

## **Your brain's sex can make you ill**

By Michelle Roberts

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### **Scientists say they have proof that the sex of the brain makes men and women more prone to different diseases.**

Doctors know that women are more likely than men to have depression, anxiety or an eating disorder, while men are at higher risk of Parkinson's disease. Post-mortem and brain imaging studies show that male and female brains are physically different. Now scientists say they can link the two together and suggest future disease cures may be "gender-specific".

#### **Male or female brain?**

The sex of a brain is decided in the mother's womb and depends, among other factors, on hormone levels. Higher levels of testosterone makes a male brain and oestrogen a female one.

Professor Dick Swaab from The Netherlands Institute for Brain Research in Amsterdam said the evidence for this comes from studies of transsexuals - people who know, often from a very early age, that they are born in the wrong gender body.

"The theory is that the sex difference in the sex organs develops early in pregnancy - in the first few months while in utero - while sexual differentiation of the brain occurs later in the second half of pregnancy and postnatally." That would mean certain factors could interfere with the sexual differentiation of the sex organs and brain in an independent way because there is a time lapse between the two.

"If that was true you would expect to see female structures in male brains. That is indeed what people have found - a reversed sex difference in the brain of transsexuals."

#### **Brain gender diseases**

He said that because men and women's brains are different "we should be looking at diseases as male and female. There is a different sex ratio for neurological and psychiatric diseases. In depression, it is very clear that sex hormones are directly interfering with the stress axis in the brain.

#### **BRAIN SEX FACTS**

Women tend to be better at empathising - guessing other's emotions and responding appropriately.

Men are generally better at systemising - investigating how a system works.

"We have shown that sensitive proteins [receptors] for sex hormones are present in the cells that form the stress axis. In women there are more oestrogen receptors and in men more androgen receptors present. That results in higher prevalence of depression in women compared to men because the stress axis is more sensitive.

The oestrogens are directly affecting the production of the stress peptides. So for the same amount of stress in the environment, women are more prone to develop depression than men. Others have shown that hormone levels could play a part in multiple sclerosis."

Dr Carlo Pozzilli and colleagues at the University La Sapienza in Italy found that women with MS had lower levels of the male hormone testosterone throughout their monthly cycle compared to women who did not have MS.

Dr Glenda Gillies and colleagues at Imperial College London have been looking at Parkinson's Disease, which is far more common in men than in women.

"The idea is that perhaps oestrogen is being neuroprotective so that the neurones that degenerate in PD don't seem to be as susceptible to the processes in women as they are in men," she said.

By looking at rats they found this was the case to some extent. Female rats who had their ovaries removed became just as prone to a chemically induced condition similar to PD as male rats. When these female mice were given extra oestrogen they got back their natural protection against PD as well. Similarly, when they took away the source of the testosterone in male rats by castrating them, the brain degeneration was lessened. However, surprisingly, when they gave the male mice oestrogen the damage was even worse.

### **His n' Hers drugs**

Dr Gillies said: "Administering oestrogen in the two sexes seems to have opposite effects.

### **I think we are realising that drugs have to be personalised**

Dr Glenda Gillies, Imperial College London

"It may well be that there is something that has been programmed differently in the brain during early development to make it respond in a different way." She said work suggested that oestrogen might also help prevent strokes and Alzheimer's disease, but that it was still very early days.

"Increasingly, I think we are realising that drugs have to be personalised and that one drug is not necessarily going to be the same for each individual."

She said that most of the drugs available today had been tested on men, which may mean they are not necessarily the best design for women. Anita Holdcroft, consultant anaesthetist also from Imperial College London, agrees. She said not only are male and female brains different, but women's brains change throughout life in relation to fluctuating hormone levels.

"That may well affect disease states and how drugs work." She scanned the brains of women before and after they were pregnant and found the brain shrank during pregnancy. The shrinkage was even greater if the woman had a complication of pregnancy called preeclampsia, but reversed by six months after delivery of the baby. "We need studies to find out why these things are happening. It may well

affect disease states and how drugs work and highlights our lack of understanding," she said.