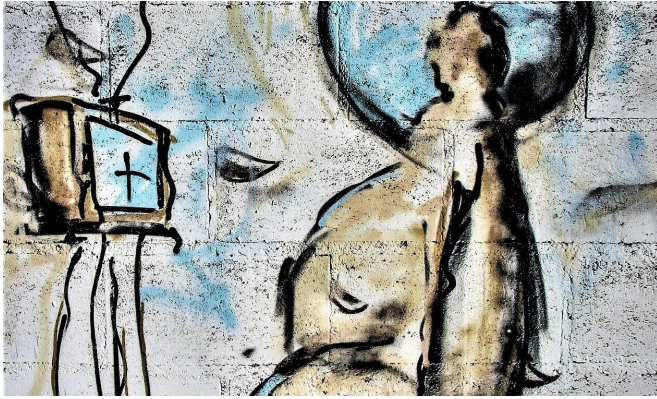


Apathy could predict onset of dementia years before other symptoms

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Apathy—a lack of interest or motivation—could predict the onset of some forms of dementia many years before symptoms start, offering a 'window of opportunity' to treat the disease at an early stage, according to new research from a team of scientists led by Professor James Rowe at the University of Cambridge.

Frontotemporal dementia is a significant cause of dementia among [younger people](#). It is often diagnosed between the ages of 45 and 65. It changes behaviour, language and personality, leading to impulsivity, socially inappropriate behaviour, and repetitive or compulsive behaviours.

A common feature of [frontotemporal](#) dementia is apathy, with a loss of motivation, initiative and interest in things. It is not depression, or laziness, but it can be mistaken for them. Brain scanning studies have shown that in people with frontotemporal dementia it is caused by shrinkage in special parts at the front of the brain—and the more severe the shrinkage, the worse the apathy. But, apathy can begin decades before other symptoms, and be a sign of problems to come.

"Apathy is one of the most [common symptoms](#) in patients with frontotemporal dementia. It is linked to functional decline, decreased quality of life, loss of independence and poorer survival," said Maura Malpetti, a cognitive scientist at the Department of Clinical Neurosciences, University of Cambridge.

"The more we discover about the earliest effects of frontotemporal dementia, when people still feel well in themselves, the better we can treat symptoms and delay or even prevent the dementia."

Frontotemporal dementia can be genetic. About a third of patients have a family history of the condition. The new discovery about the importance of early apathy comes from the Genetic Frontotemporal dementia Initiative (GENFI), a collaboration between scientists across Europe and Canada. Over 1,000 people are taking part in GENFI, from families where there is a genetic cause of Frontotemporal dementia.

Now, in a study published today in *Alzheimer's & Dementia: The Journal of the Alzheimer's Association*, Professor Rowe and colleagues have shown how apathy predicts cognitive decline even before the dementia symptoms emerge.

The new study involved 304 healthy people who carry a faulty gene that causes frontotemporal dementia, and 296 of their relatives who have normal genes. The participants were followed over several years. None had dementia, and most people in the study did not know whether they carry a faulty gene or not. The researchers looked for changes in apathy, memory tests and MRI scans of the brain.

"By studying people over time, rather than just taking a snapshot, we revealed how even subtle changes in apathy predicted a change in cognition, but not the other way around," explained Malpetti, the study's first author. "We also saw local brain shrinkage in areas that support motivation and

initiative, many years before the expected onset of symptoms."

People with the genetic mutations had more apathy than other members of their family, which over two years increased much more than in people with normal genetics. The apathy predicted [cognitive decline](#), and this accelerated as they approached the estimated age of onset of symptoms.

Professor Rogier Kievit from the Donders Institute, Radboud University Medical Center at Nijmegen and MRC Cognition and Brain Sciences Unit at Cambridge, said: "Apathy progresses much faster for those individuals who we know are at greater risk of developing frontotemporal dementia, and this is linked to greater atrophy in the brain. At the start, even though the participants with a genetic mutation felt well and had no symptoms, they were showing greater levels of apathy. The amount of apathy predicted cognitive problems in the years ahead."

"From other research, we know that in patients with [frontotemporal dementia](#), apathy is a bad sign in terms of independent living and survival. Here we show its importance in the decades before symptoms begin," said Professor James Rowe from the Department of Clinical Neurosciences, joint senior author.

Professor Rowe said the study highlights the importance of investigating why someone has apathy. "There are many reasons why someone feels apathetic. It may well be an easy to treat medical condition, such as low levels of thyroid hormone, or a psychiatric illness such as depression. But doctors need to keep in mind the possibility of [apathy](#) heralding a dementia, and increasing the chance of dementia if left unaddressed, particularly if someone has a family history of dementia.

"Treating [dementia](#) is a challenge, but the sooner we can diagnose the disease, the greater our window of opportunity to try and intervene and slow or stop its progress."

More information: Malpetti, M et al. Apathy in pre-symptomatic genetic frontotemporal dementia

predicts cognitive decline and is driven by structural brain changes. *Alzheimer's & Dementia*; 14 Dec 2020; DOI: [10.1002/alz.12252](https://doi.org/10.1002/alz.12252)

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