

## Chapter 1 : Estrogen and Progesterone: two hormones that control a woman's life

*The Effects of Estrogen on Brain Function* edited by Natalie L. Rasgon, M.D., Ph.D. This timely volume reviews current data on the effects of estrogen on the central nervous system, highlighting clinical aspects of this topic.

The Rockefeller University Q: What surprises you most about how male and female brains differ? There are fundamental sex differences between males and females that go well beyond reproduction. We have evidence, as do others, that the hippocampus, a memory-related organ unrelated to reproduction, responds differently to estrogens. The female responds to estrogen by forming new synaptic connections in the hippocampus, while the male does not. But if you block the actions of testosterone in the male at birth, then the male will respond to estrogens to induce these synapses. There are many other examples. The differences include cerebellum, the autonomic nervous system, cerebral cortex, and hypothalamus. The more we look, the more sex differences we discover. Has science done enough to take into account sex differences in basic and clinical research? Science has not done enough to take into account sex differences in either basic or clinical research. This has revitalized the study of sex differences, meaning, in large part, the study of whole animals and how they differ behaviorally and physiologically. Why has it been so difficult to nail down these effects? These non-nuclear receptors can stimulate important signaling pathways, such as cyclic AMP, very much like neurotransmitters and other hormones that work on the surface of cells. The myriad of possible mechanisms and effects has grown enormously, for estrogens as well as for other steroids. As a result, the pharmacology of estrogen antagonists is confusing. It may actually stimulate some actions in the brain produced by estrogen and block others. It becomes a matter of trade-offs between getting a beneficial effect, for example in bone or protecting against uterine or ovarian cancer, versus possibly having a negative effect elsewhere. We have to go back to the drawing board and perhaps investigate other types of therapies that involve more natural hormones, and are given in more physiological ways, which means sequentially and intermittently. We know that low-dose is always the best idea, and that sequential administration of estradiol, the natural hormone, and progesterone, the natural hormone, may be effective. A recent paper by Karen Prestwood in the Journal of the American Medical Association, suggests that low doses of natural estradiol protect bone density in post-menopausal women. We have to go back to the drawing board There is evidence from animal studies that the body in general, and the brain in particular, may lose sensitivity to estrogens if they are missing for too long. And, if the brain is continually reorganizing itself, it may adapt and not need these hormones, at least not in the same way. That suggests, and there is evidence, that if you treat around the time of menopause, perhaps even with Prempro, there may actually be some lasting protective benefit. It remains to be seen whether women should be treated around the time of the menopause and not later, or whether they have to be treated continuously for the rest of their lives, in the most physiologic manner possible. Some women are probably okay without the supplemental hormones, but if the hormones are given too late, according to WHI, they may make matters worse. What might account for this? There is a disconnect. I think, unfortunately, clinicians ignored basic research in designing Prempro. In meetings where clinicians and basic researchers are present, it sometimes feels like nobody is listening to one another. There are still people that totally ignore the basic research and just continue on their own logic. Of course, as a basic researcher, I feel that really the whole problem with Prempro was produced by a failure to recognize the basic facts on hormone action, and bowing to the pressure from pharmaceutical companies. The Europeans, incidentally, did not buy any of this; most of them stayed away from Prempro like a plague. It was also out of their experience that we now have progesterone gels, and even estradiol that can be applied topically. I think these offer hope for real benefits. University of Michigan Q: Your research focuses on sex differences in the brain, and how estrogen modulates neural systems. When I started investigating sex differences in the brain more than 25 years ago, most people thought they would be relatively minor and only in a few areas of the brain. What is surprising at this point is that we know that men and women have different brains, and yet we know very little about the consequences of these differences for neurological disorders, mental health, or drug abuse. Why has it been so difficult to nail down what estrogen is doing in the brain? In other words, in some cells estradiol does one thing, in other cells it does another, and in

many cells the effect varies with the recent history of hormone exposure. For example, in the hypothalamic brain regions important for reproductive behavior in rats, it can take 48 hours of exposure to estradiol before a female rat will exhibit sexual receptivity. In contrast, in the striatum, estradiol acts extremely rapidly within minutes to induce a change in behavior triggered by drugs like cocaine or amphetamine. So, there are both long-term effects of estradiol as well as rapid immediate effects. This is one source of the confusion about what estradiol is doing in the brain. There can also be big effects depending on how the hormone is administered. You have advocated for increased attention to gender differences in basic neuroscience and clinical research. Is enough being done? If not, what needs to happen to improve the situation? I do not think that enough research is being done on gender differences in basic neuroscience, clinical research, or in pharmaceutical testing of drugs. A number of things need to be done. Physicians also need to be more aware of sex differences in the brain and body. The only way that will happen is if the medical schools begin teaching how the brains of men and women differ, and the medical boards include questions to assess that this knowledge has been learned. Currently they are only required to include women, but are not required to include enough subjects so as to determine if women and men react differently to a drug. What have you learned about how estrogen relates to addiction vulnerability? What are the practical implications of this work? My research has shown that physiological doses of estradiol affect acquisition of cocaine-taking in female rats, so that they will start taking cocaine at lower doses than will males or females without estradiol. On the other hand, progesterone may counteract the effects of estradiol on acquisition of cocaine-taking behavior. We have also been looking at an animal model of cocaine relapse. If cocaine-taking ceases, estradiol alone does not induce a female rat to start taking cocaine again. But, if a rat gets an injection of cocaine after receiving estradiol, they respond more intensely to cocaine that is, they relapse more easily. So, there may be certain times during the menstrual cycle when a woman who has kicked a cocaine habit will be at greater risk for relapse if she is exposed to even a little cocaine. What do you tell women? We know that estradiol promotes cognitive functions related to language and fine motor skills in women. The animal research is very clear that estradiol has beneficial effects on the brain. Estradiol induces nerve growth factor, which promotes survival of neurons important for learning and memory. In the absence of estradiol, these functions are lost. Long-term hormone withdrawal can make it impossible for estradiol to restore these functions. So, a woman should decide if she is going to take HRT before she is symptomatic and work with her doctor to determine the best formulation and dose for her. I believe that the adverse effects reported in the WHI study cannot be generalized to all women, but are specific for women who have been post-menopausal without HRT for many years. Stay In Touch Get the latest neuroscience news delivered to your inbox.

**Chapter 2 : Estrogens and brain function.**

*" The effects of estrogen on mood Citing the ongoing confusion over the risks and benefits of estrogen therapy, the contributors emphasize the need for additional research on medication, doses, preparations, methods of administration, alternative therapies, and supplements.*

Cognition[ edit ] Verbal memory scores are frequently used as one measure of higher level cognition. These scores vary in direct proportion to estrogen levels throughout the menstrual cycle, pregnancy, and menopause. Furthermore, estrogens when administered shortly after natural or surgical menopause prevents decreases in verbal memory. In contrast, estrogens have little effect on verbal memory if first administered years after menopause. Sudden estrogen withdrawal, fluctuating estrogen, and periods of sustained low estrogen levels correlate with significant mood lowering. When estrogen levels were raised through the increased activity of the enzyme aromatase in male lab mice, OCD rituals were dramatically decreased. Hypothalamic protein levels in the gene COMT are enhanced by increasing estrogen levels which are believed to return mice that displayed OCD rituals to normal activity. Aromatase deficiency is ultimately suspected which is involved in the synthesis of estrogen in humans and has therapeutic implications in humans having obsessive-compulsive disorder. Contrarily, local application of estrogen has been shown to block the ability of fluvoxamine to slow serotonin clearance, suggesting that the same pathways which are involved in SSRI efficacy may also be affected by components of local estrogen signaling pathways. Hormone replacement therapy using estrogen may be a possible treatment for binge eating behaviors in females. Estrogen replacement has been shown to suppress binge eating behaviors in female mice. Women exhibiting binge eating behaviors are found to have increased brain uptake of neuron 5-HT, and therefore less of the neurotransmitter serotonin in the cerebrospinal fluid. Research has predicted increased emotional eating during hormonal flux, which is characterized by high progesterone and estradiol levels that occur during the mid- luteal phase. It is hypothesized that these changes occur due to brain changes across the menstrual cycle that are likely a genomic effect of hormones. These effects produce menstrual cycle changes, which result in hormone release leading to behavioral changes, notably binge and emotional eating. These occur especially prominently among women who are genetically vulnerable to binge eating phenotypes. Dysregulated eating is more strongly associated with such ovarian hormones in women with BEs than in women without BEs. In addition, estrogens are responsible for bone maturation and maintenance of bone mineral density throughout life. Due to hypoestrogenism, the risk of osteoporosis increases during menopause. Cardiovascular system[ edit ] Women suffer less from heart disease due to vasculo-protective action of estrogen which helps in preventing atherosclerosis.

**Chapter 3 : Does the lack of estrogen affect the brain? | Cancer Survivors Network**

*opposed to an effect on motivation or performance parameters. In monkeys, estradiol has been shown to modulate visuospatial attention (Voytko, ) 12 THE EFFECTS OF ESTROGEN ON BRAIN FUNCTION Fig. The synthetic estrogen diethylstilbestrol (DES) enhances object recognition in young ovariectomized rats.*

When they are out of balance problems follow. To better understand the consequences of these hormone disturbances, we must first discuss the normal functions of estrogen and progesterone. Estrogen, a steroid hormone, carries physiological messages to body organs and systems. These messages differ for each body organ and system. Estrogen sends messages to the uterus to grow and replace the lining that is shed during the previous menses. Bone resorption is decreased by estrogen. Bone is constantly being broken down and replaced. Estrogen is needed to maintain a proper rate of bone breakdown and prevent bone loss. The vagina and female bladder functions are maintained under the influence of estrogen. It keeps the vagina moist and prevents the bladder from leaking urine. In adolescence, estrogen is responsible for developing female sex characteristics. Estrogen causes breast to grow by increasing breast cell numbers and their multiplication. It also stimulates the development of female sexual organs. Estrogen decreases the function of thyroid hormone. Estrogen increases the production of a protein called thyroid binding globulin. This protein binds thyroid hormone making it inactive. Thereby, decreasing metabolism and increasing fat deposits. The body stores fat in order to have enough energy for a fetus if a pregnancy develops. Estrogen effects the brain. Its effect on the brain is very tenuous. At normal levels estrogen prevents depression and insomnia, increases concentration, and maintains normal sex drive. If estrogen is too high or low, depression, anxiety, insomnia, decreased sex drive and decreased concentration may result. Progesterone, a steroid hormone, also carries messages to other organs. The messages are directed to the same body organs and systems as estrogen but the messages are different. Progesterone is produced by the ovary after ovulation. It instructs the uterine lining to stop growing so that it might develop and mature in preparation for a possible pregnancy. Progesterone is produced for fourteen days after ovulation. If there is no pregnancy, progesterone decreases and signals the beginning of menses. Progesterone decreases the target organs response to estrogen by decreasing the number of receptors the organ has for estrogen. Receptors are molecules on the cells that recognize specific hormones and allows them to carry their message to the cell. Progesterone also decreases breast cell growth. It is involved in the maturation of breast cells and decreases the rate of multiplication. Progesterone also promotes normal cell death in the breast which is important in the prevention of cancer. While estrogen decreases the rate of bone breakdown, progesterone stimulates bone osteoblasts. Osteoblasts are responsible for making new bone to replace old bone. By decreasing thyroid binding globulin, progesterone increases the activity of thyroid hormone. Thyroid hormone increases metabolism, and utilizes the fat stored under estrogen influence for energy. Normal progesterone levels are important for a normal body composition. Low progesterone levels can lead to weight gain. Progesterone stimulates normal sex drive because it can be converted to testosterone which is involved in male and female sex drive. It blocks aldosterone receptors. Aldosterone promotes water retention and swelling. Progesterone blocks aldosterone causing normal fluid loss and decreasing swelling. Progesterone decreases uterine muscle contractions which cause menstrual cramps by promoting uterine muscle relaxation. In the brain, progesterone binds GABA receptors. These receptors decrease anxiety, insomnia and depression. Anti-depressants and barbiturates bind these same receptors. Progesterone is a natural antidepressant and prevents anxiety.

**Chapter 4 : Sex Differences in the Brain: The Estrogen Quandary**

*The results of small randomized trials and larger observational studies suggest a beneficial effect of estrogen therapy on cognitive function in symptomatic postmenopausal women. However, the results of the Women's Health Initiative Study (WHIMS) do not support this, at least not in women over the age of*

Side effects Estrogens are a group of sex hormones that promote the development and maintenance of female characteristics in the human body. They play an essential role in the growth and development of female secondary sexual characteristics, such as breasts, pubic and armpit hair, and the regulation of the menstrual cycle and reproductive system. During the menstrual cycle, estrogen produces an environment suitable for the fertilization, implantation, and nutrition of an early embryo. An imbalance of these hormones can lead to a range of health problems and unwanted physical changes. This MNT Knowledge Center article will explain what estrogen is, how it works in the body, its range of medical uses, and the effects of estrogen imbalance.

Fast facts on estrogen The ovaries are the main location for estrogen production. Estrogen influences the structural differences between the male and female bodies, such as females having a wider pelvis and more permanent hair on the head. Synthetic estrogen has a range of uses in medicine, including birth control and managing the effects of menopause. Estrogen is involved in the development of a range of health issues. Estrogen is a vital hormone in female development. Hormones are chemical messengers that tell specific tissues to behave in a certain way. During puberty , the ovaries begin releasing estrogen hormones in line with each monthly menstrual cycle. The estrogen level rises suddenly halfway through the cycle, which triggers the release of an egg. This level then quickly decreases after ovulation. Estrogens usually travel through the bloodstream in fluids, interact with cells in a variety of tissues in the body, and deliver a message or instruction. It is one of the most important hormones for women, alongside progesterone. Progesterone helps to maintain pregnancies and implant an egg in the uterus. The related hormones in the estrogen family include:

This is a weak form of estrogen and the only type found in women after the menopause. Small amounts of estrone are present in most tissues of the body, mainly fat and muscle. The body can convert estrone to estradiol and estradiol to estrone. This is the strongest type of estrogen. Estradiol is a steroid produced by the ovaries. It is thought to contribute to a range of gynecological problems, such as endometriosis , fibroids , and cancers that occur in females , particularly endometrial cancer. This the weakest of the estrogens and is a waste product made after the body uses estradiol. Pregnancy is the only time at which significant amounts of estriol are made. Estriol cannot be converted to estradiol or estrone. Far lower levels of estrogen are also present in men. Function Estrogen is crucial to the reproductive function and cycle of a woman. Benefits In females, estrogen affects the following areas of the body: Estrogen helps stimulate the growth of an egg follicle. It also stimulates the growth of the vagina to its adult size, the thickening of the vaginal wall, and an increase in vaginal acidity that reduces bacterial infections. It also helps lubricate the vagina. Estrogen is responsible for the growth of a thick, muscular wall in the fallopian tubes, and for the contractions that transport the egg and sperm cells. Estrogen enhances and maintains the mucous membrane that lines the uterus. It increases the size of the endometrium as well as enhancing blood flow, protein content, and enzyme activity. Estrogen also stimulates the muscles in the uterus to develop and contract. Contractions help during the delivery of an infant and placenta, and they also assist the wall of the uterus in getting rid of dead tissue during menstruation. Estrogen is thought to regulate the flow and thickness of uterine mucous secretions. This enhances the movement of a sperm cell to an egg and enables fertilization. Estrogen forms unique relationships with other hormones in the breast. They are responsible for the growth of the breasts during adolescence, the pigmentation of the nipples, and eventually stopping the flow of milk when an infant is no longer breast-feeding. Estrogen is responsible for the differences between male and female bodies. For example, in a female body: Estrogen makes the bones smaller and shorter, the pelvis broader, and the shoulders narrower. It increases fat storage around the hips and thighs, meaning that the body is more curved and contoured. Estrogen helps to slow down the growth of females during puberty and increases sensitivity to insulin. Insulin influences the amount of body fat and lean muscle a person can develop. Estrogen makes the

voice box smaller and the vocal cords shorter, giving females a higher-pitched voice than males. Estrogens suppress the activity of the glands in the skin that produce oily substances. This reduces the likelihood of acne in females. Other areas on which estrogen has an impact include: Estrogens improve the thickness and quality of the skin as well as the collagen content which prevents aging. Estrogen helps to preserve bone strength and prevent bone loss. The liver and heart: The hormone regulates cholesterol production in the liver, helping to protect the heart and arteries. Foods Some foods contain phytoestrogens, which may affect levels of estrogen in the body.

**Chapter 5 : Progesterone and the Nervous System/Brain - Women in Balance Institute**

*The Effects of Estrogen on Brain Function provides a comprehensive update on recent research findings and is an indispensable guide to clinicians and scientists.*

Prokai is the Robert A. For many women going through menopause, hormone replacement therapy HRT can be a godsend. HRT can also offer the body some important protective benefits, like helping prevent osteoporosis. But where HRT really flexes its muscles, so to speak, is in the brain. If you think about it, the symptoms of menopause are largely neurological in origin, which many women may not realize. Insomnia, hot flashes, dizziness, anxiety, depression, and fatigue are all originate in the CNS " and all are thought to occur when there is too little estrogen circulating in it. Menopausal symptoms can range from bothersome to debilitating for some women. However, there is a lot of good evidence that safer forms of estrogen are indeed possible, and will exist in the near future. This article will outline the current thoughts on how ET can best be used. Is there a certain window of time when ET should be started to have the most benefits with the least risk? How can we harness the power of ET for the protective and restorative benefits to the brain without harming other tissues of the body? Researchers are still working on many of these questions, but there is already some very strong evidence that we are on the way to developing safe and effective forms of ET. The study revealed that not only was the risk higher in the first year of using HRT, but there were continued heart risks even years down the road. Estrogen was shown to decrease the risk of hip fracture and colorectal cancer, as well as prevent hot flashes but increased the incidence of breast cancer, stroke, pulmonary embolism, and coronary heart disease. Both studies utilized a form of [estrogen made from the urine of pregnant mares] and a synthetic form of progesterone. These are not the forms of estrogen or progesterone that the human ovary produces. The ET in the WHI study was actually stopped because of the increased risk of stroke that was occurring without any benefit in the prevention of heart disease. These studies led researchers to conclude that though it clearly offers some benefits, the heightened risk of cardiovascular disease was enough to outweigh those benefits. These are not the forms of estrogen or progesterone that the human ovary produces. There are also many other variables that could affect the results of using ET, like the doses used and methods of administration patch, orally, or by injection , how long a woman stays on hormone therapy, and the age when she begins the therapy in relation to her age at menopause. Some newer studies that have reanalyzed the WHI data have actually found that if a woman takes ET within 10 years of beginning menopause, she has no more risk of developing breast cancer than anybody else. Moreover, ET in this age group provides certain protection against breast cancer. This is good news. Conversely, if a woman begins ET later than 10 years of beginning menopause, her risk of developing breast cancer does seem to increase. Findings like this show that there is a lot of value to reanalyzing old studies. However, stroke, probably due to the elevated coagulation and inflammation caused by estrogen, remains a serious risk, regardless of the time from the onset of menopause or the form of HT. Some newer research has also shown that ET " if started around the time of menopause " can reduce the cognitive decline that comes with age. So, it seems that this "critical window" may prevent multiple health problems, in both the body and the brain. In fact, some studies have shown that estrogen has a "healthy cell bias": Despite all the health benefits when hormones are started at the right time, however, stroke is still a serious risk. The risk of stroke with hormone therapy is considerable, too, regardless of when a woman starts therapy, or the form that she uses ET alone or HRT. And it would do all this without having the adverse effects in the rest of the body, like the forms of cancer mentioned earlier. It is thought that estrogen may actually rescue or prevent neurons from cell death. Estrogen may help take care of free radicals by actively scavenging for them directing or by helping to boost other endogenous substances that do the same. Rescuing Cells from Certain Death Another way that estrogen protects the brain is by regulating how cells live " and die. Estrogen can promote cell survival and the formation of neurons neurogenesis through a variety of avenues, like nerve growth factor, brain-derived neurotrophic factor BDNF , neurotrophins, and insulin-like growth factor 1 IGF As mentioned, estrogen can also affect the life-cycle of the cell by staving off cell death. A process called apoptosis a. Though cell death is sometimes considered necessary, when neurons die, they

are typically not replaced; therefore, it behooves the brain to lose as few neurons as possible. Preventing Inflammation Estrogen has also been shown to help reduce inflammation, which can lead to a host of health problems. Specifically, estrogen can reduce not only the expression of "neuroinflammatory" compounds in the brain but the selective permeability of the blood-brain barrier – if this sounds complicated, it is! But the end-goal is that inflammation in the CNS is reduced. Not surprisingly, estrogen actually works in multiple ways to prevent inflammation in the nervous system, and lead to better brain health. Targeting Estrogen Receptors in the Brain, Soy And Other New Approaches Early studies albeit in rodents gave researchers great hope for using certain kinds of estrogens to treat diseases that affected the brain. For example, it has been found to play a crucial role in how estrogen fights degeneration in the brain, as well as boosts learning and memory. Can Soy Really Help? Many women may have heard of the potential benefits of eating soy products to help with menopause symptoms. Though the research on soy has been mixed, there is some evidence that soy may mimic the effects of estrogen in the body. Soy is a phytoestrogen, which is a weaker form than the estrogen that animals produce. It is thought that phytoestrogens like soy may be behind the finding that Asians, of both sexes, have lower incidences of sex hormone-related disorders like prostate cancer in men and breast cancer and hot flashes in women, compared to Westerners. It is thought that phytoestrogens like soy may be behind the finding that Asians, of both sexes, have lower incidences of sex hormone-related disorders. One reason for this is the evidence that the GI tracts of many Asian people produce a certain end-product from soy, called equol an isoflavone, which Westerners are less likely to produce. If this is the case, it would mean that just adding soy to the diet would not necessarily have the desired effect. But some studies have found that women who are actually administered the compound equol do have some improvements in menopause symptoms depression, anxiety, and fatigue, but more research will need to be done to fully understand the link between soy and estrogen. These molecules do not function exactly like the parent hormone, estrogen, but they behave in similar ways. Sometimes these are called non-feminizing estrogens though this is a bit of a misnomer, and they should technically avoid all the side effects of chronic estrogen therapy, which affect the uterus, breast, liver, and other organs. They can also be used in both women and men, in certain circumstances. It has been difficult, however, to create good estrogen-like compounds because they need to behave in very specific ways. Much research has been devoted to designing these molecules to retain all the neuroprotective effects of estrogen, by tweaking the molecular structure in various ways, for example. Some have looked promising when they were tested in rats, but because the compounds were ultimately large and attracted too much to fat, they would not have been appropriate to move forward with drug development. Still, there is research being devoted to the development of good mimics, and researchers remain optimistic about their potential. In other words, a precursor of estrogen, or a prodrug, can be converted into estrogen after it is inside the body. Studies have found that using prodrugs can actually boost the effectiveness of a parent drug. Researchers especially like the idea of prodrugs because there is not a lot of cost or risk associated with their development. Some prodrugs are particularly good at gaining access to and remaining in the brain, which is not an easy thing to do – this is because of a tight "blood-brain barrier", which is meant to keep toxins and other unwanted molecules in the blood stream rather than the brain. Though there have been some hurdles to developing estrogen prodrugs, researchers are still hopeful about using this class of drugs for treating a variety of menopause symptoms. In fact, one promising drug, called estrogen-derived para-quinol, has been shown to act primarily in the brain, and even better, it does not seem to give off any toxic by-products. Experiments in rats have shown encouraging results, and hopefully more research will explore estrogen prodrugs for use in humans. To recap, though early studies raised some concerns about using estrogen safely, when researchers looked deeper into these findings, they saw trends that would allow them to develop better ones in the future. Some of the important variables seemed to be what kinds of hormones were being used estrogen vs. We want estrogen to work in the brain and the rest of the nervous system, not in the organs of the body. The nervous system needs it to function smoothly – when estrogen is missing, this is where the symptoms of menopause begin hot flashes, fatigue, muscle weakness, depression, anxiety, and insomnia. And researchers are working hard to discover new and clever ways to get estrogen to our nervous systems without letting it affect the rest of the body. Some of these methods –

phytoestrogens, estrogen "mimics" and the prodrugs " are looking like powerful prospects.

## Chapter 6 : Estrogen: Functions, uses, and imbalances

*This article summarizes what is known to date about the effects of estrogen on cognitive functions. News & Perspective Drugs & Diseases Estrogen & the Aging Brain.*

Progesterone and the brain By Margaret N. By the time she reaches menopause, circulating progesterone levels are so low, they are similar to those normally seen in men. However, progesterone is far more than a gestational agent. Research is now surfacing which shows that the benefits of progesterone reach to breast health, cardiovascular health, and nervous system health, most importantly brain function. The rest of this article will take a closer look at just how essential progesterone is for your brain. It is so essential that it comes from two different places to reach the brain: Secondly, progesterone that is circulating in the bloodstream also has direct access to the brain and nerves. Normal brain function is not the only thing progesterone is required for in the nervous system. An important role of progesterone is to protect the brain from damage and promote repair after injury. It actually does this by promoting the growth and repair of the myelin sheath that protects the nerve fibers. Progesterone protects the brain from damage after traumatic brain injury. Around 20 years ago, researchers who were studying rats after brain injury made a significant observation. Female rats which, at the time of the brain injury, were at the stage of their reproductive cycles when progesterone levels were the highest, had significantly less brain damage than male rats or females with lower progesterone levels. A review published this year suggests that not only should progesterone be used to treat traumatic brain injuries, but that it may also have a role in treating stroke, because of its powerful protective effects on brain tissue. This is a very exciting area of progesterone research, as researchers and clinicians acknowledge the fact that natural progesterone has an excellent safety profile without long term side effects, making it a good candidate for high dose therapy that can also be carried out in a home environment as patients recover. Progesterone and brain development – smarter kids? There is published evidence that the children of women who were treated with progesterone during pregnancy showed enhanced development during infancy, achieved better academic results at ages , and were significantly more likely to attend universities. If progesterone levels are too low, normal brain development may be affected, putting an infant at a developmental disadvantage. Progesterone eases anxiety and facilitates memory Progesterone naturally metabolizes in brain tissues to the metabolite allopregnanolone, which is known to produce calming, anti-anxiety and possibly enhanced memory effects. There is some speculation that it could be important in preserving cognitive function in women experiencing the decline in progesterone levels with age. It will be interesting to see further research on this as aging women increasingly use progesterone in hormone replacement. Progesterone as a sleeping aid? Basically, there is a large quantity of metabolites produced in the liver after oral progesterone is absorbed by the intestines. These metabolites have known sedative and hypnotic effects. On the other hand, women using progesterone cream do not produce metabolites in such large quantities because the progesterone is absorbed through the skin and bypasses the liver metabolism. Synthetic progestins are molecularly different from natural progesterone and therefore do not metabolize to the same compounds as natural progesterone. They do not show benefits for cognitive or anti-anxiety function. The progestin that has been the most extensively studied and which is commonly used in synthetic hormone replacement therapy, MPA medroxyprogesterone acetate , has been found to have negative effects on the nervous system and even reduces the beneficial effects of estrogen. Trying to find articles on hormone balance and menopause? We know how important it is for you to have quality research in order to make informed decisions about your health. Our research database contains articles that are hand-picked to provide the most up-to-date and relevant information.

## Chapter 7 : Estrogen And the Brain

*This timely volume reviews current data on the effects of estrogen on the central nervous system, highlighting clinical aspects of this topic.*

## Chapter 8 : Estrogen - Wikipedia

*Estrogens and brain function 11 A cross-sectional study by Portin et al 46 on sixty- three healthy pre-, peri- and postmenopausal wom-en evaluated the effect of estrogen levels on cogni-*

## Chapter 9 : The Effects of Estrogen on Brain Function

*Another way to retain estrogen's beneficial brain effects while avoiding the adverse organ effects is to come up with "estrogen-like" compounds. These molecules do not function exactly like the parent hormone, estrogen, but they behave in similar ways.*