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Review Article

Midnight-noon Ebb-flow (*Ziwu Liuzhu*) and Circadian Science: Comparison of Two Temporalized Models of the Body

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Abstract

Midnight-noon ebb-flow (*ziwu liuzhu*) and circadian science are both temporalized models of the body, treating time of day as an intrinsic variable of physiology and therapeutic response, yet they differ fundamentally in theoretical units, causal claims, and standards of evidence. *Ziwu liuzhu*, a time-function model of traditional Chinese medicine, maps the 12 double-hours (*shichen*) onto the ebb and flow of qi and blood in the 12 channels (meridians); circadian science, an experimentally grounded mechanistic model, describes circadian rhythms generated by an endogenous, light-entrained timing system of the suprachiasmatic nucleus, clock genes, and peripheral clocks. Existing accounts tend either to conflate the two frameworks or to dismiss one in terms of the other. This narrative review compares the two frameworks' conceptual structure, historical formation, mechanisms, evidence, and applications. Their genuine convergence lies in treating time as a variable in health and disease, not in any proven mechanism. Chronotherapy findings likewise do not validate the channel-hour correspondences. Fixed double-hour assignments do not correspond to the phase-adjustable, individually variable circadian system; the morphological basis of the channels remains unconfirmed; and the certainty of evidence for a timing-specific effect of *ziwu liuzhu* acupuncture appears low to very low. We distinguish three critical issues that are often conflated: the efficacy of timed acupuncture, its mechanism, and the anatomical status of the channels; evidence on the first two does not settle the third. We propose a layered research agenda that preserves the tradition's historical and clinical value while rigorously evaluating its testable claims, chiefly through trials comparing identical needling given on-time and off-time, scheduled both by classical clock time and relative to measured circadian phase. We conclude that *ziwu liuzhu* is best treated as a source of testable hypotheses, and that no clinical efficacy should be claimed for its timing principle until it has been demonstrated.

Introduction

Two very different frameworks share an intuition: the living body does not function identically at every hour but rises and falls with the cycles of day and night, activity and rest, and feeding and fasting.[1,2] Classical Chinese medicine elaborates this intuition through *ziwu liuzhu*, in which qi and blood flourish and recede through the 12 channels in step with the 12 double-hours of the day. Contemporary biology expresses it through circadian science, whose foundational discovery, the transcription-translation feedback loops of the cellular clock, was recognized by the 2017 Nobel Prize in Physiology or Medicine.[3,4]

Integrative medicine increasingly explores whether the temporal concepts of older healing systems can inform modern chronomedicine, and *ziwu liuzhu* is an extensively developed temporal doctrine within Chinese medicine.[1,2] However, it also circulates as a simplified "organ clock" promoted as literal physiology. The literature accordingly tends toward two diametrically opposed errors: claiming that ancient physicians had already discovered the biological clock, or dismissing the tradition wholesale because the channels have not been isolated anatomically. Whereas recent comparative scholarship has emphasized conceptual parallels between the traditional double-hour timetable and circadian rhythm,[2] this review treats the two frameworks as distinct systems and distinguishes a shared concern with time from demonstrated biological mechanisms.

Keywords: Midnight-noon ebb-flow; Ziwu liuzhu; Circadian science; Temporalized model; Circadian rhythm; Chronotherapy; Traditional Chinese medicine; Acupuncture; Suprachiasmatic nucleus; Meridians.
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A note on terminology. Terms such as qi, blood, channel, viscus, gallbladder qi, and heart qi are used in their traditional functional sense. Qi denotes the activity and movement that sustain bodily function; blood (*xue*), the nourishing substance moved by qi; a channel (*jingmai*, often rendered as meridian), a pathway linking the body surface and interior along which qi and blood are understood to circulate; and a viscus (*zangfu*), a functional system named after, but not identical to, an anatomical organ. None of these terms is equated here with a discrete anatomical structure, a laboratory quantity, or a molecular mechanism. Functional descriptions such as "coursing" and "diffusion and descent" (explained in the notes to Table 1) describe traditional functional patterns rather than modern physiological actions,[5-9] and *nazi* and *najia* refer to traditional stems-and-branches methods of timing acupoint selection, not to circadian phase markers. Where a modern parallel is offered, for example heart qi as a conceptual parallel to cardiovascular and mental vigor, it is an interpretive analogy only. "Circadian science" refers to the modern framework that investigates the biological timing system, "circadian clock" to that timing system itself, "time-function model" to *ziwu liuzhu*, and "organ clock" exclusively to the popular simplification of the latter.

We use the term *temporalized model* for an account of the body in which time of day is treated as an intrinsic variable of physiology and therapeutic response rather than as a background condition. In this sense, the two models compared here are *ziwu liuzhu*, a traditional time-function model, and circadian science, an experimentally grounded mechanistic model. The objective of this review is to compare *ziwu liuzhu* and circadian science across their conceptual structure, historical formation, mechanistic content, evidentiary basis, and clinical applications, while proposing a layered research agenda that separates testable claims from untestable ones. As a narrative review, it draws on purposively selected sources: the classical medical texts in standard translations, the later acupuncture literature, and representative chronobiological and clinical studies. Throughout, three categories of statement are distinguished: historical interpretation of what the classical sources assert, modern hypotheses generated by the comparison, and experimentally testable modifications of the traditional claims.

Viewpoint 1: *Ziwu liuzhu* as a traditional time-function model

The scaffolding of *ziwu liuzhu* is the division of the day into 12 double-hours, each named after an earthly branch and spanning roughly two modern hours. This is not a neutral clock face but a cosmological cycle: the *zi* hour falls around midnight, when yin reaches its extreme and yang begins to stir, and the *wu* hour around noon, when yang peaks and yin begins to return. The *Lingshu* names noon the height of yang (*chong yang*) and midnight the height of yin (*chong yin*) (chapter 18).[5] Onto this cycle the tradition maps a fixed sequence of channels, each said to be "in charge" (*dang ling*) during its double-hour (Table 1). Being in charge means that a functional system is held to be most prominent, and its disorders most readily observed, during that interval; it does not mean that the corresponding organ ceases to function outside it.

The *Huangdi Neijing* already relates the body to time, taking *zi* and *wu* as the warp and *mao* and *you* as the weft of a coordinate system for the movement of qi (*Lingshu*, chapter 76).[5] It describes construction qi (*ying qi*) completing a fixed circuit through the 12 channels that begins in the hand-taiyin lung channel (*Lingshu*, chapter 16), and defensive qi (*wei qi*) moving through the yang aspect of the body by day and the yin aspect by night (*Lingshu*, chapters 18 and 76).[5] The clock form of the timetable reproduces this circuit: the lung is assigned to the *yin* hour (03:00–05:00), and, read from midnight, the sequence runs from the gallbladder at the *zi* hour, as yang first stirs, to the triple energizer at the *hai* hour (21:00–23:00), after which the cycle turns again at midnight. Being in charge thus marks a phase of one continuous circulation rather than a relay of organs taking turns.

The full 12-channel timetable and its point-selection methods were systematized much later, in the acupuncture literature of the Jin to Ming dynasties, including Yan Mingguang's *Ziwu liuzhu zhenjing* (which annotates He Ruoyu's *Liuzhu zhiwei fu*) and Xu Feng's *Zhenjiu daquan*.[7,8,10] The two methods, *nazi* ("receiving the branch") and *najia* ("receiving the stem"), select acupoints according to the day and hour of the stems-and-branches calendar. *Nazi* selects points on the channel active during the current double-hour, whereas *najia* selects an "opening" point based on the heavenly stem of the day and hour. This narrow technique of time-specific opening-point acupuncture must not be equated with the broader notion that the body corresponds to the daily cycle. Many clinicians use the hour at which a symptom arises, worsens, or eases as a clue in pattern differentiation without applying *najia* or *nazi* protocols, and evidence for or against the former should not be transferred automatically to the latter.

The 12 earthly branches were also correlated with the 12 sovereign (*bi*), or waxing-and-waning (*xiaoxi*), hexagrams of the *Yijing*, a correlation developed in the Han-dynasty *guaqi* tradition associated with Meng Xi and Jing Fang, so that a single day recapitulates the seasonal cycle in miniature.[10,11] This correspondence is best understood as an interpretive heuristic that illuminates the directional logic of the sequence, in which darkness gives way to light and activity gives way to rest, rather than as a mechanism documented in the early medical sources. The same 12-double-hour framework also shaped contemplative practice in medieval Chinese Buddhism.[12]

On the tradition's own account, living in accord with the hours is a form of cultivation (*yangsheng*). The *Neijing* states that yang qi arises at dawn, peaks at midday, and wanes toward evening (*Suwen*, chapter 3); that at midnight yin and yang converge "and all people sleep" (*Lingshu*, chapter 18); and that the other viscera rely on the gallbladder for decision (*Suwen*, chapter 9).[5,9] Later *yangsheng* teaching, grounded in the principle that the body should comply with the daily waxing and waning of yin and yang,[1] built on these passages the specific advice that sleep during the *zi* hour nourishes gallbladder qi and fosters nascent yang, and that a brief rest at the *wu* hour nourishes heart qi and settles the spirit, whereas habitually violating this schedule disorders qi and, over time, depletes essence (*jing*) and unsettles the spirit (*shen*). These are normative claims internal to the tradition, offered as guidance for conduct rather than as measured quantities.

Traditional practice is individualized, but at the level of diagnosis and treatment rather than at the level of the timetable. The *Neijing* describes the age-related decline of qi, blood, and kidney essence (*Suwen*, chapter 1; *Lingshu*, chapter 54) and attributes the

Table 1. The traditional correspondences between the 12 double-hours (*shichen*) and the channels in *ziwu liuzhu*

Double-hour	Approximate clock time	Corresponding channel (viscus)	Traditional functional emphasis	Classical basis
Zi	23:00–01:00	Gallbladder Meridian of Foot-Shaoyang (GB)	Yang first stirs; decision and free coursing	*Suwen* 8: official of uprightness, from which decisions issue; *Suwen* 9: the other viscera rely on the gallbladder for decision; free coursing is a later (post-Song) doctrine
Chou	01:00–03:00	Liver Meridian of Foot-Jueyin (LR)	Storing blood; coursing; deep-night restoration	*Suwen* 10: when a person lies down, blood returns to the liver; coursing is a later (post-Song) doctrine
Yin	03:00–05:00	Lung Meridian of Hand-Taiyin (LU)	Diffusion and descent; the rhythm of respiration	*Suwen* 8: minister regulating the rhythm of the body; *Lingshu* 16: circuit of construction qi begins in the lung channel; diffusion and descent is a later formulation
Mao	05:00–07:00	Large Intestine Meridian of Hand-Yangming (LI)	Elimination and renewal; movement outward	*Suwen* 8: official of conveyance, from which change and transformation issue
Chen	07:00–09:00	Stomach Meridian of Foot-Yangming (ST)	Receiving food and drink; the morning meal	*Suwen* 8: spleen and stomach as officials of the granaries
Si	09:00–11:00	Spleen Meridian of Foot-Taiyin (SP)	Transformation of food; supplying activity	*Suwen* 8; *Suwen* 21: spleen qi disperses essence
Wu	11:00–13:00	Heart Meridian of Hand-Shaoyin (HT)	Spirit and vessels; the peak of yang	*Suwen* 8: sovereign, from which spirit brightness issues; *Lingshu* 18: noon as the height of yang (*chong yang*)
Wei	13:00–15:00	Small Intestine Meridian of Hand-Taiyang (SI)	Receiving the bounty; separating clear from turbid	*Suwen* 8: official of receiving the bounty, from which transformed things issue; separating clear from turbid is later commentary
Shen	15:00–17:00	Bladder Meridian of Foot-Taiyang (BL)	Fluid metabolism and excretion	*Suwen* 8: official of the regional capital, where fluids are stored
You	17:00–19:00	Kidney Meridian of Foot-Shaoyin (KI)	Storing essence; turning from peak to gathering	*Suwen* 9: root of sealing and storage, the place of essence
Xu	19:00–21:00	Pericardium Meridian of Hand-Jueyin (PC)	Protecting the heart-spirit; emotional settling	*Suwen* 8: *danzhong*, the envoy from which joy issues (later identified with the pericardium); *Lingshu* 71: the pericardium receives pathogens on behalf of the heart
Hai	21:00–23:00	Triple Energizer Meridian of Hand-Shaoyang (TE)	Water pathways; whole-body coordination of qi	*Suwen* 8: official of the drainage ditches, from which the waterways issue

The table is a traditional classificatory and clinical instrument. "In charge" (*dang ling*) denotes the interval in which a functional system is held to be most prominent, not a claim that the corresponding organ works only within that two-hour window. Each channel is paired with its namesake viscus (*zangfu*); channel names and abbreviations follow the World Health Organization Standard Acupuncture Nomenclature.[6] The clock assignments follow the acupuncture literature of the Jin to Ming dynasties[7,8]; their order reproduces the *Lingshu* circuit of construction qi. Clock times are modern equivalents of local solar time. In the classical basis column, "Suwen 8" denotes *Suwen*, chapter 8, and so on[5,9]; entries marked as later reflect post-*Neijing* or modern textbook interpretation. Functional terms: coursing (*shuxie*), keeping qi, emotion, and bile moving smoothly (free coursing refers to the same function in the gallbladder); diffusion and descent (*xuanfa sujiang*), the outward dispersal and downward movement of qi and fluids attributed to the lung; transformation of food (*yunhua*), digestion and distribution of nutriment attributed to the spleen; separating clear from turbid (*fenbie qingzhuo*), the sorting of usable from waste material attributed to the small intestine. These are traditional functional descriptions, not modern physiological actions; any modern parallel is an interpretive analogy. BL, bladder meridian; GB, gallbladder meridian; HT, heart meridian; KI, kidney meridian; LI, large intestine meridian; LR, liver meridian; LU, lung meridian; PC, pericardium meridian; SI, small intestine meridian; SP, spleen meridian; ST, stomach meridian; TE, triple energizer meridian.

poor daytime alertness and poor night-time sleep of the elderly to the decline of their qi and blood (*Lingshu*, chapter 18)[5,9]; later writers, most notably Zhang Jiebin, regarded yang as the body's "great treasure", on which health and longevity depend.[13] Age and constitution thus shape pattern differentiation and treatment, but the timetable itself assigns the same local hours to every person.

The ontology of the model requires a final caution. Reviews conclude that the morphological basis of the channels remains unconfirmed and that the channels cannot be equated with blood vessels, nerves, or lymphatic vessels.[14,15] Three levels of evidence must be distinguished. Measurable physiological phenomena along channel pathways, such as differences in skin electrical impedance, low hydraulic resistance, and infrared thermal signals, have been reported, although not consistently reproduced.[15-17] Anatomical hypotheses, including connective-tissue planes and interstitial fluid pathways, remain untested proposals.[15,18] No universally accepted discrete anatomical conduit has been identified. The existence of measurable phenomena should therefore not be confused with the identification of a specific anatomical structure. *Ziwu liuzhu* is best understood as a traditional time-function model with internal coherence and a long history of clinical use, though its timing-specific clinical efficacy remains insufficiently validated and its underlying functional units are not those of gross anatomy.

Viewpoint 2: Circadian science as an experimentally grounded mechanistic model

Circadian rhythms are endogenous, self-sustained oscillations with a period close to 24 hours that persist under constant conditions, can be entrained by environmental cues (zeitgebers), and are temperature-compensated. Diurnal variation, by contrast, denotes any observed day-night difference, which may be driven wholly or partly by external cycles of light, activity, and feeding and may disappear when those cues are held constant; chronobiology separates the two by means of constant-routine and forced-desynchrony protocols.[19] In mammals, the central pacemaker resides in the suprachiasmatic nucleus (SCN) of the hypothalamus, which receives light information from the retina and coordinates the rhythms of sleep and wakefulness, core body temperature, hormone secretion, and alertness; darkness is signaled by pineal melatonin, whose secretion the SCN gates.[20-22] At the cellular level, the clock consists of interlocking transcription-translation feedback loops: the transcription factors CLOCK (circadian locomotor output cycles kaput) and BMAL1 (brain and muscle ARNT-like 1) drive expression of the *Period* (*PER*) and *Cryptochrome* (*CRY*) genes, whose protein products accumulate, inhibit their own transcription, and are then degraded, so that the cycle restarts with a period of about 24 hours, while auxiliary loops involving the nuclear receptors REV-ERB and ROR (retinoic acid receptor-related orphan receptor) fine-tune its phase.[3,4] Because these components regulate much of the transcriptome, a substantial fraction of the genes in any tissue is expressed rhythmically.[23]

Peripheral tissues, including the liver, pancreas, heart, and skeletal muscle, contain cell-autonomous clocks that behave as semi-autonomous oscillators at the tissue level: the SCN coordinates rather than generates their rhythms, through neural, hormonal, body-temperature, and feeding-related signals, and the timing of meals can shift peripheral clocks independently of the SCN.[23-25] Chronic misalignment between central and peripheral clocks, as in shift work, jet lag, or mistimed eating, is associated with sleep disorders, metabolic dysregulation, mood disturbance, and cardiovascular risk.[25-27] Cortisol peaks in the early morning, core body temperature reaches its trough before dawn and its peak in the early evening, and blood pressure and digestive and immune functions vary across the day[28]; alertness and cognitive performance follow similar daily rhythms.[29-31] The phase of the system is plastic: the same clock hour corresponds to different internal times in different people, and light, meals, and sleep can advance or delay it.[21] The clock is thus an oscillator negotiated with the environment rather than a schedule imposed from outside.

Two limits follow for the present comparison. First, the traditional sources contain no equivalent of constant-routine controls and therefore cannot distinguish endogenous rhythms from diurnal variation. Second, the fact that cortisol, temperature, blood pressure, and digestive function vary across the day shows that human physiology is temporally organized; it does not validate the assignment of a particular channel or viscus to a particular double-hour, and apparent matches may reflect conventional times of eating and sleeping rather than intrinsic rhythms. The mechanistic account explains how the body keeps time, but it is not evidence for the channel-hour correspondences of *ziwu liuzhu*, whose units and causal language are of a different kind.

Viewpoint 3: Points of genuine convergence

Set side by side, the two temporalized models share a refusal to treat the body as static: both hold that when a symptom occurs is as informative as what the symptom is.[1,2] The injunction to "accord with the timing of heaven" (*shun ying tian shi*), which counsels against chronically violating the daily cycle, can be brought into genuine dialogue with modern evidence on sleep regularity, light exposure, and meal timing.[26,27,32]

The recommendations of the two frameworks, however, rest on different grounds and must be kept distinct. A regular sleep schedule, morning daylight, dim light in the evening, and consistent daytime eating are supported by chronobiological evidence; for time-restricted eating, evidence of metabolic benefit is promising, although it remains limited.[26,27,32,33] Traditional recommendations such as sleep during the *zi* hour, rest during the *wu* hour, and channel-specific timing of activities are cultural analogies without direct experimental support. A clinician may draw on both vocabularies when counseling regularity but should not present the second set of recommendations as validated by the first.

The convergence extends to treatment. Chronotherapy shows that the timing of an intervention can alter its efficacy and toxicity for some agents, notably several chemotherapeutic drugs.[34,35] Time-of-day variation in response does not, however, establish universal timing rules. Evidence on bedtime dosing of antihypertensive drugs has been conflicting, and the large pragmatic TIME trial found no difference in major cardiovascular outcomes between morning and evening dosing[36,37]; the field is moving toward timing interventions to each patient's internal phase rather than to fixed clock hours.[28,38] *Ziwu liuzhu* likewise holds that the hour of treatment matters, but the explanations differ entirely: the tradition reasons from the ascendancy of a channel, whereas modern medicine reasons from the phase of a molecular clock and of its drug targets.

Both frameworks should resist a popular misreading. In contemporary wellness writing, the timetable is often simplified into an "organ clock" in which each organ "detoxifies" or "repairs" itself within its allotted two hours. The classical sources describe the relative ascendancy of a functional channel system within one continuous circulation of qi and blood, not an hour-by-hour cleansing of anatomical organs, and circadian science describes graded, overlapping, individually phased rhythms rather than discrete maintenance slots. Neither framework supports the organ-clock claim. Table 2 summarizes the comparison, including the evidence level and validation status of each framework.

Viewpoint 4: Where the mapping breaks down

The first fault line is the structure of time itself. *Ziwu liuzhu* assigns each channel a fixed two-hour peak at the same local hours for every person, even where treatment is individualized, whereas the circadian system is defined by an adjustable phase and amplitude and by wide individual variation in chronotype, driven by genetics, age, light exposure, latitude, and work schedule.[39] A night-shift worker, an adolescent with a late chronotype, and an early-rising older adult occupy different internal phases at the same clock hour, and light can shift the entire system by several hours within days. A universal, fixed two-hour peak for each channel has no counterpart in a physiology of broad, overlapping, phase-shiftable oscillations.

The distinction between endogenous rhythms and diurnal variation applies directly to the timetable. A symptom may peak at a given hour simply because the person is then awake, upright, or eating; without constant-routine controls, an observed match between a symptom and a channel-hour may reflect behavior and environment rather than an intrinsic channel rhythm. This does not refute the clinical observation, but it constrains what the observation can prove. Attempts to detect channel-linked rhythms directly, such as an infrared thermal-imaging case series, remain preliminary.[17]

Three critical issues are routinely conflated: whether timed acupuncture is clinically effective for a given condition; through what mechanisms needling acts, whether neural, connective-tissue, endocrine, immune, or analgesic; and whether the channels constitute an independent anatomical system. Evidence on the first two issues does not settle the third.[14,15]

Clinical evidence bears mainly on the first issue, and even there it seldom isolates timing. A controlled trial in post-stroke aphasia (196 patients) compared language rehabilitation alone with the same rehabilitation plus *ziwu liuzhu* timed acupuncture, using Jiexi (ST 41) as the hour-selected main point, with supplementary points including Zusanli (ST 36) and Sanyinjiao (SP 6), combined with the Baihui (GV 20) Bazhen needling pattern for 4 weeks,[40] and a randomized trial in central neurogenic bladder (60 patients) compared device-based low-frequency electrical stimulation of fixed acupoints (Sanyinjiao [SP 6], Zhongji [CV 3], and Diji [SP 8]), timed according to the midnight-noon ebb-flow concept and added to basic rehabilitation, with rehabilitation alone.[41] Both reported benefit, but in both the control group received no acupoint stimulation at all. Such add-on designs test whether a timed acupuncture package adds to usual care, not whether timing matters, because timing is confounded with needling itself and with the additional treatment time, attention, and expectation. Because the second trial used non-invasive stimulation rather than needling, it bears on needle acupuncture only indirectly.

Two further lines of evidence sharpen the point. First, acupuncture given without reference to the double-hours can itself be effective: a sham-controlled trial in primary insomnia found benefit from untimed acupuncture,[42] and an individual patient data meta-analysis of chronic pain trials found acupuncture superior to both sham and no-acupuncture controls, although the difference from sham was modest.[43] Any timing-specific effect must therefore be detected over and above an active, untimed treatment, which may require large samples to detect small differences. Second, the design that comes closest to isolating timing is a randomized trial in which 86 older adults received a Chinese five-element music intervention either organized according to midnight-noon ebb-flow theory or delivered in the standard way; the ebb-flow arm showed greater reductions in depression and anxiety scores.[44] This is a single, modest-sized trial of a non-needling intervention, and its findings cannot be transferred to acupuncture.

Judged against the Grading of Recommendations Assessment, Development and Evaluation (GRADE) domains of risk of bias, inconsistency, indirectness, imprecision, and publication bias,[45] the certainty of evidence that timed acupuncture packages improve selected outcomes compared with usual care appears low: the trials are small to moderate in size, mostly single-center, often unblinded, and drawn from a literature in which trials from some countries report almost uniformly positive results.[46] The certainty of evidence for a timing-specific effect of *ziwu liuzhu* acupuncture appears low to very low, because no trial identified here compares identical needling given on-time and off-time, so the evidence is indirect as well as imprecise. Future trials should report the clock time of every session, the timing method used (*nazi*, *najia*, or another), and, where possible, each participant's circadian phase, as extensions of the Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA) items for acupuncture interventions.[47]

Viewpoint 5: A layered research agenda and future directions

A layered research program begins with historical interpretation of what the classical sources assert, distinguishing the cosmology of the *Neijing* from later systematization.[5,7,9] Chinese medical theory supplies the diagnostic context in which the double-hours serve as one variable among symptoms, constitution, and lifestyle. Modern hypotheses generated by the comparison are then stated explicitly, and chronobiology tests those that are empirically measurable.

The central testable proposition is simple to state but demanding to test: does needling an acupoint during the double-hour of its channel outperform the identical treatment given off-time? A rigorous design would randomize participants to on-time or off-time needling of the same points for the same condition, anchor time to objective circadian markers such as dim-light melatonin onset or the cortisol rhythm, and define each channel-hour relative to the participant's own phase.[22,39,48] Defining channel-hours by individual circadian phase is not part of the classical doctrine, which uses local solar time (in modern practice, usually clock time); it is a modified hypothesis informed by modern chronobiology and proposed here to make the traditional claim testable. A three-arm trial comparing classical clock-time scheduling, phase-adjusted scheduling, and off-time treatment

Table 2. *Ziwu liuzhu* and circadian science compared

Dimension	*Ziwu liuzhu*	Circadian science
Type of model	Traditional time-function model	Experimentally grounded mechanistic model
Basic theoretical unit	Qi, blood, 12 channels, visceral functional systems	SCN, peripheral clocks, clock genes, melatonin, physiological rhythms
Time structure	12 double-hours; each channel has a fixed two-hour peak at the same local hours for everyone	24-hour rhythm with adjustable phase and amplitude; also seasonal and other cycles
Principal entraining factors	Sun and moon, waxing and waning of yin and yang, daily routine, correspondence between heaven and humans	Light-dark cycle, feeding, activity, temperature, hormones, social time
Causal language	A channel is in charge; qi and blood flourish or ebb	Light resets the SCN; the SCN coordinates semi-autonomous peripheral clocks that regulate genes, hormones, and behavior
Primary evidence	Classical texts, clinical observation, pattern differentiation, and timed point selection	Physiological measurement, molecular biology, sleep science, and randomized trials
Ontological status	Channels not equated with anatomical conduits; measurable phenomena reported, substrate unconfirmed	SCN, hormones, neural pathways, and gene loops are directly investigable
Evidence level	Low to very low certainty for a timing-specific effect; low certainty for timed acupuncture packages on selected outcomes	High certainty for core mechanisms; variable for specific chronotherapies
Validation methods	Classical authority, clinical observation, and small to moderate-sized, mostly single-center trials with usual-care comparators	Constant-routine and forced-desynchrony protocols, genetic models, phase markers (e.g., dim-light melatonin onset), and randomized trials
Mechanistic support	No established mechanism for channel-hour timing	Transcription-translation feedback loops and SCN-peripheral coordination experimentally established
Clinical applicability	Diagnostic clue in pattern differentiation; health education on regularity; timing-specific efficacy not validated	Evidence-based sleep, light, and meal-timing advice; chronotherapy for selected agents; no universal timing rules
Kind of claim	Historical interpretation; channel-hour timing is a testable hypothesis; phase-adjusted timing is a modern modification	Experimentally established findings, with open questions on individualized timing

SCN, suprachiasmatic nucleus.

would test the original and modified claims separately. Neurophenomenological methods, which correlate first-person reports with physiological data, could complement such trials by relating patients' own reports of when symptoms arise, worsen, or ease to measured circadian phase.[49,50]

Crossover and n-of-1 designs suit this question because they can detect within-person timing effects while controlling for between-person variation. They also carry inherent constraints. They are appropriate only for stable, chronic conditions; they are vulnerable to carryover of acupuncture effects and therefore require adequate washout periods; they may be affected by period effects and dropout; and their results may not generalize to broader populations. They should therefore be complemented by adequately powered parallel-group trials.[51]

Either outcome would be informative. A positive result, with on-time needling outperforming off-time needling under phase control, would be a substantive, mechanism-neutral finding regardless of how the channels are ultimately understood. A null result would not discredit acupuncture; it would suggest that any benefit may depend on factors other than timing and could help avoid an unnecessary scheduling constraint. In either case the tradition is engaged on its strongest claim rather than caricatured, and a person-centered reading of *ziwu liuzhu*, in which the right time is defined relative to each patient's own rhythm, would align a modified form of the tradition with the direction of modern chronomedicine.[28,38]

Two constraints should govern any such program. Clinically, *ziwu liuzhu* should serve as a tool for asking when a symptom arises, worsens, or eases, and for encouraging regularity of sleep, light exposure, and meals, not as a rigid timetable of prohibitions. It cannot substitute for modern management of emergencies such as acute trauma, chest pain, or neurological crises, and patients should not discontinue medication or delay diagnosis on the basis of a channel timetable. Methodologically, application must be

individualized, because shift work, travel across time zones, age, disease, medication, and light environment all reshape a person's rhythms.[39]

Limitations

The evidence in this field suffers from several key limitations. First, clinical studies of *ziwu liuzhu* are small to moderate in size, mostly single-center, and heterogeneous; none identified here includes an off-time control, sham controls are uncommon, blinding is limited, and publication bias toward positive findings is possible.[46] Second, to our knowledge, no study has directly tested channel-hour correspondences against circadian phase markers such as dim-light melatonin onset, so the relationship between the traditional timetable and endogenous biological rhythms remains unexplored. Third, the morphological basis of the channels remains unconfirmed, which limits mechanistic interpretation of any timing effect. Fourth, comparing a traditional theoretical framework with a mechanistic biological model is inherently constrained, because their units, causal language, and standards of evidence differ, and the correspondences identified between them are interpretive rather than demonstrated.

This review also has limitations of its own. This is a narrative comparative review. No systematic literature search or meta-analysis has been performed, and no formal risk-of-bias assessment was undertaken. The viewpoints presented represent the authors' synthetic appraisal and should not be treated as conclusions from a systematic review. The certainty ratings given above reflect the authors' judgment based on GRADE domains, not the output of a formal GRADE assessment.

Conclusions

The true meeting point of *ziwu liuzhu* and circadian science is a shared conviction that life is temporally organized and that health and disease cannot be understood outside time. *Ziwu liuzhu* expresses this conviction in the language of yin and yang, qi and blood, and channels and viscera; circadian science expresses it in terms of the SCN, light entrainment, melatonin, clock genes, and peripheral oscillators. The former is a traditional time-function model and the latter an experimentally grounded mechanistic one, and they differ as much in evidence level and validation method as in vocabulary. The most productive position keeps each framework in its own context, submits the testable claims of the traditional model to rigorous evaluation, and treats *ziwu liuzhu* as a resource for generating hypotheses, organizing clinical observation, and understanding the history of medical thought, without asserting clinical efficacy for its timing principle before such efficacy has been demonstrated. So framed, the doctrine retains its cultural and clinical value, while integrative medicine keeps faith with evidence, safety, and the individuality of each patient's rhythm.

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Conflict of interest

The authors have no conflicts of interest related to this publication.

Author contributions

Study concept and design (KCH), literature search and analysis (KCH, YNC), drafting of the manuscript (KCH), and critical revision of the manuscript for important intellectual content (KCH, YNC). Both authors made significant contributions to this study and have approved the final manuscript.

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