Vincente, 87, has dementia; he is cared for at home by his daughter.

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NEUROSCIENCE

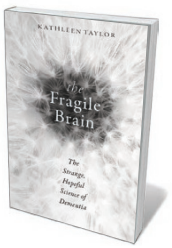
Tide of forgetting

Michael Heneka applauds a sweeping survey of dementia that explores research, diagnosis and care.

The global rise in dementia should surprise no one. The figures — such as the 9.9 million new diagnoses each year — have been known for decades. As slow as we are to accept such vast changes on a personal, societal and political level, so research is slow to uncover why our brains become fragile with age.

Neuroscientist and writer Kathleen Taylor's *The Fragile Brain* is about that research. But it is much more than a simple reflection on the best published hypotheses. Taylor has crafted a personal, astonishingly coherent review of our current state of knowledge about the causes of Alzheimer's disease and dementia, as well as possible solutions, from lifestyle adjustments to drug developments.

Filled with elegant metaphors, her study covers the detail of molecular biology and larger-scale analysis, including epidemiological observations and clinical studies. It extends to dementia due to multiple sclerosis, stroke and encephalitis. For instance, some 5–30% of people who have a first stroke develop dementia. But the book's focus is Alzheimer's disease, and rightly so: it is what up to 80% of people with dementia are diagnosed with.



The Fragile Brain: The Strange, Hopeful Science of Dementia
KATHLEEN TAYLOR
Oxford University Press: 2016.

Taylor begins with a shocking juxtaposition, setting the costs of age-related disorders and of dementia alongside the scarcity in funding. In Britain, Australia and the United States, for example, funding for dementia research is a fraction of that for cancer — in the United States, just 18%. She contextualizes with reflections on the history of dementia research, deftly unravelling the roles of pioneering scientists Alois Alzheimer, Franz Nissl and Emil Kraepelin in describing the condition.

She then walks the reader through different brain elements and regions, from single neurons, transmitters and receptors to their complex interactions and function in cognition and behaviour. She describes the functional and structural loss of synapses as well as the many ways in which amyloid folds and abnormally accumulates in our brains.

Taylor's discussion of risk is especially rich. She explains how to interpret studies on risk factors for age-related dementia and Alzheimer's, such as carrying the *APOE4* gene mutation. She emphasizes the influence of immune cells and their actions, such as clearing amyloid from the brain. She succinctly buries the long-fostered concept of the brain's immune privilege. And she isolates prime suspects in mediating further risks, from inflammation to the consequences of infection, vascular changes and production of reactive oxygen species such as hydrogen peroxide.

The big modifiable factors in early cognitive decline are, we now know, diabetes, obesity and smoking. Taylor's discussion here is sympathetic rather than hectoring, acknowledging the difficulties in shifting lifestyles. Likewise, her evidence on the influence of diet, food quality and habits is carefully handled, distilled to writer Michael Pollan's dictum: "Eat food. Not too much. Mostly plants."

Factors harder to influence by ourselves — such as stress, depression, environmental pollution or poverty — she frames as needing consideration in the larger social context. She discusses interventions to delay or prevent dementia, such as physical fitness and good education. We know from studies that these can buffer genetic disadvantages such as carrying *APOE4*.

Taylor does not glide over the limitations of current interventions,

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such as drugs that at best offer transient improvement. Despite decades of intensive research on dementia, a therapeutic breakthrough is yet to come. Taylor counters gloom by revealing avenues of current and future research, for instance further analysis of molecular pathways.

Taylor's discussion of hypotheses about the nature of dementia points to the limitations of concepts such as the physiological function of the amino acids in amyloid plaques in the brain. She offers a forthright assessment of the amyloid-cascade hypothesis and its pros and cons — for example, evidence of genetic mutations and lack of therapeutic success, respectively — and examines it in the context of ideas about the role of inflammation in the brain, particularly in Alzheimer's.

She is critical of how dementia research is conducted, discussing, for instance, the limitations of mouse models in analysing disease mechanisms. Her constructive suggestions include not restricting animal models to studies of the brain, but rather looking at the animal as a whole, because peripheral events such as infection have a neurological impact. However, as she notes, such moves would demand significant funding increases.

Finally, *The Fragile Brain* addresses how people interact with those who have dementia, and how both information and respect are needed. This is of utmost importance: information can quell many fears.

Taylor has the talent to make complex biology easy, but not trivial. There are many gems, such as her comparison of the immune system's roles of "peacekeeping" and healing with the US Marshall Plan to aid Western Europe after the Second World War. She nicely avoids over-interpretation of findings where research has not yet progressed beyond guesswork. Her provocative questions about genetics, habits, attitudes and levels of knowledge should prompt readers to reason and hypothesize for themselves, and to learn — for instance, whether a particular type of surgery and a particular anaesthetic act together to induce or aggravate dementia.

The Fragile Brain, as a trove of accessible, up-to-date science, has something to offer caregivers and families of people with dementia; medical professionals in dementia diagnosis and treatment; and specialists in memory clinics. It calls for change that reaches to the foundations of our society, suggesting that we adapt lifestyles, workplaces and institutions "to prioritize not labour and cash, but health and well-being". Some of this change has begun. We had better keep going. ■ SEE NEWS FEATURE P.156

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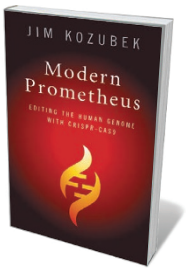
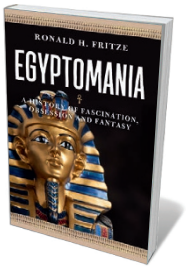
Books in brief

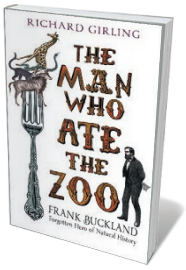


Modern Prometheus: Editing the Human Genome with Crispr–Cas9
Jim Kozubek CAMBRIDGE UNIVERSITY PRESS *(2016)*
As the CRISPR–Cas9 method for rewriting genomes revolutionizes biotechnology, bioinformatician Jim Kozubek steps into the maelstrom with a weighty exploration of its discovery and implications. It should be noted that Kozubek was recently affiliated with an institution battling for patent rights to CRISPR gene-editing. His tome is also in need of a heavy edit. But he usefully pushes the discussion beyond obvious designer-baby concerns to the technique's limitations, and its broader implications for agriculture and the commercialization of science.

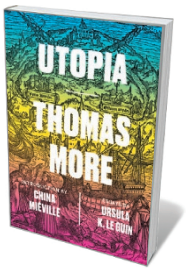
Vertical: The City from Satellites to Bunkers
Stephen Graham VERSO *(2016)*
Our view of cities is perilously partial, argues urban geographer Stephen Graham. Mustering evidence in engineering, sociology and beyond, he argues for a new, vertical perspective — satellite to sewer — to reflect today's "intensified urban stacking". Seeing cities as Gordian knots of geopolitics, he gathers an impressive range of case studies to bolster his analysis. These compel and convince, from Saudi Arabia's high-rise vanity projects to Rio de Janeiro's *favelas* — which struggle with basic services beneath cable cars full of tourists — and the ultradeep mineral mines that service urban infrastructures.



Egyptomania: A History of Fascination, Obsession and Fantasy
Ronald H. Fritze REAKTION *(2016)*
The richness, distinction and diversity of ancient Egyptian culture has fired imaginations for millennia. Here, historian Ronald Fritze examines 'Egyptomania' in detail and through time. As Herodotus and other classical scholars extolled Giza's pyramids and the great lighthouse at Alexandria, Egyptian cults and esoteric tracts seeped into Greece and Rome — to later fascinate and befuddle medieval and Renaissance scholars. The cracking of hieroglyphs, discovery of Tutankhamun's tomb and "mummymania" from the nineteenth century onwards ensured that the craze persists almost unabated today.



The Man Who Ate the Zoo
Richard Girling CHATTO & WINDUS *(2016)*
Victorian zoologist and surgeon Frank Buckland occupies a peculiar place in science history. Like his renowned naturalist father William, he was both a serious researcher — rubbing shoulders with scientific heavyweights such as Michael Faraday — and an eccentric who dined on giraffe and panther. In this lively biography, Richard Girling revels in Buckland's phenomenal drive to master animal biology in a number of contexts: domestic menageries featuring marmots, a meerkat and a bear; a flood of natural-history writing; stints as a zoo medic; and distinguished contributions to fisheries science.



Utopia
Thomas More VERSO *(2016)*
Five hundred years ago, English humanist Thomas More — who counselled Henry VIII and was executed at his order — published *Utopia*, a radical imagining of a society free from tyranny and suffering. This special edition is bookended by pieces from science-fiction greats Ursula Le Guin and China Miéville. In one essay, Le Guin suggests we edge back into history to see forward to a liveable future. How better than to revisit More, whose view of the social order as a "conspiracy of the rich" and war as inhuman resonate so powerfully today? **Barbara Kiser**