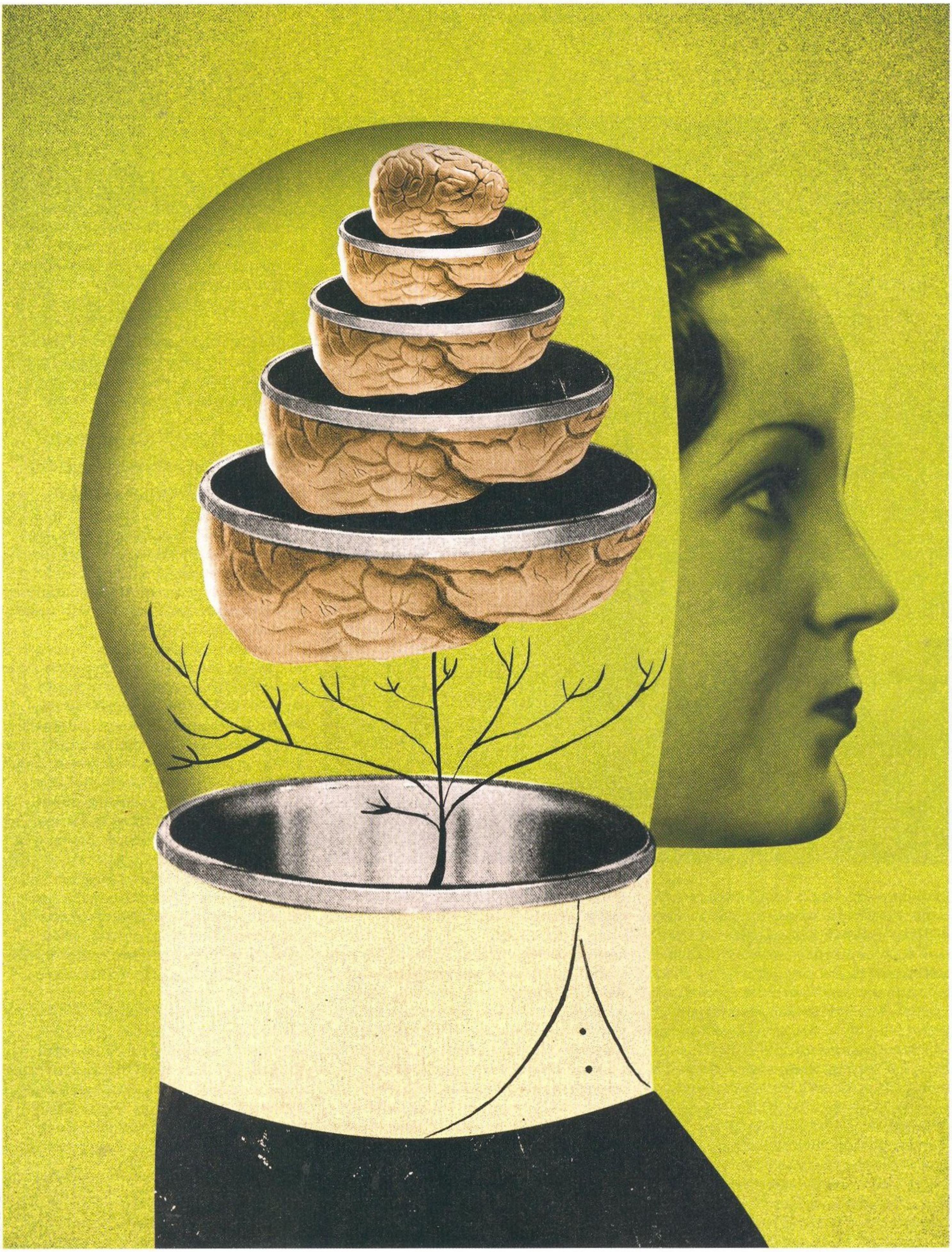


DAVID PLUNKERT

The five ages of the brain

Throughout life our brains undergo more changes than any other part of the body. These can be broadly divided into five stages, each profoundly affecting our abilities and behaviour. But we are not just passengers in this process, so how can we get the best out of our brains at every stage and pass the best possible organ on to the next? *New Scientist* investigates

GESTATION
Setting the stage

1

By the time we take our first breath, the brain is already more than eight months old. It starts to develop within four weeks of conception, when one of three layers of cells in the embryo rolls up to form the neural tube. A week later the top of this tube bends over, creating the basic structure of fore, mid and hindbrain.

From this point, brain growth and differentiation is controlled mainly by the genes. Even so, the key to getting the best out of your brain at this stage is to have the best prenatal environment possible. In the early weeks of development, that means having a mother who is stress-free, eats well and stays away from cigarettes, alcohol and other toxins. Towards the end of the brain-building process, when the fetus becomes able to hear and remember (see "Childhood", page 28), sounds and sensations also begin to shape the brain.

In the first two trimesters of pregnancy, though, development is all about putting the basic building blocks in place: growing neurons and connections and making sure each section of the brain grows properly and in the right area. This takes energy, and a variety of nutrients in the right quantity at the right time. In fact, if you consider the size of the construction job at hand – 100 billion brain cells and several million support cells in four major lobes and tens of distinct regions – it is a truly staggering feat of evolutionary engineering.

One nutrient we know the brain needs early on is folic acid, which is crucial for closing the neural tube. Deficiencies can lead to defects like spina bifida, where part of the spine grows outside the body, and anencephaly, a fatal condition in which much of the brain fails to develop. There's some evidence that vitamin B_{12} deficiency has similar effects (*Pediatrics*, vol 123, p 917).

The role of other nutrients is less well understood in these early weeks – partly because deficiencies often occur as a component of either general malnutrition or poverty, which brings in the confounding factors of poorer general health or health education, and partly because early deficiencies are difficult to link to problems that may not show up until months or years later.

We do know from animal studies, however, that malnutrition – particularly a lack of protein – stunts the growth of neurons and connections, and that iron and zinc are needed for neurons to migrate from where they form to their final location. Long-chain polyunsaturated fatty acids are required for synapse growth and membrane function.

Yet while a good diet and taking prenatal ›

RALPH HUTCHINGS/VISUALS UNLIMITED/GETTY

vitamins, if prescribed, is usually enough to take care of the fetus's early brain needs, deficiencies caused by an inefficient placenta can hinder development. Factors that can affect the placenta include maternal high blood pressure, stress and smoking. Excesses of nutrients can also be bad news. Poorly controlled diabetes, for example, can cause a potentially toxic excess of glucose in the developing brain.

Luckily, the brain has a large safety net, producing double the neurons it will ultimately need. Even so, some damage may not be reversible. Fetal iron deficiency, for instance, affects brain function for up to three years, even if the child receives supplements from birth.

As for toxic substances, the good news is that fetuses are well protected from the outside world, and even from their own mother. The placenta is a highly selective barrier studded with protein pumps that help prevent unwanted substances in the mother's bloodstream from reaching the fetus.

TOXIC EFFECTS

It is not a perfect barrier, however, and toxics such as mercury, nicotine and alcohol can squeeze through. The effects depend on the dose and timing of exposure, but in animal studies nicotine has been shown to affect the functioning of neurotransmitters, while mercury has been linked to cell loss in the cerebellum and parts of the cortex. Alcohol is known to kill off neurons and alter the action of certain neurotransmitters, although how much is needed to cause the physical and cognitive defects of fetal alcohol syndrome or more subtle forms of damage is unclear.

Some toxics do not need to go through the placenta to have an effect. For example, cigarette smoke restricts blood flow to the fetus, depriving it of oxygen and nutrients. Exactly how this affects the brain in human fetuses is unclear, although there are some indications that the corpus callosum, which links the two hemispheres, and the orbitofrontal cortex (OFC), involved in social behaviour, may be smaller in adolescents exposed to cigarette smoke in the womb. A smaller OFC correlated with less "caring" behaviour in female teens, suggesting smoking may cause behavioural problems in offspring. However a recent study found no difference in general cognitive ability between exposed and non-exposed adolescents (*International Journal of Epidemiology*, vol 38, p 158).

Stress, too, can be toxic. In animals, exposure to the mother's stress hormones can lead to anxious behaviour and hyperactivity in the offspring. A recent longitudinal study of over 7000 mothers and babies at Imperial College London concluded that maternal stress may account for up to 15 per cent of diagnoses of attention-deficit hyperactivity disorder.

If you are reading this, however, chances are you got off pretty lightly in the first nine months of life, or that any problems were outweighed by good parenting or education (see "Childhood", right). In the next age, the young brain starts to learn and remember, and that means we get our first chance to really use that amazing organ. Caroline Williams

2

CHILDHOOD
Soak it up

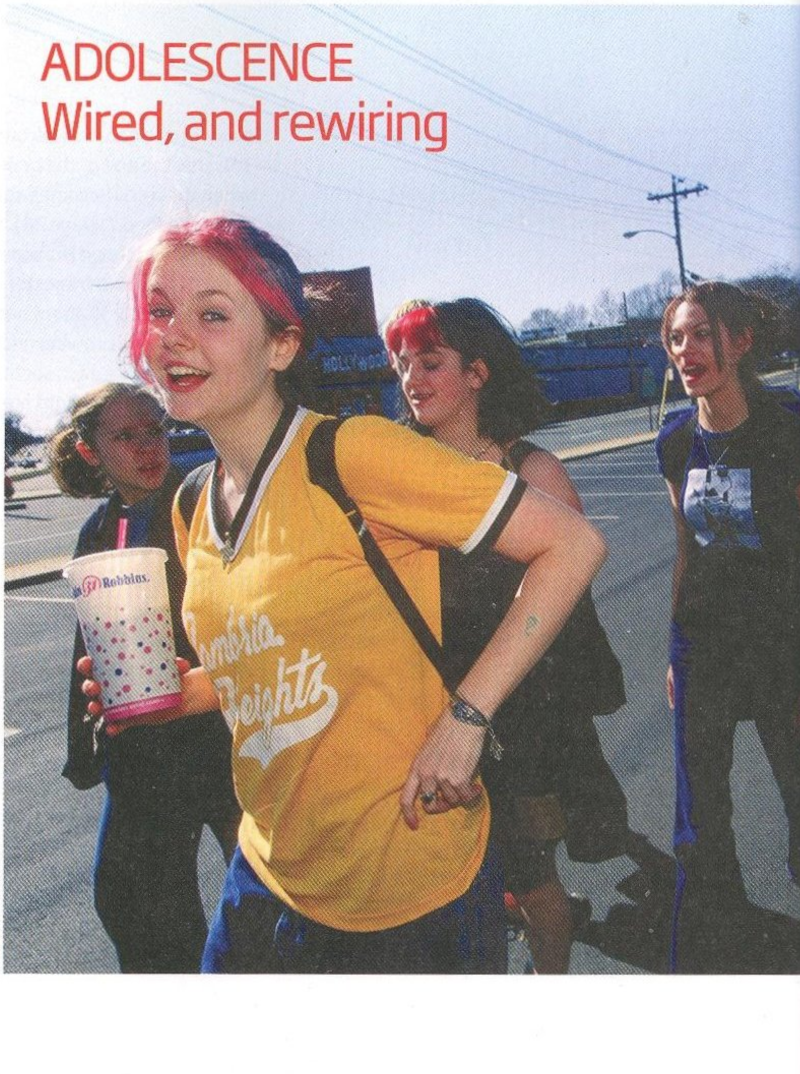
In childhood, the brain is the most energetic and flexible that it will ever be. As we explore the world around us it continues to grow, making and breaking connections at breakneck speed. Perhaps surprisingly, learning, memory and language begin before we are even born.

During the prenatal period, up to a quarter of a million new cells form every minute, making 1.8 million new connections per second, though about half of the cells will later wither and die, leaving only those reinforced by use. From birth, a child undergoes more than a decade of rapid growth and development, in which every experience contributes to the person they will become. So what can a parent do to help maximise the potential of their child's brain?

Experiences during the late prenatal period are certainly important, and perhaps vital for normal brain development. Learning can first be detected experimentally at about 22 to 24 weeks of gestation, when fetuses will respond to a noise or a touch but will ignore the same stimulus if it occurs repeatedly - a simple kind of memory called habituation. From around 32 weeks fetuses show conditioning - a more complex kind of memory in which an arbitrary stimulus

"A fetus forms up to a quarter of a million new neurons a minute and up to 1.8 million connections per second"

ADOLESCENCE
Wired, and rewiring



LAUREN GREENFIELD/VII

can be learned as a signal that something will happen, like a sound signalling a poke. Fetal memories for particular pieces of music and the mother's voice and smell have all been shown to form sometime after 30 weeks' gestation and to persist after birth.

Language acquisition, too, begins prenatally. A newborn will suck more vigorously if it hears its native language rather than a foreign one, although newborns do respond to sounds from any language until about 3 years of age. Even so, while talking to a third trimester fetus may help them recognise your voice, there is no direct evidence that exposure to multiple languages will influence future linguistic talents. The most important factor in language development is how much a parent talks to the child after birth, the complexity of their vocabulary and how well they focus the child's attention.

EARLY LEARNING

Likewise, while some companies selling "prenatal education" systems would like parents to believe that it is possible to educate a child in the womb, there is no direct evidence that such strategies provide a head start. In fact, there could be good reasons why the fetal environment provides a limited sensory experience. Too much stimulation, which may occur if mothers take certain drugs, can actually kill new brain cells.

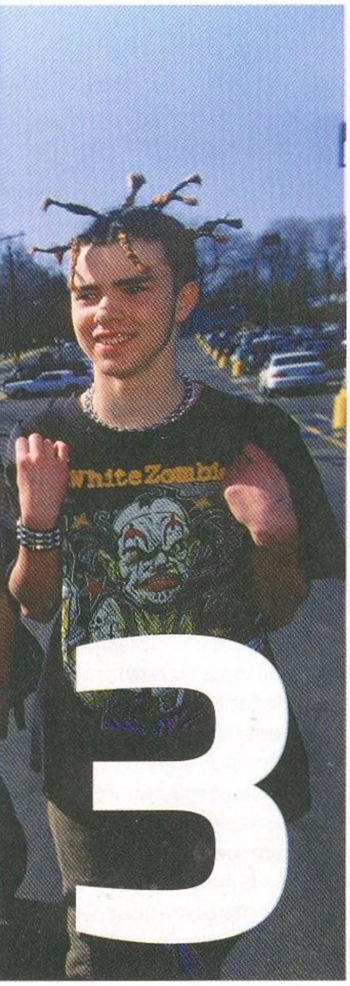
Birth alters brain function surprisingly little. Although the touch-sensitive somatosensory cortex is active before birth, it's another two or three months before there is any other activity in the cortex, which ultimately governs such things as voluntary movement, reasoning and perception. The frontal lobes become active between 6 months and a year old, triggering the development of emotions, attachments, planning, working memory and attention. A sense of self develops as the parietal and frontal lobe circuits become more integrated, at around 18 months, and a sense of other people having their own minds at age 3 to 4.

Life experiences in these early years help shape our emotional well-being, and neglect or harsh parenting may change the brain for good. Maternal rejection or trauma early in life, for example, may affect a person's emotional reactions to stressful events later on, potentially predisposing them to depression and anxiety disorders.

So how to make the most of this delicate yet fertile time in the brain's life? The good news for parents is that there is no reason for your child to stop playing and start working. Studies have shown that a nurturing environment and one-on-one playtime with games like peekaboo, building blocks, singing nursery rhymes and shape-sorting are all a child needs to increase IQ and foster a lifelong interest in learning.

Some claim that listening to Mozart improves spatial tasks and learning in people, and maze-running in rats. This "Mozart effect" – which has spawned countless prenatal and childhood learning programmes – has just as many scientific detractors as supporters, however. Learning to play music during childhood is a different matter. It has long-lasting effects on the brain which some suggest may improve spatial, mathematical and reasoning skills.

By age 6, the brain is 95 per cent of its adult weight and at its peak of energy consumption. Around now, children start to apply logic and trust and to understand their own thought processes. Their brains continue to grow and make and break connections as they experience the world until, after a peak in grey matter volume at 11 in girls and 14 in boys, puberty kicks in and the brain changes all over again. Helen Phillips



Teenagers are selfish, reckless, irrational and irritable, but given the cacophony of construction going on inside the adolescent brain, is it any wonder? In the teenage years, our brains may be fully grown, but the wiring is certainly still a work in progress.

Psychologists used to explain the particularly unpleasant characteristics of adolescence as products of raging sex hormones, since children reach near adult cerebral volumes well before puberty. More recently, though, imaging studies have revealed a gamut of structural changes in the teens and early 20s that go a long way towards explaining these tumultuous teenage years.

Jay Giedd at the National Institute of Mental Health in Bethesda, Maryland, and his colleagues have followed the progress of nearly 400 children, scanning many of them every two years as they grew up. They found that adolescence brings waves of grey-matter pruning, with teens losing about 1 per cent of their grey matter every year until their early 20s (*Nature Neuroscience*, vol 2, p 861).

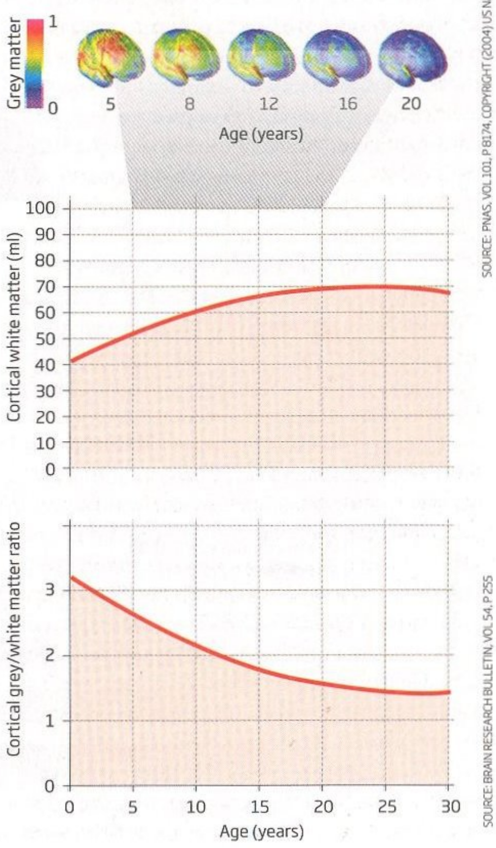
This cerebral pruning trims unused neural connections that were overproduced in the childhood growth spurt, starting with the more basic sensory and motor areas. These mature first, followed by regions involved in language and spatial orientation and lastly those involved in higher processing and executive functions (*Proceedings of the National Academy of Sciences*, vol 101, p 8174).

Among the last to mature is the dorsolateral prefrontal cortex at the very front of the frontal lobe. This area is involved in control of impulses, judgement and decision-making, which might explain some of the less-than-stellar decisions made by your average teen. This area also acts to control and process emotional information sent from the amygdala – the fight or flight centre of gut reactions – which may account for the mercurial tempers of adolescents.

As grey matter is lost, though, the brain gains white matter (see graph, right). This fatty tissue surrounds ›

Less cells, more speed

While pruning of underused pathways means we lose grey matter (brain cells), an increase in white matter speeds electrical impulses and stabilises connections



neurons, helping to conduct electrical impulses faster and stabilise the neural connections that survived the pruning process.

These changes have both benefits and pitfalls. At this stage of life the brain is still childishly flexible, so we are still sponges for learning. On the other hand, the lack of impulse control may lead to risky behaviours such as drug and alcohol abuse, smoking and unprotected sex.

Substance abuse is particularly concerning, as brain imaging studies suggest that the motivation and reward circuitry in teen brains makes them almost hard-wired for addiction. Throw in a lack of impulse control, poor judgement and a woeful underappreciation of long-term consequences and you have a hooked teen. And since drug abuse and stressful events – even a broken heart – have been linked to mood disorders later in life, this is the time when both are best avoided.

On the plus side, as teens rush towards adulthood and independence, they carry with them the raw potential to sculpt their brains into lean, mean processing machines. Making the most of this time is a matter of throwing all that teen energy into learning and new experiences – whether that means hitting the books, learning to express themselves through music or art, or exploring life by travelling the world. But whether they like it or not, while their decision-making circuits are still forming, tender teen brains still need to be protected, if only from themselves. Anna Gosline

"The peak of your brain's powers comes at age 22 and lasts for just half a decade"

JAMES BELL/WILD CARD IMAGES

4

ADULTHOOD
The slippery slope

So you're in your early 20s and your brain has finally reached adulthood. Enjoy it while it lasts. The peak of your brain's powers comes at around age 22 and lasts for just half a decade. From there it's downhill all the way.

This long, slow decline begins at about 27 and runs throughout adulthood, although different abilities decline at different rates. Curiously, the ones that start to go first – those involved with executive control, such as planning and task coordination – are the ones that took the longest to appear during your teens. These abilities are associated with the prefrontal and temporal cortices, which are still maturing well into your early 20s.

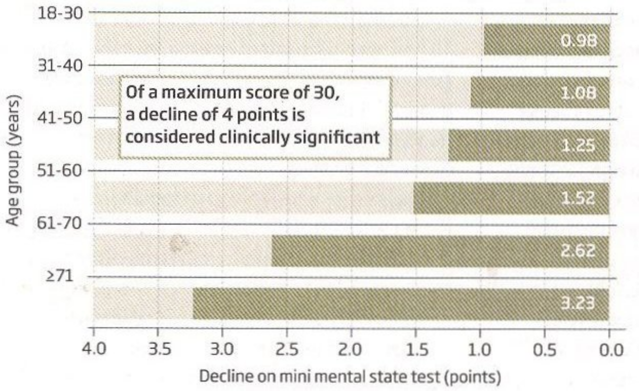
Episodic memory, which is involved in recalling events, also declines rapidly, while the brain's processing speed slows down and working memory is able to store less information.

So just how fast is the decline? According to research by Art Kramer, a psychologist at the University of Illinois in Urbana-Champaign, and others, from our mid-20s we lose up to 1 point per decade on a test called the mini mental state examination (see graph, left). This is a 30-point test of arithmetic, language and basic motor skills that is typically used to assess how fast people with dementia are declining. A 3 to 4 point drop is considered clinically significant. In other words, the decline people typically experience between 25 and 65 has real-world consequences.

That all sounds rather depressing, but there is an upside. The abilities that decline in adulthood

The brain drain

Cognitive ability, as measured by the battery of tests that make up the mini mental state examination, declines faster with every passing decade



SOURCE: AMERICAN JOURNAL OF PSYCHIATRY, VOL 156, P 58

rely on "fluid intelligence" - the underlying processing speed of your brain. But so-called "crystallised intelligence", which is roughly equivalent to wisdom, heads in the other direction. So even as your fluid intelligence sags, along with your face and your bottom, your crystallised intelligence keeps growing along with your waistline. The two appear to cancel each other out, at least until we reach our 60s and 70s (see "Old age", right).

There's another reason to be cheerful. Staying mentally and physically active, eating a decent diet and avoiding cigarettes, booze and mind-altering drugs seem to slow down the inevitable decline. And if it is too late to live the clean life, don't panic. You still have one more chance to turn it around. Graham Lawton

5

OLD AGE
Down but not out

By the time you retire, there's no doubt about it, your brain isn't what it used to be. By 65 most people will start to notice the signs: you forget people's names and the teapot occasionally turns up in the fridge.

There is a good reason why our memories start to let us down. At this stage of life we are steadily losing brain cells in critical areas such as the hippocampus - the area where memories are processed. This is not too much of a problem at first; even in old age the brain is flexible enough to compensate. At some point though, the losses start to make themselves felt.

Clearly not everyone ages in the same way, so what's the difference between a jolly, intelligent oldie and a forgetful, grumpy granny? And can we improve our chances of becoming the former?

Exercise can certainly help. Numerous studies have shown that gentle exercise three times a week can improve concentration and abstract reasoning in older people, perhaps by stimulating the growth of new brain cells. Exercise also helps steady our blood glucose. As we age, our glucose regulation worsens, which causes spikes in blood sugar. This can affect the dentate gyrus, an area within the hippocampus that helps form memories. Since physical activity helps regulate glucose, getting out and about could reduce these peaks and, potentially, improve your memory (*Annals of Neurology*,vol 64, p 698).

Coordination training could also help. Studies have shown that specifically targeting motor control and balance improves cognitive function in 60 to 80-year-olds. A few sessions on the grandchildren's Nintendo Wii could bring similar benefits.

If you're struggling to find the guitar hero in yourself, however, try a cognitive workout instead. "Brain training" was once considered flaky, but a study due to be published in the *Journal of the American Geriatrics Society* in April concludes that computerised brain exercises can improve memory and attention in the over 65s. Importantly, these changes were large enough that participants reported significant improvements in everyday activities, such as remembering names or following conversations in noisy restaurants.

Avoiding the grumps is even easier. Dopamine receptors - responsible for feelings of positive emotions - are in decline, with the potential to cause depression, but you can give yourself a regular dose of dopamine by eating certain foods, such as yoghurt, almonds and chocolate.

In fact, your brain is doing it all it can to ensure a contented retirement. During the escapades of your 20s and 30s and the trials of midlife, it has been quietly learning how to focus on the good things in life. By 65 we are much better at maximising the experience of positive emotion, says Florin Dolcos, a neurobiologist at the University of Alberta in Canada. In experiments, he found that people over the age of 60 tended to remember fewer emotionally negative photographs compared with positive or neutral ones than younger people (*Psychological Science*, vol 20, p 74).

WHEN I WAS YOUNG...

MRI scans showed why. While the over-60s showed normal activation in the amygdala, a region of the brain that processes emotion, its interaction with other brain areas differed: it interacted less with the hippocampus than in younger people and more with the dorsolateral frontal cortex, a region involved in controlling emotions. Dolcos suggests that this may be a result of more experience of situations in which emotional responses need to be kept under control. Older people really do see the world through rose-tinted glasses.

So while nobody wants to get older, it's not all doom and gloom. In fact you should probably stop worrying altogether. Studies show that people who are more laid back are less likely to develop dementia than stress bunnies. In one study, people who were socially inactive but calm had a 50 per cent lower risk of developing dementia compared with those who were isolated and prone to distress (*Neurology*, vol 72, p 253). This is likely to be caused by stress-induced high levels of cortisol, which may cause shrinkage in the anterior cingulate cortex, an area linked to Alzheimer's disease and depression in older people.

So while our brains may not wrinkle and sag like our skin, they need just as much care and attention - so don't give up on yours too soon. When you notice the signs of age, go for a walk, do a crossword and try to have a laugh - it might just counteract some of the sins of your youth. Helen Thomson