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REVIEW ARTICLE

Stress and the hypothalamic–pituitary–adrenal axis: How can the COVID-19 pandemic inform our understanding and treatment of acute insomnia?

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Summary

Stress and sleep are very closely linked, and stressful life events can trigger acute insomnia. The ongoing COVID-19 pandemic is highly likely to represent one such stressful life event. Indeed, a wide range of cross-sectional studies demonstrate that the pandemic is associated with poor sleep and sleep disturbances. Given the high economic and health burden of insomnia disorder, strategies that can prevent and treat acute insomnia, and also prevent the transition from acute insomnia to insomnia disorder, are necessary. This narrative review outlines why the COVID-19 pandemic is a stressful life event, and why activation of the hypothalamic–pituitary–adrenal axis, as a biological marker of psychological stress, is likely to result in acute insomnia. Further, this review outlines how sleep disturbances might arise as a result of the COVID-19 pandemic, and why simultaneous hypothalamic–pituitary–adrenal axis measurement can inform the pathogenesis of acute insomnia. In particular, we focus on the cortisol awakening response as a marker of hypothalamic–pituitary–adrenal axis function, as cortisol is the end-product of the hypothalamic–pituitary–adrenal axis. From a research perspective, future opportunities include identifying individuals, or particular occupational or societal groups (e.g. frontline health staff), who are at high risk of developing acute insomnia, and intervening. From an acute insomnia treatment perspective, priorities include testing large-scale online behavioural interventions; examining if reducing the impact of stress is effective and, finally, assessing whether "sleep vaccination" can maintain good sleep health by preventing the occurrence of acute insomnia, by preventing the transition from acute insomnia to insomnia disorder.

KEYWORDS
acute insomnia, cortisol awakening response, COVID-19, hypothalamic–pituitary–adrenal axis, sleep, stress

1 | INTRODUCTION

Insomnia disorder is highly prevalent: it is estimated that within industrialised societies, approximately 6%–10% of the population have insomnia, and approximately 50% of the population report having symptoms of insomnia (Ohayon, 2002; Pallesen et al., 2014). Insomnia disorder has a significant economic burden (Daley et al., 2009), and is associated with an increased risk of multiple deleterious physical and psychological health conditions (Baglioni et al., 2011; Li et al., 2014; Riemann & Voderholzer, 2003).

Theoretical models of insomnia, such as Spielman's "*3P*" model, suggest that stressful life events can potentially result in clinically significant short-term insomnia, which is known as acute insomnia (Ellis, Gehrman et al., 2012a; Spielman et al., 1987; Spielman et al., 1996). Acute insomnia refers to a self-reported disruption in sleep continuity that occurs for a duration of between 2 weeks and 3 months (Ellis, 2019; Ellis, Gehrman et al., 2012a). Indeed, a range of previous studies have demonstrated that stress is associated with various subjective and objective sleep disturbances (Bastien et al., 2004; Reynolds 3rd et al., 1992; Reynolds 3rd et al., 1993). Acute insomnia is also highly prevalent: annually, it has been estimated that the incidence of acute insomnia may be as high as 40% (Ellis, Perlis et al., 2012b; Perlis et al., 2020). A further problem is that acute insomnia can also trigger (longer-term) insomnia disorder, or cause variable disturbances to subjective sleep continuity (i.e. disturbances to sleep initiation and/or sleep maintenance that are not of a sufficient severity to be considered acute insomnia), which can subsequently lead to insomnia disorder at a later date (Perlis et al., 2020). In order to inform the aetiology and treatment of acute insomnia, it is important to understand how, and why, stressful life events may result in acute insomnia. This is important as preventing, and treating, acute insomnia may prevent the later development of insomnia disorder.

The aim of the present narrative review is to outline why the ongoing COVID-19 pandemic should be considered a stressful life event and potential cause of acute insomnia and, mechanistically, why psychological stress caused by COVID-19 is likely to result in acute insomnia through activation of the hypothalamic–pituitary–adrenal (HPA) axis. The implications of this review are twofold. Firstly, this review will directly inform future mechanistic studies that will further the understanding of the pathogenesis of acute insomnia. Secondly, this review will inform the design of future treatment studies, focussed on addressing, and preventing, acute insomnia, through targeted interventions that are likely to reduce HPA axis activity.

2 | STRESSFUL EVENTS AND THE IMPACT OF THE COVID-19 PANDEMIC UPON SLEEP

Stress can affect sleep (Altena et al., 2016; Lo Martire et al., 2020), and it is well established from a range of naturalistic studies that stressful events, including earthquakes, hurricanes and war, are shown to have a deleterious effect upon sleep (Askenasy & Lewin, 1996; Kato et al., 1996; Mellman et al., 1995). The COVID-19 pandemic, which has been ongoing since March 2020, represents one such stressful event, and potentially represents a stressor of unknown duration, accompanied by a wide range of societal and lifestyle changes (Altena et al., 2020).

Cross-sectional evidence certainly indicates that the COVID-19 pandemic disrupts sleep. This includes sleep problems related to national or local "lockdown" occurrences, sleep problems that are caused by or related to pandemic-related anxiety and stress, and sleep problems that have occurred as a direct consequence of the disease itself. For instance, the results of an online study of 842 adults, which was conducted during lockdown periods in May/June 2020, where social interaction and movement were limited, reported a significant negative impact on sleep (Perez-Carbonell et al., 2020). Specifically, this study found that a range of sleep disturbances were apparent: approximately 70% of respondents reported a change in their sleep pattern; 46% of people were sleepier in comparison with before the lockdown period; 43% reported "disrupted sleep"; 35% reported falling asleep unintentionally; and approximately 30% of respondents had difficulties falling asleep or staying asleep, and reported later bedtimes (Perez-Carbonell et al., 2020). Additionally, the majority (65%) of participants stated that the pandemic/lockdown period had an impact upon their mental health, and only 45% of respondents reported having refreshing sleep (Perez-Carbonell et al., 2020). Two further cross-sectional studies, from China and Italy, respectively, also appear to confirm the negative impact of the pandemic upon sleep (Casagrande et al., 2020; Wang et al., 2020). Evidence from Italy, in an online survey of approximately 2300 adults in March/April 2020, showed that approximately 58% of participants reported poor sleep quality, 42% reported distress, 32% reported high levels of anxiety, and 8% reported symptoms of post-traumatic stress disorder (PTSD; Casagrande et al., 2020).

In addition to cross-sectional evidence, a recent meta-analytic study has provided further evidence in support of the negative impact of the pandemic upon sleep (Jahrami et al., 2022). In this review of 250 studies ($n = 493{,}475$), the estimated global prevalence of sleep disturbances was estimated to be approximately 41%, with higher rates observed in healthcare workers (42%) and in patients who had reported having COVID-19 (52%). Another systematic review observed a similar pattern, whereby sleep problems were more frequently observed in COVID-19 patients, and that sleep problems were also positively associated with depression and anxiety (Alimoradi et al., 2021). It is particularly important to prevent the transition from acute to chronic insomnia in this context, as it is known that insomnia symptoms can continue even after the emotional consequences of the initial cause (e.g. a trauma or upsetting life event) have been effectively treated (López et al., 2019). This is also important as, for example, insomnia treatment can effectively prevent the occurrence of comorbid depression (Irwin et al., 2022; Leerssen et al., 2022).

Further recent studies have shown that the COVID-19 pandemic is considered to be a traumatic stressful event (Bridgland et al., 2021; Saalwirth & Leipold, 2021), with meta-analytic work estimating that 20%–30% of the general population may have experienced elevated stress levels (Cooke et al., 2020; Salari et al., 2020). This point is backed up by the results of recent population survey studies, which

have indicated that subjective stress levels have increased during the pandemic (Hsing et al., 2020; Robillard et al., 2020).

3 | STRESS, THE HPA AXIS AND INSOMNIA

The term "stress" refers to experiences that are considered to be emotionally or physiologically demanding, and to the adaptative response involving multiple physiological systems (Lo Martire et al., 2020; McEwen, 2007). The HPA axis is an endocrine system that has an important role in ensuring that the body adapts to bodily and environmental challenges (Fries et al., 2009; Hucklebridge et al., 2005). As part of the primary stress response, both the sympathetic nervous system and HPA axis are activated, and this leads to a "fight-or-flight" response, whereby catecholamines and glucocorticoids are released into the bloodstream (Lee & Harley, 2012; McEwen, 2007), and redirect energy resources, in order to restore homeostasis (Herman et al., 2003).

A stress marker that is of particular interest with regards to the development of acute insomnia is cortisol, which is the end-product of the HPA axis. In the context of stress, a perceived threat causes the hypothalamus to release corticotropin-releasing hormone (CRH), which then triggers the anterior pituitary gland release of adrenocorticotropin hormone (ACTH), and finally the release of cortisol from the adrenal cortex (Clow et al., 2004). Cortisol is highly responsive to physical and psychological stress, and it is well established that acute psychological stress can increase cortisol levels (Dickerson & Kemeny, 2004; Lo Martire et al., 2020).

4 | THE HPA AXIS AND INSOMNIA

Alterations to HPA axis activity are relevant to the pathogenesis of both acute insomnia and insomnia disorder. The hyperarousal theoretical model of insomnia suggests that elevated cognitive, emotional and physiological activity (expressed as, e.g., heightened autonomic or central nervous system activity) are important in the pathophysiology of insomnia disorder (Dressle et al., 2022; Riemann et al., 2010; Riemann et al., 2015). Acute insomnia, and insomnia disorder, can both be considered to be stress-related conditions, whereby an initial stressful event can result in physiological hyperarousal and, over time, insomnia disorder becomes stressful in its own right (Dressle et al., 2022).

Activation of the HPA axis is a feature of acute insomnia, where the initial stress response is observed as a consequence of the response to the initial stressor (Dressle et al., 2022). However, alterations to HPA axis activity are also a feature of the transition from acute insomnia to insomnia disorder, where following the initial stressor, heightened HPA axis activity can negatively affect sleep (Dressle et al., 2022). The initial sleep disturbance that accompanies the acute stressor can potentially cause sleep fragmentation or deprivation. This can, in itself, negatively affect the HPA axis and maintain the sleep disturbance, potentially due to chronic HPA axis hyperarousal affecting sleep and circadian rhythmicity (Buckley & Schatzberg, 2005; Dressle et al., 2022; Lo Martire et al., 2020). Additionally, stress reactivity, and sleep, could potentially moderate the relationship between acute and chronic stress, and HPA axis activity (Dressle et al., 2022; van Dalfsen & Markus, 2018). Taken together, altered HPA axis activity is relevant to acute insomnia in terms of the initial stress response, and is also relevant to the maintenance of acute insomnia, and subsequent progression towards insomnia disorder.

Certainly, several studies show that there are specific alterations to cortisol, and the cortisol awakening response (CAR), which could potentially indicate that elevated HPA axis activity is a feature of insomnia disorder (Riemann et al., 2015). Specifically, studies have observed that relative to people without insomnia disorder, those with insomnia display elevated levels of morning cortisol, increased CARs, and higher 24-hr cortisol levels (Grimaldi et al., 2021; Xia et al., 2013; Zhang et al., 2014). Despite the relevance of the HPA axis to insomnia disorder, currently, very little is known about HPA axis activity during the acute phase of insomnia; to the best of our knowledge, no studies have specifically sought to examine this, or have been able to do so, to date.

5 | THE CAR

Cortisol is a particularly suitable biological marker of stress in the context of acute insomnia, as it can be easily, reliably and non-invasively measured, in order to quantify stress. Cortisol secretion fluctuates in a circadian pattern: cortisol levels sharply increase in the hour after awakening; decline 3 hr after awakening, then gradually decline until the nadir, which occurs during the first half of the sleep period and, finally, gradually rise until awakening (Elder et al., 2014; Fries et al., 2009). Connections between the suprachiasmatic nucleus and paraventricular nucleus of the hypothalamus are responsible for synchronising the time of day to cortisol output (Buijs et al., 2003).

In contrast to other indices of HPA axis function, cortisol can be easily and reliably measured in a non-invasive manner using saliva sampling, with salivary cortisol levels showing a high level of agreement with plasma cortisol levels (Hellhammer et al., 2009). Additionally, compared with other methods of assessing HPA axis function, saliva sampling is advantageous as firstly, blood sampling is considered to be a stressor in its own right (Prinz et al., 2001) and, secondly, as blood collection is not required, this means that participants can self-collect saliva samples outside of a sleep laboratory environment (Elder et al., 2014; Elder et al., 2016). In contrast, other measures of HPA axis function, such as ACTH or CRH, are difficult to measure due to their instability, or the fact that only low levels of these measures circulate within blood (Dressle et al., 2022; Spencer & Deak, 2017).

Of particular relevance is the CAR. The CAR refers to a distinct phase of the circadian cortisol profile, whereby there is a sharp increase in cortisol levels observed upon awakening: during the CAR, cortisol levels increase by 38%–75% and peak approximately 30 min after awakening (Elder et al., 2014). The CAR is a robust marker of

HPA axis function and, although other physiological stress measures can be obtained (e.g. heart rate variability, electrodermal activity), a particular advantage of focussing upon the CAR is that the link between sleep and HPA axis activity is generally well understood (van Dalfsen & Markus, 2018). Unlike other biological markers of stress activity, there are specific CAR measurement protocols that have been designed for use in sleep medicine and sleep research environments, and that were developed with insomnia research in mind (Elder et al., 2014; Elder et al., 2016). Multiple different measurement indices of the CAR can be examined, including cortisol levels at each sampling time point, awakening cortisol levels, or total cortisol secretion, or the magnitude of change between awakening levels and peak levels or, finally, the mean increase in cortisol levels (Elder et al., 2014; Elder et al., 2016). As is the case with cortisol, the CAR is sensitive to periods of stress: the CAR is associated with periods of increased demand and/or anticipation of forthcoming demand (Brant et al., 2010; Elder et al., 2018). Finally, the CAR should also be considered an appropriate marker of HPA axis activity because our understanding of HPA axis activity is also informed by a large body of work focussing on depression, which is itself very closely linked to insomnia (Riemann et al., 2010). Taken together, the CAR is likely to be useful in understanding HPA axis function in stress-related acute insomnia.

6 | STRESS AND HPA AXIS ACTIVATION AS A RESULT OF PANDEMIC-RELATED STRESS

There are numerous stressors that have occurred in the context of the pandemic, which are relevant and could trigger acute insomnia, as they have been shown to also result in HPA axis activation. These stressors include being forced to remain at home (during lockdown periods), working from home, working more hours in stressful circumstances, and managing health risks (Altena et al., 2020). Other associated changes, such as potential or actual unemployment, are relevant: one study found that factors such as financial worry, self-rated health, perceived control, and concern in relation to catching COVID-19 were predictors of subjective stress (Newby et al., 2020).

These events have also been associated with altered HPA axis functioning. For example, unemployment can result in alterations to the CAR (Gallagher et al., 2016). Altered HPA axis function may also be useful for examining the impact of stress within particular groups of individuals or, for example, specific occupational groups. For instance, it has been shown that cortisol levels in healthcare workers were higher during the peak of the first wave of the pandemic relative to immediately before, and that those individuals who worked in higher-risk environments demonstrated increased cortisol levels compared with low-risk workers (Rajcani et al., 2021). Separate studies, conducted during the pandemic, have shown that the relative change in cortisol levels can predict subsequent burnout in healthcare workers, and that the CAR is associated with the emotional response to the pandemic (Baliyan et al., 2021; Marcil et al., 2022); importantly, one demonstrated that hair cortisol levels *increased* from pre-pandemic to post-pandemic onset (Marcil et al., 2022). Overall, this provides further support to demonstrate that the simultaneous measurement of stress and HPA axis activity is relevant to the pathogenesis of acute insomnia.

7 | RESEARCH OPPORTUNITIES: PREDISPOSITIONAL AND SITUATIONAL RISK FACTORS FOR ACUTE INSOMNIA

One potential area for research is to examine predispositional and situational factors that may increase the individual risk of developing acute insomnia from the initial pandemic-related trigger of poor sleep.

According to the Spielman 3P model of insomnia, predisposing factors are trait-like characteristics, such as worry, or specific personality traits (Spielman et al., 1996). Indeed, recent work has demonstrated that factors including anxiety, insomnia severity and personality aspects including conscientiousness and openness to experience are predictive of the development of acute insomnia following the initial sleep disturbance (Ellis et al., 2021).

More recently, the concept of "sleep reactivity" has been investigated in relation to the hyperarousal model of insomnia disorder, whereby the response to stress might be an important risk factor for future insomnia development (Drake et al., 2004; Kalmbach et al., 2018; Walker et al., 2022). Sleep reactivity is the extent to which stress can disrupt sleep, and this can be influenced by environmental stress, or other factors such as genetics, a family history of insomnia, or rumination/worry (Kalmbach et al., 2018). Indeed, it is the experienced stress, and not the number of stressful events experienced, that is predictive of the development of insomnia (Morin et al., 2003).

It is evident that there is a great deal of heterogeneity in the way in which sleep has changed in response to the pandemic. In one Canadian study, conducted in Spring 2020, three distinct profiles of sleep-related changes to behaviour were observed: those who demonstrated a reduction in their subjective time in bed, those who delayed their sleep time, and those who extended their duration of time in bed (Robillard et al., 2020). Importantly, this study examined clinically significant changes in subjective stress, and found that both the group with reduced time in bed and the delayed sleep group each had a greater proportion of individuals with a clinically significant worsening in stress, relative to the extended time in bed group.

Perhaps counterintuitively, it should be noted that various studies have also demonstrated that sleep has actually *improved* in certain groups of individuals (Kocevska et al., 2020; Partinen et al., 2021). These findings may be due to changes in sleep *timing*, where relative to before the pandemic, people may have had an increased opportunity to obtain sleep, particularly in the context of work days (Korman et al., 2020). One potential reason for this is potentially due to the marked shift towards remote, or flexible, working during the pandemic, which has also potentially led to greater levels of flexibility in the sleep schedule of some individuals (Staller & Randler, 2021; Yuan et al., 2022). Work is an important determinant of sleep quality and

timing and, additionally, other employment-related factors such as work stress, work demands and the time spent commuting to work can also affect sleep (Linton et al., 2015; Myllyntausta et al., 2022; Petrov et al., 2018). One potential reason as to why this increased flexibility could have affected sleep is that at a biological level, this societal shift might have negated the impact of "social jetlag". Specifically, for some individuals, and particularly those with a later diurnal preference, the increased flexibility offered by this societal change is likely to have negated or removed the mismatch between their actual, and desired, timing of sleep (Blume et al., 2020; Wittmann et al., 2006).

As the effect of the pandemic upon sleep has not been consistently negative across individuals, this certainly warrants the further investigation of subgroups who may have had different experiences of the stress–sleep link during the pandemic. For example, it is known from PTSD literature that not everyone develops PTSD following a major traumatic event; figures demonstrate that on average, approximately 10% of military personnel develop PTSD (Kilpatrick et al., 2013; Miao et al., 2018). It would undoubtedly be of value to understand why some groups of people do not experience negative effects upon sleep.

In addition to pertinent trait characteristics that may heighten the risk of sleep disturbances resulting in acute insomnia, there may be a range of situational factors that are relevant in the context of the pandemic, such as occupational or environmental factors. For instance, individuals who work in certain employment sectors, which may put them at a greater actual or perceived risk of COVID-19 infection, or stress, may be at a greater risk of developing stress-related sleep disturbances, and there are even likely to be variations within employment sectors. For example, one study found that healthcare workers had greater levels of subjective work-related stress, relative to non-healthcare staff and, within healthcare staff, paramedic staff reported higher levels of stress than non-paramedic medical doctor staff (Couarraze et al., 2021). In terms of environmental factors, these might include periods of forced or voluntary home confinement, either as a consequence of illness or, for example, due to the lockdown restrictions generally observed earlier in the pandemic; an increase in home-working activity, or an increase in co-sleeping with children during stressful periods, which itself can negatively impact parental sleep (Altena et al., 2020; Teti et al., 2016). All of these factors have the potential to negatively impact sleep, potentially through the sleep/stress pathway (Altena et al., 2020). This may mean that a more precise approach will need to be adopted in order to identify who may be at a high risk of developing acute insomnia. In other words, given that the potential impact of the pandemic is not equitable in terms of stress, specific groups should be targeted for sleep interventions.

There may also be a temporal effect of relative infection severity, driven by the timing of COVID infection "waves". For instance, an international online survey, which had the aim of documenting the prevalence and incidence of sleep disturbances during the pandemic, found that the pandemic severity influenced both sleep disturbances and related daytime symptoms (Partinen et al., 2021). Specifically, this study examined cumulative COVID-19-confirmed deaths as a marker of pandemic severity, and found that the prevalence of sleep disturbances, fatigue and daytime sleepiness increased in countries including the UK and USA, during a period where the pandemic severity was increasing (Partinen et al., 2021). Whilst future work could also examine the impact of case numbers, as this may be related to perceived infection risk, it may be difficult to disentangle the specific impact of this risk from other political, social and psychological factors (Partinen et al., 2021). That said, the severity of the pandemic does appear to be relevant: one large global survey showed that perceived stress was positively associated with the severity of COVID-19 in a given country (Kowal et al., 2020), and longitudinal work from Hong Kong seems to confirm that specific COVID-19 waves can negatively influence sleep disturbances (Lam et al., 2021). Wang and colleagues observed that sleep disturbances were more likely to be present in individuals who believed that COVID-19 had caused a high number of deaths, and those who considered that COVID-19 was not easy to cure (Wang et al., 2020). Taken together, this suggests that particular groups may be at a greater risk of pandemic-related sleep disturbances, and that the fear of infection may play an important role in this relationship.

Additionally, the temporal changes in relation to the pandemic also raise the possibility that as the pandemic progresses, it is possible that for some individuals, the ongoing pandemic could be considered to be a *perpetuating* factor in the context of the 3P model, whereby this may maintain the transition to insomnia disorder, rather than the *precipitating* acute stressor. Within the 3P model, perpetuating factors typically refer to behavioural and cognitive factors in relation to insomnia symptoms and their consequences (Spielman et al., 1987; Spielman et al., 1996). Speculatively, perpetuating factors could encompass pandemic-related behaviours such as reacting to a heightened fear of infection, or the perception of infection severity and/or likelihood during subsequent pandemic "waves", as this has been demonstrated to negatively affect sleep (Lam et al., 2021; Partinen et al., 2021). Other related perpetuating factors might include the mismatch between the ability and opportunity of individuals to sleep, which could also be influenced by pandemic-related factors such as poor mental and/or physical health (Perlis et al., 2021).

The impact of anticipated stress may also be relevant, even in healthy individuals without sleep disturbances, as anticipation can affect both sleep and the HPA axis; observational studies have shown that even the anticipation of future work-related tasks can disrupt objective sleep (Torsvall & Akerstedt, 1988; Torsvall et al., 1987). The anticipation of demand can also affect the magnitude (increase) of the CAR although, in this particular study, neither subjective or objective sleep were affected, most likely as a result of the stressor not being personally salient or of a sufficient duration to disrupt sleep (Elder et al., 2018). The COVID-19 pandemic is highly likely to be considered personally salient and disruptive.

Work should also examine if the HPA axis stress response can make a quantifiable contribution to the risk of acute insomnia: it is possible that individuals who may be "at risk" of acute insomnia during the pandemic may be more sensitive to stress-related sleep disturbances, and this is likely to be accompanied by increased HPA axis

activity. Although stress can be quantified using subjective self-report measures, such as the Perceived Stress Scale (Cohen et al., 1983), work could simultaneously examine the CAR, as this would allow for both subjective stress and objective HPA axis activity to be measured.

Although, as stated, sleep medicine and sleep research-focussed CAR measurement protocols exist (Elder et al., 2014; Elder et al., 2016), these were originally designed with a sleep laboratory environment in mind and may need to be modified or updated to allow for potential COVID-19 restrictions (e.g. social distancing or fear of infection), or other pandemic-related events, which may limit the ability to undertake laboratory research. This may also present a research opportunity: this might facilitate the further development of a bespoke sleep research and sleep medicine CAR protocol that can be utilised within an ambulatory environment. An advantage of this approach is that such a measurement protocol would appropriately balance cost, technical requirements and the required levels of control for the measurement of the CAR in sleep research. This could be done by using the electronic monitoring of saliva sampling, which relies upon time-stamping the opening of saliva collection bottles (Kudielka et al., 2007), and by using actigraphy to verify awakening times and light exposure. Additionally, blackout blinds and/or ultraviolet light bulbs may also be used to minimise the influence of light upon the HPA axis, as light levels can affect the CAR and lead to incorrect measurements (Elder et al., 2014). Participant screening and training to ensure high levels of adherence may also increase measurement accuracy, although the target participant group may need to be considered; for example, individuals with cognitive impairment may find this difficult. Whilst the level of agreement with sleep laboratory protocols should be tested, this may facilitate the measurement of the HPA axis in a home environment, with better levels of control than most ambulatory studies. Moreover, this could be combined with the simultaneous measurement of other relevant physiological stress variables; for example, one recent study has combined ambulatory cardiac monitoring with actigraphy to derive measures including heart rate variability (Rosler et al., 2022).

Concurrent measurement of the HPA axis would also allow for the examination of whether behavioural and/or societal changes that have occurred alongside or as a result of COVID-19 might have increased stress and concurrent HPA axis activity. This could provide a useful insight into particular groups of people, or occupations, who may be at increased risk of developing acute insomnia through this pathway. Finally, studies should focus on examining if the anticipation of highly stressful situations may trigger increased HPA axis activation and result in acute insomnia; experimental work in healthy sleepers has demonstrated that the anticipation of a short period of demand can still activate the CAR, irrespective of whether or not the demand is actually experienced (Elder et al., 2018; Elder et al., 2020).

8 | THERAPEUTIC OPPORTUNITIES FOR ACUTE INSOMNIA

It is beyond the scope of the present review to provide a comprehensive guide for the clinical treatment of acute insomnia during the pandemic, as other reviews provide practical recommendations (Altena et al., 2020). However, there are a number of intervention studies that could be trialled in order to maximise the effectiveness of existing treatments in the context of sleep disturbances caused by COVID-19, and these may also be effective post-pandemic. For instance, these include adapting treatments for use during the pandemic, or targeting particular groups who might be at high risk of developing acute insomnia.

Cognitive behavioural therapy for insomnia (CBT-I) is recommended as a first-line treatment for insomnia disorder (Riemann et al., 2017). However, a major barrier to the widespread delivery and uptake of CBT-I is in the high attrition levels and lack of qualified providers; subsequently, CBT-I may be too time-intensive and resource-intensive to be able to be rolled out at the scale required during the pandemic (Ellis et al., 2015; Sawdon et al., 2021). Although pharmacological approaches, such as benzodiazepines and hypnotic benzodiazepine receptor agonists, can be used in the treatment of insomnia in the short-term (Riemann et al., 2017), these can have a number of side-effects, including drowsiness, tolerance and negative impacts upon cognition (Kripke et al., 2012; Siriwardena et al., 2008; Stranks & Crowe, 2014). Additionally, pharmacological approaches to the treatment of acute insomnia may be particularly unsuitable for particular groups, such as older adults, who are at risk of adverse side-effects and for whom polypharmacy is especially problematic (Elder & Flo-Groeneboom, 2022; Glass et al., 2005).

Given the highly effective nature of CBT-I, and advantages over the pharmacological treatment of insomnia (e.g. the lack of interaction with other medications, good treatment durability, and concomitant reductions in anxiety and depressive symptoms), work should focus on whether the CBT-I treatment regimen can be modified to facilitate the widespread deployment. Indeed, previous work has demonstrated that "one-shot" CBT-I is effective for acute insomnia, where a single 60–70-min session of face-to-face CBT-I is provided alongside a behavioural intervention consisting of a self-help leaflet based on stimulus control, cognitive control and imagery distraction techniques (Ellis et al., 2015). Follow-up work has demonstrated that a one-shot approach is feasible and effective in a group format, and in a male prison environment (Boullin et al., 2016; Randall et al., 2019), therefore, modifications to the traditional CBT-I programme may be effective.

Aside from the advantages over a traditional CBT-I programme in terms of scale and cost, an online or remote behavioural intervention may also have other practical benefits. For instance, online and remote interventions can be delivered without it being necessary to accommodate social distancing measures and, from a feasibility point of view, can mitigate against the fear of contagion that may be present in face-to-face scenarios (Weiner et al., 2020); this is important as the fear of infection may in itself disrupt sleep and the use of remote interventions may be advantageous (Wang et al., 2020). In developing such programmes, consideration should be given as to how adherence can be improved in a remote scenario. It is known from using behavioural interventions for depressive symptoms that online interventions can sometimes result in higher drop-out rates when compared with face-to-face therapy (Webb et al., 2017); this

may be an issue for insomnia research, as attrition rates as high as 50% have been observed in some instances (Luik et al., 2019). Although online CBT-I appears to be promising, work should investigate whether this is effective in the short-term and long-term, as it is a cost-effective method of delivering CBT-I (van der Zweerde et al., 2019). For instance, it may be the case that even if behavioural interventions are shown to be effective, then sleep "booster" interventions may be required to maintain these effects (Ellis et al., 2015). Similarly, the use of videoconferencing software in the delivery of insomnia treatment (i.e. telemedicine) appears to result in good levels of efficacy (Arnedt et al., 2020).

Studies have already shown that CBT-I may help to prevent insomnia in the context of COVID-19. For instance, Cheng et al. have shown that patients with insomnia who had received CBT-I before the outbreak of COVID-19 had less insomnia and depression symptoms, less stress and less COVID-related cognitive intrusions compared with a group that had received sleep education only before the outbreak (Cheng et al., 2020). Others have provided COVID-19-related insomnia treatment to small samples of schoolchildren and university staff (Schlarb et al., 2020; Schlarb et al., 2021), while other CBT-I trials are ongoing (Becker, 2022; Sawdon et al., 2021).

Focussing on the specific impact of stress may also inform the development of specific treatments for acute insomnia. Current approaches to the treatment of acute insomnia primarily rely upon "one-shot" CBT-I techniques that aim to prevent the development of subsequent insomnia disorder (Ellis, 2019). Given the close links between stress, the HPA axis and sleep, work should also examine if interventions that specifically aim to modify and reduce stress can be used to prevent the transition from the acute insomnia phase to insomnia disorder and also reduce HPA axis activity. These could be used in tandem with CBT-I approaches, and may also improve the effectiveness of existing one-shot acute insomnia interventions. For instance, one recent study found that an 8-week mindfulness-based online intervention reduced perceived stress after the first Italian COVID-19 lockdown period (Bossi et al., 2022). Evidence from the PTSD literature indicates that imagery rehearsal, which has typically been used in the context of the treatment of post-traumatic nightmares and involves psychoeducation, imagery exercises and cognitive restructuring, is an effective treatment for post-traumatic insomnia when combined with CBT-I (Brownlow et al., 2015; Nappi et al., 2012); this combination may be applicable and effective in the context of COVID-19.

Given that the economic cost of poor sleepers to society is approximately 10 times greater than the impact of good sleepers (Daley et al., 2009), therapeutic studies should also specifically examine if the impact of an upcoming stressor upon poor sleep can be prevented. In this context, an intervention would function as a form of "sleep vaccination": instead of using an intervention to treat the resulting sleep disturbance, the intervention would be used to maintain good sleep, potentially by mitigating the impact of upcoming stressors upon sleep, in healthy normal sleepers. The sleep vaccination concept is therefore focussed upon the prevention of acute insomnia as, theoretically, it is possible to protect sleep by encouraging individuals to "bank" resources (Ellis, Gehrman et al., 2012a). As the COVID-19 pandemic should be considered an ecologically valid and provocative stressor, the sleep vaccination approach is conceptually attractive and, indeed, an ongoing trial is investigating if this approach might be effective in healthy normal sleepers (Sawdon et al., 2021).

As well as the potential economic advantages of a preventative sleep vaccination approach, there may also be clear individual and societal health benefits of this strategy; for example, sleep may affect the immune response to COVID-19 vaccination or may influence relevant disease outcomes. Sleep disturbances are likely to negatively affect antibody response and immune function (Besedovsky et al., 2012) and, indeed, sleep duration has been shown to be positively associated with post-vaccination antibody response levels (Schmitz et al., 2022), and it has also been shown that poor sleep is associated with prolonged COVID-19-related hospitalisation (Zhang et al., 2020). Therefore, maintaining good sleep health, including potentially through a preventative sleep vaccination approach, is likely to be of significant clinical and research value, both during the pandemic and beyond. For instance, if effective, one possibility is to target groups who are known to be at risk of developing sleep disturbances, including healthcare workers, or other key workers, who exhibit high levels of stress (Couarraze et al., 2021). Similarly, this may also be useful from a sleep health-focussed policy perspective: it has been shown that demographic factors can have a disproportionate negative impact upon COVID-19 outcomes, and it is known that many of these factors can affect sleep in their own right (Brown et al., 2021; Grandner, 2020). It is possible that groups who may be more negatively affected by COVID-19 may be at a greater risk of sleep disturbances related to COVID-19. In the longer term, this may enable a "precision medicine" approach to the prevention and treatment of acute insomnia.

9 | CONCLUSIONS

A range of cross-sectional studies demonstrate that poor sleep and sleep disturbances are associated with the COVID-19 pandemic. The pandemic should be considered a highly stressful life event, which is likely to trigger acute insomnia, potentially as a result of increased HPA axis function. Future work should identify those who are at high risk of acute insomnia (e.g. frontline or healthcare workers, or people with high levels of sleep reactivity) and aim to prevent the transition to insomnia disorder. From a treatment perspective, work should examine if large-scale online behavioural interventions are appropriate and effective, given the scalability and cost of these interventions, and modifying acute insomnia treatment to lessen the impact of stress in addition to improving sleep. Finally, the concept of "sleep vaccination", where interventions are used with the prevention of acute insomnia in mind, should be tested in order to maintain good sleep health.

AUTHOR CONTRIBUTIONS

Greg J. Elder drafted the initial manuscript. All authors contributed to the conceptualisation, writing, critical review and editing of the manuscript.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

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REFERENCES

Alimoradi, Z., Brostrom, A., Tsang, H. W. H., Griffiths, M. D., Haghayegh, S., Ohayon, M. M., … Pakpour, A. H. (2021). Sleep problems during COVID-19 pandemic and its' association to psychological distress: A systematic review and meta-analysis. *EClinicalMedicine*, *36*, 100916. https://doi.org/10.1016/j.eclinm.2021.100916

Altena, E., Baglioni, C., Espie, C. A., Ellis, J., Gavriloff, D., Holzinger, B., … Riemann, D. (2020). Dealing with sleep problems during home confinement due to the COVID-19 outbreak: Practical recommendations from a task force of the European CBT-I academy. *Journal of Sleep Research*, *29*(4), e13052. https://doi.org/10.1111/jsr.13052

Altena, E., Micoulaud-Franchi, J. A., Geoffroy, P. A., Sanz-Arigita, E., Bioulac, S., & Philip, P. (2016). The bidirectional relation between emotional reactivity and sleep: From disruption to recovery. *Behavioral Neuroscience*, *130*(3), 336–350. https://doi.org/10.1037/bne0000128

Arnedt, J. T., Conroy, D. A., Mooney, A., Furgal, A., Sen, A., & Eisenberg, D. (2020). Telemedicine versus face-to-face delivery of cognitive behavioral therapy for insomnia: A randomized controlled noninferiority trial. *Sleep*, *44*(1), 1–11. https://doi.org/10.1093/sleep/zsaa136

Askenasy, J. J., & Lewin, I. (1996). The impact of missile warfare on self-reported sleep quality. Part 1. *Sleep*, *19*(1), 47–51.

Baglioni, C., Battagliese, G., Feige, B., Spiegelhalder, K., Nissen, C., Voderholzer, U., … Riemann, D. (2011). Insomnia as a predictor of depression: A meta-analytic evaluation of longitudinal epidemiological studies. *Journal of Affective Disorders*, *135*(1–3), 10–19. https://doi.org/10.1016/j.jad.2011.01.011

Baliyan, S., Cimadevilla, J. M., de Vidania, S., Pulopulos, M. M., Sandi, C., & Venero, C. (2021). Differential susceptibility to the impact of the COVID-19 pandemic on working memory, empathy, and perceived stress: The role of cortisol and resilience. *Brain Sciences*, *11*(3), 348. https://doi.org/10.3390/brainsci11030348

Bastien, C. H., Vallieres, A., & Morin, C. M. (2004). Precipitating factors of insomnia. *Behavioral Sleep Medicine*, *2*(1), 50–62. https://doi.org/10.1207/s15402010bsm0201_5

Becker, P. M. (2022). Overview of sleep management during COVID-19. *Sleep Medicine*, *91*, 211–218. https://doi.org/10.1016/j.sleep.2021.04.024

Besedovsky, L., Lange, T., & Born, J. (2012). Sleep and immune function. *Pflügers Archiv-European Journal of Physiology*, *463*(1), 121–137. https://doi.org/10.1007/s00424-011-1044-0

Blume, C., Schmidt, M. H., & Cajochen, C. (2020). Effects of the COVID-19 lockdown on human sleep and rest-activity rhythms. *Current Biology*, *30*(14), R795–R797. https://doi.org/10.1016/j.cub.2020.06.021

Bossi, F., Zaninotto, F., D'Arcangelo, S., Lattanzi, N., Malizia, A. P., & Ricciardi, E. (2022). Mindfulness-based online intervention increases well-being and decreases stress after Covid-19 lockdown. *Scientific Reports*, *12*(1), 6483. https://doi.org/10.1038/s41598-022-10361-2

Boullin, P., Ellwood, C., & Ellis, J. G. (2016). Group vs. individual treatment for acute insomnia: A pilot study evaluating a "one-shot" treatment strategy. *Brain Sciences*, *7*(1), 1. https://doi.org/10.3390/brainsci7010001

Brant, H., Wetherell, M. A., Lightman, S., Crown, A., & Vedhara, K. (2010). An exploration into physiological and self-report measures of stress in pre-registration doctors at the beginning and end of a clinical rotation. *Stress*, *13*(2), 155–162. https://doi.org/10.3109/10253890903093778

Bridgland, V. M. E., Moeck, E. K., Green, D. M., Swain, T. L., Nayda, D. M., Matson, L. A., … Takarangi, M. K. T. (2021). Why the COVID-19 pandemic is a traumatic stressor. *PLoS One*, *16*(1), e0240146. https://doi.org/10.1371/journal.pone.0240146

Brown, C., Wilkins, K., Craig-Neil, A., Upshaw, T., & Pinto, A. D. (2021). Reducing inequities during the COVID-19 pandemic: A rapid review and synthesis of public health recommendations. *Public Health Reviews*, *42*, 1604031. https://doi.org/10.3389/phrs.2021.1604031

Brownlow, J. A., Harb, G. C., & Ross, R. J. (2015). Treatment of sleep disturbances in post-traumatic stress disorder: A review of the literature. *Current Psychiatry Reports*, *17*(6), 41. https://doi.org/10.1007/s11920-015-0587-8

Buckley, T. M., & Schatzberg, A. F. (2005). On the interactions of the hypothalamic-pituitary-adrenal (HPA) axis and sleep: Normal HPA axis activity and circadian rhythm, exemplary sleep disorders. *The Journal of Clinical Endocrinology and Metabolism*, *90*(5), 3106–3114. https://doi.org/10.1210/jc.2004-1056

Buijs, R. M., van Eden, C. G., Goncharuk, V. D., & Kalsbeek, A. (2003). The biological clock tunes the organs of the body: Timing by hormones and the autonomic nervous system. *Journal of Endocrinology*, *177*(1), 17–26. https://doi.org/10.1677/joe.0.1770017

Casagrande, M., Favieri, F., Tambelli, R., & Forte, G. (2020). The enemy who sealed the world: Effects quarantine due to the COVID-19 on sleep quality, anxiety, and psychological distress in the Italian population. *Sleep Medicine*, *75*, 12–20. https://doi.org/10.1016/j.sleep.2020.05.011

Cheng, P., Casement, M. D., Kalmbach, D. A., Castelan, A. C., & Drake, C. L. (2020). Digital cognitive behavioral therapy for insomnia promotes later health resilience during the coronavirus disease 19 (COVID-19) pandemic. *Sleep*, *44*(4), zsaa258. https://doi.org/10.1093/sleep/zsaa258

Clow, A., Thorn, L., Evans, P., & Hucklebridge, F. (2004). The awakening cortisol response: Methodological issues and significance. *Stress*, *7*(1), 29–37. https://doi.org/10.1080/10253890410001667205

Cohen, S., Kamarck, T., & Mermelstein, R. (1983). A global measure of perceived stress. *Journal of Health and Social Behavior*, *24*(4), 385–396.

Cooke, J. E., Eirich, R., Racine, N., & Madigan, S. (2020). Prevalence of posttraumatic and general psychological stress during COVID-19: A rapid review and meta-analysis. *Psychiatry Research*, *292*, 113347. https://doi.org/10.1016/j.psychres.2020.113347

Couarraze, S., Delamarre, L., Marhar, F., Quach, B., Jiao, J., Avilés Dorlhiac, R., … Dutheil, F. (2021). The major worldwide stress of healthcare professionals during the first wave of the COVID-19 pandemic–the international COVISTRESS survey. *PLoS One*, *16*(10), e0257840. https://doi.org/10.1371/journal.pone.0257840

Daley, M., Morin, C. M., LeBlanc, M., Gregoire, J. P., & Savard, J. (2009). The economic burden of insomnia: Direct and indirect costs for individuals with insomnia syndrome, insomnia symptoms, and good sleepers. *Sleep*, *32*(1), 55–64.

Dickerson, S. S., & Kemeny, M. E. (2004). Acute stressors and cortisol responses: A theoretical integration and synthesis of laboratory

research. *Psychological Bulletin*, *130*(3), 355–391. https://doi.org/10.1037/0033-2909.130.3.355

Drake, C. L., Richardson, G., Roehrs, T., Scofield, H., & Roth, T. (2004). Vulnerability to stress-related sleep disturbance and hyperarousal. *Sleep*, *27*(2), 285–291.

Dressle, R. J., Feige, B., Spiegelhalder, K., Schmucker, C., Benz, F., Mey, N. C., & Riemann, D. (2022). HPA axis activity in patients with chronic insomnia: A systematic review and meta-analysis of case–control studies. *Sleep Medicine Reviews*, *62*, 101588. https://doi.org/10.1016/j.smrv.2022.101588

Elder, G. J., Barclay, N. L., Wetherell, M. A., & Ellis, J. G. (2018). Anticipated next-day demand affects the magnitude of the cortisol awakening response, but not subjective or objective sleep. *Journal of Sleep Research*, *27*(1), 47–55. https://doi.org/10.1111/jsr.12569

Elder, G. J., Ellis, J. G., Barclay, N. L., & Wetherell, M. A. (2016). Assessing the daily stability of the cortisol awakening response in a controlled environment. *BMC Psychology*, *4*(1), 1–10. https://doi.org/10.1186/s40359-016-0107-6

Elder, G. J., & Flo-Groeneboom, E. (2022). How can light be used to optimise sleep and health in older adults? In *Progress in brain research* (Vol. 273, pp. 331–355). Elsevier.

Elder, G. J., Wetherell, M. A., Barclay, N. L., & Ellis, J. G. (2014). The cortisol awakening response-applications and implications for sleep medicine. *Sleep Medicine Reviews*, *18*(3), 195–204. https://doi.org/10.1016/j.smrv.2013.05.001

Elder, G. J., Wetherell, M. A., Pollet, T. V., Barclay, N. L., & Ellis, J. G. (2020). Experienced demand does not affect subsequent sleep and the cortisol awakening response. *Nature and Science of Sleep*, *12*, 537–543. https://doi.org/10.2147/NSS.S231484

Ellis, J. G. (2019). Cognitive behavioral therapy for insomnia and acute insomnia: Considerations and controversies. *Sleep Medicine Clinics*, *14*(2), 267–274. https://doi.org/10.1016/j.jsmc.2019.01.007

Ellis, J. G., Cushing, T., & Germain, A. (2015). Treating acute insomnia: A randomized controlled trial of a "single-shot" of cognitive behavioral therapy for insomnia. *Sleep*, *38*(6), 971–978. https://doi.org/10.5665/sleep.4752

Ellis, J. G., Gehrman, P., Espie, C. A., Riemann, D., & Perlis, M. L. (2012a). Acute insomnia: Current conceptualizations and future directions. *Sleep Medicine Reviews*, *16*(1), 5–14. https://doi.org/10.1016/j.smrv.2011.02.002

Ellis, J. G., Perlis, M. L., Espie, C. A., Grandner, M. A., Bastien, C. H., Barclay, N. L., … Gardani, M. (2021). The natural history of insomnia: Predisposing, precipitating, coping and perpetuating factors over the early developmental course of insomnia. *Sleep*, *44*(9), zsab095. https://doi.org/10.1093/sleep/zsab095

Ellis, J. G., Perlis, M. L., Neale, L. F., Espie, C. A., & Bastien, C. H. (2012b). The natural history of insomnia: Focus on prevalence and incidence of acute insomnia. *Journal of Psychiatric Research*, *46*(10), 1278–1285. https://doi.org/10.1016/j.jpsychires.2012.07.001

Fries, E., Dettenborn, L., & Kirschbaum, C. (2009). The cortisol awakening response (CAR): Facts and future directions. *International Journal of Psychophysiology*, *72*(1), 67–73. https://doi.org/10.1016/j.ijpsycho.2008.03.014

Gallagher, S., Sumner, R. C., Muldoon, O. T., Creaven, A.-M., & Hannigan, A. (2016). Unemployment is associated with lower cortisol awakening and blunted dehydroepiandrosterone responses. *Psychoneuroendocrinology*, *69*, 41–49. https://doi.org/10.1016/j.psyneuen.2016.03.011

Glass, J., Lanctot, K. L., Herrmann, N., Sproule, B. A., & Busto, U. E. (2005). Sedative hypnotics in older people with insomnia: Meta-analysis of risks and benefits. *BMJ*, *331*(7526), 1169. https://doi.org/10.1136/bmj.38623.768588.47

Grandner, M. A. (2020). Sleep, health, and society. *Sleep Medicine Clinics*, *15*(2), 319–340. https://doi.org/10.1016/j.jsmc.2020.02.017

Grimaldi, D., Reid, K. J., Papalambros, N. A., Braun, R. I., Malkani, R. G., Abbott, S. M., … Zee, P. C. (2021). Autonomic dysregulation and sleep homeostasis in insomnia. *Sleep*, *44*(6), zsaa274. https://doi.org/10.1093/sleep/zsaa274

Hellhammer, D. H., Wust, S., & Kudielka, B. M. (2009). Salivary cortisol as a biomarker in stress research. *Psychoneuroendocrinology*, *34*(2), 163–171. https://doi.org/10.1016/j.psyneuen.2008.10.026

Herman, J. P., Figueiredo, H., Mueller, N. K., Ulrich-Lai, Y., Ostrander, M. M., Choi, D. C., & Cullinan, W. E. (2003). Central mechanisms of stress integration: Hierarchical circuitry controlling hypothalamo–pituitary–adrenocortical responsiveness. *Frontiers in Neuroendocrinology*, *24*(3), 151–180. https://doi.org/10.1016/j.yfrne.2003.07.001

Hsing, A., Zhang, J. S., Peng, K., Lin, W.-K., Wu, Y.-H., Hsing, J. C., … Lounsbury, D. W. (2020). A rapid assessment of psychological distress and well-being: impact of the COVID-19 pandemic and Shelter-in-Place. *Available at SSRN* 3578809.

Hucklebridge, F., Hussain, T., Evans, P., & Clow, A. (2005). The diurnal patterns of the adrenal steroids cortisol and dehydroepiandrosterone (DHEA) in relation to awakening. *Psychoneuroendocrinology*, *30*(1), 51–57. https://doi.org/10.1016/j.psyneuen.2004.04.007

Irwin, M. R., Carrillo, C., Sadeghi, N., Bjurstrom, M. F., Breen, E. C., & Olmstead, R. (2022). Prevention of incident and recurrent major depression in older adults with insomnia: A randomized clinical trial. *JAMA Psychiatry*, *79*(1), 33–41. https://doi.org/10.1001/jamapsychiatry.2021.3422

Jahrami, H. A., Alhaj, O. A., Humood, A. M., Alenezi, A. F., Fekih-Romdhane, F., AlRasheed, M. M., … Vitiello, M. V. (2022). Sleep disturbances during the COVID-19 pandemic: A systematic review, meta-analysis, and meta-regression. *Sleep Medicine Reviews*, *62*(101), 591. https://doi.org/10.1016/j.smrv.2022.101591

Kalmbach, D. A., Cuamatzi-Castelan, A. S., Tonnu, C. V., Tran, K. M., Anderson, J. R., Roth, T., & Drake, C. L. (2018). Hyperarousal and sleep reactivity in insomnia: Current insights. *Nature and Science of Sleep*, *10*, 193–201. https://doi.org/10.2147/NSS.S138823

Kato, H., Asukai, N., Miyake, Y., Minakawa, K., & Nishiyama, A. (1996). Post-traumatic symptoms among younger and elderly evacuees in the early stages following the 1995 Hanshin-Awaji earthquake in Japan. *Acta Psychiatrica Scandinavica*, *93*(6), 477–481. https://doi.org/10.1111/j.1600-0447.1996.tb10680.x

Kilpatrick, D. G., Resnick, H. S., Milanak, M. E., Miller, M. W., Keyes, K. M., & Friedman, M. J. (2013). National estimates of exposure to traumatic events and PTSD prevalence using DSM-IV and DSM-5 criteria. *Journal of Traumatic Stress*, *26*(5), 537–547. https://doi.org/10.1002/jts.21848

Kocevska, D., Blanken, T. F., Van Someren, E. J. W., & Rosler, L. (2020). Sleep quality during the COVID-19 pandemic: Not one size fits all. *Sleep Medicine*, *76*, 86–88. https://doi.org/10.1016/j.sleep.2020.09.029

Korman, M., Tkachev, V., Reis, C., Komada, Y., Kitamura, S., Gubin, D., … Roenneberg, T. (2020). COVID-19-mandated social restrictions unveil the impact of social time pressure on sleep and body clock. *Scientific Reports*, *10*(1), 22225. https://doi.org/10.1038/s41598-020-79299-7

Kowal, M., Coll-Martin, T., Ikizer, G., Rasmussen, J., Eichel, K., Studzinska, A., … Ahmed, O. (2020). Who is the most stressed during the COVID-19 pandemic? Data from 26 countries and areas. *Applied Psychology: Health and Well-Being*, *12*(4), 946–966. https://doi.org/10.1111/aphw.12234

Kripke, D. F., Langer, R. D., & Kline, L. E. (2012). Hypnotics' association with mortality or cancer: A matched cohort study. *BMJ Open*, *2*(1), e000850. https://doi.org/10.1136/bmjopen-2012-000850

Kudielka, B. M., Hawkley, L. C., Adam, E. K., & Cacioppo, J. T. (2007). Compliance with ambulatory saliva sampling in the Chicago health, aging, and social relations study and associations with social support. *Annals of Behavioral Medicine*, *34*(2), 209–216. https://doi.org/10.1007/bf02872675

Lam, C. S., Yu, B. Y., Cheung, D. S. T., Cheung, T., Lam, S. C., Chung, K. F., … Yeung, W. F. (2021). Sleep and mood disturbances during the

COVID-19 outbreak in an urban Chinese population in Hong Kong: A longitudinal study of the second and third waves of the outbreak. *International Journal of Environmental Research and Public Health*, *18* (16), 1–11. https://doi.org/10.3390/ijerph18168444

Lee, J., & Harley, V. R. (2012). The male fight-flight response: A result of SRY regulation of catecholamines? *Bio Essays*, *34*(6), 454–457. https://doi.org/10.1002/bies.201100159

Leerssen, J., Lakbila-Kamal, O., Dekkers, L. M. S., Ikelaar, S. L. C., Albers, A. C. W., Blanken, T. F., … Van Someren, E. J. W. (2022). Treating insomnia with high risk of depression using therapist-guided digital cognitive, behavioral, and circadian rhythm support interventions to prevent worsening of depressive symptoms: A randomized controlled trial. *Psychotherapy and Psychosomatics*, *91*(3), 168–179. https://doi.org/10.1159/000520282

Li, M., Zhang, X. W., Hou, W. S., & Tang, Z. Y. (2014). Insomnia and risk of cardiovascular disease: A meta-analysis of cohort studies. *International Journal of Cardiology*, *176*(3), 1044–1047. https://doi.org/10.1016/j.ijcard.2014.07.284

Linton, S. J., Kecklund, G., Franklin, K. A., Leissner, L. C., Sivertsen, B., Lindberg, E., … Hall, C. (2015). The effect of the work environment on future sleep disturbances: A systematic review. *Sleep Medicine Reviews*, *23*, 10–19. https://doi.org/10.1016/j.smrv.2014.10.010

Lo Martire, V., Caruso, D., Palagini, L., Zoccoli, G., & Bastianini, S. (2020). Stress & sleep: A relationship lasting a lifetime. *Neuroscience and Biobehavioral Reviews*, *117*, 65–77.

López, C. M., Lancaster, C. L., Wilkerson, A., Gros, D. F., Ruggiero, K. J., & Acierno, R. (2019). Residual insomnia and nightmares postintervention symptom reduction among veterans receiving treatment for comorbid PTSD and depressive symptoms. *Behavior Therapy*, *50*(5), 910–923. https://doi.org/10.1016/j.beth.2019.01.006

Luik, A. I., van der Zweerde, T., van Straten, A., & Lancee, J. (2019). Digital delivery of cognitive behavioral therapy for insomnia. *Current Psychiatry Reports*, *21*(7), 50. https://doi.org/10.1007/s11920-019-1041-0

Marcil, M. J., Cyr, S., Marin, M. F., Rosa, C., Tardif, J. C., Guay, S., … Brouillette, J. (2022). Hair cortisol change at COVID-19 pandemic onset predicts burnout among health personnel. *Psychoneuroendocrinology*, *138*(105), 645. https://doi.org/10.1016/j.psyneuen.2021.105645

McEwen, B. S. (2007). Physiology and neurobiology of stress and adaptation: Central role of the brain. *Physiological Reviews*, *87*(3), 873–904. https://doi.org/10.1152/physrev.00041.2006

Mellman, T. A., David, D., Kulick-Bell, R., Hebding, J., & Nolan, B. (1995). Sleep disturbance and its relationship to psychiatric morbidity after hurricane Andrew. *The American Journal of Psychiatry*, *152*(11), 1659–1663.

Miao, X.-R., Chen, Q.-B., Wei, K., Tao, K.-M., & Lu, Z.-J. (2018). Posttraumatic stress disorder: From diagnosis to prevention. *Military Medical Research*, *5*(1), 32. https://doi.org/10.1186/s40779-018-0179-0

Morin, C. M., Rodrigue, S., & Ivers, H. (2003). Role of stress, arousal, and coping skills in primary insomnia. *Psychosomatic Medicine*, *65*(2), 259–267. https://doi.org/10.1097/01.psy.0000030391.09558.a3

Myllyntausta, S., Kronholm, E., Pulakka, A., Pentti, J., Vahtera, J., Virtanen, M., & Stenholm, S. (2022). Association of job strain with accelerometer-based sleep duration and timing of sleep among older employees. *Journal of Sleep Research*, *31*(2), e13498. https://doi.org/10.1111/jsr.13498

Nappi, C. M., Drummond, S. P., & Hall, J. M. (2012). Treating nightmares and insomnia in posttraumatic stress disorder: A review of current evidence. *Neuropharmacology*, *62*(2), 576–585. https://doi.org/10.1016/j.neuropharm.2011.02.029

Newby, J. M., O'Moore, K., Tang, S., Christensen, H., & Faasse, K. (2020). Acute mental health responses during the COVID-19 pandemic in Australia. *PLoS One*, *15*(7), e0236562. https://doi.org/10.1371/journal.pone.0236562

Ohayon, M. M. (2002). Epidemiology of insomnia: What we know and what we still need to learn. *Sleep Medicine Reviews*, *6*(2), 97–111. https://doi.org/10.1053/smrv.2002.0186

Pallesen, S., Sivertsen, B., Nordhus, I. H., & Bjorvatn, B. (2014). A 10-year trend of insomnia prevalence in the adult Norwegian population. *Sleep Medicine*, *15*(2), 173–179. https://doi.org/10.1016/j.sleep.2013.10.009

Partinen, M., Holzinger, B., Morin, C. M., Espie, C., Chung, F., Penzel, T., … Bjorvatn, B. (2021). Sleep and daytime problems during the COVID-19 pandemic and effects of coronavirus infection, confinement and financial suffering: A multinational survey using a harmonised questionnaire. *BMJ Open*, *11*(12), e050672. https://doi.org/10.1136/bmjopen-2021-050672

Perez-Carbonell, L., Meurling, I. J., Wassermann, D., Gnoni, V., Leschziner, G., Weighall, A., … Steier, J. (2020). Impact of the novel coronavirus (COVID-19) pandemic on sleep. *Journal of Thoracic Disease*, *12*(Suppl 2), S163–S175. https://doi.org/10.21037/jtd-cus-2020-015

Perlis, M. L., Morales, K. H., Vargas, I., Posner, D. A., Grandner, M. A., Muench, A. L., … Ellis, J. G. (2021). The natural history of insomnia: Does sleep extension differentiate between those that do and do not develop chronic insomnia? *Journal of Sleep Research*, *30*, e13342. https://doi.org/10.1111/jsr.13342

Perlis, M. L., Vargas, I., Ellis, J. G., Grandner, M. A., Morales, K. H., Gencarelli, A., … Thase, M. E. (2020). The natural history of insomnia: The incidence of acute insomnia and subsequent progression to chronic insomnia or recovery in good sleeper subjects. *Sleep*, *43*(6), zsz299. https://doi.org/10.1093/sleep/zsz299

Petrov, M. E., Weng, J., Reid, K. J., Wang, R., Ramos, A. R., Wallace, D. M., … Patel, S. R. (2018). Commuting and sleep: Results from the Hispanic community health study/study of Latinos Sueno ancillary study. *American Journal of Preventive Medicine*, *54*(3), e49–e57. https://doi.org/10.1016/j.amepre.2017.11.006

Prinz, P., Bailey, S., Moe, K., Wilkinson, C., & Scanlan, J. (2001). Urinary free cortisol and sleep under baseline and stressed conditions in healthy senior women: Effects of estrogen replacement therapy. *Journal of Sleep Research*, *10*(1), 19–26. https://doi.org/10.1046/j.1365-2869.2001.00236.x

Rajcani, J., Vytykacova, S., Solarikova, P., & Brezina, I. (2021). Stress and hair cortisol concentrations in nurses during the first wave of the COVID-19 pandemic. *Psychoneuroendocrinology*, *129*(105), 245. https://doi.org/10.1016/j.psyneuen.2021.105245

Randall, C., Nowakowski, S., & Ellis, J. G. (2019). Managing acute insomnia in prison: Evaluation of a "one-shot" cognitive behavioral therapy for insomnia (CBT-I) intervention. *Behavioral Sleep Medicine*, *17*(6), 827–836. https://doi.org/10.1080/15402002.2018.1518227

Reynolds, C. F., 3rd, Hoch, C. C., Buysse, D. J., Houck, P. R., Schlernitzauer, M., Frank, E., … Kupfer, D. J. (1992). Electroencephalographic sleep in spousal bereavement and bereavement-related depression of late life. *Biological Psychiatry*, *31*(1), 69–82. https://doi.org/10.1016/0006-3223(92)90007-M

Reynolds, C. F., 3rd, Hoch, C. C., Buysse, D. J., Houck, P. R., Schlernitzauer, M., Pasternak, R. E., … Kupfer, D. J. (1993). Sleep after spousal bereavement: A study of recovery from stress. *Biological Psychiatry*, *34*(11), 791–797. https://doi.org/10.1016/0006-3223(93)90068-O

Riemann, D., Baglioni, C., Bassetti, C., Bjorvatn, B., Dolenc Groselj, L., Ellis, J. G., … Spiegelhalder, K. (2017). European guideline for the diagnosis and treatment of insomnia. *Journal of Sleep Research*, *26*(6), 675–700. https://doi.org/10.1111/jsr.12594

Riemann, D., Nissen, C., Palagini, L., Otte, A., Perlis, M. L., & Spiegelhalder, K. (2015). The neurobiology, investigation, and treatment of chronic insomnia. *Lancet Neurology*, *14*(5), 547–558. https://doi.org/10.1016/S1474-4422(15)00021-6

Riemann, D., Spiegelhalder, K., Feige, B., Voderholzer, U., Berger, M., Perlis, M., & Nissen, C. (2010). The hyperarousal model of insomnia: A review of the concept and its evidence. *Sleep Medicine Reviews*, *14*(1), 19–31. https://doi.org/10.1016/j.smrv.2009.04.002

Riemann, D., & Voderholzer, U. (2003). Primary insomnia: A risk factor to develop depression? *Journal of Affective Disorders*, *76*(1–3), 255–259. https://doi.org/10.1016/s0165-0327(02)00072-1

Robillard, R., Saad, M., Edwards, J., Solomonova, E., Pennestri, M. H., Daros, A., … Kendzerska, T. (2020). Social, financial and psychological stress during an emerging pandemic: Observations from a population survey in the acute phase of COVID-19. *BMJ Open*, *10*(12), e043805. https://doi.org/10.1136/bmjopen-2020-043805

Rosler, L., van der Lande, G., Leerssen, J., Vandegriffe, A. G., Lakbila-Kamal, O., Foster-Dingley, J. C., … van Someren, E. J. W. (2022). Combining cardiac monitoring with actigraphy aids nocturnal arousal detection during ambulatory sleep assessment in insomnia. *Sleep*, *45*(5), zsac031. https://doi.org/10.1093/sleep/zsac031

Saalwirth, C., & Leipold, B. (2021). Well-being and sleep in stressful times of the COVID-19 pandemic: Relations to worrying and different coping strategies. *Stress and Health*, *37*(5), 973–985. https://doi.org/10.1002/smi.3057

Salari, N., Hosseinian-Far, A., Jalali, R., Vaisi-Raygani, A., Rasoulpoor, S., Mohammadi, M., … Khaledi-Paveh, B. (2020). Prevalence of stress, anxiety, depression among the general population during the COVID-19 pandemic: A systematic review and meta-analysis. *Globalization and Health*, *16*(1), 57. https://doi.org/10.1186/s12992-020-00589-w

Sawdon, O. L., Elder, G. J., Santhi, N., Alfonso-Miller, P., & Ellis, J. G. (2021). Testing an early online intervention for the treatment of disturbed sleep during the COVID-19 pandemic in self-reported good and poor sleepers (sleep COVID-19): Study protocol for a randomised controlled trial. *Trials*, *22*(1), 913. https://doi.org/10.1186/s13063-021-05888-0

Schlarb, A. A., Fründ, J. P., Kovacevic, T., & Faber, J. (2021). Modularized iCBT-I self-learn training for university staff—Prevention and early intervention in the SARS-CoV-2 crisis. *Somnologie*, *25*(1), 29–37. https://doi.org/10.1007/s11818-021-00301-z

Schlarb, A. A., Schulte, H., Selbmann, A., & Och, I. (2020). Online cognitive behavioral group therapy (iCBT-I) for insomnia for school children and their parents. *Somnologie*, *24*(4), 259–266. https://doi.org/10.1007/s11818-020-00280-7

Schmitz, N. C. M., van der Werf, Y. D., & Lammers-van der Holst, H. M. (2022). The importance of sleep and circadian rhythms for vaccination success and susceptibility to viral infections. *Clocks & Sleep*, *4*(1), 66–79. https://doi.org/10.3390/clockssleep4010008

Siriwardena, A. N., Qureshi, M. Z., Dyas, J. V., Middleton, H., & Orner, R. (2008). Magic bullets for insomnia? Patients' use and experiences of newer (Z drugs) versus older (benzodiazepine) hypnotics for sleep problems in primary care. *British Journal of General Practice*, *58*(551), 417–422. https://doi.org/10.3399/bjgp08X299290

Spencer, R. L., & Deak, T. (2017). A users guide to HPA axis research. *Physiology & Behavior*, *178*, 43–65. https://doi.org/10.1016/j.physbeh.2016.11.014

Spielman, A. J., Caruso, L. S., & Glovinsky, P. B. (1987). A behavioral perspective on insomnia treatment. *The Psychiatric Clinics of North America*, *10*(4), 541–553.

Spielman, A. J., Nunes, J., & Glovinsky, P. B. (1996). Insomnia. *Neurologic Clinics*, *14*(3), 513–543.

Staller, N., & Randler, C. (2021). Changes in sleep schedule and chronotype due to COVID-19 restrictions and home office. *Somnologie*, *25*(2), 131–137. https://doi.org/10.1007/s11818-020-00277-2

Stranks, E. K., & Crowe, S. F. (2014). The acute cognitive effects of zopiclone, zolpidem, zaleplon, and eszopiclone: A systematic review and meta-analysis. *Journal of Clinical and Experimental Neuropsychology*, *36*(7), 691–700. https://doi.org/10.1080/13803395.2014.928268

Teti, D. M., Shimizu, M., Crosby, B., & Kim, B. R. (2016). Sleep arrangements, parent-infant sleep during the first year, and family functioning. *Developmental Psychology*, *52*(8), 1169–1181. https://doi.org/10.1037/dev0000148

Torsvall, L., & Akerstedt, T. (1988). Disturbed sleep while being on-call: An EEG study of ships' engineers. *Sleep*, *11*(1), 35–38.

Torsvall, L., Castenfors, K., Åkerstedt, T., & Fröberg, J. A. N. (1987). Sleep at sea: A diary study of the effects of unattended machinery space watch duty. *Ergonomics*, *30*(9), 1335–1340. https://doi.org/10.1080/00140138708966027

van Dalfsen, J. H., & Markus, C. R. (2018). The influence of sleep on human hypothalamic–pituitary–adrenal (HPA) axis reactivity: A systematic review. *Sleep Medicine Reviews*, *39*, 187–194. https://doi.org/10.1016/j.smrv.2017.10.002

van der Zweerde, T., Lancee, J., Ida Luik, A., & van Straten, A. (2019). Internet-delivered cognitive behavioral therapy for insomnia: Tailoring cognitive behavioral therapy for insomnia for patients with chronic insomnia. *Sleep Medicine Clinics*, *14*(3), 301–315. https://doi.org/10.1016/j.jsmc.2019.04.002

Walker, J. L., Vargas, I., Drake, C. L., Ellis, J. G., Muench, A., & Perlis, M. L. (2022). The natural history of insomnia: High sleep reactivity interacts with greater life stress to predict the onset of acute insomnia. *Sleep*, *45*(9), zsac149. https://doi.org/10.1093/sleep/zsac149

Wang, J., Gong, Y., Chen, Z., Wu, J., Feng, J., Yan, S., … Yin, X. (2020). Sleep disturbances among Chinese residents during the coronavirus disease 2019 outbreak and associated factors. *Sleep Medicine*, *74*, 199–203. https://doi.org/10.1016/j.sleep.2020.08.002

Webb, C. A., Rosso, I. M., & Rauch, S. L. (2017). Internet-based cognitive-behavioral therapy for depression: Current progress and future directions. *Harvard Review of Psychiatry*, *25*(3), 114–122. https://doi.org/10.1097/HRP.0000000000000139

Weiner, L., Berna, F., Nourry, N., Severac, F., Vidailhet, P., & Mengin, A. C. (2020). Efficacy of an online cognitive behavioral therapy program developed for healthcare workers during the COVID-19 pandemic: The reduction of stress (REST) study protocol for a randomized controlled trial. *Trials*, *21*(1), 870. https://doi.org/10.1186/s13063-020-04772-7

Wittmann, M., Dinich, J., Merrow, M., & Roenneberg, T. (2006). Social jetlag: Misalignment of biological and social time. *Chronobiology International*, *23*(1–2), 497–509. https://doi.org/10.1080/07420520500545979

Xia, L., Chen, G. H., Li, Z. H., Jiang, S., & Shen, J. (2013). Alterations in hypothalamus-pituitary–adrenal/thyroid axes and gonadotropin-releasing hormone in the patients with primary insomnia: A clinical research. *PLoS One*, *8*(8), e71065. https://doi.org/10.1371/journal.pone.0071065

Yuan, R. K., Zitting, K. M., Maskati, L., & Huang, J. (2022). Increased sleep duration and delayed sleep timing during the COVID-19 pandemic. *Scientific Reports*, *12*(1), 10937. https://doi.org/10.1038/s41598-022-14-782-x

Zhang, J., Lam, S. P., Li, S. X., Ma, R. C., Kong, A. P., Chan, M. H., … Wing, Y. K. (2014). A community-based study on the association between insomnia and hypothalamic–pituitary–adrenal axis: Sex and pubertal influences. *The Journal of Clinical Endocrinology and Metabolism*, *99*(6), 2277–2287. https://doi.org/10.1210/jc.2013-3728

Zhang, J., Xu, D., Xie, B., Zhang, Y., Huang, H., Liu, H., … Yuan, S. (2020). Poor-sleep is associated with slow recovery from lymphopenia and an increased need for ICU care in hospitalized patients with COVID-19: A retrospective cohort study. *Brain, Behavior, and Immunity*, *88*, 50–58. https://doi.org/10.1016/j.bbi.2020.05.075

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