

Why are women twice as likely to get Alzheimer's?: Experts think it's linked to hormones - and having a hysterectomy can hugely increase your risk

By [Jerome Burne](#)

We badly need new and effective treatments for Alzheimer's.

But they may be proving so hard to find because researchers are looking in the wrong place.

That's the remarkable claim by experts in the field.

They are questioning why so much research into Alzheimer's focuses on male brains — despite women being twice as likely to get the disease, and their brains having a fundamentally different make-up.

New studies show female hormones could be the reason women are more at risk, suggesting hormone replacement therapy could have a protective effect.

It's no secret that men and women's brains are wired differently — sophisticated scanners have shown this for years.

For instance, women are more likely to suffer from depression, but are less vulnerable to the kind of brain damage you can get in a car accident.

But strangely, research into a disease that devastates brain cells too often ignores such fundamental features that could hold clues about the roots of Alzheimer's.

And because women are at double the risk, they are going to suffer more from this blind spot.

'We need much better data about gender differences,' says Glenda Gillies, professor of neuroendocrine pharmacology at Imperial College London, who researches the effect of drugs and hormones on the brain.

She is one of the few British scientists who is seriously concerned about this neglected area.

'It's women who are losing out because of this. And because they live longer, at any one time significantly more women will have the disease than men.

'So we need to know a lot more about what works for them.'

It's well known that victims of Alzheimer's have clumps of damaged proteins — called plaques and tangles — in their brains.

Less well known is that depending on your sex, the tangles are found in very different places, according to Larry Cahill, professor of neurobiology at the University of California.

About 90 per cent of male sufferers have them in the hypothalamus, a central area of the brain controlling hunger, eating and sex — but only 10 per cent of women do, he says.

Women have them in a nearby area involved in controlling production of a neurochemical called acetylcholine. But why this is or what difference it makes to symptoms and behaviour hasn't been researched properly.

Wherever the plaques or tangles are, men seem to be able to handle them better — women can have worse symptoms, even though they have much less damaged protein in their brains.

Researchers at Rush University Medical Center in Chicago have shown the same amount of tangles in the brain caused much more severe symptoms in women than in men.

The female hormone oestrogen seems to protect the brain but, yet again, no one has investigated why symptoms vary so much.

And just last week researchers from the University of Hertfordshire reported that women suffering from Alzheimer's deteriorate faster than men — even when they are apparently at the same stage of the disease, suggesting men's brains are better at coping with the ravages of the disease.

Furthermore, research from Kansas University found that if your mother had Alzheimer's, that doubles your risk of developing the disease compared with having a father who had it.

Scientists usually try to solve such puzzles by doing research on the brains of rats.

But here the failure to focus on sex differences strikes again: brain researchers are much more likely to use male rats for their basic investigations because the females are more agitated and difficult to work with.

'The assumption sex influences may be safely ignored by neurobiologists is invalid and must be abandoned,' writes Professor Cahill in the June issue of the journal *Endocrinology*.

This failure to investigate gender difference in a chronic disease isn't new.

'Twenty years ago, doctors were less likely to spot a woman was having a heart attack because they misinterpreted symptoms,' says Lynn Posluns, founder of a new charity called Women's Brain Health Initiative, which aims to encourage research into male-female differences in Alzheimer's.

'Doctors were trained that the classic symptom of a heart attack — a stabbing pain in the heart and pain down the left arm — applied to women, too.

'But female heart attack symptoms can include nausea, breathlessness, an upset stomach and a feeling of exhaustion.

'As a result, women took longer to get vital treatment. We are determined not to let it happen all over again with Alzheimer's.'

As yet no one has tried to analyse the risk factors for Alzheimer's along sex lines, so there is not much practical action you can take to cut your general risk.

But Professor Walter Rocca, a neurologist at the Mayo Clinic in Minnesota, has found something important for any woman who has to have her ovaries removed before she naturally moves into the menopause.

'When a woman has a hysterectomy, often because of fibroids or pain and heavy periods, the surgeon often removes the ovaries as well,' he says.

He has found this raises the risk of Alzheimer's by 140 per cent. Ovaries produce the female hormone oestrogen.

Professor Rocca found that giving oestrogen replacement to women who had lost their ovaries reduced their risk of Alzheimer's back to normal.

'Doctors have been nervous of giving oestrogen to protect the brain because of the link with cancer and heart disease,' he says.

'But the latest finding is that there is a therapeutic window between 50 and 60.

'The danger doesn't seem to be there if oestrogen is given close to the menopause.'

So does the drop in oestrogen that is part of the menopause push up the risk of Alzheimer's?

'It doesn't seem to. But it's also not certain if prescribing oestrogen can lower the risk.

'And if it did we don't know how long oestrogen should be given for and in what dose,' says Professor Rocca.

Oestrogen isn't the only hormone playing a role here.

In women, having low thyroid function for several years is linked with cognitive decline and dementia.

Men are less at risk from a low thyroid function, but may suffer more from the rise in the steroid hormones pumped out in response to stress.

Pushing up steroid levels for years damages brain cells, which raises the risk of Alzheimer's.

But too often, sex specific findings, even when they're discovered, can be effectively ignored.

'Women with a certain variant of a gene called ApoE4 are 50 per cent more likely to develop Alzheimer's,' says Dr Pauline Maki, a psychiatrist at the University of Illinois in Chicago, with a special interest in brain-hormone links.

'That was discovered 15 years ago and affects around 20 per cent of the population, but it has never been followed up.'

So why is research into Alzheimer's apparently so biased?

Ironically, Dr Maki suggests male rats are used more because the hormonal cycles the females go through complicate results.

Cost is another issue.

'Trials would have to be twice as large to produce reliable results about male and female responses, while sales of sex specific drugs would be cut by half,' she says.

The other problem is that rats don't normally develop Alzheimer's, so they have to be genetically modified. This makes females more agitated and dangerous.

'They need a separate cage each, making them more expensive,' says Dr Tiffany Chow, a neurologist at the University of Toronto.

But going for the easier option could be costing lives.

'Sex differences in Alzheimer's hasn't become much of a live issue in Britain yet,' says Professor Gillies.

'But it is certainly an area that needs more attention.'