Ray Peat's Newsletter

Eternity is in love with the productions of time. --William Blake

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Consciousness, nootropics, and progesterone

In the last few decades there has been a lot of overlap between the cultures of "artificial intelligence" and the nootropics (things that improve mental processes or protect the brain) or "smart drugs" (usually referring to stimulants of some sort). These cultures, to the extent that they overlap, are contributing to a view of the mind that I think is harmful.

> **To exist is to change, to change is to mature, to mature is to go on creating oneself endlessly.**
>
> ***Henri Bergson***

I want to consider progesterone's effects on the brain and consciousness as a context for, and alternative to, those cultural trends.

It has been known for several decades that progesterone is an essential factor for nerve growth, and since the 1990s the brain has been known to synthesize it, and to maintain a local concentration of progesterone which is higher than the concentration in the blood stream. Both animal and human studies have shown that providing larger than average amounts of progesterone during fetal development results in larger than average brains and superior abilities in the offspring. Women, in proportion to their height, have on average significantly larger brains than men. In animals generally, a larger brain is associated not only with higher intelligence, but with greater longevity (Jensen and Fuller, 1978, Mallouk, 1975, Hoffman, 1983).

There has been surprisingly little interest in investigating the ways in which progesterone's presence in the brain leads to improved growth, stress resistance, and functioning, but other lines of investigation have made it clear that progesterone's effects are antagonistic to the effects of the other major steroid hormones, especially estrogen, cortisol, and aldosterone. Those hormones interfere with energy metabolism, specifically with the oxidation of glucose.

The other main experimental treatment of fetuses that has resulted in the growth of bigger brains is the provision of additional energy, especially sugar. It seems likely that a basic part of progesterone's ability to protect the brain against stress is its support for the high energy mitochondrial oxidation of glucose to carbon dioxide.

The cortex of the brain, especially the frontal lobes, is the part most sensitive to energy adequacy or deprivation. The outstanding function of the frontal lobes is temporal or sequential thinking, the

ordering of images and actions through time (Romine and Reynolds, 2004). The understanding of time is where there is the most radical difference between mainstream philosophy of science and the anti-reductionist dissenters.

> **It has long been recognized that no analysis of a natural science, whether it be physics or biology, is complete unless we possess a proper analysis of its appropriate time concept.**
>
> ***Norbert Wiener***

In 1948, there were two important publications, one of which, Claude Shannon's "A Mathematical Theory of Communication," is seen by many in the artificial intelligence culture as their charter document. Defining information in terms of abstract discrete units, it stated the computability principle of the logical atomists in a way that was useful for processing electronic signals to eliminate noise (by eliminating the gradations, where random electronic noise degrades the signal). The "digital" units simply had to be a signal that was very much larger than the random noise of the system, so that its presence, or non-presence, was unmistakable.

The other, Norbert Wiener's *Cybernetics, or Control and Communication in the Animal and the Machine,* considered the way natural control systems operate in the midst of noise, by continuous interactions of perception and action. In this approach, understanding is an analog of reality, or creates a model of it that resembles it in form and substance as closely as is practical. Continuity is the property that gives the system reliability, since the system is always in some meaningful state that can be evaluated according to the intended actions.

"Meaning," our intention, has extension through time, while noise has no extension through time. The continuous gradations allow the signal to be distinguished from the noise.

Consciousness and control involve understanding, "modeling," the environment in a way that anticipates changes in the environment. Wiener's 1948 book put time and biology at the center of his thinking, and that same year he published an article focused entirely on "Time, communication, and the nervous system."

As soon as electrical means of communication became part of the culture, they were used as models of the nervous system—sensations were said to be transmitted like telegraphic messages, the brain was like a telephone switchboard. Shannon's information theory based on digital, all-or-none signals, was perfectly compatible with the telegraphic models of nerve impulses and synaptic transmission.

A Russian approach to the nervous system typified by P.K. Anokhin had developed an understanding similar to Wiener's; Anokhin pointed out physiological processes that were incompatible with the telegraphic all-or-none model of nerve function.

Shannon's digitized computational and communication approach to information was formally similar not only to the telegraphic theory of consciousness, but to a reductionist approach to being itself, in which the units of matter, atoms, have no

individual history---if they come to an end by fission, it's a random, uncaused event. If atoms are a-temporal, time is only a statistical description of systems. If consciousness is composed of digital signals, each of which has only one kind of meaning—on or off—time has only an abstract meaning for the conscious system.

The experience of time governs the way we behave, and our metabolism governs the way we experience time. Progesterone, as a central neurosteroid, is a crucial part of our metabolism that shapes our consciousness as it projects itself into time (e.g., Koonce and Frye, 2013).

If a model of the world is written in arbitrary symbols, such as the words of a natural language, or the binary digits of a computer code, the message is the same, regardless of what it's written on—paper, semiconductors, or levers, strings, and pulleys. But if the representation of the world is developed in the flowing metabolism and physiology of an organism, the properties of the model will change as the condition of the organism changes. Norbert Wiener and P.K. Anokhin both considered some of the implications of fine-grain, continuous, modeling of reality.

Accurate prediction of the outcome of one's actions in a changing environment is a major purpose of consciousness. An acrobat and a drunk represent different degrees of accuracy in the representation of movement through time. If we think of our model of the world as the source of hypotheses, the acrobat will habitually produce hypotheses that are useful, those of the staggering drunk are likely to be arbitrary and useless.

In the Wiener worldview, everything has a history which is an intrinsic part of itself, to be taken into account as it moves into the future. New situations and possibilities are produced when different histories interact, and those possibilities will be limited by the extent of the richness, the complexity and flexibility, of the physiology which is supporting the interactions. Anokhin observed that nerves seem to vary in the complexity of the signal that they can transmit.

If the doors of perception were cleansed everything would appear to man as it is, Infinite. For man has closed himself up till he sees all things thro' narrow chinks of his cavern. ***William Blake***

In every circumstance, adaptive metabolism is occurring in an organism, and when the environment is unfavorable, the organism can defend itself by limiting its needs and its range, but when the environment is rich, satisfying needs easily, the organism will tend to expand its range and abilities. The "orienting" or exploratory, curiosity reflex, a need to discover and understand, becomes powerful as the other needs are met. The opportunity to exercise the exploratory reflex expands not only the organism's functional range, but that of the cells and tissues that are exercised in exploration and discovery, and their energetic metabolism. In discovering something about the world, the organism creates something new in itself.

During stress, idle tissues are dismantled to provide materials for the actively adapting tissues, but during constructive exploration, energy is abundant, and cells with the highest energy needs are protected by progesterone, testosterone, DHEA, and other steroids. Besides directly stabilizing the internal structures of the cell, progesterone increases the ATP concentration and oxygen consumption, decreases excitatory systems and numerous inflammation-related processes, decreases intracellular calcium concentration, and increases the use of glucose, leading to increased carbon dioxide production, as well as adjusting breathing and pH.

Until about 1990, the ovaries were believed to be the only significant source of progesterone, and it was clear that stress blocked their synthesis of it, while the presence of progesterone activated the ovary's synthetic apparatus in a self stimulating process. (The negative feedback idea from cybernetics has been widely misapplied in endocrinology.)

Unlike other needs, the appetite for exploration is self stimulating, as long as it's satisfied, and it is dulled, rather than intensified, by frustration. The increased alertness of the orienting state intensifies learning and memory. For example, researchers watched brain responses by MRI when various questions or issues were presented, and noticed that the hippocampus, an area important for remembering, was activated when the person was most curious about a topic, and they found that learning was improved when the person was in a state of increased curiosity.

The fortunate condition of the brain with adequate progesterone is in a high energy state of readiness, metabolically supporting alertness while protecting against excitatory fatigue. I think this state is analogous to the high energy resting state of a healthy muscle, able to relax immediately after a contraction, and very resistant to the cramping and swelling of fatigue. The reticular activating system of the brain stem, which is responsible for waking alertness and muscle relaxation, is central to the orienting reflex, and is responsive to progesterone (Camacho-Arroyo, et al., 1999). This reticular formation of the brain stem is also responsible for the REM, rapid eye movement, phase of sleep, in which dreams occur. REM sleep and the orienting reflex both promote flexibility and fluidity of thinking, with increased sensitivity to motion, and they both show a unique electrical activity pattern, the ponto-geniculo-occipital (PGO) wave, which is probably a product of activation of the reticular formation. It has been suggested (Sanford, et al., 1993) that the presence of these waves in REM sleep "indicates that the brain is in a state of more-or-less continual orienting." When progesterone is given during sleep, it increases the amount of REM.

Colin Wilson described the (somewhat rare) state of being fully awake as "dreaming into the world." When the perceptual system is strong enough, he believed, it could be fully realistic about its situation, while grasping the possibilities existing in the complexity that provide a basis for optimism.

The "pro-cognitive" effects of an enriched environment and of progesterone can to some extent substitute for each other, and they are additive; both of them resist

the metabolic changes caused by stress. Both estrogen and the stress-induced glucocorticoids are reduced by environmental enrichment, allowing progesterone to function with less interference (Meng, et al., 2015, Welberg, et al., 2006). Environmentally enriched animals, progesterone animals, are more novelty seeking, and that trait is probably good for health and longevity (Cavigelli, et al., 2006).

There has been a general medical antagonism toward the "novelty seeking trait," based on the fear that adventurous people will usually get in trouble, but C. R. Cloninger is leading a trend in the other direction, having seen the trait's benefits when it's combined with a basic sociability.

Sociability, curiosity, appreciating novelty, being open to the perception of new possibilities, are traits that make life enjoyable, and although they aren't as spectacular as some of progesterone's other effects, they are traits that would be very valuable in the world's developing social and economic circumstances.

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