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# Human Responses to the Geophysical Daily, Annual and Lunar Cycles

Review



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**Collectively the daily, seasonal, lunar and tidal geophysical cycles regulate much of the temporal biology of life on Earth. The increasing isolation of human societies from these geophysical cycles, as a result of improved living conditions, high-quality nutrition and 24/7 working practices, have led many to believe that human biology functions independently of them. Yet recent studies have highlighted the dominant role that our circadian clock plays in the organisation of 24 hour patterns of behaviour and physiology. Preferred wake and sleep times are to a large extent driven by an endogenous temporal program that uses sunlight as an entraining cue. The alarm clock can drive human activity rhythms but has little direct effect on our endogenous 24 hour physiology. In many situations, our biology and our society appear to be in serious opposition, and the damaging consequences to our health under these circumstances are increasingly recognised. The seasons dominate the lives of non-equatorial species, and until recently, they also had a marked influence on much of human biology. Despite human isolation from seasonal changes in temperature, food and photoperiod in the industrialised nations, the seasons still appear to have a small, but significant, impact upon when individuals are born and many aspects of health. The seasonal changes that modulate our biology, and how these factors might interact with the social and metabolic status of the individual to drive seasonal effects, are still poorly understood. Lunar cycles had, and continue to have, an influence upon human culture, though despite a persistent belief that our mental health and other behaviours are modulated by the phase of the moon, there is no solid evidence that human biology is in any way regulated by the lunar cycle.**

## Introduction

Geophysical cycles dominate much of the activity of life on earth. The daily (24 hours ± 30 seconds), seasonal (365.24 days), lunar (29.53 days) and tidal (12.8 hour) cycles provide the temporal cues for the coordination of most behaviours ranging across daily feeding patterns, daily and seasonal migration, growth, reproduction, hibernation and much else. The extent to which humans respond to, and are influenced by, each of these cycles will be explored in this review. Like almost all life on the planet, much of human physiology and behaviour is controlled, modulated or at least 'fine-tuned' by an internal ~24 hour circadian timer in anticipation of the varying demands of the day/night cycle. As in other mammals, light perceived by the eye provides the primary cue for the entrainment of our circadian program [1] and, despite the imposition of social time and a world divided into time zones, human behaviour is still dominated by geophysical sunrise and sunset [2]. Yet society is moving increasingly towards a 24/7 structure and atemporality.

The increasing tendency to work at odds with biological time is having a marked impact on our health, exacerbating, for example, cardiovascular disease, cancer, obesity and mental health problems [3]. Whilst circadian cycles dominate our physiology and behaviour, the impact of annual cycles is less obvious. Human patterns of birth, death, suicide and disease show seasonal changes, and despite an increasing isolation from seasonal variation in the developed economies, and a corresponding decrease in the amplitude of these annual rhythms, they can be detected in population studies [4]. In contrast to other vertebrates, many of which are known to have endogenous annual timing mechanisms that predict seasonal change [5], in humans, the mechanisms that generate seasonality remain poorly defined. Whether we use an endogenous timer or simply respond to seasonal change is much debated. What is clear, however, is that an understanding of these seasonal affects is likely to provide important insights into our susceptibility to conditions such as schizophrenia and multiple sclerosis.

Many organisms living in tidal zones use the lunar cycle to anticipate the tides [6]. Human culture has been greatly influenced by the obvious waxing and waning of the moon and it is likely that some of the first calendars generated by the early civilisations were based upon twelve lunations in a solar year, a period of 354.37 days. Whilst lunar cycles have dominated human culture, and despite the persistent belief that our mental health can be modulated by the phase of the moon, there is no reliable evidence that the moon can influence our biology.

## Daily Rhythms

Jürgen Aschoff was the first to investigate experimentally the circadian clock of humans. Together with Rüdger Wever, he had a 'bunker' built into a hill near the monastery at Andechs which was famous for brewing among the best Bavarian beers. For more than 20 years, this isolation facility was used for the investigation of the human circadian system under constant conditions and under many different entrainment regimes [7]. The studies of Charles Czeisler, Josephine Arendt, Anna Wirz-Justice, Derk-Jan Dijk and many others have built upon Aschoff's observations regarding the mechanisms that generate and regulate (entrain) the circadian activities of humans. This impressive body of work has been reviewed recently [8]. Here we focus upon how humans are influenced by geophysical cycles under non-laboratory conditions.

Humans provide an excellent opportunity to investigate entrainment under real-life conditions by simply asking individuals about their sleep times. An ongoing study using the Munich ChronoType Questionnaire (MCTQ) [9] has sampled well over 70,000 subjects, mainly from Europe and India.

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Analyses of this database are providing important insights into human entrainment. Assessment of the phase of entrainment (chronotype) is based on the mid-time of sleep on free days without social constraints. If a subject slept, for example, from midnight to eight o'clock, his/her mid-sleep on free days would be at four o'clock. This entrainment marker shows an almost normal distribution in a given population, with slightly more late than early chronotypes [10]. Most people sleep at different times during the working week compared to free days.

Although sleep timing and sleep duration are independent traits, there are systematic differences when sleep duration of different chronotypes is compared between work and free days. The later chronotypes tend to get less sleep on work days, because their sleep-onset is largely controlled by the circadian clock whilst their sleep end is dictated by the alarm clock [11]. The relatively few extreme early types experience sleep deprivation on free days, in this case, because social demands (the majority of late types) keep them up beyond their preferred bedtime while their circadian clock wakes them at their habitual time in the morning. Thus, sleep times on free days are influenced by the sleep schedules during the work-week, so that the assessment of chronotype can be improved by a correction for sleep-debt [12]. The difference in sleep timing on work and on free days has been coined *social jetlag* [13] and can be used as a quantitative variable for many research issues, including the affects of shift-work on the circadian system or for correlations with factors such as mood, nicotine and caffeine consumption. For example, the stronger the social jetlag people experience, the more likely they are to be smokers. Among people with no social jetlag the percentage of smokers is at around 10%, but in individuals whose sleep time differs four hours or more between work and free days, this increases to 60% [13].

The phase of entrainment changes with age. Children are usually relatively early chronotypes, while the circadian programme progressively delays throughout puberty and adolescence until it reaches a 'peak' of lateness around the age of 21 (1.5 years earlier in women than in men). From that age, the phase of entrainment becomes progressively earlier again (Figure 1) [12]. The fact that male adolescents delay for longer than female adolescents also explains why in a given age group adult males are, on average, later chronotypes than females. The importance of an accurate chronotype assessment is proving useful not just as a marker for human development but also in a broad range of other 'real-life' situations, including individual shift work scheduling, interpretation of medical results and optimal timing of medical interventions.

It is becoming increasingly evident that internal time (as represented by chronotype) is more important than external time (as represented by social time) for understanding human 24 hour biology. A recent study has shown that the human circadian clock entrains predominantly to sun time, rather than social time (Figure 2) [2], and in this regard humans are comparable to other animals. A subsequent study investigated the impact of daylight saving time on the phase of entrainment. The results demonstrated that phase systematically tracks the moving dawn/dusk with season but this seasonal adaptation is disrupted by the onset of daylight saving time [14]. In addition, this study showed that the daily activity patterns do not fully adjust to daylight saving time (clock time), especially in later chronotypes.

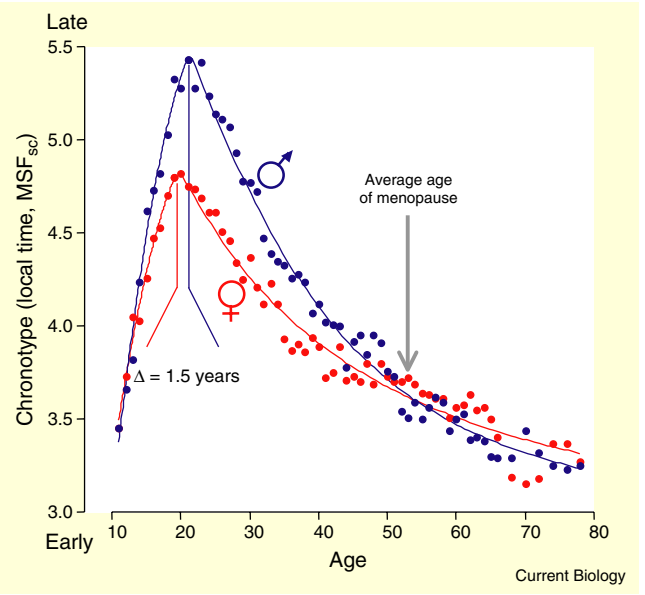


Figure 1. Changes in chronotype with age.

As children, we are early chronotypes, but during puberty and adolescence we progressively delay our body clock by up to two hours. In the early twenties, the gradual delay turns around and our sleep times become increasingly earlier with age. Women reach the turn-around point on average at around 19.5 years of age, while men continue to delay until ~21. As a consequence, men are, on average, later chronotypes than women but since men advance their clocks more, the sex difference disappears at around the age of 52 which coincides with the average age of menopause. The graph shown here represents age-related changes in chronotype for the central European population (redrawn incorporating a larger data-set of ~60,000 individuals from [4]). Similar kinetics exist in rural parts of Northern Italy, Eastern Europe, India and New Zealand (T.R., unpublished data).

## Seasonal Rhythms

With some exceptions, non-equatorial animals do not breed all year round. They save energy by effectively 'turning-off' their reproductive organs for much of the year [5]. In many species, the gonads regress and in some they almost vanish. In the non-breeding state, the reproductive organs of many seasonally reproductive birds weigh no more than 0.02% of body weight, but in full breeding condition the testes of the male can weigh between 1–2% of total body weight (more than the weight of the brain) [15]. Many animals also show seasonal patterns of migration and hibernation, underpinned by profound changes in their physiology and behaviour. The seasonal change in daylength and temperature, and the consequent availability of food, dominates the lives of most non-equatorial species. The extent to which our species is affected by and responds to seasonal change continues to be a much discussed, but poorly understood, component of our biology.

### *Seasonal Birth*

It is worth making the point at the outset of this discussion that many seasonally reproductive species produce and wean their offspring over a short time period: from birth to maternal independence can take a few weeks in rodents or a few months in the smaller primates. By contrast, human offspring have a period of prolonged dependency on the mother, estimated as two years or more in early humans [16]. Because the energy demands of both pregnancy and

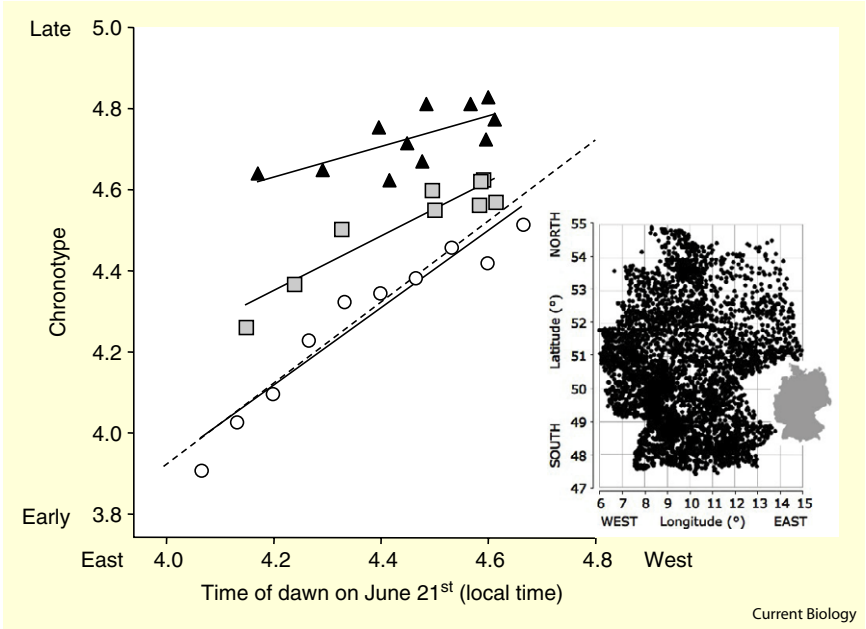


Figure 2. Chronotype depends on the times of dawn and/or dusk rather than on social time.

The inset shows the geographical distribution of the places of residence of German individuals in our database (n = 60,000; a map of Germany is shown in grey). The graph shows the dependency of chronotype on dawn times (arbitrarily chosen for the summer solstice) at the different longitudes. Average chronotypes of people living in areas with up to 300,000 inhabitants are shown as circles (representing 82% of the German population), of those living in cities with up to half a million inhabitants as squares and of those living in even larger cities as triangles. The time difference of dawn between longitude 6° and 15° is 36 minutes. (Adapted from [2].)

lactation are so high and are spread over such a long period of time in humans, there may be no optimal time of year for conception based upon food availability alone. Rather the mother has to be able to sustain good nutritional health across multiple seasons. On this basis, one might predict that seasonal reproduction in humans will be complex, dependent upon multiple environmental and biological variables, and as a consequence have a very variable timing and amplitude across different societies and living conditions.

Human societies show, until recently at least, a significant variation in birth-rate over the year. The range in amplitude of seasonal births in pre-industrialised societies has been 60% or greater, but now seasonality is far less marked in the industrialised nations, being either non-detectable or of very low amplitude (~5%) and requiring large population statistics to detect [4]. What mechanisms have driven this seasonality in the past, and what factors account for the marked drop in seasonal births today remains a matter of much debate. Diligent studies of parish records and local and national censuses have built up a picture of the seasonality of birth and conception in several northern European countries, including Sweden, Finland, England, Germany and Holland, dating back well into pre-industrial times. Whilst there is some inter-country variation, conception rates peak around the end of April beginning of May followed by a secondary much smaller winter peak [17]. The records from North America also show a marked seasonality in birth, but unlike the largely unimodal European conception rate, the pattern is markedly bimodal with a peak in conception around April and a second peak around November. A bimodal pattern of births also occurs in some Eastern European countries and to a lesser extent in Japan [17].

In contrast to these large scale population studies, Condon and Scaglion [18] selectively compared the birth season in two very different cultures. The Copper Inuit live in the Canadian Arctic, where the winter temperature drops to −30°C and the summer high is just over 7°C, accompanied by huge changes in the amount of daylight, wind speed and direction and, of course, ice condition. The Samukundi Abelam live in Papua New Guinea. There is a wet and dry season but the average daily temperature seldom varies much from 25°C and most days are relatively humid. Although both societies had been in contact with Westerners and the Inuits in particular were already beginning to live a very different life from their ancestors, Condon and Scaglion [18] were still able to piece together the traditional patterns of reproduction. Samukundi life revolves around yams. The males tend the crop and their status is dependent on the size of the tubers they grow. The centrality of yams is associated with taboos and rituals. There is a six-month prohibition against sexual activity from July until the January harvest, and during this time there is a ban on sexual innuendo and joking and also on contact with menstruating women. Births peak in October and this is associated with the cultural sex taboo as there is no such seasonality among neighbouring tribes. The taboo is self-reinforcing because women who conceive soon after the harvest are in the third trimester and so are not sexually receptive during the critical yam growing months of August and September [18].

Among the Inuit, "social and economic patters of winter concentration and summer dispersal are regulated by the change of seasons" [18]. Winter is the time for socialising and the dark months are spent in the settlement. As the weather improves in the spring, Inuit families go off on their own to camp outside the settlement and go ice-fishing and duck hunting. This enables them to have more privacy and intimacy. As a result, the vast majority of conceptions take place in the spring and summer, and most births are in the first half of the year. The rhythmicity in rainfall and humidity synchronises the yam-growing season for the Samukundi and social behaviours and cultural taboos 'cement' this seasonality into their lives by the restrictions on sexual congress. This social rhythm synchronises the annual birth rhythms and imposes pronounced birth seasonality in the absence of any dramatic seasonal variation in the environment, including photoperiod and temperature. By contrast, in the Copper Inuit, climatic rhythms appear to directly drive economic activities, social behaviours and physiological response, all of which, Condon and Scaglion [18] conclude, contribute to the non-random distribution of births throughout the year.

Straightforward biological resource factors appear to broadly account for conception/birth seasonality in many

societies. Near universal weight loss is a common feature of the pre-harvest season among the Lese women in the Ituri Forest of the Democratic Republic of the Congo. This weight loss is accompanied by lower levels of salivary progesterone and oestradiol, longer intermenstrual intervals, and shorter durations of menstrual bleeding. All these trends are reversed after the harvest as a positive energy balance is established. Over time this seasonal variation in ovarian function is reflected in a statistically significant seasonal pattern of conceptions after the harvest [19,20]. Such metabolic effects may also help disentangle the cultural *versus* biological basis for why in all hunter-gatherer societies it is the males who do the hunting and females the gathering. When women started training for athletic events to the same intensity as men, menstruation and ovulation became intermittent and often stopped altogether [21]. In hunter gatherer societies, the hunters cover about fifty kilometres a day, every day. If women participated in the hunting then the birth rate in those societies would drop dramatically and that society would quickly disappear. As a result, the only hunter-gatherer societies to survive would be those in which men hunted and the women gathered [21,22].

Overall reproductive fitness has been studied in Canadian women living in the Saguenay region on the north shore of the St Lawrence River in Quebec, Canada ($\sim 48^{\circ}$ north) in the nineteenth century [23]. This is a tough climate with a vegetative season from mid-May to mid-September, but frost at the end of May and at the beginning of September is not unusual. The study examined the cohort of individuals born between 1850 and 1879, including the survival and complete reproductive history of their surviving offspring (born between 1866 and 1926) who married in the same population [23]. The female population they studied was almost entirely French speaking, Catholic, mainly agricultural and culturally homogeneous. Remarkably, the month of birth, which was used as a marker for the conditions experienced during conception and early development, predicted a woman's genetic fitness as measured by the number of grandchildren produced. Women born in June (the 'best' month) had on average at least seven more grandchildren than those born in October (the 'worst' month). Those born in high-success months got married earlier (if under 30), gave birth to their last child later, had a longer reproductive lifespan, gave birth to more children and raised more to reproduce. This differential was caused primarily by differences in the reproductive rates of both mothers and their offspring, rather than differences in their survival. Furthermore, the offspring of those women born in the best months also had greater reproductive rates, suggesting that month of conception/birth also influenced a mother's ability to invest in her offspring.

But what precisely is the crucial factor or factors for these Canadian women? A strong case has been made for conception. Ellison [21] argues that the ability of a woman to divert metabolic energy towards reproduction in the early gestation period is a significant factor in the success of that pregnancy. Indeed, even though the direct energetic costs of the embryo and placenta are minimal in the first few months of gestation, significant fat accumulation occurs during this period. These stores are later drawn upon to meet the high costs of late gestation and early lactation. The efficiency of fat storage is increased in early pregnancy in direct proportion to oestrogen levels. Successful reproduction depends on a continuous diversion of energy from a woman's current metabolic budget. It is the potential for sustaining an ongoing investment that matters most [21]. This strategy of linking female metabolic state to conception to best cope with gestation would allow for a late spring/early summer peak in conception, when the food availability and female metabolic state would have been at their highest, and a subsequent birth peak around the spring equinox. So food availability drives maternal metabolic state, which in turn modulates successful conception and gestation. This attractive hypothesis seems to explain the seasonal reproduction of these Canadian women in Quebec. Whether it applies more universally remains unclear because of the paucity of similarly detailed longitudinal studies in other human societies.

Strikingly, gestation events affect not only the immediate offspring but also the subsequent generation, as has been demonstrated among women who became mothers during or soon after the Dutch famine of 1944–1945. About 30,000 Dutch people starved to death during the Hongerwinter. There was a 300-gram decrease in mean birth-weight of the babies of women who had conceived at the start of the famine and so had endured poor nutrition throughout the pregnancy. These low birth-weight babies did not suffer from adverse effects on their subsequent fecundity in adulthood, but they were themselves more likely to give birth to offspring of reduced birth weight. This reduced birth weight in the second generation was associated with a high frequency of still-births and early infant mortality. The result was that females exposed to the famine *in utero* had reduced reproductive success compared with those who were born before or after the famine [24,25]. In the Dutch famine, the foetuses were developing within the womb of nutritionally deprived mothers and so the foetus was under nutritional stress. Detailed studies in adult life of babies born during the famine found that maternal nutrition during early gestation can permanently influence the lipid profile in later life. Exposure to famine in early gestation led to a higher LDL:HDL cholesterol ratio in adult life.

These results confirmed findings from other studies in humans that maternal nutritional intake during pregnancy can have permanent effects on health in later life [26]. Perhaps, in response to the nutritional stress, the foetus adopts a 'thrifty' metabolism which it keeps throughout its adult life, even though the nutritional stress was relieved in early infancy. When this generation conceived, the maternal metabolism was still 'thrifty' and so the foetus received fewer nutrients than required and so it in turn developed a 'thrifty' metabolism [26]. Long-term effects of chronic stress in pregnancy on foetal programming are now well established in rodent models and the epigenetic mechanisms that allow such cross-generational effects are emerging (for example [27]). Such mechanisms might also account for the observations seen in the children of the Dutch famine.

While seasonal timing of conception/births might be expected to be related to biological resources in pre-industrial societies, low-amplitude seasonal birth rhythms can be detected in modern societies, whether urban or rural. Quite why this 'residual' seasonality in birth still exists is again difficult to explain, particularly as food availability is largely constant and seasonal changes in temperature are masked by central heating and air-conditioning in homes and offices [17,28]. It is not just conceptions and births that show seasonal variation. The frequency of sexual activity, sexually transmitted diseases and the sale of contraceptives are all seasonal [29]. Where might this seasonality have its origins in our evolutionary history? The assumption is that these

phenomena are residual responses evolved originally by our ancestors using one or both of the following mechanisms. The first is that, even though our species is thought to have evolved in the tropics, this does not mean that reproduction would have been entirely random. Many equatorial species possess a circannual clock to time their physiology, but instead of using daylength signals, use local seasonal cues such as rainfall, humidity or even food availability [30]. Perhaps we have retained a circannual timer that can be synchronised by some aspect of our metabolic status or even photoperiod in northern latitudes. Alternatively, as our ancestors moved out of Africa into the higher latitudes and encountered variation in food availability, these ancient hominins evolved a strongly photoperiodic response based upon a daylength dependent melatonin signal from the pineal gland [5]. Support for this idea is based upon the fact that humans, along with other primates, appear to have the basic biological machinery that would drive such a response [31,32].

Bronson [33] suggests that some humans are indeed highly photoperiodic and that the variation in seasonal reproduction among humans around the globe reflects a spectrum of photo-responsiveness between individuals, some of whom respond to changes in photoperiod whilst others do not, and there are a range of intermediate types. The mechanistic basis for such responses to seasonal change remains obscure. In contrast to our increasing understanding of the involvement of circadian clock genes in the morning preference of people described as 'larks' and the evening preference of 'owls' [34,35], nothing similar has been described for a tendency towards photoperiodic phenomena. By contrast, Doblhammer *et al*. [36] argue that neither photoperiodism nor the weather causes birth seasonality, but they have a role to play in that "climate and photoperiod appear to explain shifts in the amplitude of the peaks and troughs across region, but not the fundamental presence of the peaks and troughs in the first place". Based on a detailed historical study of Austrian birth patterns, Doblhammer *et al*. [36] put forward the 'resilience hypothesis': that a multiplicity of small causes slightly shift, dampen, and enhance the patterns, which are themselves caused by a very few resilient and much stronger causes. But once again, these much stronger causes/critical factors remain largely ill defined.

There is no doubt that humans are able to procreate all year round and that many factors could modulate this capability in a systematic seasonal fashion, ranging from cultural restraints or preferences such as in the case of the Samukundi [37] to factors related to the different metabolic workload throughout the year [26] or simply the seasonality of food resources [21]. But the extent to which a seasonal modulation of human reproduction is influenced by those environmental factors which are known to control reproduction in so many other species — photoperiod and temperature — remains elusive. The question stands: is seasonality in humans independent of photoperiod and temperature? It is easy to dismiss any biological modulation of reproduction by these two factors when generalizing from studies that have focused upon human societies in which there is a strong cultural influence upon seasonal activity such as the Samukundi [37]. However, because such societies are so specialised, generalisations to all human kind may not be appropriate.

So what do the larger population studies actually tell us? As discussed above, there are striking differences between North America and Western/Central Europe in seasonal conception rates. The former showing clear bimodal patterns with two peaks per year and the latter a unimodal pattern with one dominant annual peak around the spring equinox and a second minor 'blip' in autumn. It became clear that the bimodal pattern of conception, typical for North America, also exists in Eastern Europe and this then suggested a climatic influence, specifically of temperature. The amplitude of annual temperature oscillations does not correlate with latitude. Because of the influences of the Gulf stream, the annual temperature amplitudes of Northern Norway (~78°N) are comparable with those in Virginia (~37°N), but also with those in many Eastern European countries from Estonia (~58°N) right down to the Balkans (~43°N). Thus the bimodal pattern in conception/births might be attributed to a higher environmental temperature amplitude in the different locations. Very hot summers and cold winters are generally found in continental regions (such as North America or Eastern Europe), whilst milder climates with less severe seasonal differences are found in more coastal regions (Western/Central Europe) [28,38]. Furthermore, a worldwide comparison of seasonal reproduction shows a clear trend with temperature.

In countries which never experience high temperatures, such as those in the arctic and near-arctic, conception maxima generally correlate with the time of highest annual temperatures. By contrast, in those predominantly equatorial and near-equatorial countries which never experience really low temperatures, conception correlates with the annual lowest temperature [28]. Thus there appears to be a negative correlation between conception and temperature in hot locations while this correlation is positive in cold environments. In regions between these extremes, conceptions are always highest when morning minimum temperatures reach approximately 12°C. A comparison between nine equatorial countries (covering latitudes from 13°N to 9°S) illustrates the power of global comparisons when trying to identify the influence of environmental influences on conception rates. Temperature shows a high negative correlation with conception in all these countries, except one, Columbia (5°N), which is the only country among them that is characterised by low (daily minimum) temperatures (~10°C, as opposed to ~21°C in the other countries) [4,28].

A clear latitudinal cline exists in the timing of human reproduction from the poles to the equator (from later to earlier). This cline could well be related to temperature (as for the clines in plant and tree flowering). It is worth stressing that although in all regions the largest increases of conception rates are found around the spring equinox ($20^{th}$/$21^{st}$ March in the Northern hemisphere and six months later in the Southern hemisphere), the time of the maximum is reached later the further away from the equator (the colder the annual average temperature). In regions around 30°N, the morning temperatures reach 12°C by the spring equinox, but in regions further north morning temperatures barely reach 12°C even by August.

Collectively there appears to be good evidence for a temperature modulation of conception in humans, but what about photoperiod? As discussed above, seasonality in human reproduction has become progressively weaker with industrialisation which may reflect an increased shielding of individuals from both temperature and photoperiod. Historically, shielding against photoperiod (by working inside) has preceded shielding against temperature (by heating and air-conditioning) and there is some suggestion that changing the light exposure of a population does indeed affect the

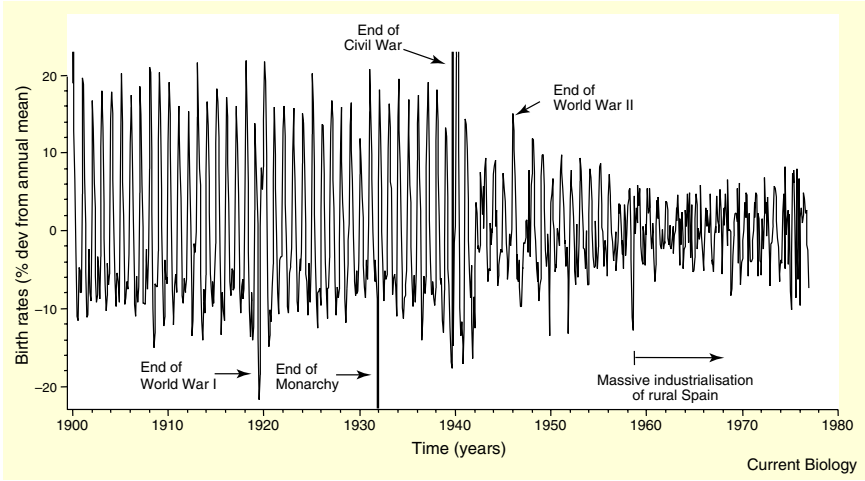


Figure 3. Seasonal and social influences on human reproduction exemplified by the monthly birth rates in Spain from 1900 to 1978.

Before 1940 the birth rhythm was highly regular with a peak of conceptions in spring and annual differences around 30% (peak to trough). Social interventions, such as wars, introduce irregularities but have little effect on the overall rhythmicity. During and after World War II, the rhythm's amplitude decreased but otherwise continued with the same characteristics. During the 1960s, Franco launched a massive industrialization campaign introducing more extensive electrification and factories into many rural areas. Concurrently, the annual birth rhythms changed drastically. The amplitude declined even more and the phase of the conception peaks shifted to autumn/winter. (Adapted from [4].)

timing of conception. For example, the seasonal conception rhythm in pre-industrial Spain peaked around March/April and remained relatively rhythmic, despite wars, until the 1960s when Franco initiated a massive industrialisation campaign that included introducing extensive electrification and factories into rural areas. Industrialisation would have meant working indoors and losing the photoperiodic signal, but would not have greatly altered the exposure to temperature, yet the conception peak largely collapsed (Figure 3) [4].

### *Seasonal Death*

In the same way that human conception shows a seasonal rhythm, so does our susceptibility to illness and many other traits. It seems absurd that the month you are born/conceived can affect your future life chances. But how long you live [39], adult height [40], and how likely you are to develop a range of diseases, including devastating conditions such as schizophrenia, all appear to be associated with the month of birth/conception (Figure 4). A recent and detailed study [41] of more than two million Danes and Austrians who died in the last three decades of the last century suggests that in these two countries, at least, life span and month of birth are associated. The studies excluded deaths under 50 and were carefully controlled for possible confounding effects, such as the seasonal distribution of death which is higher in winter than summer. In Austria, for all major groups of causes of death including accidents and suicides, mean age at death of those born in the second quarter (April to June) is significantly lower (101 days below average) than that of individuals born in the fourth quarter (October to December; 115 days above average).

Similar studies on life span in the United States showed that those born in the autumn live about 160 days longer than those born in spring, and there is a significant month-of-birth pattern for all major causes of death including cardiovascular disease, malignant neoplasms, in particular lung cancer, and other natural diseases like chronic obstructive lung disease [39]. In the Southern Hemisphere, the pattern is shifted by six months. The mean age at death of people born in Australia in the second quarter (March–May) of the year is 78; those born in the fourth quarter (October–December) die 125 days earlier. Furthermore, the lifespan pattern of British immigrants to Australia is similar to that of Austrians and Danes and significantly different from that of Australians [39].

At any time in the UK, there are about two to three adults in every 1,000 with schizophrenia. In the USA, more than 2 million people have been diagnosed with a schizophrenic disorder. The illness wrecks lives and families. One of every 10 people with schizophrenia eventually commits suicide. People who develop schizophrenia in Europe and North America are more likely to be born in the winter and early spring (February and March in the Northern Hemisphere) The subjects who were born during these months had a slightly higher than average rate of schizophrenia, while subjects born in August and September had a slightly lower than average rate. There seems to be about a 10% difference in risk of schizophrenia between the high (Winter and Spring) and low risk months of birth [42]. Of course statistical assertions based on large population studies tell us nothing about any individual. The vast majority of individuals with these diseases are not born during the months of excess births, and most individuals born during these months do not develop schizophrenia. It is important to stress that a 6–10% variance is relatively small in terms of its impact on the overall incidence of these diseases.

Could the findings in schizophrenia and other pathologies outlined in Figure 4 represent anything more than a statistical artefact? For example, in the case of schizophrenia, the condition is age linked. As somebody born in the first quarter of the year is older than somebody born in the last quarter of the same calendar year, this age-lag has been suggested as a possible explanation for a birth month effect in a given calendar year. But when this age effect has been corrected, the seasonal effect still stands. Another possibility is that, as there are more births overall in spring, the rhythm in schizophrenia results from the same causes [43]. This seems unlikely, however, as the pattern of conception/birth differs between North America and Europe (see section above), but the peak birth months for schizophrenia are the same for both regions (late winter/early spring). So the general consensus is that for conditions such as schizophrenia, and many other pathologies, there is a conception/pregnancy/birth influence and that the results are not just a statistical artefact. A biological explanation remains elusive, but multiple theories abound ranging from levels of prenatal vitamin D [44] to exposure to infectious agents and viruses such as influenza in particular [45].

The incidence of multiple sclerosis (MS) varies with latitude. Ebers has co-ordinated a study [46] that examined

| | Month of Birth | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Condition** | **Jan** | **Feb** | **Mar** | **April** | **May** | **June** | **July** | **Aug** | **Sept** | **Oct** | **Nov** | **Dec** | **Reference** |
| ***General pathologies*** | | | | | | | | | | | | | |
| **Asthma (UK)** | | | | | | | | | | | | | [55] |
| **Asthma (UK)** | | | | | | | | | | | | | [103] |
| **Asthma (Denmark)** | | | | | | | | | | | | | [104] |
| **Crohn's disease (Israel)** | | | | | | | | | | | | | [105] |
| **Childhood diabetes mellitus** | | | | | | | | | | | | | [106] |
| **Glaucoma** | | | | | | | | | | | | | [107] |
| **Hodgkin disease** | | | | | | | | | | | | | [108] |
| ***Psychiatric disorders*** | | | | | | | | | | | | | |
| **Alcohol abuse** | | | | | | | | | | | | | [42] |
| **Autism** | | | | | | | | | | | | | [42] |
| **Bipolar** | | | | | | | | | | | | | [42] |
| **Eating disorder** | | | | | | | | | | | | | [42] |
| **Personality disorder** | | | | | | | | | | | | | [42] |
| **Neuroses** | | | | | | | | | | | | | [42] |
| **SAD** | | | | | | | | | | | | | [42,109] |
| **Schizoaffective disorder** | | | | | | | | | | | | | [42] |
| **Schizophrenia (N. hemisphere)** | | | | | | | | | | | | | [42,109–112] |
| **Schizophrenia (S. hemisphere)** | | | | | | | | | | | | | [110,111] |
| **Suicidal behaviour (W. Australia)** | | | | | | | | | | | | | [113] |
| ***Neurological illness*** | | | | | | | | | | | | | |
| **Alzheimer's disease** | | | | | | | | | | | | | [42] |
| **Amyotrophic lateral sclerosis** | | | | | | | | | | | | | [66] |
| **Down's syndrome** | | | | | | | | | | | | | [42] |
| **Epilepsy** | | | | | | | | | | | | | [66] |
| **Mental retardation** | | | | | | | | | | | | | [42] |
| **Motor neuron disease** | | | | | | | | | | | | | [42] |
| **MS (Northern hemisphere)** | | | | | | | | | | | | | [46,66,109,114] |
| **MS (Southern hemisphere)** | | | | | | | | | | | | | [46] |
| **Narcolepsy** | | | | | | | | | | | | | [115] |
| **Parkinson's disease** | | | | | | | | | | | | | [42,66,109] |

Current Biology

Figure 4. Summary of pathologies/conditions in humans that have been reliably associated with the season of birth.

Gray shading indicates the peak month of birth for the different conditions. Unless otherwise stated the results presented are from populations in the Northern hemisphere. This figure is based upon two excellent reviews of the literature [42,66] and additional papers. It is important to stress that although the percentage differences of a gradient are relatively small, they are statistically significant and do not occur by random chance. For example, in the Northern hemisphere, significantly fewer (8.5%) people with MS were born in November and significantly more (9.1%) were born in May. In the Southern hemisphere, the situation is reversed and November is the peak month and May the lowest. Likewise, multiple studies have shown there is an ~10% greater chance of developing schizophrenia if born in the winter/spring and a corresponding drop of approximately 10% if born in summer/autumn. This is also true for the Southern hemisphere [42].

more than 40,000 Canadian, British, Danish and Swedish patients with multiple sclerosis. The results show that in the Northern hemisphere, significantly fewer (8.5%) people with MS were born in November and significantly more (9.1%) were born in May. In the Southern hemisphere, the situation is reversed and November is the peak month and May the lowest. There are several clues as to the cause. An important study [47] compared the risk of two or more siblings having multiple sclerosis to the risk of its occurrence in both twins in a non-identical pair. There should be no difference, but non-identical twins do have a significantly higher risk of both having MS than non-twin siblings. This suggests that the pre-natal and post-natal environment affects the overall risk. Pinpointing the actual environmental factor has been problematic.

Correlations have been made between the incidence of MS, the availability of dietary vitamin D, and the availability of sunlight to drive vitamin D3 synthesis. In Japanese populations, who consume plenty of fish rich in vitamin D (90% of the Japanese vitamin D requirement comes from fish, 3% from eggs and 3% from milk), the MS prevalence is three per 100,000 population. MS has a very low frequency in equatorial regions where, it is argued, there is plenty of sunlight to drive vitamin D3 synthesis in the skin, whilst the incidence of MS increases dramatically with latitude in both hemispheres. In Scotland (in the north) and Tasmania (in the south), the prevalence is 250 per 100,000 population. Such arguments have also been used to explain two peculiar geographic anomalies on MS frequency, one in Switzerland with high MS rates at low altitudes and low MS rates at high altitudes, and one in Norway with a high MS prevalence inland and a lower MS prevalence along the coast. Ultraviolet light intensity is higher at high altitudes, resulting in a greater vitamin D3 synthetic rate, thereby accounting for low MS rates at higher altitudes. On the Norwegian coast, fish is consumed at high rates and fish oils are rich in vitamin D3 [48].

## Lunar Rhythms

The orbital motions of the earth, moon and sun and their gravitational and centrifugal forces generate the tides. As a result, life in the inter-tidal zone experiences a 12.8 hour rise and fall of water level, and twice every lunar month will experience high amplitude spring tides (an interval of 14.76 days). In addition to these gravitational forces, many nocturnal species, and species that sleep in the open, are also exposed to marked changes in the brightness of the light reflected from the lunar surface every lunar month (a period of 29.53 days). At full moon the illuminance (~0.25 lux) is approximately 25 times greater than at the quarter moon, and 250 times greater than a moonless clear starry night sky. In response to these predictive events in the environment numerous species have evolved endogenous clocks to anticipate these tidal (circa-tidal ~12.8 hours), semi-lunar and lunar (circa-lunar ~29.53) cycles. (This area of rhythmic biology is reviewed in detail in [49–53].)

One well known example will suffice to illustrate lunar related rhythms in the animal world. The Palolo worm (*Eunice viridis*) is found on several coral islands near to Samoa and the Fiji Islands. The palolos reproduce by swarming during the last quarter of the moon in October and November. The terminal parts of their bodies drop off and float over the surface of the water, releasing sperm and eggs. The natives of the Samoan Islands have known this for centuries and predict the date and time of day when the emergence occurs so that they can be ready to catch the worms for food. Studies have attempted to determine whether it is the direct effect of lunar illuminance which stimulates swarming. This seems unlikely because cloudy or clear whether conditions have no effect on the spawning date. Furthermore, the Palolo worm lives at depths of 3-5 metres within coral rocks, where moonlight would not easily penetrate. Studies in an allied species of polychaete worm have demonstrated that moon-related rhythms in behaviour continue in isolation from any environmental influence. Collectively the data suggest that the Palolo worm and other polychaete worms have an endogenous circa-lunar timer [6,54].

The moon is by far the most obvious celestial object in the night sky. It has always dominated human culture and continues to do so. The passage from full to crescent moon provided the basis for the earliest calendars of most civilisations. There are even claims that lunar calendars were painted on the Lascaux cave walls and that 30,000 years ago early humans were recording the lunar cycle by cutting lines and notches on stones and bones. Most lunar calendars are in fact lunisolar calendars. That is, months are kept on a lunar cycle, but then intercalary months are added to bring the lunar cycles into synchronisation with the solar year. For example, the early Romans had a primitive lunar calendar with ten lunar months, beginning with the spring moon in March and ending about 300 days later in December [55]. There are multiple modern examples of the moon dictating cultural events. Easter is determined by the phase of the moon and can move in date by as much as six weeks.

Whilst it is clear that some animals are clearly influenced by the moon and possess internal clocks that can predict the lunar cycle [6,50], and that human culture has been markedly affected by the phases of the moon [56], there is no convincing evidence that the moon can affect the biology of our own species. We stress that, unlike the seasonal rhythms of birth and death in humans discussed in the previous sections, the moon appears to have no effect upon our physiology. This literature has been reviewed in several detailed papers (for example [57,58]), and has been partially summarized in Table 1.

Table 1. Pathologies and some physiological and behavioural phenomena in humans which have been linked to the lunar cycle but which in reality occur independently of the phase of the moon.

| Condition/event with no consistent lunar influence | Reference |
|---|---|
| Psychosis, depression, anxiety | [67–75] |
| Violent behaviour/aggression | [76–80] |
| Seizures | [81] |
| Suicide | [79,82–87] |
| Absenteeism rates | [88] |
| Coronary failure | [89] |
| Conception (*in vitro* fertilization) | [90] |
| Birth | [91–93] |
| Menstruation | [94] |
| Surgery and survival of breast cancer | [95] |
| Postoperative outcome (general) | [96–98] |
| Renal colic | [99] |
| Outpatient admissions (general) | [100] |
| Automobile accidents | [101,102] |

Despite the empirical evidence, belief that the moon exerts an influence on humans remains strong. Many midwives still believe that more babies are born at full moon than at new moon but the statistics show that this is a purely subjective association [59]. The moon has been associated with mental health since ancient times, the word 'lunacy' itself, is derived from Luna, the Roman goddess of the moon. Surveys of workers in the mental health professions show a persistent belief that the full moon can alter behaviour [60,61]. The belief that the moon can have an affect on human physiology is usually justified on the basis that the human body contains 80 percent water and that the moon exerts its influence, like the tides, due to its gravity. The first point to make is that the gravitational forces which generate the tides are dependent upon the distance between the earth and the moon, and on the alignment of the moon, earth and sun, and not on the phases of the moon. So a full moon does not mean a specific gravitational effect on earth. The second point is that gravity is a remarkably weak force. Whilst the moon clearly influences oceanic tides, it does not produce tides in smaller bodies of water such as lakes and even some seas, let alone a human. Roger Culver and colleagues [62] have summarised this point elegantly by pointing out that the moon's gravitational pull was less than that of a wall of a building six inches away.

So why is the belief in a lunar effect on human biology still so strong? Until the introduction of some form of street and then domestic lighting, cities were enveloped by a profound darkness on a moonless night. The luxury of generating artificial light, for example by burning a candle, remained the province of the rich until well into the 19th century [63]. Moonlight, especially around the three days of full moon, would have permitted many activities, including work, hunting, travel and even social gatherings. Thus, real changes in many aspects of human behaviour would have become associated with the lunar phase. But why has mental health become so uniquely associated with the full moon? Perhaps this belief arose because of the disruption to sleep that would have occurred in societies regulated by lunar illuminance: thus sleep disruption and sleep loss would have occurred in association with the full moon.

Significantly, since the 1980s multiple studies have shown that partial sleep loss, even for only one night, can induce mania in those individuals vulnerable to bipolar disorder. Such finding gave rise to the hypothesis that sleep deprivation may be a final common pathway in the triggering of mania, and that the ongoing sleep disturbance of mania may function as a self-sustaining positive feedback loop once a manic episode has begun [64]. In a pre-industrialised age, when moonlight would have determined night-time activity, perhaps moonlight was an additional factor involved in inducing mania. Seizures have also been associated with both sleep deprivation and the full moon [57]. Patients with temporal lobe epilepsy are remarkably sensitive to even moderate sleep deprivation. Only 1.5 hours of sleep loss from baseline can markedly increase the occurrence of seizures the following day [65]. As with mania, disruption of sleep in pre-industrialised societies may be the cause of the association between seizures and the full moon [57].

## Conclusions

We began this review with the observation that there is considerable confusion and ignorance about the influence of the geophysical cycles on human biology. There is a strong belief by many that the moon has marked effects upon our health and wellbeing. Yet, study after study has failed to find any consistent association with the moon and human pathology, physiology or behaviour. Occasional reports have proposed correlations between the phase of the moon and human phenomena, but nothing has been sufficiently replicated to conclude that there is a causal relationship. The reason for this belief is probably linked to the importance of moonlight in allowing human activity at night before artificial light was freely available, coupled with the endless re-telling of stories about behavioural changes associated with the lunar phase. If an individual expects certain behaviours to occur with the full moon then selective recall and/or selective perception will reinforce this view. As Saint Augustine wrote in the 5$^{th}$ century ''Faith is to believe what you do not yet see; the reward of this faith is to see what you believe''.

We lack a response to the moon, but human biology remains profoundly dependent upon the 24 hour revolution of the earth upon its axis. We have an endogenous circadian clock that is locked to the solar day and allows an optimal response to the differing demands of the day and night. Working against this temporal programme, as in shift-work, is associated with a broad range of interconnected pathologies ranging from poor vigilance and memory, reduced mental and physical reaction times, reduced motivation, depression, insomnia, metabolic abnormalities, obesity, immune impairment, and even a greater risk of cancer [3]. The work culture of long hours, shift work, extended commutes, 24 hour global communication, freedom from many economic and social constraints, and the 24 hour availability of almost everything are all conspiring to warp normal physiology. In an attempt to cope, many individuals depend upon a cycle of stimulants and sedatives. Stimulants such as caffeine and nicotine are used during the day and sedatives such as hypnotics and alcohol are used at night to induce sleep. The following morning stimulants are needed once again to override the sedatives and impaired sleep. This stimulant/sedative loop characterizes the life of many and is fuelled by a failure to appreciate that our physiology is rooted in a 24 hour temporal program that cannot be overridden by the recent imposition of a 24/7 culture [3].

The seasons to many individuals of the developed economies only impinge upon the consciousness because of the yearly cycle of Father Christmas, followed by the Easter bunny and then Halloween pumpkins. Yet our biology is affected by the seasons. Seasonally related metabolic status, temperature, photoperiod and social structures all appear to modulate, in varying degrees of importance, the reproductive timing of human births [28]. Disentangling how these factors interact to influence the long and opportunistic breeding strategy of humans has turned out to be frustratingly complex. No single unifying biological explanation can fully account for the well documented pattern of seasonal births in the recent past or explain why the amplitude of these rhythms has flattened in the past 50–60 years. But the lack of an all-encompassing biological explanation for seasonal reproduction in humans is no reason to ignore this aspect of our physiology particularly as seasonal reproduction appears to be just one example of our response to annual change. An individual's month of conception modulates susceptibility to illness. There is an increasing recognition of the importance of the foetal or neonatal environment in the expression of the developmental programme. This early environment will be influenced by multiple seasonal influences, and as a result, it is perhaps not too surprising that the season of conception/birth is a significant factor for our health and sickness. The problem is that we still have very little fundamental understanding of how the seasonal environment might impinge upon our early developmental program. Characterising the genetic variation in human responsiveness to environmental change will provide not only insights into our fundamental biology but also new opportunities for therapeutic intervention.

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