Ray Peat's Newsletter

. . . Pray God us keep From Single vision & Newton's sleep! Blake

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Sleep and Aging

Research on sleep, as on other physiological processes, is guided by our assumptions and culture. Our understanding of the nature of consciousness affects our thoughts about what happens during these periods of its absence, but in attempting to understand what's happening in the brain when it isn't conscious some researchers have freed themselves from the dominant "philosophy of mind" of the neuroscientists, and I think their more objective look at the sleeping brain is opening some new perspectives on the functions of the waking brain—and on life in general.

> **The disastrous separation of body and mind which has been fixed on European thought by Descartes is responsible for this blindness of science.** ***A. N. Whitehead***

Many "cognitive scientists" have thought of the brain as a computer, in which synapses represent switches, and digital patterns represent information and logical relationships. When the logic circuits aren't operating, this model simply represents nothing, but those who follow Norbert Wiener's example, viewing the brain as a cybernetic control system, rather than as a logic machine, have a fruitful model that can represent the brain as it goes through various changes of state.

For Lamarck, irritability or sensibility, the ability to be stimulated and to react, was life's basic property. The ability to relax after being stimulated, in preparation for another reaction, is probably just as essential, for organisms that do something more than replicate themselves. The ability to relax and to accumulate energy and substance for differentiation corresponds to the presence of oxidative, high efficiency energy production. The intensity of the metabolic cycle, alternating activity and quiescence, sustains the complexity and intensity of life.

Bacteria, which are always in the process of replicating if food is available, don't have anything that corresponds to sleep, or at least no one has observed it. Many people assume that the same would apply to a more complex single cell animal such as the amoeba, but few people have bothered to look. In 1908, two researchers took turns, during 6 days and 5 nights, continuously observing the activities of a group of Amoeba proteus, and concluded that "Activity, or the performing of work, requires energy which the protoplasm must supply. The period of rest appears to be simply the result of organic satisfaction, or a period of recuperation. It suggests the lowest form of sleep; for this tendency to rest, to sleep, as a food reaction is illustrated by the higher animals. In this respect this lowest form of life does not differ essentially from the higher forms." (Gibbs and Dellinger, 1908.)

The sleep of all animals, flies, worms, reptiles, fish, etc., resembles human sleep in various ways, especially in its importance for good health. If a fly is deprived of sleep, it's sleepier the next day, its learning is impaired, and if it's kept awake for three days it will die. In rats, prolonged sleep disruption produces a syndrome of increased food intake, weight loss, increased noradrenaline, decreased thyroxine, decreased body temperature, and death (Rechtschaffen, et al., 1989).

The whole organism sleeps, though the brain regulates the process. In some aspects of its metabolism, especially the turnover of phospholipids, the brain is very active during sleep, but its energy consumption decreases, and it causes the skeletal muscles to relax, reducing their consumption of glucose. Although free fatty acids normally increase during the night, their increase is much greater when sleep is inadequate, and a diabetes-like metabolism appears, with a shift toward the oxidation of fat rather than glucose.

In an experiment in which blood samples were taken at 15 minute intervals during the night, the concentration of cortisol was found to start increasing when the light was turned off, whether the person was asleep or not, but the rise was slower when the person was asleep. In animal experiments, it was found that their mitochondria progressively deteriorated during the hours of darkness. The well known peak of cortisol at dawn is sometimes said to be caused by "the biological clock, preparing for the day's activity," but the experiments show that the stress of darkness creates an inefficient catabolic state, in which cortisol breaks down tissues to provide glucose, and that sleep, to some extent, reduces the stress.

Although nerves and muscles are called "excitable cells," they work best when they aren't too excitable, and fatigue, or interference with their energy supply, makes them too excitable—muscles cramp, nerves die from "excitotoxicity." A deficiency of energy, from either hypoglycemia or hypoxia, makes nerves and muscles too excitable, producing seizures and vascular spasms. When a nerve cell is using oxygen to produce energy, it becomes much more electrically charged than other cells, becoming an "electron sink." That causes the head to have an electrically positive polarity, relative to other parts of the body.

When the electrical activity of a cell is measured with an intracellular electrode, the "membrane potential" is high when it's ready for work, and decreases or disappears during the excited working state. This applies to all sorts of differentiated cells. When cells are in the process of dividing, they stop their differentiated functioning, and lose their electrical membrane potential, as they shift completely away from oxidative energy metabolism. They are in a low energy active state. When cell division is finished, oxidative metabolism resumes, and with the higher energy state, a measurable electrical potential returns.

The high energy resting state is achieved when energy production is greater than energy expenditure. Thyroid hormone and oxidation of sugar produce energy; progesterone and carbon dioxide prevent wasteful expenditure of energy.

For about 150 years, it has been known that electrical current applied to the brain could induce sleep or anesthesia**;** people who were aware that sleep can be therapeutic have proposed using electricity to prolong sleep, and possibly to correct age related conditions. In recent decades, several experimenters have shown that applying a positive current to the head of an animal or person improves learning (Marshall, et al., 2004). This externally applied electrical current seems to be

reinforcing a process that occurs during sleep, a deepening of the resistance to excitatory influences.

> **"You start with a random clump of atoms, and if you shine light on it for long enough, it should not be so surprising that you get a plant."**
>
> **Jeremy England**

Groups of brain cells, removed from a brain and observed in vitro, interact in a way that's analogous to resonance of electrons in molecules or of molecules in physical objects; their electrical activity gradually becomes coordinated, producing electrical signals resembling the EEG (electroencephalogram) signal of a brain in the state of slow wave (deep) sleep. If the cells in the culture dish are electrically stimulated, the sleep rhythm disappears, and they show an EEG pattern resembling that of a waking brain. The day after being electrically stimulated, their sleep rhythm is deepened, the way a person's sleep is deeper after losing sleep (Krueger and Roy, 2016).

When cells are excited, they release some ATP into their local surroundings, where it signals fatigue or injury, activating the formation of inflammatory factors such as TNF-alpha, which promote the sleep rhythm. A breakdown product of ATP is adenosine, which accumulates during waking, and decreases during sleep. A small area of the brain can go into the sleep rhythm earlier than other areas, if it has been more strongly stimulated. Experimenters found that prolonged stimulation of the left hand, by holding a vibrator, caused the subsequent sleep intensity, represented by higher amplitude of the slow waves, to be greater on the right side of the brain, which received the increased sensory stimulation from the left hand. If an arm is immobilized during the day, the sleep waves on the corresponding side of the brain will be weaker in the following sleep.

At the onset of slow wave deep sleep, there is a surge of ATP concentration (Dworak, et al., 2010), coinciding with a decrease of the enzyme AMPK, indicating a shift away from catabolic processes. The brain's consumption of glucose and oxygen is very low during this time. During the hours of normal sleep, this elevated level of ATP gradually declines toward the normal daytime level, and the excitability of the neurons gradually rises to the normal waking level.

The electrical and metabolic properties of this high energy resting state of the brain can be seen in a healthy skeletal muscle, which has a high ATP content, and relaxes immediately after stimulation and contraction. If the ATP is depleted by prolonged intense stimulation, or if it isn't replenished quickly enough, because of hypothyroidism, the relaxation is very slow, leading to cramping. The Achilles reflex relaxation test used for identifying hypothyroidism makes the slow relaxation visible. Since thyroid hormone is needed for oxidative metabolism everywhere in the body, its deficiency makes brain cells slow to relax, delaying the onset of sleep, and can even prevent the deepest restorative sleep. Since all cells are regulated by excitatory and inhibitory processes, hypothyroidism can create a bias toward excitatory states, leading to abnormal secretion and proliferation, for example.

The diastolic, relaxed phase of the heart contraction cycle commonly fails under stress or old age—even in fruit flies. The heart stiffens, and fails to fill completely, so it pumps less with each stroke. In old age, the deep phase of sleep becomes shorter and shallower. When fruit flies are kept active for 2 and a half hours during the day, their deep sleep the following night is improved, and their heart

function is improved (Klassen, et al., 2017; Zheng, et al., 2015).

Bright light during the day strongly stimulates the brain, and improves the depth and duration of deep sleep during the night (Wams, et al., 2017).

Beginning around 1910, Pavlov began studying the ways in which stimulation can bring on sleep, and although electrical techniques such as the EEG hadn't been developed yet, he and his associates gave very detailed descriptions of the interactions of excitation and inhibition in the cortex of the brain, showing that sleep begins in the cortex, and spreads to other parts of the brain and body. They found that the character of an individual governs the way the nervous system responds to fatigue and stress. Outside of Russia, the popularity of Freudian psychology and Behaviorism caused that work to be ignored.

One of Pavlov's students, T. Hayashi, identified the structures in the brainstem that integrate eye movement, the inner ear vestibular system, the cerebellum, and the regulators of muscle tone. The familiar events at the onset of sleep can be understood in terms of the spread of inhibition from the cortex to the brainstem and adjoining structures.

The brain's inhibition of some of the body's functions during sleep is important, because the progressive failure of mitochondria during darkness wastes glucose, leading to a catabolic metabolism (with increased growth hormone, free fatty acids, prolactin, parathyroid hormone, thyroid stimulating hormone, cortisol, histamine, and inflammatory cytokines), converting protein to glucose, liberating free fatty acids, and breaking down bone. During the night, even with the quieting actions of sleep, breakdown of protein is much faster than synthesis, and calcium is lost from the bones.

Exposure of the whole body to red light at the beginning of the night not only improves the quality of sleep, but also endurance and performance the next day (Zhao, et al., 2012). Optimizing mitochondrial function at the beginning of the night makes the brain's inhibitory signals more effective, preserving glycogen stores and reducing noctural catabolism.

The pavlovians' approach to sleep research recognized that the body's needs are always part of the way the organism relates to the world, affecting the meaning of each experience, so that the previous life experience of an individual affects the way that particular daily events will affect the sleep that follows. Stimulation and excitation always have a particular structure, according to the perceived meaning, and for Pavlov, the resulting inhibition was also structured. He saw the dreams that occurred during sleep as residual shadows or fragments of the meanings that were experienced during the day. When sleep wasn't fully restorative, patterns of excitation and inhibition could persist, becoming chronic influences on behavior and physiology.

In order to acquire learning, we must first shake ourselves free of it. We must grasp the topic in the rough, before we smooth it out and shape it. ***A. N. Whitehead***

Pavlov recognized that character types, in his dogs and in people, were influenced by hormones and by personal history. Present knowledge of prenatal influence on the development of autistic traits, in people and in experimental animals, is consistent with Pavlov's observation that some animals were overwhelmed by stimulation that other animals could adapt to easily. Individuals who are hypometabolic are more susceptible to the harmful effects of sleep deprivation, being less able to quickly restore the high energy

resting state. In that state, even relatively weak stimulation can be damaging. For the generation of therapists who followed Pavlov, such as K.I. Platonov (1930), the induction of sleep was considered to be the most effective aspect of psychotherapy.

The rise of free fatty acids in the serum during the night coincides with a high rate of turnover of the brain's phospholipids. Polyunsaturated fatty acids are preferentially liberated from fat stores, in proportion to their degree of unsaturation (Raclot, 2003; Conner, et al., 1996), so their interchange with the brain's lipids means that each night the brain will become enriched with the highly unsaturated fats that are most susceptible to lipid peroxidation. The intensity of lipolysis during the night is decreased during the most restorative deep sleep, but the free fatty acids themselves, by blocking oxidation of glucose to carbon dioxide, tend to increase lactate and to depress glucose metabolism, creating an inflammatory and excitatory state that interferes with deep sleep.

The accumulation of arachidonic acid with aging will tend to increase the formation of prostaglandins, which promote wakefulness and inhibit both slow wave and REM sleep (Matsumura, et al., 1988, 1989; Onoe, et al., 1992). Producing a deficiency of the "essential fatty acids" in animals increases the duration of their slow wave sleep (Dzoljic, 1978). Using aspirin at bedtime, to inhibit prostaglandin synthesis, is likely to be helpful in age related insomnia. Progesterone and vitamin E act in various ways to prevent excessive stimulation by prostaglandins.

Using snacks to minimize the nocturnal increase of free fatty acids and hypoglycemia is an effective way to support restorative sleep, and to retard the brain-aging effects of the accumulation of the unstable fatty acids. Calcium and vitamin D, sufficient to keep parathyroid hormone low, contribute to that process.

Salty snacks are especially helpful for bringing on sleep, probably by stabilizing blood glucose and lowering adrenalin. Ice cream, combining sugar, calcium, and some fat that prolongs the absorption of the sugar, is often effective for improving the quality of sleep.

Thyroid hormone, by promoting the oxidation of glucose, and increasing ATP, is extremely important for the ability to achieve and maintain the needed deep sleep. Hypothyroid people who often find that sleep isn't refreshing, sometimes enter only the first superficial stage of sleep. Thyroxin, T4, helps to reduce the nocturnal level of the proinflammatory thyroid stimulating hormone, TSH, but 5 or 10 mcg of the immediately active T3 at bedtime will usually produce sleep within a few minutes.

Even coffee, if it's used in the right amounts at the right time, can improve the quality of sleep, by supporting the body's energy processes.

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