

Estrogen in the fight against schizophrenia

January 20 2010

Many American women are prescribed estrogen to combat the negative effects of menopause, such as bone loss and mood swings. Now, new evidence from a Tel Aviv University study suggests that hormone replacement therapy might also protect them — and younger women — from schizophrenia as well.

Prof. Ina Weiner of Tel Aviv University's Department of Psychology and her doctoral student Michal Arad have reported findings suggesting that restoring normal levels of estrogen may work as a protective agent in menopausal women vulnerable to schizophrenia. Their work, based on an animal model of menopausal psychosis, was recently reported in the journal *Psychopharmacology*.

"We've known for some time that when the level of estrogen is low, vulnerability to psychotic symptoms increases and anti-psychotic drugs are less likely to work. Now, our pre-clinical findings show why this might be happening," says Prof. Weiner.

A hormonal treatment to address a behavioral condition

In their study, Weiner and Arad removed the ovaries of female rats to induce menopause-like low levels of estrogen and showed that this led to schizophrenia-like behavior. The researchers then tried to eliminate this abnormal behavior with an estrogen replacement treatment or with the antipsychotic drug haloperidol. Estrogen replacement therapy effectively alleviated schizophrenia-like behavior but haloperidol had no effect on

its own. Haloperidol regained its effect in these rats when supplemented by estrogen.

"When the level of estrogen was low, we could see psychotic-like behavior in the animals. Moreover, the sensitivity to psychosis-inducing drugs went up, while the sensitivity to anti-psychotic drugs went down," Prof. Weiner says. This is exactly what we observe in women with low estrogen levels," she says. "But we also found that estrogen, all by itself, combats psychosis in both male and female rats." Furthermore, in low amounts estrogen increases the effectiveness of anti-psychotic drugs.

Prof. Weiner points out that the medical community is hotly debating the pros and cons of estrogen replacement as an add-on to conventional treatment in schizophrenia. Detractors point to higher chances of cervical cancer and heart attacks in those who receive estrogen supplements. But according to her study, which looked at very specific factors possibly related to schizophrenia, estrogen replacement therapy could have positive behavioral effects, she concludes.

Assessing the possibility for prevention

During the course of a woman's lifetime, estrogen levels do not remain constant. During her reproductive years, these levels are affected by the menstrual cycle. There are also dramatic changes in the levels of estrogen just after a woman gives birth — a change, which can trigger "post-partum blues", and in extreme cases lead to clinical depression and psychosis.

As a preventative therapy, estrogen could be given to women at certain points in time when they are most at risk for schizophrenia, Prof. Weiner suggests: in their mid-twenties and later during the menopausal years.

"Antipsychotic drugs are less effective during low periods of estrogen in the body, after birth and in [menopause](#)," says Prof. Weiner. "Our research links schizophrenia and its treatment to estrogen levels. Men seem less likely to begin schizophrenia after their 40s, which also suggests that [estrogen](#) is the culprit."

Prof. Weiner is continuing her research.

Provided by Tel Aviv University

Citation: Estrogen in the fight against schizophrenia (2010, January 20) retrieved 30 April 2024 from <https://medicalxpress.com/news/2010-01-estrogen-schizophrenia.html>

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