Epilepsy and Progesterone

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The length of the life-span, and of the period of youth or immaturity, is closely associated with the size of the brain, and the brain has a very high rate of metabolism. When something interferes with this very high metabolic rate, the consequences may be instantanteous,* or developmental, or chronic and degenerative, or even transgenerational. The issue of epilepsy centers on questions of brain metabolism, and so it has all of those dimensions.

As I discuss the mechanisms known to predispose a person to epilepsy, I will emphasize the centrality of oxidative energy production, and show how "stroke," "stress," "hyperactivity," "dementia," and other brain syndromes are related to "epilepsy." (Similar processes are being studied in the heart and other tissues; eventually, we might have a general language that will make it easier to understand the parallels in the various kinds of "seizure" in any organ.)

As an old term, "epilepsy" has aquired a burden of pseudoscientific ideas, covering old superstitions with an overlay of new superstitions. [Hereditary epilepsy has been discussed in countless textbooks and medical journals, but I think a much better case could be made for the inheritance of a tendency to offer stupid genetic explanations.] "Hereditary epilepsy" and "idiopathic epilepsy" are seriously pathogenic terms; "brain scar" sometimes has a factual basis, but most often the term is an evasion of understanding.

As long as we realize that the essential meaning of the word is "something that grabs you," "epilepsy" is a convenient way to refer to a cluster of convulsive states, fainting spells, night-terrors and nightmares, and strange sensations.

Seizures can be caused by lack of glucose, lack of oxygen, vitamin B6 deficiency, and magnesium deficiency. They are more likely to occur during the night, during puberty, premenstrually, during pregnancy, during the first year of life, and can be triggered by hyperventilation, running, strong emotions, or unusual sensory stimulation. Water retention and low sodium increase susceptibility to seizures. When I was in high school, our dog found and ate a pint of bacon grease, and shortly afterward had a convulsive seizure. I knew of veterinarians who treated seizures in dogs with a vermifuge, so it seemed obvious that a metabolic disturbance, especially if combined with intestinal irritation, could cause fits.

It was undoubtedly such observations that led some physicians to advocate removal of the colon as treatment for epilepsy. Pregnancy and the menstrual cycle have been recognized as having something to do with seizures, but when seizures occurred only during pregnancy, they were classified as nonepileptic, and when they had a clear premenstrual occurrence, they were likely to be classified as "hysterical fits," to be treated with punishment.

It has been observed that all "recognized" anti-seizure drugs are teratogenic, and women who are taking such drugs are told that pregnancy might kill them if they stop the drug, but that their babies will have a greatly increased risk of birth defects if they take the drugs during pregnancy. This is why a better understanding of epilepsy is very important. Old therapies are mainly important for the insight they can give into the nature of the physiological problem. Some of the well established clinical-laboratory observations (F. Mora, and C. S. Babel, for example) give strong hints as to the physiological problem, for example, low albumin, high prealbumin, low magnesium and high calcium all suggest hypothyroidism. (Problems with the bowel, liver, and sex hormones are highly associated with hypothyroidism, both as causes and as effects.) Water retention was so clearly involved in seizures that increased water intake was used as a diagnostic procedure. (R. Grinker) Unfortunately, animal experiments showed that water intoxication increased susceptibility to seizures even in normal individuals. Low sodium content in the body fluids also predisposed to seizures, so that someone with hyponatremia (low blood sodium) would be more susceptible to induction of a seizure by excessive water intake. (Excessive water uptake is still recognized as a factor in seizures, but now it is seen as part of a complex process, involving energy, hormones, and transmitter substances. E.g., Kempski; Chan.)

Hypothyroid people tend to lose sodium easily, and unopposed estrogen increases water retention, without an equivalent sodium retention, so low thyroid, high estrogen people have two of the conditions (edema and hyponatremia) known to predispose to seizures. Another outstanding feature of seizures of various sorts is that they are most likely to occur at night, especially in the early pre-dawn hours. Low blood sugar and high adrenalin predominate during those hours. Hypoglycemia, in itself, like oxygen deprivation, is enough to cause convulsions.

Progesterone and thyroid promote normal energy production, and their deficiency causes a tendency toward hypoglycemia, edema and instability of nerves.

Twenty years ago, a woman who was considered demented visited me. From the age of 21, she had been increasingly disabled by premenstrual migraines. When she was 35 she was a school teacher, and during the summer a neurologist told her that dilantin would help her headaches, because "migraine is similar to epilepsy." Although she told the neurologist that the drug made her "too stupid to teach school," he offered her no alternatives, and didn't mention that sudden withdrawal from the drug could trigger a seizure. When classes started she discontinued the dilantin and had a seizure. The neurologist said the seizure proved that migraines were a form of epilepsy. At the age of 52, she spent about 20 hours a day in bed, and couldn't go outside by herself, because she would get lost. After using a little progesterone for a few days, she stopped having seizures, discontinued her drugs, and was able to work. When she returned to graduate school, she got straight As, and earned her masters' degree in gerontology. But she had lost 17 years because the drug industry had covered up the role of the hormones in epilepsy, migraine, and the perimenstrual syndrome.

The most popular anticonvulsant drugs are both neurotoxic and teratogenic, that is, they damage the patient's brain, and greatly increase the incidence of birth defects. The Nazis justified their horrible medical experiments as "science," but the effects of epilepsy medicine in the last half century have been similar in effect, grander in scale, and without any scientific

justification.

Besides the specific promotional efforts of the drug industry and their branch of government, there is a broader situation that makes their work easier. It is a culture of goony ideas, that ultimately emanates from the academic elite, which (since Descartes, and before) places "thought" above evidence. In biology, "genes" and "membranes" are confused ideas that are used to justify actions that aren't based on evidence. For the Nazis, "cultural degeneracy" was a medical-biological-political category based on that style of thinking. In the United States, "genes" for epilepsy, hyperactivity, language development, IQ, eclampsia, etc., are "found" at Harvard/MIT/Stan- ford/Yale/Univ. of California, etc., by an elite whose wits have been dulled by environmental deprivation, that is, by a lack of criticism.

By manipulating the diet and environment, animals can be made more or less seizure-prone, and it happens that the changes that affect the brain affect all other organs, in ways that are now fairly well understood. Examining the cellular events associated with a seizure is useful for therapy and prevention of seizures, but the same methods are helpful for many other conditions. It is now clearly established that stress can cause brain damage, as well as other diseases. Now that our public health establishment has eliminated smoking from public places, maybe they can find a way to reduce stress and disease by removing morons from positions of power.

Excitotoxicity, in its simplest sense, is the harmful cellular effect (death or injury) caused by an excitatory transmitter such as glutamate or aspartate acting on a cell whose energetic reserves aren't adequate to sustain the level of activity provoked by the transmitter. Once an excitotoxic state exists, the consequences of cell exhaustion can increase the likelihood that the condition will spread to other cells, since any excitation can trigger a complex of other excitatory processes. As calcium enters cells, potassium leaves, and enzymes are activated, producing free fatty acids (linoleic and arachidonic, for example) and prostaglandins, which activate other processes, including lipid peroxidation and free radical production. Protein kinase C (promoted by unsaturated fats and estrogen) facilitates the release of excitatory amino acids. (See J. W. Phillis and M. H. O'Regan, "Mechanisms of glutamate and aspartate release in the ischemic rat cerebral cortex," Br. Res. 730(1-2), 150-164, 1996.) Estrogen supports acetylcholine release, which leads to increased extracellular potassium and excitatory amino acids. (See R. B. Gibbs, et al., "Effects of estrogen on potassium-stimulated acetylcholine release in the hippocampus and overlying cortex of adult rats," Br. Res. 749(1), 143-146, 1997.)

Estrogen also stimulates the production of free radicals. Calcium, free radicals, and unsaturated free fatty acids impair energy production, decreasing the ability to regulate potassium and calcium. The increased estrogen associated with seizures is associated with reduced serum calcium (Jacono and Robertson, 1987). Feedback self-stimulation of free radicals, free fatty acids, and prostaglandins create a bias toward increased excitation.

Ammonia is produced by stimulated nerves, and normally its elimination helps to eliminate and control the excitotoxic amino acids, glutamate and aspartate. The production of urea consumes aspartic acid, converting it to fumaric acid, but this requires carbon dioxide, produced by normal mitochondrial function. A deficiency of carbon dioxide would reduce the delivery of oxygen to the brain by constricting blood vessels and changing hemoglobin's affinity for oxygen (limiting carbon dioxide production), and the failure to consume aspartate (in urea synthesis) and glutamate (as alpha-ketoglutarate) and aspartate (as oxaloacetate) in the Krebs cycle, means that as energy becomes deficient, excitation tends to be promoted. This helps to explain the fact that seizures can be induced by hypoxia. (Balloonists and mountain climbers at extremely high elevations have mentioned suffering from severe insomnia. The mechanisms of excitotoxicity are probably involved in other forms of insomnia, too.) Antioxidants help to control seizures, by reducing the excitatory contribution of free radicals and lipid peroxidation. Since excitation can promote the toxic forms of oxidation, many surprising substances turn out to have an "antioxidant" function. Magnesium, sodium (balancing calcium and potassium), thyroid and progesterone (increasing energy production), and in some situations, carbon dioxide. Aspirin, by inhibiting prostaglandin synthesis (and maybe other mechanisms) often lowers free radical production. Adenosine seems to have a variety of antioxidant functions, and one mechanism seems to be its function as an antiexcitatory transmitter. One of estrogen's excitant actions on the brain probably involves its antagonism to adenosine (Phillis and O'Regan, 1988).

Albumin, besides maintaining blood volume and preventing edema, serves to protect respiration, by binding free fatty acids. Estrogen blocks the liver's ability to produce albumin, and increases the level of circulating free fatty acids. Free fatty acids cause brain edema. This is probably another aspect of estrogen's contribution to seizure susceptibility. Magnesium sulfate has been used for generations in India to treat eclampsia and "toxemia" of pregnancy, and its effectiveness is gradually coming to be recognized in the U.S. Increasingly, magnesium deficiency is recognized as a factor that increases susceptibility to seizures. (Valenzuela and Benardo, 1995; Slandley, et al., 1995). Hypothyroidism reduces the ability of cells to retain magnesium. Thyroid does many things to protect against seizures. It keeps estrogen and adrenal hormones low, and increases production of progesterone and pregnenolone. It facilitates retention of magnesium and of sodium, and prevents edema in a variety of ways.

Progesterone, because of its normal anesthetic function (which prevents the pain of childbirth when its level is adequate), directly quiets nerves, and in this way suppresses many of the excitotoxic processes. It has direct effects on mitochondria, promoting energy production, and it facilitates thyroid hormone functions in various ways. It promotes the elimination of estrogen from tissues, and is a "diuretic" in several benign ways, that are compatible with maintenance of blood volume. It antagonizes the mineralocorticoids and the glucocorticoids, both of which promote seizures. (Roberts and Keith, 1995.) The combination of hypoglycemia with elevation of cortisone probably accounts for the nocturnal incidence of seizures.

If progesterone's antiepileptic effectiveness were not enough (and it is very effective even in irrational pharmaceutical formulations), the fact that it reduces birth defects, and promotes brain development and nerve repair should assure its general use in women with a history of seizures, until it is established that they are no longer "epileptic." Although thyroid, progesterone, and a high quality protein diet will generally correct the epilepsy problem, it is important to mention that the involvement of unsaturated fats and free radicals in seizure physiology implies that we should minimize our consumption of the unsaturated fats. Even years after eliminating them from the diet, their release from tissue storage can prolong the

problem, and during that time the use of vitamin E is likely to reduce the intensity and frequency of seizures. Coconut oil lowers the requirement for vitamin E, and reduces the toxicity of the unsaturated fats (see Cleland, et al.), favoring effective respiration and improving thyroid and progesterone production. Endotoxin formed in the bowel can block respiration and cause hormone imbalances contributing to instability of the nerves, so it is helpful to optimize bowel flora, for example with a carrot salad; a dressing of vinegar, coconut oil and olive oil, carried into the intestine by the carrot fiber, suppresses bacterial growth while stimulating healing of the wall of the intestine. The carrot salad improves the ratio of progesterone to estrogen and cortisol, and so is as appropriate for epilepsy as for premenstrual syndrome, insomnia, or arthritis.

NOTES:

When the brain loses its oxygen supply, consciousness is lost immediately, before there is much decrease in the ATP concentration. This has led to the proposal of interesting "electronic" ideas of consciousness, but there is another way of viewing this. While ATP constitutes a kind of reservoir of cellular energy, the flow of carbon dioxide through the brain cell is almost the mirror image of the flow of oxygen. Oxygen scarcity leads directly to carbon dioxide scarcity. The "sensitive state," consciousness, might require the presence of carbon dioxide as well as ATP, to sustain a cooperative, semi-stable, state of the cytoplasmic proteins. The ability of ordinary light to trigger a conformation change in the hemoglobin-carbon monoxide-carbon dioxide system shows how sensitive a system with only a few elements can be. At the other extreme from consciousness, there is the evidence that carbon dioxide is essential for even the growing/living state of protozoa, algae, and bacteria.(O. Rahn, 1941.)

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