

HORMONES ON THE BRAIN

Vascular Health in the Brain and Eye across the Menstrual Cycle

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Fluctuations in hormone level across a woman's life show associations with brain health.

What are hormones?

Hormones are chemical messengers that travel around the body via blood vessels. They promote a wide range of functions essential for health and wellbeing.

Hormones that change across the reproductive lifespan and beyond include **oestrogen**, **progesterone**, and **testosterone**, in both sexes.

How do they change in cisgender women?

Oestrogen and progesterone – These hormones fluctuate greatly across a menstrual cycle and pregnancy. They also gradually decrease across a lifespan, before dramatically decreasing with menopause.

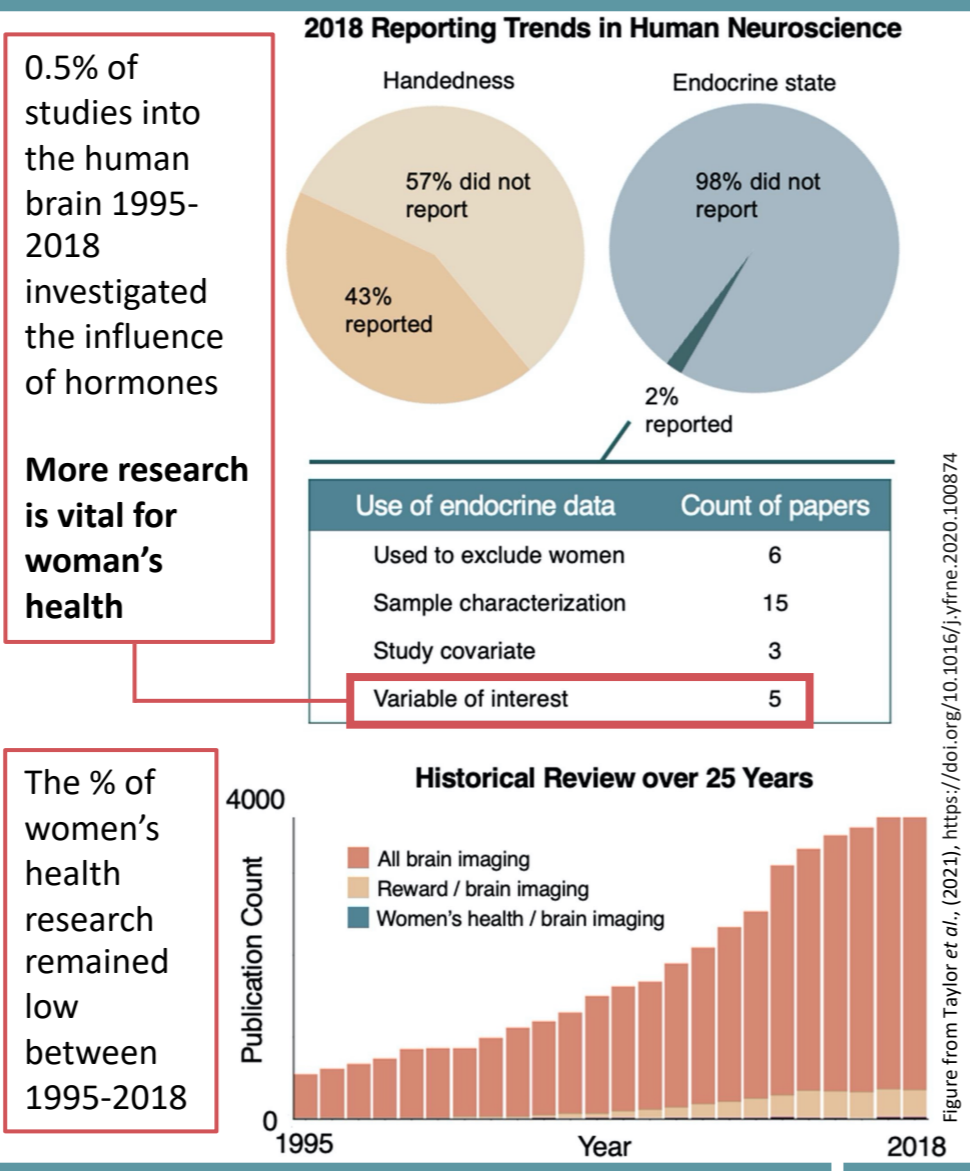
Testosterone – Gradually decreases throughout a woman's lifespan. People with Polycystic Ovary Syndrome (PCOS); about 1 in 10 women in the UK often show elevated testosterone.

What impact do these changes have on brain health?

Oestrogen is protective against **dementia** and **stroke**. A woman's risk of these conditions increase with menopause. Other hormonal changes (e.g., menstruation) can be associated with **debilitating symptoms** (e.g., 'brain fog', migraine, mood and vision changes) that may relate to brain and eye health.

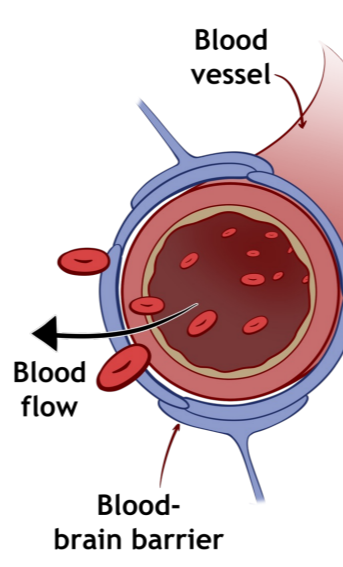
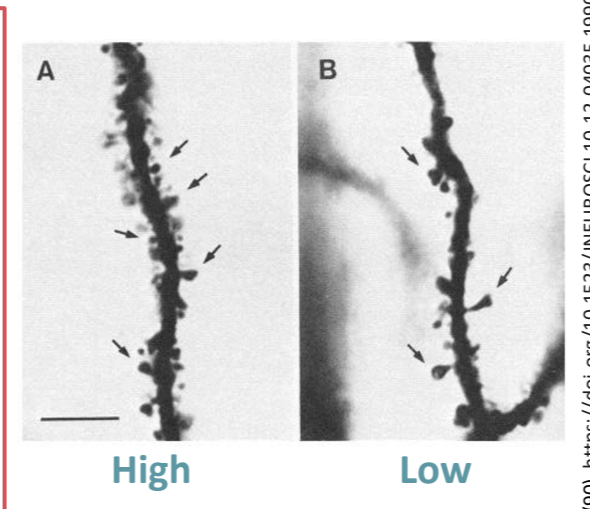
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There is a stark lack of research into the impact of hormones (i.e., endocrine states like pregnancy, menopause, menstruation) on the human brain.



Animal research suggests that hormones are closely tied to brain health and functioning. Cells that detect hormones are present all over the eye and brain.

Animal research has imaged individual neurons (cells that carry electrical information around the eye and brain) and found that the shape and connections of these cells are closely tied to oestrogen levels.



Animal research also finds that oestrogen effects the vascular system, which supports the body's blood supply.

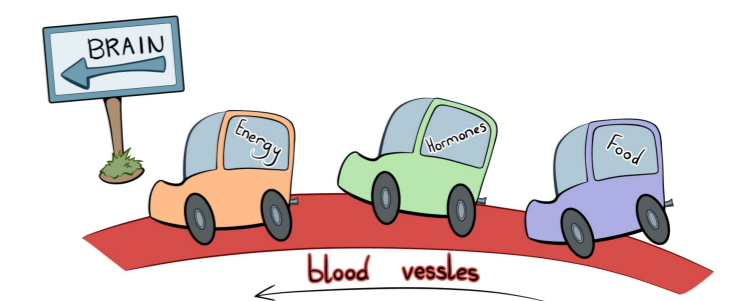
Oestrogen increased blood flow, altered blood-brain barrier permeability and improved recovery from ischemic conditions such as stroke in rodent models.

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Brain and eye functioning and health rely on a healthy blood supply via the vascular system.

A healthy vascular system is **essential** for delivering energy, organ-to-organ communication (such as via hormones) and nutrition around the body.

The brain and retina (the neural tissue at the back of the eye) are highly energy-hungry organs and require a constant and steady supply of oxygen-rich blood to maintain essential functioning.



However, **little is known about how oestrogen influences this vascular supply in humans.**

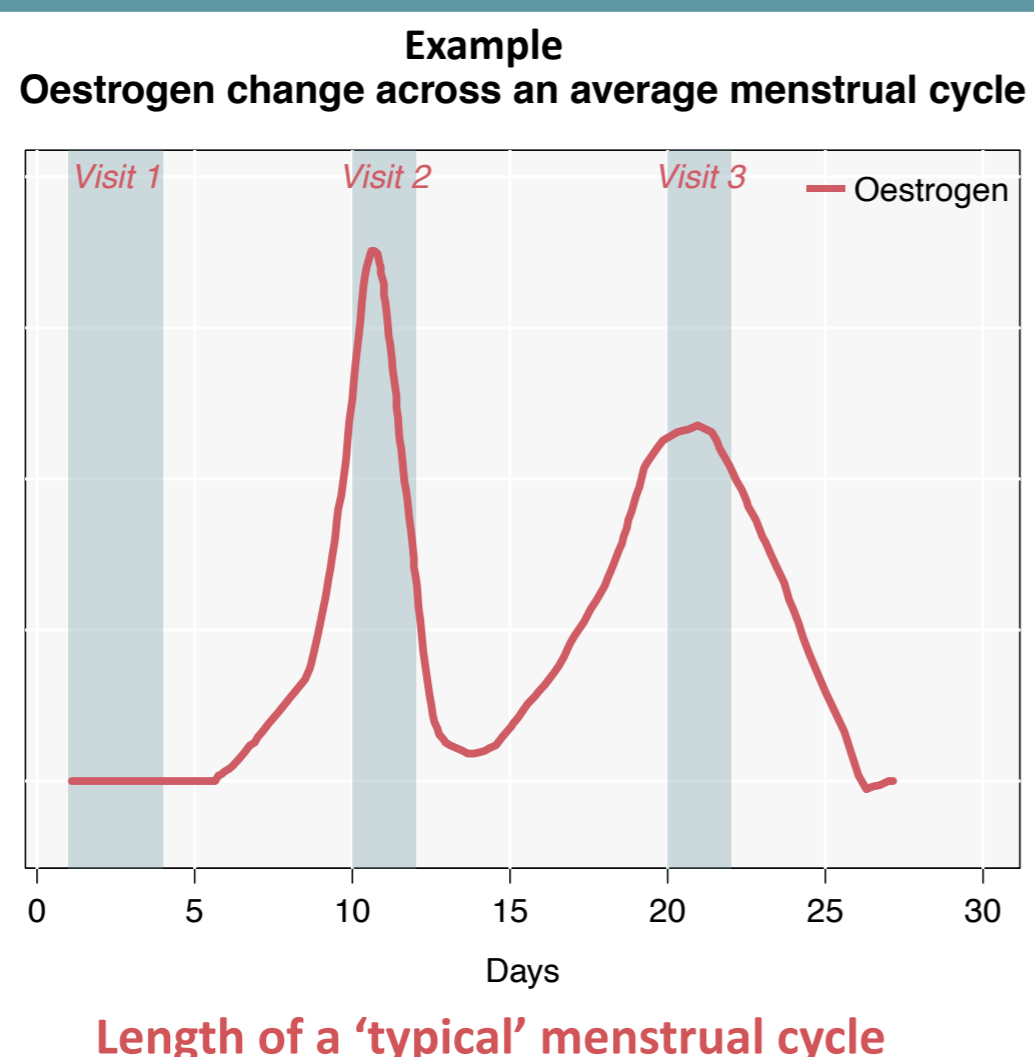
It can't be assumed that what we see in animal models will translate to humans. Each cohort of interest (e.g., menstrual cycle, menopause, PCOS) has unique aspects that mean they must be investigated individually and specifically, such as age, fitness, history, comorbidities, interactions with other hormones, use of external hormones...

METHODS

In this study, we investigated how changes of the hormone oestrogen across a menstrual cycle influence vascular health in a sample of 27 healthy young menstruating women, using advanced imaging techniques.

A sample of 27 **healthy menstruating women** were recruited for this study (average age= 22.9 years) and took part in a testing session at **three different timepoints** across their menstrual cycle, which are typically associated with different levels of oestrogen (see right).

All participants had a history of regular cycles and had no health conditions that could have predictably influenced the results. Participants fasted before testing to avoid the effects of food or caffeine on blood flow.



Hormone Analysis

A blood sample was taken so the exact hormone level could be investigated. How **oestrogen** levels vary across a menstrual cycle can differ between people and months, so it is important to measure the exact hormone level for that day.



Brain Imaging

Brain imaging was carried out using advanced **Magnetic Resonance Imaging (MRI)** sequences.

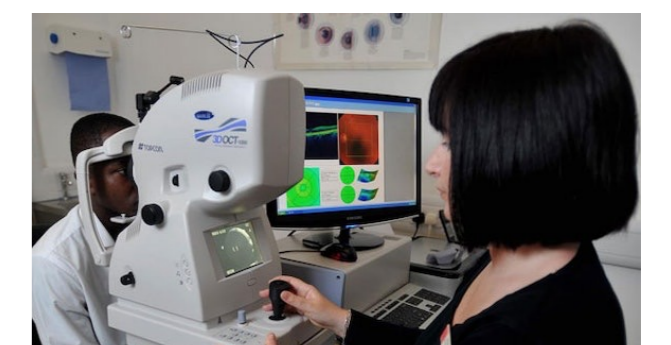


This allows for brain blood flow and oxygen metabolism (how much oxygen is extracted from the blood and used by the brain) to be measured throughout the brain.

Eye Imaging

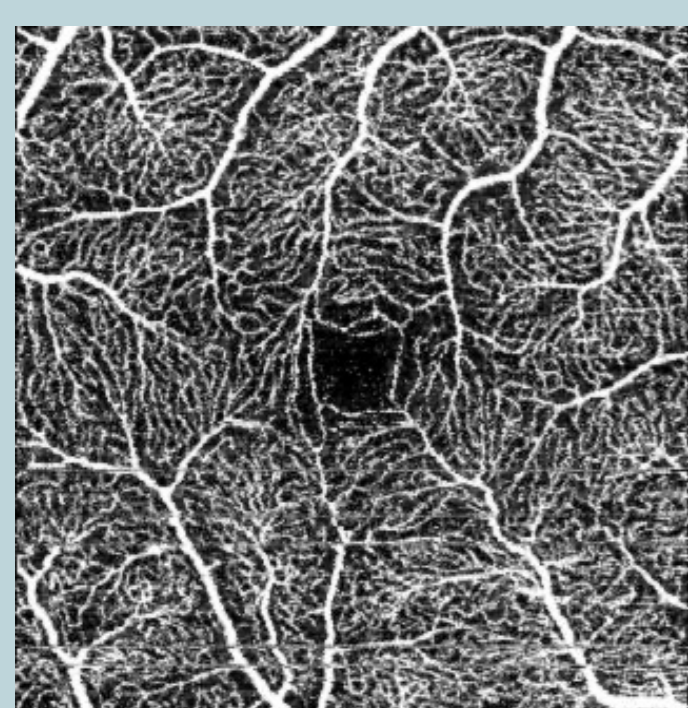
The part of the eye investigated was the retina, a neural layer at the back of the eye that transforms incoming light into electrical information and then sends it to the brain.

Using **Optical Coherence Tomography-Angiography (OCT-A)**, we can image the blood vessels that support the retina and allow it to function. Retinal blood flow and blood vessel density was examined.



RESULTS

Oestrogen changes across a menstrual cycle were associated with increasing blood flow in both the eye and the brain.



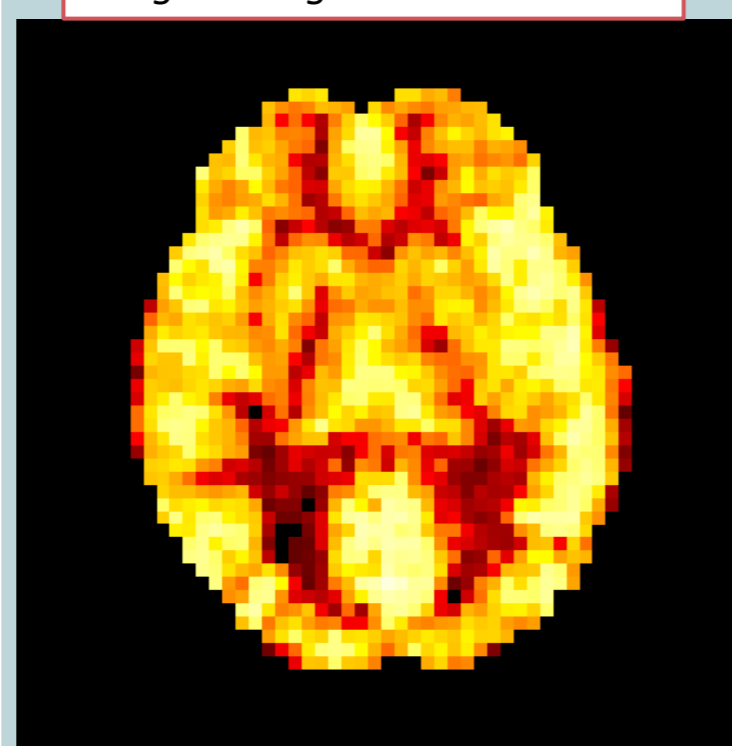
An example image of the blood vessels in the retina (back of the eye) taken using OCT-A.

Oxygen metabolism and retinal vessel density remained relatively stable across the short-term hormonal changes of the menstrual cycle.

However, circulating oestrogen was positively associated with blood flow, which was found globally across the brain and in the retina. It was also associated with faster blood flow speeds in the brain.

Increasing oestrogen therefore increased blood flow to both the brain and eye, which may explain symptoms such as menstrual migraine and 'brain fog' during stages when oestrogen is decreasing sharply.

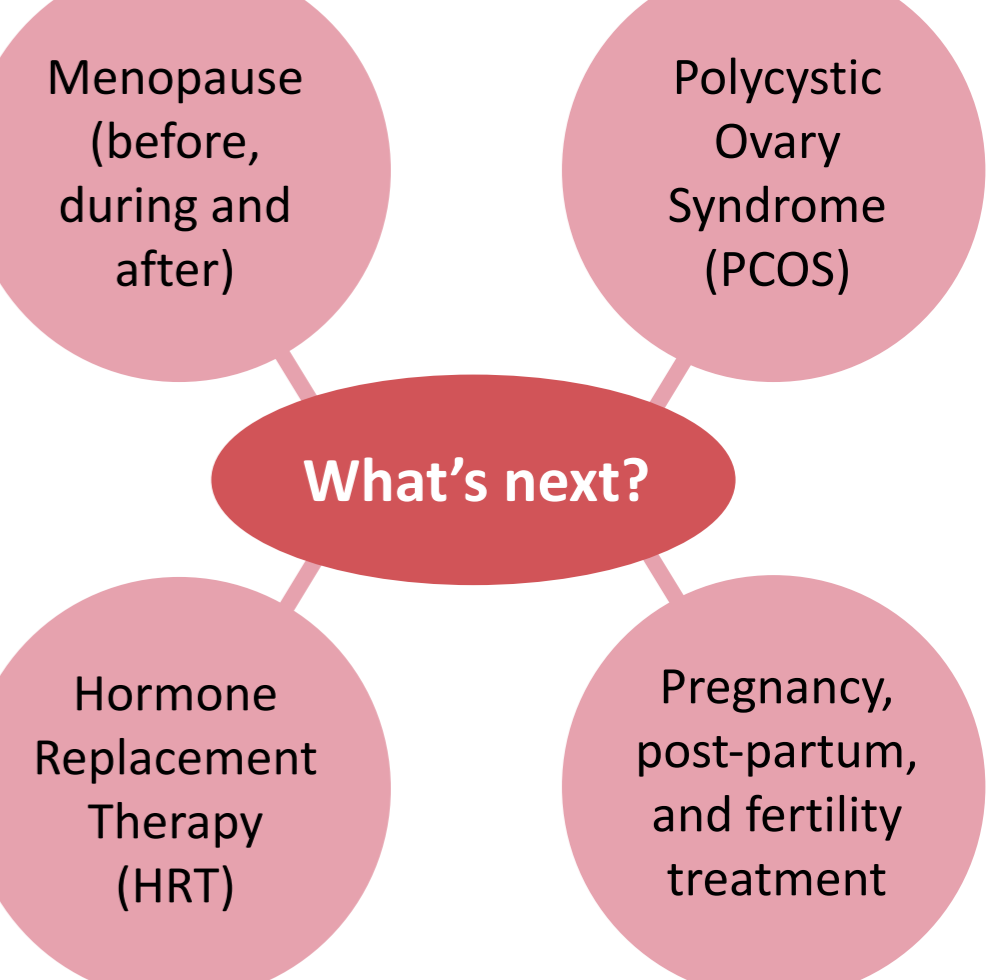
An example scan of the amount of blood flow in the brain imaged using an MRI scanner



CONCLUSIONS

This study highlights how oestrogen may influence the vascular system in healthy menstruating women, which may explain its protective effect.

- This study investigated the influence of oestrogen levels across a menstrual cycle on vascular health in both the eye and brain.
- Oestrogen was found to influence brain and eye blood flow, which may help to explain menstrual-related symptoms.
 - Current work at Cardiff University is investigating the link between hormone-driven changes in the vascular system and menstrual symptoms in more detail.
- Importantly, this study highlights how oestrogen may influence vasculature and in turn may be protective against dementias and cardiovascular disease.
- This also opens up questions in other areas of women's/ hormonal health



Take home messages

- Hormone changes across a menstrual cycle impact blood supply in both the eye and brain.
- This could explain menstrual symptoms, such as migraines.
- We need more women's health research!



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This research was funded in whole, or in part, by the Wellcome Trust (WT224267).

