Research Article

Circadian Rhythm Disruption and Myopia: A New Paradigm in Eye Growth Regulation — A Scoping Review

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Abstract

Objective: To organize the evidence connecting circadian disruption with myopia and to judge whether this framework has matured enough to be called a paradigm of ocular growth regulation.

Methods: A scoping review was carried out in PubMed/MEDLINE, Scopus and Web of Science Core Collection for records published from 1 January 2000 to 31 October 2026. Three concept blocks — refractive error and ocular growth; circadian rhythm, melatonin and sleep; and lens-based spectral manipulation — were combined with Boolean operators. Records were eligible only if published as full peer-reviewed articles; conference abstracts, supplements, data deposits, preprints and unpublished material were excluded. Data were charted for design, population, circadian measurement, ocular endpoint and stated limitation, and summarized narratively.

Results: Thirty-nine records were analyzed — 24 primary studies and 15 syntheses. In 6,295 schoolchildren followed for two years, bedtimes after 21:30 h were associated with myopia prevalence (OR 1.55, p = 0.04), two-year incidence (OR 1.44, p = 0.02) and 24-month progression (p = 0.005). Among 30,188 children, prevalence was 49.8%. Of 1,902 children with complete data, 588 (30.9%) were myopic in both eyes and 1,129 (59.4%) had abnormal sleep-habit scores. In 34 young adults, axial length and subfoveal choroidal thickness varied significantly across the day (each $p < 0.05$), and a one-hour summer phase advance was associated with axial change ($R^2 = 0.81$) and choroidal thickening ($R^2 = 0.54$).

Conclusions: Ocular rhythmicity is measurable and reproducible, but the human evidence remains small, largely cross-sectional and methodologically fragmented. Circadian disruption is a testable mechanistic hypothesis, not an established causal pathway.

Descriptors: Myopia; Circadian Rhythm; Melatonin; Sleep; Refractive Errors; Review.

1. Introduction

The standard account of myopia centres on optical defocus, accommodative lag and inherited susceptibility. That account explains a great deal, yet it leaves three observations unaccounted for. Axial elongation does not proceed at a constant rate through the year, deprivation experiments generate growth oscillations with a period close to twenty-four hours, and exposing the eye to optically comparable stimuli at different points of the light–dark cycle does not yield comparable growth. These anomalies have gradually been consolidated into a competing proposition: that eye growth is paced by a circadian system, and that its disturbance is one of the routes by which myopia develops [1].

The biochemical core of that proposition is an antagonism between dopamine and melatonin that has been studied in the retina for decades. Eyes developing myopia show lower concentrations of dopamine and of its metabolite 3,4-dihydroxyphenylacetic acid than control eyes, and the difference appears only while the eye is light-adapted — a pattern that locates the deficit in the daytime signal rather than in global synthesis [2]. Experimental manipulation of dopaminergic signaling has been described as acting on axial growth more than on equatorial growth, which would make the pathway dimensionally selective [2]. The rhythm itself also carries information: vitreous levels of 3,4-dihydroxyphenylacetic acid follow a diurnal cycle, and that cycle is reshaped when visual input is altered in ways that change eye growth [3]. Melatonin, which interacts reciprocally with retinal dopamine and with clock-gene transcription, has been proposed as the element that couples light timing to turnover of the scleral matrix [1].

Alongside this experimental literature, a clinical one has grown around bedtime, light exposure and refractive status in children. The relevant question is not whether such reports exist they clearly do but whether their convergence supports the stronger assertion that circadian disturbance governs eye growth, and what evidence, measurement and design would be needed for that assertion to hold. The most comprehensive synthesis of myopia risk factors classifies both sleep and circadian rhythms as weak contributors, confounded by educational demands and by light exposure itself [4]. At the same time, strategies that extend time outdoors appear to lower

both the incidence of myopia and the rate of its progression [5], leaving unresolved whether light operates through image quality, through circadian entrainment, or through both.

Three objectives guided this review: to map the human and experimental evidence; to examine the methodological sources of the field's divergent results; and to state what would be required for the circadian account to move from plausible hypothesis to defensible paradigm.

2. Method

2.1 Study design and reporting

A scoping design was selected because the literature is heterogeneous and still forming. Reporting followed the PRISMA extension for scoping reviews. The protocol was not registered and no pooling of effect estimates was attempted: outcome definitions, melatonin assays and biometric measurement windows differed too much between studies for meta-analysis to be defensible.

2.2 Sources and search period

PubMed/MEDLINE, Scopus and Web of Science Core Collection were searched. The window ran from 1 January 2000 to 31 October 2026, with the final search executed on 31 October 2026. The lower bound reflects the fact that both the light–dark manipulation experiments in refractive development and the earliest clock-gene hypotheses in this field appeared after that date. Reference lists of the included reviews were examined manually, and forward citation tracking was applied to the two most recent systematic reviews.

2.3 Search strategy

Three concept blocks were combined with the operator AND, while terms within each block were joined with OR. In PubMed, controlled vocabulary was combined with free-text terms in title and abstract.

The refractive block used "Myopia"[MeSH] OR "Refractive Errors"[MeSH] OR "Emmetropization"[MeSH] together with the free-text terms myopi*[tiab], "refractive error"[tiab], "refractive errors"[tiab], "refractive status"[tiab], "axial length"[tiab], "axial elongation"[tiab], "eye growth"[tiab], "ocular growth"[tiab], emmetropi*[tiab] and "choroidal thickness"[tiab].

The circadian block used "Circadian Rhythm"[MeSH] OR "Circadian Clocks"[MeSH] OR "Melatonin"[MeSH] OR "Sleep"[MeSH] OR "Sleep Wake Disorders"[MeSH] together with circadian[tiab], "circadian clock"[tiab], "clock gene"[tiab], "clock genes"[tiab], Bmal1[tiab], ARNTL[tiab], PER2[tiab], Cry1[tiab], diurnal[tiab], melatonin[tiab], "melatonin receptor"[tiab], "dim light melatonin onset"[tiab], DLMO[tiab], chronotype[tiab], "social jetlag"[tiab], "social jet lag"[tiab], "light at night"[tiab], "light pollution"[tiab], melanopsin[tiab], ipRGC*[tiab], "intrinsically photosensitive"[tiab], "sleep duration"[tiab], "sleep quality"[tiab], "sleep timing"[tiab] and "sleep onset"[tiab].

A third block identified studies in which the spectrum reaching the eye had been deliberately modified: "Eyeglasses"[MeSH] OR "Lenses"[MeSH] OR "blue light"[tiab] OR "blue blocking"[tiab] OR "blue-cut"[tiab] OR "short wavelength"[tiab] OR "spectacle lens"[tiab] OR "spectacle lenses"[tiab].

The date restriction was applied as ("2000/01/01"[dp] : "2026/10/31"[dp]) OR ("2000/01/01"[edat] : "2026/10/31"[edat]), so that the publication-date limit was paired with an Entrez-date limit and records available ahead of print were not lost. Duplicates were removed in reference management software. The complete strategy, set by set and database by database, is reproduced in the appendix tables.

2.4 Eligibility criteria

A record was eligible if it presented original data or a formal synthesis on circadian phase, melatonin secretion, sleep timing or diurnal ocular rhythms in relation to refractive error, axial length or choroidal thickness, in humans or in animal models of myopia. Inclusion was restricted to full articles published in peer-reviewed journals with a retrievable DOI, PMID or ISSN. Conference abstracts and proceedings, supplementary files and questionnaire appendices, dataset deposits, preprints, theses and unpublished manuscripts were excluded, as were records in languages other than English and studies of circadian rhythm in ocular disease unrelated to refractive development. Narrative reviews were retained only when they supplied a mechanistic synthesis unavailable from primary sources.

2.5 Data charting and synthesis

A standardized form recorded the objective, design, sample size, population and age, method of refractive classification, circadian measurement and sampling frequency, ocular endpoint and instrument, principal quantitative results, and the limitation acknowledged by the authors. Synthesis was narrative and was organized by type of evidence rather than by ocular endpoint, since merging biomarker studies with biometry studies would obscure exactly the methodological contrasts the review set out to examine.

3. Literature review

3.1 Profile of the included evidence

The 39 records comprised 24 primary studies and 15 reviews, meta-analyses or evidence syntheses. Of the primary studies, twelve were conducted in humans and twelve were experimental or preclinical. Human designs were almost entirely cross-sectional or short-term observational; none was powered for a refractive or axial endpoint within a circadian intervention. Paediatric epidemiological data were concentrated geographically in East Asia.

3.2 Comparative summary of representative studies

Table 1. Objectives, samples, methods, circadian measurements, findings and limitations of representative included studies

Study	Objective	Sample	Population	Methodology	Circadian / ocular measurements	Main findings	Limitations
Ulaganathan et al. [6]	Examine whether objectively measured ambient light relates to daily variation in axial length and choroid, and to longitudinal change	34	Young adults, emmetropic and myopic	Serial biometry approximately every 3 h between 09:00 and 21:00, on a weekday and a weekend in winter, repeated in summer; wrist-worn light sensor for 14 days	Axial length; subfoveal choroidal thickness; personal light exposure	Significant within-day variation in axial length and choroidal thickness (each $p < 0.05$)	Daylight-only sampling with no nocturnal readings; small sample; short follow-up
Nilsen et al. [7]	Test whether diurnal ocular and systemic rhythms vary with season	Cohort of adolescents and young adults, emmetropic and myopic	Adolescents and young adults	Repeated diurnal assessment of melatonin timing and ocular biometry in summer and winter	Melatonin phase; axial length phase	One-hour phase advance of melatonin and axial length in summer ($P < 0.001$); axial change related to phase advance ($R^2 = 0.81$) and to choroidal thickening ($R^2 = 0.54$)	Observational; only two seasonal assessments; phase estimated at group level
Liu et al. [8]	Relate demographic, behavioural and environmen	6,295 enrolled	Schoolchildren in Shanghai, 6–9 years at baseline	Prospective school-based study over two years; questionnai	Reported bedtime; refractive error; axial length	Bedtime after 21:30 h associated with prevalence	Bedtime self-reported; confounded by study load, private

	tal factors, including sleep, to myopia			re on sleep and near work; refraction and 24-month progression		(OR 1.55, p = 0.04), two-year incidence (OR 1.44, p = 0.02) and 24-month progression (p = 0.005)	tuition and socioeconomic position; no circadian biomarker
Xu et al. [9]	Examine whether sleep–wake schedules relate to myopia	30,188	Schoolchildren and adolescents, Baoan District, Shenzhen	Cross-sectional survey with stratified cluster sampling and self-administered questionnaire	Sleep–wake regularity; myopia inferred from age at first spectacle use	Overall prevalence 49.8%; prevalence higher among students with irregular sleep–wake schedules	Myopia self-reported without cycloplegia; no biomarker; recall-based questionnaire
Zhou et al. [10]	Examine whether disordered sleep is associated with myopia	1,970 recruited; 1,902 (96.5%) with complete data	Urban primary schoolchildren, mean age 9.80 ± 0.44 years	Automated cycloplegic refraction with subjective refinement; parent-completed Children's Sleep Habits Questionnaire	Sleep-habit score; sleep duration; near work; time outdoors	Myopia ≤ −0.50 D in both eyes in 588 children (30.9%); 1,129 (59.4%) scored above 41 on the sleep-habit questionnaire	Parental report; cross-sectional; instrument captures sleep behaviour rather than circadian phase

3.3 Sleep timing and refractive status

The behavioural studies agree in direction while remaining coarse in resolution. In the two-year Shanghai cohort of 6,295 children aged 6–9 years at entry, a bedtime later than 21:30 h was associated with prevalence (OR 1.55, p = 0.04), two-year incidence (OR 1.44, p = 0.02) and progression over 24 months (p = 0.005) [8]. In the Shenzhen survey of 30,188 students, prevalence reached 49.8% and was greater among those reporting irregular sleep–wake schedules [9]. In the third dataset, drawn from 1,970 recruited urban primary schoolchildren with complete data for 1,902, bilateral myopia of ≤ −0.50 D affected 588 children (30.9%) and 1,129 (59.4%) had sleep-habit scores above 41 [10].

What unites these three studies is also what limits them: in each, the exposure is a reported behaviour. Bedtime and sleep regularity describe a schedule, not a phase, and a schedule is shaped by school timetables and household routine as much as by endogenous timing. The distinction is pursued in Section 4.1.

3.4 Ocular rhythms as the more informative endpoint

The most consequential finding for the paradigm is not any difference between refractive groups, but the demonstration that the eye oscillates measurably and that its rhythms are coupled across tissues. In children, ocular and systemic rhythms were shown to be robust, with axial length and intraocular pressure approximately in phase and both in antiphase to choroidal thickness [11]. In adults, anterior and posterior segment biometry varied over the day, with choroidal variation correlating with axial variation [12]. Serial biometry across a daylight window in 34 young adults confirmed significant within-day change in both axial length and subfoveal choroidal thickness [6].

Seasonal entrainment offers the strongest available argument that these rhythms are circadian in origin rather than mechanical. Melatonin timing and axial length phase both advanced by about one hour in summer (P <

0.001), and the size of the axial change was related to the size of the phase advance ($R^2 = 0.81$) and to choroidal thickening ($R^2 = 0.54$) [7]. This is the only dataset in the corpus in which a shift in circadian timing and a change in ocular biometry were quantified in the same individuals.

An anatomical route for such entrainment is available. Intrinsically photosensitive retinal ganglion cells that express melanopsin drive photoentrainment and other non-image-forming responses independently of rods and cones [13].

3.5 Experimental evidence

Human studies cannot establish causation in this field; animal work can, in principle. In myopic sclera, hypoxia-related signaling is activated, experimental myopia selectively up-regulates HIF-1α in mice and guinea pigs, and antihypoxia treatment slows progression without altering normal growth — establishing scleral hypoxia as a target that can be manipulated [14]. Transcriptomic and proteomic profiling of sclera from guinea pigs with lens-induced myopia has catalogued the accompanying matrix and signaling changes [15]. Diurnal gene-expression patterns in retina and choroid have been reported to separate progression from onset in a mammalian model, which implies that the circadian transcriptome differs by disease stage [16]. At receptor level, dopamine D1 receptors appear necessary for apomorphine-induced inhibition of deprivation myopia in mice [17].

4. Discussion

4.1 Why the studies disagree

Divergence in this literature is patterned rather than random, and five methodological fault lines account for most of it.

Melatonin polarity remains unsettled. Group differences in melatonin have not been shown to run in one direction across refractive groups. Part of the explanation is analytic rather than biological: serum, saliva and urinary metabolite index different phenomena, none of them interchangeable, and a single timed specimen estimates neither phase nor total secretion. Two studies that both describe themselves as measuring melatonin in myopia may therefore be reporting different quantities, and papers seldom state which inference their design can support.

Sampling frequency dictates what can be detected. Phase estimation requires repeated sampling across a bedtime-anchored window under dim light. Questionnaire studies measure bedtime, which is a behaviour molded by school schedules, private tuition and parental employment [4]. The two are not interchangeable exposures, and the corpus shows the consequence clearly: the largest datasets rest entirely on self- or parent-report [8,9], whereas studies that measure rhythmicity directly are necessarily small [6,11]. Precision and statistical power are almost perfectly inversely related here, and no included study achieves both.

Measured light does not behave as a simple dose model predicts. If ambient light determined the amplitude of ocular rhythms, objectively measured exposure should track that amplitude. In young adults it did not: prior light exposure was unrelated to the amplitude of diurnal variation in axial length, choroidal thickness, ocular perfusion pressure, body temperature, melatonin or cortisol [18]. Objectively measured exposure profiles nonetheless differ between myopic and non-myopic children outside school hours [19], so a signal exists but does not pass through to biometric amplitude in any straightforward way. This inconsistency is seldom acknowledged in reviews that treat light dose as the operative variable.

Definitions and instruments are not standardized. Myopia was defined at −0.50 D in some studies [10] and at stricter thresholds in others, with or without cycloplegia. Non-cycloplegic autorefraction and questionnaire-based case definition both introduce detection bias [20]. Because axial length and refraction are imperfectly coupled, effect estimates are not directly comparable, and heterogeneity read as biological may be partly artefactual.

Onset and progression are treated as one outcome. Within a single dataset, associations with prevalence, incidence and progression differ substantially in magnitude [8], and the experimental transcriptome separates onset from progression [16]. Pooling all three under the heading of myopia risk is itself a source of apparent contradiction.

4.2 Mechanistic pathways from photon to sclera

A paradigm requires a mechanism, and the available evidence supports one provided its gaps are stated.

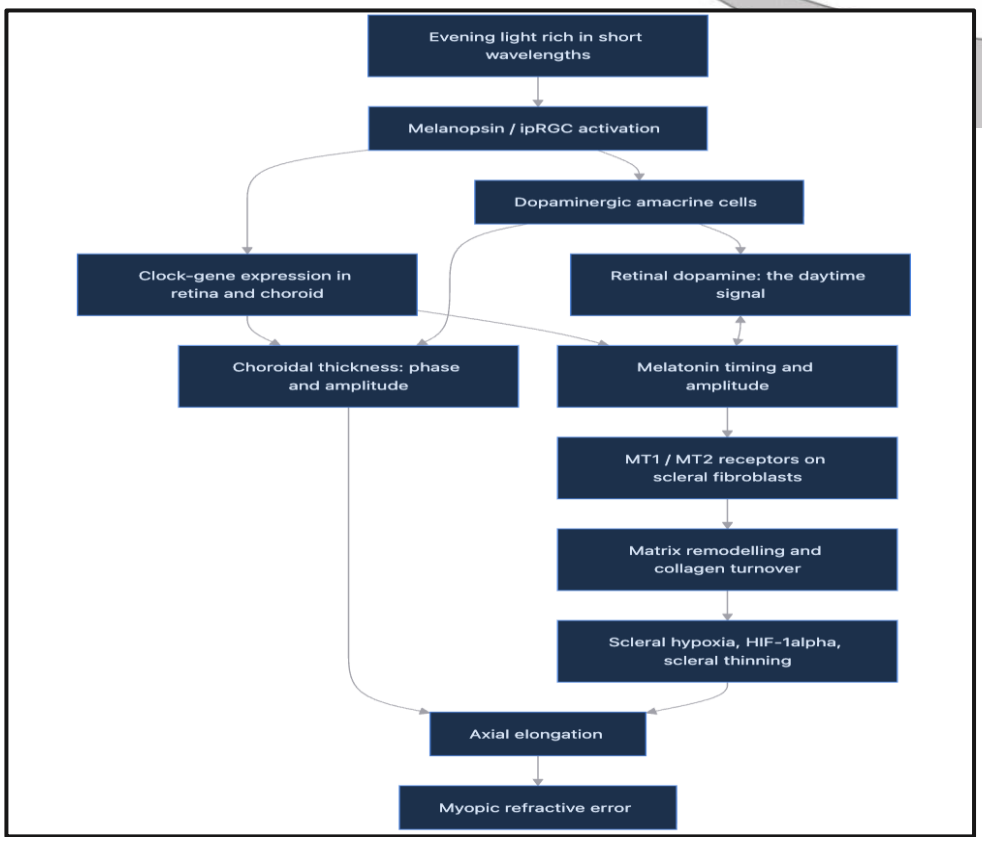


Figure 1. Proposed pathway linking circadian light input to axial elongation.

Retinal dopamine. The pathway begins with melanopsin-based photoreception, which governs non-image-forming light responses independently of image-forming vision [13]. The dopaminergic link is the best characterized: dopamine and its metabolite fall in myopic eyes, and the fall is confined to the light phase, locating the deficit in the daytime signal rather than in overall synthesis [2]. The rhythm carries information of its own — vitreous metabolite levels cycle over the day, and that cycle is altered by visual conditions that change eye growth, which places dopamine downstream of light–dark timing and not merely downstream of defocus [3]. Pharmacology supports a specific rather than a generic pathway, since D1 receptors are required for apomorphine-induced inhibition of deprivation myopia [17].

Choroidal thickness. The choroid responds faster than any other tissue in the pathway and is for that reason the most useful intermediate phenotype. Its thickness oscillates in antiphase to axial length in children [11], varies with axial variation in adults [12], and changes measurably across a single day in young adults [6]. For a circadian account, the informative quantity is the phase relationship between choroid and axial length rather than absolute thickness: choroidal thickening tracked the summer phase advance ($R^2 = 0.54$) instead of lagging behind it [7].

Scleral remodeling. Matrix change is the final common pathway. Scleral hypoxia is a demonstrated target, with selective HIF-1α up-regulation in experimental myopia and slower progression under antihypoxia treatment [14]. Profiling of myopic sclera shows coordinated shifts across matrix and signaling pathways [15], low-dose atropine modifies the transcriptional profile of scleral fibroblasts, suggesting that pharmacological control acts at least partly through fibroblast phenotype [21], and OPN5 expression in human scleral fibroblasts under hypoxic conditions has been linked to matrix-preserving responses, indicating that scleral cells mount protective as well as degradative programs [22].

Melatonin as the coupling node. Melatonin is where the circadian and scleral literatures intersect. Acting through MT1/MT2 receptors and interacting with clock genes, it influences synthesis and remodeling of extracellular matrix in scleral fibroblasts and has been proposed to favour axial elongation [1]. It also contributes to circadian regulation of ocular physiology more broadly, with rhythms in intraocular pressure and ocular perfusion among its documented targets [23]. This step is what gives the paradigm clinical interest and is simultaneously its weakest link, since no included study measured scleral melatonin signaling and axial elongation in the same system.

Where the pathway is inferential. Three arrows are not demonstrated. First, retinal dopamine has never been measured in vivo during human refractive development, so that link is entirely model-derived. Second, it has not been shown that a phase shift in the choroidal rhythm causes rather than accompanies altered elongation; the seasonal covariation is equally compatible with either direction [7]. Third, the polarity of melatonin's scleral effect is unresolved, which is why differences in melatonin concentration between groups cannot yet be given a mechanistic sign.

4.3 Confounding

Any association between circadian markers and myopia has to be read against a dense confounder structure. The most comprehensive synthesis identifies education and restricted time outdoors as the major causal factors, classifies parental myopia as strong and screen time as equivocal, and classifies near work, sleep, circadian rhythms and light spectrum as weak, naming dopamine, night-time light and educational pressure as specific sources of confounding [4].

Educational load. Late bedtime cannot be separated from homework, tutoring and academic pressure, each of which predicts myopia independently [4]. Every hour of delay carries an unmeasured quantity of near work and indoor time. That bedtime remained associated with incidence after adjustment for screen time and outdoor time is reassuring [8] but not decisive.

Outdoor light as a shared cause. Time outdoors is the best supported protective exposure in the corpus, with more daily outdoor time associated with lower incidence and slower progression [24]. Outdoor light is also the principal zeitgeber, so a child who spends more time outside is at once better entrained and less myopic through an independent optical route. Separating the two requires objective measurement of dose and spectrum, and smartwatch-based measurement in children has shown that quantified outdoor exposure relates to myopic shift in a way questionnaire estimates do not [25].

Socioeconomic position, urbanization and ancestry. Socioeconomic position has been positively associated with myopia in some studies and not in others; the inconsistency is plausibly an artefact of definition, with the effect operating through more near work and less time outdoors [26]. Environmental and lifestyle exposures in general, urbanization among them, show the same dependence on context [26,27].

Near work and its interaction with outdoor time. Near-work estimates are confounded by outdoor exposure and by inconsistent cycloplegia [20], and interaction has been reported, with children who spent more time outdoors and less time on near tasks progressing more slowly [24]. Other candidates — sleep quantity, diet, birth season, birth order, urbanization, pollution — have been proposed with conflicting results, and each faces the same difficulty of establishing independence from the two dominant exposures [27].

Reverse causation. Myopia may itself disturb sleep: uncorrected refractive error, asthenopia and reduced outdoor play could all alter sleep timing, and a child who becomes myopic is fitted with spectacles that may change evening light exposure. Designs with repeated biomarker sampling before onset are needed; none was identified.

4.4 What kind of variable is circadian disruption?

Three readings are compatible with the current evidence, and they lead to different research agendas.

The first treats circadian disruption as a *cause* of excessive elongation, acting through the melanopsin–dopamine–melatonin axis on matrix turnover. This is the reading implied by most reviews and by the consumer framing of evening blue-light filters. It requires a prospective dose–response relationship between light timing and axial growth in children, and no included study supplies one: the corpus contains no trial using circadian phase as the intervention target with axial elongation as the primary endpoint, and syntheses of blue-light-filtering spectacle lenses have not found consistent benefit on visual or ocular outcomes [28,29].

The second treats circadian disruption as a *correlate* of the myopic phenotype — a marker of a shared developmental program rather than a driver. Ocular rhythms are already robust and normally phased in children [11], so a modest group difference may reflect individual chronotype rather than pathology. This reading also accommodates the null association between measured light and rhythm amplitude [18], which the first reading struggles to explain.

The third, and in my view the most defensible, treats *light itself as the common cause*, with circadian timing as a downstream marker of an exposure pattern that also affects growth optically. On this reading the circadian signal is genuine but not the operative pathway; it is a sensitive index of evening indoor light and reduced daytime outdoor light, both of which carry independent myopia risk [4]. This accounts for why the signal survives adjustment for reported outdoor time — questionnaire outdoor time is a poor proxy for light dose [25] and why objective measurement weakens rather than strengthens the circadian association [18].

Two further points are usually omitted. Melatonin is highly light-sensitive, so a study conducted without controlled lighting measures recent light behaviour as much as endogenous rhythmicity; controlled conditions are a requirement for validity, not merely good practice. And the field has an unusual measurement problem:

biomarkers are sensitive but clinical endpoints are slow, so studies end up powered for the surrogate and underpowered for the outcome that matters [6].

5. Final considerations

Contribution. What this review adds is not the observation that circadian and sleep measures differ across refractive groups that has been reported many times but the argument that the field's central disagreement is measurement-theoretic rather than biological. Separating behavioural from biometric evidence, showing that precision and power vary inversely across the corpus, and mapping the mechanistic pathway step by step together expose three specific gaps: a dopamine link that is entirely model-derived, an undemonstrated causal direction between choroidal phase and axial elongation, and an unresolved polarity for melatonin's scleral effect.

Clinical implications. Three conclusions can be acted on now. Circadian timing is not yet a screening or prognostic measure; no threshold, assay standard or sampling protocol is validated for individual decisions. Evening light management is defensible as general sleep hygiene, especially in children, but should not be presented to families as myopia control, since no included trial tested a circadian-timed intervention against an axial endpoint and the lens-filtering literature does not support consistent benefit [28,29]. Time outdoors remains the exposure with the strongest causal support [5,24], and it plausibly acts partly through entrainment so the circadian rationale reinforces existing public health advice rather than replacing it.

Unresolved questions. Five would need answers before the paradigm could be adopted. Does circadian timing predict incident myopia prospectively, before refraction changes? Is melatonin's scleral effect protective or permissive? Does a phase-advancing intervention produce a measurable axial benefit, and of what magnitude? Which light metric intensity, duration, timing or spectrum carries the effect? And does light act on growth through the circadian system at all, or is circadian timing simply a marker of the light behaviour that matters optically? Until at least the first and third are answered, circadian disruption is best described as a compelling candidate mechanism in eye growth regulation, not yet a new paradigm.

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