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Insomnia disorder in adolescence: diagnosis, impact, and treatment

Massimiliano de Zambotti, PhD[1,*], **Aimee Goldstone, PhD**[1], **Ian M Colrain, PhD**[1,2], and **Fiona C Baker, PhD**[1,3]

[1]Center for Health Sciences, SRI International, Menlo Park, CA, USA

[2]Melbourne School of Psychological Sciences, University of Melbourne, Parkville, Victoria, Australia

[3]Brain Function Research Group, School of Physiology, University of the Witwatersrand, Johannesburg, South Africa

Summary

Insomnia disorder is very common in adolescents; it is particularly manifest in older adolescents and girls, with a prevalence comparable to that of other major psychiatric disorders (e.g., depressive disorders). However, *insomnia disorder* in adolescence is poorly characterized, under-recognized, under-diagnosed, and under-treated, and the reason for the female preponderance for insomnia that emerges after puberty is largely unknown. *Insomnia disorder* goes beyond an individual complaint of poor sleep or a sleep state misperception, and there is emerging evidence supporting the association of insomnia symptoms in adolescents with alterations in several bio-systems including functional cortical alterations and systemic inflammation. *Insomnia disorder* is associated with depression and other psychiatric disorders, and is an independent risk factor for suicidality and substance use in adolescents, raising the possibility that treating insomnia symptoms in early adolescence may reduce risk for these adverse outcomes. Cognitive behavioral treatments have proven efficacy for adolescent insomnia and online methods seem to offer promising cost-effective options. Current evidence indicates that insomnia in adolescence is an independent entity that warrants attention as a public health concern in its own right.

Keywords

Hyperarousal; insomnia; adolescents; polysomnography; depression; pubertal development; mental health

[*]**Corresponding Author:** Massimiliano de Zambotti, PhD, SRI International, 333 Ravenswood Avenue, Menlo Park, CA, 94025; Tel: (650) 859-2714; Fax: (650) 859-2743; massimiliano.dezambott@sri.com.

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1. Introduction

Insufficient sleep and sleepiness in adolescents is a serious public health issue (1). Typical developmental changes and challenges to sleep faced by adolescents have been the topic of several recent reviews (1–3). Over and above these typical changes in sleep is the emergence of *insomnia disorder* in a portion of adolescents, which has received less attention in the literature.

Insomnia disorder is the most severe clinical manifestation of recurrent and chronic perceived sleep dissatisfaction (difficultly falling asleep and staying asleep despite having an adequate opportunity to sleep) occurring several times per week, resulting in significant distress and daytime consequences (e.g., sleepiness; difficulties with attention, concentration and memory; mood lability). Insomnia in adolescence is common, particularly in older adolescents and in girls (4, 5), with a prevalence that is comparable of that of other major psychiatric disorders (e.g., depressive disorders) (6). Further, insomnia tends to be chronic with 88% of adolescents with a history of insomnia reporting current insomnia (4). Insomnia is frequently comorbid with other mental conditions, with half of adolescents with insomnia also reporting comorbid psychiatric disorders (4).

This review aims to offer a picture of *insomnia disorder* in the context of social, behavioral and bioregulation changes normally occurring in adolescence. Adolescence is the transitional period between childhood and adulthood, and is considered part physiological, part psychological, and part social construct (7). Adolescence is different from puberty, which describes the period during which the reproductive system matures, ending with the cessation of bone growth (7). The World Health Organization (WHO) defines adolescents as those people between 10 and 19 years (http://apps.who.int/adolescent/second-decade/section2/page1/recognizing-adolescence.html). Chronotype has been suggested as a physiological marker of the end of adolescence, with peak eveningness being reached at around the age of 20 years (8). For the purposes of this review, therefore, we have focused on research about insomnia in the second decade. In cases where we have deviated from this age range, we have specified ages of included participants. Topics covered in this review include the challenge in diagnosing insomnia in adolescence, risk factors for insomnia that emerge during adolescence including sex-specific differences in risk profiles, associations between insomnia and psychiatric disorders, physiological functioning, and cognition, and available treatment options. Finally, we highlight some of the gaps in the literature and suggest future directions for research to enable greater recognition of *insomnia disorder* and its impact in adolescents.

Comprehensive literature searches were conducted on epidemiological, clinical, and experimental studies published in the English language on *insomnia disorder* in adolescents using the electronic databases, PubMed, Google Scholar, Web of Science, PsycINFO. For this narrative review, in combination with the words “insomnia”, “adolescen*”, “pediatric”, one or more of the following search terms were used to obtain articles published in peer-reviewed journals: risk factors, etiology, polysomnography, actigraphy, female, sex difference, non-restorative sleep, poor sleep, sleep quality, electroencephalogram, psychiatric disorder, depression, suicide, substance use, cognition, autonomic nervous

system, hypothalamic pituitary axis, sleep duration, treatment, cognitive behavioral therapy. Full-text manuscripts were reviewed for relevance and reference lists were cross-checked for additional relevant studies. A review of the articles that cited the most relevant references was also performed using Google Scholar. Given the low number of studies that have confirmed the presence of *insomnia disorder* according to clinical criteria, we have included studies in which specific insomnia symptoms in adolescents were considered. Due to the heterogeneity of *"insomnia"*, for each study we specified if the insomnia samples consisted of individuals with insomnia symptomatology (nocturnal symptoms of the disorder with or without daytime dysfunction) or whether insomnia sufferers met specific diagnostic criteria of the disorder.

2. Prevalence and clinical diagnosis of insomnia in adolescence

Insomnia is the most prevalent sleep disorder in adolescence (4, 6) with a 10.7% lifetime and a 9.4% current prevalence according to the diagnostic and statistical manual of mental disorders (DSM) fourth edition (DSM-IV) in a US sample of 13–16 year old adolescents (4). Importantly, the chronicity of insomnia is high in adolescents (4) and there is a strong female prevalence of the disorder with sex differences emerging after puberty (4–6).

Rates of adolescent insomnia in other studies range between 4% and 39%, with differences in prevalence rates related to the diagnostic criteria used (e.g., use of different classification systems, evaluation of nocturnal symptoms with or without the presence of daytime dysfunction, use of dichotomized or continuous variables to assess symptoms presence, partial or no evaluation of comorbidities, use of quantitative criteria to evaluate frequency and severity of the disorder alone or in conjunction with other criteria), how insomnia was determined (e.g., inperson or phone interview, survey and sleep diary), time of the assessment, and population characteristics (e.g., age range) (5, 6, 9–12). Recently, a prevalence rate of 18.5% (23.6% in girls and 12.5% in boys) was reported for insomnia diagnosed by DSM fifth edition (DSM-5) criteria in older adolescents (16–18 years) (5). In the same study, a prevalence of 23.8% was reported when insomnia was defined according to DSM-IV criteria, and 13.6% based on quantitative criteria (as defined by difficult in initiating and maintaining sleep at least three times per week, with sleep onset latency and/or wake after the sleep onset of more than 30 min), with girls having a higher prevalence of insomnia than boys independent of the criteria used (5). It is unclear which aspects of the different classification systems are responsible for the differences in the prevalence of the disorder. For example, the DSM-5 applies stricter requirements for frequency and duration of the disorder, which could result in a lower prevalence of the disorder. On the other hand, DSM-5 allows the coexistence of potential comorbidities [e.g., depression] which could involve the inclusion of more insomnia cases, compared to DSM-IV (unfortunately not many studies consider the presence of comorbidities in the diagnosis of insomnia). Thus, although it is clear that there is a high prevalence of insomnia in adolescence, no matter what diagnostic system is used, reasons for discrepancies in the prevalence of the disorder according to different systems need to be further elucidated.

According to the most recent diagnostic criteria, i.e. the DSM-5 (13), "i*nsomnia disorder"* is defined by a predominant dissatisfaction with sleep despite an adequate opportunity for

sleep, and includes difficulties in initiating sleep and/or in maintaining sleep and/or early-morning awakening with inability to return to sleep. The sleep disturbance has to cause clinically significant distress or impairment in daytime functioning, and the sleep difficulties need to occur at least 3 nights/week and for at least 3 months. The DSM-5 groups together *"primary insomnia"* and *"insomnia related to another mental disorder"* in a single diagnostic entity, however, it requires specification if *"insomnia disorder"* coexists with other mental or medical comorbidities and/or sleep disorders. Also, the DSM-5 states that insomnia has to be better explained by, and does not occur exclusively, during the course of another sleep and/or mental disorder and/or medical condition and/or substance use. Similarly, the recent international classification of sleep disorders (ICSD) third edition (ICSD-3) (14) grouped the secondary categories of insomnia and the several subtypes (*"psychophysiological insomnia", "idiopathic insomnia", "inadequate sleep hygiene"* and *"paradoxical insomnia"*) into a single category of *"chronic insomnia disorder".* Thus, recent editions of ICSD and DSM are better aligned. Although not a core part of the criteria, age-related differences in insomnia symptomatology are listed in the DSM-5 and the ICSD-3. For example, the DSM-5 states *"Changes in sleep patterns associated with the normal developmental process must be differentiated from those exceeding age-related changes"*, thus contextualizing insomnia within the individuals' lifetime. It also states that, *"The onset of insomnia symptoms can occur at any time during life, but the first episode is more common in young adulthood. Less frequently, insomnia begins in childhood or adolescence"*, although current estimates of DSM-5 *insomnia disorder* prevalence in adolescence (18.5%) (5) are on a par or higher with that for adults, and with the overall population-based prevalence of the disorder (13).

The diagnosis of insomnia in adolescence has unique challenges. For example, a diagnosis of insomnia requires the presence of *"sleep dissatisfaction despite an adequate opportunity to sleep"*, however an *"adequate opportunity to sleep"* particularly during normal school days in adolescence may not be easily achieved. To illustrate the stark differences in sleep patterns between school weeks and vacations, Bei et al. (15) followed adolescents (N=146) through a transitional period between school time and vacation time. School time was characterized by significant sleep restriction and sleep patterns gradually shifted to later sleep timing and extended sleep opportunities, with a progressive rise in sleep disruption including a progressive delay in sleep onset latency, and more variable sleep timing as adolescents progressed through the 2-week vacation period. Authors hypothesized that there are two processes responsible for this change: a shifting toward later sleep timing that may reflect a combination of shifting in adolescents' circadian preference (possibly in combination with reduced parental control during vacation time); and, a recovery from a condition of sleep restriction typical of school-weeks, with sleep pressure progressively decreasing into the vacation time. Importantly, the sleep pattern seems to stabilize at the end of the second week of vacation, which may reflect the "true adolescents' sleep pattern" in a condition in which obligations are removed. This data shows how critical the time of the assessment of *insomnia disorder* is, from a diagnostic perspective. Thus, careful documentation of the adolescent's sleep pattern on school days vs. week-end, school-time vs. vacation-time, desired sleep-time vs. actual sleep-time is needed. Also, delayed sleep phase disorder (DSPD), syndrome or type, common in this age group, needs to be excluded (see below). Another challenge to diagnosing *insomnia disorder* in adolescents is the

evaluation of DSM-5 criteria H (*"Coexisting mental disorders and medical conditions do not adequately explain the predominant complaint of insomnia"*). There is a high comorbidity of insomnia and other psychiatric disorders (e.g. depressive disorders), and the time-course of the development of insomnia and other psychiatric disorders overlaps in adolescence.

Among the several factors potentially confounding diagnosis and characterization of insomnia in adolescence, DSPD requires particular attention. Accordingly to the DSM-5, DSPD (or *"delayed sleep phase type"*) typically begins in adolescence and is characterized by a delay in the desired (or conventionally acceptable) sleep and wake up time resulting in insomnia symptoms and excessive sleepiness (13).

Unfortunately, most of the studies investigating *insomnia disorder* in adolescence do not specifically screen for the presence of DSPD such that it cannot be completely ruled out as a potential confounding factor in the study outcomes. Among the few studies assessing the prevalence of DSPD in adolescence, Silversten et al. (16), reported a strong overlap (~50%) of ICSD-R (17) defined DSPD and insomnia defined accordingly to quantitative criteria (difficulty initiating and maintaining sleep, tiredness or sleepiness occurring at least three time per week, and sleep onset latency and/or wake after sleep onset greater than 30 min). However, in the sample of 10,220 16–18 years adolescents considered, authors reported an prevalence of 1.4% for DSPD only, 11.3% for insomnia only and 1.7% for the combination of insomnia and DSPD. Thus, the potential coexistence of DSPD and insomnia in adolescence seems to involve a small fraction of the potential insomnia cases. Similarly, Johnson et al. (4) found that DSPD did not account for a significant proportion of DSM-IV insomnia cases (4.2%). Thus, whether almost half of adolescents with DSPD may also have co-occurring insomnia (reflecting the diagnostic criteria of DSPD in which insomnia is a symptom), a small proportion of adolescents with insomnia seems to have co-occurring DSPD. Even so, a comprehensive sleep assessment (preferably through in-person structured clinical interviews) is required to differentiate DSPD from late sleep behaviors, "typical" of adolescents (but which do not cause significant distress), and from *insomnia disorder.* In particular, monitoring of sleep patterns (e.g., using sleep diaries and/or actigraphic-type devices) over prolonged periods (for at least 7 days) including times when social constraints and other obligations are removed (e.g., during week-ends) could improve the differentiation of the circadian alteration typical of DSPD from *insomnia disorder.*

Overall, an accurate diagnosis of *insomnia disorder*, which should include an exhaustive sleep history and circadian sleep assessment, is required to successfully manage the disorder and to ensure that the appropriate treatment option is selected (see Section 8).

3. Understanding insomnia in the context of normal development

The manifestation of insomnia in adolescence needs to be considered against the backdrop of the dramatic changes that occur in sleep architecture, duration, and timing as a result of changes in circadian and homeostatic processes in association with reorganization of the central nervous system (CNS) (1, 2, 18) combined with social and environmental pressures on sleep (1, 3).

Sleep architecture changes across adolescence, with a decrease in N3 sleep associated with a steep decline in delta power (slow wave activity, SWA; 0.3–4 Hz)(reviewed in (2)), hypothesized to reflect the process of reorganization in the adolescent brain (18). Limited evidence suggests that the buildup of homeostatic sleep pressure during wakefulness is slower in more mature adolescents, contributing to their delayed bedtime (19).

Changes in circadian and homeostatic bioregulatory processes together with external factors such as involvement in extracurricular activities, high homework load, evening technology use, and early school start times (20) lead to later bedtimes and shorter sleep duration (1, 3). Adolescents also show a shift in chronotype towards eveningness, with a preference for evening activities (*"owls"*) (8). Adolescents reach the maximum in their eveningness tendency at around the age of 20 years, with young women reaching their maximum significantly earlier than young men (8). School start times are a major restricting factor on wake-up times during the week, and early school start time is recognized by the American Academy of Pediatrics as a modifiable factor that is a key contributor to adolescents' insufficient sleep and circadian sleep disruption (21). As a result of early school start times, adolescents tend to accumulate a sleep debt during the school week which they attempt to recover on weekend nights, referred to as *"social jet lag"* (1, 3). Importantly, when parents set bedtimes, adolescents sleep longer and have improved daytime functioning, suggesting that parents may play a key role in improving their children's sleep (20).

Changes in sleep timing and duration may be considered a normal part of adolescent development, evident around the world (22), although sleep duration in adolescents varies geographically and culturally: adolescents in Asian countries report less sleep than those from the U.S. who, in turn, report shorter sleep durations than those from Australia and Europe (22). These differences are, in part, driven by differences in school start times, however, other factors play a role; for example, 11^{th} and 12^{th} grade Korean students have less than 6 hours sleep, on average, which is due to a combination of early school start times and because a high percentage of students attend additional night classes (23). Data in the U.S. also indicate that a large percentage (69%) of high school students average less than 7 hours on school nights (24). Having less than 8 hours of sleep per night is associated with increased sleepiness, impaired attention, decreased mood and motivation during the day in adolescents (20). There is growing awareness of the impact of insufficient sleep in adolescents and a call to reduce sleep loss at this critical time of development through improved education, later school start times, and identifying protective factors for adolescent sleep (20, 25, 26). A recent important position statement from the American Academy of Sleep Medicine (27), *"the leading voice in the sleep field"* clearly recommends that middle and high schools implement start times no earlier than 8:30 $_{AM}$ to promote adolescents' sleep needs, alertness, learning, safety, mental health and well-being. This position is also supported by the Centers for Disease Control and Prevention, see https://www.cdc.gov/features/school-start-times.

The global changes in sleep behavior and biology and the high prevalence of chronic sleep loss and daytime sleepiness in adolescents make it challenging to distinguish the development of a sleep disorder like insomnia. There may even be an interaction between "normal" adolescent sleep changes and development of insomnia, which could operate both

ways: chronic insufficient sleep (due to a chronic pattern of sleep restriction) may increase sleep pressure, paradoxically protecting against insomnia. Alternatively, chronic short sleep, irregular sleep-wake patterns, and associated daytime impact could contribute to the development of insomnia. Experimental manipulations to alter an adolescent's sleep timing and homeostatic sleep pressure are needed to investigate their role in the development of insomnia during this period. For example, the evaluation of *insomnia disorder* (other than changes in standard sleep metrics, daytime sleepiness, academic performance) in the context of public health interventions such as delayed school start times (designed to better align school start time and adolescents' circadian timing), may provide some insight.

4. Risk factors for developing and maintaining insomnia in adolescents

Insomnia is a complex disorder, with genetic factors (28) as well as biological, environmental, and social factors all contributing to its development. Here, we highlight some of the factors that may play a role in insomnia development in the adolescent period.

4.1. Female sex and puberty

Female sex is a major risk factor for insomnia. Sex differences in insomnia emerge after the onset of menses in adolescence (4), suggesting that hormonal changes underlying puberty may be directly or indirectly involved. Recent work including a large community-based sample of Chinese children and adolescents (6–17 years) has also shown an interaction between self-report stages of pubertal development and sex on the prevalence of insomnia symptoms (as defined by difficulty falling asleep, nighttime and early morning awakenings with difficulty returning to sleep occurring at least three times per week, as well as by the insomnia severity index (ISI) (29) scores ≥9), which increased 3.6-fold in girls from pubertal stage 1 to 5, compared with 2.1-fold in boys, with a clear sex difference evident in late/post puberty stages (30). The finding of increased risk for insomnia symptoms across pubertal development even in boys is in contrast to previous research (4) and highlights the importance of the pubertal transition for both boys and girls as a time of increased risk for the emergence of insomnia. The sexual differentiation in the prevalence of insomnia in adolescence could, in part, relate to the higher prevalence of depression in girls, which also emerges after puberty (31). Several social and biological changes occur during puberty that are sexually differentiated, such as higher stress level and greater stress reactivity in girls (30) and differential changes in sex steroids associated with increased neuroendocrine sensitivity (31), which may increase risk for both depression and insomnia. Zhang and colleagues (30) explored the association between insomnia symptoms, lifestyle, and emotional and behavioral problems in girls and boys. While some relationships were common in boys and girls (such as between insomnia symptoms and poorer mental and overall health scores), interactions with sex were also apparent in that insomnia symptoms were associated with greater consumption of energy drinks and alcohol in boys only whereas insomnia symptoms were associated with self-reported poorer emotional and behavioral wellbeing in girls only. These findings suggest, for the first time, that not only is there sexual differentiation in the prevalence of insomnia in adolescence but there is also differentiation in behaviors associated with insomnia. Importantly, the current evidence is correlational and future work is needed to determine directionality of these relationships.

4.2. School stress

High school is a period during which students are under enormous pressure to keep up with academic situations (e.g. exams, work groups, homework), deal with parental and societal expectations, balance social life, sports, and extra-curricular activities while studying. School pressure increases with age and is higher in girls compared to boys (32). The American Psychological Association in the 2014 nationwide “Stress in America” survey (33) clearly indicated stress as a major concern in teens: perceived stress may have a detrimental effect on health by affecting mood, eating behaviors, and sleep (33). Twenty-seven percent of teens report experiencing high levels of stress with school being the most common source of stress (83%) following by getting into college or deciding what to do after high school (69%).

Few studies have empirically evaluated the impact of school-stress on the development of insomnia in adolescents. In a longitudinal study, Roberts and colleagues (6) examined several risk and protective factors, including school stress, associated with the incidence and chronicity of insomnia as defined by an approximation of DSM-IV criteria of the disorder (authors assessed difficulty initiating and maintaining sleep, early morning awakening and nonrestorative sleep that “should” cause significant distress or impairment over the past 4 weeks; the disorder was not occurring exclusively during another mental disorder or due to the effect of a substance or to a medical condition; the assessment of potential comorbid sleep disorders was not performed) in 3134 adolescents (11–17 years) from Teen Heath 2000. Multivariate analyses indicate middle (OR: 3.23, 95%CI: 1.69–6.16) and high (OR: 4.34, 95%CI: 2.20–8.54) school stress as significant independent predictors of insomnia. Despite several limitations, including only assessing insomnia symptoms over the past 4 weeks without controlling for potential comorbid sleep disorders, this study suggests that school pressure may be a precipitating factor for insomnia that warrants further attention.

Given that many adolescents face similar stressors, it is plausible that different levels of vulnerability to insomnia exist, with increasing school-stress across adolescence triggering insomnia in those adolescents who are more vulnerable to developing the disorder. Interestingly, in adults it has been shown that appraisal and perceived lack of control over stress, more than the number of stressors, seems to increase the vulnerability to insomnia, with pre-sleep arousal and coping skills mediating the stress-insomnia relationship (34). Stress-reactivity, which has been recently proposed as a key factor in the psycho-bio-behavioural model of vulnerability to insomnia (28), seems to play a major role in the onset of insomnia. The assessment of stress-reactivity could be particularly valuable during early adolescence, to identify those adolescents “at risk” for developing insomnia before stress became more pervasive (e.g. during high school) and before the risk of developing insomnia increases (e.g. after puberty).

4.3. Electronic media use

Use of electronic media, and particularly the use of stimulating technology in which the users constantly interact with the devices (e.g., game consoles, mobile phones), has received attention as a disruptor to sleep in adolescents. It is common for adolescents to have and use electronic items (mobile phones, computers, TVs, game consoles) in their bedroom.

Specifically in adolescence, the progressive delay in circadian phase results in later bedtimes leaving adolescents more time to perform various activities until late at night. Electronic media use at bedtime, may impact subsequent sleep through several mechanisms: the direct reduction of time available to sleep and awakenings caused by incoming messages/calls at night, the melatonin-suppression effect of bright screen light, as well as the increase of pre-sleep psychophysiological arousal secondary to the engagement and content of the media (35), which prevents the psychophysiological withdrawal necessary to fall asleep. The increase in pre-sleep arousal levels is probably the most relevant factor in the context of insomnia, being a potential precipitating factor for the development of the disorder. As part of the National Sleep Foundation's 2011 Sleep in America Poll involving 1,508 Americans (13–64 years), Gradisar and colleagues (36) reported a high use of electronic media in adolescents (13–18 years) in the hour before bed (72% of them use cell phones, 60% computers/laptops, 64% electronic music devices, 23% video games console, with 18% of them reporting being awakened by their cell phone at least a few nights a week). Analysis of the whole sample (13–64 years) showed that the amount of media use was significantly related to difficulty falling asleep, but when analyses were conducted separately for "passive" and "interactive" devices, only the use of interactive devices (phones, computers, gaming consoles) was associated with difficulty sleeping. To note, pre-sleep engagement with stimulating technology was particularly high in adolescents, followed by young adults, and significantly less by middle-aged and older adults. Similar results were provided by Harbard et al. (37), who found that even when controlling for chronotype, among the several pre-bedtime behaviors analyzed in a sample of 146 adolescents, playing video games in the hour before bed was associated with delayed bedtimes during both school and vacation time, whereas online social media was associated with delayed sleep onset latency during vacation time, as mediated by higher pre-sleep cognitive arousal. Interestingly, pre-bedtime "passive" engagement (e.g., watching TV) was higher during vacation time whereas pre-bedtime "active" behaviors (e.g., playing video games) was greater during school time. In the same study, nontechnology-related pre-bedtime behaviors such as increased time spent with family was associated with earlier bedtimes and longer sleeping time on school nights, thus potentially acting as a protective factor. Among studies specifically investigating insomnia symptomatology and electronic media use in adolescents, a large cross-sectional survey of 7,533 German adolescents (11–17 years) reported a positive association between use of electronic media and insomnia complaints (defined as an approximation of DSM-IV criteria of insomnia including symptoms of difficulty in sleep initiation and/or maintenance, "feeling tired" and "lack of energy" during the past week rated as "often" or "always" on a five-point Likert-scale), with some evidence of sex differences related to the type of media used (for boys significant associations were found for computer/internet use while for girls, for listening to music) (38). Another nationwide epidemiological study involving 95,680 Japanese adolescents, reported that calling (8.3% of the respondents) and texting (17.6% of the respondents) after lights-out were independently associated with poor sleep, daytime sleepiness and insomnia symptoms (difficulty falling asleep, nighttime and early morning awakenings with difficulty returning to sleep) (39). Similarly, other studies reported positive associations between electronic media use, including problematic internet use (40), internet addiction (41), and insomnia symptoms in adolescents.

Despite evidence indicating an association between electronic media use and insomnia symptoms in adolescents, the causality and direction of the relationship needs to be determined. In fact, despite the general belief that the bedtime use of electronic media causes sleep problems (e.g. bedtime delay), it is also possible that insomnia symptomatology leads to a greater use of electronic media as a compensatory activity due to the inability to sleep.

4.4. High caffeine intake

Another potential factor implicated in delaying bedtimes in adolescents is the consumption of caffeinated beverages (42). Caffeine is a central nervous system stimulant acting as an adenosine receptor antagonist; it is the most widely used psychoactive drug, it is legal and "generally recognized as safe" by the Food and Drug Administration, easily to access, and socially acceptable to use. The disruptive effect of caffeine on sleep in adults, children and adolescents is well known (43). However, recent concerns have been raised about the consumption of caffeinated beverages in adolescents coincident with the introduction and exponential grown of the market for energy drinks - beverages containing high and unregulated amounts of caffeine (44). Importantly, these potentially harmful drinks seem to be targeted particularly at the adolescent market (45), and the availability and appeal of these new high-caffeine-products makes children and adolescents a fast growing population of caffeine users, with energy drinks regularly consumed by >30% of adolescents (46). Consumption of caffeinated beverages in adolescents seems to be an alarming countermeasure to overcome excessive sleepiness (44), despite a vicious loop among caffeine consumption – poor sleep – sleepiness. High caffeine consumption may precipitate or perpetuate insomnia via caffeine-induced physiological hyperarousal (47) which in turn prevents individuals from falling asleep and having a restful night sleep. In a school-based nationally-representative sample of 15,686 US adolescents, high daily caffeine intake (coffee and soda), compared to "low intake", was associated with 1.9 times greater likelihood of having difficulty sleeping and 1.8 times greater likelihood of being tired in the morning (48). A recent cross-sectional study on 7,698 German adolescents (11–17 years) found that tobacco, alcohol, marijuana, and coffee use were all related to insomnia complaints (dichotomically defined by assessing problems in falling asleep or staying asleep, and daytime tiredness), however, the effect was greatest for caffeine consumption (49). While current research shows the separate detrimental effects of these substances on sleep, it remains to be determined what is the combined effects of caffeine consumption with other substances (e.g. alcohol, tobacco) and other sleep-disruptive behaviors (e.g. use of electronic media late at night) on sleep and insomnia in adolescence.

5. Objective sleep in adolescence with insomnia

Despite a large body of evidence characterizing the polysomnographic (PSG) profile of adults with insomnia (50), few studies have investigated objective sleep in adolescents with insomnia. The analysis of large samples of adolescents from the Penn State Child Cohort (PSCC) examining the relationship between self-report insomnia symptoms (difficulty falling asleep and/or staying asleep) with inflammation (N=378) (51) as well as with internalizing and externalizing behavior problems (N=397) (52), failed to show PSG

differences in standard sleep metrics between adolescents with compared to those without self-reported insomnia symptoms. However, the same authors showed pronounced group differences in objective PSG macro- and micro-structure by analyzing a smaller randomly selected, case-control sample of the same cohort (N=44) (53). Specifically, authors reported greater sleep onset latency (~22 min), wake after sleep onset (~30 min) and elevated low- and high-beta EEG power across the falling asleep period and during NREM sleep, less total sleep time (~51 min) and sleep efficiency (~9 %) in those adolescents with self-reported insomnia compared to controls, with greater variance in these metrics for adolescents in the insomnia group. Elsewhere, Carotenuto and colleagues (54) found poor PSG sleep macrostructure in 25 adolescents with ICSD-2 *psychophysiological insomnia* (as determined by a screening interview; 2 years of insomnia was required) at baseline before treatment was initiated. Specifically, these adolescents had on average a total sleep time of less than 6h, a sleep efficiency of less than 75%, and spent more than 30 min falling asleep and more than 80 min awake at night. Unfortunately, no control group was used, and adolescents had to report insomnia symptoms for at least 2 years for inclusion in the study, thus probably reflecting a severe insomnia population.

Few actigraphic studies including adolescent samples with and without insomnia exist and findings are mixed. No differences were found between Hong Kong Chinese adolescents with (N=57) compared to those without (N=148) DSM-IV insomnia (as determined by an interview with a psychiatrist) (55). In another actigraphic study of adolescents (12–19 years) meeting DSM-IV criteria for primary insomnia (N=116) as determined by a face-to-face interview, de Bruin and colleagues (56) found that adolescents with DSM-IV insomnia had an overall pattern of poor sleep with a sleep efficiency of less than 80%.

Subjective complaints of poor sleep do not necessary match objectively measured sleep in insomnia sufferers (13). In addition group differences in PSG sleep are not always visible in single studies, possibly due to a high night-to-night variability in sleep in insomnia sufferers, coupled with the use of a single (sometime the first night in the lab) or few PSG nights for group comparisons (50). Thus, from a diagnostic point of view, clinical utility of PSG is limited and currently, PSG is not required or recommended for the diagnosis of the disorder, and is not routinely used in clinical practice (57). Objective sleep data, however, are critical in the research setting to evaluate etiology of *insomnia disorder*, to determine whether there are sub-groups of insomnia sufferers with and without objective sleep disturbances and their implication for severity and treatment of the disorder (58). In particular, it is important to evaluate the potential combined effect of insomnia and objective sleep disruption on psychophysiological functioning. For example, growing evidence indicates that insomnia with short sleep duration affords increased risk for hypertension, type 2 diabetes, poor neuropsychological performance, and mortality (reviewed in (58). In addition, as pointed out in the meta-analysis of Baglioni et al. (50), specific insomnia PSG features of abnormality in SWS and REM sleep are implicated in alterations of cognitive and emotional processes, and are manifest in psychopathology. A first attempt to delineate different behavioral phenotypes of insomnia in adolescents based on sleep patterns (PSG sleep duration) (52), revealed that adolescents with insomnia symptoms and short sleep duration were characterized by more internalizing problems (e.g. depression) whereas those with normal (>7h) sleep duration had

more externalizing problems (e.g. rule breaking behaviors), suggesting the importance of assessing objective sleep in adolescence with insomnia.

6. Physiological alterations in adolescents with insomnia: evidence of hyperarousal

Growing evidence supports *"hyperarousal"* as the main etiological factor in the pathogenesis of *insomnia disorder* with abnormal elevated levels of cognitive (worry, rumination, intrusive thoughts) and physiological (elevated cortical activity, metabolism, inflammation, sympathetic nervous system activity, systolic blood pressure) activity preventing individuals from falling asleep and having a restorative night's sleep (47, 59).

Few studies have investigated evidence of hyperarousal in *insomnia disorder* in adolescence. Importantly, psychophysiological alterations associated with insomnia at this young age - in which critical bio-systems (e.g., CNS, autonomic nervous system [ANS]) necessary for adaptive homeostasis are still maturating - may set the stage for the development of mental and physical pathology later in life. Fernandez-Mendoza and colleagues (53) provided evidence, for the first time, of CNS hyperarousal (elevated beta activity [15–35 Hz]) during sleep onset and sleep in adolescents with insomnia symptoms (difficult falling and/or staying asleep), suggesting that functional cortical alteration may manifest in insomnia as early as adolescence. This cortical hyperarousal was more evident in those individuals with insomnia who also had objective short sleep duration (PSG sleep efficiency <85 %), and was particularly evident in the high beta range (25–35 Hz). Alterations in cortical functioning are implicated in altered information processing as reflected by increased worry, rumination, intrusive thoughts, particularly evident at bedtime and though to interfere with the process of falling asleep and maintaining sleep, as well as with the perception of sleep quantity and quality (60).

Studies of ANS hyperarousal in adolescents are lacking although our group previously showed that ANS hyperarousal is evident in young college students (19–28 years) with an inperson DSM-IV diagnosis of primary insomnia who were otherwise healthy and free from other psychiatric disorders. These subjects had a selective hyperactivation of the sympathetic nervous system (SNS), as indexed by a faster pre-ejection period (measured with impedance cardiography) across the falling asleep process (61) and throughout the night (62), compared with controls. Insomnia symptoms and objective short sleep duration have been linked to an adverse ANS profile (reduced heart rate variability and elevated heart rate, increased sympathovagal balance) even in children (9.2±1.7 years) (63). In addition, objective sleep disturbances have been related to an adverse ANS profile in both children (5–11 years) (64) and adolescents (16.7±2.3 years) (65). Importantly, hyperactivation of major stress systems including ANS alterations and dysfunctions in the hypothalamic-pituitary-adrenal (HPA) axis, together with the presence of objective sleep alterations (58), is recognized as the main pathophysiologic mechanism linking insomnia with poor health, particularly, increased risk for cardiovascular (CV) disease (66). The pathogenesis of CV disease follows a consistent progression beginning early in life and becoming clinically evident in middle-age with risk factors in youth predicting the development of clinical and sub-clinical CV disease in

adulthood (67). Recently Fernandez-Mendoza et al. (51) found that adolescents with insomnia symptoms and short sleep (<7 hours) had greater plasma C-reactive protein levels compared to adolescents with insomnia symptoms sleeping more than 7 hours and those without insomnia symptoms but sleeping less than 7 hours. These data suggest an association between insomnia and markers of inflammation although authors failed to found alterations in other major inflammatory indices including interleukin-6, tumor necrosis factor-alpha, leptin and adiponectin. Zhang et al. (55) specifically investigated the association between insomnia and saliva cortisol (the primary stress hormone produced by the adrenal gland), as well as the interaction between sex, pubertal development and insomnia in a sample of 205 adolescents with and without DSM-IV insomnia. Post- but not pre-pubertal adolescents with insomnia had larger cortisol awakening responses compared to adolescents without insomnia, supporting the link between stress and insomnia in adolescence. The long-term consequences of chronic alterations of any of these systems, and whether these alterations manifest as a trait vulnerability before insomnia develops, or appear as a consequence of insomnia and/or poor sleep, remains unknown.

7. Consequences of insomnia in adolescence

Insomnia in adolescents is associated with a worsening quality of life and increased risk of somatic, interpersonal, and psychiatric problems (4, 6), as described in the next section.

7.1. Mental health

7.1.1. Depression and Suicidality—About 20% of adolescents have a diagnosable mental disorder, with depression being the single most common type (68). Depression increases in adolescence and occurs at double the rate in girls than boys (31). There is a reciprocal relationship between insomnia and depression in adolescents as in adults (69–71), with a high rate of insomnia and sleep disturbances in depressed adolescents, and with insomnia being a strong predictor for subsequent development of depression in both boys and girls. Sivertsen et al. (70) found that the greatest risk group for the development of depression is adolescents with short sleep duration (<6 hours) in combination with insomnia (as defined by difficulties initiating and maintaining sleep occurring at least 3 times per week and for at least 6 months with sleep onset latency and/or wake after sleep onset of greater than 30 min, presence of tiredness or sleepiness at least 3 times per week). In their longitudinal study, Roane and Taylor (72) also reported insomnia (defined as *“almost every day”* or *“every day”* presence of trouble falling asleep or staying asleep over the past 12 months) as a predictor of later depression in adolescents. It has been argued that insomnia in early adolescence leads to the development of later depressive symptoms by altering corticolimbic circuitry (73) possibly via the disruptive effect of hyperarousal and insufficient sleep, thus impacting adolescents’ emotional regulation and cognitive functioning. Others have suggested that sleep disruption in adolescents (e.g., increased wakefulness in bed) may reinforce ruminative thinking styles, perpetuating further sleep disturbance, and that these processes could develop into depression over time (74). Depression is closely related with suicidal ideation, suicide attempts, and suicide in adolescents (75), and suicide is the second leading cause of death for the ages of 10 to 14 and 15 to 24 behind unintentional injury (76). Even after controlling for depression, however, sleep disturbances remain independent

predictors of suicidality (77). In a survey of 10,123 adolescents, Wong and colleagues (77) reported that insomnia symptoms were significantly related to suicidal ideation, plans, and attempts. Having three insomnia symptoms was associated with a 6.2-fold increased risk of suicidal ideation, 10.4-fold increased risk of making a suicide plan and a 10.5-fold risk if making a suicide attempt when compared to those with no insomnia symptoms. Multivariate analysis, controlling for covariates such as alcohol and substance use, and mood and anxiety disorders, revealed lower, but still significant relations between insomnia and suicidal thoughts and plans for the previous year. Longitudinal reports from the same group support cross-sectional findings, showing that trouble sleeping predicted endorsement of suicidal thoughts at follow-up (78). In fact, a one-unit increase in sleep problems across one year was associated with a 20 % increase in likelihood of suicidal ideation (78) and the relationship remained after controlling for suicidal thoughts, depression symptoms, substance use and demographic variables at time 1. Sleep problems at the first time point also predicted suicide attempts a year later (78).

One of the most compelling analyses was conducted by Goldstein et al. (79) who conducted psychological autopsies of 140 adolescent suicide victims by using structured clinical interviews of friends and family. These data were then compared to 131 community dwelling control adolescents. They found that the rate of sleep disturbance (insomnia and hypersomnia) was higher for the suicide victims than the controls within the depressive episode leading to their death and in the final week before it. In most cases this was reflected in difficulties getting to sleep. Higher insomnia rates were still seen in the suicide group after controlling for the presence of affective disorders and the severity of the terminal depression.

Clearly not all adolescents with sleep difficulties, or even clinically diagnosed insomnia, will have suicidal thoughts, make suicide plans or attempt suicide. However, the data are very clear that presence of insomnia substantially elevates the risk of these phenomena occurring. Parents and medical professionals need to be aware of the need to intervene early when insomnia develops as a way of helping to prevent an all too common tragic outcome. Recently, it has been suggested that suicide prevention program should include discussion and evaluation of sleep-related issues including management of insomnia (77).

7.1.2. Anorexia Nervosa—There is growing recognition that there may be a link between adolescent insomnia symptoms and Anorexia Nervosa (80). The general trend for insomnia symptoms to be more related to Anorexia Nervosa than other eating disorders such as Bulimia Nervosa, has led to the hypothesis that the malnutrition associated with Anorexia leads to up regulation of the orexin/hypocretin system that is involved in both feeding and sleep regulation (81). In this case it is possible that insomnia symptomatology is a result of the anorexia rather than a cause, but nonetheless, awareness of the link might help trigger treatment earlier for this notoriously challenging condition.

7.1.3. Substance use—Adolescent substance use is an important public health issue, with 39 % and 25 % of 12th graders reporting use of alcohol and/or illicit drugs, respectively, in the past 30 days (82). Research, including large population-based studies, consistently shows an association between *insomnia disorder*, insomnia symptoms or sleep problems and

alcohol, cannabis, tobacco, and other substance use in adolescents (72, 83), and this association remains, albeit attenuated, after controlling for other mental health problems such as depression (83). In a national sample of adolescents in the USA, Wong et al (84) showed that sleep difficulties (short sleep, trouble sleeping) measured in the first wave predicted substance use problems (e.g., binge drinking, driving while drunk, using illicit substances) measured a year later, after controlling for substance use problems at first wave. Recently, Mike et al (85) characterized the longitudinal relationship between early adolescent sleep and subsequent substance use in boys: they reported that lower sleep quality and shorter sleep duration at age 11 were associated with earlier alcohol use, intoxication, and repeated use, and that lower sleep quality at age 11 was associated with earlier cannabis intoxication and repeated use, after controlling for several covariates. In the longitudinal National Consortium on Adolescent Neurodevelopment and Alcohol study, Hasler et al. (86) also showed that poor sleep quality at time 1 predicted cannabis use one year later in a large cohort of adolescents (although eveningness at time 1 showed more substantial relationships with substance use at follow-up). A number of mechanisms linking insomnia symptoms and substance use have been proposed, including an imbalance between affective and control systems due to disrupted sleep, leading to increased risk-taking behaviors, as described in the next section. The strong link between insomnia symptoms and substance use has potential clinical implications: adolescents may use substances as self-medication for insomnia, further exacerbating the sleep problems, and potentially also increasing risk for the development of other disorders related to both sleep and substance use (83). Treating insomnia symptoms early may reduce the likelihood of this vicious circle from developing.

7.2. Cognitive processing and risk-taking behavior

Over and above its negative association with mental health, *insomnia disorder* can also lead to negative developmental outcomes including cognitive and academic functioning, critical during this period of intense learning. Currently, the literature investigating the impact of clinical insomnia on cognitive ability during adolescence, is lacking. However, a number of studies have reported the negative association between insomnia-type characteristics and cognitive performance in this age group.

In early adolescence (11–13 years), actigraphically-defined poor sleep was related to poorer executive functioning (87). In girls, higher amount of wake after sleep onset and sleep fragmentation were marginally significantly related to poorer performance on the Wisconsin card sorting task, whereas in boys lower sleep efficiency, shorter sleep duration, greater sleep fragmentation and greater amount of wake within the sleep period were associated with faster, but more error prone performance on a continuous performance test (suggesting a more careless response style). For both boys and girls, no associations were identified with measures of sleep quality and memory or general intelligence, suggesting that insomnia symptoms are associated with more complex cognitive abilities (87). By directly assessing insomnia symptomatology based on ISI scores in undergraduate students, Schmidt at al. (88) divided participants into three groups: no insomnia, sub-threshold insomnia and clinical insomnia based on their ISI scores, as determined by the norms provided by Bastien et al. (29). Delayed recall memory performance differed significantly between the groups and performance was negatively associated with ISI scores, so that greater ISI was associated

with poorer memory performance. The authors suggested that potentially differing strategies/abilities were responsible for worse memory in those with greater ISI scores. However, although the average age of the participants in this study was 22, the age range was 18–46, meaning that these results require further validation in an entirely adolescent population.

Perhaps the most consistent finding, to date, is the link between adolescent insomnia symptoms and increased risk taking. A number of authors have utilized large data sets of national surveys from high school students and have identified an association between sleep-wake behavior problems (e.g., found it particularly difficult to fall asleep, arrived late to class because of oversleeping) and greater risk taking, (e.g., drug use, drink-driving) (89). In a study by Catrett and Gaultney (90) 16 % of an adolescent sample were classified as having 'possible insomnia', based on their response to two items on the Add Health survey, (http://www.cpc.unc.edu/projects/addhealth) which asked about trouble sleeping and morning tiredness in the past year. At year 1, depressive symptoms and possible insomnia were associated with a number of risky behaviors. Although risky behavior at year 2 was best predicted by risky behavior at year 1, those with possible insomnia were twice as likely as those without possible insomnia to drink and drive at year 2, even after controlling for depressive symptoms. In another study, Thomas et al. (91), risk taking behavior in late adolescence was not found to be directly associated with sleep problems, but instead, sleep problems were associated with poorer working memory performance which in turn, predicted risk taking. This study suggests that the association between insomnia *symptomatology* and risk taking during adolescence may be explained by the impact of insomnia on other cognitive abilities, such as working memory and executive function, which results in a greater likelihood of engaging in risky behavior.

Recently, researchers have investigated how the association between insomnia and cognitive performance may be explained by disrupted brain functioning and provide some evidence for the mechanism by which insomnia may result in increased risk taking. Telzer et al. (92) investigated cognitive control and risk taking in 14–16 years old adolescents using functional magnetic resonance imaging (fMRI) tasks. Authors found that higher scores on the Pittsburgh sleep quality index (PSQI) (indicating poorer sleep quality) were associated with more risk taking, as assessed by both self-report and the risk-taking task, and poorer selfreported decision making. Furthermore, poor sleep quality was associated with heightened insula response during reward processing, which was fully mediated by reduced dorsolateral prefrontal cortex (dLPFC) response during a cognitive control task. Authors report that the association between poor sleep and greater risk taking may be driven by an imbalance between affective and control systems, likely caused by disrupted sleep. Therefore, adolescents with poor sleep may exhibit increased arousal to reward and impaired cognitive control which results in a greater orientation towards risk and poorer decision making abilities.

In a longitudinal study of insomnia symptoms (obtained from The Schedule for Affective Disorders and Schizophrenia in School-Age Children [K-SADS]) (93) in adolescent girls for 5 consecutive years, starting at 9 years old, and an fMRI task, which assessed neural response during anticipation of reward when they were 16 years, symptoms of non-

restorative sleep were associated with a greater reward-related dorsal medial prefrontal cortex response, which in turn, was associated with higher depression scores (94). The significant association between greater non-restorative sleep in early adolescence and later adolescence depression scores, was entirely moderated by the increased dmPFC response to reward. The authors suggest that insomnia symptoms in early adolescence may disrupt neural reward processing which may be associated with later adolescent depression.

However, in all of these studies, it cannot be ruled out that increased risk taking, poorer decision making abilities and disrupted neural processing did not precede insomnia symptoms. Adolescents may be predisposed to *insomnia disorder* if they have a neural imbalance between reward and cognitive control resulting in greater risk-taking and poorer decision making, which inevitably results in inadequate sleep. Similarly, adolescents who engage in risky or delinquent behaviors may exhibit symptoms of insomnia due to their chosen activities (e.g., staying up late, using substances or alcohol) as opposed to insomnia preceding and causing such behaviors. Longitudinal research is required to establish the direction of this potential association between insomnia, impaired reward processing, cognitive control and decision making and greater risk taking behavior.

A number of studies have reported an association between poor sleep, daytime sleepiness and worse academic performance. In healthy adolescents, the outcome of three separate metaanalytic reviews (95) revealed that sleep quality and duration, and daytime sleepiness, were all moderately associated with academic performance. Daytime sleepiness had the largest association, followed by sleep quality and then sleep duration. These general measures of sleep (quality, duration and daytime sleepiness) may be affected in those with *insomnia disorder* and thus it is plausible that adolescents with insomnia would exhibit poorer academic performance compared to their counterparts. However, to date, no study investigated the impact of sleep and sleepiness on academic performance in adolescents with a clinical diagnosis of insomnia. Furthermore, it remains to be seen exactly how the increased use of substances, such as caffeine, which are also associated with altered cognitive function, may mediate the relationship between insomnia and poor academic and/or cognitive functioning in adolescents.

8. Treating insomnia in adolescence

There are two main approaches for the treatment of *insomnia disorder* in adolescence, which are used in isolation or combination; cognitive behavioral interventions and pharmacotherapy (96), although alternative methods have also been reported to improve insomnia symptoms (54). To date, the research into the effectiveness of treatments in this population is largely lacking.

8.1. Pharmacological interventions

There is currently a lack of controlled studies into the effectiveness and long-term effects of pharmacological interventions for adolescent *insomnia disorder* (97, 98). In the absence of empirical evidence, several medications have been traditionally used in pediatric and adolescent insomnia, such as benzodiazepines, α-receptor agonists (e.g., clonidine and guanfacine), pyrimidine derivatives (e.g., zaleplon and zolpidem), sedating antidepressants

(e.g. trazodone and mirtazapine), melatonin, and sedating antihistamines (e.g., diphenhydramine and hydroxyzine) (99), descriptions and reviews of which are presented in Owens and Moturi (97). The American Academy of Sleep Medicine has published consensus statements for the use of these substances and recommends strongly that additional research is required to ascertain appropriate use, dosing, safety, tolerance, and efficacy in children and adolescents (98, 100). Of particular concern is that a number of these treatments are available as over the counter medications and not currently regulated by the US Food and Drug Administration. However, despite these uncertainties, both prescribed and non-prescribed medications are commonly recommended by physicians to adolescents with insomnia symptoms (101).

Melatonin is one of the substances that is currently unregulated and easily accessible over-the counter and online, in varying forms and strengths, and is a commonly used method for treating adolescent insomnia. Endogenous melatonin is a hormone, primarily synthesized by the pituitary gland and released by the hypothalamus and is commonly considered to be one of the main mechanisms by which the sleep-wake cycle is maintained in humans. Several studies have identified that administration of melatonin may improve sleep quality in children with co-morbid disorders (98, 102) and improve sleep problems associated with delayed sleep-phase disorder in adolescence (103, 104). Ivanenko et al. (105) identified that, following melatonin treatment, 90.6 % of a sample of 32 children and adolescents (2–18 years) all seeking treatment for insomnia, showed a significant improvement in insomnia symptoms, as derived from parent-reported sleep diaries. A meta-analysis of 19 randomized-placebo controlled trials for a variety of sleep disorders conducted by Ferracioli-Oda et al. (106), which included both children and adults identified that melatonin significantly reduced sleep onset latency and that larger doses demonstrated greater effects on sleep time and latency. Melatonin, compared to placebo, was reported to significantly improve sleep quality. However, few studies have systematically investigated the effectiveness of melatonin in adolescent-only samples. A placebo-controlled, randomized, double-blind study by van Geijlswijk et al. (107) reported that for a group of children and adolescents aged 6–12 years diagnosed with chronic sleep onset insomnia, melatonin significantly advanced sleep onset and dim-light melatonin onset by approximately 1 h and decreased sleep-onset latency by 35 min, when given at least 1 hour prior to bedtime. A follow-up study reported that there were no long-term consequences to melatonin use, that is; that social and pubertal development in melatonin users was not different compared to controls. However, the long-term effectiveness was inconsistent across participants. Future work is required to establish the efficacy and potential side-effects of using melatonin (and other pharmacological interventions) in adolescent insomnia, compared to behavioral methods (see below), using randomized, controlled trials. Furthermore, future regulation will also be required to ensure appropriate, effective use of such methods.

8.2. Cognitive behavioral therapies

Cognitive behavioral therapies (CBT), designed to alter thoughts, beliefs and attitudes about sleep to exact change on an observable behavior, are the most commonly evaluated approach for the treatment of adolescent insomnia and are largely reported to be successful. As well as challenging negative cognitions or catastrophizing thoughts (108), CBT for insomnia (CBT-

I) includes a variety of methods, including: stimulus control (adopt regular schedules, consolidate sleep to night-time, and improve bed-sleep association), arousal reduction (quieting pre-bedtime activities and relaxation-imagery), cognitive therapy, improving sleep hygiene practices (increase behaviors and environmental conditions that promote improved sleep quality) and sleep restriction (temporarily limit hours in bed to increase sleep efficiency). A number of studies have provided evidence that CBT-I can improve sleep quality in children and adolescents with insomnia symptoms (109). However, when treating adolescent insomnia, some CBT-I methods may be more appropriate than others. For example, sleep restriction is not a method typically reported in the literature as being used within this age group, presumably because adolescents already experience restricted sleep schedules (e.g., due to later bedtimes and early school start times) and thus the process of restricting sleep schedules further may exacerbate the consequences of *insomnia disorder* in adolescence. However, a recent study suggested that some sleep restriction, the amount of which was determined weekly during personalized bedtime advice, may be beneficial for adolescents with insomnia disorder (110). However, at follow-up restriction of time in bed was not maintained. One issue with current studies investigating the effectiveness of CBT-I in adolescents is that studies employ a variety of methods (listed above) however, they typically do not evaluate the efficacy of the individual components. Future work could establish specifically which combinations of CBT-I methods are most effective for treating *insomnia disorder* in adolescence.

Given the high prevalence of co-morbid disorders in adolescence, and the effectiveness of insomnia treatments for concurrently improving depression symptoms (111) and suicide ideation (112) in adults, there may be a similar outcome in adolescents. In a group of participants aged 12–20 years, meeting research diagnostic criteria of insomnia and a DSM-IV diagnosis of depression, treatment with CBT-I resulted in a significant improvement in actigraphy determined total sleep time, ISI scores and depression outcomes, although not all improvements were fully maintained at 26-week follow-up (113). Similarly, a randomized controlled trial utilized the SENSE intervention (114), which combines CBT and mindfulness to improve sleep, found that adolescents ‘at-risk’ for major depressive disorder had significantly improved self-reported and objective measures of sleep quality as well as a small improvement in anxiety, but not depression, following treatment, compared to an active control-group (115).

Efforts have been made to adapt behavioral treatments of *Insomnia disorder* in special pediatric populations, such as those with autism spectrum disorders, Tourette syndrome, cerebral palsy and epilepsy, as well as in childhood cancer patients (reviewed in (109)). For example, CBT-I (consisting of an abbreviated CBT-I intervention delivered both in person and via videoconference) was successfully used in adolescents and young adult cancer survivors (15–40 years) with DSM-5 *insomnia disorder*, who showed improvements in insomnia symptomatology immediately after the CBT-I treatment and at 2 months follow-up (116). While sample size was small (10 participants across a wide age range), this study shows the feasibility and potential benefit of adapted CBT-I in vulnerable populations.

Recently, researchers have provided evidence for the successfulness of a novel form of CBT-I in adolescents who met either the DSM-IV or DSM-5 diagnostic criteria for insomnia, as

determined by a diagnostic interview, administered via the internet. A randomized controlled trial conducted by de Bruin et al. (56) identified that compared to a waiting-list control group, both CBT-I and internet therapy resulted in significantly improved sleep efficiency, sleep onset latency, wake after sleep onset, and total sleep time at post-treatment, as assessed by both objective actigraphic and subjective measures, with little difference in outcome between the two treatment methods. Insomnia complaints and symptoms of chronic sleep reduction also decreased significantly in both treatment conditions compared to the waiting-list control. Furthermore, these improvements were maintained at follow-up. In another randomized trial de Bruin et al.(117) identified that insomnia symptoms and the cognitive functioning of some cognitive domains but not others, were significantly improved post-treatment for an internet based therapy. Furthermore, de Bruin et al. (118) reported that group and internet therapy were equally effective treatments for adolescent insomnia, but with greater cost-effectiveness, over 12 months, for internet based therapy.

Despite the apparent successfulness of behavioral interventions for adolescent insomnia, one common problem is compliance with the protocol (119). This may be particularly true for internet-based treatment, in which there is, typically, no face-to-face contact with a sleep therapist to provide feedback and motivation. Preliminary research suggests that reducing alcohol intake, enhancing treatment-related self-efficacy, and monitoring and providing feedback on sleep, early in treatment, may affect adherence to insomnia treatments in older adolescents and young adults (17–25 years) (120) However, further research is required to fully determine the type of feedback that is useful for adolescents engaging in internet-based CBT-I. In one study (110), out of four distinct factors of therapeutic feedback, only sleep expertise (i.e. explanation of sleep efficiency and bedtime advice) contributed to improvements in sleep efficiency at post-treatment and reduction in insomnia symptoms at two-month follow-up. Furthermore, qualitative evidence suggests that for depressed adolescents, in-person therapy may be a preferred method for insomnia treatments and that the necessity of completing sleep logs may be a barrier for treatment adherence (121).

Finally, one area of research that is currently lacking is the feasibility of preventative methods to target insomnia early before chronicity develops. Plausible barriers to seeking treatment for insomnia in adolescence include: the stigma attached to seeking help, the lack of awareness of the disorder and the common misconception that insomnia symptoms are a normal part of adolescent development. School-based preventative methods may provide a mechanism by which to improve adolescent’s knowledge of sleep, including insomnia awareness and the potential outcomes of poor sleep, promote good sleep hygiene and decrease stigma attached to seeking treatment. A school-based intervention that utilized mindfulness mediation and training on sleep hygiene, resulted in significant improvements in objective (from actigraphy) sleep measures and reduced PSQI scores (122). Furthermore, preventative, educational methods may also be an effective mechanism by which to abate the widespread anxiety amongst parents, media and adolescents themselves, regarding the consequences of insufficient sleep in this age-group. This is particularly important as unhelpful beliefs about sleep (e.g., “when I sleep poorly on one night I know it will disrupt my sleep for the rest of the week”) have been shown to be associated with more sleep complaints (123), which suggests that harboring anxiety and unhelpful beliefs about sleep may serve to perpetuate insomnia in at-risk adolescents. Any preventative methods should,

therefore, strike a balance between educating adolescents (and parents) on the importance of adequate sleep whilst also normalizing some degree of sleep restriction within this age group. Future, longitudinal, research should investigate the feasibility of such preventative methods and the impact of targeting such interventions during the pubertal transition period. Preventative and/or coping strategies may be the most beneficial during this time, which is a period of great developmental and social change and uncertainty.

9. Conclusion

Insomnia disorder in adolescence is common and is associated with poorer quality of life, increased risk for psychopathology, and compromised functioning. The diagnosis of insomnia in adolescence is complex and needs to be evaluated in the context of social, behavioral and bioregulation changes normally occurring in adolescence. Evidence of cortical hyperactivation supports the existence of hyperarousal as a pathophysiological mechanism underlying the disorder, as early as adolescence but further studies are needed to investigate potential dysregulation of the ANS and HPA and associated detrimental long-term cardiovascular consequences of insomnia in early life. A better understanding of the physiological perturbations of *insomnia disorder* in adolescence and factors that could contribute to the vulnerability for insomnia, such as female sex, could improve awareness and inform specific treatment early in life before a clustering of risk factors and comorbidities occurs. Sleep disruptive behaviors that are becoming increasingly common, such as consumption of beverages containing high levels of caffeine or caffeinated drinks mixed with alcohol, and the 24/7 access to digital information, may interact with biological factors in adolescents vulnerable to the development of *insomnia disorder*. Increasing awareness about insomnia as a disorder distinct from typical changes in sleep across adolescence, and other sleep disorders such as DSPD, is needed so that treatment can be implemented early to minimize negative consequences and possibly also limit the chronicity of the disorder. Developing flexible solutions, which can be delivered in a variety of different ways e.g. in-person, online, group therapy, school settings, may allow for more specific tailoring of treatments to the individual, facilitating compliance with treatment protocols and ultimately improving the effectiveness of the treatment.

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Abbreviations

ANS	Autonomic nervous system
CBT	Cognitive behavioral therapy
CNS	Central nervous system
CV	Cardiovascular
CVD	Cardiovascular disease

DSM	Diagnostic and statistical manual of mental disorders
DSPD	Delayed sleep phase disorder
EEG	Electroencephalography
HPA	Hypothalamic–pituitary–adrenal
ICSD	International classification of sleep disorders
NREM	Non rapid-eye-movement
PSG	Polysomnography
REM	Rapid-eye-movement
SNS	Sympathetic nervous system
SWS	Slow wave sleep

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Practice Points

- *Insomnia disorder* is common in adolescence, particularly in late adolescence and in girls. Importantly, sex differences are manifest not only in the prevalence of the disorder but also characterize insomnia comorbidities, precipitating factors of the disorder, cognitive and physical consequences of insomnia.
- The increasing trends for unhealthy sleep-related behaviors (e.g. electronic media use at bed- and night-time, high-caffeine consumption) and other factors such as school pressure affect sleep in adolescents and may precipitate or perpetuate insomnia.
- Insomnia is associated with mental health disorders, including depression and substance use, and may be a precursor to the development of these disorders in adolescents. Importantly, insomnia is a risk factor for suicidal ideation, plans, and attempts even after controlling for mood disorders.
- Complex cognitive abilities, particularly those involving executive function necessary to regulate risk-taking behaviors, seem to be compromised in adolescents with insomnia. However, the impact of *insomnia disorder* on adolescents' school performance is still unclear.
- Cognitive behavioral therapy is an effective intervention for *insomnia disorder* in adolescents although further research is needed to determine optimal protocols and methods of delivery to ensure sustained adherence in this population.

Research Agenda

- Future studies need to clearly operationalize insomnia as a disorder determined from a structured clinical interview (suitable to capture the complexity of the disorder in adolescence), according to the major classification systems (DSM or ICSD). Type, frequency and severity of nocturnal and diurnal insomnia symptoms, timing of the assessment (e.g., examining insomnia symptomatology during both weekdays and weekend, school-time and vacation-time), duration of insomnia, and presence of comorbid psychiatric conditions should be clearly examined and reported.
- Research is needed to determine how cultural and social factors, including school pressure, economic factors, and change in health policy (e.g., delay in school start-times), could shape the development of insomnia in different adolescent populations around the world.
- Prospective longitudinal studies are needed to investigate the causal role of hyperarousal in the pathophysiology of insomnia in adolescents. Adolescence offers a critical time-frame in which incidence of insomnia increases, particularly after puberty in girls, allowing determination if hyperarousal manifests as a trait-like vulnerability to insomnia or if it develops as a consequence of the disorder.
- Despite some studies indicated alterations in several bio-systems, there is insufficient evidence to reach a conclusion about the impact of insomnia on an adolescent's physical health. Prospective and experimental studies are needed to investigate mental and physical consequences (e.g. development of psychopathology and cardiometabolic diseases) of *insomnia disorder* developed in adolescence.
- Actigraphic sleep assessments should be implemented in research and clinical setting to characterize and evaluate different insomnia phenotypes based on objective sleep features of *insomnia disorder* in adolescence. This would be highly relevant to potentially guide treatment decisions.
- More randomized controlled trials of CBT-I are needed to evaluate their efficacy in improving insomnia symptoms as well as other comorbid symptoms of mental disorders. Preventative interventions should also be explored as a potential means to prevent later dysfunction.