



Circadian Rhythms in Obsessive-Compulsive Disorder: Recent Findings and Recommendations for Future Research

Rebecca C. Cox¹ · Bunmi O. Olatunji¹

Published online: 4 June 2019

© Springer Science+Business Media, LLC, part of Springer Nature 2019

Abstract

Purpose of Review Circadian rhythms are a topic of growing interest in mental health, particularly in obsessive-compulsive disorder. However, the consistency of this link has not been carefully examined. Thus, the present review integrates findings from the past 5 years in order to determine the strength of such a relationship and identify areas for clarification and extension.

Recent Findings Findings revealed inconsistent evidence for a link between circadian rhythms and OCD. Chronotype is unrelated to OCD symptoms in adolescents but predicts OCD symptoms in adults. Results on delayed sleep timing are equivocal. Circadian rhythm disorders predict OCD treatment outcome. Preliminary evidence implicates decreased light exposure and diurnal symptom variability in OCD.

Summary The relationship between circadian rhythms and OCD may vary by age, diagnostic status, and assessment method. Recent findings are limited by an overreliance on convenience samples and singular self-report methods. Recommendations for future research on the role of circadian rhythms in OCD are discussed.

Keywords Obsessive-compulsive disorder · OCD · Circadian rhythms · Chronotype · Eveningness · Sleep timing

Introduction

Circadian rhythms are autonomous 24-h cycles in processes ranging from gene expression to behavior that occur independent of environmental input, and misalignment in these rhythms can result in pathology [1]. Considerable research has delineated the negative consequences of “living against the circadian clock” for physical health [1], and increasing attention is now being directed towards the role of circadian rhythms in psychopathology [2, 3]. Indeed, multiple systems linked to circadian rhythms are also implicated in psychopathology, including functions of monoaminergic neurotransmitters, the immune system, and the hypothalamic-pituitary-adrenal axis [4]. Though much of the extant literature on circadian rhythms in psychopathology has focused on

depression [e.g., 5], a small body of work also implicates circadian rhythms in obsessive-compulsive disorder (OCD). For example, individuals with delayed sleep phase disorder (DSPD) report increased OCD symptoms compared to healthy controls [6]. Similarly, DSPD is linked to severe, treatment-resistant OCD [7, 8]. However, evidence for variability in circadian-controlled hormone output in OCD is inconsistent, with some studies indicating alterations in cortisol and melatonin secretion [9, 10] while others studies report no such effects [11, 12]. Finally, individuals with OCD also exhibit decreased total sleep time (TST) compared to healthy controls (see [13] for a review), which may represent a consequence of a mismatch between internal rhythms (i.e., delayed sleep timing) and environmental demands.

These findings offer preliminary evidence for a role of circadian rhythms in OCD. Given increased theorizing on a circadian-OCD link [e.g., 14], a review of recent findings in this area may clarify inconsistencies and highlight areas for replication and extension. Thus, the present review aims to integrate findings on circadian rhythms in OCD over the past 5 years. Conclusions and recommendations for future research on the role of circadian rhythms in OCD will be discussed.

This article is part of the Topical Collection on *Sleep Disorders*

✉ Rebecca C. Cox
rebecca.cox.1@vanderbilt.edu

¹ Department of Psychology, Vanderbilt University, 301 Wilson Hall, 111 21st Avenue South, Nashville, TN 37240, USA

Recent Findings on Circadian Rhythms and OCD

Chronotype

Recent research has yielded mixed evidence for the role of circadian rhythms in OCD. The majority of work in this area has examined chronotype in OCD. Chronotype represents individual differences in circadian preference and phase of entrainment [15]. Chronotype is described by a spectrum from morningness to eveningness, such that those who trend towards eveningness have a later sleep-wake schedule and later peaks in circadian markers such as cortisol, core body temperature, and subjective alertness and vice versa [16, 17]. Importantly, eveningness may be indicative of desynchrony in circadian rhythms and environmental demands [15] and has been linked to symptoms of mood and anxiety disorders [18]. However, recent evidence for a link between chronotype and OCD is equivocal. A study of undergraduates found that evening types report increased intrusive cognition compared with morning types [19]. Cross-sectional survey studies also indicate a small association between eveningness and OCD symptoms in adolescents [20] and adults [21•]. However, both of these studies also found that the relationship between chronotype and OCD symptoms becomes non-significant when depression is controlled [20, 21•]. Thus, it is unclear whether there is a unique relationship between concurrent chronotype and OCD symptoms in unselected samples.

Interestingly, findings diverge between age groups when the link between chronotype and OCD is examined over time. Among adolescents, chronotype at baseline is unrelated to OCD symptoms over 6 months [22•]. However, among adults, eveningness significantly predicts increased OCD symptoms over 4 months, even when controlling for baseline symptoms of OCD and depression [21•]. Importantly, this finding suggests that the link between circadian rhythms and OCD is not accounted for by depression. These discrepant findings between age groups may be explained by developmental changes in chronotype. That is, the signal for a link between chronotype and OCD may be obscured by normative eveningness in adolescence. In contrast, those who do not phase shift towards morningness in adulthood may be vulnerable to adverse outcomes, such as increased OCD symptoms. Additional research examining the developmental trajectories of chronotype and OCD symptoms is necessary to determine whether persistent eveningness predicts OCD symptom onset.

Recent studies examining chronotype in OCD samples has likewise yielded mixed results. In a study comparing individuals with OCD who had undergone treatment to healthy controls, there was a trend towards more evening types and fewer morning types in the OCD group [23]. In contrast, eveningness was unrelated to symptom severity in the OCD group. Importantly, no other study has compared chronotype

in OCD versus healthy controls in the last 5 years. However, one recent study compared those with OCD to a mixed psychiatric disorder group. Findings indicate no difference in chronotype between groups and no association between chronotype and OCD symptom severity in the OCD group, though there was a small association between eveningness and increased negative affect that was unique to the OCD group [24]. Together, these findings suggest a potential small signal for increased eveningness in OCD that may also extend to other forms of psychopathology.

Though few studies of the link between chronotype and OCD have examined potential intervening processes, one recent study found that the prospective relation between eveningness and OCD symptoms was partially mediated by sleep disturbance [21•]. This finding is consistent with a recent model proposing insufficient and disturbed sleep as potential mechanisms linking evening chronotype to mental illness more broadly [3].

Sleep Timing

In addition to chronotype, delayed sleep timing may also indicate circadian rhythm abnormalities in OCD [25]. The timing of sleep has been suggested as the preferred method for measuring chronotype [26], as sleep timing is more strongly correlated with indicators of circadian phase, such as melatonin [27], relative to morningness-eveningness measures of chronotype. However, it is important to note that sleep timing is also impacted by psychosocial factors and is not uniquely driven by circadian rhythms [28]. Indeed, recent findings provide inconsistent evidence for a link between delayed sleep timing and OCD. In an undergraduate sample who self-reported habitual sleep timing, individuals with delayed sleep timing reported increased intrusive thoughts compared with individuals with non-delayed sleep timing, and this effect was independent of sleep duration and negative affect [29]. Further, individuals with delayed bedtimes endorsed increased urges to neutralize or suppress intrusive thoughts. However, though one study of an undergraduate sample found a small association between later self-reported bedtimes and OCD symptoms [19], this finding was not replicated in a later study [30]. Further, clinical comparisons of both adolescents and adults with OCD to healthy controls indicated no differences in sleep timing as measured by actigraphy [31•, 32]. Thus, recent findings do not consistently implicate delayed sleep timing in OCD.

Circadian Rhythm Disorders

Despite minimal recent evidence for delayed sleep timing in OCD, two recent findings indicate a link between circadian rhythm disorders and OCD. In a population survey of over 9000 adolescents, there was a trend towards increased DSPD

in those meeting criteria for probable OCD [33]. Further, a study comparing adults with OCD to healthy controls found evidence for a large effect of increased circadian rhythm disorders in the OCD group [31•]. Further, this study also found baseline circadian rhythm disorders and sleep timing together predicted non-response to repetitive transcranial magnetic stimulation treatment, as well as a trend-level effect for more severe circadian rhythm disorder symptoms among treatment non-responders compared with responders. Thus, circadian abnormalities may characterize clinical levels of OCD and may likewise represent a barrier to effective treatment.

Time of Day Effects on OCD Symptoms

Circadian rhythm abnormalities in OCD may also be indicated by diurnal variation in OCD symptoms. Indeed, Nota, Gibb, and Coles [34] found that the likelihood of experiencing obsessions peaks in the afternoon in a sample of untreated OCD adults. This pattern is similar to previous research showing anxiety-related symptoms peak mid-day in a sample of adults with panic attacks [35] but is notably distinct from findings suggesting that anxiety declines across the day in healthy adults [36, 37]. Thus, elevated OCD symptoms in the afternoon may represent a deviation from the normative diurnal rhythm of anxiety. Additional research utilizing ecological momentary assessment approaches is needed to fully characterize time of day effects for OCD symptoms.

Latitude and Light Exposure

Importantly, despite increased theorizing on a role of circadian rhythms in OCD [e.g., 14, 38], no recent studies have examined mid-sleep, the preferred method for measuring chronotype [39] or physiological indicators of circadian rhythms, such as dim light melatonin onset or core body temperature in OCD. However, one study found a medium to large association between OCD prevalence and latitude, such that increasing latitude is associated with increased OCD prevalence [40•]. Previous circadian rhythm research suggests that decreased light exposure at increased latitudes impacts circadian-controlled processes [41]. Indeed, Coles et al., [40•] also found a medium association between fewer hours of light exposure and increased OCD prevalence. Notably, these effects were specific to OCD and did not extend to panic disorder. Thus, decreased light exposure at higher latitudes may contribute to circadian dysregulation and confer vulnerability for OCD. However, it is important to note that few studies have reported prevalence rates of OCD in high latitude regions (> 40°); thus, replication of this effect is needed in more extreme latitudes.

Conclusions and Future Directions

Taken together, recent findings offer mixed evidence for the role of circadian rhythms in OCD. Though small associations between chronotype and OCD in cross-sectional samples are inconsistently detected [20, 21•], there is preliminary evidence for a prospective link between chronotype and OCD symptoms in adults [21•]. Similarly, circadian rhythm disorder symptoms predict OCD treatment outcome [31•], again suggesting that circadian measures may hold predictive utility for OCD trajectories over time. These findings highlight the importance of prospective designs when examining the links between circadian rhythms and OCD and suggest that concurrent relations between indicators like chronotype may be too small to be detectable in models that include other relevant covariates.

Interestingly, evidence for links between delayed sleep timing and OCD symptoms in unselected samples does not appear to extend to clinical OCD populations. However, these discrepant findings are difficult to interpret due to notable differences in study design. First, undergraduate students may not be appropriate samples for studies of sleep timing. That is, delayed bedtimes in the pursuit of goal-directed behavior (e.g., studying for exams) may be fundamentally distinct from delayed bedtimes underpinned by circadian rhythm variability. Second, the studies of OCD samples also utilized an objective measure of sleep timing (i.e., actigraphy [31•, 32]). Thus, it is unclear if the lack of evidence for delayed sleep timing in recent clinical comparison studies suggests that those with OCD do not exhibit delayed sleep timing or rather that delayed sleep timing in relation to OCD is not detected by actigraphy. Alternatively, the studies indicating a link between delayed sleep timing and OCD utilized a retrospective measure of bedtimes over the past month [19, 29]. Thus, it is possible that the relation between sleep timing and OCD is better explained by retrospective bias. Additional work utilizing multiple indicators of sleep timing in those with and without OCD is necessary to clarify these conflicting findings.

Recent findings on the role of circadian rhythms in OCD also diverge by age. Though recent studies detect no unique link between chronotype or delayed sleep timing and OCD in adolescents [20, 22•, 32], studies of adults find a relatively more consistent signal across circadian indicators. Again, such discrepancies findings may reflect the developmental trajectory of circadian rhythms. Given typical phase delay in adolescence [42], a link between delayed circadian rhythms and OCD may be difficult to detect in this stage of development. However, a more consistent link between delayed circadian rhythms and OCD in adult samples suggests that a relative phase delay that persists beyond adolescence and into adulthood may confer vulnerability for OCD. This interpretation is supported by a similar pattern evident in recent studies

examining the prevalence of DSPD status in OCD which found a trend level effect in an adolescent sample [33], but a large effect in an adult OCD sample [31•]. These findings suggest that longitudinal studies tracking OCD symptoms and disorder onset in the transition between adolescence and adulthood may yield important findings on physiological factors that contribute to OCD onset.

Finally, recent findings in this area also highlight new areas for future research. For example, evidence for a large association between OCD prevalence and latitude [40•] suggests that light exposure may be an understudied mechanism in OCD. Likewise, preliminary evidence for diurnal variation in OCD symptoms [34] suggests that additional research is necessary to fully characterize time of day effects in this population. Careful delineation of the timing of peaks in OCD symptoms is necessary in order to identify concurrently peaking processes that may be contributing to OCD pathology.

Taken together, these studies offer evidence for a small, but inconsistent link between circadian rhythms and OCD that may vary by age, sampling period, and diagnostic status. However, recent findings are limited by an overreliance on unselected samples and underutilization of gold standard circadian methods. Thus, the results of this review suggest that circadian rhythms may be disrupted in OCD, but claims made about this link should be tempered and findings interpreted with caution. Still, given growing appreciation for the role of circadian rhythms in mental and physical health [e.g., 1, 2], circadian rhythms remain an important area for future research within the context of OCD. The following recommendations may increase the clarity and utility of subsequent circadian-focused OCD research: (1) Increased examination of clinical OCD populations. The majority of recent work has examined unselected samples, making it difficult to generalize findings to individuals with OCD. (2) Decreased reliance on undergraduate samples. Purposeful delays in sleep/wake timing engaged in by undergraduates may obscure any true effect of circadian delays in OCD. (3) Increased use of multiple indicators of circadian rhythms. Single-method approaches are vulnerable to measurement error [43], an issue which is likely particularly problematic when variables measured are proxies of the desired construct (e.g., sleep timing to indicate circadian rhythms). (4) Increased use of preferred circadian methods (e.g., mid-sleep, dim light melatonin onset), as well as experimental methods (e.g., forced desynchrony). Overreliance on self-report measures introduces bias and ignores considerable research detailing appropriate methods for circadian rhythm measurement [44]. (5) Increased use of prospective designs, as well as ecological momentary assessment methods. Though cross-sectional studies are an important first step, ultimately the question should be one of mechanism, in which case prospective designs are critical. Likewise, cross-sectional measures represent a blunt approach to processes which are likely dynamic and variable over time. Thus, utilization of

ecological momentary assessment may offer a more valid characterization of circadian rhythms in OCD. (6) Recruitment of large samples in order to detect what is likely a small effect. Recent findings converge on a small effect size for circadian rhythms in OCD. Thus, studies utilizing small samples may be misleading.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:

- Of importance

1. Roenneberg T, Merrow M. The circadian clock and human health. *Curr Biol*. 2016;26:R432–43.
2. Wulff K, Gatti S, Wettstein JG, Foster RG. Sleep and circadian rhythm disruption in psychiatric and neurodegenerative disease. *Nat Rev Neurosci*. 2010;11:1–11.
3. Taylor BJ, Hasler BP. Chronotype and mental health: recent advances. *Curr Psychiatry Rep*. 2018;20:59.
4. McClung CA. How might circadian rhythms control mood? Let me count the ways. *Biol Psychiatry*. 2013;74:242–9.
5. Kronfeld-Schor N, Einat H. Circadian rhythms and mood: human psychopathology and animal models. *Neuropsychopharmacol*. 2012;62:101–14.
6. Schubert JR, Coles ME. Obsessive-compulsive symptoms and characteristics in individuals with delayed sleep phase disorder. *J Nerv Ment Dis*. 2013;201:877–84.
7. Drummond LM, Wulff K, Rani RS, White S, Mbangi-Sibanda J, Ghodse H, et al. 2012. How should we measure delayed sleep phase shift in severe, refractory obsessive-compulsive disorder? *Int J Psychiatry Clin Pract* 2012;16:268–276.
8. Turner J, Drummond LM, Mukhopadhyay S, Ghodse H, White S, Pillay A, et al. A prospective study of delayed sleep phase syndrome in patients with severe resistant obsessive-compulsive disorder. *World Psychiatry*. 2007;6:08–111.
9. Kluge M, Schussler P, Kunzel HE, Dresler M, Yassouridis A, Steiger A. Increased nocturnal secretion of ACTH and cortisol in obsessive compulsive disorder. *J Psychiatr Res*. 2007;41:928–33.
10. Monteleone P, Catapano F, Tortorella A, Di Martino S, Maj M. Plasma melatonin and cortisol circadian patterns in patients with obsessive-compulsive disorder before and after fluoxetine treatment. *Psychoneuroendocrinol*. 1995;20:763–70.
11. Catapano F, Monteleone P, Fuschino A, Maj M, Kemali D. Melatonin and cortisol secretion in patients with primary obsessive-compulsive disorder. *Psychiatry Res*. 1992;44:217–25.
12. Millet B, Touitou Y, Poirier MF, Bourdel MC, Hantouche E, Bogdan A, et al. Plasma melatonin and cortisol in patients with obsessive-compulsive disorder: relationship with axillary temperature, physical activity, and clinical symptoms. *Biol Psychiatry*. 1998;44:874–81.

13. Cox RC, Olatunji BO. A systematic review of sleep disturbance in anxiety and related disorders. *J Anxiety Disord.* 2016;37:104–29.
14. Nota JA, Sharkey KM, Coles ME. Sleep, arousal, and circadian rhythms in adults with obsessive-compulsive disorder: a meta-analysis. *Neurosci Biobehav Rev.* 2015;51:100–7.
15. Duffy JF, Rimmer DW, Czeisler CA. Association of intrinsic circadian period with morningness-eveningness, usual wake time, and circadian phase. *Behav Neurosci.* 2001;115:895–9.
16. Bailey SL, Heitkemper MM. Circadian rhythmicity of cortisol and body temperature: morningness-eveningness effects. *Chronobiol Int.* 2001;18:249–61.
17. Kerkhof GA, Van Dongen HPA. Morning-type and evening-type individuals differ in the phase position of their endogenous circadian oscillator. *Neurosci Lett.* 1996;218:153–6.
18. Antypa N, Vogelzangs N, Meesters Y, Schoevers R, Penninx BWJH. Chronotype associations with depression and anxiety disorders in a large cohort study. *Depress Anxiety.* 2016;33:75–83.
19. Nota JA, Coles ME. Duration and timing of sleep are associated with repetitive negative thinking. *Cogn Ther Res.* 2015;39:253–61.
20. Alvaro PK, Roberts RM, Harris JK. The independent relationships between insomnia, depression, subtypes of anxiety, and chronotype during adolescence. *Sleep Med.* 2014;15:934–41.
21. Cox RC, Tuck B, Olatunji BO. The role of eveningness in obsessive-compulsive symptoms: cross-sectional and prospective approaches. *J Affect Disord.* 2018;235:448–55 **Eveningness predicts OCD symptoms over 4 months, controlling for depression.**
22. Alvaro PK, Roberts RM, Harris JK, Bruni O. The direction of the relationship between symptoms of insomnia and psychiatric disorders in adolescents. *J Affect Disord.* 2017;207:167–74 **Eveningness does not predict OCD symptoms over 6 months in adolescents.**
23. Kani AS, Poyraz CA, Poyraz BC, Bayar MR, Akin E, Kose S. The role of affective temperaments and chronotype in pharmacotherapy response in patients with obsessive-compulsive disorder. *Psychiatry Clin Psychopharmacol.* 2018;28:58–65.
24. Simor P, Harsanyi A, Csigo K, Miklos G, Lazar AS, Demeter G. Eveningness is associated with poor sleep quality and negative affect in obsessive-compulsive disorder. *J Behav Addict.* 2018;7:10–20.
25. Coles ME, Schubert JR, Sharkey KM. Delayed bedtimes and obsessive-compulsive symptoms. *Behav Sleep Med.* 2012;10:258–65.
26. Roenneberg T. What is chronotype? *Sleep Biol Rhythms.* 2012;10:75–6.
27. Kantermann T, Burgess HJ. Average mid-sleep time as a proxy for circadian phase. *Psych J.* 2017;6:290–1.
28. Paine SJ, Gander PH. Differences in circadian phase and weekday/weekend sleep patterns in a sample of middle-aged morning types and evening types. *Chronobiol Int.* 2016;33:1009–17.
29. Schubert JR, Coles ME. The experience and impact of intrusive thoughts in individuals with late bedtimes. *Biol Rhythm Res.* 2015;46:81–9.
30. Nota JA, Schubert JR, Coles ME. Sleep disruption is related to poor response inhibition in individuals with obsessive-compulsive and repetitive negative thought symptoms. *J Behav Ther Exp Psychiatry.* 2016;50:23–32.
31. Donse L, Sack AT, Fitzgerald PB, Arns M. Sleep disturbances in obsessive-compulsive disorder: association with non-response to repetitive transcranial magnetic stimulation (rTMS). *J Anxiety Disord.* 2017;49:31–9 **Adults with OCD report increased symptoms of circadian rhythm disorders compared to healthy controls. Circadian rhythm disorders and bedtime predict treatment outcome.**
32. Jaspers-Fayer F, Lin SY, Belschner L, Mah J, Chan E, Bleakley C, et al. A case-control study of sleep disturbances in pediatric obsessive-compulsive disorder. *J Anxiety Disord.* 2018;55:1–7.
33. Sivertsen B, Harvey AG, Pallesen S, Hysing M. Mental health problems in adolescents with delayed sleep phase: results from a large population-based study in Norway. *J Sleep Res.* 2015;24:11–8.
34. Nota JA, Gibb BE, Coles ME. Obsessions and time of day: a self-monitoring study in individuals with obsessive-compulsive disorder. *J Cogn Psychother.* 2014;28:134–44.
35. Kenardy J, Fried L, Kraemer HC, Taylor CB. Psychological precursors of panic attacks. *Br J Psychiatry.* 1992;160:668–73.
36. English T, Carstensen LL. Emotional experience in the mornings and the evenings: consideration of age differences in specific emotions by time of day. *Front Psychol.* 2014;5:1–9.
37. Willis TA, O'Connor DB, Smith L. The influence of morningness-eveningness on anxiety and cardiovascular responses to stress. *Physiol Behav.* 2005;85:125–33.
38. Boland EM, Ross RJ. Recent advances in the study of sleep in the anxiety disorders, obsessive-compulsive disorder, and posttraumatic stress disorder. *Psychiatr Clin N Am.* 2015;38:761–76.
39. Roenneberg T, Kuehne T, Juda M, Kantermann T, Allebrandt K, Gordijn M, et al. Epidemiology of the human circadian clock. *Sleep Med Rev.* 2007;11:429–38.
40. Coles ME, Wirshba CJ, Nota J, Schubert J, Grunthal BA. Obsessive compulsive disorder prevalence increases with latitude. *J Obsessive-Compulsive Relat Disord.* 2018;18:25–30 **Higher latitude and fewer hours of light exposure associated with increased OCD prevalence.**
41. Adamsson M, Laike T, Morita T. Annual variation in daily light exposure and circadian change of melatonin and cortisol concentrations at a northern latitude with large seasonal differences in photoperiod length. *J Physiol Anthropol.* 2017;36:6.
42. Crowley SJ, Acebo C, Carskadon MA. Sleep, circadian rhythms, and delayed phase in adolescence. *Sleep Med.* 2007;8:602–12.
43. Cole DA, Maxwell SE. Testing mediational models with longitudinal data: questions and tips in the use of structural equation modeling. *J Abnorm Psychol.* 2003;112:558–77.
44. Broussard JL, Reynolds AC, Depner CM, Ferguson SA, Dawson D, Wright KP. Circadian rhythms versus daily patterns in human physiology and behavior. In Kumar V, editor. *Biological timekeeping: clocks, rhythms and behaviour.* Springer; 2017.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.