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re:search

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Is this your ancestor?

re: search editorial

I do like a good controversy

As one of my heroes, Arthur Holmes, used to say, good science progresses by erecting 'wickets to be bowled at'. If they haven't been knocked down within 50 years then they are pretty robust, although could still fall if someone throws a really good googly.

We have two wickets in this issue that have had a few googlies thrown at them recently. The first questions who our distant ancestors were. The latest evidence suggests that when early modern humans moved out of Africa and arrived in Europe, they interbred with the Neanderthals. This is a shock to our cultural values, given that it was previously believed we were descended from a superior race who out-competed the Neanderthals in all ways – can we really be descended from those brutes? Or is it, perhaps, that we need to re-evaluate our understanding of this sophisticated, technically advanced and much-maligned race?

The second wicket to be fending off a lot of fast balls lately is global warming. *The Great Global Warming Swindle* and *An Inconvenient Truth* demonstrated two ends of the spectrum of our understanding about climate change – the former implying we are all being conned into believing that a change in the climate is occurring at all, and the latter supporting what most scientists seem to believe, but sensationalising it.

The *Swindle*, in particular, incensed our climatolgiststs. It implied that in our secular world 'global warming' has become the new religion, and cutting CO_2 emissions the new stick with which to flagellate ourselves. It also claimed that because the global warming band-wagon is now rolling so fast and so many jobs depend on it, views of dissenters who contributed to the IPCC's report on climate change were suppressed. Interestingly, though, an article in *New Scientist* claims the opposite – ie, that references to 'feedback mechanisms' which could point to even faster warming than predicted, were also suppressed.

What is the public to believe? Well, to help inform the debate, I asked some of our climatolgiststs to give their views on what they think are the undisputed facts. You can read their opinions on page 14, and all about our Neanderthal ancestors on page eight. Which wickets do you think are toppling?

Cherry Lewis
Editor

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Articles about research at Bristol University are welcome, please contact the editor.

Editor Cherry Lewis
Research Communications Manager, Communications & Marketing Services, University of Bristol, Senate House, Tyndall Avenue, Bristol BS8 1TH.
email re-search@bristol.ac.uk
tel +44 (0)117 928 8086

Head of Public Relations Office
Jill Cartwright

Communications & Marketing Director Barry Taylor

Design, print and production
cw-design.co.uk

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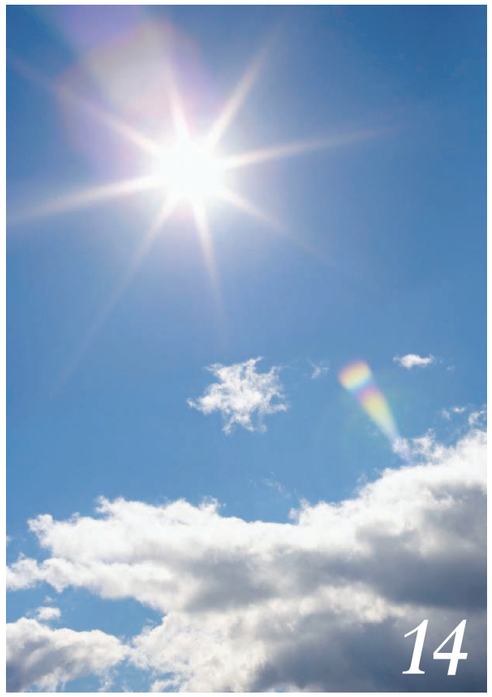

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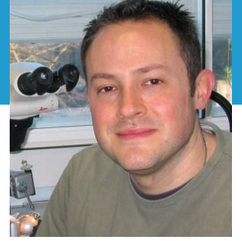
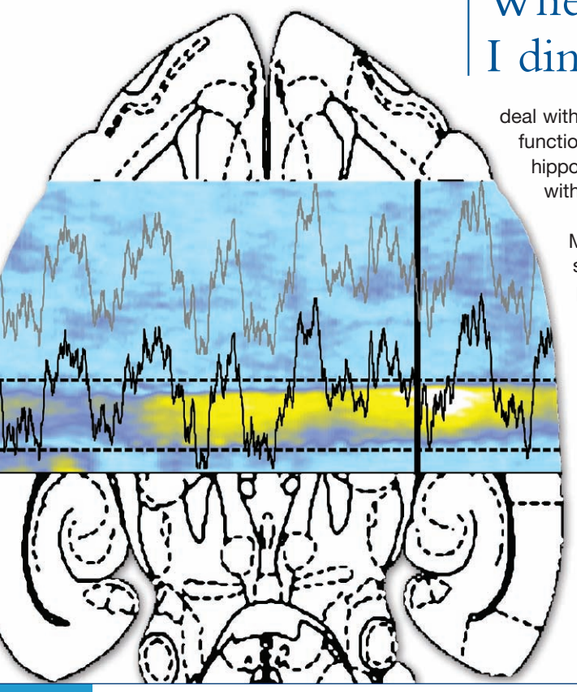


Dr Matt Jones

Brain waves make a splash

Ever jammed a sword up your nose? Not something to try at home, folks, but accidents do happen. Dr ***Matt Jones***, an RCUK Academic Fellow in the Department of Physiology, tells us what happened to the unfortunate NA – and what that tells us about how our brains function.

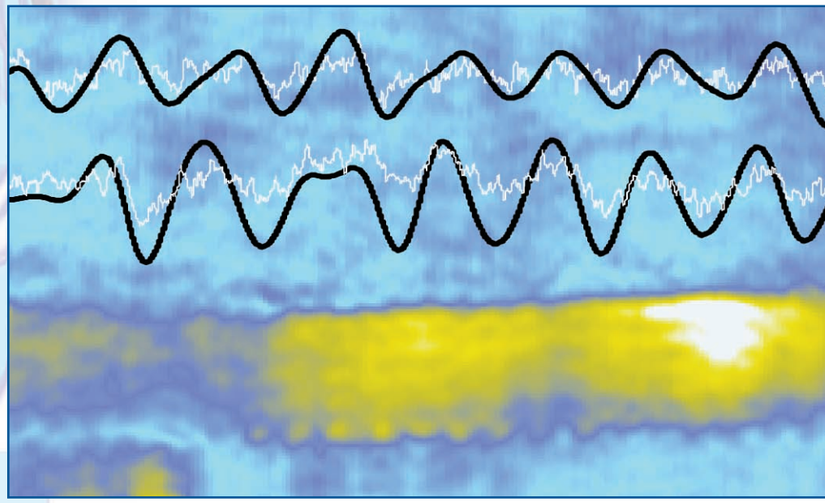


There he was, quietly building a model airplane, when NA spun round on his chair to be greeted by his friend's fencing foil. The sharp tip of the foil found its way – via his right nostril – into a discrete region near the middle of NA's brain known as the hippocampus (ouch!). But despite this damage, NA was able to function surprisingly normally, though he was left with a specific neurological disorder called 'anterograde amnesia'. This meant that NA was unable to form certain types of new memory, particularly those conscious memories that involve distinct times and locations – for example, "Where was that restaurant I dined in last night?". The unfortunate NA thereby demonstrated first, that the brain is segregated into specialised structures that have evolved to deal with particular aspects of brain function, and second, that the hippocampus deals in particular with learning and memory.

Where was that restaurant I dined in last night?

Multiple lines of evidence support these conclusions: pathological amnesia in Alzheimer's disease is associated with degeneration of the hippocampus and neighbouring regions; experimental lesions of the hippocampus leave rats and mice unable to learn and remember where hidden food is buried; and functional brain imaging in healthy taxi drivers shows the hippocampus becoming active as they recall tortuous routes through the London traffic. But next time you find yourself staring at the back of a taxi driver's head, remember that as well as learning and remembering all those routes, he needs to be processing all the visual information rushing through the windscreen, following the commands you bark from the rear seat, obeying road traffic regulations, controlling the sharp jabs of his feet on accelerator and brake, and chatting excitedly about the latest football results. All that takes a lot of brain, and the simultaneously active specialised brain structures that deal with vision, hearing, rule learning, movement, language and emotion must somehow co-ordinate their activities and interactions with one another.

Decoding how these networks of neurons are co-ordinated across multiple brain regions during complex functions and behaviour presents a challenge at the forefront of neuroscientific research. Our approach to addressing this challenge is relatively direct: we use bundles of extremely fine electrodes to record the electrical activity produced by hundreds of neurons in the brains of rats and mice as they perform 'taxi-driver' tasks while navigating their way around mazes in search of chocolate. The electrodes used are approximately 15 micrometers in diameter (the average human hair is about 100 micrometers), and up to 128 of them can be monitored simultaneously, 32,000 times per second. Since these electrodes can record simultaneously ➜



Below left: EEG data superimposed on a schematic diagram of a rat brain.

Right: The yellow and white band in this coherogram reflects coordination between neuronal activity in the hippocampus and prefrontal cortex (shown in the upper traces) as rats decide whether to turn left or right to find their chocolate.

➜ from multiple neurons in multiple brain structures, this technology allows us to detail the fundamental nature of the neuronal activity and interactions underlying behaviour.

But what of our own mental health?

A striking feature of neuronal activity in the hippocampus as these rats and mice run around mazes is its rhythmicity: individual neurons tend to fire short, high-frequency bursts of activity about ten times per second (10 Hz). Furthermore, populations of hippocampal neurons become co-ordinated with one another on this timescale, leading overall hippocampal activity to oscillate at about 10 Hz – this is known as the 'theta rhythm'. The brain's net electrical activity can be recorded through electrodes on the scalp, and is known as the electroencephalogram (EEG). Like in rats, the theta rhythm in human EEG recordings becomes prevalent as volunteers perform learning tasks, or navigate around the virtual mazes common in computer games. In fact, human and rodent EEG recordings share many common motifs, including a range of 1-200 Hz rhythms that become prominent in different brain regions and during different types of behaviour and sleep. But are all these brain waves important, or simply phenomenological ripples?

Using multi-neuron recordings in trained rats, we recently demonstrated that the hippocampal theta rhythm becomes synchronised with rhythmic activity in another specialised brain structure – the prefrontal cortex – when rats approach a decision point on a maze. In fact, just by examining the degree of hippocampal-prefrontal synchrony, we were able to predict whether the rat was about to make the right choice (and win his chocolate) or make a mistake. We hypothesised that theta rhythm synchrony allowed neurons in the prefrontal cortex to 'borrow' information from the hippocampus, which was subsequently used to guide the rats' decisions. This is one of many laboratory and clinical observations which suggest that synchronous brain rhythms reflect, or underlie, functional interactions within and between neuronal populations. Neuronal oscillations therefore present a tantalising target for both reading and shaping brain activity. For example, EEG activity can be used as a signal to control prosthetic limbs, and a recent study in Germany showed that rhythmical stimulation of volunteers' brains during sleep improved their memories of previously learned facts.

If the normal brain is complicated, the diseased brain challenges neuroscientists yet further. Most psychiatric disorders cannot be explained by overt pathology in a single brain region, but arise as a consequence of dysfunctional interactions between brain regions. Schizophrenia – which afflicts up to one per cent of the world's population – is thought to involve dysfunctional interactions between the hippocampus and the prefrontal cortex, and similar principles are likely to apply to depression and Attention Deficit Hyperactivity Disorder. All these disorders are associated with abnormal neural synchrony and EEG oscillations, but the molecular and cellular bases of these abnormalities are not known; successful treatments therefore remain elusive.

This is where our neuronal network recordings in rodents come to the fore: measuring co-ordinated, rhythmic activities between the hippocampus and prefrontal cortex in rat and mouse models of schizophrenia constitutes a test system with which to define the cause of the disease and investigate novel therapies. Deciphering the mechanisms and roles of co-ordinated neural activity is therefore fundamental not only to our understanding of normal brain function, but also to the development of animal models of psychiatric disorders, with the ultimate goal of clinical diagnosis and treatment of brain disease in humans.

But what of your own mental health? Well, be sure to compliment taxi drivers on their remarkable feats of neuronal co-ordination. And don't push swords up your nose. ■

www.bristol.ac.uk/Depts/Physiology

Dr Lucy Donaldson (left)
Dr Jan Melichar (right)

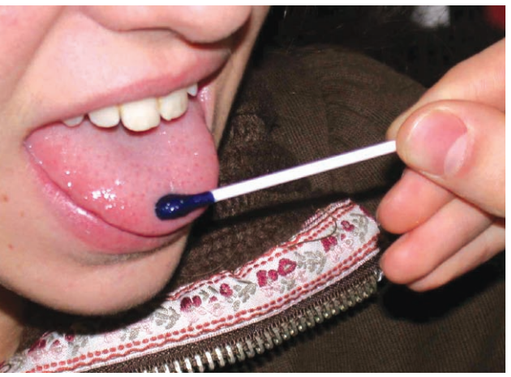
A taste of depression

Many depressed people have reduced appetite and in the severely depressed this may be linked to a reduced ability to detect different tastes. But exactly how depression might affect taste is unknown. Is there really a direct effect – on the taste buds, for example – or could an apparent effect simply be due to a general loss of interest in things? Dr ***Lucy Donaldson*** from Physiology and Dr ***Jan Melichar*** from Community-based Medicine devised a test to find out.

Depression has been linked to a reduction in serotonin and/or noradrenaline levels. In the brain these key chemicals are involved in setting people's mood, but they have also been found in taste buds and are released from taste cells when a taste such as sugar activates the cell. Donaldson and Melichar reasoned that if serotonin or noradrenaline were reduced in someone with depression, the reduction of these chemicals throughout the body might also affect the taste buds and how they respond to different tastes, and that this would effect a depressed person's ability to taste. They therefore decided to test whether changes in these chemicals could directly affect taste by using antidepressant drugs to *enhance* serotonin or noradrenaline levels in healthy volunteers – effectively creating the opposite situation to that found in depression.

> These tests may help us choose the best drugs to treat depression

Tom Heath, a Masters student on the project, first tested the volunteers for their ability to taste four different compounds – sweet, salt, bitter and sour. He then gave them antidepressant drugs that rapidly increased their levels of the neurotransmitters serotonin and noradrenaline. Three different drugs were given: an SSRI (serotonin specific reuptake inhibitor) to raise serotonin levels; an NARI (noradrenaline reuptake inhibitor) to raise noradrenaline levels; and an inactive placebo. Two hours later the volunteers were asked to take the taste tests again.



Taking a taste test.

What Heath found was that when serotonin levels were increased, the volunteers could recognise sweet and bitter tastes at much lower concentrations than when their serotonin levels were normal. The effect on bitter was the most dramatic – the volunteers were able to taste it at concentration levels half of what they had been before being given the drug. The effect on sweet was also profound, with the concentrations of sugar people could taste being lowered by a third.

Increasing noradrenaline levels had different effects – instead of sweet and bitter taste recognition being enhanced, the same people could recognise bitter and sour tastes at lower concentrations. Salt taste did not seem to be affected at all by altering either of the neurotransmitters. Neither did the placebo have any effect, showing that the identified effects were real – ie, the changes in peoples' taste were not because they got better at performing the test or were better at guessing after taking the drugs, but that the drugs directly affected their ability to taste things at different concentrations.

At each testing session the volunteers were also assessed for their anxiety levels and the researchers then ➜ determined whether their overall level of anxiety was related to their ability to taste. Some of the volunteers were quite anxious, and surprisingly, considering that these were normal healthy volunteers with no history of depression or anxiety, their level of anxiety was shown to be related to their ability to taste. The more anxious a person was, the less sensitive to bitter and salt taste they were. Taste is often thought to be determined genetically and, until now, people assumed it was fairly fixed throughout life, but these studies show that the ability to recognise different tastes can be altered by both the neurotransmitters serotonin and noradrenaline, and also by people's mood.

These results, which were published at the end of last year in the *Journal of Neuroscience*, are exciting for taste research as they link previous work where serotonin and noradrenaline were shown to be important transmitters in the taste cells on the tongue with the effects of these transmitters on taste thresholds in normal people. This not only shows us that serotonin and noradrenaline are both important in changing peoples' ability to recognise certain tastes, but it also gives us information on which transmitters signal which tastes. These findings may also explain why anxious and depressed individuals have diminished appetite. In addition, the ability to recognise which tastes are most affected in someone with depression might give us some idea of the neurochemical basis for their disease – do they have reduced serotonin, noradrenaline, or both?

But perhaps the most exciting outcome of this research is the possibility that by identifying which neurotransmitter has been reduced, using these taste tests, we may then be able to chose the best drug with which to treat someone with depression. Until now there has been no easy way of deciding which is the best medication for an individual who is depressed. As a result, we only get it right about 60-80 per cent of the time. It then takes up to four weeks to see if the drug is working or if we need to change it, during which time the person who is depressed may not be getting better. With a taste test we may be able to get it right first time. This research will be extended to look at taste in people with depression and anxiety in order to further explore these possibilities. ■

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Translating research into saving lives

Establishing links between risk factors and the development or progression of diseases can often identify the best ways to prevent and treat them. However, traditional techniques are sometimes unable to work out what is actually causing a disease, because there are so many potential risk factors. To tackle this problem, the University has been awarded funding from the Medical Research Council (MRC) to set up a new Centre for Causal Analyses in Translational Epidemiology. The aim of research done in the centre will be to apply new molecular-based methods to identifying the causes of disease. This approach requires scientists from across several disciplines to work and learn together.

> "Conventional study of patterns of disease has made important contributions to understanding their causes"

George ***Davey Smith***, Professor of Clinical Epidemiology and head of the new MRC Centre, said: "Conventional study of patterns of disease has made important contributions to understanding their causes. A notable example is the work pioneered by Sir Richard Doll that identified the link between cigarette smoking and lung cancer, heart disease and other health problems. Those findings have already saved millions of lives. This centre aims to take this type of work into the 21st century, making full use of the wealth of data and methods we now have at our fingertips."

The Bristol centre is one of six new MRC Centres being set up around the country with the ultimate aim of finding ways to translate research findings into practice. The MRC has provided a total of £15.5 million over the next five years to fund the six centres which will encourage collaboration between scientists working in different disciplines. ■

Are we facing a poverty-stricken old age?

The University's Centre for Market and Public Organisation aims to better understand how to organise and deliver public services, which in turn informs policy-makers. ***Sarah Smith***, Senior Research Fellow in the Centre, was interviewed by Romesh Vaitilingam about her work on pension policy in the UK.

Sarah, tell me, just what is the pension crisis really about?
In the UK the issues are quite different to those faced by a lot of other countries that have more generous state pensions than we do. Without reform, those countries are looking at spending an increasing proportion of GDP on pensions in the future. Now that isn't the case in the UK. Due to reforms going back more than 20 years, state spending on pensions is not likely to increase that substantially as a percentage of GDP, in spite of increasing longevity.

But the system is creaking under a number of different pressures. One of the problems with a less generous state pension is that a lot of pensioners end up living in poverty. New Labour has targeted extra resources at the very poorest of pensioners through increasing means-tested benefits, but that was at the cost of increased complexity and reduced incentives for people to make their own provisions. Currently, around 40 per cent of pensioners receive some form of means-tested benefit; without reform that is set to increase to more than three quarters of pensioners by 2050.

Another problem is what's happening to private pensions. In the UK, many people have enjoyed quite generous occupational pensions linked to final salaries. But for a number of reasons many companies have been closing these schemes and a lot of people haven't been taking out individual personal and stakeholder pensions to replace them. So we have both a declining state pension and fewer people making any additional private provision.

> The system is creaking under a number of pressures

What solutions is the Government proposing?
The Government's recent proposals have three main elements. The basic state pension is going to be more generous and, in the future, linked to earnings, not prices. Partly this is going to be funded out of higher taxes, but partly it is going to be funded by the second main change, which is raising the state pension age from 65 to 68 by 2050. The third element is an attempt to increase the level of private provision via a National Pension Savings Scheme. The Government rejected compulsory additional saving – instead, you will be automatically enrolled in the scheme and will have to make a conscious decision to opt out. The aim with auto-enrolment is to overcome the inertia that often acts as a barrier to saving. Evidence shows that where firms have introduced auto-enrolment into their firm-based schemes, it does have a positive effect. If you are in the scheme, you will have to contribute four per cent of your earnings but, as an additional incentive, the equivalent of three per cent of your earnings will be paid in by your employer and a further one per cent by the government. If you stick with the scheme throughout your working life, that should give you enough for a decent additional pension on top of the basic state pension. ➜

➜ So assuming these proposals are implemented, who would be the winners from the changed system and who would be the losers?
For those at the bottom in terms of pension income, the set of proposals doesn't really help very much, it just changes the form of help they get. Currently, they get money in the form of means-tested benefit; in the future, they will get it as a basic state pension. However, because benefits don't get through to everyone who needs them – some people don't claim through stigma or ignorance – the shift to higher state pension will help. But generally, if you are claiming the full amount of means-tested benefits, you won't gain in terms of the amount per week that you get. In fact, if you take into account the fact that those on lower incomes tend to have a shorter life expectancy, the increase in the state pension age will be a bigger hit out of their total pension income. Those who are better off will lose relatively less from the increase in state pension age and will tend to gain from having income in the form of a basic state pension, rather than means-tested benefits.

> Raising the state pension age from 65 to 68 may not encourage people to work longer

And finally, do you think the Government has come up with proposals that will work?
The proposals go some way to addressing the problems in the current system but there is a possibility that this is not the final set of proposals we will see in the next few years. The future growth of means-tested benefits will be less, but still around one third of pensioners are predicted to receive some money from means-tested benefit by 2050. I think auto-enrolment and the National Pension Savings Scheme will give some people the push through the door they need to start saving, but I am not sure it will achieve the same kind of results as it has in individual firms. Where auto-enrolment has been introduced by individual firms, it has been the employer driving the process. That's completely different to introducing a scheme nationally, when many employers are going to be quite resistant to something they have to contribute three per cent to. And if people don't have additional savings, they are going to have to rely on a fairly low basic state pension in retirement.

Finally, raising the state pension age from 65 to 68 may not be enough to encourage people to work longer. Many people are retiring in their 50s and 60s, well before the current state pension age; those who are less well qualified may face barriers to getting employment, others may leave work on health grounds. These people aren't necessarily going to work longer because the state pension age has increased, and they may find themselves facing real hardship if they don't qualify for a state pension until they are 68. ■

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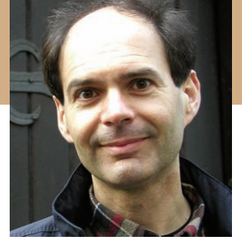

The Neanderthals: human ancestors or aliens from outer time?

The first humans appeared in Africa some two million years ago and, soon after, dispersed into Asia and Europe. Subsequent geographic and genetic isolation eventually led to the differentiation of two lineages: Homo sapiens in Africa, and Neanderthals in western Eurasia. ***João Zilhão***, Professor in Palaeolithic Archaeology, from the Department of Archaeology and Anthropology, puts the case for our badly misunderstood cousins.

Above: Pierced and grooved pendants from Châtelperronian level X of the Grotte du Renne, France, which also yielded skeletal remains of their Neanderthal makers.

Opposite page: The Oase 2 cranium (top) and the Oase 1 mandible (below), Europe's earliest modern human fossils, feature diagnostic Neanderthal traits.

Almost since their discovery in 1856 Neanderthals have suffered from a bad press, especially in the English-speaking world, where the term entered daily language as a widely used deprecating adjective. Nowadays, such views of Neanderthals as the archetypal cavemen are no longer found in academia; nevertheless, the predominant view still is that they should be construed as a side branch of humanity, a dead-end of evolution, both distinct from and somewhat inferior to *sapiens* people. Such a prevalence largely arose from the fact that mitochondrial (mt)DNA studies of present populations, coupled with mtDNA data extracted from Neanderthal fossils, have provided much support for the notion that today's humans descended entirely from a second out-of-Africa dispersal of evolved *Homo sapiens* that took place some time after 60,000 years ago. Upon arriving in Europe, where their earliest fossil represent-atives are now dated to between 40,000 and 42,000 years ago, the theory continues, these modern humans would have out-competed local populations as a result of being superior in cognition, culture and adaptation; for the Neanderthals extinction would have been swift, leaving no descendants.

The out-of-Africa expansion of modern humans involved interbreeding with Neanderthals

Thanks to new insights and new finds during the past decade, this notion of the Neanderthals' fundamental 'otherness' is on the wane. Where the fossil record is concerned, it is now clear that all early European modern humans feature a diverse mix of skeletal features that are either diagnostic of Neanderthals, or that correspond to generically primitive traits that had been lost in the African lineage prior to dispersal into Eurasia. A case in point is the fossils from the Oase cave (Romania), which I ➜

➜ excavated and study in collaboration with Erik Trinkaus (Washington University, St. Louis). A skull found there had the same proportions as modern human crania and shared a number of modern human features. However, there were some important differences, which included frontal flattening of the face, a large bone protuberance at the base of the skull and exceptionally large upper molars, all features found principally among Neanderthals.

This evidence suggests that the out-of-Africa expansion of modern humans involved interbreeding with the Neanderthals. Once closer and more intensive contact was established, the small, peripheral gene pool – Neanderthals – underwent assimilation, not extinction. Further support for this theory is found in the fact that in the many lineages of mammals for which fossil or molecular data are available, the minimum amount of time required for complete reproductive separation is some 350,000 generations or, in humans, seven million years. This is at least ten times more than is estimated for the Neanderthal/*sapiens* split (500,000 years, or 25,000 generations ago) and carries the implication that, at the time of contact in Europe, some 42,000 years ago, interbreeding would have resulted in viable, fertile offspring.

Data provided by important genetic studies published in November 2006 are also consistent with this suggestion of interbreeding. One study concluded that a variant of a gene involved in the control of brain size (*microcephalin*), and now found in 70% of today's humans, was introduced some 37,000 years ago into the *sapiens* lineage from an archaic lineage – most probably Neanderthals. The second study, from the Max Planck Institute in Germany, announced preliminary results from the Neanderthal genome project, which aims to sequence the entire nuclear DNA from extracts of a Neanderthal bone. Looking at sites in the DNA molecule where we can investigate how often the Neanderthal had the ancestral (that is, the chimpanzee) or the derived (that is, the human) variant, they found the derived one in 30% of cases. Given the estimated time of divergence between Neanderthals and modern humans, the team concluded that such a high percentage implied gene flux between the two lineages, due to interbreeding.

This conclusion is of great significance because the Neanderthal individual sequenced by the German team *predates* by many millennia the actual dispersal of modern humans into the European continent. The inescapable implication is that, despite geographical isolation and ensuing morphological differentiation, gene flux between Europe and Africa was never completely interrupted and, therefore, biologically, Neanderthals and modern humans must be construed as different populations of a *single* species, not as different species.

This new fossil and genetic evidence dovetails nicely with the rapidly increasing body of archaeological data showing that, at the time of contact between late European Neanderthals and immigrating modern humans, both lineages had attained comparable levels of cultural achievement. Over the past ten years, working in close partnership with Francesco d'Errico, in Bordeaux, and other French colleagues, I have been able to demonstrate that the Châtelperronian – an archaeological culture with sites extending from the Paris basin in the north to the Spanish Basque country in the south – is an independent Neanderthal development. The significance of this finding resides in the fact that, with its objects of personal ornamentation and decorated bone tools, the Châtelperronian has ➜

Neanderthals and immigrating modern humans attained comparable levels of cultural achievement

Oase skull in situ.

➜ been widely recognised since the 1960s as the first stage of the artistic and symbolic 'revolution' of the European Upper Palaeolithic period.

At the same time, German colleagues were producing evidence for the sophisticated cognitive and intellectual capabilities of the Neanderthals derived from artefacts related to more mundane subsistence activities. Analysis of two fragments of birch bark pitch used for stone tool hafting recovered at the site of Königsaue, on the margins of the Aschersleben paleolake, in Saxony-Anhalt, and directly dated to more than 50,000 years ago, showed that they had been produced through a smouldering process several hours long, that required a strict manufacture protocol: under exclusion of oxygen, and at tightly controlled temperatures (between 340 and 400°C). These items document the manufacture by Neanderthals of the first artificial raw material known in human history, a feat of chemistry that experimental archaeologists have so far been unable to replicate using Palaeolithic technology alone. Last year, the same kind of pitch was reported from a site in Italy dating to more than 120,000 years ago, giving extended time-depth to the evidence for advanced cognition in the Neanderthal lineage.

If one were to form an opinion on the basis of how Neanderthal-related scientific discoveries are reported to the public, one would hardly guess that this much-revised view of Neanderthals as a cognitively sophisticated, fully human part of our ancestry has already been endorsed by a significant number (if not a clear majority) of archaeologists and palaeoanthropologists directly involved with the research. Thus one of the most fascinating features of contemporary studies of the origins of modern humans lies in the continued popularity, particularly in the media and more conservative quarters of the academic world, of traditional views of the Neanderthals as aliens – not from outer space but from outer time. Although there are reasons to be found strictly in the domain of the scientific history of the subject, the particular role played by Neanderthals in late 19th-century debates over evolution goes a long way to explain such current attitudes.

> The first artificial materials known in human history were manufactured by Neanderthals

At that time, Neanderthals were used as supporting ancillary evidence in mainstream ethnological views of the racial ladder, to which they added a temporal dimension. Today, ranking human races is no longer acceptable but, in western culture, the philosophical or religious need to place 'us' at the top of the ladder of life is still very prevalent and explains the continued search for images of what 'we' are *not* (or *not anymore*) that, by contrast, enhance the basics of what 'we' *are*. Thus, depending on different perceptions of the fundamental basis for the triumphant status of civilized society and industrial capitalism, so the tendency arose for Neanderthals to be represented as lacking in the corresponding behavioural features. For instance, to give but a few examples, the Enlightenment emphasised the power of reason, Adam Smith stressed the importance of the division of labour, and David Ricardo explained the role of international trade and comparative advantage. And, sure enough, explanations for the demise of the Neanderthals have variously postulated competitive inferiority caused by their lack of symbolic cognition, labour specialisation and long-distance circulation of raw materials.

The fact that such propositions are demonstrably in complete contradiction with the empirical record does not seem to deter their uninterrupted flow. This suggests that the Victorians were not completely wrong, Neanderthal studies do have the potential to bring progress not only to the understanding of past humans as *they* were in the past but also to the understanding, through philosophy, sociology and the historiography of science, of present humans as we are in the present. Put another way, despite the apparent cacophony, the field of Neanderthal studies has at least one uncontroversial conclusion to offer: that Neanderthals should not be left to archaeologists and palaeoanthropologists alone. ■

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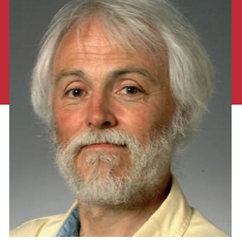


Professor Peter Fleming (left)
Dr Peter Blair (right)

Back to sleep during the day

In the mid-1980s it was recognised that the number of babies dying from Sudden Infant Death Syndrome (SIDS, commonly referred to as cot death) had increased in many countries, but no-one knew quite why.

Peter Fleming, Professor of Infant Health and Developmental Physiology, was just starting the Avon Cot Death Study when he read a Dutch report which suggested that putting babies to sleep on their fronts led to a high risk of cot death. Fleming immediately analysed the Avon data and found that indeed, 93 per cent of the babies who had died had been put to sleep lying on their fronts.

Initially researchers refused to believe that something as simple as this could have such a profound effect and it wasn't until a follow-up study in 1991 that Fleming felt confident enough to approach the government's health advisers with his findings. Following a high profile campaign on the issue by TV presenter Anne Diamond – who lost her own child through SIDS – the Government gave its official support to the study and launched the highly successful *Back to Sleep* campaign. As a direct result, cot deaths across the country fell by 70% – the equivalent of saving 12 babies a week.

Since then, much work has been done on this distressing syndrome, by Fleming and others, and parents have further been advised that for the first six months the safest place for a baby to sleep is in a cot by the parents' bedside. But new research by Dr ***Peter Blair***, a Senior Research Fellow working alongside Fleming, reveals that this advice is just as important for an infant's day-time naps as it is for their night-time sleep.

> Day or night, the advice is the same

The new study found that the babies who died during the day were more likely to have been placed on their side than on their back for their day-time naps; they were more likely to be found with their heads covered by the bedclothes than the babies who didn't die; and, in particular, 75 per cent of the babies who died in the day-time were sleeping in a room where there was no adult present.

One important aspect of the study looked at the time that had elapsed since the baby was last seen alive. Three quarters of the infants who died during the night were observed alive after midnight; a fifth were still alive within two hours of death. Of those who died during the day, over a third were alive 30 minutes prior to death and nine per cent were alive within 10 minutes of death. The fact that most parents described their infants as seeming to be well the last time they saw them alive suggests that for some of these deaths the onset of the final event was very quick. The protective effect of having an adult in the same room as the sleeping infant is therefore important as it may reduce the risk of young infants rolling onto their front, or bedclothes covering their head.

In summary, most of the risks associated with SIDS were significant for both night-time and day-time deaths, although the fact that the father smoked was only significant for night-time deaths, and placing infants on their side to sleep was more marked amongst the day-time deaths. So fundamentally the advice remains the same – put your baby to sleep on its back – whether it's at night or during the day. ■

Dr Jemma Wadham (left)
Dr Jon Telling (right)

Building

Antarctica in central Bristol

The search for life on other planets, and research into climate change, will be the focus for top scientists and glaciologists using the recently-opened LOWTEX laboratories in the School of Geographical Sciences. Dr ***Jemma Wadham***, Director, and Dr ***Jon Telling***, Experimental Officer, explain how these state-of-the-art facilities will help in their quest for a better understanding of our planet.

The cryosphere is that part of the Earth that contains water in its frozen state. This includes glaciers, seasonal snow, lake ice, sea ice, ice caps, ice sheets and permafrost. Somewhat surprisingly, the cryosphere covers more than 60 per cent of the Earth's land surface, so an understanding of the cryosphere and its relationship with the rest of the Earth system is essential to understanding the past, present, and future behaviour of the Earth as a whole.

We once thought these icy settings were very barren environments, but we now know them to be viable habitats for microbial life. As such, they also serve as possible model habitats for life on other icy terrestrial planets, such as Mars and the moons of Jupiter. Many microbes in icy ecosystems are adapted to extreme conditions and play a role in regulating key biogeochemical cycles on Earth. Permafrost environments, for example, are significant producers of the greenhouse gas methane, known to be a significant contributor to global warming. Knowledge of the survival mechanisms utilised by such microbes and their role in biogeochemical cycles is therefore required in order to understand the evolution and persistence of life on Earth, and feedback between the climate and the Earth's biosphere. The LOWTEX (LOW Temperature EXperimental) facilities will thus provide key analytical and experimental facilities that are required to improve our understanding of extreme icy environments.

Achieving a full understanding of biogeochemical processes in such places is currently limited by a lack of instruments that can be used for *in situ*, remote monitoring. Chemical and biosensors that can be used to infer life-mediated processes, or the characteristics of life itself, just do not exist for these extreme ecosystems. This programme unites the efforts of glaciologists, space scientists, oceanographers and biotechnologists derived from six UK universities and aims to develop sensing technologies for icy environments. The temperature-controlled facilities in LOWTEX will provide the testing site for such chemical and biosensors as they are developed. As Wadham said of the facilities: "One of the key ways to better understand the effect of climate on the polar regions is to recreate these icy environments close to home."

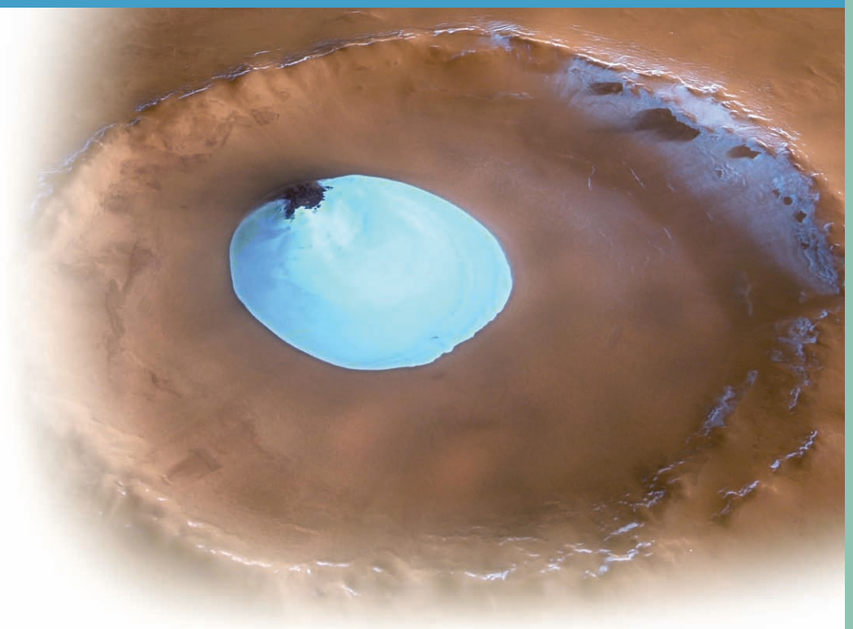
Another project looks at whether the melting of glaciers might be accompanied by the release of methane trapped at the glacier bed, thereby amplifying the effects of global warming. Significant populations of micro-organisms have recently been found beneath such ice masses, but almost nothing is known about the carbon sources for these microbes (ie, what do they live on and where does their food come from?); the rates of microbial activity; and the full spectrum of products (gases) that they emit. This information is important for understanding the global carbon cycle on Earth. The fate of large amounts of organic carbon

> Permafrost environments are significant producers of the greenhouse gas methane

One of the projects already underway includes the development and testing of miniaturised sensors to detect life in icy environments on Earth and Mars.

during the advance of the glaciers over the boreal forest during the last Ice Age, for example, is unknown and is likely to depend fundamentally ➜

Bottom left: Part of LOWTEX's analytical facility
Below: Residual water ice in Vastitas Borealis Crater. Photo: ESA



> One way to understand the effect of climate on the polar regions is to recreate icy environments close to home

➜ on microbial processes in sub-ice environments. The possibility that this carbon is used by subglacial microbes and converted to carbon dioxide and methane has not previously been considered, but it may explain the variation in the Earth's atmospheric greenhouse gas composition seen over the last two million years.

This last project represents an international effort, led from Bristol University, aimed at constraining details of the subglacial carbon cycle for the first time. It will also address the question of whether subglacial environments could be significant sources of greenhouse gases during periods of rapid ice wastage. Analytical and experimental investigations of microbial activity will be undertaken in LOWTEX and in specialist laboratories in the School of Chemistry and Department of Earth Sciences.

LOWTEX will become a unique national facility for cryospheric biogeochemical research. At its core is a series of seven temperature-controlled walk-in cold rooms for experimentation and sample storage, supported by a suite of interconnected wet/sediment laboratories for biological and non-biological sample preparation. LOWTEX also houses a research-grade analytical laboratory, with the latest instrumentation for the biogeochemical analysis of dilute solutions. The commissioning of LOWTEX reflects wider UK research council interest in the 'hot' scientific areas of climate change and life in extreme environments. To reflect this interest, LOWTEX has received almost £2 million in investment over the past 18 months from research councils, the University, and the EU.

The launch of the laboratories took place in Mongolian yurts on the only day of the year that Bristol had any snow. Frozen vodka shots were handed round to break the ice and chill-out tunes were provided by the *Poles Apart* string ensemble. Let's hope that the research done at LOWTEX will help prevent such freezing conditions becoming a regular feature in Bristol. ■

www.ggy.bristol.ac.uk

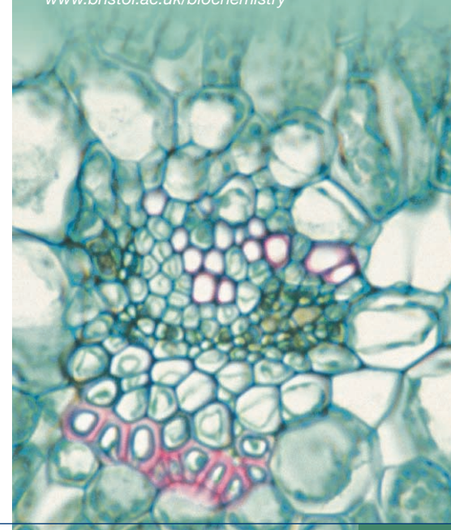
RESEARCH REVIEW • APRIL 2007

Turning off cancer

A way of switching off the development and growth of certain cancer cells has been identified by scientists at ProXara Biotechnology Limited, a spin out company from the University of Bristol, UK. Results to date have proved so positive that the University team now plans to develop the drug compound to a point at which it would be close to entering clinical trials, using funding of £2.8 million from the Wellcome Trust's Seeding Drug Discovery initiative.

The ability of cells to commit suicide, or apoptosis, is an important and normal process in the body's development. All cells contain an enzyme called protein kinase B (PKB) which, when activated, triggers a signal that prevents apoptosis.Certain types of genetic damage, common to many cancer cells, lead to the movement of PKB from the interior of the cell to its surface membrane. When this happens, PKB becomes active, halting apoptosis. *Professor Tavaré*, lead scientist on the project, believes that by preventing PKB binding to the cell's membrane he can ensure that apoptosis continues, thereby driving the cancer cells to commit suicide and preventing them from forming tumours. ■

www.bristol.ac.uk/biochemistry





From left: Dr Rich Pancost, Professor Paul Valdes and Ian Ross

In our opinion…

Science in the public spotlight

Man's role in causing climate change has been a topic of much interest over the past 30 years. It is a primary focus of UK and international scientific strategy and a political issue that guides public policy. It may also decide elections. As with all such issues, a major arena for debate is the media but, just as there are many sensible articles discussing climate change and, in particular, global warming, there are just as many that distort and misrepresent the science. Dr ***Rich Pancost***, Professor ***Paul Valdes*** and ***Ian Ross***, on behalf of the University's Global Change Initiative, put their side of the argument.

The University contains many scientists, across many departments, who investigate both modern and past processes in order to better anticipate future climate change. Although there are many nuances to the problem that demand further study, we consider that some key aspects of global warming are now known, and that these should provide an unambiguous foundation for such debates:

1. Carbon dioxide concentrations in the atmosphere are increasing due to human activity.
Carbon dioxide concentrations are higher now (approximately 380 ppm) than they have been for the past 650,000 years (between 190 to 290 ppm). Human activity has been directly implicated as the cause of this increase by direct measurements of CO_2 inputs and a shift in the isotopic composition of CO_2 towards a 'fossil fuel signature'.

2. The concentrations of other greenhouse gases have also increased.
The most striking example of this is methane, the concentrations of which have increased from approximately 700 ppb to 1800 ppb over the past 200 years, despite being below approximately 700 ppb for the previous 650,000 years.

3. Increased CO_2 concentrations will cause global warming.
It is important to realise that atmospheric CO_2 concentration is not the main control on the Earth's climate – the sun, albedo (how much incoming light is reflected) and water vapour all have a much greater effect. However, due to the ability of CO_2 to absorb infrared radiation, any significant changes in its concentrations alter the energy balance of the Earth and this causes a change in the climate. It is not yet clear what impact the current rate of carbon dioxide release will have on the climate system over the next 100 years, but the uncertainty is related to the magnitude, which could range from 1°C to 5°C of warming.

4. The Earth's climate varies naturally.
Examination of the geologic record indicates that the Earth's climate has varied widely over billions of years; in fact, some changes are probably more dramatic than human activity will ever achieve. However, those ➜

> There seems to be evidence that humans have caused 0.6°C of warming since the 1960s

➜ changes generally occurred over millions of years. Even climate variability on shorter timescales appears far less dramatic and much slower than the changes observed in the past 100 years.

5. The climate has warmed by about 1°C over the past 100 years, which is greater than natural temperature variation over the previous 1,000 years.
This particular point has been the focus of a great deal of debate because warming trends do not perfectly match the change in carbon dioxide concentrations. However, this appears to be due to the multiple controls on the Earth's temperature, including the influence of volcanoes and solar activity. Those controls are routinely incorporated into climate models but over and above them there seems to be evidence that humans have caused 0.6°C of warming since the 1960s.

These points are supported by numerous observations but, as with all topics that are truly worth understanding, simplistic explanations rarely reveal the whole truth and our current understanding is incomplete. So with a view to informing the debate, we are currently constructing a list of frequently asked questions regarding climate change that will address these issues in greater detail than can be covered here, or is typically presented in the media. We hope that this will clarify which aspects of global warming are well understood, highlight those that are not, and provide a helpful guide to people interested in understanding how humans affect the Earth's climate.

This page is available at www.paleo.bristol.ac.uk. We invite you to take a look and give us your comments. ■

www.chm.bristol.ac.uk
www.ggy.bristol.ac.uk

15 minutes of football?

A report by Professor ***Andy Ness*** and his 'Children of the 90s' team at Bristol, together with Professor ***Chris Riddoch*** from Bath University, offers new hope for parents concerned about the growing obesity epidemic. It suggests that making even small increases to a child's daily exercise routine, such as walking them to school instead of taking the car, could have dramatic long-term results.

While a poor diet and lack of exercise have long been known to cause obesity, what researchers have been unable to discover until now, is exactly how major a role activity plays in the battle to keep obesity at bay. Using the latest techniques, they discovered that doing 15 minutes a day of moderate exercise lowered a child's chances of being obese by almost 50 per cent. As long as the activity was at least at the level of a brisk walk – enough to make your child a little out of breath – it seemed to be of benefit.

Researchers monitored 5,500 12-year-olds from the 'Children of the 90s', a unique ongoing research project based in the University that enrolled 14,000 mothers during pregnancy in 1991-2, and has followed most of the children and parents in minute detail ever since.

Each child wore a special 'Actigraph activity monitor', which sits on a belt around the waist and records their activity levels for 10 hours a day. Most wore the movement-sensitive monitor for a week but all used the Actigraph for at least three days. They also had their body fat measured using an X-ray emission scanner, which differentiates both muscle and fat deposits in the body.

Professor Ness commented how even modest increases in physical activity could lead to important reductions in childhood obesity. ■

www.alspac.bristol.ac.uk

Dr Christopher Lowry

Professor Graham Collingridge

New insights into the brain

Getting dirty may lift your mood

Work by Dr ***Christopher Lowry*** in the Laboratories for Integrative Neuroscience and Endocrinology, and colleagues from UCL, has identified novel mechanisms through which the immune system can signal to the brain to influence behaviour and emotional state.

In studies of mice they identified a small group of neurons containing the neurotransmitter serotonin that was activated by the 'friendly' bacterium *Mycobacterium vaccae*, normally found in the soil. Treatment of mice with *M. vaccae* led to increases in serotonin metabolism in the prefrontal cortex, a region of the brain involved in cognitive function and regulation of mood. The lack of serotonin in the brain is thought to cause depression in people, thus *M. vaccae's* effects on the behaviour of mice may be due to increasing the release of serotonin in parts of the brain that regulate mood. Indeed, treatment with *M. vaccae* led to antidepressant-like behavioural responses.

The authors hypothesise that this small group of serotonin neurons normally increases the ability to cope with stressful life events, but when the system is over-activated, for example by prolonged immune activation or chronic stress, it can desensitise, leading to an inability to effectively cope with everyday stress (a common feature of major depression). The work raises interesting questions relating to how the body communicates with the brain to regulate our behaviour and our emotions. It also help us understand how the body communicates with the brain and why a healthy immune system is important for maintaining mental health.

> "This research makes us wonder if we shouldn't spend more time playing in the dirt"

LAURA ROSA BRUNET

Colonies of *Mycobacterium vaccae*.

The interest in *M.vaccae* arose following its discovery in soil samples from the shores of Lake Kyoga in Uganda when colleagues were looking for a bacterium that could help the human immune system respond to virulent bacteria like *M. tuberculosis*, which causes tuberculosis. Subsequently, they found that *M. vaccae* was also an effective vaccine for leprosy and could improve the autoimmune symptoms of leprosy patients free from bacterial infection. Since then, *M. vaccae*-based products have been evaluated in clinical trials for the treatment of asthma, cancer and tuberculosis.

Interest in the antidepressant qualities of *M.vaccae* emerged after human cancer patients treated with *M. vaccae* unexpectedly reported increases in their quality of life. Lowry and his colleagues reasoned that this effect could be mediated by activation of serotonin-containing neurons in the brain. The new research supports this hypothesis but future studies will be designed to determine if *M. vaccae* or other bacteria have antidepressant properties, through activation of this group of serotonin neurons. ■

www.bristol.ac.uk/clinicalsciencesouth/dhbg/dhbg.html

Laying down memories

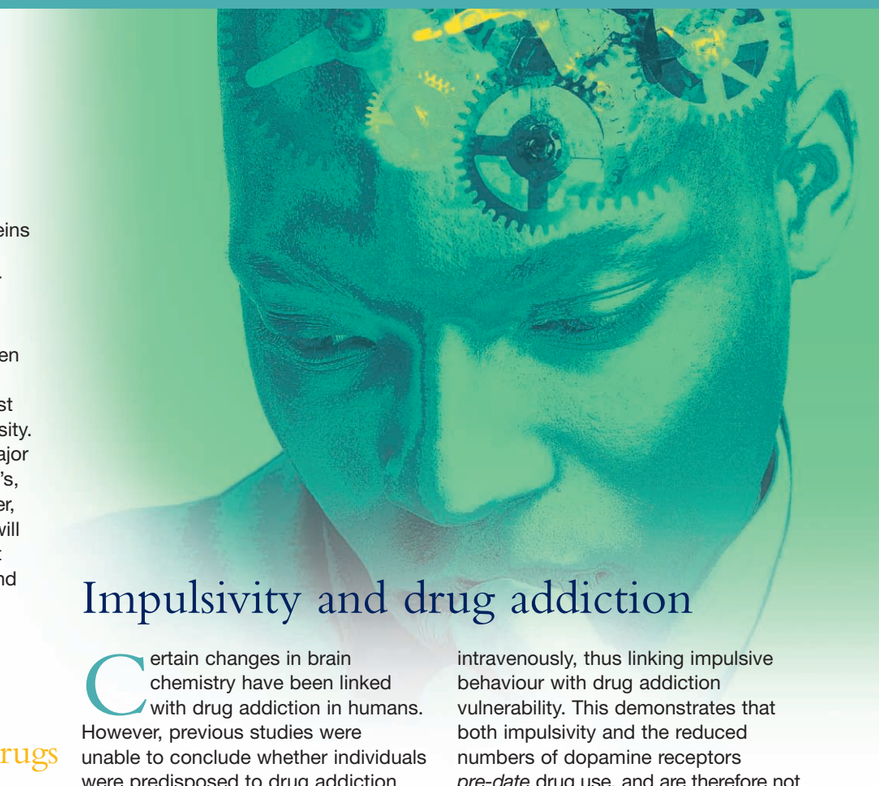
Enzymes are important proteins in the body that speed up chemical reactions of other substances, without themselves being destroyed. The function of one enzyme in the brain – glycogen synthase kinase-3 (GSK3) – has recently been identified for the first time by researchers at the University. Strongly linked to a number of major brain diseases such as Alzheimer's, schizophrenia and bi-polar disorder, our new insight into this enzyme will help in the understanding of what goes wrong in these disorders, and how memories are laid down.

> "This research will help pharmaceutical companies develop drugs to inhibit GSK3 when things go wrong."

Professor ***Graham Collingridge*** and his team from the Department of Anatomy, with colleagues from the University of British Columbia, revealed in the journal *Neuron* that the activity of GSK3 regulates a form of 'cross-talk' between the two major forms of synaptic plasticity in the brain. Synaptic plasticity is the strength of a connection between neurons and forms the basis of learning and memory. The research showed how controlling the activity of GSK3 might prevent a memory being erased by improving the strength of connections between neurons, thus allowing better consolidation of new information.

Professor Collingridge said: "While GSK3 has previously been implicated in major neurological disorders, until now its role in normal neuronal function has been largely unknown. Our new understanding will help pharmaceutical companies develop drugs to inhibit GSK3 when things go wrong." ■

www.bristol.ac.uk/Depts/Anatomy



Impulsivity and drug addiction

Certain changes in brain chemistry have been linked with drug addiction in humans. However, previous studies were unable to conclude whether individuals were predisposed to drug addiction because of these chemical changes, or if chronic drug use itself caused the chemical changes in the brain.

Dr ***Emma Robinson*** from the Department of Pharmacology, and her colleagues at the Cambridge Behavioural and Clinical Neuroscience Institute, may have resolved this debate. Using positron emission tomography (a PET scan), the team discovered that rats that were behaviourally impulsive, but which had not been exposed to drugs, had significantly less brain dopamine receptors than their more restrained counterparts. Dopamine is a neurotransmitter in the brain that has been implicated in the rewarding effects of drugs of abuse. These changes in dopamine receptors suggest that the animals may have altered sensitivity to reward.

> "The findings could help us understand why some individuals are more susceptible to drug addiction."

Additionally, these same impulsive rats were found to be considerably more likely to self-administer cocaine intravenously, thus linking impulsive behaviour with drug addiction vulnerability. This demonstrates that both impulsivity and the reduced numbers of dopamine receptors *pre-date* drug use, and are therefore not the result of prolonged drug addiction.

The new findings, published in *Science*, one of the world's most prestigious journals, may lead to more targeted treatments for drug addiction and other compulsive behaviour disorders, with less side effects than current alternatives.

Government reports estimate there are up to half a million individuals addicted to Class A drugs in England and Wales. This new research should help understand why and how people become addicted. Dr Robinson said "The findings may have important ramifications for a range of addictive substances and could help us understand why some individuals are more susceptible to drug addiction."

The next step is to identify the gene or genes that cause this diminished supply of brain receptors. ■

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Public Relations Office
Communications & Marketing Services
University of Bristol
Senate House
Tyndall Avenue
Bristol BS8 1TH

www.bristol.ac.uk
Email: re-search@bristol.ac.uk

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