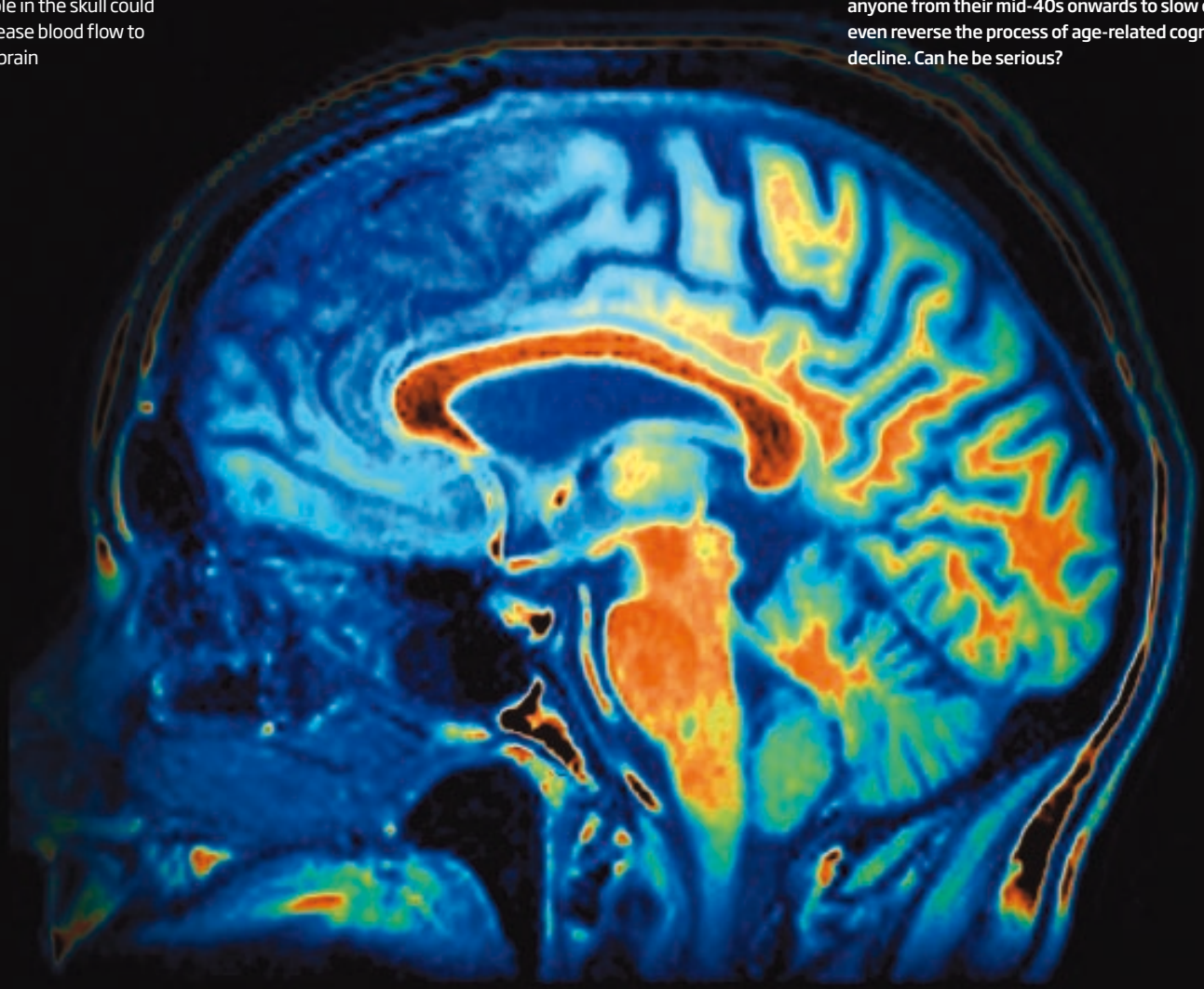
Our ancestors used trepanation to expel demons – now drilling a hole in the skull is being touted as a cure for dementia. **Arran Frood** investigates

Like a hole in the head

IN THE early 1960s, a young Russian neurophysiologist called Yuri Moskalenko travelled from the Soviet Union to the UK on a Royal Society exchange programme. During his stay, he co-authored a paper published in *Nature*. "Variation in blood volume and oxygen availability in the human brain" may not sound subversive, but it was the start of a radical idea.

Decades later, having worked in Soviet Russia and become president of the Sechenov Institute of Evolutionary Physiology and Biochemistry at the Russian Academy of Sciences in St Petersburg, Moskalenko is back in the UK. Now collaborating with researchers at the Beckley Foundation in Oxford, his work is bearing fruit.

And strange fruit it is. With funding from the foundation, he is exploring the idea that people with Alzheimer's disease could be treated by drilling a hole in their skull. In fact, he is so convinced of the benefits of trepanation that he claims it may help anyone from their mid-40s onwards to slow or even reverse the process of age-related cognitive decline. Can he be serious? ›



A hole in the skull could increase blood flow to the brain

ZEPHYR/SPL

"A 4-square-centimetre hole increases cerebral blood flow by between 8 and 10 per cent"

For thousands of years, trepanation has been performed for quasi-medical reasons such as releasing evil spirits that were believed to cause schizophrenia or migraine. Today it is used to prevent brain injury by relieving intracranial pressure, particularly after accidents involving head trauma.

In the popular imagination, though, it is considered crude, if not downright barbaric. Yet such is the desperation for effective treatments for dementia that drilling a hole in the skull is not even the strangest game in town (see "Desperate measures to treat dementia", below).

The problem is huge and growing. Alzheimer's, the most common form of dementia, affects 700,000 people in the UK and nearly 5 million in the US. In addition, 1 in 5 Americans over the age of 75 have mild cognitive impairment, which often leads to Alzheimer's. As people live longer, the numbers seem certain to grow. Yet we have few ideas about what causes dementia and even fewer about how to treat it. Most patients get a mixture of drugs and occupational therapy, which at best stalls the apparent progression of their illness by masking its symptoms.

The causes of dementia are many and poorly understood, but there is growing evidence that one factor is the flow of blood within the brain. As we age, cerebral blood flow decreases, and the earlier this happens the more likely someone is to develop early onset dementia. It remains unclear, however, whether declining cerebral blood flow is the cause, or an incidental effect of a more fundamental change. Moskalenko's research indicates that cerebral blood flow is more closely correlated with age than with levels of dementia, so he decided to delve more deeply.

The brain's buffer

As well as delivering oxygen to the brain, cerebral blood flow has another vital role: the circulation and production of cerebrospinal fluid. This clear liquid surrounds the brain, carrying the nutrients that feed it and removing the waste it produces, including the tau and beta-amyloid proteins that have been implicated in the formation of plaques found in the brains of people with Alzheimer's (*Cerebrospinal Fluid Research*, vol 5, p 10).

How blood flow influences cerebrospinal fluid flow can be gauged from something called "cranial compliance", a measure of the elasticity of the brain's vascular system. "The cranium is a bony cavity of fixed volume, with the brain taking up most of the space," says Robin Kennett, a neurophysiologist from the Oxford Radcliffe Hospitals in the UK. "Every time the heart beats and sends blood into the cranium, something else has to come out to prevent the pressure rising to levels that would damage the brain." So, as fresh blood flows into the brain's blood vessels, cerebrospinal fluid flows out into the space around the spinal cord through a hole in the base of the skull called the foramen magnum.

As we age, the proteins in the brain harden, preventing this system from working as it should. As a result, the flow of both blood and cerebrospinal fluid is reduced, impairing the delivery of oxygen and nutrients as well as the removal of waste. Moskalenko's research

Desperate measures to treat dementia

RDF MEDIA

Terry Pratchett tries a laser helmet to slow his brain's decline

"THE LASER HELMET"
As worn by sci-fi and fantasy author Terry Pratchett, who was diagnosed with posterior cortical atrophy, a rare type of Alzheimer's, in 2007. Inventor Gordon Dougal, director of British company Restorelite, says the device uses light at a wavelength of 1072 nanometres to penetrate the skull and repair brain cells damaged by the ageing processes.

OMENTAL TRANSPOSITION
Not for the faint-hearted. It entails cutting into the omentum, a blood-vessel-rich part of the lower abdominal cavity, and stretching a strip of this tissue so that it can be "tunnelled" under the skin and laid directly onto the brain. The operation's pioneer, Harry Goldsmith from the University of Nevada, believes this increases cerebral blood flow, improving neuronal activity.

CRANIAL OSTEOPATHY
Manipulating the skull by hand. The practice controversially assumes that adult skull plates are not fused, but move a fraction. Mark Rosen, president of The Cranial Academy in Indianapolis, Indiana, says there is evidence that cranial osteopathy increases intracranial blood flow.

STANDING ON YOUR HEAD
Albert Hoffman, the discoverer of LSD, swore by it. So do many devotees of yoga. Studies have shown that some yoga breathing techniques can significantly increase cerebral blood flow. Whether hanging upside down for 15 minutes a day can stave off dementia is another matter.

suggests that this normally begins between the ages of 40 and 50. Moreover, in a study of 42 elderly people with dementia, he found that the severity of their cognitive disorder was strongly correlated with cranial compliance: those with the severest dementia had the lowest compliance (*International Journal of Psychophysiology*, vol 69, p 307). "Cranial compliance is a significant component of the origin of certain cases of brain pathology," he says.

This view gets qualified agreement from Conrad Johanson, a clinical neuroscientist at Brown University in Providence, Rhode Island. Although the link between low compliance and dementia has yet to be comprehensively shown, he says, "there's a gestalt that it's broadly true".

So where does trepanation come into all this? "A hole made in the bony cavity would act as a pressure-release valve," says Kennett, and this would alter the flow of fluids around the brain. This is exactly what Moskalenko observed when he carried out one of the first neurophysiological studies on trepanation.

Moskalenko studied 15 people who had undergone the procedure following head injuries. He found that their cranial compliance was around 20 per cent higher than the average for their age. Based on this, he calculates that a 4-square-centimetre hole increases cerebral blood flow by between 8 and 10 per cent, which is equivalent to 0.8 millilitres more blood per heartbeat (*Human Physiology*, vol 34, p 299). This, he says, shows that trepanation could be an effective treatment for Alzheimer's, and he even goes so far as to suggest that it might provide a "significant" improvement in the mental functions of anyone from their mid-40s, when cranial compliance starts to decline.

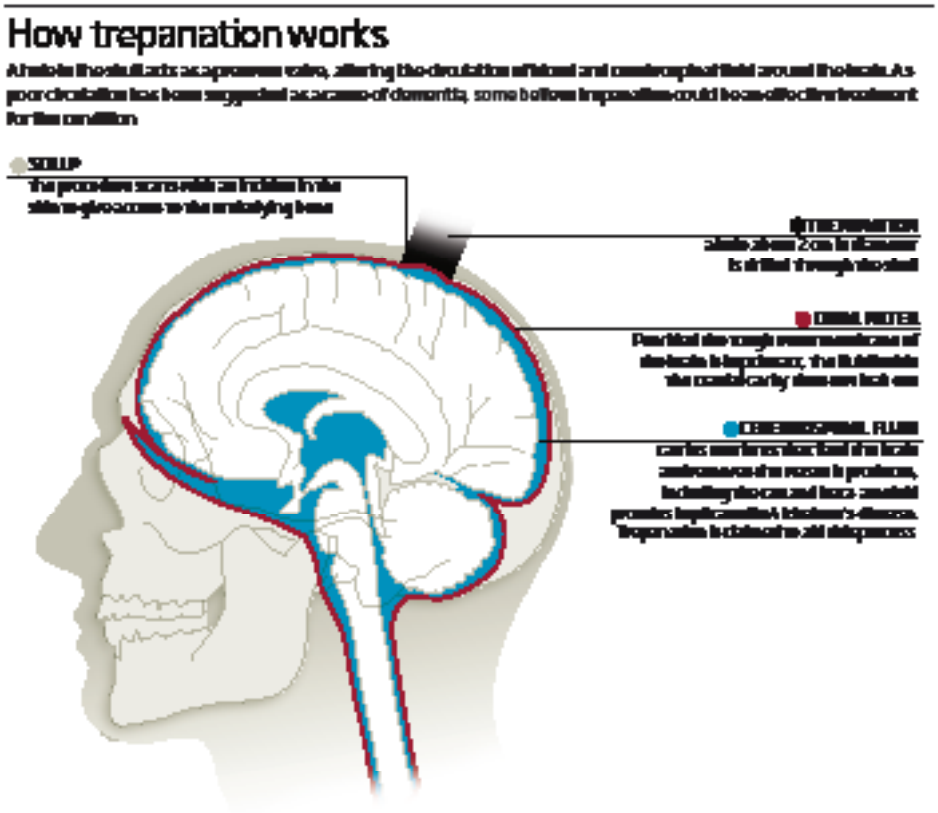
Spinal taps

Surprisingly, his most vociferous critics do not challenge his support for trepanation. Instead they question his ideas about how it works. Gerald Silverberg at the Stanford School of Medicine in California points out that drilling a hole in the skull may temporarily drain the cranial cavity of cerebrospinal fluid together with any toxins that may have accumulated in it, effectively flushing out the system. "Metabolite clearance, or the lack of it, is felt to be an important factor in the development of age-related dementias," he says. A similar intervention, known as a lumbar shunt or "spinal tap", in which a needle is inserted into the spinal column to remove cerebrospinal fluid, can dramatically improve the cognitive performance of people who undergo the procedure, Silverberg says. Spinal taps are normally used as a treatment for hydrocephalus – water on the brain – but Silverberg is now trying it out on people with Alzheimer's, and early studies suggest it helps (*Neurology*, vol 59, p 1139).

Olivier Baledent, a neurophysiologist based at the University Hospital of Amiens, France, also questions Moskalenko's focus on cranial compliance (*Journal of Cerebral Blood Flow & Metabolism*, vol 27, p 1563). Like Silverberg, he believes cerebrospinal fluid itself is key. Baledent's unpublished research shows that in people with mild cognitive impairment, there is reduced activity in a part of the brain called the choroid plexus, where cerebrospinal fluid is formed. He suspects this results in impaired fluid formation and reabsorption, leading to a build-up of toxins, and that a spinal tap may be able to stop or decrease dementia by improving fluid turnover. Trepanation could work in a similar way.

So will dementia patients and their families ever accept trepanation as a treatment for the condition? Johanson, who sees trepanation as no more alarming than a spinal tap, admits that it is always going to be a hard sell. "People think it's witchcraft when you drill a hole in the skull and patients are improving."

Harriet Millward, deputy chief executive of UK-based charity Alzheimer's Research Trust, is keeping an open mind. "The procedure has been understudied so far and, until further research has been undertaken, the possibility of beneficial effects remains open," she says. David Smith, a neuropharmacologist and head of the Oxford Project to Investigate Memory and Ageing, is even more receptive. "I think the observations look pretty robust," he says. In the absence of drug treatments for dementia, "these rather drastic surgical ones are worth considering", he says. ■



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Arran Frood is a freelance science writer based in the UK