

The Secret Life of the Brain

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Weird and wonderful things start to happen when you put your brain in neutral, finds **Douglas Fox**

IN 1953 a physician named Louis Sokoloff laid a 20-year-old college student onto a gurney, attached electrodes to his scalp and inserted a syringe into his jugular vein.

For 60 minutes the volunteer lay there and solved arithmetic problems. All the while, Sokoloff monitored his brainwaves and checked the levels of oxygen and carbon dioxide in his blood.

Sokoloff, a researcher at the University of Pennsylvania in Philadelphia, was trying to find out how much energy the brain consumes during vigorous thought. He expected his volunteer's brain to guzzle more oxygen as it crunched the problems, but what he saw surprised him: his subject's brain consumed no more oxygen while doing arithmetic than it did while he was resting with his eyes closed.

People have long envisaged the brain as being like a computer on standby, lying dormant until called upon to do a task, such as solving a Sudoku, reading a newspaper, or looking for a face in a crowd. Sokoloff's experiment provided the first glimpse of a different truth: that the brain enjoys a rich private life. This amazing organ, which accounts for only 2 per cent of our body mass but devours 20 per cent of the calories we eat; fritters away much of that energy doing, as far as we can tell, absolutely nothing.

"There is a huge amount of activity in the [resting] brain that has been largely unaccounted for," says Marcus Raichle, a neuroscientist at Washington University in St Louis. "The brain is a very expensive organ, but nobody had asked deeply what this cost is all about."

Raichle and a handful of others are finally tackling this fundamental

question – what exactly is the idling brain up to, anyway? Their work has led to the discovery of a major system within the brain, an organ within an organ, that hid for decades right before our eyes. Some call it the neural dynamo of daydreaming. Others assign it a more mysterious role, possibly selecting memories and knitting them seamlessly into a personal narrative. Whatever it does, it fires up whenever the brain is otherwise unoccupied and burns white hot, guzzling more oxygen, gram for gram, than your beating heart.

"It's a very important thing," says Giulio Tononi, a neuroscientist at the University of Wisconsin-Madison. "It's not very frequent that a new functional system is identified in the brain, in fact it hasn't happened for I don't know how many years. It's like finding a new continent."

The discovery was slow in coming. Sokoloff's experiment 55 years ago drew little attention. It wasn't until the 1980s that it started to dawn on researchers that the brain may be doing important things while apparently stuck in neutral

Eavesdropping on the mind

In those days a novel brain scanning technique called PET was all the rage. By injecting radioactive glucose and measuring where it accumulated, researchers were able to eavesdrop on the brain's inner workings. In a typical experiment they would scan a volunteer lying down with their eyes closed and again while doing a mentally demanding task, then subtract one scan from the other to find the brain areas that lit up.

Raichle was using PET to find brain areas associated with words

when he noticed something odd: some brain areas seemed to go at full tilt during rest, but quietened down as soon as the person started an exercise. Most people shrugged off these oddities as random noise. But in 1997 Raichle's colleague Gordon Shulman found otherwise.

Shulman sifted through a stack of brain scans from 134 people. Regardless of the task, whether it involved reading or watching shapes on a screen, the same constellation of brain areas always dimmed as soon as the subject started concentrating. "I was surprised by the level of consistency," says Shulman. Suddenly it looked a lot less like random noise. "There was this neural network that had not previously been described."

Raichle and Shulman published a paper in 2001 suggesting that they had stumbled onto a previously unrecognised "default mode" – a sort of internal game of solitaire which the brain turns to when unoccupied and sets aside when called on to do something else. This brain activity occurred largely in a cluster of regions arching through the midline of the brain, from front to back, which Raichle and Shulman dubbed the default network (*Proceedings of the National Academy of Sciences*, vol 98, p 676).

The brain areas in the network were known and previously studied by researchers. What they hadn't known before was that they chattered non-stop to one another when the person was unoccupied but quietened down as soon as a task requiring focused attention came along. Measurements of metabolic activity showed that some parts of this network devoured 30 per cent more calories, gram for gram, than nearly any other area of the brain.

“Daydreaming may sound like a mental luxury but its purpose is deadly serious”

All of this poses the question – what exactly is the brain up to when we are not doing anything? When Raichle and Shulman outlined the default network, they saw clues to its purpose based on what was already known about the brain areas concerned.

One of the core components is the medial prefrontal cortex (see diagram), which is known to evaluate things from a highly self-centred perspective of whether they're likely to be good, bad, or indifferent. Parts of this region also light up when people are asked to study lists of adjectives and choose ones that apply to themselves but not to, say, Britney Spears. People who suffer damage to their medial prefrontal cortex become listless and uncommunicative. One woman who recovered from a stroke in that area recalled inhabiting an empty mind, devoid of the wandering, stream-of-consciousness thoughts that most of us take for granted.

Parts of the default network also have strong connections to the hippocampus, which records and recalls autobiographical memories such as yesterday's breakfast or your first day of kindergarten.

To Raichle and his colleague Debra

Gusnard, this all pointed to one thing: daydreaming. Through the hippocampus, the default network could tap into memories – the raw material of daydreams. The medial prefrontal cortex could then evaluate those memories from an introspective viewpoint. Raichle and Gusnard speculated that the default network might provide the brain with an “inner rehearsal” for considering future actions and choices.

Randy Buckner, a former colleague of Raichle's now at Harvard, agrees. To him the evidence paints a picture of a brain system involved in the quintessential acts of daydreaming: mulling over past experiences and speculating about the future (*New Scientist*, 24 March 2007, p 36). “We're very good at imagining possible worlds and thinking about them,” says Buckner. “This may be the brain network that helps us to do that.”

There is now direct evidence to support this idea. Last year, Malia Mason of Dartmouth College in Hanover, New Hampshire, reported that the activity of the default network correlates with daydreaming. Using the brain imaging technique fMRI, Mason found that people reported daydreaming when their default

network was active, but not when it dimmed down. Volunteers with more active default networks reported more wandering thoughts overall (*Science*, vol 315, p 393).

Daydreaming may sound like a mental luxury, but its purpose is deadly serious: Buckner and his Harvard colleague Daniel Gilbert see it as the ultimate tool for incorporating lessons learned in the past into our plans for the future. So important is this exercise, it seems, that the brain engages in it whenever possible, breaking off only when it has to divert its limited supply of blood, oxygen and glucose to a more urgent task.

But people are starting to suspect that the default network does more than just daydream. It started in 2003 when Michael Greicius of Stanford University in California studied the default network in a new way. He got his subjects to lie quietly in an fMRI scanner and simply watched their brains in action. This led him to find what are called resting state fluctuations in the default network – slow waves of neural activity that ripple through in a coordinated fashion, linking its constellation of brain areas into a coherent unit. The waves lasted 10 to 20 seconds from crest to crest, up to 100 times slower than typical EEG brain waves recorded by electrodes on the scalp.

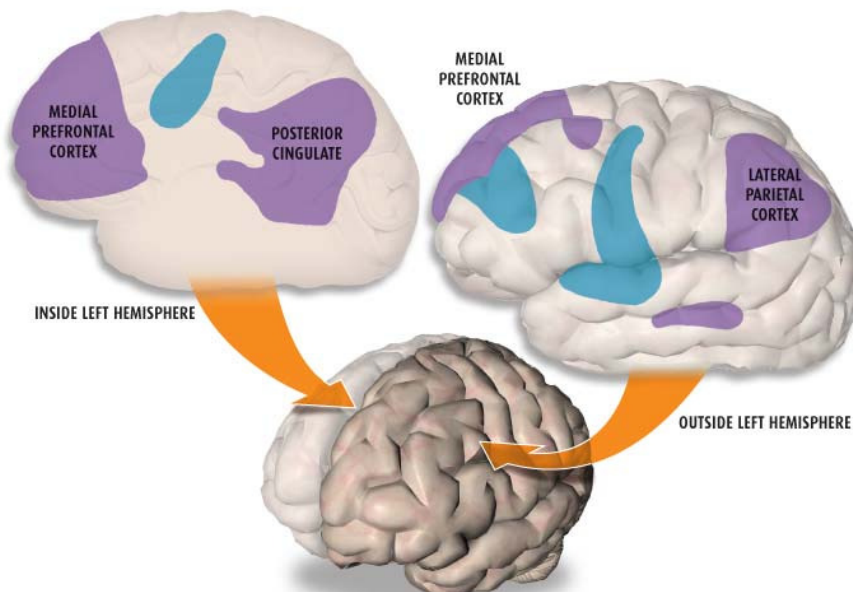
Until then scientists had studied the default network in the old-fashioned way, subtracting resting scans from task scans to measure changes in brain activity. But Greicius's work showed that you could eavesdrop on the network by simply scanning people as they lay around doing nothing. This allowed scientists to study the network in people who weren't even conscious, revealing something unexpected.

Raichle reported last year that the network's resting waves continued in heavily anaesthetised monkeys as though they were awake (*Nature*, vol 447, p83). More recently, Greicius reported a similar phenomenon in sedated humans, and other researchers have found the default network active and

THE BRAIN IN NEUTRAL

When you switch off, a distinctive network of brain areas not involved in focused attention bursts into action

● Default network ● Areas involved in focused visual attention



synchronised in early sleep (*Human Brain Mapping*, vol 29, p 839 and p 671).

It threw a monkey wrench into the assumption that the default network is all about daydreaming. "I was surprised," admits Greicius. "I've had to revamp my understanding of what we're looking at."

Given that the default network is active in early sleep it's tempting to link it with real dreaming, but Raichle suspects its nocturnal activity has another purpose – sorting and preserving memories. Each day we soak up a mountain of short-term memories but only a few are actually worth adding to the personal narrative that guides our lives.

Raichle now believes that the default network is involved, selectively storing and updating memories based on their importance from a personal perspective – whether they're good, threatening, emotionally painful, and so on. To prevent a backlog of unstored memories building up, the network returns to its duties whenever it can.

In support of this idea, Raichle points out that the default network constantly chatters with the hippocampus. It also devours huge amounts of glucose, way out of proportion to the amount of oxygen it uses. Raichle believes that rather than burning this extra glucose for energy it uses it as a raw material for making the amino acids and neurotransmitters it needs to build and maintain synapses, the very stuff of memory. "It's in those connections where most of the cost of running the brain is," says Raichle.

With such a central role, it shouldn't be surprising that the default network is implicated in some familiar brain diseases. In 2004, Buckner saw a presentation by William Klunk of the University of Pittsburgh School of Medicine. Klunk presented 3D maps showing harmful protein clumps in the brains of people with Alzheimer's. Until then people had only looked at these clumps in one brain location at a time, by dissecting the brains of deceased patients. So when Klunk projected his whole-brain map on the screen, it was the first time many people had seen the complete picture. "It was quite surprising," says

Buckner. "It looked just like the default network."

Raichle, Greicius and Buckner have since found that the default network's pattern of activity is disrupted in patients with Alzheimer's disease. They have also begun to monitor default network activity in people with mild memory problems to see if they can learn to predict who will go on to develop Alzheimer's. Half of people with memory problems go on to develop the disease, but which half? "Can we use what we've learned to provide insight into who's at risk for Alzheimer's?" says Buckner.

The default network also turns out to be disrupted in other maladies including depression, attention-deficit hyperactivity disorder (ADHD), autism and schizophrenia. It also plays a mysterious role in victims of brain injury or stroke who hover in the grey netherworld between consciousness and brain death known as a minimally conscious or vegetative state. Steven Laureys, a neurologist at the University of Liège in Belgium, has used fMRI to look at patterns of activity in the default networks of people in this state. "You can really see how this network breaks down as coma deepens," he says. He is now looking for a link between default network activity and whether patients will regain consciousness after, say, 12 months. "We're hoping to show that it will have prognostic value," he says.

All of this has been a long time coming since Sokoloff's surprising observation 55 years ago. Watching the brain at rest, rather than constantly prodding it to do tricks, is now revealing the rich inner world of our private moments. So the next time you're mooching around doing nothing much, take a moment to remind yourself that your brain is still beaver away – if you can tear yourself away from your daydreams, that is.

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The Meditating Mind

WHEN Zen Buddhists meditate, they may be deliberately switching off their default network, a recently discovered system within the brain that has been strongly linked with daydreaming (see main story).

The goal of Zen meditation is to clear the mind of wandering, stream-of-consciousness thoughts by focusing attention on posture and breathing. Giuseppe Pagnoni, a neuroscientist at the University of Modena and Reggio Emilia in Italy, wondered whether this meant they had learned to suppress the activity of their default network.

He recruited a group of volunteers trained in Zen meditation and put them in an fMRI scanner. He presented them with random strings of letters and asked them to determine whether each was an English-language word or just gibberish. Each time a subject saw a real word, their default network would light up for a few seconds – evidence of meandering thoughts triggered by the word, such as apple... apple pie... cinnamon.

Zen meditators performed just as well as non-meditators on word recognition, but they were much quicker to rein in their daydreaming engines afterwards, doing so within about 10 seconds, versus 15 for non-meditators (*PLoS ONE*, vol 3, p e3083).