

# Alzheimer's and cancer: a strange relationship...

They are among the commonest, most feared diseases of old age. Now research shows that patients with a history of cancer are 25% less likely to develop Alzheimer's disease, and vice versa.

Theres Lüthi reports

**W**ith age comes disease. Cancer and Alzheimer's dementia are among the commonest and most feared health conditions – particularly in countries with ageing populations such as the UK. Several decades ago, researchers at a psychiatric centre in New York observed a curious relationship between these two diseases. At autopsy, they found an inverse relation between cancer and Alzheimer's disease.

In one of the first epidemiological studies on the topic Jane Driver of Brigham and Women's Hospital in Boston, Massachusetts in the US followed 1,278 participants aged 65 and older for a mean of 10 years. Published in 2012, the results showed that cancer survivors had a 33% decreased risk of subsequently developing Alzheimer's disease compared with people without a history of cancer.

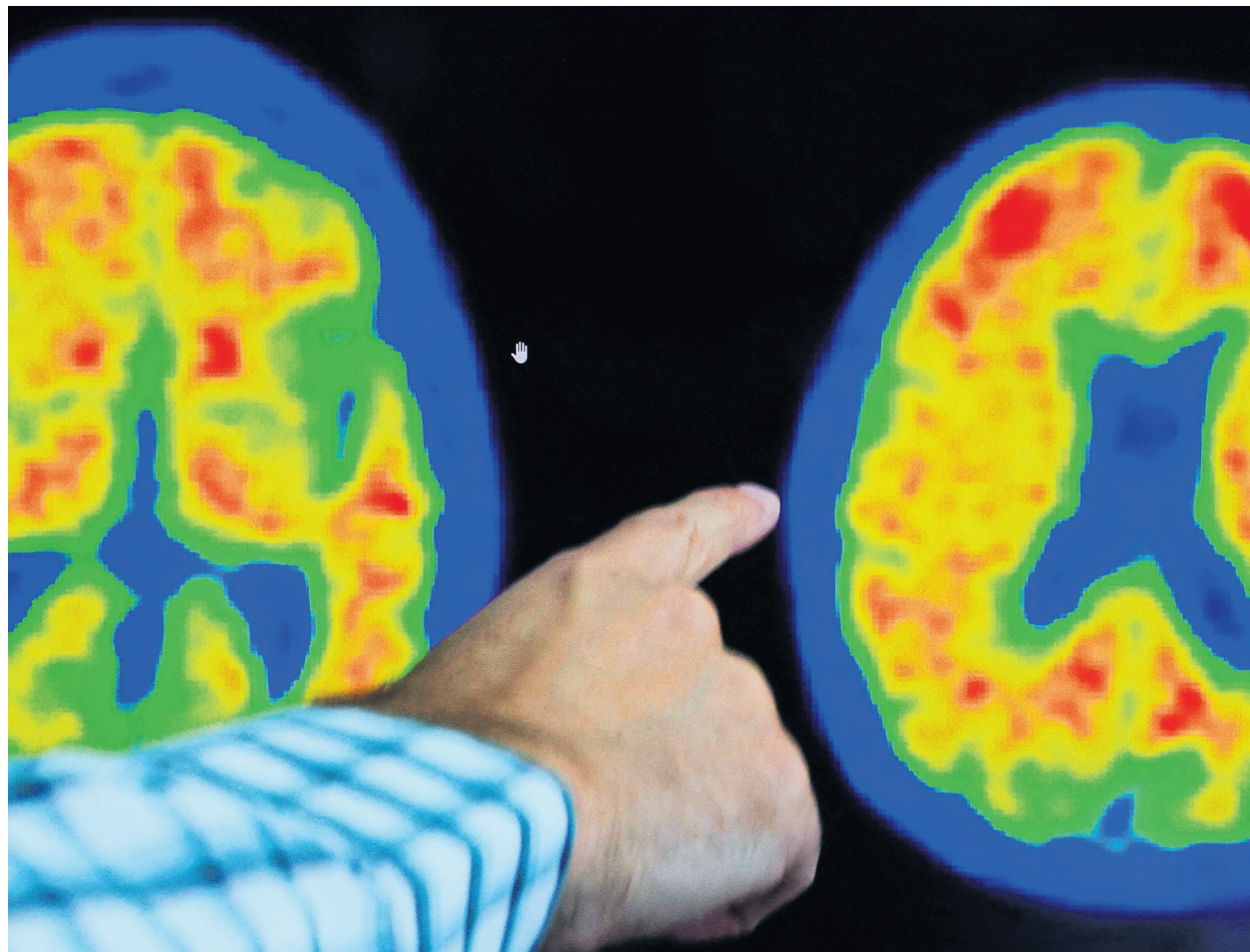
As intriguing as the finding was, the scientific community urged caution and pointed out potential pitfalls in dealing with age-related

diseases. One of them concerned a so-called survival-bias: perhaps people with a history of cancer simply do not live long enough to develop Alzheimer's disease.

Since then, scientists have analysed the relationship between cancer and Alzheimer's disease in more detail and built an increasingly compelling case. In the largest study to date, published in July this year, researchers at Imperial College London provide convincing evidence of a lower incidence of dementia following a cancer diagnosis. They looked at the NHS health data of more than three million people aged 60 and over and followed them for a mean period of 9.3 years, taking extra care to correct for potential biases. Their results show that cancer survivors have a 25% lower risk of developing age-related dementia compared with people without a history of cancer. The inverse association was observed for the most common types of cancers such as prostate, colon, lung and breast.

"The relationship between cancer and Alzheimer's disease is very intriguing and it's persistent," says Erin Abner, a professor at the University of Kentucky. "A lot of people questioned the results and tried hard to find other explanations for the inverse association, but it just keeps showing up, even after taking confounding factors into account."

Two years ago, Abner published clinical evidence for the inverse association. Unlike previous epidemiological studies, she looked at brain autopsies of patients at the University's Alzheimer's Disease Research Center. "We found a pretty consistent association between someone having had



cancer and having lower levels of amyloid pathology in their brain, which is a hallmark of Alzheimer's disease," she says.

In her study the inverse association was seen only with Alzheimer's disease and not with dementia in general. In contrast, many of the previous epidemiological studies did not differentiate between Alzheimer's and other age-related dementias. The majority of elderly patients with dementia, however, have Alzheimer's.

But that is not the whole story; there is another twist to the inverse relationship. Not only do those with a history of cancer have a decreased risk of dementia, but those with Alzheimer's disease are less likely to develop cancer. In her 2012 study Jane Driver reported that the inverse relation goes in both directions, a finding that was replicated in

northern Italy looking at more than one million residents, and more recently in South Korea. According to this study, patients with Alzheimer's disease show a 37% lower likelihood of developing overall malignancy compared to those without dementia. Again, the finding was met with scepticism. Perhaps, critics argued, people with dementia were less likely to be screened for cancer given the potentially limited benefit of therapies.

"The results have been replicated again and again, and most experts in the field now believe the inverse relation appears to be real," says Elio Riboli who led the study at Imperial College London that also confirmed the bidirectionality. "The next step is to understand the biology behind this phenomenon."

Some researchers have suggested that cancer treatment itself may

be having an effect on dementia risk. In recent years, inflammation has emerged as a central process in the onset and progression of Alzheimer's disease, so it is possible that chemotherapy may be protecting neurons by suppressing inflammation.

But for Elio Riboli, that is not the whole story. The fact that the inverse relationship is bidirectional suggests there may be underlying biological mechanisms that influence the two groups of diseases in opposite directions. The researchers at Imperial College performed genetic analyses. "Looking at hundreds of genes, we identified a genetic profile that predicts an increased risk of cancer and we found that this profile is tied to a lower risk of dementia."

According to Riboli, the specific genetic factors may be involved in tissue regeneration. "Growth factors

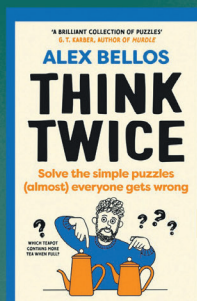
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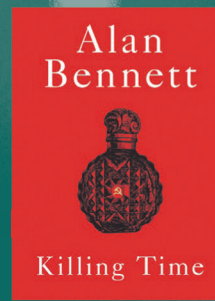
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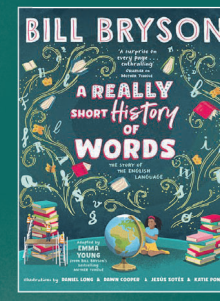
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*A doctor looks at evidence of Alzheimer's disease on a Pet scan of a patient's brain at Brigham and Women's Hospital, Boston, Massachusetts.*  
Brian Snyder/Reuters

are a large family of molecules that regulate tissue renewal and growth. They are generally associated with better cardiovascular health," he says. "Having a genetic makeup that favours replication allows for better renewal of tissues and arteries, but may also slightly increase the risk of some cancers."

Surprising findings can open new lines of research, says Riboli. For instance, it has long been known that people with diabetes have an increased risk of developing cancer, with one notable exception: men with diabetes have a 10-20% reduced risk of developing prostate cancer. "Why does being diabetic come with a reduced risk of prostate cancer, a cancer for which we are desperately trying to understand the risk factors?" asks Riboli. Similarly, research into the inverse association between cancer and dementia may shed light on new molecular pathways that contribute to, or protect people from, the development of dementia. "You open a window and suddenly you see a new horizon," he says.

Cancer is linked to uncontrolled cell growth, whereas dementia is tied to excessive neuronal death. Mikyoung Park of the Korea Institute of Science and Technology in Seoul, South Korea, recently published a review of molecular mechanisms that operate inversely in cancer and neurodegeneration – some leading to enhanced resistance to cell death and others to a higher risk of cell death. Dysfunctional mitochondria, the cellular power plants, might provide a crucial link between cancer and neurodegeneration, a hypothesis put forward a decade ago by Jane Driver and Lloyd Demetrius, based on mathematical arguments.

Unravelling the inverse association between cancer and neurodegenerative diseases may ultimately help treat or prevent these common conditions. But many questions remain unanswered. "Both cancer and dementia are actually a bunch of different diseases," says Erin Abner. "We don't have the granularity of data to draw strong conclusions about any one type of disease." Additionally, there is a long latency period between the development of pathology and the start of symptoms, both in cancer and Alzheimer's, raising questions around the timing of this inverse relation.

These enigmatic findings have no practical relevance for the time being. "But even now, it may be just a little piece of comfort for cancer survivors, that something is going to be a bit easier for them down the road," says Abner.

The networker

## John Naughton



### Elon Musk is not America's new king. But he might be its new Thomas Cromwell

**P**icture, if you will, the scene at Mar-a-Lago on election night at the moment when it has become clear that Trump has won. The atmosphere is hysterical. Trump is in expansive form. He stands surrounded by his ghastly tribe of dependants, plus AN Other. In his victory speech, the president-elect praises his campaign staff, his prospective vice-president, and his family. Each gets a few seconds of adulation.

But AN Other gets a whole four minutes. He is Elon Musk, the richest manchild in history. Trump calls him a "super genius", a "special guy" and a "star". He has flown from Texas in his Gulfstream to bask in the adulation of his new lord and master. He has also paid several hundred million dollars, plus a month of his time, to be here. But now his time has come.

Hold that thought. We will return to it later.

Now imagine what Musk's peers in Silicon Valley were thinking, as they sat chewing their pencils composing slavish messages of congratulation to The Donald. And believe me, they were toe-curlingly obsequious. All around the valley, though, the prevailing sound was of teeth being gnashed. After all, most of these tech titans had spent months wondering how to curry favour with Trump in case he actually won. And there was Musk, who had done an end-run around them and inserted himself into the heart of the new administration. It must have been maddening.

Spool forward a few days and we find that it gets worse: Trump has chosen Musk and a wannabe titan, Vivek Ramaswamy, to lead a "department of government efficiency" (or "Doge", after Musk's favourite cryptocurrency, Dogecoin), thereby putting the two dudes in charge of a concerted effort to slash rules, bureaucracy and spending throughout the federal government. "Together, these two wonderful Americans," declared their new boss, "will pave the way for my administration to dismantle government bureaucracy, slash excess regulations, cut wasteful expenditures, and restructure federal agencies."

Presumably he was impressed by Musk's claim that he could cut at least \$2 trillion from the government's \$6.8tn budget, and by Ramaswamy's promise, made during his failed campaign for the Republican nomination, to



*Musk and Trump: the president called him a 'super genius' in his victory speech.*  
Andrew Harnik/Getty

### What I'm reading

#### John Naughton's recommendations

##### The narrow path from despair

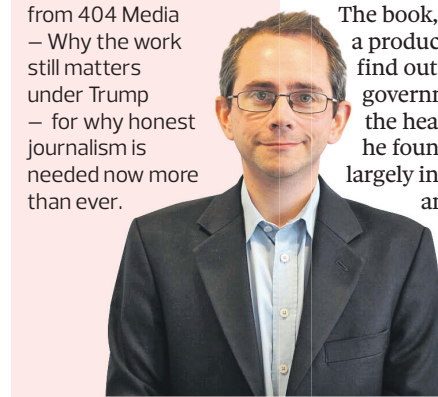
Diane Coyle's beautifully succinct review on Enlightenment Economics of Sam Freedman's (below) book *Failed State: Why Nothing Works and How We Fix It*.

##### Congratulations, boss

The Verge's compilation of all the nauseatingly obsequious messages sent by tech titans to the president-elect.

##### Reason to carry on

A really good argument from 404 Media – Why the work still matters under Trump – for why honest journalism is needed now more than ever.



eliminate the FBI, the Department of Education and the Nuclear Regulatory Commission.

Although this new outfit is called a "department", it won't actually be a government agency. If it were, Musk would have innumerable conflicts of interest that would cause legal difficulties if he started slashing the regulators with which he is currently in conflict. These include the Federal Aviation Authority, the National Labor Relations Board, the Securities and Exchange Commission, the Federal Communications Commission and the Federal Trade Commission. Also, last year his various companies had \$3bn worth of government contracts from 17 federal agencies. But if he's "outside" the system, he'll be freer to slash and burn as he likes.

In 2018, Michael Lewis published *The Fifth Risk*, a remarkable book examining the implications of Trump's political appointments in his first term, especially with respect to three government agencies: the Department of Energy, the Department of Agriculture, and the Department of Commerce.

The book, Lewis explained, was a product of his own desire to find out what branches of the government that never make the headlines actually *do*. And he found that what they do largely involves keeping people and society *safe*.

If Musk's past behaviour is anything to go by, such concern with safety will cut little ice. After he had been forced by a Delaware court

to proceed with his purchase of Twitter, the first thing he did was to fire 6,500 people – about 80% of the staff, by his own reckoning. And those dismissed included people whose job was to moderate content on the platform and keep it relatively "safe". After they'd gone, the platform was opened to allcomers, which is why it has degenerated into a toxic sewer of anti-woke fanatics, white supremacists, misogynists, conspiracy theorists and other inhabitants of alternative universes. He also tweaked the platform's algorithms to prioritise his own posts to its 200 million users, thus in effect giving him a broadcast medium for his political views and preferences.

Musk's strategy, once he decided to back Trump, was to go all-in, much as he did years ago when the production of the Tesla Model 3 was running into trouble and he claimed to have slept in the factory for weeks. He moved to Pennsylvania for the last month of the campaign and was active on the ground every day, energising campaigners and generally raising the campaign's profile, especially in rural areas.

In other words, he made himself indispensable to Trump, and therein lies what may come to be his problem. Narcissists do not like to be under an obligation to *anyone*, no matter how useful they have been. Thomas Cromwell made himself indispensable to Henry VIII in the 1530s and – as viewers of *Wolf Hall: The Mirror and the Light* are soon to discover – ultimately that was not a great career move. History may not repeat itself, but this time, as Mark Twain is supposed to have said, it might just rhyme.