotional/behavioral problems

Unconditional GMMs with 1–5 latent trajectory classes were estimated separately for sleep problems and dysregulation profile, emotional/behavioral problems. Tables 5–9 presents the model fit and selection criteria, as well as group sizes of these solutions. Based on these criteria, usefulness of the trajectory classes, and consistency of the identified classes with prior theoretical and empirical work, the two-class solutions were chosen. Latent trajectory classes of sleep problems and dysregulation profile, emotional/behavioral problems are shown in Figure 1.

For sleep problems, the first trajectory class with the majority of adolescents (91.9%) was labeled *Normal Sleepers*. This class included adolescents with a lower initial level of sleep problems ($i = 1.19$, $p < 0.01$), which decreased by an accelerating rate over time, as indicated by the significant negative linear slope ($s = -1.05$, $p < 0.01$) and a significant positive quadratic slope ($q = 0.44$, $p < 0.01$). The second trajectory class consisted of adolescents who followed a persistent higher sleep problems trajectory (8.1 %) and was labeled *Troubled Sleepers*. This class was described by a higher initial level of sleep problems ($i = 2.88$, $p < 0.01$) and a highly stable developmental course as indicated by a nonsignificant positive linear slope ($s = 2.51$, $p = 0.16$) and a nonsignificant negative quadratic slope ($q = -1.60$, $p = 0.32$).

The trajectory classes in dysregulation profile and emotional/behavioral problems were quite similar. For the dysregulation profile, the first trajectory class with the majority of adolescents (91.4%) was labeled *Low Dysregulation*. This class included adolescents with a lower initial level of dysregulation ($i = 160.67$, $p < 0.01$), which tended to decrease over time, as indicated by the nonsignificant negative linear slope ($s = -1.35$, $p = 0.22$) and a significant negative quadratic slope ($q = -3.87$, $p < 0.01$). The second trajectory class consisted of adolescents who followed a persistent higher dysregulation trajectory (8.6%) and was labeled *High Dysregulation*. This class was described by a higher initial level of dysregulation ($i = 180.13$, $p < 0.01$) that appeared to be stable over time as indicated by a nonsignificant negative linear slope ($s = -0.14$, $p = 0.99$) and a nonsignificant positive quadratic slope ($q = 6.80$, $p = 0.31$). For anxiety and depression, the majority of adolescents (*Low Anxiety/depression*, 90.3%) were characterized by a lower initial level of anxiety and depression ($i = 53.02$, $p < 0.01$), which slowly decreased over time ($s = 1.4$, $p < 0.01$, $q = -2.73$, $p < 0.01$). The remaining adolescents (*High Anxiety/depression*, 9.7%) had a higher level of anxiety and depression that appeared stable over time ($i = 57.59$, $p < 0.01$, $s = 0.76$, $p = 0.78$, $q = 3.59$, $p = 0.10$). For AP, most adolescents (*Low AP*, 89.9%) had lower AP which gradually decreased over time ($i = 53.44$, $p < 0.01$, $s = -0.80$, $p = 0.06$, $q = -1.09$, $p < 0.01$), only a

Table 5. Model selection criteria to determine trajectory classes of sleep problems

Class #	BIC	aBIC	Entropy	LMRT	BLRT	Class 1	Class 2	Class 3	Class 4	Class 5
1	24883.104	24838.628	-	-	-	1.000				
2	**24297.815**	**24240.632**	**0.950**	**0.018**	**0.000**	**0.919**	**0.081**			
3	24084.759	24014.868	0.943	0.057	1.000	0.889	0.056	0.055		
4	23796.536	23713.939	0.905	0.224	1.000	0.798	0.135	0.041	0.026	
5	23607.375	23512.070	0.922	0.377	1.000	0.778	0.136	0.040	0.031	0.014

aBIC = Sample-size Adjusted BIC. Best-fitting model is showed with bold font.

Table 6. Model selection criteria to determine trajectory classes of dysregulation profile

Class #	BIC	aBIC	Entropy	LMRT	BLRT	Class 1	Class 2	Class 3	Class 4	Class 5
1	59213.996	59169.520	-	-	-	1.000				
2	**58431.585**	**58374.402**	**0.946**	**0.027**	**0.000**	**0.914**	**0.086**			
3	58067.409	57997.519	0.938	0.093	0.375	0.863	0.071	0.066		
4	57746.373	57663.776	0.943	0.120	1.000	0.832	0.086	0.075	0.008	
5	57476.108	57380.803	0.905	0.474	0.667	0.766	0.131	0.062	0.033	0.009

aBIC = Sample-size Adjusted BIC. Best-fitting model is showed with bold font.

Table 7. Model selection criteria to determine trajectory classes of anxiety and depression

Class #	BIC	aBIC	Entropy	LMRT	BLRT	Class 1	Class 2	Class 3	Class 4	Class 5
1	45603.425	45558.950	-	-	-	1.000				
2	**44695.598**	**44638.415**	**0.931**	**0.021**	**0.000**	**0.903**	**0.097**			
3	44176.238	44106.348	0.934	0.205	0.600	0.847	0.125	0.028		
4	43669.367	43586.769	0.926	0.458	1.000	0.818	0.104	0.066	0.012	
5	43345.512	43250.208	0.935	0.014	1.000	0.807	0.107	0.056	0.020	0.010

aBIC = Sample-size Adjusted BIC. Best-fitting model is showed with bold font.

Table 8. Model selection criteria to determine trajectory classes of attention problems

Class #	BIC	aBIC	Entropy	LMRT	BLRT	Class 1	Class 2	Class 3	Class 4	Class 5
1	45492.478	45448.003	-	-	-	1.000				
2	**44570.131**	**44512.948**	**0.946**	**0.029**	**0.000**	**0.899**	**0.101**			
3	44108.976	44039.086	0.931	0.326	1.000	0.831	0.119	0.050		
4	43545.326	43462.728	0.930	0.064	1.000	0.788	0.128	0.074	0.009	
5	42973.565	42878.260	0.939	0.218	1.000	0.781	0.113	0.065	0.033	0.009

aBIC = Sample-size Adjusted BIC. Best-fitting model is showed with bold font.

Table 9. Model selection criteria to determine trajectory classes of aggressive behaviors

class #	BIC	aBIC	Entropy	LMRT	BLRT	Class 1	Class 2	Class 3	Class 4	Class 5
1	46023.178	45978.703	-	-	-	1.000				
2	**45110.882**	**45053.699**	**0.948**	**0.059**	**0.000**	**0.922**	**0.078**			
3	44523.509	44453.618	0.955	0.104	0.500	0.876	0.112	0.012		
4	43823.998	43741.400	0.941	0.123	0.667	0.824	0.103	0.061	0.011	
5	43369.546	43436.039	0.940	0.215	1.000	0.818	0.100	0.041	0.031	0.010

aBIC = Sample-size Adjusted BIC. Best-fitting model is showed with bold font.

small proportion of the adolescents (*High AP*, 10.1%) recorded comparatively higher levels of AP (i = 60.91, $p < 0.01$, $s = 4.81$, $p = 0.09$, $q = -1.64$, $p = 0.42$). For ABs, both adolescents who had lower levels of aggression (*Low ABs*, 92.2%) and higher levels of aggression (*High ABs*, 7.8%) at the first time point showed a declining trend overtime ($i_{Low} = 53.97$, $p < 0.01$, $s_{Low} = -2.12$, $p < 0.01$, $q_{Low} = -0.25$, $p = 0.47$; $i_{High} = 62.72$, $p < 0.01$, $s_{High} = -8.11$, $p = 0.04$, $q_{High} = 10.48$, $p < 0.01$).

Joint courses/trajectories of sleep problems and dysregulation profile, emotional/behavioral problems

Joint trajectory models of sleep problems and the dysregulation profile, emotional/behavioral problems were built based on the separate best solutions. Classification accuracies of adolescents into joint trajectory classes were assessed as satisfactory (entropy for joint model of sleep problems and dysregulation,

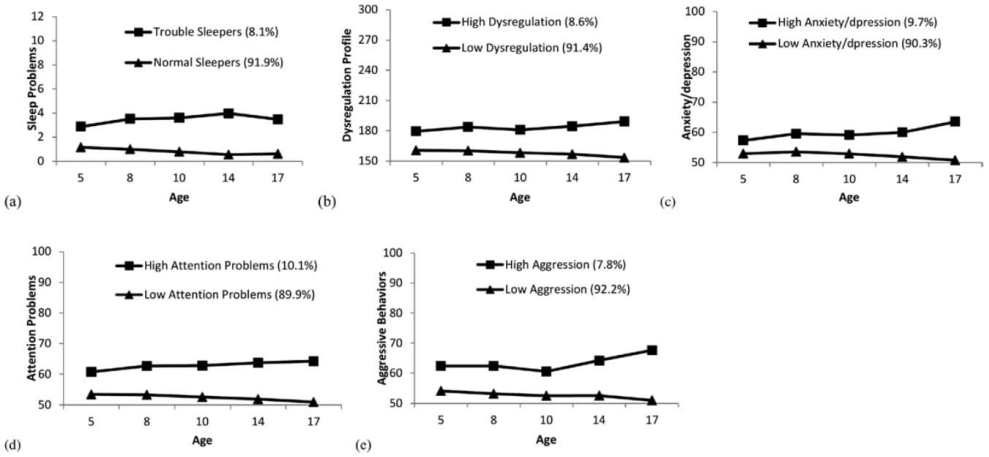


Figure 1. Latent trajectory classes of development from age 5 to 17: (a) sleep problems; (b) dysregulation profile; (c) anxiety/depression; (d) attention problems; and (e) aggression behaviors.

anxiety/depression, AP, ABs were 0.951, 0.937, 0.955, and 0.951, respectively). The joint probabilities were shown in the first panels of Tables 10–13, which yielded four potential trajectory classes (2*2) characterized by different developmental patterns of sleep problems and co-occurring difficulties. The joint probabilities indicated that the majority of adolescents followed the same trajectory class. For sleep problems and the dysregulation profile, 87.4% of the adolescents followed the low trajectory class for both sleep problems and dysregulation profile and 4.9% belonged to the high trajectory classes. The ratios for sleep problems and anxiety/depression, AP, ABs were 85.6% and 5.2%, 85.6% and 4.2%, 86.8%, and 3.9%, respectively. Only a minority of adolescents were found to be in a different trajectory class. Specifically, 4.0% of participants belonged to the *Normal Sleepers* and *High Dysregulation* and 3.7% followed a *Troubled Sleepers* and *High Dysregulation* trajectory; 4.5% of participants belonged to the *Normal Sleepers* and *High Anxiety/depression* and 4.7% followed a *Troubled Sleepers* and *High Anxiety/depression* trajectory; 5.6% of participants belonged to the *Normal Sleepers* and *High AP* and 4.6% followed a *Troubled Sleepers* and *High AP* trajectory; 3.8% of participants belonged to the *Normal Sleepers* and *High ABs* and 5.4% followed a *Troubled Sleepers* and *High ABs* trajectory.

We were especially interested in how sleep problems and psychopathology developed over time within those individuals who were both *Troubled Sleepers* and had high levels of psychopathology. From the joint developmental trajectories (Figure 2), we can conclude that sleep problems and its co-occurring difficulties of dysregulation, anxiety/depression, AP, and ABs share highly associated developmental patterns.

The second panel of Tables 10–13 shows the probabilities for adolescents in the sleep problems trajectories to be conditional on their dysregulation, anxiety/depression, AP, and ABs. Adolescents in the low co-occurring difficulties trajectory class were most likely in the *Normal Sleepers* than *Troubled Sleepers* trajectory class (96.0:4.0 for dysregulation, 94.8:5.2 for anxiety/depression, 94.9:5.1 for AP, 94.1:5.9 for ABs). By comparison, adolescents in the high co-occurring difficulties trajectory class had recorded similar ratios to fall in the *Normal Sleepers* and *Troubled Sleepers* trajectory class (44.9:55.1 for dysregulation, 46.0:54.0 for anxiety/depression, 56.9:43.1 for AP, 49.6:50.4 for ABs).

Similarly, results were found in the probabilities of dysregulation, anxiety/depression, AP, and ABs trajectory classes given the sleep problems trajectory classes (see third panel of

Table 10. Joint and conditional probabilities of sleep problems and dysregulation profile

	Dysregulation profile	
Sleep problems	Low	High
Joint probabilities of sleep problems and dysregulation profile		
Normal	0.874	0.040
Troubled	0.037	0.049
Probabilities of sleep problems conditional on dysregulation profile		
Normal	0.960	0.040
Troubled	0.449	0.551
Probabilities of dysregulation profile conditional on sleep problems		
Normal	0.956	0.044
Troubled	0.429	0.571

Table 11. Joint and conditional probabilities of sleep problems and anxiety/depression

	Anxiety/depression	
Sleep problems	Low	High
Joint probabilities of sleep problems and anxiety/ depression		
Normal	0.856	0.045
Troubled	0.047	0.052
Probabilities of sleep problems conditional on anxiety/ depression		
Normal	0.948	0.052
Troubled	0.460	0.540
Probabilities of anxiety/ depression conditional on sleep problems		
Normal	0.950	0.050
Troubled	0.472	0.528

Table 12. Joint and conditional probabilities of sleep problems and attention problems

	Attention problems	
Sleep problems	Low	High
Joint probabilities of sleep problems and attention problems		
Normal	0.856	0.056
Troubled	0.046	0.042
Probabilities of sleep problems conditional on attention problems		
Normal	0.949	0.051
Troubled	0.569	0.431
Probabilities of attention problems conditional on sleep problems		
Normal	0.939	0.061
Troubled	0.521	0.479

Table 13. Joint and conditional probabilities of sleep problems and aggression behavior

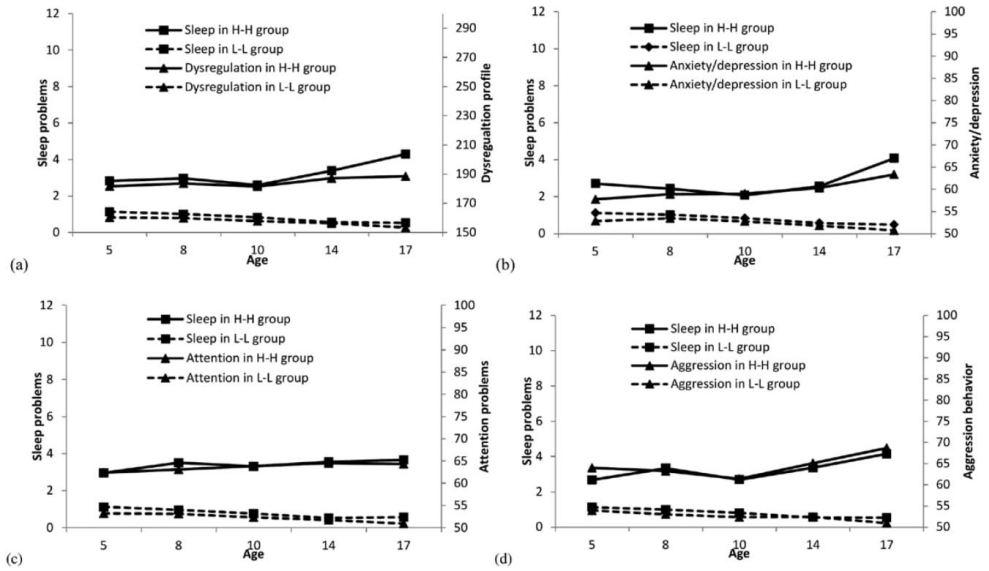
	Aggressive behaviors	
Sleep problems	Low	High
Joint probabilities of sleep problems and aggressive behaviors		
Normal	0.868	0.038
Troubled	0.054	0.039
Probabilities of sleep problems conditional on aggressive behaviors		
Normal	0.941	0.059
Troubled	0.496	0.504
Probabilities of aggressive behaviors conditional on sleep problems		
Normal	0.958	0.042
Troubled	0.583	0.417

Tables 10–13). Being in the *Normal Sleepers* trajectory class had overwhelming ratios of resulting in the low co-occurring difficulties trajectory class compared to the high counterparts (95.6:4.4 for dysregulation, 95.0:5.0 for anxiety/depression, 93.9:6.1 for AP, 95.8:4.2 for ABs). On the contrary, those in the *Troubled Sleepers* trajectory class were evenly distributed in the low and high co-occurring difficulties trajectory classes (42.9:57.1 for dysregulation, 47.2:52.8 for anxiety/depression, 52.1:47.9 for AP, 58.3:41.7 for ABs).

Discussion

We used data from a large cohort sample of adolescents who were followed longitudinally to describe the developmental courses/trajectories of subgroups with sleep problems and dysregulation profile, anxiety/depression, AP, Abs, and provided new insights into the mutual relationship between these phenomena, by subsequently examining the associations between their latent trajectories.

Descriptively, for the whole group, the levels of sleep problems and dysregulation profile, anxiety/depression, AP, ABs were all low and decreased over time. However, using the person-oriented approach of growth mixture modeling, we were able to explore the hidden heterogeneity, that is, the presence of subgroups with distinctly different developmental patterns which were otherwise masked in the general trends. We have previously documented, the existence of different trajectory classes of sleep problems [65] and shown that most adolescents (about 90%) report few sleep problems and follow a low and declining trajectory of sleep problems from childhood to



Note. H-H = High-High group; L-L = Low-Low group. The former H/L indicate the class of sleep problems, the latter H/L indicate the class of dysregulation.

Figure 2. Joint development from age 5 to 17: Sleep and (a) dysregulation profile; (b) anxiety/depression; (c) attention problems; and (d) aggressive behaviors.

adolescence. This developmental pattern of the majority of population was manifested as a general decline in the overall prevalence as has also been shown in previous studies [38, 66, 67]. However, what this general course obscures is the finding that there is a small group of about 10% beyond the large majority who are persistently troubled with higher levels of sleep problems throughout childhood and adolescence. The findings of both groups reveal that during childhood and adolescence, the long-term development of sleep problems is dominated by its stability. Heterogeneity in the development course of sleep problems is mainly reflected in the level of symptom severity, rather than the shape of growth curve. Similar results were found in the development of dysregulation profile, anxiety/depression, AP, and ABs. It may be suggested that individuals at high risk could be identified from early screening and then carefully assessed in order to treat early and prevent increasing psychopathology.

This is supported by the results from these joint trajectory models which showed a clear and strong association between the trajectory classes of sleep problems and dysregulation profile, anxiety/depression, AP, ABs. It is consistent with prior evidence on within-time associations [12, 13] and longitudinal predictive value [4, 17]. These results indicated that, even over time, the mentioned dimensional psychic difficulties are highly comorbid, at least during the period of childhood and adolescence, and may substantially co-occur across time. Furthermore, *Troubled Sleepers* (i.e. those adolescents with chronic sleep problems), are at significantly higher risk, as much as about 10 times, for also engaging in persistently high dysregulation (0.571/0.044 ≈ 13.0), anxiety/depression (0.528/0.050 ≈ 10.6), AP (0.479/0.061 ≈ 7.9) and ABs (0.417/0.042 ≈ 9.9), compared to their counterparts (i.e. *Normal Sleepers*). Specifically, it was even more efficient for the prediction of dysregulation profile as a broad syndrome than for anxiety/depression, AP, and ABs as single specific problems. Similarly, adolescents with enduring high dysregulation, anxiety/depression, AP, and ABs were more likely to be persistently *Troubled Sleepers* compared to their unaffected counterparts. Correspondingly, the broad syndrome of dysregulation profile (0.551/0.040 ≈ 13.8 times) provided higher predictive value than anxiety/depression (0.540/0.052 ≈ 10.4 times), AP (0.431/0.051 ≈ 8.5 times) and ABs (0.504/0.059 ≈ 8.5 times) as specific problems. These mutual associations highlight the risk these individuals are at when any of the above-mentioned difficulties are screened out. Thus, in clinical practice, possible concurrent psychopathology should be considered when studying the developmental course of sleep problems.

This study has a number of limitations that should be kept in mind when interpreting the findings. First, sleep problems were measured using six items derived from CBCL to assess the general sleep problems (composed of different kinds of sleep problems) and thus might not generalize to specific categorical and isolated disorders of sleep, like insomnia, hypersomnia, and parasomnia. Therefore, we suggest that future studies should apply more specific (or even objective, e.g. actigraphy) sleep assessments in longitudinal designs, to investigate the unique features of these disturbances. Second, all of the measures were based exclusively on parent-reports and there is potential for rater bias. Although self-reports may be more appropriate than parent-reports in assessing older children particularly for internalizing problems, we used a single source in order to obtain a reliable longitudinal developmental course. Future studies would benefit from including different informants, such as self-report and teacher's report. Third, all participants in the present study were from Western Australia. Thus, findings may be sample dependent and might not generalize to other countries or cultures. Future research should replicate these findings in other cultures. Moreover, considering the excluded sample (who had less data than four out of the five measurement points) had higher levels of both sleep and psychopathological difficulties, interpretation of findings needs to be cautious that the true relationships might be underestimated. Fourth, given the focus on anxiety/depression, AP and aggression as specific problems and joint as a broad syndrome of dysregulation profile, we did not examine other difficulties that may be co-occurring with sleep problems during childhood and adolescence, such as autism [68, 69], trauma and stress-related disorders [70, 71] or other potential influences on the development of sleep problems, such as family/parental factors [72, 73]. It would be of particular value if future research could take into account these risk factors.

In conclusion, this study provides new theoretical and practical insight into the developmental course of sleep problems and its co-occurring difficulties of dysregulation, anxiety/depression, AP, and ABs. Our results, based on a large longitudinal population sample, suggest that there exist heterogeneous subgroups in the general population with distinct developmental courses of sleep and psychopathology. One of it is a small group (about 10%) of adolescents suffering from enduring problems. Sleep problems and dysregulation, anxiety/depression, AP, ABs share strong mutual associations in their developmental courses/trajectories over time. Future research should be aimed at understanding the underlying processes in their longitudinal comorbid nature.

Acknowledgments

We are thankful to the Raine Study participants and their families, and the Raine Study Team for cohort co-ordination and data collection. We acknowledge the NH&MRC for their long-term support and contribution to funding the study over the last 29 years. We are thankful to Dr. Andreas Schroeder from Institute of Aerodynamics and Flow Technology, German Aerospace Center, Goettingen, Germany, who kindly provided check of statistical methods.

Funding

We would like to acknowledge the NHMRC and The Raine Medical Research Foundation for supporting the Year 5, 8, and 10 follow-ups; the NHMRC (Sly et al., Grant ID 211912), the NHMRC Program Grant (Stanley et al., Grant ID 003209) and the Raine Medical Research Foundation for supporting the Year 14 follow-up; and the NHMRC Program Grant (Stanley et al., Grant ID 353514) for supporting the Year 17 follow-up. Finally, core management of the Raine Study is funded by The University of Western Australia (UWA), Curtin University, Telethon Kids Institute, Women and Infants Research Foundation, Edith Cowan University, Murdoch University, the University of Notre Dame Australia, the Raine Medical Research Foundation, and the UWA Faculty of Health and Medical Sciences. The development of this

article was supported by a scholarship from the Overseas Study Program of Guangzhou Elite Project to B. Wang.
Conflict of interest statement. None declared.

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3.3 Original Article 3

Wang, B., Runions, K., Eastwood, P. R., Poustka L., Becker, A., Wong, J., ... & Rothenberger, A. (submitted). Causality and mutuality of predictors in children along a 13-year period: dysregulation profile impacts on sleep problems.

Title:

Causality and mutuality of predictors in children along a 13-year period: dysregulation profile impacts on sleep problems

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Abstract

Objective: The first time, this study explored longitudinally the reciprocal relationship between general sleep problems and the dysregulation profile (DP) of the Child Behavior Checklist (CBCL) as a broad psychopathological syndrome in children.

Method: Young people from the large community cohort Raine Study (N = 1625) were followed over 13 years. Sleep problems and a dysregulation profile as defined within deficiency of self-regulation in affective, behavioral and cognitive functions were assessed at ages 5, 8, 10, 14 and 17 years. The presence of developmental pathways was assessed using a series of autoregressive cross-lagged models tested using an exploratory approach.

Results: The longitudinal stability of both sleep problems and dysregulation profile were reflected by consistently high autoregressive paths in the model, especially for the dysregulation profile. Concurrent associations between those two domains were high (0.40 – 0.59) for each assessment panel. Overall, after controlling for cross-sectional correlations and autoregressive effects over time, the dysregulation profile consistently accounted for significant variance in subsequent sleep problems.

Conclusion: Our findings provide evidence of temporal precedence, which is important in considering potential causality. The dysregulation profile should be considered and treated as a primary factor for clinical interventions related to concurrent problems in sleep and dysregulation.

Keywords:

Sleep problems, dysregulation profile, childhood and adolescence, Raine Study

Introduction

Difficulties with self-regulation and poor sleep are both common problems during childhood and adolescence.[1-4] Emerging research indicates the presence of important overlap between impairments in sleep and the ability to self-regulate in emotional, cognitive, and behavioral domains. Emerging research indicates the presence of important overlap between impairments in sleep and the ability to self-regulate in emotional, cognitive, and behavioral domains, with robust concurrent associations observed in children and adolescents.[5-8] The focus of this mutuality as well as the nature of their temporal association (i. e. "causality") are clinically important but still unknown.

Understanding the temporal precedence of sleep versus dysregulation problems is an important step toward determining causality, over and beyond their internal stability and co-occurrence.[9, 10] Additionally, further understanding of the temporal sequencing of interrelations between sleep and dysregulation problems can inform the focus and timing of clinical interventions that would be optimal for each of the two domains.[11]

The Development of Sleep Problems

Behavioral sleep problems, in the form of dyssomnias (such as insomnia and hypersomnia) and parasomnias (such as sleep walking, nightmares, and night terrors), are distinguished from physical sleep problems, such as breathing or movement-related sleep disorders. Sleep problems affect not only children and adolescents' academic, neurocognitive and behavioral performance, but can also significantly impact family members and their functioning.[12-14] Numerous studies have reported prevalence rates of such disturbances at different stages of childhood and adolescence.[15, 16] However, longitudinal investigations on this topic are scarce and often limited by short time frames designs.[4] Studies that have examined the development of behavioral sleep problems during childhood and adolescence descriptively or longitudinally typically have found a general decrease in the average level of sleep problems

with modest stability.[17, 18] The longitudinal stability of individual differences in sleep problems has also been reflected through robustly high autoregressive.[19, 20]

The Development of Dysregulation Problems

Concurrent impairments in regulating emotion, attention, cognition and behaviour have recently been considered as a broad syndrome dubbed a 'dysregulation profile'.[21, 22] The dysregulation profile has been shown to be associated with various adverse outcomes such as psychological disorders, suicidality, and substance use,[21-24] and represents a useful index for identifying children and adolescents at risk for psychiatric problems in early adulthood.[25] The phenotype of 'severe dysregulation' can be assessed with the Anxious/Depressed, Attention Problems and Aggressive Behavior subscales of the Child Behavior Checklist,[26] yet the profile appears to supersede these specific problems.[27, 28] The co-occurring elevations in anxiety/depression, attention problems and aggressive behaviours that mark the dysregulation profile can be heritable [29, 30] and are suggested to be highly stable throughout childhood and adolescence due to genetic factors.[1, 31, 32] Although most previous studies have focused on childhood dysregulation profiles as predictors of later problems, some have mapped the developmental trajectories of the dysregulation profile.[2, 33] Overall, these studies indicate inter-individual stability and a decreasing within-person course of dysregulation during childhood and adolescence. Such findings are consistent with the views of Gestsdottir[34] and Raffaelli[35], who note that children's ability to self-regulate typically increase across development.

Bidirectional Relationship of Sleep Problems and Dysregulation Profile

High rates of comorbid sleep disturbance and difficulties with various facets of self-regulation have been found in both epidemiological and clinical studies.[8, 36, 37] Current studies on comorbidity have been dominated by single-direction (i.e., the effects of sleep on self-regulation or the effects of self-regulation on sleep) and/or cross-sectional designs. However,

such studies provide limited insight into the potential co-development of sleep and dysregulation problems. For example, insufficient sleep appears to interfere with the capacity to regulate emotions, which is associated with increases in negative emotions, a reduction in positive emotions, and an alteration in individuals' ways of understanding, expressing, and modifying emotions.[38, 39] Conversely, in the short term, emotional arousal appears to lead to difficulty falling asleep, in addition to eliciting further sleep disruptions.[40, 41] Inadequate or disrupted sleep may also be linked to aggression and violence.[42-44] Studies have also shown that children with conduct problems may experience more disordered breathing during sleep.[6] Sleep problems exist as a common complaint in children and adolescents with ADHD.[8, 45] Sleep deprivation or disruption may lead to compromised alertness and neurobehavioral functioning in developing children, it may contribute to the origination and deterioration of symptoms such as periodic limb movement disorder/restless legs syndrome and sleep-disordered breathing in children.

Only a handful of studies have investigated the bidirectional relationship between sleep problems and regulatory functioning. With a sample of children aged 5-13 years, Mulraney found weak evidence of a bidirectional relationship between sleep problems and emotional problems, and no evidence of bidirectional relationships between sleep and externalizing problems.[46] Studies by Gregory[47] and Foley[19] provided support for the influence of sleep problems on anxious-depressed symptoms and depression. Johnson found two predominant pathways for the relationships from anxiety to insomnia and from insomnia to depression, with other pathways consisting of lesser or non-significant effects.[48] But their study only examined adolescents (aged 13-16), leaving earlier relationship unclear, and relied on retrospective reports of age of onset. Jansson-Frojmark followed adult participants over the course of a single year and found that baseline anxiety and depression predicted insomnia at follow-up; insomnia at baseline also predicted subsequent new episodes of anxiety and

depression.[49] Williams found inconsistent bidirectional relationships between sleep problems and emotional regulation from the first year of life through nine years of age; attention regulation and sleep problems had very little bidirectional relationship.[20] These inconsistent findings make it difficult to draw definitive conclusions regarding the bidirectionality of sleep and regulatory functioning, and warrant additional studies to further delineate this complex relationship.[11, 38] Moreover, most studies have only examined impairments in regulatory domains in isolation, failing to account for the concurrent difficulties in ability to regulate emotion, cognition and behavior, namely, the broad syndrome of the dysregulation profile. Although a recent study (Wang et al., submitted) showed that the development of behavioural sleep problems and the broad syndrome of the dysregulation profile consistently share strong coexistence throughout childhood and adolescence, their temporal precedence over development remains unclear.

The current study

To address the aforementioned research gaps, the present study followed a community sample of Australian children for 13 years and tested bidirectional relationships between general sleep problems and the dysregulation profile as a broad syndrome, which consists of anxiety/depression, attention problems and aggressive behaviors from early childhood to adolescence. The overarching aim of the current study was to explore the nature of the reciprocal relationship between sleep problems and dysregulation profile. We took an exploratory approach to investigate a series of autoregressive cross-lagged models, assessing the presence of developmental cascade effects while accounting for continuity in constructs across time and thereby uncovering the direction of effects.[50]

Material and methods

Participants and procedures

Participants were from the Western Australian Pregnancy Cohort (Raine) Study. The study design and recruitment strategy for this study have been described in detail.[51, 52] Pregnant women between 16 and 20 weeks gestation (mean 18 weeks) were recruited from the public antenatal clinic at King Edward Memorial Hospital (KEMH) in Perth, Western Australia, and surrounding private clinics between May 1989 and November 1991. Eligibility criteria for participation were having sufficient English-language skills to give informed consent, an expectation to deliver at KEMH, and an intention to reside in Western Australia to make future follow-ups of their child feasible. A total of 2900 women ('Generation 1') were enrolled into the study. There were 2868 live births–the index participants of 'Generation 2'–including 60 sets of twins (n = 120) and two sets of triplets (n = 6), from 2826 mothers. These children were assessed at birth, and follow-ups were carried out at ages 1, 2, 5, 8, 10, 14, 17, 20, and 22 years of age using well-validated questionnaires and physical assessments. The study described in this paper had a primary focus on the 5, 8, 10, 14 and 17-year follow-ups, as these follow-ups contained detailed data on sleep problems and difficulties with self-regulation measured as emotional and behavioural problems.

Available data on sleep problems were as follows: 2,116 participants at age 5 (73.8% retention); 2,037 participants at age 8 (71.0% retention); 1,994 participants at age 10 (69.5% retention); 1,774 participants at age 14 (61.9% retention); and 1,380 participants at age 17 (48.1% retention); corresponding data on difficulties with self-regulation measured by emotional and behavioral problems were available for 2,170 participants at age 5 (75.7% retention); 2,075 participants at age 8 (72.4% retention); 2,017 participants at age 10 (70.3% retention); 1,784 participants at age 14 (62.2% retention); and 1,355 participants at age 17 (47.2% retention). For the sake of ensuring validity of data, only participants with complete data for more than 80% (four out of the five) measurement points for all studied variables were selected into the current study. This screening procedure resulted in an effective sample

of 1,625 participants (56.7% retention). Those who were excluded from the study (n = 1,243) were rated as significantly higher in the following categories and respective time points; sleep problems and anxious/depressed problems at age 14, the dysregulation profile and aggressive behaviour at ages 5, 8 and 14 years, and attention problems at all time points. Data collection was in accordance with Australian National Health and Medical Research Council (NH&MRC) Guidelines for Ethical Conduct and was approved by the ethics committees of KEMH and Princess Margaret Hospital for Children. At recruitment and at each follow-up, written consent was obtained from the parent of participants.

Measures

Sleep Problems

Children and adolescents' sleep problems were measured by the sleep composite consisting of six items from the Child Behavior Checklist for ages 4-18 (CBCL/4-18).[53] The CBCL sleep composite, although not a standard CBCL scale, is shown to be strongly correlated with validated sleep measures such as the Children's Sleep Habits Questionnaire (CSHQ)[54] and with clinical sleep disorder diagnoses. In addition, it has been proved to have similar external correlations with social problems and psychopathology symptoms as the CSHQ score.[55] The CBCL sleep composite has been widely used as a measure of overall sleep functioning in previous research.[18, 56] The six specific sleep-related items are: "trouble getting to sleeping", "nightmares", "overtired without good reason", "sleeps less than most kids", "talks or walks in sleep", and "sleeps more than most kids during day and/or night". Each item was rated on 3-point scale (0 = not true, 1 = somewhat or sometimes true, 2 = very true or often true). The sum score of the 6-items scale was used to represent the level of children and adolescents' sleep problems (range 0-12) with higher score representing more problematic sleep.

Difficulties with self-regulation reflected as anxiety/depression, attention problems and aggressive behaviors

Difficulties with self-regulation were reflected by problems in three aspects: Anxious/Depressed, Attention Problems, Aggressive Behavior, which was measured respectively by corresponding subscales from the parent-report of CBCL.[53] The Anxious/Depressed scale consists of 14 items, sample items of the subscale included "feels or complains that no one loves him/her" and "too fearful or anxious". The Attention Problems scale consists of 11 items, sample items of the subscale included "daydreams or gets lost in his/her thoughts" and "can't sit still, restless, or hyperactive". The Aggressive Behavior scale consists of 20 items, sample items of the subscale included "cruelty, bullying, or meanness to others" and "destroys things belonging to his/her family or others". Each item was rated on a 3-point scale (0 = not true, 1 = somewhat or sometimes true, 2 = very true or often true). The sum score of all the items of a subscale was calculated (range 0-28 for Anxious/Depressed, range 0-22 for Attention Problems, range 0-40 for Aggressive Behaviour) with higher scores indicating higher levels of problems. Raw scores were converted to gender- and age- standard T-scores (M = 50 and SD = 10). A minimum T-score of 50 was assigned to scores that fell at midpoint percentiles of $\leq$ 50 on the syndrome scales to permit comparison of standardized scores across scales.[57] Severe dysregulation was defined as positive by a score of $\geq$ 70 on each subscale of anxiety/depression, attention problems and aggressive behaviours, while deficient self-regulation was defined as positive by a score of $\geq$ 60 but $<$ 70.[58] Importantly, there is no overlap between the CBCL items for sleep problems and dysregulation profile.

Statistical Analysis

The effective and excluded samples were examined in a descriptive manner before examination of bivariate correlations between sleep problems and emotional/behavioral problems (i.e., anxious/depressed, attention problem, aggressive behaviors) measured at the five time points outlined above.

The construct of the dysregulation profile was adopted as an underlying latent variable comprised of three aspects of difficulties with self-regulation, namely anxious/depressed (emotional dysregulation), attention problems (attention dysregulation), and aggressive behavior (behavioral dysregulation). Therefore, testing the longitudinal measurement invariance of the latent construct of the dysregulation profile at each measurement point was the precondition for testing the full cross-lagged model. Nested configural (invariant factor structure), metric (invariant factor structure and loadings), and scalar models (invariant factor structure, loadings, and item thresholds) were estimated. Integral to these analyses was the need for the invariant models to display a good fit to the data in order to ensure that the latent dysregulation profile measured the same construct at each measurement point, i.e., that any observed changes over time reflected true changes in the level of dysregulation profile, rather than changes referent of latent structure.

To identify the reciprocal longitudinal relationships between sleep problems and dysregulation profile, autoregressive cross-lagged models were used, allowing an exploration of longitudinal influences among constructs while controlling for their concurrent associations and the stability within each construct over time.[50] Autoregressive effects describe the effect of a construct on itself measured at a later time point. Smaller autoregressive coefficients (closer to zero) indicate more variance in the construct, indicating less stability from the previous time point. Larger autoregressive coefficients indicate little inter-individual variance over time, meaning more stability from the previous time point. Cross-lagged effects describe the influences from one construct on another measured at a later time point; controlling for concurrent and autoregressive effects.

In the current study, children and adolescents' sleep problems and dysregulation profile measured at five time points from childhood to adolescence were used as outcome variables to explore reciprocal longitudinal relationships. Several nested models with different

autoregressive and cross-lagged effects were tested: Model 1 was the base model in which only autoregressive paths between adjacent time points were included. In Model 2, autoregressive paths between distant time points were included, i.e., all possible autoregressive effects were modelled. The following models took cross-lagged effects into consideration: Model 3 added cross-lagged paths between adjacent time points, Model 4 included early cross-lagged effects by adding cross-lagged paths between age 5 and other time points. Model 5 added all remaining potential cross-lagged paths. In Model 6, all the non-significant paths in Model 5 were removed to obtain a more parsimonious model.

To compare model fits, the chi-square index was reported, with a non-significant chi-square reflecting a good fit to the data. As chi-square is sensitive to sample size and may reflect statistical significance even though a model fits the data well when sample sizes are large, multiple model selection criteria were applied including the root mean square of approximation (RMSEA), the Tucker-Lewis index (TLI), and the comparative fit indices (CFI). As recommended, RMSEA values <.05, TLI and CFI value >.95, respectively, indicate a good fit to the data.

Tests of the longitudinal measurement invariance and autoregressive cross-lagged models were conducted using Mplus version 7.3.[59] Missing data were handled through full information maximum likelihood estimation in Mplus as a standard procedure under the assumption of missing at random.[59] Other analyses were carried out using SPSS version 23.

Results

Descriptive Statistics

Table 1 presents descriptive statistics of the effective sample (n = 1,625). Comparisons of each variable at age 5 (i.e. the earliest timepoint) and age 17 (the latest time point) using *t*-tests showed that average sleep problems ($t = 9.806$, $df = 1206$, $p < .001$, Cohen's $d = 0.565$), anxious/depressed ($t = 7.487$, $df = 1215$, $p < .001$, Cohen's $d = 0.430$), attention problems ($t =$

10.862, *df* = 1215, $p < .001$, Cohen's $d = 0.623$), and aggressive behaviours ($t = 13.617$, *df* = 1215, $p < .001$, Cohen's $d = 0.781$) generally decreased from childhood to adolescence.

Correlations within and between groups as defined by sleep problems and difficulties with self-regulation in terms of anxiety/depression, attention problems and aggressive behaviours measured at each of the five time points are shown in Table 2. All variables were significantly inter-correlated ($p < .01$) in the expected direction. The magnitude of associations between scores of attention problems (range of $r = .377$-$.671$) and aggressive behaviours (range of $r = .365$-$.687$) were greater than those between sleep problems (range of $r = .307$-$.522$) and anxious/depressed (range of $r = .253$-$.563$). Focusing on the correlation between sleep problems and difficulties with self-regulation, cross-sectional correlations (range of $r = .378$-$.501$) were also greater than those between adjacent (range of $r = .258$-$.339$) and distant (range of $r = .181$-$.321$) time points.

Measurement Invariance

To examine the longitudinal measurement invariance of the latent variable dysregulation profile, the configural (invariant factor structure), metric (invariant factor structure and loadings), and scalar (invariant factor structure, loadings, and item thresholds) invariant models were tested. The configural invariance model, χ^2 (50) = 97.049, $p < .001$, CFI = .997, TLI = .993, RMSEA = .024 (90% CI = .017-.031), the metric invariance model, χ^2 (58) = 170.469, $p < .001$, CFI = .992, TLI = .986, RMSEA = .035 (90% CI = .029-.041) and the scalar invariance model, χ^2 (66) = 355.921, $p < .001$, CFI = .980, TLI = .968, RMSEA = .052 (90% CI = .47-.057), all showed good fit to the data, indicating the latent variable dysregulation profile measured at each time point represented the same underlying construct and therefore could be used in further longitudinal modeling. Standardized factor loadings for the dysregulation profile at age 5 were 0.724 (anxious/depressed), 0.775 (attention problem) and 0.739 (aggressive behaviours), at age 8 were 0.712 (anxious/depressed), 0.781 (attention

problem) and 0.800 (aggressive behaviours), at age 10 were 0.694 (anxious/depressed), 0.745 (attention problem) and 0.816 (aggressive behaviours), at age 14 were 0.685 (anxious/depressed), 0.769 (attention problem) and 0.720 (aggressive behaviours), and at age 17 were 0.709 (anxious/depressed), 0.810 (attention problem) and 0.754 (aggressive behaviours), respectively. All factor loadings were significant at the p<0.01 level.

Longitudinal Cross-Lagged Model

To examine the longitudinal reciprocal relationship between sleep problems and dysregulation profile, we tested several nested models in steps by adding different autoregressive and cross-lagged effects (Table 3). In general, all models presented good fit to the data and were improved by including more autoregressive and cross-lagged paths and removing non-significant paths. The final model (Model 6) , χ^2 (118) = 273.116, p < .001, CFI = .992, TLI = .986, RMSEA = .028 (90% CI = .024-.033) provided the best fit and is shown in Figure 1 with all significant standardized path coefficients presented.

The autoregressive paths between all adjacent time points were significant, while decreasing stability of sleep problems and dysregulation profile were seen as decreasing estimates for the autoregressive paths over time (β_{age5} = .74 to β_{age17} =.48 for dysregulation profile and β_{age5} = .38 to β_{age17} = .29 for sleep problems). Most of the autoregressive paths between distant time points were also significant with some exceptions (i.e., age 5 and age14, age 5 and age 17 for dysregulation profile, age 5 and age 17, age 8 and age 17 for sleep problems). The cross-sectional correlations between sleep problems and dysregulation profile were significant at all-time points (rs = .40-.59), with greater levels of sleep problems associated with higher scores on the dysregulation profile. The cross-lagged paths from dysregulation profile to sleep problems were consistently significant (βs = .14-.24) at 0.01 level, indicating that dysregulation profile were associated with more sleep problems at later time points. On the contrary, the cross-lagged paths from sleep problems to dysregulation profile were not

significant in most cases, with only sleep problems at age 5 associated with greater levels of the dysregulation profile at age 14 (β = .10). Moreover, an inconsistent effect showed that sleep problems at age 10 tend to be associated with less dysregulation profile at age 14 (β = -.06, p = .03). This final model of sleep problems and dysregulation profile from age 5 to 17 accounted for 33.0% and 46.9% of total variance in sleep problems and dysregulation profile at age 17, respectively.

Discussion

Using longitudinal data from a large cohort sample, we were able to explore nature of the reciprocal relationships between sleep problems and dysregulation profile, the latter being defined as difficulties with emotional, attentional and behavioral self-regulation as manifested respectively in anxious/depressed problems, attention problems, aggressive behaviours. Autoregressive cross-lagged models of sleep problems and dysregulation profile were tested with a five-measurement design from early childhood (age 5) to adolescence (age 17). Even when accounting for relevant concurrent and auto-regressive relationships, dysregulation profiles showed robust associations with subsequent sleep problems. These findings provide strong evidence for a temporal precedence of cross-domain problems with self-regulation on later behavioural sleep disturbances.

The present study showed that, in general, the magnitudes of sleep problems and difficulties with self-regulation in terms of anxiety/depression, attention problems and aggressive behaviours showed decreasing trends over time. Such a finding is consistent with results from previous studies.[17, 18, 60-62] Correlations between sleep problems and difficulties with self-regulation were significant at all time points, with the magnitude of correlation coefficients ranging from moderate to small. As expected, cross-sectional correlations (i.e. at the same

time-point) were greater than those between adjacent time points, while the correlation coefficients between distant time points were very small in most cases.

Longitudinal Stability of Sleep Problems and Dysregulation Profile

For both sleep problems and the dysregulation profile, significant autoregressive coefficients were found not only in paths between adjacent time points, but also in most distant time points. Such high stabilities are consistent with the results of previous research on those domains.[2, 18, 63, 64] However, it was notable that their internal stability gradually reduced from early childhood to adolescence, possibly due to the maturational changes over puberty[65, 66] or perhaps to the increasing influence of other interpersonal factors, such as social stress and peer relationships.[67, 68]

Temporal Precedence of Dysregulation and Sleep Problems

Variations in the longitudinal development of sleep problems and dysregulation profile were further explained by bidirectional concurrent and cross-lagged associations. Correlations within time-points between sleep problems and dysregulation profile as a latent construct were consistently strong. As a construct comprised of emotional, attentional and behavior dysregulation, this finding is consistent with prior research.[20, 56, 69]

With regard to cross-lagged associations, sleep problems did not consistently have the expected effect on dysregulation profile at later adjacent time points. The only significant predictions of dysregulation profile were made indirectly by sleep problems from distant time points: sleep problems at age 5 and 10 predicted higher dysregulation at age 14 and 17, respectively. Dysregulation profile, in contrast, showed robust associations with sleep problems at each subsequent time point, with larger path effect sizes than the sleep-driven paths. These results provide strong evidence for a temporal precedence of cross-domain dysregulation features over sleep problems, providing evidence toward a causal understanding of their relationship. It is possible that the dysregulation profile as a broad syndrome, which

is indicated by the co-occurrence of problems with anxiety/depression, attention, and aggressive behaviours, may play a more important role in the development of general sleep problems. Given the strong autoregressive effects for the dysregulation profile from age five, and that lagged effects are present from that age, further research on developmental antecedents may help to clarify the biological, psychological or social precursors. As well, neuropsychological research may help to understand brain processes that might account for the lagged effect of dysregulation on sleep problems. Finally, targeted intervention research to address dysregulation from an early age could seek to assess the course of sleep problems to determine if improved dysregulation has a beneficial flow-on effect on sleep.

Limitations and Implications

The present study represents the first attempt, to our knowledge, to explore the reciprocal relationship between sleep problems and the dysregulation profile during the key developmental stage from early childhood to adolescence. The large sample size (N = 1,625), longitudinal design over a span of 13 years, and cohort sample which clarified the true age effect, are among the strengths of this study. But there are also a number of limitations that should be considered when interpreting the findings. First, to ensure all participants provided reliable longitudinal data, only those with 80% or more valid data were included in the main analysis. This resulted in retention of 56.7% of the original sample. Differences were noted between the effective and excluded sample in all studied variables were reported, thus interpretation of our findings should consider these differences. Moreover, since the excluded sample had higher levels of both sleep and psychopathological difficulties, it is possible that the magnitudes of the true relationships might be underestimated. Second, all participants in the present study were from Western Australia. Therefore, the extent to which one can generalize findings to other countries or cultures is unclear. Future research should replicate these findings in other contexts and/or cultures. Third, although self-reports may be more

appropriate than parent-reports in assessing older children particularly for internalizing problems, we relied on a single source of information in a quest for more reliable and comparable results in the long term. Rater bias shouldn't have a particular impact on the cross-lagged associations since we have included autoregressive effects. Fourth, a short list of items from CBCL was used to measure general sleep problems and thus might not generalize to specific categorical and isolated disorders of sleep, like parasomnias. Future studies could apply more specific (and ideally objective, like actigraphy) sleep assessments in longitudinal designs, to investigate the unique features of these disorders. Fifth, given the focus on dysregulation profile as a broad syndrome, deficient self-regulation in anxiety/depression, attention problems and aggressive behaviours was only adopted as a component of the dysregulation profile. The potential reciprocal relationships between sleep problems and anxiety/depression, attention problems, aggressive behaviours as separate impairments may be the interest of future research.

Despite these limitations, our study, based on a large longitudinal population sample provides new insight into the understanding of development and reciprocal relations between sleep problems and dysregulation profile. Our results indicate that in addition to strong internal stability and cross-sectional associations, the longitudinal bi-directional relations between sleep problems and dysregulation profile were dominated by paths driven by the latter. These findings suggest that dysregulation profile should be treated as the primary factor for the clinical intervention of concurrent problems in sleep and dysregulation, especially when its persistence over time is taken into consideration. In the case that concurrent therapy for sleep problems and dysregulation is not practical, promoting self-regulatory functioning prior to sleep rather than the other way around would most likely maximize the improvement in both domains.

Acknowledgments:

We are thankful to the Raine Study participants and their families, and the Raine Study Team for cohort co-ordination and data collection. This work is supported by the NH&MRC for their long term support and contribution to funding the study over the last 29 years. In particular, we would like to acknowledge the NH&MRC and The Raine Medical Research Foundation for supporting the Year 5, 8, and 10 follow-ups; the NH&MRC (Sly et al., Grant ID 211912), the NH&MRC Program Grant (Stanley et al., Grant ID 003209) and the Raine Medical Research Foundation for supporting the Year 14 follow-up; and the NH&MRC Program Grant (Stanley et al., Grant ID 353514) for supporting the Year 17 follow up. Finally, core management of the Raine Study is funded by The University of Western Australia (UWA), Curtin University, Telethon Kids Institute, Women and Infants Research Foundation, Edith Cowan University, Murdoch University, The University of Notre Dame Australia, the Raine Medical Research Foundation, and the UWA Faculty of Medicine, Dentistry and Health Sciences. The development of this paper was supported by a scholarship from the Overseas Study Program of Guangzhou Elite Project to B. Wang.

TABLE 1 | Descriptive statistics of effective sample

		Effective sample (n = 1625)				
		n_{valid}	*Min*	*Max*	*Mean*	*SD*
(1)	Sleep problems at age 5	1557	0	11	1.29	1.479
(2)	Sleep problems at age 8	1573	0	9	1.20	1.530
(3)	Sleep problems at age 10	1599	0	9	1.01	1.401
(4)	Sleep problems at age 14	1562	0	9	0.82	1.313
(5)	Sleep problems at age 17	1275	0	9	0.83	1.342
(6)	Anxious/depressed at age 5	1583	50	89	53.37	5.491
(7)	Anxious/depressed at age 8	1589	50	95	54.18	6.407
(8)	Anxious/depressed at age 10	1610	50	92	53.51	6.037
(9)	Anxious/depressed at age 14	1569	50	87	52.68	5.212
(10)	Anxious/depressed at age 17	1258	50	81	52.05	4.470
(11)	Attention problems at age 5	1583	50	92	54.14	6.336
(12)	Attention problems at age 8	1589	50	93	54.23	6.738
(13)	Attention problems at age 10	1610	50	95	53.56	6.692
(14)	Attention problems at age 14	1569	50	89	53.03	5.549
(15)	Attention problems at age 17	1258	50	86	52.11	4.604
(16)	Aggressive behaviors at age 5	1583	50	95	54.76	6.993
(17)	Aggressive behaviors at age 8	1589	50	97	53.89	6.825
(18)	Aggressive behaviors at age 10	1610	50	100	53.11	6.121
(19)	Aggressive behaviors at age 14	1569	50	91	53.44	6.276
(20)	Aggressive behaviors at age 17	1258	50	88	52.03	4.923

Note. Sleep problems raw score. Anxious/depressed, attention problems and aggressive behaviors T score.

TABLE 2 | Correlations among the variables and descriptive statistics

			(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)	(17)	(18)	(19)	(20)
Sleep problems at age	5	(1)	1	.512**	.407**	.373**	.307**	.452**	.347**	.269**	.273**	.223**	.423**	.290**	.260**	.254**	.205**	.444**	.348**	.307**	.286**	.194**
	8	(2)		1	.522**	.436**	.335**	.325**	.462**	.335**	.289**	.247**	.328**	.412**	.298**	.276**	.272**	.337**	.426**	.316**	.247**	.247**
	10	(3)			1	.512**	.346**	.245**	.329**	.448**	.281**	.186**	.294**	.310**	.413**	.339**	.210**	.286**	.337**	.378**	.289**	.181**
	14	(4)				1	.470**	.233**	.309**	.315**	.458**	.276**	.252**	.245**	.300**	.417**	.258**	.284**	.321**	.333**	.421**	.266**
	17	(5)					1	.216**	.254**	.268**	.305**	.501**	.225**	.202**	.217**	.265**	.450**	.262**	.292**	.285**	.316**	.454**
Anxious/depressed at age	5	(6)						1	.550**	.414**	.273**	.253**	.516**	.337**	.276**	.215**	.189**	.546**	.404**	.336**	.263**	.195**
	8	(7)							1	.563**	.418**	.359**	.392**	.571**	.396**	.366**	.310**	.435**	.601**	.429**	.368**	.298**
	10	(8)								1	.501**	.393**	.348**	.414**	.551**	.391**	.306**	.357**	.431**	.572**	.393**	.296**
	14	(9)									1	.551**	.278**	.316**	.357**	.495**	.387**	.266**	.345**	.377**	.522**	.356**
	17	(10)										1	.232**	.281**	.301**	.317**	.590**	.235**	.311**	.323**	.325**	.511**
Attention problems at age	5	(11)											1	.650**	.565**	.483**	.377**	.613**	.485**	.432**	.352**	.249**
	8	(12)												1	.660**	.581**	.466**	.467**	.625**	.476**	.376**	.308**
	10	(13)													1	.671**	.490**	.396**	.470**	.624**	.429**	.348**
	14	(14)														1	.588**	.366**	.438**	.472**	.588**	.396**
	17	(15)															1	.298**	.375**	.365**	.391**	.600**
Aggressive behaviors at age	5	(16)																1	.687**	.590**	.502**	.365**
	8	(17)																	1	.684**	.603**	.480**
	10	(18)																		1	.665**	.508**
	14	(19)																			1	.587**
	17	(20)																				1

Note. $^{**}p<.001$, $^{*}p<.01$

TABLE 3 | Model selection criteria to determine best fitting model of the reciprocal relations between sleep problems and dysregulation profile.

Model		χ^2	*df*	*p*	CFI	TLI	RMSEA [90% CI]
Model 1	autoregressive paths between adjacent time points	739.098	132	<.001	.967	.952	.053 [.049-.057]
Model 2	add autoregressive paths between distant time points	417.517	120	< .001	.984	.974	.039 [.035-.043]
Model 3	add cross-lagged paths between adjacent time points	278.383	112	<.001	.991	.985	.030 [.026-.035]
Model 4	add early-effect (age 5) cross-lagged paths	262.202	106	<.001	.991	.985	.030 [.026-.035]
Model 5	add remainder of potential cross-lagged paths	251.667	100	< .001	.992	.984	.031 [.026-.035]
Model 6	remove non-significant paths	273.116	118	<.001	.992	.986	.028 [.024-.033]

Note. Models 1 through 6 are nested within each other. CFI = comparative fit index; TLI = Tucker-Lewis index; RMSEA = root mean square error of approximation; SRMR = standardized root mean square residual

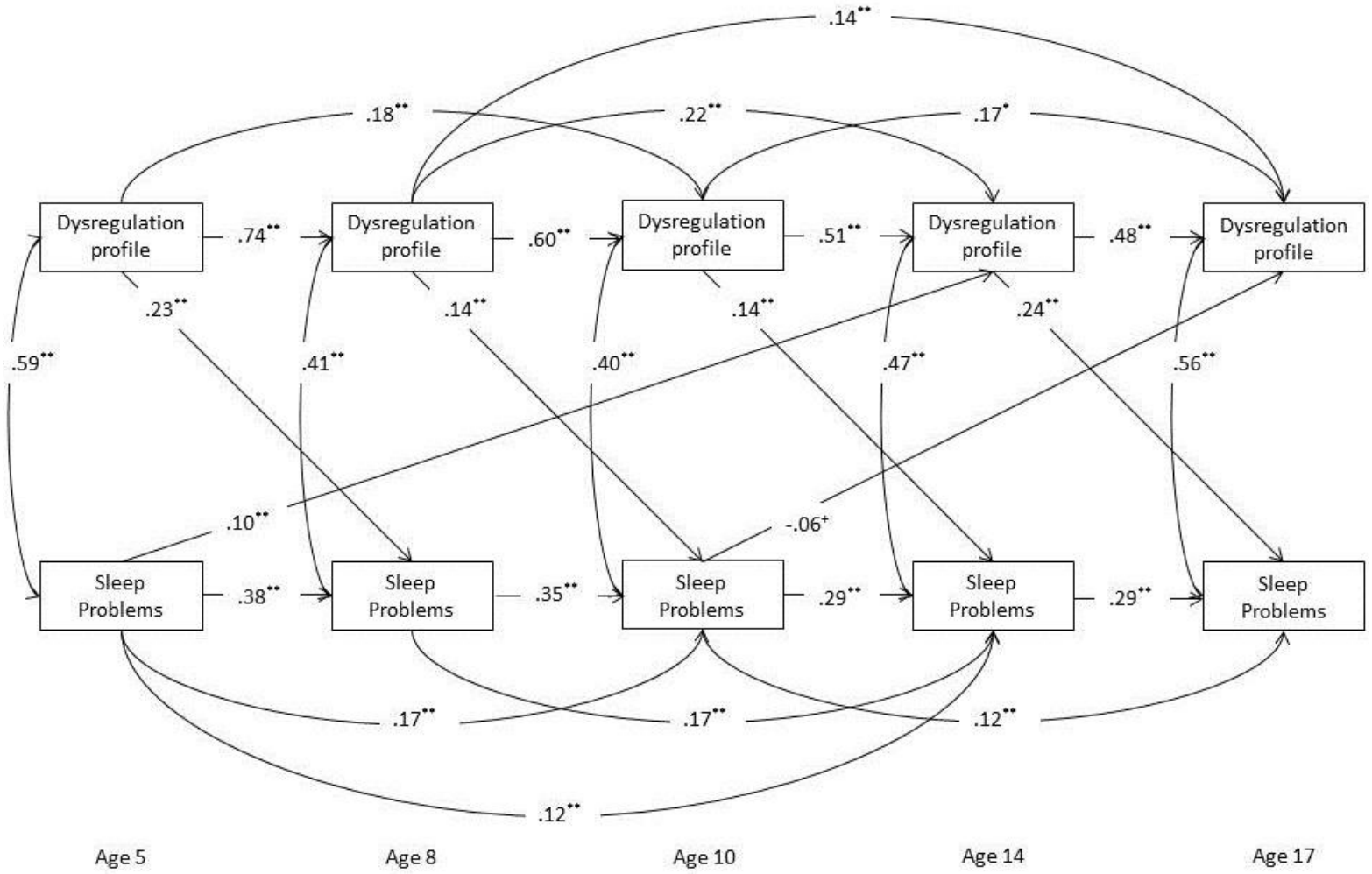

FIGURE 1 | Final model for the reciprocal relations between sleep problems and dysregulation profile from childhood to adolescence. All estimates are standardized. All potential paths and cross-sectional correlations were estimated but only significant paths are shown. **p<.001,*p<.01, +p<.05.

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Chapter 4 - Summary Discussion

4.1 Findings and Relevance to Current Knowledge

This cumulative work explored the longitudinal relationship between sleep problems and self-regulatory impairments in a large cohort sample from early childhood to adolescence over five measurement points. Results provided new evidence and insights. Hence, they improved current knowledge of the above-mentioned relationship and offer a better platform for future approaches to screening and prevention.

Across the period of childhood and adolescence, the general course of sleep problems showed a gradual declining trend, which is consistent with previous findings (Gregory & O'Connor, 2002) from a community sample with similar age range (5-14 years vs. 4-15 years), despite of different cultural background (Australian vs. American) and statistical method (latent growth curve modeling vs. repeated measures analyses). However, the significant variances observed for both average initial level and growth of the general course (slope) suggested inter-individual differences i.e. within group heterogeneity concerning developmental aspects of sleep problems.

This kind of heterogeneity was revealed by applying growth mixture modeling. Two latent classes of individuals following distinct developmental course of sleep problems from childhood to adolescence were identified. The majority of children and adolescents (Normal Sleepers, 89.4%) reported consistently lower sleep problems as reflected by the general course. Covered by this general course, there was a small group of children and adolescents (Troubled Sleepers, 10.6%) with persistent higher level of sleep problems. The presence of Troubled Sleepers echoes (in a similar

frequency) previous literature on the continuation and persistence of sleep problems (Fricke-Oerkermann et al., 2007). Notably, this group experienced a sudden increase of symptoms in adolescence probably due to the pubertal developmental phase. Considering the predictive value of adolescence sleep disturbances to adulthood sleep disturbances (Dregan & Armstrong, 2010), such problems might reflect a persistent disturbance and help to explain the high prevalence of sleep disturbances in late adolescence (25%, see Ohayon et al., 2000) and even adulthood (37%, see Morphy, Dunn, Lewis, Boardman, & Croft, 2007). These findings suggest that due to the stable nature of sleep problems, children with sleep problems at early times face great chance/risk of maintaining or even aggravating their symptoms over time. Therefore, early time screening could be particularly important to finding and supporting individuals at elevated risk.

Early childhood self-regulatory impairments manifested as emotion, attention and aggression problems at age 5 were tested as predictors of the development of sleep problems. The presence of anxiety/depression, attention problems and aggressive behavior predicted a higher initial level of sleep problems, suggesting that these risk factors are active already in the earlier years of life. Furthermore, children of both sexes with early attention problems or aggressive behavior, and, specifically, girls with early anxiety and depression were more likely to be Troubled Sleepers compared to their counterparts. This interaction between emotional problems, sleep problems and gender may stem from girls' greater vulnerabilities for anxiety and depression (see Hyde, Mezulis, & Abramson, 2008; McLean & Anderson, 2009for review) and calls for further investigation into this complex relationship. Correspondingly, latent class membership of sleep problems was predictive of attention problems and aggressive behavior in adolescence, with Troubled Sleepers

reporting significantly higher symptoms levels. These results are partly consistent with previous findings (Gregory & O'Connor, 2002; Pieters et al., 2015) and thus indicated that the longitudinal relationship between sleep problems and self-regulatory impairments from early childhood to adolescence to be complex and bi-directional.

Developmental course of regulatory difficulties in emotion, attention and aggression domain, both separately estimated as specific problems and jointly formed the broad syndrome of dysregulation profile, were mapped during childhood and adolescence using the same procedure as with sleep problems. Growth mixture modeling revealed individuals following a distinct developmental pattern of regulatory difficulties with lower and higher symptoms. Similar to the case of sleep problems, small groups of individuals (prevalence rates between 7.8%-10.1%) reported enduring problematic developmental courses.

Based on separate developmental courses, joint trajectory models were built to reflect their longitudinal co-occurrence. Results from these joint trajectory models showed that, during the period of childhood and adolescence, these difficulties share an overlap rate between 89.8%-92.3%. Sleep problems and self-regulatory impairments, while representing different phenomena, are highly comorbid. This finding is consistent with prior evidence on the above-mentioned relationship on cross-sectional (Astill, Van der Heijden, Van IJzendoorn, & Van Someren, 2012; Fredriksen, Rhodes, Reddy, & Way, 2004) and longitudinal (Gregory et al., 2008; Williams, Berthelsen, Walker, & Nicholson, 2017) associations. More importantly, the presence of one of these persistent problems (compared to their unaffected counterparts) was associated with a dramatic increase in the risk of having the other at 8-14 times. Therefore, it may be suggested that a positive screening of any of the

above-mentioned psychopathological dimensions should lead to careful further assessments for the consideration of potential co-occurring problems before treatment decisions are made.

With evidence of the strong mutual association in the development of sleep problems and difficulties of dysregulation, their longitudinally reciprocal relationships were explored by autoregressive cross-lagged models. Significant autoregressive paths were found in sleep problems and dysregulation. Such high stabilities overtime are consistent with the results of previous research on those domains (Deutz et al., 2017; Gregory & O'Connor, 2002). It is worth mentioning that their internal stability gradually reduced with time, possibly due to the maturational changes during puberty (Dahl & Lewin, 2002; Soffer-Dudek, Sadeh, Dahl, & Rosenblat-Stein, 2011). Corresponding to their concurrent development, within time-points correlations between sleep problems and dysregulation profile were consistently strong. The effect of sleep problems on self-regulatory impairments and vice versa were reflected in the cross-lagged paths. Dysregulation profile showed stronger and more consistent influence on subsequent sleep problems than the sleep-driven paths, after controlling for relevant autoregressive and concurrent effects. These findings provide strong evidence for a temporal precedence of the cross-domain problems of self-regulation on later sleep disturbances, which is critical in the understanding of their causal relationship. Hence, it may be suggested that, when there exist concurrent problems in sleep and dysregulation, the dysregulation problems should be considered as the primary factor for clinical interventions.

4.2 Strengths and Limitations

Several strengths of this cumulative work should be highlighted. From the perspective of sample, we benefited from the large, population-based cohort sample of Raine Study to conduct the investigation in a large community sample which is representative of the general population. The longitudinal design over a span of 13 years enabled us to examine the content during the key developmental stage from early childhood to adolescence. The nature of the cohort sample ensured that the developmental patterns we found are reflecting true age effects. With respect to the methods, we conducted the analysis in three successive steps: firstly, we tested the longitudinal course for each aspect separately and whether there were longitudinal similarities between sleep problems and dysregulation profile; secondly, we tested how did their associations present overtime and what was the extent of their co-occurrence, lastly, what was their reciprocal relationship and whether temporal precedence, i.e., direction of impact, could be determined. Such order of investigation followed a complete flow of rationality and thus improved the validity and rigor of this study. In the first and second study, the person-centered approach of growth mixture modeling and joint growth mixture modeling were applied. The utilization of these methodologies allowed us to identify subgroups following distinct developmental patterns. To our knowledge, this is the first set of study to empirically investigate subgroups in the longitudinal development of general sleep problems and examine its concurrent development with self-regulatory impairments. The third study adopted autoregressive cross-lagged models to explore the research question of temporal precedence between sleep problems and dysregulation profile, it represents the first attempt, to our knowledge, to examine the reciprocal relationship between difficulties in sleep and self-regulation.

However, some limitations of this cumulative work should be kept in mind when interpreting the findings. First, all participants in the present study were from Western Australia and thus findings may be sample dependent. Future research should replicate these findings in other contexts and/or cultures. Second, to improve the validity of longitudinal analysis, we only included participants who had data in 80% or more measurement points. Such data management resulted in retention of 56.7% (study 2 and 3) to 69.4% (study 1) of the original sample. Differences between the effective and excluded sample in all studied variables were reported in detail, which should be considered when interpreting the findings. Since the excluded sample had higher levels of both sleep and psychopathological difficulties, it is possible that the magnitudes of the true relationships might be underestimated. Third, all of the measures were based exclusively on parent- reports and there is potential for rater bias. Although self-reports may be more appropriate than parent-reports in assessing older children particularly for internalizing problems, we relied on a single source of information in a quest for more reliable and comparable results in the long term.

4.3 Future Research Perspectives

The present cumulative dissertation examined a clinically relevant topic, namely difficulties of sleep and self-regulation from early childhood to adolescence about their longitudinal association, concurrence and reciprocal relationships. Results provided evidence for stable and heterogeneous developmental patterns for both contents, strong mutual associations with concurrent symptoms and longitudinal bi-directional relations, dominated in impact by the dysregulation-driven paths. Future studies should explore the underlying mechanisms of these relationships in greater detail to improve our understanding. The current cumulative work relied solely on a

population-based sample. Hence, the replication in broader clinical samples may be especially informative, since both problem areas studied should be exaggerated in the more vulnerable population of psychiatric patients, such as those with autism (Cohen et al., 2014; Richdale, 2009). This would allow to putting our findings in a more specific but also broader context.

Another direction of future research may lie in the measurement of sleep problems. In the current work, items from the CBCL were used to access general sleep problems. Although the CBCL sleep composite is a valid and reliable measurement of sleep problems, the inclusion of formal diagnoses of sleep disorders would have strengthened the results. Moreover, for the consideration of specific features of sleep disturbances, more detailed sleep assessments, such as actigraphy could be included.

As this cumulative work represents, to the best of our knowledge, the first detailed and systematic examination of the longitudinal relationship between difficulties of sleep and self-regulation, focus was given on the content of interest itself (i.e., behavioral sleep problems, regulatory difficulties in emotion, attention and aggression domain separately estimated as specific problems and jointly formed the broad syndrome of dysregulation profile) without considering potential influences from family/parental factors (Adam, Snell, & Pendry, 2007; Cousins, Bootzin, Stevens, Ruiz, & Haynes, 2007). It would be of particular value if future investigations could take into account these factors.

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Acknowledgements

First and foremost I would like to express my sincere gratitude to my supervisor Prof. Aribert Rothenberger for the continuous support of my doctoral study and related research. I appreciate all his contributions of time, ideas and knowledge to make this experience joyful, productive and stimulating. His great passion and enthusiasm for science is and will always be inspiring for my future research. I could not imagine having a better supervisor and mentor for my doctoral study and following career.

I would like to thank the members of my thesis committee: Prof. Nicole von Steinbüchel and Prof. York Hagmayer, not only for their time devoted to my project, but also for their insightful advices and warm encouragements. I would also like to thank my program promoter, Prof. Martin Oppermann, and Ms. Kornelia Ewens from the promotion office, for their project management and help in my doctoral program.

I am greatly thankful to my colleagues in the clinic for child and adolescent psychiatry and psychotherapy: Prof. Luise Poustka, Dr. Corinna Isensee, Dr. Henrik Uebel-von Sandersleben, Ms. Ute Bolt, Dr. Björn Albrecht, for their constant help and support during my study. Specially, I am extremely grateful to Dr. Andreas Becker, for his countless help in both work and life. I am very lucky to have an advisor and friend so kind as he is. My sincere thank you also goes to Ms. Barbara Kunze, who generously offered her help when I begin my life in Goettingen. I would also like to say thanks to my great office mates, former and present, Ms. Parisa Ganje, Ms. Olga Müller, Ms. Chrinstina Kälble, Mr. Mohammad Rostami for their sweet companion along the way.

I would like to thank Prof. Thomas Meyer, Dr. Geza Brüni, Prof. Florian Zepf, Prof. Peter Eastwood, Dr. Kevin Runions, Dr. Janice Wong, Dr. Rae-Chi Huang, Dr. Richard Stewart whom I have done collaboration work with, for their high level of expertise, constructive suggestions, inspiring discussions and generous help as

experienced researchers. I am also thankful to the Raine Study for both children and their families for years of participation, and the management team for cohort co-ordination and data collection, the research ideas and work from this thesis would not be possible without your efforts.

Furthermore, I would like to thank my funding, Overseas Study Program of Guangzhou Elite Project, for providing financial support during my doctoral study, and Guangzhou Service Center for Scholarly Exchange office, especially Ms. Huiting Mai, for providing excellent project management and great support.

Finally, I would like to express my utmost gratitude to my husband Shi Cheng, my family and my friends, for their endless love and unconditional support in all of my pursuits. You are the source of my strength and l love you too.