

Effects of progesterone on Alzheimer's disease

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The first study on progesterone and Alzheimer's disease has found no clear preventive benefit for the widely prescribed hormone in an animal model.

Progesterone is given with estrogen in hormone replacement therapy. Previous studies have suggested that estrogen offers women some protection against Alzheimer's disease.

The study's authors, led by gerontologist Christian Pike of the University of Southern California, asked if the same could be true of progesterone.

In a study highlighted in this week's issue of the *Journal of Neuroscience*, Pike's group reports that progesterone has only limited benefit for mice with Alzheimer's symptoms when taken alone.

When taken with estrogen, progesterone actually inhibits some of the other hormone's beneficial effects, the study found.

The problem is not necessarily progesterone itself, Pike said. It could be the constant daily dosage, which fails to replicate the pre-menopausal body's natural cycles of hormone production.

"This is probably not the best way to be delivering progesterone," Pike said. "Giving a constant dose of progesterone appears to antagonize a lot of the beneficial effects of estrogen."

Pike's group tested progesterone on female mice whose hormone production had been blocked to simulate menopause. The mice, which were genetically predisposed to develop an Alzheimer's-like disease, showed symptoms within months.

Treatment with estrogen reversed the symptoms, Pike's group reported. Treatment with progesterone did not.

When the two hormones were given together, progesterone appeared to hinder estrogen's main beneficial function: preventing the buildup of beta amyloid protein, the key risk factor in Alzheimer's.

"Estrogen no longer decreases the amount of beta amyloid" when progesterone is present, Pike said.

Progesterone's effects were not all bad, Pike added. The hormone appeared to inhibit tau hyperphosphorylation, another chemical process implicated in Alzheimer's.

Progesterone also is known to counteract the increased risk of endometrial cancer from estrogen therapy, which is one reason most women receive both hormones.

Pike said his group's study should provide guidance for the design of human trials studying hormone therapy and Alzheimer's. He added that future studies might need to focus both on the dosage and the formulation of progestins -- the synthetic versions of progesterone given to humans -- as well on the starting age for hormone therapy.

Prior to the study, "we really had no idea what the progestins were doing," Pike said.

The study was funded by the National Institute on Aging under a large

grant to USC's Roberta Brinton, (Progesterone in Brain Aging and Alzheimer's Disease), who is leading a university-wide effort to study the effects of hormone therapy on women's health.

Doctors prescribe hormone therapy to counter some of the harmful consequences of menopause, such as losses in bone density. But other large studies have shown that hormone therapy also increases the risk of breast cancer.

"Our study mirrors to some extent recent clinical observations in women that hormone therapy appears to have both beneficial and deleterious effects," Pike said.

Source: University of Southern California

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