Dementia in detail: amyloid, tau and Alzheimer’s disease

Research suggests that the build-up of two proteins, called **amyloid** and **tau**, in the brain plays a central role in the development of Alzheimer’s disease. These proteins damage the cells in our brains, including, but not limited to, nerve cells. Nerve cells send messages throughout the body.

Amyloid forms plaques **between** all types of brain cells, and tau forms tangles **inside** nerve cells. These proteins eventually disrupts the nerve cells, and this damage spreads throughout the brain, affecting regions involved in important functions such as memory, thinking, and movement.

Although we currently don’t have a full picture of what causes the proteins to build up, we know that this can start to occur **decades** before symptoms like memory problems appear.
What is a protein?

Proteins are molecules that form the building blocks of life. There are thousands of different types in your body, and these have a variety of roles, including transporting things around the body, providing structural support within cells and maintaining our tissues and organs. Your DNA is an instruction manual for all the proteins that your body builds.

Proteins are made up of long chains of smaller units called amino acids. There are 20 different amino acids. The combination and order of amino acids determines the 3D shape a protein will fold into - this shape determines how it behaves, and what role it plays, in our body.

The proteins we eat are broken down in our guts into amino acids, which then get made back into different proteins by our cells. So, the protein in our diet is not the same as any amyloid and tau in our brains.

Alzheimer’s disease symptoms often depend on where in the brain these toxic proteins build-up. As damage spreads to different regions of the brain, more complex symptoms can develop, and people are less able to do things like eat and move around.
What goes wrong with amyloid and tau?

Proteins sometimes misfold into an abnormal shape. This affects how they work and is thought to be the primary cause of degenerative diseases like Alzheimer’s, Huntington’s and Parkinson’s.

Proteins can misfold because of:

- A **DNA mutation** that causes a change in a protein’s amino acid sequence.
- A **missing enzyme** required for the protein to fold correctly. An enzyme is a type of protein that helps processes take place.
- An accumulation of **damage** to the healthy protein that causes it to change shape.

This misfolding can result in a number of issues, including:

- The protein **stops working** properly.
- The protein becomes ‘**sticky**’, and builds up, disrupting the cells and blood vessels nearby.

Why is understanding amyloid and tau important?

Methods to detect amyloid and tau in living people will allow for earlier and more accurate diagnosis.

For example, collection of **cerebrospinal fluid** (CSF) and **brain imaging** methods such as PET scanning are now established methods of imaging amyloid, and show promise in imaging of tau, too. These are gradually becoming available on the NHS.

**Blood tests** also show promise in detecting the presence of these proteins at an early stage.
What is amyloid?

Amyloid is a protein found in healthy bodies and brains. Research suggests that “normal” amyloid is part of the immune system, and appears to have antibacterial, antifungal and antiviral properties.

A misfolded version of amyloid called amyloid-beta (Aβ) is found in the brains of people with Alzheimer’s disease. This misfolded amyloid sticks together and forms clumps, or plaques, which build up between nerve cells in the brain. They are a hallmark feature of Alzheimer’s disease.

Stages of amyloid plaque formation

- **Misfolded amyloid-beta proteins**
- A few proteins clump together to form a toxic oligomer
- As proteins keep joining the oligomer, it becomes a toxic protofibril
- As the protofibril continues to grow, it forms an amyloid fibril
- Fibrils join together to form an amyloid plaque

Amyloid Plaque
Credit: Prof Tammaryn Lashley

Aβ is formed when a larger protein called amyloid precursor protein (APP) is chopped into smaller, sticky proteins that clump together and form plaques.
How does amyloid affect cells in Alzheimer's disease?

It is not currently fully understood how amyloid-beta affects cells, but some theories suggest:

- Amyloid plaques are **directly toxic** to nerve cells. They damage the cell membranes, disrupting their ability to transmit messages and maintain normal function.
- Amyloid plaques lead to problems with the **tau** protein in what's known as the amyloid cascade hypothesis. Read more [here](#).
- Smaller clumps of amyloid called **oligomers** damage the membrane surrounding nerve cells. The cell membrane is a vital part of a nerve cell, and damage to it can affect how the cells conduct signals.

The factors which contribute to amyloid building up are important for researchers to understand. This is because they may prove an even more important drug target than amyloid itself, stopping amyloid from building up at all.

The precise link between Aβ plaques and Alzheimer’s disease is unclear. Not everyone with high levels of Aβ plaques has Alzheimer’s symptoms, and some people with Alzheimer’s disease have low levels of amyloid.
What is tau?
All our cells contain an internal scaffolding made of many specialist proteins. Tau is an important protein that helps to add structural support inside our brain cells.

Changes in the way tau behaves have been found in many brain diseases, including Alzheimer’s disease, frontotemporal dementia, and corticobasal degeneration.

In Alzheimer’s disease, other molecules stick to tau, which changes its shape and causes it to detach from the nerve cell’s scaffolding and no longer provide structural support. This detached tau is more likely to misfold and stick together to form tau tangles. Without tau’s support, the cell’s scaffolding disintegrates, which interferes with the nerve cell’s ability to function properly.

In contrast with Aβ plaques, the link between tau tangles and problems with thinking and memory is much clearer and stronger.
Current research suggests that tau detaches from a nerve cell’s scaffolding during Alzheimer’s disease because normal cell processes become impaired, so there are more molecules that attach to, and change the shape of tau.
New treatments that target amyloid and tau aim to slow down disease progression, rather than simply targeting the symptoms. In 2022, an anti-amyloid drug called lecanemab became the first drug to slow the decline in memory and thinking in people with early Alzheimer’s disease. [Find out more here.](#)

Alzheimer’s Research UK has funded crucial research that has helped researchers understand amyloid and tau. This includes funding [Prof. Sir John Hardy](#) (pictured) who first suggested the main theory of how amyloid triggers Alzheimer’s disease, leading many pharmaceutical companies to develop drugs that clear amyloid from the brain.

Recently, we awarded a Research Fellowship to [Dr Amy Pooler](#), who discovered vital clues about how tau spreads from cell to cell. The impact of this work has rippled throughout the scientific community and is bringing researchers closer to developing approaches to stop the protein’s abnormal behaviour, keeping nerve cells healthier for longer.

For more information, contact the Dementia Research Infoline: infoline@alzheimersresearchuk.org or call 0300 111 5 111

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