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RESEARCH ARTICLE

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Influence of social jetlag on daytime sleepiness in obstructive sleep apnea

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Summary

Social jetlag is the discrepancy between socially determined sleep timing on workdays and biologically determined sleep timing on days free of social obligation. Poor circadian timing of sleep may worsen sleep quality and increase daytime sleepiness in obstructive sleep apnea (OSA). We analysed de-identified data from 2,061 participants (75.2% male, mean [SD] age 48.6 [13.4] years) who completed Sleep Apnea Global Interdisciplinary Consortium (SAGIC) research questionnaires and underwent polysomnography at 11 international sleep clinic sites. Social jetlag was calculated as the absolute difference in the midpoints of sleep between weekdays and weekends. Daytime sleepiness was assessed using the Epworth Sleepiness Scale (ESS). Linear regression analyses were performed to estimate the association between social jetlag and daytime sleepiness, with consideration of age, sex, body mass index, ethnicity, insomnia, alcohol consumption, and habitual sleep duration as confounders. Of the participants, 61.5% had <1 h of social jetlag, 27.5% had 1 to <2 h, and 11.1% had ≥2 h. Compared to those with <1 h of social jetlag, those with ≥2 h of social jetlag had 2.07 points higher ESS (95% confidence interval [CI] 0.77–3.38, $p = 0.002$), and those with 1 to <2 h of social jetlag had 0.80 points higher ESS (95% CI 0.04–1.55, $p = 0.04$) after adjustment for potential confounding. Interaction with OSA severity was observed; social jetlag appeared to have the greatest effect on daytime sleepiness in mild OSA. As social jetlag exacerbates daytime sleepiness in OSA, improving sleep timing may be a simple but novel therapeutic target for reducing the impact of OSA.

KEYWORDS

circadian rhythm, cross-sectional study, obstructive sleep apnea, polysomnography, sleep habits, sleepiness

1 | INTRODUCTION

Obstructive sleep apnea (OSA) is an increasingly prevalent sleep disorder thought to affect almost 1 billion people globally (Benjafield et al., 2019). OSA is characterised by recurring episodes of partial or complete upper airway collapse during sleep. The repetitive obstructions and intermittent hypoxaemia associated with sleep fragmentation can lead to excessive daytime sleepiness (He & Kapur, 2017).

However, there are many factors known to contribute to excessive daytime sleepiness, beyond OSA. Residual sleepiness occurs in a significant proportion of patients with OSA despite seemingly adequate treatment, especially in younger individuals (Pepin et al., 2009). Circadian disruption may potentially exacerbate the negative health consequences of OSA. However, this has not been previously explored.

Social jetlag is conceptualised as the discrepancy between socially determined sleep timing on workdays and biologically determined sleep timing on free days that is, days free of work or educational commitments (Wittmann et al., 2006). Social jetlag is a highly prevalent form of circadian disruption, with an estimated 30% of Australians experiencing >1 h of social jetlag and 30% of Europeans experiencing >2 h of social jetlag (Lang et al., 2018; Roenneberg et al., 2012). Social jetlag has been associated with depression, obesity, diabetes, and academic underachievement (Diaz-Morales & Escribano, 2015; Islam et al., 2020; Parsons et al., 2015). Sleep–wake timing is regulated by endogenous circadian rhythms, an internal homeostatic process, and exogenous social constraints such as work timing (Borbely, 1982; Foster et al., 2013). Early work schedules may force individuals to sleep and wake at inappropriate times compared to their internally regulated circadian preference. In particular, people who prefer a late sleep onset often suffer from sleep deprivation on weekdays (workdays), which causes them to sleep longer on weekends to compensate (Roenneberg et al., 2003). Social jetlag is a chronic form of circadian misalignment that causes sleep disruption. Increasing social jetlag decreases sleep quality in shift workers and patients with sleep disorders (Kang et al., 2020; Reis et al., 2020). Poor sleep quality and fragmented sleep both impair daytime function and increase daytime sleepiness (Stepanski, 2002).

To date, no studies have examined the effect of social jetlag on daytime sleepiness in patients with OSA. Poor circadian timing of sleep potentially contributes to poorer sleep quality, decreased sleep duration, and increased daytime sleepiness in OSA. If this hypothesis is correct, then changing the timing of sleep may be a simple but novel therapeutic target for reducing the impact of circadian disruption in OSA. This study aimed to examine whether social jetlag exacerbates the impact of OSA on daytime functioning by evaluating the severity of social jetlag and its association with daytime sleepiness in patients with OSA, while adjusting for a range of potential confounding factors. We hypothesised that social jetlag increases daytime sleepiness in patients with OSA.

2 | METHODS

2.1 | Study design

This study used de-identified data from the Sleep Apnea Global Interdisciplinary Consortium (SAGIC). Founded in 2012, SAGIC involves 11 sleep clinic sites, including Chang Gung Memorial Hospital in Taipei, Taiwan; Charité University Hospital in Berlin, Germany; Korea University in Seoul, South Korea; Universidade Federal de São Paulo in São Paulo, Brazil; Landspitali University Hospital in Reykjavík, Iceland; Ohio State University in Columbus, USA; the University of Pennsylvania in Philadelphia, USA; Royal North Shore Hospital in Sydney (University of Sydney), Australia; Sir Charles Gairdner Hospital in Perth, Australia; Ruijin Hospital in Shanghai, China; and Peking University in Beijing, China. SAGIC recruits patients who have presented to these sites for sleep testing (Keenan et al., 2018; Qin et al., 2021; Sutherland et al., 2019). Recruited participants complete SAGIC research questionnaires and undergo polysomnography. Sleep studies were scored by technicians at each site to the same standard and high concordance (Magalang et al., 2013; Magalang et al., 2019).

2.2 | Ethics

The data were collected with ethics approval from each of the SAGIC sites. The use of the de-identified data for this study was approved by the SAGIC investigators, who act as the data custodians. No further ethics approval was required for this study according to the University of Sydney Human Ethics Committee.

2.3 | Social jetlag

Sleep and wake times were obtained from participant responses to questions about usual bed and wake-up times on weekdays and weekends. The midpoint of sleep (mid-sleep) was calculated from usual bed and wake-up times on weekdays and weekends. Social jetlag was calculated as the absolute time difference between mid-sleep on weekdays and mid-sleep on weekends (Wittmann et al., 2006). This definition of social jetlag assumes that participants have regular sleep–wake patterns (which excludes shift workers), weekdays correspond to workdays and weekend days correspond to free days.

2.4 | Daytime sleepiness

Daytime sleepiness was assessed using the Epworth Sleepiness Scale (ESS) (Johns, 1991). This scale consists of eight questions describing eight different activities. Participants rate their chances of falling asleep for each activity, ranging from 'would never doze off' to 'high chance of dozing off'. Each question is scored on a scale from 0 to 3 and the total ESS score ranges from 0 to 24. A higher ESS score represents a greater degree of subjective daytime sleepiness. The reliability and validity of the ESS in patients with OSA has been well established in multiple languages (Beiske et al., 2009; Chen et al., 2002; Chiner et al., 1999; Vignatelli et al., 2003).

2.5 | Participants

The participant selection flow chart is shown in Figure 1. The total number of participants in the SAGIC dataset was 5,829 as of

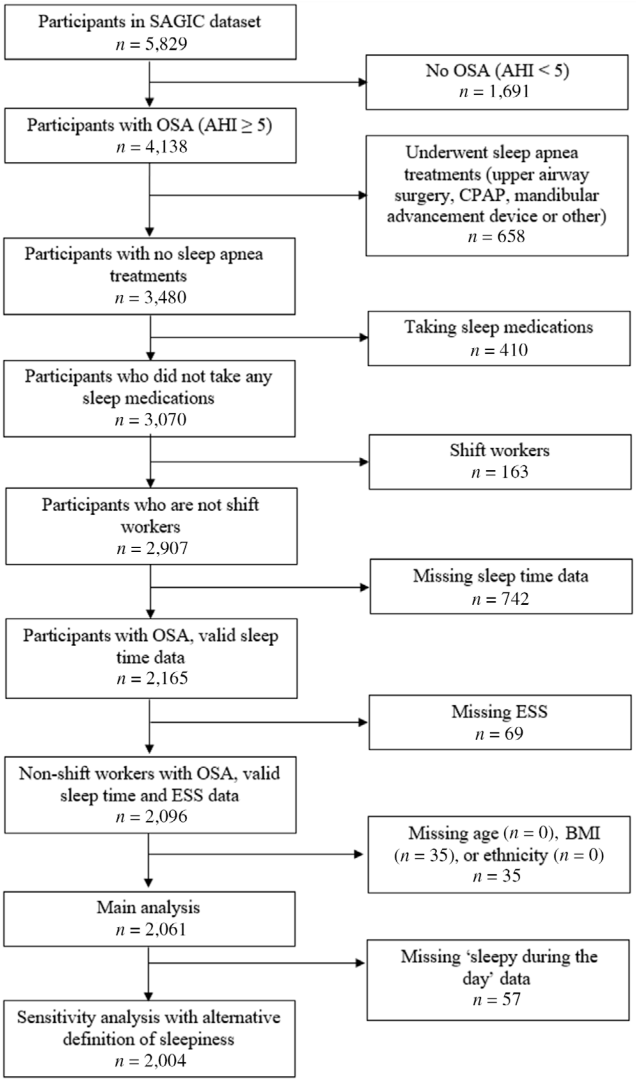

FIGURE 1 Flow chart of the analysis of participants. Abbreviations: AHI, Apnea–Hypopnea Index; BMI, body mass index; CPAP, continuous positive airway pressure; ESS, Epworth Sleepiness Scale; OSA, obstructive sleep apnea; SAGIC, Sleep Apnea Global Interdisciplinary Consortium

January 24, 2022. Only participants with diagnosed OSA (Apnea–Hypopnea Index [AHI] ≥5 events/h) were included in the present study. Participants who were previously treated for sleep apnea (with upper airway surgery, continuous positive airway pressure, mandibular advancement device or other) were excluded because the treatments reduce the severity of OSA and daytime sleepiness. Those who took sleep medications were also excluded due to potential effects on daytime sleepiness. Shift working participants were excluded due to potentially irregular sleep–wake patterns and difficulties in ascertaining social jetlag. Participants with invalid or missing sleep time data, ESS data, or covariate data were further excluded. The remaining 2,061 participants were included in the main analysis on social jetlag and daytime sleepiness.

2.6 | Covariates

The AHI was taken from polysomnography and used for categorising OSA severity (i.e., mild, AHI 5 to <15; moderate, AHI 15 to <30; severe, AHI ≥30 events/h). Age and body mass index (BMI) were assessed as part of the overnight sleep study visit. Sex, ethnicity, shift work, insomnia, alcohol consumption, and habitual sleep duration were self-reported as part of the SAGIC Sleep Questionnaire. Ethnicity categories included 'Asian', 'Caucasian', 'Central/South American', and 'Other' (which combined Pacific Islander, African, Other, Do not know, and Multiple). Alcohol consumption was reported as consuming alcohol 0, 1 or ≥2 days/week. Habitual sleep duration was based on self-report in response to 'How many hours do you sleep on average?', with responses measured in hours and minutes. We note that 558 participants did not report their habitual sleep duration (27.8% of analysis sample). Insomnia was assessed using the Insomnia Symptom Questionnaire (Okun et al., 2009). A diagnosis of insomnia was assigned to participants if they experienced at least one of three sleep symptoms (difficulty initiating sleep, difficulty maintaining sleep, or unrefreshing sleep) at least 3 times/week for ≥4 weeks and at least one aspect of daily life was affected 'quite a bit' or 'extremely' by these symptoms.

2.7 | Statistical analysis

The IBM® Statistical Package for the Social Sciences (SPSS®) version 26 was used for statistical analysis. Social jetlag was calculated as the absolute difference in the midpoints of sleep between weekdays and weekends and split into three groups (<1, 1 to <2, and ≥2 h). Associations between social jetlag and other variables were assessed using the chi-square test for categorical variables and one-way analysis of variance for continuous variables.

Age, sex, BMI, ethnicity, insomnia, alcohol consumption, and habitual sleep duration were considered potential confounders. A directed acyclic graph was constructed to consider the causal interrelationships between the exposure, outcome, and potential confounding variables and to evaluate which of the variables was necessary to include in adjusted models in order to estimate the association between social jetlag and sleepiness. The advantage of this approach is that it explicitly considers the network of causal relationships between the exposure and outcome variables and potential covariates. Only age and ethnicity were considered necessary covariates in adjusted models estimating the relationship between social jetlag and daytime sleepiness (Appendix S1, Figure S1).

Linear regression analyses were performed to estimate the effect of the predictor social jetlag (<1, 1 to <2, ≥2 h, categorical) on the outcome of daytime sleepiness (continuous), with adjustment for confounding. Model 0 is a simple regression between social jetlag and ESS. Model 1 adjusted only for OSA severity (AHI, continuous). To explore potential interactions between OSA severity and social jetlag on daytime sleepiness, an interaction term was

TABLE 1 Participant characteristics according to social jetlag categories ($n = 2061$)

Participant characteristic		Social jetlag			Test statistic (df), p [a]
		Nil/minimal <1 h	Moderate 1 to <2 h	Severe ≥2 h	
Number of participants, *n* (row %)		1,267 (61.5)	566 (27.5)	228 (11.1)	
ESS score, mean (SD)		10.6 (5.5)	10.8 (5.0)	11.5 (5.5)	F (2, 2058) = 2.79, 0.061
AHI, events/h *n* (col %)	5 to <15	545 (43.0)	241 (42.6)	92 (40.4)	$X^2(4) = 1.00$, 0.910
	15 to <30	318 (25.1)	145 (25.6)	64 (28.1)	
	≥30	404 (31.9)	180 (31.8)	72 (31.6)	
Age, years, mean (SD)		51.2 (13.6)	45.1 (11.9)	43.1 (12.2)	F (2, 2058) = 67.35, < 0.001
Sex (male), *n* (col %)		963 (76.0)	421 (74.4)	166 (72.8)	$X^2(2) = 1.35$, 0.510
BMI, kg/m^2, mean (SD)		29.1 (5.5)	30.6 (6.8)	32.8 (8.6)	F (2, 2058) = 38.68, < 0.001
Ethnicity, *n* (col %)	Asian	865 (68.3)	323 (57.1)	79 (34.6)	$X^2(6) = 116.93$, < 0.001
	Caucasian	255 (20.1)	153 (27.0)	84 (36.8)	
	Central/South American	67 (5.3)	36 (6.4)	41 (18.0)	
	Other[b]	80 (6.3)	54 (9.5)	24 (10.5)	
Habitual sleep duration, h, mean (SD)		6.9 (1.7)	6.9 (1.7)	6.5 (1.4)	F (2, 1501) = 3.72, 0.025
Missing data, *n* (col %)		355 (28.0)	148 (26.1)	54 (23.7)	
Insomnia, *n* (col %)		217 (17.1)	99 (17.5)	64 (28.1)	$X^2(2) = 15.85$, <0.001
Alcohol consumption, *n* (col %)	0 days/week	564 (51.1)	226 (44.8)	92 (45.1)	$X^2(14) = 43.87$, <0.001
	1 day/week	232 (21.0)	163 (32.3)	65 (31.9)	
	≥2 days/week	307 (27.9)	116 (22.9)	47 (23.0)	
Missing data, *n* (col%)		164 (12.9)	61 (10.8)	24 (10.5)	
Site, *n* (col %)	Australia	95 (7.5)	28 (4.9)	14 (6.1)	$X^2(8) = 149.76$, <0.001
	Brazil	103 (8.1)	58 (10.2)	57 (25.0)	
	China and Taiwan	868 (68.5)	318 (56.2)	77 (33.8)	
	Europe	124 (9.8)	93 (16.4)	48 (21.1)	
	USA	77 (6.1)	69 (12.2)	32 (14.0)	

Abbreviations: AHI, Apnea–Hypopnea Index; BMI, body mass index; ESS, Epworth Sleepiness Scale; SD, standard deviation.
[a]Based on chi-square test for categorical variables and one-way analysis of variance for continuous variables.
[b]Other ethnicities include Pacific Islander, African, Other, Do not know and Multiple.

created. Model 2 adjusted for age (years, continuous), ethnicity (categorical), and the interaction term (social jetlag × AHI). Potential site differences were explored and reported in (Appendix S2, Table S1).

Two sensitivity analyses were performed. The first sensitivity analysis examined whether social jetlag is associated with an alternative definition of excessive daytime sleepiness defined as ESS scores and the question 'Do you feel sleepy during the day?' from the Basic Nordic Sleepiness Questionnaire (BNSQ) (Partinen & Gislason, 1995). This definition of sleepiness may be better for detecting clinically significant sleepiness that has an impact on health consequences and quality of life (Thorarinsdottir et al., 2019; Thorarinsdottir et al., 2021) (Appendix S3, Table S3). The second sensitivity analysis was performed to examine whether social jetlag is associated with daytime sleepiness using the traditional approach of adjusting for all covariates that were significantly different between the social jetlag groups (the traditional 'Table 1 approach') (Appendix S4, Table S4). The significance level was defined as $p < 0.05$ for all analyses.

3 | RESULTS

3.1 | Participant characteristics

Participant characteristics are summarised by categories of social jetlag in Table 1. Social jetlag was significantly associated with younger age, higher BMI, ethnicity, shorter habitual sleep durations, and greater rates of insomnia. There were no significant differences in social jetlag by OSA severity or gender groups. There was no significant difference in the mean ESS score by social jetlag categories, although there was a trend towards higher ESS scores with increasing social jetlag (Table 1). When sleepiness was defined as feeling sleepy, having risk of dozing off, or both symptoms, social jetlag was significantly associated with sleepiness ($p = 0.01$, Appendix S3, Table S2).

3.2 | Linear regression results

The results of the regression modelling are presented in Table 2. Compared to social jetlag of <1 h, severe social jetlag (of ≥2 h) was

TABLE 2 Multivariable linear regression analysis of the relationship between social jetlag and Epworth Sleepiness Scale (ESS) score ($n = 2,061$)

B coefficient (95% CI)	Model 0	*p*	Model 1[a]	*p*	Model 2[b]	*p*
Social jetlag <1 h	Reference	-	Reference	-	Reference	-
Social jetlag 1 to <2 h	0.21 (−0.32, 0.74)	0.443	0.17 (−0.35, 0.69)	0.523	**0.80 (0.04, 1.55)**	**0.040**
Social jetlag ≥2 h	**0.91 (0.15, 1.67)**	**0.019**	**0.80 (0.06, 1.53)**	**0.035**	**2.07 (0.77, 3.38)**	**0.002**
AHI	-	-	**0.05 (0.04, 0.06)**	**<0.001**	**0.06 (0.04, 0.07)**	**<0.001**
Social jetlag × AHI	-	-	-	-	**−0.26 (−0.51, −0.01)**	**0.044**
Age	-	-	-	-	−0.01 (−0.03, 0.01)	0.470
Ethnicity						
Asian	-	-	-	-	Reference	-
Caucasian	-	-	-	-	**−1.13 (−1.73, −0.53)**	**<0.001**
Central/South American	-	-	-	-	−0.22 (−1.15, 0.71)	0.643
Other[c]	-	-	-	-	**−1.68 (−2.56, −0.80)**	**<0.001**

Note: Bold values statistically significant at $p < 0.05$.

Abbreviations: AHI, Apnea–Hypopnea Index; CI, confidence interval; ESS, Epworth Sleepiness Scale.

[a]Model 1 adjusted only for AHI (continuous).

[b]Model 2 additionally adjusted for age (year, continuous), ethnicity (Asian, Caucasian, Central/South American, or Other), and the social jetlag × AHI interaction term.

[c]Other ethnicities include Pacific Islander, African, Other, Do not know and Multiple.

significantly associated with daytime sleepiness on unadjusted analysis, but moderate social jetlag (1 to <2 h) was not (Table 2). After adjusting for age and ethnicity, moderate and severe social jetlag were significantly associated with daytime sleepiness compared to nil/minimal social jetlag (Table 2). Moderate social jetlag was associated with an increase of 0.80 points on the ESS (95% confidence interval [CI] 0.04–1.55, $p = 0.04$), and severe social jetlag an increase of 2.07 points compared to nil/minimal social jetlag (95% CI 0.77–3.38, $p = 0.002$). There was a significant interaction between OSA severity and social jetlag on daytime sleepiness (Figure 2). Social jetlag appears to have the strongest effect on daytime sleepiness in patients with mild OSA (Figure 2).

Stratification by site of recruitment revealed significant associations between severe social jetlag and daytime sleepiness in Brazil after adjusting for confounding but found no other significant associations at other sites (Appendix S2, Table S1). While the effect sizes for moderate and severe social jetlag for each site are consistent with the overall findings, there is large uncertainty around the results due to the diminished sample sizes, and as such we cannot make firm conclusions about differences by recruitment site/country (Appendix S2, Table S1).

In the sensitivity analysis using an alternative definition of sleepiness defined as a risk of dozing off (ESS score >10), feeling sleepy, or both symptoms, results showed that the difference in sleepiness among social jetlag categories was largely driven by subjects who were both at risk of dozing off and were feeling sleepy (Appendix S3, Table S3). In this sleepiness category, severe social jetlag was associated with 2.24 points higher ESS compared to nil/minimal social jetlag (95% CI 1.19–4.23, $p = 0.01$) after adjusting for confounding. However, among those with only one of the two sleepiness symptoms, the ESS score was not significantly associated with social jetlag (Appendix S3, Table S3).

We note that social jetlag was not significantly associated with daytime sleepiness after adjusting for all significant covariates from Table 1 (Appendix S4, Table S4); however, we do not believe this approach is appropriate given that adjusting for sleep duration and insomnia may include over-adjustment for the consequences of social jetlag that contribute to greater sleepiness.

4 | DISCUSSION

This is the first study to examine the effect of social jetlag on daytime sleepiness in a clinic-based cohort of patients with OSA. Although there were no significant differences in daytime sleepiness among the different categories of social jetlag, moderate and severe social jetlag were significantly associated with daytime sleepiness in OSA after accounting for confounding. Severe social jetlag was associated with a 2.07-point higher ESS score compared to nil/minimal social jetlag. With a minimum clinically important difference in ESS score estimated to be at least 2 points in OSA (Patel et al., 2018), patients with severe social jetlag may experience a noticeable improvement in daytime sleepiness if they are able to eliminate their social jetlag. Social jetlag also seemed to have the greatest effect on daytime sleepiness in mild OSA. This may be due to a ceiling effect in those with more severe OSA, that is, social jetlag may contribute more significantly to sleepiness in mildly sleepy patients than in those already who are already quite sleepy. When we examined an alternative definition of

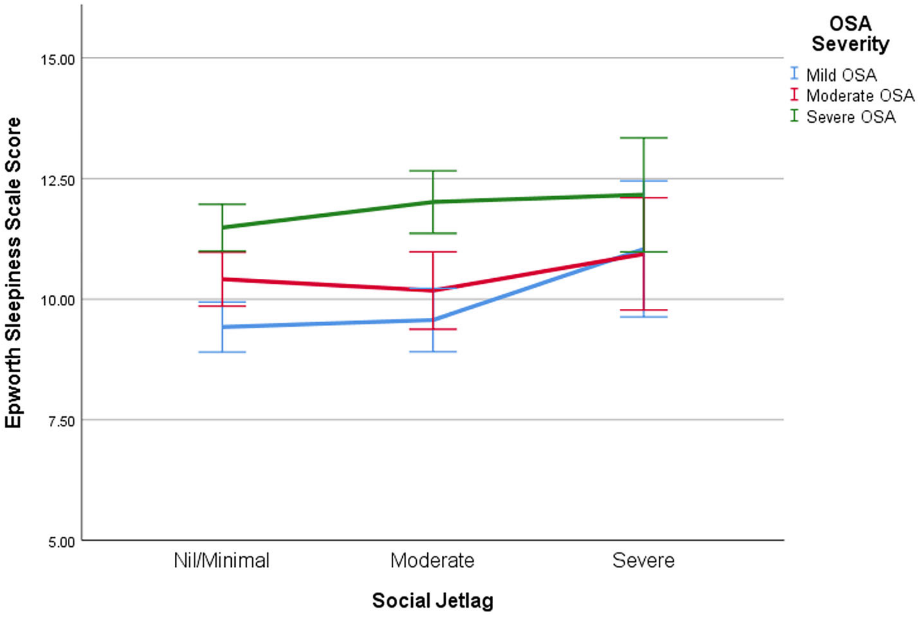

FIGURE 2 Interaction effect of obstructive sleep apnea severity and social jetlag on daytime sleepiness. Social jetlag: Nil/minimal = <1 h, moderate = 1 to <2 h, severe = ≥2 h. OSA severity: mild = AHI 5 to <15, moderate = 15 to <30, severe = ≥30 events/h. Abbreviations: OSA, obstructive sleep apnea. Error bars are 95% confidence intervals

sleepiness classified as a risk of dozing off, feeling sleepy three or more times during the day, or both symptoms, we found that the association appeared to be driven by patients who reported both a risk of dozing off and feeling sleepy.

The present findings are consistent with the results of a previous study that found a significant association between social jetlag and daytime sleepiness in Japanese adults without OSA (Okajima et al., 2021). In that study, social jetlag significantly contributed to daytime sleepiness in individuals with <2 h of sleep debt. However, social jetlag was no longer significantly associated with daytime sleepiness in individuals with >2 h of sleep debt (Okajima et al., 2021). In the present study, both moderate and severe social jetlag were associated with increased daytime sleepiness compared to nil/minimal social jetlag in OSA. This suggests that regular sleep timing to reduce social jetlag may reduce excessive daytime sleepiness in patients with OSA. This simple therapeutic approach could be easily trialled in patients with OSA. While our study examined only untreated patients, the impact of social jetlag in treated patients should be explored in the future. This is particularly important given the high prevalence of residual sleepiness in patients with OSA who are treated with positive airway pressure devices. Previous studies have found that 12%–55% of patients with OSA have residual sleepiness despite efficacious treatment (Gasa et al., 2013; Koutsourelakis et al., 2009; Pepin et al., 2009). Understanding the association between social jetlag and residual sleepiness might open new pathways and offer more personalised approaches when treating patients with OSA.

We did not adjust for sleep debt (sleep duration) in our modelling because of the potential for overadjustment according to our causal diagram and the large amount of missing data for habitual sleep duration, which would lead to selection bias. However, habitual sleep durations are on average lower in those with more severe social jetlag (Table 1), and less habitual sleep is also a cause of social jetlag. Future studies should clarify whether social jetlag and other forms of circadian disruption significantly contribute to sleepiness and other OSA symptomology once sleep debt is taken into account.

Another factor in patients with OSA that may contribute to the association between social jetlag and daytime sleepiness is the amount of rapid eye movement (REM) sleep. People with more severe social jetlag typically sleep later and longer on weekends. REM sleep has an inherent circadian variation, with greater amounts of REM sleep in the morning (Czeisler et al., 1980; Endo et al., 1981). REM sleep has been associated with more severe OSA due to an increase in upper airway collapsibility and reduced respiratory drive (Varga & Mokhlesi, 2019). Consequently, it is possible that elevated daytime sleepiness is due to increased severity of OSA in people who experience more social jetlag and have more REM sleep on free days. The increased duration of REM sleep due to social jetlag may also exacerbate other health consequences associated with REM OSA, such as hypertension and insulin resistance (Varga & Mokhlesi, 2019). Future studies should examine the relationship between social jetlag and the proportion of REM and non-REM sleep at different severities of OSA.

There are several limitations in this study. Firstly, a causal relationship cannot be established based on the results of a cross-sectional study. Future intervention studies should examine whether a regular sleep schedule that reduces disparities in sleep timing between work and free days can reduce daytime sleepiness in patients with OSA. The second limitation is the estimation of social jetlag based on a self-reported sleep questionnaire, which is prone to recall bias. This decreases the accuracy of the social jetlag measurements (non-differential misclassification) and increases the likelihood of a null result. Furthermore, the questions about sleep timing only asked about weekdays and weekends rather than workdays and work-free days, a distinction which would better reflect disparities in sleep timing due to work schedules. Thirdly, although age and ethnicity were identified as potential confounders, the observed associations may be due to other unrecognised and unmeasured confounding variables. Finally, although excessive daytime sleepiness is the most common presenting complaint in OSA, the symptom is not reported by all patients. One review reported that only 3%–18% of men with OSA and 1%–17% of women with OSA experienced excessive daytime sleepiness (Franklin & Lindberg, 2015). Other studies have found that approximately 40% of patients with OSA belong in a distinct cluster of 'excessively sleepy' patients, one of three distinct OSA clusters based on symptoms and comorbidities (Keenan et al., 2018; Ye et al., 2014). Hence, patients with OSA might not experience daytime sleepiness despite being socially jetlagged, suggesting other consequences of circadian disruption on OSA should be explored in future studies. The major strengths of this study include adjustment for major confounders and a large sample size of 2,061 participants from 11 different sites across many continents. The findings are likely generalisable to other populations with OSA.

As the mechanism by which OSA contributes to daytime sleepiness is currently unknown, it may be worthwhile for future studies to determine the contribution of social jetlag to other factors that predispose to daytime sleepiness in OSA. Additionally, there may be a role for investigating other impacts of social jetlag in OSA as circadian disruption may exacerbate the effect of OSA on other health consequences. For example, OSA has been associated with changes in cortisol, insulin resistance, blood pressure and body temperature, all of which exhibit circadian rhythmicity, and which may be further exacerbated by social jetlag (Koritala et al., 2021; Stenvers et al., 2019). OSA has also been found to alter the circadian rhythmicity of blood pressure (Butler et al., 2020). OSA has been associated with increased risks of cardiovascular disease, metabolic dysfunction, and cognitive impairment (Krysta et al., 2017; Levy et al., 2007), and circadian misalignment has also been linked to a similar range of health conditions (Chen et al., 2020; James et al., 2017; Sudy et al., 2019). Thus, further studies should explore the contribution and impact of circadian disruption in OSA and examine the relationship between social jetlag and other consequences of OSA.

5 | CONCLUSION

In conclusion, social jetlag is a form of chronic circadian disruption that contributes to greater sleepiness in OSA. Reducing social jetlag may alleviate subjective daytime sleepiness, particularly in patients with mild OSA. Future studies should examine the relationship between social jetlag and other consequences of OSA. If such relationships are discovered, then improving the circadian timing of sleep may be a simple method of reducing the impact of OSA.

AUTHOR CONTRIBUTIONS

Conceptualisation and design: Charley Ximing Jin, Yu Sun Bin. Data analysis and interpretation: all authors. Drafting the article: Charley Ximing Jin, Yu Sun Bin, Kate Sutherland, Peter Cistulli. Critical revision of the article: all authors. Final approval of the version to be published: Charley Ximing Jin, Yu Sun Bin.

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CONFLICT OF INTEREST

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All other authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the the Sleep Apnoea Global Interdisciplinary Consortium upon reasonable request.

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REFERENCES

Beiske, K. K., Kjelsberg, F. N., Ruud, E. A., & Stavem, K. (2009). Reliability and validity of a Norwegian version of the Epworth sleepiness scale. *Sleep & Breathing*, *13*(1), 65–72. https://doi.org/10.1007/s11325-008-0202-x

Benjafield, A. V., Ayas, N. T., Eastwood, P. R., Heinzer, R., Ip, M. S. M., Morrell, M. J., … Malhotra, A. (2019). Estimation of the global prevalence and burden of obstructive sleep apnoea: A literature-based analysis. *The Lancet Respiratory Medicine*, *7*(8), 687–698. https://doi.org/10.1016/S2213-2600(19)30198-5

Borbely, A. A. (1982). A two process model of sleep regulation. *Human Neurobiology*, *1*(3), 195–204.

Butler, M. P., Thosar, S. S., Smales, C., DeYoung, P. N., Wu, H., Hussain, M. V., … Shea, S. A. (2020). Effects of obstructive sleep apnea on endogenous circadian rhythms assessed during relaxed wakefulness; an exploratory analysis. *Chronobiology International*, *37*(6), 856–866. https://doi.org/10.1080/07420528.2020.1740723

Chen, N. H., Johns, M. W., Li, H. Y., Chu, C. C., Liang, S. C., Shu, Y. H., … Wang, P. C. (2002). Validation of a Chinese version of the Epworth sleepiness scale. *Quality of Life Research*, *11*(8), 817–821. https://doi.org/10.1023/a:1020818417949

Chen, P. S., Chiu, W. T., Hsu, P. L., Lin, S. C., Peng, I. C., Wang, C. Y., & Tsai, S. J. (2020). Pathophysiological implications of hypoxia in human diseases. *Journal of Biomedical Science*, *27*(1), 63. https://doi.org/10.1186/s12929-020-00658-7

Chiner, E., Arriero, J. M., Signes-Costa, J., Marco, J., & Fuentes, I. (1999). Validation of the Spanish version of the Epworth sleepiness scale in patients with a sleep apnea syndrome. *Archivos de Bronconeumología*, *35*(9), 422–427. https://doi.org/10.1016/s0300-2896(15)30037-5

Czeisler, C. A., Zimmerman, J. C., Ronda, J. M., Moore-Ede, M. C., & Weitzman, E. D. (1980). Timing of REM sleep is coupled to the circadian rhythm of body temperature in man. *Sleep*, *2*(3), 329–346.

Diaz-Morales, J. F., & Escribano, C. (2015). Social jetlag, academic achievement and cognitive performance: Understanding gender/sex differences. *Chronobiology International*, *32*(6), 822–831. https://doi.org/10.3109/07420528.2015.1041599

Endo, S., Kobayashi, T., Yamamoto, T., Fukuda, H., Sasaki, M., & Ohta, T. (1981). Persistence of the circadian rhythm of REM sleep: A variety of experimental manipulations of the sleep-wake cycle. *Sleep*, *4*(3), 319–328. https://doi.org/10.1093/sleep/4.3.319

Foster, R. G., Peirson, S. N., Wulff, K., Winnebeck, E., Vetter, C., & Roenneberg, T. (2013). Sleep and circadian rhythm disruption in social jetlag and mental illness. *Progress in Molecular Biology and Translational Science*, *119*, 325–346. https://doi.org/10.1016/B978-0-12-396971-2.00011-7

Franklin, K. A., & Lindberg, E. (2015). Obstructive sleep apnea is a common disorder in the population-a review on the epidemiology of sleep apnea. *Journal of Thoracic Disease*, *7*(8), 1311–1322. https://doi.org/10.3978/j.issn.2072-1439.2015.06.11

Gasa, M., Tamisier, R., Launois, S. H., Sapene, M., Martin, F., Stach, B., … Scientific Council of the Sleep Registry of the French Federation of Pneumology, F.F.P. (2013). Residual sleepiness in sleep apnea patients treated by continuous positive airway pressure. *Journal of Sleep Research*, *22*(4), 389–397. https://doi.org/10.1111/jsr.12039

He, K., & Kapur, V. K. (2017). Sleep-disordered breathing and excessive daytime sleepiness. *Sleep Medicine Clinics*, *12*(3), 369–382. https://doi.org/10.1016/j.jsmc.2017.03.010

Islam, Z., Hu, H., Akter, S., Kuwahara, K., Kochi, T., Eguchi, M., … Mizoue, T. (2020). Social jetlag is associated with an increased likelihood of having depressive symptoms among the Japanese working population: The Furukawa nutrition and health study. *Sleep*, *43*(1), zsz204. https://doi.org/10.1093/sleep/zsz204

James, S. M., Honn, K. A., Gaddameedhi, S., & Van Dongen, H. P. A. (2017). Shift work: Disrupted circadian rhythms and sleep-implications for health and well-being. *Current Sleep Medicine Reports*, *3*(2), 104–112. https://doi.org/10.1007/s40675-017-0071-6

Johns, M. W. (1991). A new method for measuring daytime sleepiness: The Epworth sleepiness scale. *Sleep*, *14*(6), 540–545. https://doi.org/10.1093/sleep/14.6.540

Kang, H., Lee, M., & Jang, S. J. (2020). The impact of social jetlag on sleep quality among nurses: A cross-sectional survey. *International Journal of Environmental Research and Public Health*, *18*(1), 47. https://doi.org/10.3390/ijerph18010047

Keenan, B. T., Kim, J., Singh, B., Bittencourt, L., Chen, N. H., Cistulli, P. A., … Pack, A. I. (2018). Recognizable clinical subtypes of obstructive sleep apnea across international sleep centers: A cluster analysis. *Sleep*, *41*(3), zsx214. https://doi.org/10.1093/sleep/zsx214

Koritala, B. S. C., Conroy, Z., & Smith, D. F. (2021). Circadian biology in obstructive sleep apnea. *Diagnostics*, *11*(6), 1082. https://doi.org/10.3390/diagnostics11061082

Koutsourelakis, I., Perraki, E., Economou, N. T., Dimitrokalli, P., Vagiakis, E., Roussos, C., & Zakynthinos, S. (2009). Predictors of residual sleepiness in adequately treated obstructive sleep apnoea patients. *The European Respiratory Journal*, *34*(3), 687–693. https://doi.org/10.1183/09031936.00124708

Krysta, K., Bratek, A., Zawada, K., & Stepanczak, R. (2017). Cognitive deficits in adults with obstructive sleep apnea compared to children and adolescents. *Journal of Neural Transmission*, *124*(Suppl 1), 187–201. https://doi.org/10.1007/s00702-015-1501-6

Lang, C. J., Reynolds, A. C., Appleton, S. L., Taylor, A. W., Gill, T. K., McEvoy, R. D., … Adams, R. A. (2018). Sociodemographic and behavioural correlates of social jetlag in Australian adults: Results from the 2016 National Sleep Health Foundation Study. *Sleep Medicine*, *51*, 133–139. https://doi.org/10.1016/j.sleep.2018.06.014

Levy, P., Tamisier, R., & Pepin, J. L. (2007). Obstructive sleep apnea syndrome. *La Revue du Praticien*, *57*(14), 1569–1580.

Magalang, U. J., Chen, N. H., Cistulli, P. A., Fedson, A. C., Gislason, T., Hillman, D., … Investigators, S. (2013). Agreement in the scoring of respiratory events and sleep among international sleep centers. *Sleep*, *36*(4), 591–596. https://doi.org/10.5665/sleep.2552

Magalang, U. J., Johns, J. N., Wood, K. A., Mindel, J. W., Lim, D. C., Bittencourt, L. R., … Pack, A. I. (2019). Home sleep apnea testing: Comparison of manual and automated scoring across international sleep centers. *Sleep & Breathing*, *23*(1), 25–31. https://doi.org/10.1007/s11325-018-1715-6

Okajima, I., Komada, Y., Ito, W., & Inoue, Y. (2021). Sleep debt and social jetlag associated with sleepiness, mood, and work performance among workers in Japan. *International Journal of Environmental Research and Public Health*, *18*(6), 2908. https://doi.org/10.3390/ijerph18062908

Okun, M. L., Kravitz, H. M., Sowers, M. F., Moul, D. E., Buysse, D. J., & Hall, M. (2009). Psychometric evaluation of the insomnia symptom questionnaire: A self-report measure to identify chronic insomnia. *Journal of Clinical Sleep Medicine*, *5*(1), 41–51.

Parsons, M. J., Moffitt, T. E., Gregory, A. M., Goldman-Mellor, S., Nolan, P. M., Poulton, R., & Caspi, A. (2015). Social jetlag, obesity and metabolic disorder: Investigation in a cohort study. *International Journal of Obesity*, *39*(5), 842–848. https://doi.org/10.1038/ijo.2014.201

Partinen, M., & Gislason, T. (1995). Basic Nordic sleep questionnaire (BNSQ): A quantitated measure of subjective sleep complaints. *Journal of Sleep Research*, *4*(S1), 150–155. https://doi.org/10.1111/j.1365-2869.1995.tb00205.x

Patel, S., Kon, S. S. C., Nolan, C. M., Barker, R. E., Simonds, A. K., Morrell, M. J., & Man, W. D. (2018). The Epworth sleepiness scale: Minimum clinically important difference in obstructive sleep apnea. *American Journal of Respiratory and Critical Care Medicine*, *197*(7), 961–963. https://doi.org/10.1164/rccm.201704-0672LE

Pepin, J. L., Viot-Blanc, V., Escourrou, P., Racineux, J. L., Sapene, M., Levy, P., … Mallart, A. (2009). Prevalence of residual excessive sleepiness in CPAP-treated sleep apnoea patients: The French multicentre study. *The European Respiratory Journal*, *33*(5), 1062–1067. https://doi.org/10.1183/09031936.00016808

Qin, H., Keenan, B. T., Mazzotti, D. R., Vaquerizo-Villar, F., Kraemer, J. F., Wessel, N., … Penzel, T. (2021). Heart rate variability during wakefulness as a marker of obstructive sleep apnea severity. *Sleep*, *44*(5), zsab018. https://doi.org/10.1093/sleep/zsab018

Reis, C., Pilz, L. K., Keller, L. K., Paiva, T., & Roenneberg, T. (2020). Social timing influences sleep quality in patients with sleep disorders. *Sleep Medicine*, *71*, 8–17. https://doi.org/10.1016/j.sleep.2020.02.019

Roenneberg, T., Allebrandt, K. V., Merrow, M., & Vetter, C. (2012). Social jetlag and obesity. *Current Biology*, *22*(10), 939–943. https://doi.org/10.1016/j.cub.2012.03.038

Roenneberg, T., Wirz-Justice, A., & Merrow, M. (2003). Life between clocks: Daily temporal patterns of human chronotypes. *Journal of Biological Rhythms*, *18*(1), 80–90. https://doi.org/10.1177/0748730402239679

Stenvers, D. J., Scheer, F., Schrauwen, P., la Fleur, S. E., & Kalsbeek, A. (2019). Circadian clocks and insulin resistance. *Nature Reviews. Endocrinology*, *15*(2), 75–89. https://doi.org/10.1038/s41574-018-0122-1

Stepanski, E. J. (2002). The effect of sleep fragmentation on daytime function. *Sleep*, *25*(3), 268–276. https://doi.org/10.1093/sleep/25.3.268

Sudy, A. R., Ella, K., Bodizs, R., & Kaldi, K. (2019). Association of social jetlag with sleep quality and autonomic cardiac control during Sleep in young healthy men. *Frontiers in Neuroscience*, *13*, 950. https://doi.org/10.3389/fnins.2019.00950

Sutherland, K., Keenan, B. T., Bittencourt, L., Chen, N. H., Gislason, T., Leinwand, S., … Investigators, S. (2019). A global comparison of anatomic risk factors and their relationship to obstructive sleep apnea severity in clinical samples. *Journal of Clinical Sleep Medicine*, *15*(4), 629–639. https://doi.org/10.5664/jcsm.7730

Thorarinsdottir, E. H., Bjornsdottir, E., Benediktsdottir, B., Janson, C., Gislason, T., Aspelund, T., … Arnardottir, E. S. (2019). Definition of excessive daytime sleepiness in the general population: Feeling sleepy relates better to sleep-related symptoms and quality of life than the Epworth sleepiness scale score. Results from an epidemiological study. *Journal of Sleep Research*, *28*(6), e12852. https://doi.org/10.1111/jsr.12852

Thorarinsdottir, E. H., Janson, C., Aspelund, T., Benediktsdottir, B., Juliusson, S., Gislason, T., … Keenan, B. T. (2021). Different components of excessive daytime sleepiness and the change with positive airway pressure treatment in patients with obstructive sleep apnea: Results from the Icelandic sleep apnea cohort (ISAC). *Journal of Sleep Research*, *31*, e13528. https://doi.org/10.1111/jsr.13528

Varga, A. W., & Mokhlesi, B. (2019). REM obstructive sleep apnea: Risk for adverse health outcomes and novel treatments. *Sleep & Breathing*, *23*(2), 413–423. https://doi.org/10.1007/s11325-018-1727-2

Vignatelli, L., Plazzi, G., Barbato, A., Ferini-Strambi, L., Manni, R., Pompei, F., … GINSEN. (2003). Italian version of the Epworth sleepiness scale: External validity. *Neurological Sciences*, *23*(6), 295–300. https://doi.org/10.1007/s100720300004

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

Ye, L., Pien, G. W., Ratcliffe, S. J., Bjornsdottir, E., Arnardottir, E. S., Pack, A. I., … Gislason, T. (2014). The different clinical faces of obstructive sleep apnoea: A cluster analysis. *The European Respiratory Journal*, *44*(6), 1600–1607. https://doi.org/10.1183/09031936.00032314

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