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Research Article

The Case Against Adenosine and Melatonin: How is Sleep Induced in the Body with Natural Hormones and Manufactured Drugs?

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Abstract: This article deals with quantum biology, the new tool to help traditional biology solves difficult questions related to living organisms. We expose adenosine molecules and melatonin hormones and explain how they build up in the body. We differentiate natural sleep from manufactured drug-induced sleep and clearly state the three conditions required for natural slumber to occur in the body.
Keywords: Entangled System Degradation/Synthesis, Complex Systems, Dissipative Structures, Cortisol, Serotonin, Entropy-hormone, Happy-hormone.

1. Introduction

We will not say it enough; sleep is still a mystery; however, when we apprehend the topic with quantum tools, we get some clarity [1]. And the first recommendation and the paramount advice we give in sleep study is to "know thyself." As we have learned from the Nobel laureate Ilya Prigogine's research, humans are complex systems; thus, there is not and will never be a standard model to apprehend them; each individual is unique. Living beings don't produce and manage entropy in the same way. For that cause, everyone must know how his organism behaves and responds to the surroundings. As dissipative structures, living organisms firmly depend on their environment [2]. Therefore, our sleep pattern is often contingent on our surroundings. Seasons vary across the globe, and Nordic people don't experience the same weather as people living at the equator [3].

Melatonin is often the hormone commonly associated with the sleep-wake cycle. Scientists said it regulates the sleep patterns of living organisms according to the sun's movement in the sky; therefore, it must trigger our slumber. Among several researchers who attempt to elucidate the mystery of sleep, another group has concluded that adenosine is the cause of why living organisms drop off. They target this molecule as a sleep-inducing factor because its concentration is higher during wakefulness than sleep [4]. Moreover, caffeine, the antagonist to adenosine, keeps humans awake and alert.

It is well-documented that adenosine and melatonin are highly involved in the sleeping process but are these molecules the cause of why living organisms drop off?

This paper will give a closer look at these two molecules and explain what they cannot do based on the literature researchers provide and the observation of sleep phenomenon in living organisms. Science offers rational explanations for natural phenomena; it is also about data analysis, logic, common sense, and critical thinking [5]. Since sleep is a phenomenon everyone experiences, no one needs anybody to tell him how he or she feels. Our approach here will be pragmatic so that anyone can relate. Thus, after explaining how adenosine molecules and melatonin hormones build up in the body, we will differentiate natural sleep from manufactured drug-induced sleep and clearly state the three conditions required for a natural slumber.

2. Adenosine ($\mathbf{C_{10}H_{13}N_5O_4}$)

Adenosine is a purine nucleoside base, more precisely, a ribonucleoside (code + sugar) composed of a molecule of adenine attached to a ribose. It is one of the main components of ATP (Adenosine Tri-Phosphate), the living cell's energy carrier, and the RNA's building block (RiboNucleic Acid). Adenosine accumulates in the body due to ATP degradation as a result of physical and intellectual activities. When the

individual wakes up in the morning and starts working, cells break the phosphate bond of ATP to release energy. When one bond is broken, we have ADP (Adenosine Di-Phosphate) as an outcome product; however, when two bonds are broken, AMP (Adenosine Mono-Phosphate) is left as a final product. Thus, adenosine appears as a by-product of ATP degradation. At the end of the day, this compound is abundant in the body systems. The accumulation of adenosine is also a sign of energy depletion since the molecule emanates from ATP degradation; hence a synonym for fatigue. The body asks for sleep not because adenosine has built up but because ATP is depleted, and the systems request to synthesize a new pool of ATP; the call for synthesis[1] is a response to the ongoing degradation (entropy). Professor Prigogine stated it clearly in chapter V of his book "Order Out of Chaos," I quote:

"ADP accumulation inside the cell thus signifies intensive energy consumption and the need to replenish stocks." [6]

Adenosine has a twin sister; researchers have found that caffeine ($C_8H_{10}N_4O_2$), a psychoactive compound is an antagonist to adenosine because both bind the same receptors but produce opposite effects. Adenosine and caffeine are of the same purine family, two-ringed structures with four nitrogen atoms each. The additional nitrogen atom in adenosine comes from the amine group (NH_2) attached to one of the rings. The similarity of these two molecules with contradictory effects leads many researchers to conclude that adenosine is responsible for sleep since caffeine promotes wakefulness and alertness.

As a manufactured drug, adenosine is administered as an antiarrhythmic medication against tachycardia, and it calms and slows the heart down. Science describes adenosine as a vasodilator, meaning it decreases blood pressure. It is a drug used to suppress abnormally fast heart rhythms.

Critical thinking: *if adenosine induces sleep, why do some people fail to drop off at night after a hectic day at work? Isn't insomnia a strong piece of evidence against adenosine as the cause of sleep?*

3. Melatonin ($\mathbf{C_{13}H_{16}N_2O_2}$)

Science classifies melatonin as both a neurotransmitter and a hormone. As a neurotransmitter, melatonin is a monoamine of the same class as serotonin ($C_{10}H_{12}N_2O$), fabricated from the essential amino acid tryptophan ($C_{11}H_{12}N_2O_2$). Contrary to popular belief, this molecule is produced throughout the day but peaks at night as the sun sets. Recent investigations show that the pineal gland's secretion, which occurs at night, accounts for 5% of all production of this natural compound. Researchers discovered that melatonin has another role in the organism; instead of the notorious circadian rhythm regulation, it is now established that the primary function of melatonin is to serve as an antioxidant in the clean-up of metabolic waste. Thus, it has been hypothesized that mitochondria produce melatonin to protect this energy factory against free radicals [7]. The study also shows that a significant amount of this natural compound is produced in the digestive tract; it makes sense when we realize how pleasant it feels when we eat food and the drowsiness that follows the meal.

The production of melatonin follows a well-definite pattern: $Tryptophan \rightarrow Serotonin \rightarrow Melatonin$. Tryptophan is supplied to the body through diet; then, it converts into serotonin and melatonin. First comes pleasure, then follows sleep. Serotonin appears to be linked to sleep onset, while melatonin works better with ongoing rest. As a powerful antioxidant, melatonin is involved in the clean-up process. Before an individual drops off naturally, serotonin must be present in the body abundantly. The increase of this neurotransmitter triggers the diminution of cortisol. As we used to say, "well people sleep well; unwell people struggle to drop off." Anyone who slept well had had a good secretion of serotonin in his body previously. That's why people often feel drowsy and sleepy after pleasurable activities such as food ingestion or sex. After pleasure, he that makes room for sleep will drop off because conditions are gathered to induce sleep.

Critical thinking: *First call, why don't bat sleep at night if melatonin induces sleep and all animals produce melatonin? Second call, if melatonin is the cause of sleep, it must not be degraded by the light because, in the Summer, the sun never sets from May to July in certain places in Norway, Iceland, Alaska, Finland, Greenland, or Canada. Do the inhabitants of these regions stay awake for several weeks?*

[1]Synthesis does occur during wakefulness, but it is more efficient during sleep; that's why degradation and synthesis form an entangled system; both work in synergy to maintain homeostasis and sustain life in the organism.

4. Cortisol ($C_{21}H_{30}O_5$)

Science classifies cortisol as a glucocorticoid, the primary stress hormone of the body, mainly produced by the adrenal glands. The hypothalamic-pituitary-adrenal axis, or HPA axis, regulates the production and secretion of this hormone. The hypothalamus in the brain stimulates the pituitary gland that commands the adrenal glands, which sit on top of the kidneys via a series of tropic hormones. The HPA axis appears to be the most important key element sleep researchers must focus on to unravel the mystery of sleep; this axis controls cortisol levels in the body.

Cortisol levels raise blood sugar as stored glucose is released into the bloodstream [8]; this phenomenon confirms cortisol as the hormone of wakefulness and alertness; its concentration is high in the morning and lowest at midnight. Several studies show cortisol production hitting its nadir during sleep; this hormone is notoriously associated with wakefulness [9]. Melatonin appears to have some relationships with cortisol in a sense that both peak naturally at opposite moments: cortisol in the day and melatonin at night.

Cortisol is a vasoconstrictor, meaning it increases blood pressure, which again confirms its role in wakefulness and alertness [10]. The study also shows tryptophan degradation in the presence of cortisol [11]; it makes sense since tryptophan converts into serotonin and melatonin to promote sleep. Stressful people are unwell, thus, struggle to drop off.

Critical thinking: *Some people believe melatonin decreases in advancing age; if so, why can a melatonin supplement not address the problem? Isn't that cortisol level rising instead? We all know that life challenges in human society augment as we age; human physical capacity does not improve as age advances; this concern alone stresses many. Isn't it right to think that the rising cortisol level is the source of adults sleeping problems instead of decreasing melatonin?*

5. Why Do Living Organisms Sleep?

The answer to this question is straightforward; living organisms, as dissipative structures, sleep to avoid spontaneous symmetry breaking, which leads to the collapse of their body systems [12]. As we have always said, sleep is a temporary loss of consciousness or awareness in the physical body. It is a mechanism of protection to prevent the body from premature death. Sleep, syncope, and death are kin; they are all losses of awareness in the body. Sleep shuts the body down for repair.

The entire sleep process could be divided into two distinct parts: onset and rest. Science is a collective enterprise, and right now, there is no consensus on whether stage one and two or only stage one is the onset [13]; however, one thing is evident, and it appears clear that the sleeping process has two mechanisms: one shuts the body down and the other repairs it. The first is a protective mechanism, while the second is a therapeutic process. During the resting period, the body overhauls and refurbishes its systems.

Without degradation in the body, there is no need for a slumber; we sleep because of entropy fluctuation. Some individuals who miraculously succeed in maintaining their entropy production minimal and constant do not need to sleep; this was the case with the Hungarian soldier Paul Kern [14]. Entropy fluctuation is the leading cause of why living organisms must sleep.

In his book "What is Life?" Nobel laureate Erwin Schrodinger identified two components of this fluctuating phenomenon and labeled them entropy positive and negative [15]. Later in his research, the Japanese Nobel laureate Yoshinori Ohsumi independently reached a similar conclusion and labeled these two components as degradation and synthesis [16]. He postulates that a tightly controlled balance between degradation and synthesis maintains life in the body; in other words, death settles when the controlled balance ruptures. Today, we understand this balance is not physical but a quantum phenomenon known as entanglement. For instance, an individual who loses four limbs will not necessarily die, although degradation is high. Notice that the patient almost loses one-third of his body weight during amputation. People survive such amputation because degradation and synthesis are always entangled to sustain life in the body.

Behind this entangled system, two cocktails of hormones are at work, which I label entropy-hormone (E) and happy-hormone (H). A few of these hormones related to the sleep study are norepinephrine, epinephrine, and cortisol; the second cocktail comprises endorphin, oxytocin, serotonin, and melatonin. The study shows a strong correlation between the elevation of norepinephrine and cortisol; both follow the same movement pattern: they rise together and decrease together, making them kin [17]. Everything about sleep boils down to the fluctuation of these two cocktails of hormones. Thus, we postulate that when entropy-hormone

increases, happy-hormone must decrease and vice versa because both are entangled; they cannot simultaneously have the same movement at the quantum level. Therefore, two configurations are possible in the physical body: E↓/H↑= sleep or synthesis and E↑/H↓=wakefulness or degradation.

At the beginning of the day, cortisol increases in the body to support activities as the individual wakes up; this situation is materialized by E↑/H↓, characterized mainly by degradation. In the evening, adenosine accumulates in the body after a hectic day due to ATP degradation as a consequence of physical or intellectual activities. The individual returns home and enjoys a meal. As the sun sets, serotonin starts converting into melatonin. When the entropy-hormone decreases to a minimal critical value, sleep is triggered automatically in the body; the new configuration is E↓/H↑, characterized mainly by protein synthesis where the body systems will be revamped and refurbished for a new day [18].

6. Natural Sleep Vs. Manufactured Drug-Induced Sleep

Above, we have sketched the pattern of natural sleep. Three conditions were required: adenosine accumulation, serotonin gradually converting into melatonin, and cortisol cutback. The third condition is the sine qua non; it is the critical condition for sleep to occur naturally in the body. However, there is another sleep pattern that does not necessarily need the first two conditions.

Manufactured drug-induced sleep occurs when artificial molecules force the adrenal glands to shut down their production; this is the case for most anxiolytic, sedative, and anti-convulsant drugs [19]. The study shows that benzodiazepines interact with gamma-aminobutyric acid (GABA) in the central nervous system. Still, the ultimate step of these sedative compounds is to make a hard shutdown of the adrenal glands. As cortisol, norepinephrine, and epinephrine withdraw from the system, breathing and the heart rate slow down; as a result, the blood flow to the brain diminishes, and the mind flips into sleep mode.

So, our second postulate in this article stipulates that all manufactured drugs which induce sleep as a side effect must act on the HPA axis and coerce the adrenal glands to shut down their production.

7. Discussion

Adenosine and melatonin promote sleep but do not trigger the phenomenon. People feel tired, but many fail to drop off, although they vividly desire to shut their eyes and rest. The sunset is not always a synonym for sleep because babies don't care about the sun's position in the sky. Their bodies secrete melatonin at night, yet many keep their parents awake. My younger sister sleeps with the light on. I often fall asleep while working on my computer. Countless people drop off in front of their TV. The key in sleep study is not melatonin/light story, although it is an issue.

The secretion of melatonin by the pineal gland alerts the body systems that it is time for clean-up. The hormone itself does not induce sleep; it is a harbinger. Human slumber is more mind-related than hormonal since we must distinguish voluntary sleep from involuntary one. At the end of the day, when it gets dark, the accumulation of adenosine and the gradual conversion of serotonin into melatonin are not enough to induce sleep in the body. When the individual has an issue going on in his mind, he will never sleep; humans are thinking animals equipped with volition, desire, and reason. Life challenges put tremendous pressure on the mind and cause this latter to falter in its mission in the sleeping process. To address the problem, scientists have invented countless artificial molecules. Among these molecules, as sleep aids, are diphenhydramine, doxylamine succinate, melatonin supplement, and the barbiturate class of drugs [20]. What may work for an individual might not work for another because each organism is unique. However, as powerful the drug appears to coerce the adrenal glands to shut down, the more potent it is in its sedative function.

One alternative to medication is to hit the gymnasium, shower, and enjoy a meal before bedtime. The workout at the gym helps accumulate adenosine as energy is needed during exercise. The bath offers relaxation to the body, and the meal increases the secretion of serotonin; these steps augment the individual's wellness. As serotonin goes up, cortisol must go down because both are entangled; thus, the three conditions are gathered. In a good mood, if nothing serious happens in the mind, sleep is induced as the individual goes to bed.

8. Conclusion

Life is about entropy management, and sleep is the best tool to regulate and control chaos in the body. However, as humans age, this process does not come up easily because of life challenges that put more burden upon the mind; physical degradation is another aspect of aging, hence an additional weight. The most

important key component in the sleep mechanism is the mind; it controls the sleeping process, but not always; thus, how humans drop off naturally differs from how manufactured drugs induce sleep in their bodies. Natural sleep needs three conditions to be gathered before the mind sends the body into slumber:

1) adenosine accumulation
2) serotonin converting to melatonin
3) cortisol cutback

The third condition is the sine qua non; it is also the only condition required when manufactured drugs are administered. Adenosine and melatonin are not the triggers of sleep; they are promoters and must yield to the whims of the mind.

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