Why are well-educated, active people more able to fend off the symptoms of dementia and brain damage? **Lisa Melton** investigates

Use it don't lose it

RICHARD WETHERILL was intolerably good at chess. Hardly surprising, for the retired university lecturer could think a mind-boggling eight moves ahead. But in recent months, his razor-sharp mind had started to dull. When he found he could no longer think five moves ahead, he was sure something was seriously wrong and arranged to meet neurologist Nick Fox at University College London's Institute of Neurology. Though his wife dismissed his complaints, Wetherill was adamant that he needed help. Yet Fox's battery of tests revealed nothing amiss: his patient sailed through every test designed to spot early dementia. Under a brain imager, his brain looked normal.

Two years later, in 2003, Wetherill died suddenly. Imagine Fox's amazement when the autopsy revealed a brain riddled with plaques and tangles, the hallmark of Alzheimer's disease. The anatomical evidence indicated advanced disease, with a level of physical damage that would have reduced most people to a state of total confusion. Yet for Wetherill the only impact was that he could no longer play chess to high standards. What on earth was he doing differently? What was cushioning the blow?

Wetherill's experience is a perfect example of a phenomenon that has long puzzled scientists: people who lead more intellectually stimulating lives, who are more intelligent, better educated and have high-status occupations, are somehow protected from the mental decline that comes with age. And not just age, but other insults too, from head injuries and alcohol intoxication to stroke, HIV, Alzheimer's and Parkinson's disease.

Some psychologists and neuroscientists have started to call this mental padding "cognitive reserve". The higher your reserve, they argue, the more damage you can sustain without showing signs of mental decline. But the idea of cognitive reserve is controversial. Some dismiss it as nothing more than common sense – people who start off smarter have further to fall. Nevertheless, a growing number of studies are bolstering the idea that cognitive reserve is real.

MILAN HORACEK/BILDERBERG/NETWORK

SIMON ROBERTSON/NB PICTURES

PHOTOLIBRARY/IMAGESTATE

Who would have thought that staying active can build an emergency stash of brainpower?

In the past few years, for example, epidemiologists have confirmed that people with high literacy and IQ cope better with the progress of Alzheimer's disease. They also recover from stroke, head injury, intoxication and poisoning with neurotoxins more rapidly than the average person. Meanwhile, neuroscientists are making headway using brain scans to discover the biological ▶

underpinnings of cognitive reserve. For anyone hoping to enjoy a ripe old age, the implications are huge – especially if you could predict how much cognitive reserve you had left, and could then take action to ratchet it up.

Like it or not, after the age of 25 or so, our mental abilities start to fade. The speed at which we process information, our ability to stash away new memories, our reasoning powers and spatial abilities are at their best in our early 20s, and it's all downhill from there.

The first inkling that some people have an emergency stash of brainpower came in 1992 when Yaakov Stern, a neurobiologist at the University School of Medicine in California found that highly educated people were less likely to experience a pronounced dip in IQ after a head injury.

If cognitive reserve does exist, then what is it? One obvious possibility is that it's simply a function of brain size: the larger your brain, the more able you are to cope with the loss of neurons. Ian Deary, a psychologist at the University of Edinburgh, UK, says that brain size does correlate with reserve. But he insists that there's more to it than just spare brain capacity. "It is more than the hardware," he says. "It's in the software."

ED KASHI/CORBIS

Physical exercise seems to protect the brain from insult and injury, though no one understands why

"People with a lot of mental padding can compensate for the effects of ageing"

Sergievsky Center at Columbia University in New York, looked at the blood flow in the brains of Alzheimer's patients. All showed symptoms of equal severity, though they had varying levels of education. But despite all the subjects being outwardly equally affected, Stern found that in terms of damage to the structure of the brain there were clear differences: those who had received more education also had more severe brain pathology.

The findings suggested that some kind of "padding" was shielding the more educated patients from the full force of clinical symptoms that would be expected from the physical condition of their brains. This made sense of long-reported findings that some people who had all the features of Alzheimer's disease at autopsy had remained lucid right up to their deaths.

Since then, evidence has piled up in favour of cognitive reserve. In 2001, a team led by Lawrence Whalley of the University of Aberdeen, UK, found that better-educated people suffer less cognitive impairment for a given level of damage to their white matter, which is known to be linked to mental decline in old age. And in 2003 Shelli Kesler of Stanford

The brain's wiring matters as well as its size, according to Colette Fabrigoule, a psychologist at the University of Bordeaux 2 in France. "What is crucial in the brain is the way it works, its dynamics and networks," she says. For the past three years her team has been using magnetic resonance imaging to watch what is going on in the brains of people with Alzheimer's disease while they perform a cognitive task: what circuits they engage, and how they work together.

Switch to plan B

The team has found that people who are highly educated are better at recruiting alternative neuronal networks to compensate for the deterioration of their cortical areas, which deal with complex behaviour and thought. This, Fabrigoule believes, is what cognitive reserve is about. "Once you have a lesion or an insult, from a neurochemical point of view the network won't work normally," she explains. "Better-educated, intelligent people are better at recruiting compensatory mechanisms."

What is more, her results so far suggest that cognitive reserve resides in a specific area of the brain: the dorsolateral prefrontal cortex, which is critical in controlling learning, short-term memory, attention and language. These compensating areas light up even in early Alzheimer's disease, indicating that the brain is starting to tap into its reserve capacity.

Stern is also convinced it's all down to the brain's ability to switch to plan B. "What gives people with high reserve the upper hand is the ability to summon that compensatory response," he says. "They are used to engaging these networks and can do it more easily."

But Stern thinks there is another ingredient to cognitive reserve: information-processing efficiency. He has scanned the brains of volunteers, young and old, as they perform increasingly difficult memory tests, to see how the activity levels in their brains change as they move from easy tasks to more difficult ones. He found that the higher a person's IQ, the less effort their brains had to make to complete the tests. Rather like a car with a more powerful engine, their brains found it easier to accelerate. Stern speculates that this mental efficiency could play a role in cognitive reserve, by allowing people with a higher IQ to cope when confronted with brain damage or disease. "Having more efficient networks keeps these people in higher stead when faced with ageing or lesions," he says.

So it looks as though there are two ways in which people with a large cognitive reserve compensate for the effects of ageing or brain damage: either they recruit alternative networks or they increase the efficiency of their existing ones.

It seems paradoxical, then, that once people with high IQ, good education or occupational achievement are diagnosed with dementia, they tend to go downhill unusually fast. Stern, for example, has looked at the impact of Alzheimer's disease on well-educated people and found that they seem to die sooner after diagnosis than people without good education.

But psychologist Michael Rutter from the Institute of Psychiatry in London points out that this is compatible with the idea of cognitive reserve. "It's not that people with high education and with Alzheimer's disease deteriorate faster." What is happening, he says, is that by the time symptoms appear, these people are at a relatively late stage of the disease. If you measure the progress of the disease by plaques and tangles, they are already far gone. As long as they have cognitive reserve in the bank, outward signs are not apparent. Yet the disease progresses regardless, and once that extra cushioning goes, the outward decline is dramatic. Wetherill's story is a case in point. "By the time he couldn't dress himself, he would have been at death's door,"

says Michael Marmot, an epidemiologist from University College London.

With growing evidence that cognitive reserve is something we want – and as much of it as possible – the next question is how to get it. Is it just a matter of luck, or is it possible to boost your cognitive reserve?

According to Marcus Richards, an epidemiologist at University College London, building cognitive reserve is a lifetime enterprise, and the earlier we start the better. "There are a massive number of factors that shape and develop cognitive function throughout our lifetimes, but some strike me as the most fundamental," says Richards, who has been sifting though data from a large study of people in England, Scotland and Wales born just after the second world war, known as the 1946 British cohort.

Richards has found that social class, occupation and education at age 26 help shape cognitive ability at age 53. The upbeat conclusion is that education makes a difference to cognitive performance later in life, and this almost certainly equates to a higher cognitive reserve. "Education works," says Richards. Stern would agree: he thinks that education may be critical in training people to recruit the alternative mental networks that enable them to compensate for damage or disease. "Cognitive reserve is not something you are born with," he says. "It's something that changes, and can be modified over time."

Yet above education stands intelligence. The best predictor of cognitive ability in middle age is your IQ score at age 8. And intelligence is to a large extent inherited. But this does not necessarily mean we are stuck with whatever cognitive reserve our genetic cards dealt us.

According to Deary, it is possible to rack up brainpower beyond your childhood potential. He and Richards recently analysed the findings of the Scottish Mental Survey, which followed a group of several hundred children born in 1921 who took an IQ test aged 11 and then again at 80. They found that, although IQ scores at 11 were a strong predictor of scores later in life, some people managed to significantly increase their IQ. "Something is pushing them up from where they were, and where you'd expect them to be based on their childhood ability," says Deary. That something is likely to be education and socio-economic status. Similarly, in September this year, Ross Andel and James Mortimer of the University of South Florida in Tampa published a study using data from the Swedish Twin Registry in which they found that people engaged in complex occupations were to some extent protected against the risk of dementia and Alzheimer's disease.

And it's never too late to start. Fighting senility with mental gymnastics has become part of the anti-ageing folklore, and there is now evidence that mental activity really does cushion people against age-related decline. In December 2004, for example, Stern and colleagues published a study in the journal *Neurology* showing that intellectual activities such as reading could reduce the severity of Alzheimer's symptoms. Meanwhile, animal studies and small-scale trials in humans are hinting at all kinds of other ways to maintain or even boost cognitive performance, and hence cognitive reserve (see "Maintain that brain", above).

Mental activity is not the only thing that helps. Preliminary results from researchers at Trinity College Dublin in Ireland, who are following a group of over-60s taking part in a four-month aerobic exercise programme, suggest that physical activity can also be beneficial. According to Ian Robertson, who is leading the study, exercise has a remarkable impact on their mental performance.

Stern and Fabrigoule acknowledge that it has yet to be established which brain-boosting exercises work best at building cognitive reserve, but they think that any activity that stimulates mental processing – even something as ordinary as meeting friends or gardening – may help. Others are not convinced it's that simple. "These are encouraging findings and it's a good place to start," says Carol Brayne, an epidemiologist at the University of Cambridge. "But we need more evidence, more painstaking large trials, before we can say it really works in practice."

Even so, the US Alzheimer's Association has already started encouraging people to build up their cognitive reserve. In a society faced with an ageing population, in which dementia, Alzheimer's and Parkinson's disease are bound to become more common, that can't do any harm. Beyond 65, the risk of dementia doubles every five years, and nearly 25 per cent of people over the age of 85 suffer from dementia. Any way of lessening the impact of such diseases will have enormous benefits. "This is as powerful as any drug we will ever have to stop Alzheimer's progression," Stern says. ●

Lisa Melton is science writer in residence at the Novartis Foundation in London

Don't underestimate the lifelong power of a good education

SAMUEL BOLLENDORFF/DEL PUBLIC

Maintain that brain

Animal studies and small-scale human trials suggest that there may be many routes to a bigger cognitive reserve, though all these techniques remain unproven:
STAY ALERT Mental activity builds up reserves of brain cells and connections, which protect against age-related decline. Get a challenging job, and don't veg out in front of the TV. Read or do crosswords instead.
KEEP FIT Exercise keeps the blood flowing and might trigger the birth of new brain cells. Cardiovascular fitness also strengthens the brain's executive functions and preserves white and grey matter.
MINIMISE STRESS People who score high on the personality trait called neuroticism have a faster rate of cognitive decline and an increased risk of Alzheimer's disease.
EAT RIGHT A diet high in the mono and polyunsaturated fatty acids (found in fish and olive oil) and vitamin E, polyphenols and antioxidants (found in citrus and dark-skinned fruits and vegetables) may slow cognitive decline. Avoid saturated fat.
STAY SOBER Don't smoke, lay off the alcohol and don't take street drugs.

www.newscientist.com/channel/being-human/brain