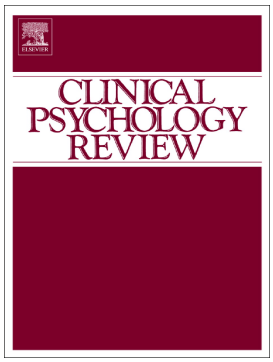

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Mechanisms Underlying the Association between Insomnia, Anxiety, and Depression in Adolescence: Implications for Behavioral Sleep Interventions

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Nicholas Allen is the Ann Swindells Professor of Clinical Psychology at the University of Oregon, and the Director of the Center for Digital Mental Health. His work focuses on adolescent mental health, particularly risk factors for adolescent emergent mental disorders such as depression and substance misuse. The ultimate aim of this work is to inform innovative approaches to early intervention and prevention that utilize novel, developmentally-informed interventions to target modifiable early risk factors for mental and substance use disorders, such as sleep, parenting, and teen sexual and romantic relationships.

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Introduction

There is growing recognition that many adolescents obtain insufficient and/or poor quality sleep, which is increasingly being regarded as an epidemic of sleep deprivation amongst adolescents and an important public health problem (American Medical Association, 2010; Office of Disease Prevention and Health Promotion, 2011). Adolescents are thought to optimally require approximately nine hours of sleep per night (Fuligni, Arruda, Krull, & Gonzales, 2017). However, a meta-analysis found that 53% obtain less than 8 hours of sleep on school nights, and 36% report difficulty falling asleep (Gradisar, Gardner, & Dohnt, 2011).

Insomnia is the most prevalent sleep disorder among adolescents (Johnson, Roth, Schultz, & Breslau, 2006). It is defined as chronic dissatisfaction with sleep quantity and/or quality (American Psychiatric Association, 2013). Insomnia is associated with difficulty initiating and/or maintaining sleep, early morning awakening, and unrefreshing sleep (Johnson et al., 2006). Approximately 8-11% of young people meet diagnostic criteria for insomnia at any one time (Dohnt, Gradisar, & Short, 2012), which tends to persist over time (Roberts, Roberts, & Duong, 2009).

A number of factors may combine to increase vulnerability to insomnia in adolescence. First, adolescence is associated with a progressive reduction in the accumulation of homeostatic sleep pressure during wakefulness, which leads to a reduction in sleep drive (Feinberg, Higgins, Khaw, & Campbell, 2006). The homeostatic sleep-wake system controls the need to sleep; with pressure increasing the longer an individual stays awake and decreasing as sleep occurs. Accumulated sleep drive before going to bed helps to control the quantity and quality of sleep. Second, adolescence is associated with a delay in the timing of sleep, which is related to a lengthening of the intrinsic period of the endogenous circadian oscillator (Carskadon, Acebo, & Jenni, 2004). The endogenous circadian oscillator is an internal clock system that regulates the daily, 24-hour rhythmic cycle, in concert with environmental time cues (e.g., the dark–light cycle). The secretion of melatonin is consistently associated with the human circadian system (Cajochen, Kräuchi, & Wirz‐Justice, 2003; Klerman, Gershengorn, Duffy, & Kronauer, 2002), and melatonin is released later in the evening amongst adolescents than children, which delays the onset of evening sleepiness (Carskadon, Vieira, & Acebo, 1993). In other words, sleep/wake rhythms are delayed in

adolescents compared to children, meaning their natural inclination is to go to bed later and sleep later. Combined with individual chronotypes (e.g., preference for morningness or eveningness), the circadian system helps regulate optimum sleep schedules and sleep window; the timing of sleep is therefore delayed even further in adolescents with evening chronotypes and circadian rhythm disruptions (e.g., delayed sleep phase disorder; Gau et al., 2007; Gradisar & Crowley, 2013). Third, adolescents develop responsibilities and social interests (e.g., homework, employment, friendships) that encourage remaining awake later into the evening (Adam, Snell, & Pendry, 2007; Maume, 2013). Fourth, parental control over bedtime is lessened during adolescence (Short et al., 2011). Fifth, electronic devices have a deleterious impact on sleep in adolescence, including delaying sleep onset and reducing sleep duration (Bartel, Gradisar, & Williamson, 2015; Hale & Guan, 2015). Sixth, caffeine intake increases in adolesence, contributing to sleep initiation and maintenance problems (Orbeta, Overpeck, Ramcharran, Kogan, & R, 2006; Owens, Mindell, & Baylor, 2014). Finally, adolescents are subject to the same physiological susceptibilities and psychological and social vulnerabilities that cause insomnia in adults (Keller & El-Sheikh, 2011), such as predisposition to cognitive-emotional hyperarousal (Fernandez-Mendoza et al., 2014). These physiological maturational processes and psychological/social factors may interact in adolescence so that reduced sleep propensity in the late evening becomes permissive of continued waking activities and delayed bedtimes (Carskadon, 2011; Jenni & LeBourgeois, 2006). This can have two potential sleep related consequences: (1) prolonged sleep onset latency (SOL) and poor sleep efficiency (SE), because sleep tends to occurs at an inappropriate circadian phase; and (2) sleep restriction, because school starts early in the morning (Carskadon et al., 2004).

Adolescent insomnia severely impacts future health and functioning (Roberts et al., 2009), and is thought to precipitate and maintain many emotional and behavioral problems, particularly anxiety and depression (Dahl & Harvey, 2007). Sleep, arousal, and affect represent overlapping regulatory systems, with dysregulation in one system impacting on the others, so sleep disruption during key periods of maturational development may provide a pathway toward later affective dysregulation, and vice versa (Dahl, 1996). Adolescence is therefore a critical developmental window for understanding the mechanisms underlying the association between insomnia and internalizing symptoms to inform early intervention and prevention.

Despite the strong relationship between insomnia, anxiety, and depression in adolescence, the mechanisms underlying these associations are not well established. Research using different methodologies (cross-sectional, longitudinal, twin studies, experimental, intervention) point to the role of biological, psychological, and social mechanisms, and suggest the presence of sequential, parallel, and interacting underlying risk factors. The aim of this review is to advance our understanding of these processes by providing a description and synthesis of these mechanisms, and to explore implications for the design of adolescent behavioral sleep interventions. Specifically, we examine whether insomnia symptoms are a mechanism for the development of internalizing disorders in adolescence and whether sleep interventions are an effective treatment for both insomnia and internalizing disorders in adolescence because they target the common mechanisms underlying these disorders. While researchers have proposed a reciprocal relationship between insomnia and internalizing symptoms in adolescence (Dahl, 1996), recent reviews have suggested that wakefulness in bed (e.g., prolonged SOL and poor SE) precede the development of anxiety and depression in adolescence more than the reverse (Lovato & Gradisar, 2014; McMakin & Alfano, 2015). Thus, the likelihood that insomnia plays a critical etiological role in adolescent internalizing symptoms suggests that the treatment of insomnia might improve resilience against the development of internalizing symptoms. We will sometimes focus on internalizing symptoms as a whole because while anxiety and depression symptoms have specific components, they share considerable overlap. For example, the tripartite model of depression and anxiety suggests that while depression is specifically characterized by anhedonia (or low positive affect) and anxiety is specifically characterized by physiological hyperarousal, general negative affect (or emotional distress that includes moods such as fear, sadness, anger, and guilt) is a nonspecific factor that relates to both depression and anxiety (Clark & Watson, 1991). Indeed, the tripartite model of depression and anxiety has been shown to be a good fit to data generated by child and adolescent inpatient psychiatric samples (Joiner, Catanzaro, & Laurent, 1996). Furthermore, adolescent generalized anxiety disorder and major depressive disorder (MDD) share five common symptoms (irritability, diminished concentration, fatigue, sleep disturbance, and restlessness/agitation) according to the Diagnostic and Statistical Manual of Mental Disorders – Fifth Edition (DSM-5; American Psychiatric Association, 2013). Additionally, recent network analyses have revealed that while individual symptoms of depression

and anxiety are more related to other symptoms within each disorder than to symptoms between disorders, symptoms of depression and anxiety share strong connections (Beard et al., 2016; Cramer, Waldorp, van der Maas, & Borsboom, 2010). Finally, we adopt a 'biopsychosocial' model because it is a systems-based approach that attributes disease outcomes to the intricate and variable interactions between biological, psychological, and sociological factors (Engel, 1977).

Potential biological mechanisms

Genetic vulnerability and neurotransmitter polymorphisms

A study conducted among 1412 twin pairs (8–16 y) found a strong overlap between genetic influences on symptoms of insomnia, depression, and anxiety disorders (Gehrman et al., 2011). Specifically, while there was support for insomnia-specific unique environmental effects over and above overlapping effects with depression and overanxious disorder, there was no evidence for insomnia-specific genetic effects. These findings suggest that genetic factors related to the etiology of insomnia overlap with those related to depression and anxiety but that there are distinct insomnia-specific environmental effects. Given the association between serotonin (5-HT), sleep, anxiety, and depression (Jouvet, 1969; Lesch et al., 1996; Mann et al., 2000), it is likely that genes involved in the 5-HT pathways play a role in the insomnia-anxiety-depression relationship in adolescence. 5-HT is a monoamine neurotransmitter that is important for attention, cognition, information processing, and mood (Richtand & McNamara, 2008). A range of evidence suggests that the sleep/circadian systems are intimately related to serotonergic function, and vice versa (Harvey, Murray, Chandler, & Soehner, 2011). For example, evidence suggests that 5-HT enhances the overall stability of circadian rhythmicity in adults (Hannibal & Fahrenkrug, 2006), while circadian function also modulates the 5-HT system in animals (Mistlberger, Antle, Glass, & Miller, 2000). Additionally, it has been hypothesized that 5-HT mediates the phase-shifting effects of behavioral stimuli on circadian rhythms, and that 5-HT projections from the medial raphe nuclei to the suprachiasmatic nuclei are an anatomical interface between circadian function and internalizing disorders (Reghunandanan & Reghunandanan, 2006; Sprouse, 2004). Human 5-HT transporter (5-HTT) gene transcription is modulated by a common polymorphism in its upstream region, and the short variant of the polymorphism has been shown to reduce the transcriptional efficiency of the 5-HTT gene promoter, resulting in decreased 5-HTT expression and 5-

HT uptake in lymphoblast's (Lesch et al., 1996). In combination with environmental adversity, the short allele has been shown to increase vulnerability to anxiety (Lesch et al., 1996; Petersen et al., 2012), depression (Sharpley, Palanisamy, Glyde, Dillingham, & Agnewa, 2014) and insomnia (Deuschle et al., 2010), in both adolescents and adults.

Disturbed dopamine (DA) functioning is also implicated in the insomnia-anxiety-depression relationship. DA is a monoamine neurotransmitter that is important for motivation, reward processing, and the ability to experience pleasure (Bressan & Crippa, 2005). It is also critical to the neurobiology of sleep, particularly neurons in the ventral tegmental area and substantia nigra pars (Monti & Monti, 2007). Disturbed DA has been associated with anxiety (Kienast et al., 2008), depression (Malhi & Berk, 2007), and sleep problems (Volkow et al., 2012) in adults. Specifically, sleep deprivation reduces dopamine D2/D3 receptor availability in the striatum (Volkow et al., 2012), which may increase susceptibility to internalizing disorders, in concert with individual differences in the dopamine storage capacity of the amygdala (Kienast et al., 2008). While these relationships have not been evaluated in adolescents, several authors have hypothesized that dysregulation in the mesolimbic DA system may be related to the faulty reward processing seen in depressed adolescents with anhedonia (Auerbach, Admon, & Pizzagalli, 2014; Harvey et al., 2011). This is particularly important because research suggests that adolescence is associated with an experience-expectant increase in dopamine that is genetically determined to prepare young people for experiences that characterize pre-adulthood, and to ensure that adolescents will want to seek out opportunities for autonomy, personal freedom, and biologically salient rewards (Luciana, 2013; Spear, 2000). This pattern of timing is important for our understanding of how disruptions in these processes might result in later dysregulation. Sleep deprivation in adolescence may decrease the availability of dopamine in limbic and striatal areas and lead to underactive reward seeking behaviors, thereby increasing vulnerability to internalizing symptoms.

Of note, interactions between 5-HT and DA can be traced to circadian function, particularly the endogenous circadian pacemaker (Harvey et al., 2011). There have been numerous reports of genetic associations between polymorphisms in clock genes and psychiatric disorders, including MDD and anxiety disorders, in both adolescents and adults (Dueck et al., 2017; Partonen, 2012). Clock genes are thought to

play an essential role in modulating the communication between different cerebral regions and circuits, and in complex processes such as learning and development. Vanderlind and colleagues (2014) found that a polymorphism in the circadian clock gene (rs11932595) was associated with self-reported sleep difficulty in a sample of young people (18–23 y). The authors speculated that this process might affect cognitive control and flexibility, and subsequently contribute to an increase in depressive symptoms. A more recent study by Liberman and colleagues (2017) found that two mutations in the circadian clock gene PERIOD3 (PER3), a variable number tandem repeat allele and a single-nucleotide polymorphism, were associated with diurnal preference and higher trait-anxiety scores in young people (18–38 y), supporting a role for PER3 in circadian and affective modulation. Similarly, Zhang and colleagues (2016) identified two rare variants in PER3 (P415A/H417R) in adults with familial advanced sleep phase and depression. The authors showed that these variants recapitulate circadian and mood phenotypes in mouse models, and uncovered a sleep trait similar to that seen in humans in flies carrying the human variants. Molecular studies also revealed that the variants led to less stable PER3 protein and reduced the stabilizing effect of PER3 on PER1/PER2. Collectively, these findings suggest that circadian clock genes may be a nexus for sleep and mood regulation. Future exploration of the developmental pattern of these effects, especially in early–mid adolescence when the sleep system is changing (Colrain & Baker, 2011) and the incidence of depressive and anxiety disorders is dramatically increasing (Kim-Cohen et al., 2003), will be critical.

In sum, polymorphisms and dysregulation in 5-HT, DA, and circadian clock genes may contribute to the development and maintenance of insomnia and internalizing disorders in adolescence, in combination with precipitating factors such as stress (Esposito, Di Matteo, & Di Giovanni, 2008). It also possible that social experiences, behavior, and thoughts may in turn influence the activity of 5-HT, DA, and circadian clock genes (Born, Hansen, Marshall, Molle, & Fehm, 1999; Robinson, Fernald, & Clayton, 2008). Studies evaluating *interactions* between 5-HT, DA, circadian clock genes, and environmental variables in adolescent samples are needed.

Dysregulation of corticolimbic brain circuits

Inadequate sleep has been shown to increase negative emotions, reduce positive emotions, and change the way in which adolescents comprehend, express, and modify emotions (Palmer & Alfano, 2016).

These results are most evident with neuroimaging studies investigating limbic system activity and its prefrontal regulation. In general, hyperarousal and insufficient sleep have been shown to disrupt the function of corticolimbic circuitry in young people (18–32 y), including the prefrontal cortex (PFC), amygdala, striatum, and anterior cingulate cortex (ACC), thereby impairing affective reactivity and regulation (Chuah et al., 2010; Motomura et al., 2013; Yoo, Gujar, Hu, Jolesz, & Walker, 2007). The PFC is critical in the regulation of sleep (Horne, 1993) as well as the regulation of attentional, arousal, and affective systems (i.e., executive functioning; Dahl, 1996), and sleep disruption in young people (18–26 y) has been shown to weaken the monitoring and regulatory abilities of the PFC, which in turn, leads to further dysregulation (Chuah et al., 2010). This pattern of activation is consistent with impaired top-down regulation of emotional responses. In contrast, other studies have shown that sleep, and specifically rapid eye movement (REM) sleep, provides a renewal of adaptive next-day emotional reactivity and salience discrimination (Goldstein & Walker, 2014).

Insomnia may be especially damaging for adolescents with internalizing disorders, who are already prone to exaggerated physiologic response and cognitive/emotional biases. Children and adolescents with anxiety disorders (5–23 y) exhibit exaggerated hypoconnectivity between the PFC and amygdala (Hamm et al., 2014), and adolescents and young adults with depression (13–25 y) show elevated activity in extended medial network regions, including the ACC, ventromedial and orbitofrontal cortices, and the amygdala (Kerestes, Davey, Stephanou, Whittle, & Harrison, 2014). This is likely to further compromise their emotion regulation, especially under conditions of sleep deprivation. Furthermore, prefrontal maturation is incomplete and executive control capacities are still developing in childhood and adolescence (Luciana, 2013). In support of this, poor sleep is associated with lower emotional competence and empathy among adolescents (Brand et al., 2016).

Dysregulation of reward/approach related brain function

Accumulating evidence suggests that insomnia disrupts reward/approach related brain function and, moreover, that this process may also be important in the development and maintenance of internalizing disorders in adolescents. For example, Talbot, McGlinchey, Dahl, Kaplan, and Harvey (2011) found that sleep restriction diminished positive/approach-related affect more than negative affect in a sample of healthy

adolescents (10–16 y). Additionally, Dagys and colleagues (2012) found that sleep deprivation in healthy adolescents (10–16 y) resulted in less positive affect and a lower positive to negative affect ratio, as well as increased anxiety. McMakin and colleagues (2016) found that experimental sleep restriction increased negative affect in healthy adolescents (11–15 y; as evidenced by self-report and pupil reactivity) and negative affective behavior in a social context primed for peer conflict. Moreover, McGlinchey and colleagues (2011) found that sleep deprived adolescents (11–15 y) displayed significantly fewer positive emotions compared to sleep deprived adults (30–60 y), suggesting that adolescents may be particularly vulnerable to emotional dysregulation following insufficient sleep.

There is also emerging evidence that neural response to approach-related cues is disrupted in adolescents with sleep disturbance. Holm and colleagues (2009) examined 58 healthy adolescents (11–13 y), who completed functional magnetic resonance imaging using a guessing task with monetary rewards. During reward anticipation, less activation in the caudate (a part of the ventral striatum) was associated with less total sleep time (TST), later sleep onset time, and lower sleep quality. During the reward outcome, less caudate activation was associated with later sleep onset time, earlier sleep offset time, and lower sleep quality.

These findings are likely to have particular relevance for the development of internalizing disorders. Several studies have shown that low levels of positive affect are specifically associated with depressed states. Indeed, both anhedonia (the inability to feel pleasure in normally pleasurable activities) and disturbed sleep are core criteria of MDD (American Psychiatric Association, 2013). In support of this, several studies have shown an increase in depression (Baum et al., 2015; Forbes et al., 2006; Fredriksen, Rhodes, Reddy, & Way, 2004) and anxiety (Sagaspe et al., 2006) symptoms following sleep deprivation in healthy adolescent samples. For example, Baum and colleagues (2015) found that after just five nights of shortened sleep (6.5 h per night), healthy adolescents (14–17 y) showed worsened mood and decreased ability to regulate emotions.

Consistent with this, a recent study by Casement, Keenan, Hipwell, Guyer, and Forbes (2016) tested the hypothesis that disturbance in neural responses to rewards is a mechanism by which insomnia symptoms during early adolescence contribute to depressive symptoms in later adolescence. Nonrestorative sleep

during early adolescence (9–13 y) was associated with increased dorsomedial PFC (dmPFC) response during expectation of rewards and more depressive symptoms in later adolescence (16 y). The finding is consistent with meta-analytic results suggesting that depression is usually associated with decreased response to reward in the striatum and increased response in the dmPFC (Zhang, Chang, Guo, Zhang, & Wang, 2013). These findings suggest that puberty and sleep deprivation may have synergistic effects on reward processing, increasing vulnerability for the development of internalizing disorders.

Hyperarousal

There may be other biological responses to sleep disturbances, such as increased cortisol and hypothalamic–pituitary–adrenal (HPA) axis dysregulation (van Dalfsen & Markus, 2018), which contribute to the development of anxiety and depression in adolescence. For example, research suggests that changes in hormonal cortisol excretion during pubertal maturation play a particularly important role in the relationship between insomnia and internalizing disorders in adolescence. Recent studies have shown that hormone levels at bedtime are different in adolescents with anxiety and depression compared to children with anxiety and depression (Forbes et al., 2006). Cortisol secretion is decreased during normal deep sleep, but adults and adolescents with insomnia and internalizing disorders exhibit elevated levels of cortisol (Elnazer & Baldwin, 2014; Herbert, 2013; Vgontzas & Chrousos, 2002). For example, Zhang and colleagues (2014) found that 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. Indeed, recent evidence suggests that sleep problems predict cortisol reactivity to stress in adolescents. Mrug, Tyson, Turan, and Granger (2016) examined the role of sleep problems on stress-related HPA axis reactivity among 84 adolescents (11–16 y). Parents provided information on the adolescents' sleep problems, and adolescents completed self-report measures of sleep disturbance and a standardized social stress test in the laboratory (the Trier social stress test). More sleep problems predicted higher cortisol reactivity to the social stress test. Self-reports of sleep were more reliably related to stress-related cortisol reactivity than parent reports. These results suggest that sleep problems may place adolescents at risk for HPA axis hyper-reactivity to stress, and vice versa, which may contribute to academic, behavioral, and mental and physical health problems. The

association between stress and internalizing disorders has been consistently recognized in the scientific literature (Burke, Davis, Otte, & Mohr, 2005).

Overall, this research suggests that alterations of the arousal system may partially explain the close association between insomnia, anxiety, and depression in adolescence. Hyperarousal models of insomnia have received widespread support and assume that (1) sleep and arousal represent opposing processes in a larger system of arousal regulation; (2) the regulation of sleep, arousal, and affect overlap in physiological, neuroanatomical, clinical, and developmental domains; and (3) the experience of insomnia may have a critical impact on the development of anxiety and depression, and vice-versa (Dahl, 1996; Riemann et al., 2010). For example, Mendoza and colleagues (2016) found that adolescents and young adults (10–22 y) with insomnia symptoms had elevated levels of cortical hyperarousal (increased electroencephalographic beta power) prior to, and during, sleep. Alfano, Pina, Zerr, and Villalta (2010) found that the presence of pre-sleep arousal was associated with greater self-reported sleep problems among children and adolescents (7–14 y) who were diagnosed with an anxiety disorder.

Inflammatory cytokines

The correlation between sleep quality and immunological processes has also been confirmed in a number of research reports. A recent systematic review and meta-analysis of 72 studies (n > 50,000) found that disturbed sleep (defined as symptoms and/or diagnosis of a sleep disorder) was associated with immune functioning and increased inflammation (Irwin, Olmstead, & Carroll, 2016). In particular, disturbed sleep was associated with higher levels of the pro-inflammatory markers interleukin IL-6 and the acute-phase protein 'C-reactive protein' (CRP). However, neither experimental sleep deprivation nor sleep restriction was associated with IL-6 or CRP. Few studies have evaluated these processes in adolescents with insomnia. Fernandez-Mendoza and colleagues (2016) found that adolescents and young adults (10–22 y) with insomnia symptoms and short sleep duration (i.e., less than seven hours) had greater plasma CRP levels compared to adolescents with insomnia symptoms and normal sleep duration (i.e., more than seven hours). Further longitudinal and experimental studies are needed to explore the directions of these relationships.

Dysregulated inflammatory processes are also associated with internalizing symptoms. A recent meta-analysis of 24 studies found significantly higher concentrations of the pro-inflammatory cytokines

TNF-α and IL-6 in depressed adults compared with healthy controls (Dowlati et al., 2010), and elevated levels of CRP have been found in adults with anxiety symptoms (Copeland, Shanahan, Worthman, Angold, & Costello, 2012; Liukkonen et al., 2011). However, again, studies among younger populations are lacking. Blom and colleagues (2012) found that mid–late adolescents with MDD (14–18 y) showed significantly higher IL-2 and IL-10 compared to healthy control adolescents. Conversely, Brambilla, Monteleone, and Mai (2004) found that younger children and adolescents with MDD (8–14 y) did not have significantly higher Il-1β or TNF-α compared to healthy controls. These findings suggest that dysregulated inflammatory processes may not appear until midway through adolescence. In support of this, Nelson and colleagues (2017) recently found that stable temperament dimensions of effortful control and negative emotionality predicted CRP levels more strongly than depressive symptoms in a sample of early-mid adolescents (10–14 y) who were followed over three years. These findings suggest that adolescents with low effortful control and higher negative emotionality may be at greater risk of depressive symptoms and later inflammation.

In sum, it is possible that changes in the activity of inflammatory factors following poor quality sleep may compromise the functioning of the central nervous system, which may affect brain functioning, and have a key impact on the development and course of different psychiatric disorders, particularly internalizing disorders. In other words, poor sleep may be a significant contributor to chronic levels of increased inflammation, and in turn, cytokine-induced mental health symptoms. However, studies in this area have been largely cross-sectional, and longitudinal studies examining *interactions* between insomnia, inflammation, and internalizing disorders are needed to establish directions of effects.

Biased memory consolidation

As reviewed by McMakin and Alfano (2015), another expanding area of research emphasizes the role of memory and learning in the relationship between sleep and internalizing disorders. Synaptic pruning and reorganization occurs during sleep, supporting a process of memory consolidation (Rasch & Born, 2013). As part of this consolidation process, memories evolve and change as sleep promotes the identification of 'gist', or bottom line meaning (Landmann et al., 2014). The brain identifies the most relevant information, and emotional memories are preferentially retained (Payne, Chambers, & Kensinger, 2012), a process that appears at least partly mediated by corticolimbic activity (e.g., amygdala,

hippocampus, and PFC; McGaugh, 2004; Nili, Goldberg, Weizman, & Dudai, 2010) interacting with hormones such as cortisol (Bennion, Payne, & Kensinger, 2015). These processes are likely to be particularly powerful during adolescence, a period of high synaptic plasticity and learning (Colrain & Baker, 2011; Spear, 2000, 2009). They are also likely to be pertinent to the development of internalizing disorders in adolescence, given that anxious and depressed adolescents tend to show high emotional reactivity to perceived threat, which could negatively bias selection of memories for consolidation, and reactivation of these memories during the pre-sleep period (i.e., worrying and ruminating) could exacerbate these processes (Dahl, 1996). This may drive a shift in 'gist' representation resulting in over-general interpretative biases (e.g., that the world is a threatening place).

Changes in sleep architecture

In the past few decades, researchers have focused on changes in sleep architecture as a potential neurophysiological substrate of insomnia, anxiety, and depression.

Reductions in slow-wave sleep

Reductions in slow-wave sleep (SWS) may contribute to the development and maintenance of insomnia and internalizing disorders in adolescence. Slow waves are low frequency (0.4–4.6 Hz), high amplitude, synchronized neuronal oscillations, abundant at the beginning of sleep, declining over the course of sleep, generated in the cortex, and modulated by the thalamus (David, 2013). They are the dominant characteristic of non-REM sleep. Slow waves are associated with deeper and better quality sleep and are more frequent following sleep deprivation, suggesting that they are markers of sleep homeostasis (i.e., sleep drive; Tononi & Cirelli, 2006). They are also more frequent in adolescents compared to adults and decline dramatically across adolescence, suggesting that they play a role in restoration, including synaptic rescaling (Tarokh & Carskadon, 2010). As mentioned previously, adolescence is a time of extensive brain remodeling, including synaptic pruning and myelination (Luciana, 2013). This reflects a transition from high plasticity and interconnectedness in childhood to high efficiency and faster processing in adulthood (Colrain & Baker, 2011; Spear, 2000, 2009). Volumes of cortical grey matter increase during childhood, reaching peak levels at puberty onset, after which they gradually decline (Paus, Keshavan, & Giedd, 2008). There is a general thinning of the cortex into adolescence, particularly in the frontal and parietal lobes, as well as

'synaptic pruning' in subcortical structures such as the ventral striatum (Luciana, 2013). Functions performed by the PFC also improve at a slow and linear rate through adolescence and into young adulthood (Luciana, 2013). Together, these brain changes promote increasingly efficient functioning in frontal, striatal, thalamic, and brain-stem networks and functional connectivity between major information-processing centers (Hwang, Hallquist, & Luna, 2013). This pattern of timing has implications for the expected levels of executive control in childhood (when prefrontal maturation is incomplete and executive control is low); in adolescence (when executive control capacities are present but inconsistently applied); and in adulthood (when executive control capacities are intact and incentive motivational drives have declined; Luciana, 2013). There is emerging evidence that slow-wave activity (SWA) mirrors synaptic reorganization of cortical areas from early childhood to late adolescence (Campbell & Feinberg, 2009), and that higher SWA is associated with more efficient cognitive functioning (Tononi & Cirelli, 2014) and consolidation of memories related to emotions, thoughts, and actions (Rasch & Born, 2013).

Robust evidence (including several reviews) suggests that adults with insomnia, anxiety, and depression exhibit significant reductions in SWS, which results in daytime dysfunction (Armitage, 2007; Baglioni et al., 2013). For example, a meta-analysis of 23 studies found that adult insomnia patients (n=582) showed a significant reduction of SWS compared to good sleeper controls (n=485; Baglioni et al., 2013). Furthermore, Cheng, Goldschmied, Deldin, Hoffman, and Armitage (2015) compared a large sample of young adults with clinical levels of depression to a sample of healthy controls (mean age 29 y), and found that the depressed group were characterized by decreases in SWA, particularly in the beginning of the night, which was associated with elevated anxiety and depression symptoms the following morning. There is also emerging evidence that children and adolescents with internalizing disorders have significant reductions in SWS. For example, Forbes and colleagues (2009) demonstrated that children and adolescents with anxiety disorders (7–17 y) had marked reductions in SWS. Furthermore, Lopez, Hoffmann, Emslie, and Armitage (2012) found lower SWA in depressed adolescent males (8–15 y) compared to controls. Additionally, Rao and colleagues (2002) found that SWS was reduced in depressed adolescents (12–18 y) who later developed borderline personality disorder (18–27 y). Finally, Silk and colleagues (2007) showed that at-risk children (6–11 y) who spent more time in SWS were less likely to develop depressive disorders as adults (18–29 y).

However, no studies have compared SWS in adolescents with and without insomnia.

In sum, these findings suggest that children and adolescents who are vulnerable to internalizing disorders may experience deficits in the build-up of sleep pressure during wakefulness, which may result in reduced SWS, inadequate restorative value of sleep, synaptic overload in the daytime (e.g., reductions in neuronal excitability, increased synaptic failure, and reduced plasticity), and related daytime dysfunction (e.g., fatigue, anhedonia, irritability, impaired attention and concentration, and decreased motivation; Cheng et al., 2015; Tononi & Cirelli, 2006).

Low sleep spindle activity

Recent evidence also suggests that individual differences in sleep spindle activity may contribute to differential susceptibility to insomnia and internalizing disorders, in combination with stress. Sleep spindles are transient (1–3 seconds), rhythmic, high frequency (11–16 Hz) neuronal oscillations, considered a hallmark of non-REM sleep (Loomis, Harvey, & Hobart, 1935). Sleep spindles are generated through thalamocortical loops (Steriade, Deschenes, Domich, & Mulle, 1985), and appear to play a functional role in memory consolidation, cognitive development, and maintenance of sleep continuity (Fogel & Smith, 2012). For example, it has been hypothesized that sleep spindles synchronize the flow of information from limbic structures to the cortex, carrying information about cortical functioning and circuit integrity supporting cognitive function (Lopez, Hoffmann, & Armitage, 2010; Tarokh, Saletin, & Carskadon, 2016). Furthermore, sleep spindles are more abundant in childhood and adolescence than in adulthood, and show a linear increase across adolescence (Scholle, Zwacka, & Scholle, 2007), suggesting they are associated with cortical myelination (Tarokh et al., 2016), and are integral to neuroplasticity during brain maturation (Lopez et al., 2010).

Lower sleep spindle activity has been shown to prospectively predict larger increases in insomnia symptoms in response to stress among healthy adolescents and young people (17–25 y; Dang-Vu et al., 2015), signifying that lower spindle activity might predispose vulnerable adolescents to neurobiological hyperarousal and psychophysiologically driven sleep disruption. Furthermore, lower spindle activity has been shown to characterize children and adolescents (8–15 y) with MDD and those at high risk for MDD

(Lopez et al., 2010), suggesting that lower spindle activity may be a biological risk marker for early-onset depression, and that the onset of depressive symptoms is associated with decreased neuroplasticity.

Changes in REM sleep

Changes in REM sleep may also contribute to the development and maintenance of internalizing disorders in adolescence. REMs are rapid, desynchronized, small amplitude neuronal oscillations, similar to waking states. The timing of REM sleep is linked to circadian rhythms, closely mirroring core temperature – REM sleep is more likely after the nadir of core temperature, usually towards the end of the sleep bout (Borbély, Daan, Wirz-Justice, & Deboer, 2016). Across adolescence, REM sleep decreases in absolute terms, but not as a percentage of TST (Ohayon, Carskadon, Guilleminault, & Vitiello, 2004). REM sleep also appears to play a role in memory consolidation and emotion regulation, specifically decreasing next-day brain reactivity to recent waking emotional experiences. In support of this, corticolimbic and paralimbic areas are specifically activated during REM sleep in adolescents and young adults (18–30 y; van der Helm et al., 2012).

Adolescents and adults with internalizing disorders show decreased REM latency (the time between sleep onset and first REM period) and increased REM length and density, particularly adolescents with a family history of internalizing disorders, further suggesting that genetic factors play a role in the development of sleep abnormalities in anxiety and depression (Benca, Obermeyer, Thisted, & Gillin, 1992; Riemann, Berger, & Voderholzer, 2001). The transition to REM sleep is accompanied by a decrease in monoaminergic tone (5-HT, norepinephrine, and DA), an increase in cholinergic tone (Pace-Schott & Hobson, 2002), and activation of amygdala-hippocampal networks (van der Helm et al., 2012). As described previously, dysregulation of monoamine neurotransmitters and emotional neural networks are associated with insomnia and internalizing disorders, and may be responsible for REM sleep irregularities in adolescents with internalizing disorders. Furthermore, REM instability (defined as REM sleep with a high number of arousals) has been shown to be a signature of insomnia, depression, and anxiety (Duncan, Pettigrew, & Gillin, 1979; Mellman, Bustamante, Fins, Pigeon, & Nolan, 2002; Riemann et al., 2012) and hinders resolution of overnight emotional distress (Wassing et al., 2016) in adults. REM instability may promote chronic hyperarousal, biased memory consolidation (e.g., pre-sleep worries extending to dreams),

and dysfunction in emotional neural networks, increasing risk for internalizing disorders. Furthermore, increased and unperturbed REM sleep has been associated with consolidation of fear extinction memories in animals (Datta & O'Malley, 2013). Further studies are needed to explore the impact of adolescent development on these processes.

In sum, adolescents with insomnia and internalizing symptoms/disorders may experience disruption in both homeostatic and circadian drives to sleep. SWS is linked to the homeostatic sleep system and REM sleep to the circadian system (Borbély et al., 2016).

Summary of biological mechanisms

In total, the research literature suggests that insomnia, anxiety, and depression may represent different facets of a single dynamic neurobiological diathesis, where dysregulation in shared neural regions leads to insomnia and internalizing symptoms (Uhde, Cortese, & Vedeniapin, 2009). The number of shared processes across multiple biological systems suggests that a systemic approach is likely to be required in order to fully understand these phenomena. Moreover, these processes are all part of adaptive systems that are known to influence, and be influenced by, psychological and social/environmental factors.

Potential psychological mechanisms

Lying awake at night

Lovato and Gradisar (2014) have argued that adolescents with insomnia symptoms spend more time in an environment conducive to repetitive and intrusive thoughts due to the lack of other visual and auditory stimuli with which to engage. This increased wakefulness in bed may serve to reinforce negative cognitions and hence perpetuate anxiety and low mood. Over time, these processes may develop into anxiety and depressive disorders. In support of this, and as described previously, recent evidence suggests that wakefulness in bed precedes the development of anxiety and depression in children and adolescence more than the reverse (Lovato & Gradisar, 2014; McMakin & Alfano, 2015). Additionally, children and adolescents with sleep problems have reported several maladaptive cognitive patterns linked to anxiety and depression, including interpretational biases (i.e., catastrophizing, overgeneralization, personalizing, and selective abstraction), judgment biases (i.e., lack of control over external threats, negative internal emotions, and bodily reactions), and negative attribution styles (internal, stable, and global attributions for the

occurrence of negative events; Alfano, Zakem, Costa, Taylor, & Weems, 2009; Gregory & Eley, 2005; Gregory, Noone, Eley, & Harvey, 2010).

Similarly, Perlis and colleagues (2016) have argued that being awake at night could contribute to suicidal ideation/behavior by increasing an individual's sense of hopelessness, isolation, and distress. Specifically, they argued that being awake at night when one is not biologically predisposed to being awake (i.e., not sleep sated and/or in a circadian phase that is associated with alertness and higher cognitive functioning), may result in a decrease in frontal lobe function (i.e., hypo-activation of the frontal lobes due to sleep loss/sleep deprivation and/or circadian effects). Hypofrontality, in turn, may result in poor executive functioning, diminished problem-solving abilities, and increased impulsive behavior, which may increase risk for suicide. This may place an individual in a situation where s/he lacks the resources to make helpful choices. These factors are likely to interact with other sleep issues (e.g., sleep loss) and social factors (e.g., lack of social support at night) and place individuals at greater risk for suicidal ideation/behavior, particularly in those already at risk due internalizing symptoms and/or challenging life circumstances.

The model proposed by Perlis and colleagues (2016) was originally developed for adults, but can be generalized to adolescents. The model also has the potential to be transdiagnostic, in that being awake at night may bestow risk for any unhelpful cognition (e.g., worry and rumination), emotion (e.g., sadness, fear, and anger) and behavior (e.g., substance abuse) that requires an individual to be motivated not to engage in and/or that requires high levels of impulse control and regulation. The incidence of maladaptive cognitions, emotions, and behaviors should therefore be highest during the night.

Several lines of evidence support this perspective. First, insomnia and poor sleep quality significantly and independently and prospectively predict increased risk for suicidal ideation, suicide attempts, and deaths by suicide, in adolescents (Wong & Brower, 2012), young adults (Becker, Dvorsky, Holdaway, & Luebbe, 2018), and adults (Pigeon, Pinquart, & Conner, 2012). Second, there is a comparative increase in the number of suicides committed at night and this finding is consistent across age groups (e.g., in both adolescents and adults; Perlis et al., 2014). For example, Gangwisch and colleagues (2010) found that adolescents with parental set bedtimes of midnight or later are 24% more likely to suffer from depression and 20% more likely to have suicidal ideation than adolescents with parental set bedtimes of

10:00 PM or earlier. Third, hypofrontality occurs in conjunction with sleep restriction (i.e., more frontal cortex theta and delta activity and less beta and gamma activity; Cajochen, Brunner, Krauchi, Graw, & Wirz-Justice, 1995; Verweij et al., 2014), and this pattern of activity is consistent across adulthood (20–74 y; Munch, Knoblauch, Blatter, Wirz-Justice, & Cajochen, 2007) but is exaggerated in young adults with internalizing disorders (20–31 y; Frey et al., 2012). Fourth, cognitive/executive function is impaired by sleep restriction in both adolescents (de Bruin, van Run, Staaks, & Meijer, 2017) and adults (Drummond, Paulus, & Tapert, 2006; McKenna, Dicjinson, Orff, & Drummond, 2007; Valdez, Ramirez, Garcia, Talamantes, & Cortez, 2010). Finally, positive mood in young people (18–30 y) is lowest during the circadian night and this is exaggerated by sleep deprivation (Murray et al., 2009).

Worry and rumination

Worry and rumination are cognitive processes "characterized by thinking about personal concerns in unproductive, repetitive ways, and experiencing difficulties terminating these chains of thoughts" (Verstraeten, Bijttebier, Vasey, & Raes, 2011, p. 365). Worry is thought to be future oriented, while rumination is thought to be past oriented (Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008). Worry and rumination have various consequences; worry interferes with emotional processing, the extinction of fear, and adaptive coping (Borkovec, 1994), while rumination interferes with problem-solving and depletes energy and motivation (Lyubomirsky, Tucker, Caldwell, & Berg, 1999). Worry and rumination correlate significantly with anxiety and depression symptoms in adolescents (9–13 y), even when worry scores are covaried out of rumination and vice versa (Verstraeten et al., 2011).

Harvey (2002) proposed a highly influential cognitive model of insomnia that posited that a tendency to worry and ruminate during the day may extend to the pre-sleep period, resulting in biased attention to threat, unpleasant intrusive thoughts, and excessive and uncontrollable worry about getting enough sleep and the consequences of sleeplessness. This may trigger autonomic arousal and emotional distress, precipitating attentional narrowing and preferential allocation of attentional resources to sleep related threat cues, both internal (e.g., bodily sensations) and external (e.g., environmental noises). This selective attention may further exacerbate worry, anxiety, and low mood, as individuals become more attuned to minor cues that

would otherwise be undetected. Escalating anxiety and dysphoria may culminate in a real sleep deficit as well as counter-productive behaviors such as avoiding bed or getting out of bed.

Harvey's cognitive model of insomnia has received widespread support in studies with adults (Hiller, Johnston, Dohnt, Lovato, & Gradisar, 2015). Electrophysiological, autonomic, neuroendocrine, neuroimmunological, neuroimaging, daytime performance, and experimental studies have consistently shown that adults with insomnia display heightened cognitive (e.g., worry and rumination), emotional (e.g., fear), and somatic (muscular tension, autonomic activity) arousal, particularly in the pre-sleep period (Riemann et al., 2010). Cross-sectional studies have also shown that adults with insomnia have dysfunctional beliefs and attitudes about sleep (Morin, Vallières, & Ivers, 2007). Moreover, an emerging literature has examined these relationships in younger populations. Several studies have shown that children and adolescents with sleep problems report elevated levels of dysfunctional beliefs and attitudes about sleep (Gradisar, Wright, Robinson, Paine, & Gamble, 2008; Gregory, Cox, Crawford, Holland, & Harvey, 2009). Additionally, Hiller, Lovato, Gradisar, Oliver, and Slater (2014) found that 87% of adolescents (11–19 y) with a sleep disorder reported catastrophic thinking in the pre-sleep period, with concerns about performance and interpersonal aspects of school most central. Similarly, Ottaviani, Medea, Lonigro, Tarvainen, and Couyoumdjian (2015) found that perseverative cognition, which is characterized by a rigid and defensive pattern of thinking, predicted poor sleep quality and low mood in a healthy sample of young adults (mean age 26.68 y). Furthermore, Danielsson, Norell-Clarke, and Hagquist (2016) found that sleep disturbance in adolescents (15–16 y) increased the odds of worrying about a range of themes, including financial security, accidents/illness, being bullied, and terrorist attacks (odds ratio, 2.65–3.35). However, these studies were limited by cross-sectional designs, which cannot attribute causality, ascertain directions of effects, or ascertain if an association between two variables is due to a third (unknown) variable. In an important extension of this work, Danielsson, Harvey, MacDonald, Jansson-Frojmark, and Linton (2013) found that sleep disturbance predicted depressive symptoms one-year later among a group of high school students (16–18 y), and that catastrophic worry partially mediated this relationship. These results suggest that sleep disturbance and worry may be early indicators of depression. Further longitudinal studies are needed to confirm the directions of these relationships.

Other cognitive processes

It is also possible that other negative cognitive styles may precipitate and/or maintain insomnia and internalizing symptoms among adolescents, including misperception of sleep deficit, cognitive inflexibility, and selective attention and monitoring (Hiller et al., 2015; Provencher & Hawke, 2011). For example, a number of studies have established the presence of attentional biases (e.g., vigilance and avoidance of negative cues) in individuals with insomnia, anxiety, and/or depression (Hallion & Ruscio, 2011; Harris et al., 2015; Milkins, Notebaert, MacLeod, & Clarke, 2016; Nota & Coles, 2018; Price et al., 2016). These findings suggest that adolescents with insomnia and internalizing disorders may selectively attend to more negative information. In support of this, Price and colleagues (2016) found that eye tracking patterns suggestive of threat avoidance predicted increased depression scores at two-year follow-up among a group of anxious adolescents (9–14 y), suggesting that avoidance of threat could restrict the development of adaptive emotion regulation skills in adolescents, resulting in the broad behavioural deactivation characteristic of depression. In another recent study, Milkins, Notebart, MacLeod, and Clarke (2016) demonstrated that an attention-bias modification procedure (designed to encourage attentional avoidance of sleep-negative stimuli) in the pre-sleep period resulted in significant reductions in subjectively assessed SOL and pre-sleep cognitive arousal among a small group of adolescents and young adults who self-identified as having sleeping difficulties. However, studies examining *interactions* between attentional biases, insomnia, and internalizing disorders in adolescents are needed.

Summary of psychological mechanisms

In sum, there is accumulating evidence that maladaptive cognitions may contribute to the relationship between insomnia and internalizing problems in adolescents. In general, cognitive inflexibility, interpretational biases, judgment biases, negative attribution styles, worry, rumination, and biased attention to threat may extend to the pre-sleep period, resulting in hypofrontality, unpleasant intrusive thoughts, dysfunctional beliefs and attitudes about sleep, selective attention and monitoring to sleep-related threat, and misperception of sleep deficit. These psychological processes may culminate in insomnia (e.g., prolonged SOL and poor SE) and internalizing (e.g., low mood and anxiety) symptoms/disorders.

Potential social mechanisms

Social withdrawal and amotivation

Poor sleep may change behaviors in ways that decrease the likelihood of experiencing positive social contexts. For example, adolescents with insomnia may prioritize sleep over other important waking activities, have reduced energy for, and motivation to, seek out enjoyable social activities, and have low overall anticipation of social reward. Indeed, recent reviews have shown that sleep duration in children and adolescents has decreased by 75 minutes over the past century (Matricciani, Olds, & Petkov, 2012) and that adolescents are experiencing more internalizing symptoms compared to previous cohorts (Bor, Dean, Najman, & Hayatbakhsh, 2014). In support of this, Carney, Edinger, Meyer, Lindman, and Istre (2006) found that young people (18–39 y) who slept poorly engaged in fewer social activities compared with good sleepers. Furthermore, sleep problems have been shown to increase daytime sleepiness and reduce goal-directed behavior in adolescents, which may reduce arousal needed for complex social and cognitive tasks (Dewald, Meijer, Oort, Kerkhof, & Bögels, 2010; Peterman, Carper, & Kendall, 2015). For example, Meijer (2008) found that chronic sleep reduction in children and adolescents (9–13 y) was linked to lower achievement motivation, a poorer self-view as a pupil, and a more negative perception of teacher's behavior. In sum, sleep disturbance and resulting daytime sleepiness may cause social withdrawal and amotivation in adolescents, which may precipitate and/or maintain internalizing symptoms. Approximately 50% of adolescents report feeling too tired/sleepy during the day, and over 20% report falling asleep in school or while doing homework at least once per week (National Sleep Foundation, 2006). It is also possible that social withdrawal may lead to sleep disturbance in adolescents. For example, social withdrawal may lead to rumination, which may in turn lead to insomnia and internalizing disorders. Longitudinal and experimental studies are needed to explore the directions of these relationships.

Impaired social interactions

Poor sleep may also impair the quality of adolescent's social interactions via compromised decision-making, poor impulse control, behavioral inhibition, and diminished emotion expressivity and recognition. Emerging evidence suggests that insufficient and/or poor quality sleep may impair the ability to recognize an emotion as problematic, to choose a suitable emotion regulation approach, and to use that strategy in an effective way (Palmer & Alfano, 2016). This has particular relevance for social interactions, including social

intelligence, social competence, affiliative behaviors, theory of mind, and empathy (Beattie, Kyle, Espie, & Biello, 2014). For example, emotional dysregulation arising from sleep difficulties may increase adolescents' likelihood of experiencing peer rejection, which may lead to feelings devaluation, low self-worth, sadness, hopelessness, and loneliness, which may in turn precipitate and/or maintain internalizing symptoms/disorders.

In support of this, several cross-sectional studies have shown that sleep disturbance in adolescence is associated with impaired social interactions. Conden, Ekselius, and Aslund (2013) found that adolescents (15–18 y) with sleep disturbance were more likely to inhibit self-expression in social interactions. Gilbert, Pond, Haak, DeWall, and Keller (2015) found that poor sleep (lower quality and quantity) exacerbated the emotional consequences of interpersonal rejection in late adolescents (mean age 19 y), highlighting the importance of sleep for coping with daily interpersonal events. Likewise, Sarchiapone and colleagues (2014) found that reduced sleep duration on school nights was associated with greater self-reported peer problems in adolescents (14–17 y). Additionally, Mahon (1994) found that adolescents with sleep disturbance reported more loneliness than adolescents without sleep problems, and Tu, Erath, and El-Sheikh (2015) found that sleep moderated the role between peer victimization and adolescents' adjustment. In the latter study, those with higher levels of sleep problems reported more peer victimization, while those with high levels of both sleep problems and peer victimization had the highest level of internalizing symptoms. Similarly, Williams, Chambers, Logan, and Robinson (1996) found that children (7–10 y) who slept poorly were more likely to feel sad and be the victim of bullying. Many other studies have found that loneliness increases risk of anxiety and depressive symptoms in children and adolescents (Fontaine et al., 2009; Lasgaard, Goossens, & Elklit, 2011).

Although these results are consistent with the suggestion that sleep disturbance in adolescence leads to impaired social interactions, they are by no means conclusive – the associations could be mere coincidence. More definitive conclusions can be garnered from longitudinal investigations, which can directly examine the temporal order of phenomena. Indeed, longitudinal studies have demonstrated that the relationship between sleep disturbance in adolescence and impaired social interactions is most likely bi-directional. Roberts, Roberts, and Chen (2002) found that adolescents with insomnia symptoms experienced

more difficulties in peer relationships 12-months later, even after controlling for initial levels of peer functioning. Furthermore, Soffer-Dudek, Sadeh, Dahl, and Rosenblat-Stein (2011) found that adolescents (10–11 y) who had poor sleep quality (elevated night awakenings and decreased SE) exhibited lower performance in a face-emotion information-processing task over time. However, there is also emerging evidence for the reverse relationship – that difficult social interactions prospectively predict sleep disturbance and internalizing problems in adolescents. Harris, Qualter, and Robisnon (2013) found that pre-adolescents (mean age 8 y) with persistent loneliness reported longer SOL, more sleep disturbance, and high depressive symptoms three years later. Yip (2015) found that adolescents (13–16 y) who reported high levels of ethnic/racial discrimination and sleep disturbance experienced a corresponding increase in depressive symptoms over time. Maume (2013) found that positive peer relationships at age 12 predicted longer school night sleep duration at age 15. Finally, Tavernier and Willoughby (2015) found that there were bi-directional relationships between sleep problems and social ties among a group of young people (17–25 y) who were followed over three years. Importantly, analyses of indirect effects showed that emotion regulation mediated these links, such that better sleep quality led to more effective emotion regulation, which, subsequently, led to more positive social ties, while more positive social ties led to more effective emotion regulation, which, in turn, led to less sleep problems. These findings particularly highlight the critical role of emotional regulation in the relationship between sleep problems and social ties in adolescence.

Unhelpful parenting practices and family stress

Parenting practices and family stress may also contribute to the relationship between insomnia, anxiety, and depression in adolescence. Specifically, parental over-accommodation (e.g., protection behaviors, permitting avoidance behaviors, modifying family routines, facilitating anxious and depressed thoughts) may contribute to the development and maintenance of insomnia and internalizing disorders. Over-accommodating parents may permit late and variable bedtimes, poor sleep hygiene behaviors (e.g., electronic devices in the bedroom), perfectionism (e.g., completing homework late into the night), and excessive re-assurance seeking. Additionally, it is also possible that parents with insomnia may model poor sleep habits and/or set fewer sleep rules/boundaries for their children. In other words, the relationship

between parent and adolescent sleep may be representative of both genetic and environmental risk for insomnia (or, more likely, their interaction; Barclay, Eley, Buysse, Maughan, & Gregory, 2012).

In support of this, several studies have found that the sleep patterns of parents and their adolescent children show similarities. Brand, Greber, Hatzinger, Beck, and Holsboer-Trachsler (2009) found that the self-reported sleep quality of adolescents' (mean age 17 y) and their parents were significantly correlated; moreover, mother's sleep poor sleep had a direct impact on parenting style, which in turn affected adolescents' anxiety and depression symptoms. Similarly, Bajoghli, Alipouri, Holsboer-Trachsler, and Brand (2013) found that self-reported sleep quality, depressive symptoms, and perceived stress of Iranian adolescents (12–20 y) and their parents were inter-related; specifically, mothers' sleep and psychological functioning were more related to adolescents' sleep and psychological functioning than were those of fathers. Kalak and colleagues (2012) were the first to show that the objective sleep patterns of adolescents and their parents were associated. In particular, sleep continuity and architecture, subjective sleep quality, and depression scores of adolescents and their mothers were associated. Brand, Hatzinger, Beck, and Holsboer-Trachsler (2009) found that adverse parenting styles (e.g., low positivity and high negativity) were associated with low sleep quality, negative mood, daytime sleepiness, and anxiety/depression symptoms among adolescents (mean age 17 y). Furthermore, Short and colleagues (2011) found that the absence of parent set bedtimes was associated with later bedtimes, less night-time sleep, more fatigue, and poorer daytime functioning among a group of adolescents (13–18 y). Conversely, Adam, Snell, and Pendry (2007) found that stricter parental rules were associated with longer weekday sleep in adolescents (12–19 y). Similarly, Vazsonyi and colleagues (2015) found that positive parenting behaviors promoted good sleep behaviors and in turn reduced risk for problematic sleep behaviors among adolescents (15–18 y). However, again, there is a relative dearth of experimental and longitudinal studies in this area. Maume (2013) found that parental divorce at age 12 predicted shorter school night sleep duration and/or more sleep disruption at age 15, while higher levels of parental control and monitoring (i.e., set bedtimes) predicted longer school night sleep duration and less sleep disruption at age 15. Further studies are needed to explore the directions of these relationships.

Finally, family stress has been associated with both insomnia and internalizing symptoms in adolescents. Adam and colleagues (2007) found that family economic strain predicted later bedtimes in adolescents (12–19 y). Additionally, Chiang and colleagues (2017) found that stressful family events were associated with depressive symptoms in late adolescents (15–20 y), and that this relationship was strongest among those with lower SE. These results suggest that the chronic experiences of lower SE may render adolescents vulnerable to the negative effects of family stress on emotional adjustment.

Summary of social mechanisms

These findings emphasize the need to consider a young person's sleep in their social and family context (Dahl & El-sheikh, 2007). In general, insomnia may decrease the likelihood of experiencing positive social contexts, undermine emotional and behavioral regulation, and overwhelm a young person's coping resources in social and family situations, either physically or cognitively, creating conditions for the disruption of interpersonal relationships, which can in turn increase risk for development of anxiety and depression. A number of mechanisms may explain these processes. First, disturbed sleep may interfere with the restorative processes that occur during sleep, including the neurobiological alterations that help to resolve strong emotions related to challenging social situations. Second, disturbed sleep, especially wakefulness in bed, may reflect difficulty-decreasing vigilance following social stressors. Adolescents who are vulnerable to insomnia and internalizing disorders may find it difficult to de-arouse following interpersonal conflict and/or social rejection (e.g., on social media). Third, because poor sleep impairs executive functioning, including impulse control and attention, adolescents who sleep poorly may depend more on automatic processing and less on effortful cognitions. Therefore, they may have difficulty resolving interpersonal conflicts, coping with peer/family stressors, and attending to subtle social cues. Finally, because poor sleep impairs emotion regulation, adolescents who sleep poorly may find it difficult to disengage from rewarding activities prior to bed (e.g., television, smart phones, parties). This is an area where more research is needed to assess these hypothesized mechanisms.

Interim summary

In sum, sequential, parallel, and interacting biological, psychological, and social mechanisms may contribute to the development of insomnia, anxiety, and depression in adolescence. Indeed these disorders

may often share a common diathesis. Insomnia, anxiety, and depression may be independent, but mutually influencing conditions, *or* may represent different symptomatic expressions of common underlying processes. In general, however, evidence suggests that insomnia symptoms precede the development of anxiety and depression in adolescence more than the reverse (Lovato & Gradisar, 2014; McMakin & Alfano, 2015). To the extent that insomnia, anxiety, and depression in adolescence share common etiological underpinnings, early treatment programs for insomnia may reduce the risk of developing anxiety and depressive disorders, and may even prevent suicide.

Figure 1 presents a diagrammatic representation of the different etiological processes reviewed in this manuscript and their hypothesized relationships to each other, and to symptoms of insomnia, anxiety, and depression. Although this model is complex, and involves a variety of mechanisms working across multiple levels of analysis (i.e., biological, psychological, social), as we have shown, the extant literature provide empirical support for these hypothesized associations and multilevel interactions. An important agenda for future research on risk processes is to more fully understand the systemic nature of the dynamic interactions between these phenomena, so that we can more fully understand which mechanisms work as part integrated networks, versus which can operate independently. A deeper understanding of these issues will help to elucidate points of leverage that can be utilized in designing preventative and treatment programs that target these disorders.

Implications for adolescent behavioral sleep interventions

Given that insomnia may precipitate and/or maintain anxiety and depression symptoms in adolescents, the application of sleep interventions is of potential significance for mental health promotion and prevention. Adolescent insomnia can be treated using a range of approaches (de Zambotti, Goldstone, Colrain, & Baker, 2018).

Few controlled studies have evaluated the effectiveness and long-term effects of pharmacological interventions for adolescent insomnia (Owens & Moturi, 2009). The American Academy of Sleep Medicine has published a consensus statement recommending that additional research is needed to determine the appropriate use, dosing, safety, tolerance, and efficacy of pharmacological interventions for adolescent

insomnia, such as benzodiazepines, sedating antidepressants, sedating antihistamines, and melatonin (Owens et al., 2005).

School-based sleep education programs have the potential to reach a large number of adolescents. However, recent reviews have suggested that while these programs are effective in increasing students' knowledge about sleep, they are less effective in improving sleep behavior or mental health (Blunden, Chapman, & Rigney, 2012; Blunden & Rigney, 2015; Gruber, 2017). These findings are consistent with research showing that sleep hygiene education does not guarantee positive outcomes in adults (Irish, Kline, Gunn, Buysse, & Hall, 2015), and that targeted interventions are more effective than universal interventions in preventing child and adolescent mental health problems (Rohde, 2015).

Cognitive-behavior therapy for insomnia (CBT-I) is recommended as a first line treatment for adult insomnia (Qaseem, Kansagara, Forciea, Cooke, & Denberg, 2016), based on evidence from several systematic reviews and meta-analyses that the intervention improves sleep and mental health, including objective and self-reported indices of sleep, anxiety, and depression (Ballesio et al., 2017; Taylor & Pruiksma, 2014; Trauer, Qian, Doyle, Rajaratnam, & Cunnington, 2015; van Straten et al., 2017), with effect sizes that are similar to those for hypnotics, such as benzodiazepines (Huedo-Medina, Kirsch, Middlemass, Klonizakis, & Siriwardena, 2012; Nowell et al., 1997). However, different to hypnotics, CBT-I effects are likely to continue after treatment cessation (Sivertsen et al., 2006) and to have fewer side effects, such as adverse effects and rebound insomnia after discontinuation (Buscemi et al., 2007; Kales et al., 1991). CBT-I involves behavioral techniques such as sleep education, sleep hygiene instruction, stimulus control, sleep restriction, and relaxation training, but also addresses unhelpful beliefs and attitudes about sleep (Edinger & Means, 2005). There is also emerging evidence that sleep problems can be treated successfully using protocols that include a mindfulness component (for a meta-analytic review, see Gong et al., 2016). Mindfulness meditation is particularly indicated for sleep-related problems, because it aims to reduce the hyperarousal and negative emotional states (e.g., anxiety and worry) that are frequently reported by individuals experiencing sleep problems.

A recent systematic review and meta-analysis found that nine trials (n = 357) have examined the efficacy of cognitive-behavioral sleep interventions among adolescents with self-identified sleep problems

or a diagnosis of a sleep disorder (mean age = 14.97 y, range 11–20 y; Blake, Sheeber, Youssef, Raniti, & Allen, 2017). Two of the studies evaluated "manualized" CBT-I, whereas the other interventions included added treatment components (e.g., mindfulness, anxiety/depression specific modules). The results showed that the sleep interventions produced marked and statistically significant improvements in objective and self-reported indices of sleep, daytime sleepiness, anxiety, and depression at post-intervention time points. Moreover, gains were generally maintained over time. As with adults, improvements tended to be stronger for wakefulness in bed variables compared to sleep duration variables. However, much remains unknown about the mechanisms underlying the effectiveness of these interventions. Based on the literature reviewed above we suggest that adolescent CBT-I and mindfulness-based sleep interventions may be effective because they target the sequential, parallel, and interacting mechanisms underlying insomnia, anxiety, and depression. An understanding of these mechanisms is especially important because concurrent insomnia has been linked with poorer response to treatment for internalizing disorders in children, adolescents, and adults (Emslie et al., 2001; Thase, Simons, & Reyndolds III, 1996). Residual insomnia symptoms are also a major feature of partially remitted internalizing disorders in both young people and adults (Becker & Sattar, 2006; Kennard et al., 2006; Smith, Huang, & Manber, 2005) and increase the risk of depression recurrence in adults (Dombrovski et al., 2008). Therefore, sleep interventions may increase the efficacy of subsequent anxiety and depression treatments, or may even render them unnecessary.

First, adolescent CBT-I and mindfulness-based techniques may reduce limbic activation and improve prefrontal regulation. CBT-I focuses on improving emotion regulation via re-appraisal, labeling, and distraction. Similarly, mindfulness-based sleep interventions encourage a detached and decentered view of emotions and thoughts, and have been described as a method of desensitization to negative affect and an exposure strategy to reduce automatic avoidance of negative emotions (Britton et al., 2010). In support of this, cognitive therapy has been associated with reduced activation of the amygdalohippocampal subcortical regions, which are implicated in the generation of negative emotion, and increased activation of higher-order frontal regions involved in cognitive control of negative emotion (Clark & Beck, 2010). Similarly, mindfulness meditation has been associated with changes in parts of the brain controlling affect regulation, and stress reaction, including prefrontal and limbic areas (Hölzel et al., 2011; Lazar et al., 2005). However,

no studies have measured changes in brain structure or function following adolescent CBT-I and/or mindfulness-based sleep interventions.

Second, adolescent CBT-I and mindfulness-based sleep interventions may reduce mesolimbic brain dysregulation by encouraging disengagement from rewarding stimuli in the pre-sleep period (e.g., watching television) and/or management of compulsive checking behavior in bed (e.g. checking social media on smart phones). For example, urge surfing ('riding the wave') was developed as a mindfulness-based relapse prevention technique for individuals who misuse substances (Marlatt, Bowen, Chawla, & Witkiewitz, 2008), but has demonstrated efficacy for a range of unhelpful behaviors/habits, including nicotine addiction and unhealthy eating practices (Bowen & Marlatt, 2009; Jenkins & Tapper, 2014). Urge surfing is based on the premise that urges and impulses (e.g., to stay up late watching television or check social media in bed) can manifest as physical sensations in the body, and rise in intensity, peak, and eventually subside. Urge surfing encourages the adoption of open and curious attitudes to unhelpful urges. Individuals are encouraged to observe their impulses in a non-judgmental manner, until they eventually subside.

Third, adolescent CBT-I and mindfulness-based sleep interventions may decrease hyperarousal and improve stress management, thereby reducing cortisol hyperreactivity to stress and inflammatory cytokine dysregulation. CBT-I includes several components likely to reduce hyperarousal, including relaxation (e.g., breathing exercises), sleep hygiene instruction (e.g., reducing caffeine and sugar consumption, limiting electronic device use near bedtime), stimulus control therapy (e.g., regularizing sleep-wake schedules, avoiding using bed/bedroom for engaging activities), and cognitive restructuring (e.g., managing worries at night, addressing upsetting beliefs about sleep). Mindfulness meditation is also likely to reduce hyperarousal (e.g., mindfulness of the breath, body scan, leaves on a stream). In support of this, several studies have shown that adults with insomnia show significant reductions in pre-sleep arousal following CBT-I (Schwartz & Carney, 2012). Moreover, a recent study showed that improvements in pre-sleep arousal contributed to the effectiveness of an adolescent cognitive behavioral and mindfulness-based sleep intervention (Blake, Schwartz, et al., 2017). However, no studies have measured changes in cortisol or inflammatory cytokines following an adolescent CBT-I and/or mindfulness-based sleep intervention.

Fourth, adolescent CBT-I and mindfulness-based sleep interventions may improve sleep architecture. The goal of sleep restriction therapy is to initially limit sleep opportunities to increase sleep drive and improve homeostatic sleep regulation, which may increase SWS. Furthermore, CBT-I and mindfulness-based techniques may increase sleep spindle activity and decrease REM instability, by reducing hyperarousal before sleep. However, no studies have measured changes in sleep microarchitecture following adolescent CBT-I and/or mindfulness-based sleep interventions. In particular, randomized controlled trials (RCTs) that incorporate polysomnography, neuroimaging, and neuropsychological techniques are needed: improvements in SWS, sleep spindle activity, and REM sleep may be associated with improvements in synaptic integrity, synaptogenesis, neuroplasticity, myelination, consolidation of memories, cognitive functioning, emotion regulation, and related daytime functioning (e.g., daytime sleepiness, fatigue, anxiety, depression, school attendance, academic performance, quality of life, and physical health).

Fifth, adolescent CBT-I and mindfulness-based sleep interventions may decrease maladaptive cognitions. CBT-I includes a core focus on reducing wakefulness in bed and overcoming worry, rumination, and dysfunctional beliefs and attitudes about sleep. Similarly, mindfulness includes a core focus on re-perceiving negative thoughts from a non-judgmental, objective, and non-elaborative stance. In support of this, several studies have shown that adults with insomnia show significant reductions in wakefulness in bed and maladaptive cognitions following CBT-I (e.g., worry, rumination, mind-racing, dysfunctional beliefs and attitudes about sleep, self-efficacy; Schwartz & Carney, 2012; Trauer et al., 2015). Furthermore, a recent systematic review and meta-analyses found that mindfulness is effective because it reduces cognitive reactivity, worry, and rumination (Gu, Strauss, Bond, & Cavanagh, 2015). Only two studies have measured changes in cognitive style following an adolescent CBT-I and/or mindfulness-based sleep intervention. Bootzin and Stevens (2005) found significant reductions in worry following an adolescent CBT-I and mindfulness-based sleep intervention, but this study was limited by a small sample size, lack of control group, and high attrition rate. A recent RCT found that adolescents with low levels of self-efficacy showed blunted response to a cognitive-behavioral and mindfulness-based sleep intervention (Blake, Blake, et al., 2017).

Sixth, group-based adolescent CBT-I and mindfulness-based sleep interventions may improve

resilience and self-regulatory skill in social situations, by normalizing the experience of insomnia, anxiety, and depression, emphasizing peer support and positive interactions between group members, and providing opportunities to practice interpersonal communication skills. In support of this, group CBT-I and mindfulness-based sleep interventions have been associated with meaningful improvements in sleep problems and mental health among adolescents (Blake et al., 2016; Bootzin & Stevens, 2005).

Seventh, the literature reviewed here suggests that it may be important to supplement adolescent CBT-I and mindfulness-based sleep interventions with additional treatment components. For example, parental psycho-education about healthy sleep practices and parenting behaviors may decrease unhelpful parenting behaviors (e.g., parental over-accommodation). Furthermore, exercise, diet, and pleasant event scheduling may improve 5-HT and DA functioning – there is emerging evidence that monoamines can be modified non-pharmacologically (Young, 2007). Additionally, social rhythm training and bright light therapy may stabilize circadian rhythms: the circadian system is primarily entrained by light and the social environment (e.g., timing of sleep, eating, and exercise; Harvey et al., 2011). In support of this, interventions incorporating early morning running (Kalak, Gerber, Kirov, et al., 2012), bright light therapy (Gradisar, Dohnt, et al., 2011), and pleasant event scheduling (Clarke et al., 2015) have been associated with meaningful improvements in sleep and internalizing symptoms among adolescents. For example, the study by Kalak and colleagues (2012) found that thirty minutes of running in the morning during weekdays for 3 consecutive weeks improved objectively measured sleep (SWS, SOL), self-reported sleep, mood, concentration, and daytime sleepiness in healthy adolescents (17.5–19.5 y) compared with healthy controls. Also, trauma-based exposure therapies may reduce biased memory consolidation, as they focus on reducing fear response and hyper-reactivity to negative memories (Gillies, Taylor, Gray, O'Brien, & D'Abrew, 2013). Similarly, savoring may reduce pre-sleep hyperarousal and negative cognitions – savoring involves the practiced recollection and enhancement of positive emotions related to past positive experiences or anticipation of positive future experiences, and can be seen as a mirror-image (positive version) to the process of worry and rumination (Bryant & Veroff, 2007). For example, savoring may encourage positive affect stimulation in the pre-sleep period (McMakin, Siegle, & Shirk, 2011). Furthermore, structured problem solving may reduce negative daytime cognitions (e.g., worry and rumination). As described

previously, attention modification procedures may reduce hypervigilance for threat (Milkins et al., 2016).

Finally, it is worth noting that acute sleep deprivation (total, partial, selective REM) can also have mood *improving* effects in individuals with depression (Kahn, Sheppes, & Sadeh, 2013). Specifically, it has been hypothesised that REM-sleep deprivation decreases the odds of consolidating dysfunctional cognitions and emotions. In a systematic review of the early literature, Wu and Bunney (1990) found that 59% of depressed patients experienced an antidepressant response to total sleep deprivation. However, mood improvements were lost following recovery sleep; 50-80% of patients relapsed following the next sleep bout. Surprisingly, few studies have evaluated these processes in adolescents. Naylor and colleagues (1993) found that severely depressed adolescents showed a significant decrease in depression severity and subjective arousal following 36 hours of sleep deprivation, whereas depressed adolescents in remission and control adolescents worsened after sleep deprivation. Moreover, in contrast to findings in depressed adults, the beneficial effects on sleep deprivation persisted after one night recovery sleep. The underlying mechanism for this clinical improvement is still unclear, but the results do challenge the idea that more sleep is always better. Clearly, further research is needed to establish the specific role of insufficient or disrupted sleep in the development of poor emotion regulation in adolescents.

Conclusion

This review described sequential, parallel, and interacting biological, psychological, and social mechanisms underlying the relationship between insomnia, anxiety, and depression in adolescence. These risk mechanisms hold promise as feasible treatment targets and suggest that behavioral sleep interventions may be particularly effective for adolescents with concomitant sleep and internalizing problems.

However, much remains unknown about the insomnia-anxiety-depression relationship in adolescence. Further cross-sectional, longitudinal, twin, experimental, and intervention studies are needed to explore these relationships. For example, which biopsychosocial mechanisms are most important? When do they appear? How do they interact? Are there gender differences? Additionally, studies that investigate mechanisms of therapeutic improvement in interventions are needed. For example, do adolescent behavioral sleep interventions improve sleep microarchitecture, neural functioning, brain structure and function, hormone regulation, inflammatory cytokine regulation, emotion regulation, executive functioning, cognitive

style, and interpersonal relationships, and are these improvements specifically related to improvements in objective and subjective sleep (e.g., SOL, SE, TST) and functional outcomes (e.g., daytime sleepiness, fatigue, anxiety, depression, school attendance, academic performance, quality of life, physical health)? Studies that examine the therapeutic efficacy and specificity of different treatment components for adolescents with different symptom profiles are also needed. A personalized approach to adolescent behavioral sleep interventions (i.e., tailoring the interventions based on biopsychosocial symptom profiles) may improve their therapeutic efficacy and cost-effectiveness.

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Conflict of interest

There are no conflicts of interests to declare.

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Figure 1: Biopsychosocial model describing the mechanisms underlying the association between insomnia, anxiety, and depression in adolescence. Note that symptomatic outcomes associated with insomnia are represented in the box titled "Wakefulness in bed", and those associated with internalizing symptoms are represented in the boxes entitled "Emotional dysregulation" and "Negative emotionality". *ACC* anterior cingulate cortex, *BT* bedtime, *DA* dopamine, *DBAS* dysfunctional beliefs and attitudes about sleep, *dmPFC* dorsomedial prefrontal cortex, *HPA axis* hypothalamic-pituitary-adrenal axis, *PER3* circadian clock gene PERIOD3, *PFC* prefrontal cortex, *REM* rapid eye movement, *SE* sleep efficiency, *SOL* sleep onset latency, *SWS* slow-wave sleep, *SWA* slow-wave activity, *TST* total sleep time, *WASO* wake after sleep onset, *5-HT* serotonin

Highlights

- Biological, psychological, and social mechanisms may underlie the relationship between insomnia, anxiety, and depression in adolescence
- Biological mechanisms may include genetic, brain, cortisol, cytokine, memory, and sleep architecture dysregulation
- Psychological mechanisms may include cognitive and attention biases and dysfunctional beliefs and attitudes about sleep
- Social mechanisms may include reduced and impaired social interactions, unhelpful parenting behaviors, and family stress
- We propose an integrative multilevel model of how these mechanisms may interact to increase vulnerability and explore implications for the design of adolescent behavioral sleep interventions

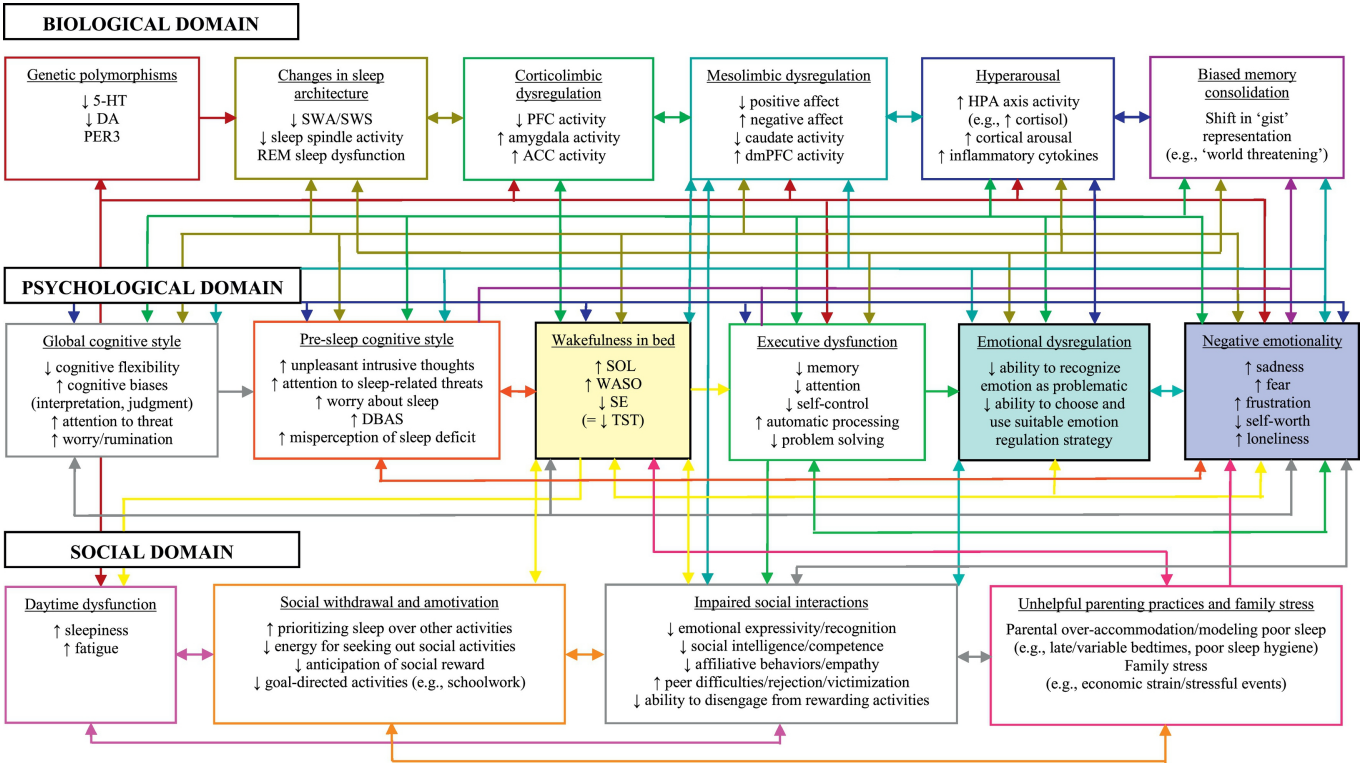
BIOLOGICAL DOMAIN
Genetic polymorphisms
↓ 5-HT
↓ DA
PER3
Changes in sleep architecture
↓ SWA/SWS
↓ sleep spindle activity
REM sleep dysfunction
Corticolimbic dysregulation
↓ PFC activity
↑ amygdala activity
↑ ACC activity
Mesolimbic dysregulation
↓ positive affect
↑ negative affect
↓ caudate activity
↑ dmPFC activity
Hyperarousal
↑ HPA axis activity
(e.g., ↑ cortisol)
↑ cortical arousal
↑ inflammatory cytokines
Biased memory consolidation
Shift in 'gist' representation
(e.g., 'world threatening')
PSYCHOLOGICAL DOMAIN
Global cognitive style
↓ cognitive flexibility
↑ cognitive biases
(interpretation, judgment)
↑ attention to threat
↑ worry/rumination
Pre-sleep cognitive style
↑ unpleasant intrusive thoughts
↑ attention to sleep-related threats
↑ worry about sleep
↑ DBAS
↑ misperception of sleep deficit
Wakefulness in bed
↑ SOL
↑ WASO
↓ SE
(= ↓ TST)
Executive dysfunction
↓ memory
↓ attention
↓ self-control
↑ automatic processing
↓ problem solving
Emotional dysregulation
↓ ability to recognize emotion as problematic
↓ ability to choose and use suitable emotion regulation strategy
Negative emotionality
↑ sadness
↑ fear
↑ frustration
↓ self-worth
↑ loneliness
SOCIAL DOMAIN
Daytime dysfunction
↑ sleepiness
↑ fatigue
Social withdrawal and amotivation
↑ prioritizing sleep over other activities
↓ energy for seeking out social activities
↓ anticipation of social reward
↓ goal-directed activities (e.g., schoolwork)
Impaired social interactions
↓ emotional expressivity/recognition
↓ social intelligence/competence
↓ affiliative behaviors/empathy
↑ peer difficulties/rejection/victimization
↓ ability to disengage from rewarding activities
Unhelpful parenting practices and family stress
Parental over-accommodation/modeling poor sleep
(e.g., late/variable bedtimes, poor sleep hygiene)
Family stress
(e.g., economic strain/stressful events)

Figure 1