

# YOUR MENTAL HEALTH

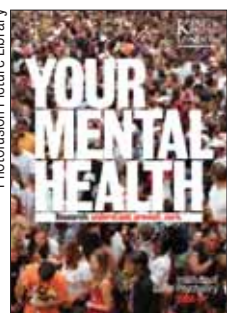
Research: **understand, prevent, cure.**

Institute of  
Psychiatry  
**2008-9**

Scientists and researchers who work at the Institute of Psychiatry (IoP) in south London are dedicated to finding out more about mental health problems and diseases of the brain. Their ultimate goal is to develop treatments and services that can cure or dramatically improve people's quality of life, and to eventually prevent mental illness and brain disease from developing.

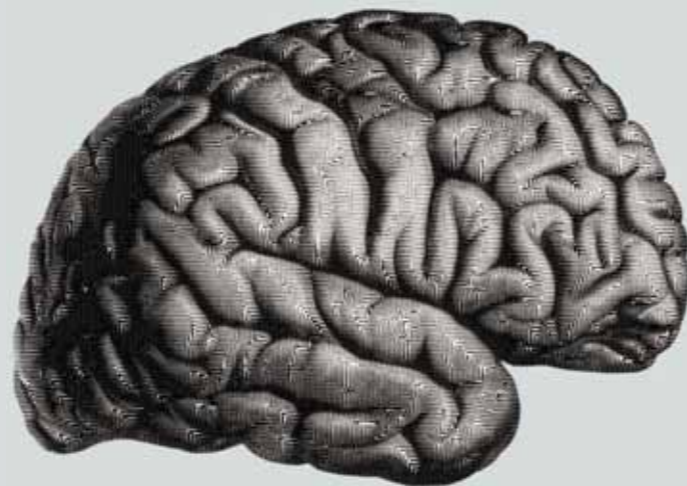
Many of them also work directly with people who have mental ill health and neurological disorders in clinics and wards run by South London and Maudsley and King's College Hospital NHS Foundation Trusts. In turn, many of these service users and their families participate in the IoP's research projects, some of which are highlighted in the pages of this publication.

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The contents of this report are not a comprehensive list of the work carried out by the IoP: its portfolio also includes, for example, research into motor neurone disease, obsessive compulsive disorder, personality disorder, the mental health needs of children who are adopted and fostered, amnesia, depersonalisation, the mental health of people with cancer and other physical illnesses, including chronic pain and insomnia. For information about all of the work of the IoP, visit [www.iop.kcl.ac.uk](http://www.iop.kcl.ac.uk)

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## What's in a brain?

The human brain is probably the most complex structure in the known universe. That is why understanding brain function – and brain dysfunction – presents such a challenge.

Perhaps the simplest concept to begin with is that the brain is composed of billions of cells, each smaller than the full stop at the end of this sentence. There are more types of brain cells than we can even count, but they all fall into one of two groups. They are either neurons, the 'communicating' cells, or glia, the 'support' cells. Two types of glia – astrocytes and microglia – are immensely important in the brain's response to injury and disease.

The neurons carry information around the brain and beyond. For example, nerve fibres (called 'axons') from neurons in the spinal cord have to reach all the way to the toes in order to move muscles, or bring back sensations of touch, temperature or pain. The brain is divided into different regions (such as the cerebral cortex, the thalamus and the hippocampus) with different responsibilities and functions, and all are connected by tracts of millions of such axons. The precision of this wiring is what assures normal brain function, and it is the loss of this precision that underlies brain disease. Sometimes the dysfunction is a subtle disruption of information flow, as in schizophrenia, autism or depression. Sometimes, however, the cause is the death of the neurons themselves, as happens in neurodegenerative diseases. Unlike tissues such as liver or skin, the brain has a very limited capacity to replace lost cells. So once neurons are lost, they are gone for ever. However, there is hope that neural stem cells might provide a therapy for neurodegenerative diseases precisely because they can replace lost brain cells.

The number of cells is just the start of the complexity of the brain. Not only are there billions of neurons, each neuron has as many as a thousand contacts with other neurons. The result is a brain with computing power IBM can only dream of. Information is carried by axons in the form of electrical signals, but the signals are not the same 'electricity' that runs through a power socket. They take the form of a slower current carried by electrically-charged sodium, potassium and calcium atoms: one reason why we need such substances in our diet. The contacts between neurons are called 'synapses'. This is where the axon from one neuron connects with the next nerve cell to create neural networks or 'brain circuits' that drive thought, emotion, memory and all mental activity, and govern all the physical activity of our bodies.

As the electrical signal moving along an axon arrives at the synapse, it performs a complicated trick. The 'electrical' signal is converted into a 'chemical' signal. The chemical produced – a 'neurotransmitter' – diffuses across the small gap that separates the two neurons at the synapse, so causing the next neuron in the chain to 'fire', thus propagating the signal. The receiving neuron in the synapse recognises the neurotransmitter signal by means of 'receptors' on its surface. There are many different neurotransmitters (like dopamine and serotonin) used by brain cells, each with their own receptors. Indeed, most neurotransmitters have multiple different receptors – D1, D2, D3, and D4 for dopamine, for example – adding even more to the complexity.

Brain cells, synapses, neurotransmitters, receptors, and indeed every element required to construct a human body, are made up of proteins. A third of all the proteins that contribute towards the whole are exclusive to the brain. A gene is essentially the set of instructions required for a cell to make

a protein. So when we say 'the gene for the D1 dopamine receptor,' what we really mean is 'the bit of chromosomal DNA that carries the instruction of how and when to make the D1 receptor protein.' Proteins vary enormously in their function: they include enzymes that assist in making (or inactivating) the neurotransmitters, or in transmitting the signal from the synapse to the rest of the neuron. Any problem with the gene is likely to transmit itself to the protein, which in turn results in altered activity. Out of that emerges altered brain function. It is these changes that probably ultimately explain the brain changes associated with disease. But as well as being the essence of the problem, these changes also hold out the prospect for diagnosis. This is the concept of 'biomarkers' – detectable changes in proteins in blood or some other body fluid that might allow us to measure otherwise invisible disease processes.

We already know that some mental illnesses are partly caused by genes inherited from parents, and partly caused by environmental factors such as stress, drug-taking or brain injury. We are beginning to learn more about epigenetic factors, chemical changes to the genes that do not change the genetic code itself, but do influence how the code is read, and can themselves be caused by environmental factors, such as diet and maternal care.

In the past, scientists relied on studying the anatomy of the brain to try to understand more about function and dysfunction. Today, grasping its complexities is made easier thanks to modern imaging technology that allows us to literally see the brain in action, and sophisticated machinery that can analyse proteins and DNA. Finding out more about how cells work at the most basic level while at the same time learning about the role of environmental factors takes us ever closer to prevention and cure. ■

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# Preventing teenage binge drinking



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Practical support and counselling to make young people understand more about their personalities, and why they feel the urge to behave in a certain way, can help them steer themselves away from binge drinking and alcohol dependency.

The school-based *Preventure* programme has been proven in two studies to cut down on drinking and improve mental well-being in teenagers at risk of misusing alcohol because of certain personality traits.

'There has been a lot of research looking at psychological risk factors for addiction, concentrating on temperament and personality,' said Dr Patricia Conrod, an Action on Addiction Research Fellow who developed and successfully evaluated the programme in Canada before joining the IoP.

'We know there are four personality traits that are risk factors for alcohol misuse, and that they are very strong predictors of who goes on to have problems in later life.'

These traits, she says, are the product of an interaction between genetic and environmental factors, which 'converge during a critical period in adolescence to influence personality and behaviour.'

The *Preventure* programme targets young people who are full of hopelessness, who are depression-prone and expect the worst to happen; those who are full of anxiety, fearful, shy, and keep away from public attention or anything that puts them centre stage; those who are the impulsive type, for whom alcohol over-use is one of a spate of behavioural problems, who put no stops on their behaviour; and those who are the thrill-seeking type – not necessarily impulsive but consistently looking for new and exciting experiences. The latter are those most likely to binge drink in early adolescence, she said, and the most recent London-based trial of *Preventure* is showing a 'robust effect' on this harmful behaviour one year after teenagers

participated in the programme's two 90-minute group sessions at school.

The trial has shown that those with the thrill-seeking trait who were given only regular curriculum-based drugs education were twice as likely to be binge drinking than their peers with the same personality feature who had been randomly allocated to the programme 12 months previously. The research team continues to follow up all the 800 14-year-olds who have participated in this trial to see what effect *Preventure* has had after two years. But the results a year after the first wave of students joined the programme show dramatic effects not only on their drinking habits, but also on other mental health problems associated with the four personality traits. 'The number

**'There are four personality traits that are risk factors for alcohol misuse'**

of panic attacks students experienced went down and there was a positive effect on truancy, and on shoplifting too.'

What's more, the students really approve of the programme. 'The feedback has been very positive,' said Dr Conrod. 'They said they really liked thinking about how to have control, how to consider their actions, realising it was up to them to make decisions, and that they have choices in how they behave. So the next step for us is to work out how to help every school deliver this programme, in an effective and sustainable way.'

The *Preventure* programme involves grouping young people with similar personality traits together. Until now, a qualified therapist has helped them explore their personality and ways of coping with potentially problematic behaviour that arises as a result of the specific risk trait, including discussions of real-life experiences and possible scenarios to encourage them to think about why they drink heavily or binge drink. 'We incorporate evidence-based cognitive behavioural techniques used to treat depression, anxiety and ADHD (attention deficit hyperactivity disorder), and motivational interviewing,' she said.

Dr Conrod and her colleagues want to find out if *Preventure* can be incorporated into secondary schools using existing staff resources rather than bringing in outside experts. An Action on Addiction-funded project now aims to discover whether

teachers can be trained to deliver the programme, or whether independent professional psychologists and counsellors are the only ones who can successfully lead the two confidential group sessions. 'Students may not feel comfortable about being entirely honest about their lifestyles with the same person who has the job to enforce the school rules,' said Dr Conrod. 'On the other hand, only school staff can be available to work with students on a regular basis, and as real-life situations arise.'

Twenty-four schools in London have signed up to the new trial, called *Adventure*.

## **'British youth are among the heaviest drinkers and binge drinkers in Europe'**

The research team in Addictions at the IoP is training teachers to deliver the programme in 12 of them. The students in the other half will carry on receiving information about the dangers of alcohol and advice about general coping strategies through the national curriculum. In the schools where the programme is being delivered, students are recruited on the basis of a simple questionnaire, developed to measure their personality traits. All year 9s in all participating schools will be followed up for two years, so the research team can find out about the drinking behaviour of those with risk traits, and compare what happens to those who take part in a teacher-led programme with what happens to those who attend classroom-based drug education

lessons. By measuring the drinking habits of all year 9s, the research team wants to discover if targeting those at greatest risk for alcohol misuse has a knock-on effect on all pupils, including those with no personality risk. They will also be monitoring behaviour at school and academic performance to see if there are any patterns or links to be made.

The teachers are being trained at three-day workshops, and then supervised by trained therapists in practice sessions and 'passed out' before they run the real programme. The rules agreed are that anything confidential revealed in a session must stay confidential.

'The schools we are working with are really enthusiastic,' said Dr Conrod. 'If this works, if the results are as good when teachers are delivering the programme, we would feel extremely comfortable to put a lot of pressure on the UK government to roll this out nationally.'

'British youth are among the heaviest drinkers and binge drinkers in Europe. Yet the maturing adolescent brain is highly vulnerable to the effects of alcohol. We know that the earlier the onset of alcohol misuse, the more likely young people are to use other substances and engage in risky sexual behaviour. Of particular concern is the strong relationship between early onset drinking and alcohol dependence in adulthood. It has been estimated that we could potentially reduce the rate of adult alcohol dependence by 10 per cent for each year that adolescent drinking is delayed.' ■

# Cutting down on alcohol before serious health problems take hold



About one in four adults regularly exceeds the UK government's sensible drinking guidelines, yet regular and heavy consumption of alcohol causes liver disease and contributes to strokes, cancers, heart disease and mental health problems. About 70 per cent of the people who visit accident and emergency departments in England between midnight and 5am do so because they have injuries or illnesses caused as a result of alcohol consumption: excessive drinking contributes to violence and death.

Now a £3.2 million programme of research, funded by the Department of Health, aims to find the best way to help people who are drinking too much cut down before serious problems caused by alcohol take hold. SIPS (*Alcohol Screening and Brief Intervention Trailblazers Research Programme*) is being led by Professor Colin Drummond here at

continues over the page →

the IoP and its results will inform national strategies designed to prevent the numerous health problems people who drink excessively can face as a result of misuse or dependency.

More than 2,600 people will be recruited through GP surgeries, accident and emergency departments and services that are part of the criminal justice system to allow the research team to gauge how effective and acceptable different screening questionnaires – designed to spot those who are drinking in a potentially harmful way – are. Staff working within these services will be asked for feedback on how easy it is to incorporate these screening tools into their everyday work.

Researchers will keep in touch with the 2,600 participants for six months to find out whether their drinking patterns have changed after receiving advice and information about the dangers of alcohol consumption, or support designed to motivate them. They will be testing different ways of offering help to find out which ones work best: one method is to give people *How much is too much?*, a Department of Health publication containing information and advice on sensible drinking. Another way is to supplement this leaflet by training

**'We aim to recommend the most cost-effective method of helping people who are drinking in a hazardous or harmful way'**

health and criminal justice professionals to work with individuals for five minutes, giving them personal advice. A third approach being evaluated in casualty departments and criminal justice services – prisons, youth offending services and probation services, for example – is a longer session of lifestyle counselling with a specialist Alcohol Health Worker, specially trained to help people change their patterns of drinking.

SIPS is being carried out in collaboration with the Universities of Newcastle and York, St George's and Imperial College, University of London, and Alcohol Concern and its results will help shape the development and the implementation of the government's *National Alcohol Harm Reduction Strategy in England*. 'We aim to be able to recommend to the government the most cost-effective method of helping people who are drinking in a hazardous or harmful way,' said Professor Drummond.

Previous research has shown that interventions like those being tested can make a difference, he said. 'What SIPS will do is show how best to implement them into routine work in GP surgeries, casualty departments and criminal justice services in order to reach a large number of people at risk from the effects of prolonged and excessive consumption of alcohol.' ■



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## Can blood reveal what's happening in the brain?

Imagine a blood test for Alzheimer's disease. One that could be used for diagnosis, but perhaps more importantly, could tell doctors about the progress of the disease and inform treatment decisions; one that could be used in trials to monitor the effect of new drugs; one that could even predict the likelihood of the disease developing.

It seems far-fetched that a vial of blood could tell doctors what is happening in the brain, and therefore it was a 'leap of faith' when Professor Simon Lovestone and his team started searching in the blood of patients with Alzheimer's for biomarkers – changes associated with disease – five years ago. It's still very early days, but so far it looks like Professor Lovestone's hunch was a good one, that the amount of certain

proteins in the blood can indicate whether a person has Alzheimer's or not. At the moment, Alzheimer's disease is detected by memory tests and brain scans, but a definite diagnosis can only be given at postmortem.

Researchers think proteins have a central role to play in the development of Alzheimer's disease. Our bodies manufacture thousands of them, each made up of a sequence of amino

**'The research team now has a panel of proteins that show up in abnormal amounts in the blood of people with Alzheimer's'**

acids, each with crucial, different roles to play almost everywhere – from building bones and skin to regulating neural pathways. Scientists have known for some time that two proteins – tau and beta-amyloid – are involved in the creation of the 'tangles' and 'plaques' found in the brains of people with Alzheimer's.

The search for biomarkers in the blood will enable scientists to understand more about other proteins involved in the progressive damage to the brain, leading ultimately, they hope, to the development of medication that can inhibit or prevent their destructive action and potentially reverse or improve the symptoms of the disease.

The first foray by the research team, based in the MRC Centre for Neurodegeneration Research at the IoP, was to look for differences in the blood of patients with Alzheimer's compared with the blood of healthy people,

using techniques involved in 'proteomics', the name given to the study of proteins.

Working in collaboration with Proteome Sciences plc, which has its UK laboratory at the IoP, the research team used a proteomics technique called 2DGE (two dimensional gel electrophoresis), routinely used to analyse complex samples of proteins in blood or postmortem brain

**'The search for biomarkers has so far involved some 1,500 volunteers who donated blood for analysis'**

tissue. Proteins are first separated horizontally by their electric charge, then vertically by their size or molecular weight. The resulting patterns of protein 'spots' were stained to allow researchers to compare the patterns in the blood of those with Alzheimer's and those without. 'This comparison showed that on the simplest level there were differences in the amount of certain proteins in the blood of people with Alzheimer's and healthy people,' said Professor Lovestone.

The task then was to try to identify which 'spot' represented which protein. To do this, the proteins were effectively 'weighed' in a mass spectrometer machine. Identification is possible because each amino acid involved in a protein has a unique mass.

As a result, the research team now has a panel of proteins that show up in abnormal amounts in the blood of people with Alzheimer's that could be important in the progression of the disease. One of these is CFH (complement factor H), a protein that is involved in the immune system, and researchers are now exploring its potential role in the creation of the plaques and tangles that develop in the structure of the brain prior to the actual death of cells.

'What's really interesting about this discovery is that people with age-related macular degeneration (AMD) are more likely to get Alzheimer's, and AMD is associated with the genes responsible for producing CFH,' said Professor Lovestone. 'AMD is a degenerative condition of the central retina and when you look into the eye, you see deposits of proteins there. One of those proteins is beta-amyloid, the same protein that deposits on the outside of brain cells in Alzheimer's, forming plaques.'

As well as investigating CFH, the research team wants to try out different proteomics techniques to analyse blood samples, techniques that could see and identify many more proteins, much more quickly. '2DGE is very labour intensive and sees only the proteins that are more abundant in the blood,' said Professor Lovestone. 'There has been a slew of

advances in proteomics – something called isobaric tagging in the mass spectrometer machine, for example, is able to see 100 proteins and identify all of them.'

Initially funded by the Alzheimer Research Trust, the search for biomarkers in the blood has so far involved some 1,500 volunteers who donated blood for analysis and regularly help the work of Professor Lovestone's team by participating in research projects.

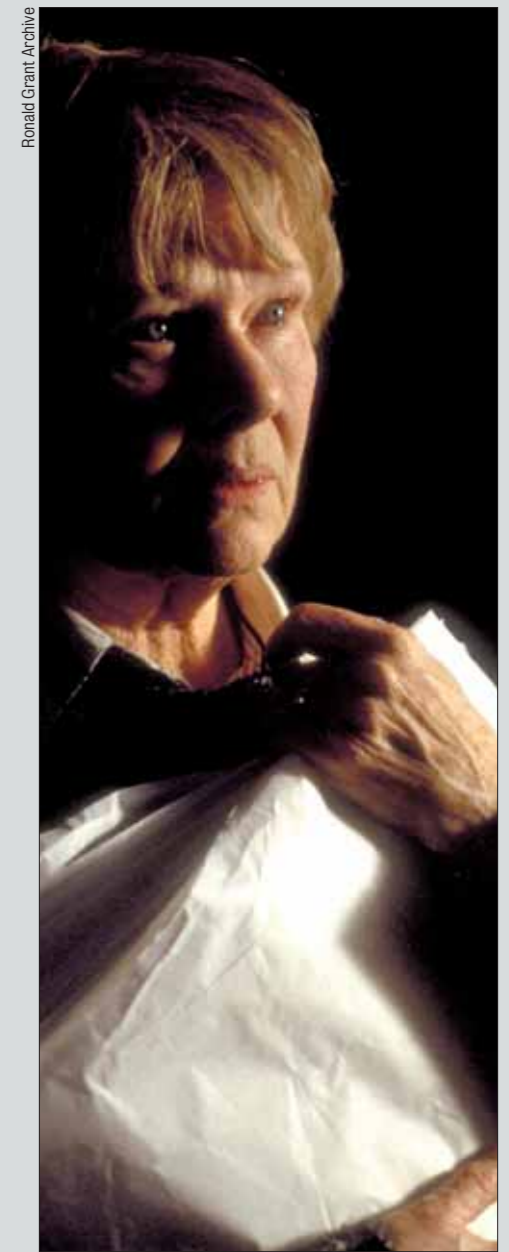
Now European Commission funding has widened the scope of the biomarker work, and volunteers from six cities in Europe are giving blood several times a year. Some volunteers are also having regular brain scans so researchers can correlate what the candidate proteins are doing in the blood with what's happening inside the brain as the disease progresses.

*AddNeuroMed* is the name of this pan-European project, led by King's College London, and one of two pilot projects funded under the umbrella of the European Commission's *Innovative Medicine Initiative*. This initiative brings together pharmaceutical companies, academic institutions and private enterprises – including Proteome Sciences plc – from across Europe. The aim of *AddNeuroMed* is to look for biomarkers in Alzheimer's that in future can lead to the development of more effective medication, but with the help of a huge investment in technology to facilitate research and collaboration across countries. 'The technology means the research is much quicker and more effective,' said Professor Lovestone, 'and gives researchers in collaborating teams access to the same information and sophisticated software that can analyse it.'

**'An investment in technology means the research is much quicker and more effective'**

Looking for biomarkers of Alzheimer's is a big field of research around the world, but the only other large-scale study collecting detailed clinical and imaging information as well as samples for biomarker analysis is the USA-based *Alzheimer's Disease Neuroimaging Initiative*, with which the IoP-based team is in close contact.

'Most other people are looking in cerebrospinal fluid (CSF),' said Professor Lovestone, 'but we felt uncomfortable about asking elderly, frail people to have a spinal tap to remove a sample of the fluid on a regular basis. A spinal tap is, at best, uncomfortable, and it's also costly because it has to be done in hospital. It was a bit of a leap of faith to look in the blood...but so far, it's looking promising.' ■



Ronald Grant Archive

Dame Judi Dench won critical acclaim for her portrayal of writer Iris Murdoch's journey into dementia in the film *Iris*. Dame Judi is a patron of both the **Alzheimer's Society**, [www.alzheimers.org.uk](http://www.alzheimers.org.uk) and the **Alzheimer Research Trust**, [www.alzheimers-research.org.uk](http://www.alzheimers-research.org.uk). Both charities provide information and advice, and support research.

**and...**

According to the *Dementia UK Report* (February 2007), commissioned by the Alzheimer's Society and prepared by the IoP and the London School of Economics and Political Science, there are nearly 420,000 people with Alzheimer's disease in the UK. These figures are forecast to increase dramatically over the next 50 years.

**Albert Smith had been a London black cab driver, like his father before him, and his passion was the history of the capital.** He even wrote a book called *Dictionary of City of London Street Names*, published in 1970 and still a point of reference on websites. 'He first started having problems when he was 63,' says his wife Vivienne. 'He was vague, and kept repeating his words and his actions, and wasn't really aware that he was doing it.'



Photo courtesy Vivienne Smith

Albert had to take early retirement from his job in traffic control in a London local authority where he had worked for the previous decade and Vivienne took him to their GP. 'There was a degree of anxiety in Albert's behaviour, and the GP gave him calming medication first of all and then suggested he go for further mental agility tests. Eventually he was diagnosed. He stayed on the calming medication, but if he was given too many, he would be in a semi-drugged state.'

'His behaviour became more and more strange. There came a time when it became obvious he could not go out unsupervised. If we went out together, it became more and more stressful. I would have to lead him and hold on to him, otherwise he might approach people and try to grab them or start speaking to them in an odd way. If he went out on his own, he went missing. There was one time on a very cold day in February when he went out without a coat, bus pass or money, about midday, and didn't come back. We had to ring the police and eventually he was found at about 9pm on the other side of London.'

## and...

Sube Banerjee, Professor of Mental Health and Ageing, has been appointed to jointly lead the development of the UK government's first ever strategy to improve dementia services in England, plans for which were unveiled by Health Minister Ivan Lewis in August 2007. The strategy, to be announced in 2008, will include ways of tackling the stigma associated with dementia which stops people seeking help; ways of helping families recognise the early signs; a plan to enable early diagnosis and treatment by professionals; and a focus on making sure people are offered high-quality treatment and support, from diagnosis to the end of life. Professor Banerjee is working with the Alzheimer's Society and representatives from a range of professional bodies, service providers and voluntary organisations.

'I had to lock him in then, and he would try to get out, stand at the door and pull at it for two hours at a time. Sometimes he would wake up in the middle of the night and try to go out, and pull me out of bed.'

After three years, Vivienne tried working from home, then two years later, gave up her job with a specialist travel company that arranged trips for schools, in order to become a full-time carer.

'Albert could become quite agitated and needed to be supervised, even in the house, so I had to put locks on all the internal doors.'

'As the disease progressed, he didn't know who I was, or who my daughters were. Sometimes he would say to me: "I think we should get married".'

'In the last year he couldn't speak at all. He became immobile, practically couldn't walk, and was doubly incontinent. He lost so much weight, because he lost the ability to know when to swallow, so all his food had to be pureed so it was safe to eat.'

'I wanted to care for him because I loved him. Right at the beginning, you have no idea of what is ahead of you. I felt that I could cope and I wanted to cope on my own. I cared for him with the help of my daughters for eight years, and then had support from Social Services, with a carer coming in for half a day here and there so I could get out. It became more and more difficult at home, and eventually we found a nursing home that could care for him in a way that I wasn't able to any more. The staff were caring and lovely and I was able to visit almost every day.'

'During that last year, when he was in the home, his eyes never flickered when I came in, there was no recognition of me, he just looked. But on the day he died, he gave me the most precious gift. I was at his bedside and had been talking to him all that day, and I told him I loved him. And he put his mouth together in a kiss, and gave me three kisses, one for me and one for my two daughters, and I felt he knew who I was.'

Albert died in 2007. He and Vivienne had been married for 41 years.



# Untangling tau protein

The symptoms of Alzheimer's disease are caused by the death of brain cells and the synapses that connect them. In a quest to find out why the cells die and cause the brain to atrophy, scientists are trying to discover what makes the characteristic 'tangles' and 'plaques' of Alzheimer's form in and around the cells prior to their death.

A team led by Dr Diane Hanger in the MRC Centre for Neurodegeneration Research is concentrating on what happens to tau, the protein involved in the creation of tangles inside the cells.

**'Tangles in the brain are created when an abnormal amount of phosphate becomes attached to the protein tau'**

Thousands of different proteins – organic molecules made up of chains of amino acids – are involved in many different crucial roles in our bodies, and the code for making them all is stored in our genes. Plaques in Alzheimer's are created when beta-amyloid proteins behave abnormally, 'sticking' together and forming clumps on the outside of brain cells. Tangles are created when an abnormal amount of phosphate becomes attached to tau.

Phosphate is a chemical in the brain that is needed for lots of everyday functioning. In healthy brains, it attaches in the right amount, when needed, to help tau hold the scaffold of a brain cell together. But when too much phosphate becomes attached, tau is no longer able to behave as it should, and the cell destabilises.

Finding a way to stop the phosphate build up on tau might be a good treatment for preventing or reversing some of the effects of Alzheimer's, says Dr Hanger, but in order to do that, scientists need to understand why the phosphate sticks when it shouldn't.

For some years, Dr Hanger's team has been looking for sites on the tau molecule where the phosphate abnormally collects, taken from brains affected by Alzheimer's. As the proteomics technology available for scrutinising and analysing the 441 amino acids in the tau chain has become more sophisticated, more sites have been identified. To find these sites, parts of tau affected by Alzheimer's are 'weighed' in a mass spectrometer machine to detect the position of the phosphate along the chain. The latest piece of research, carried out in collaboration with Proteome Sciences plc and funded by the Medical Research Council, the Alzheimer's Society and the Progressive Supranuclear Palsy Association, has brought the total number

of known sites where phosphorylation occurs on tau in Alzheimer's up to 39.

At the same time, the team has been looking for enzymes (or kinases) – proteins involved in the everyday workings of the brain – that might be involved in the abnormal build-up of phosphate.

Previous work from Dr Hanger's laboratory had already found that GSK3 was an enzyme that appeared to add phosphate to tau at several different sites, but this latest piece of research also discovered that another enzyme, CK1 (or casein kinase 1), could also add phosphate in 33 places on tau.

'These results confirmed the likely role of CK1 as an important enzyme in the creation of tangles in Alzheimer's,' said Dr Hanger. 'Together, GSK3 and CK1 may be responsible for putting on the majority of phosphate but it is likely that there will be other kinases involved and a combination of enzymes makes the extra phosphate stick.'

Much of this research has involved the analysis of tau extracted from postmortem Alzheimer's brains, donated by patients to the IoP-based MRC London Brain Bank for Neurodegenerative Disease. The research team also worked with synthetic tau created in the laboratory: they added the candidates GSK3 and CK1 and observed the phosphorylation of many of the sites they had identified in the analysis of tau involved in Alzheimer's tangles.

The work continues to uncover other enzymes and tau phosphorylation sites that may have a part to play. Each result is a small contribution to unlocking the mystery of cell death in Alzheimer's and in other disorders where tau forms tangles, such as progressive supranuclear palsy, and a step on the path to developing new, more effective, targeted medication.

**'It's a small contribution to unlocking the mystery of cell death in Alzheimer's'**

'If we can identify all the enzymes involved in putting the extra phosphate on tau, we could develop drugs that target the right ones, and inhibit their action,' said Dr Hanger. 'These enzymes do have a normal function though, so it will be important in future to develop inhibitors that may not necessarily knock them out altogether but perhaps only dampen their action, so the tau would no longer sit there as a tangle but get on with doing what it's supposed to do.' ■

A mass spectrometer machine in the laboratory of Proteome Sciences plc, based at the IoP, 'weighs' proteins.

# Treating agitation

Alzheimer's disease not only causes the ability to remember, understand, communicate and reason to decline. About a quarter of people with Alzheimer's who live at home, and about half who live in residential care, also have agitation, a cluster of symptoms that include anxiety, irritability, pacing, wandering, shouting and aggression. These symptoms are very distressing for both patients and their carers.

Agitation has traditionally been treated with tranquillisers, many of which have unpleasant side effects. The Committee for the Safety of Medicines has now warned about the increased incidence of stroke when tranquillisers are given to patients with Alzheimer's. 'It is becoming increasingly clear that tranquillisers are not an adequate treatment for managing distressing behaviour in Alzheimer's patients, and their use is associated with serious potential side effects,' said Rob Howard, Professor of Old Age Psychiatry and Psychopathology.

The search is on then for safer alternative treatments: one candidate was donepezil, part of a family of drugs called cholinesterase inhibitors, an anti-dementia medication used to slow down loss of mental ability in the early stages of Alzheimer's. But when a team of UK researchers led by Professor Howard carried out a major Medical Research Council and Alzheimer's Society-funded trial, they found that donepezil made no difference to the symptoms of agitation.

They worked with almost 300 Alzheimer's patients with severe agitation, many of whom were in nursing homes. Doctors at eight clinical centres prescribed half of them with 10mg of donepezil a day for 12 weeks, and gave the other half a placebo. There was a small improvement in memory and attention in those patients who took the donepezil, but there was no significant difference between the effects of the placebo and the drug on the symptoms of agitation. 'Sadly, but importantly, our results show that while donepezil may improve memory and attention in some patients, it is not effective in the management of agitation,' said Professor Howard.

'For severely agitated patients, we desperately need to find treatments that work. Improving cognition in Alzheimer's patients is important, but there are often other neglected features of the disease. Research to provide effective and safe treatments for agitation is a huge priority.' ■

# Genes and events of childhood can predict antisocial behaviour

One thousand men and women who turn 38 in 2010 have helped researchers find out about the biological and life causes of antisocial behaviour since they were born. They are part of the *Dunedin Multidisciplinary Health and Development Study* which started in New Zealand in 1972, and they have given information about their health, circumstances and lifestyles at regular intervals since then.

The information they share, along with their family histories and samples of their DNA, has helped different research teams based in the UK, Canada and New Zealand to investigate the effects of nature and nurture on a plethora of health and behaviour problems, from childhood to adulthood. Here at the IOP, a team led by Professors Terrie Moffitt and Avshalom Caspi, has concentrated on antisocial behaviour, mental and general physical health.

And over the years, the Moffitt/Caspi team has discovered genetic influences and identified risk factors that exist in childhood that can predict a life of crime and multiple problems as an adult.

An early Dunedin study found that boys whose genes produced low levels

of the enzyme monoamine oxidase in the brain were more likely to develop antisocial personality traits if they were maltreated during the first 10 years of life – if they were rejected by their mothers, or suffered physical or sexual abuse, for example. The enzyme is responsible for maintaining a healthy balance of several different neurotransmitters, including serotonin and dopamine, and is produced by the MAOA gene. Boys whose genes produced high levels of the enzyme were unlikely to develop antisocial problems, even if they had similar experiences.

The longitudinal study has confirmed that antisocial behaviour is much more common in boys, and that such behaviour around the time they start primary school can be a normal part of development. 'Many boys have problematic behaviour in early childhood,' said Professor Moffitt, 'but most settle into school and grow out of it as they are socialised by teachers and peers.' Adolescent bad behaviour – 'teenage delinquency' – can also be normal and end in early adulthood. But a small group of children who start to display antisocial behaviour in childhood – aggression, violence, disobedience, reckless

behaviour, lying and stealing – will continue in this manner for the majority of their lives.

The Dunedin boys who were convicted of violent crimes in their 20s were more likely to have been brought up in homes with harsh and inconsistent parenting. They were more likely to have had reading difficulties and symptoms of hyperactivity as children. They were more likely to have been raised by a single parent, or a teenage mother. As they reached their 30s, they were more likely to be abusing alcohol, have mental health problems, be violent towards their families and less supporting of their children. As adults, they are more likely to be in low-income, low-status jobs, unemployed or homeless.

The most recent follow-up, when the cohort was aged 32, showed too that lifelong antisocial behaviour has an impact on physical health. In addition to problems associated with heavy alcohol and drug use, the men who had been consistently behaving in an antisocial way since the age of five were more likely to be at risk for heart disease (high blood pressure, high cholesterol), more likely to have sexually transmitted diseases, gum disease, immune system problems and signs of precocious ageing. 'Their bodies are deteriorating at a faster rate than their peers,' said Professor Moffitt.

One of the problems for professionals designing interventions to steer children away from this sort of future is working out which ones will grow out of problems,

and which ones are set on a path towards antisocial adulthood.

Another analysis of the information gathered from assessments of the Dunedin men when they were aged 32 showed that family history can help clinicians predict which children who behave in an antisocial way when they are very young are likely to go on and develop lifelong problems. The research team collected information from 4,000 members of the 526 men's families – parents, grandparents and siblings. Those who had become persistently antisocial in

## 'Lifelong antisocial behaviour has an impact on physical health too'

adulthood were more likely to have parents and grandparents who had been antisocial themselves, who had had ADHD (attention deficit hyperactivity disorder), had been dependent on alcohol or drugs, and had smoked. The research team found the worst prognosis of lifelong antisocial behaviour could be predicted if both biological parents and grandparents had drinking problems. 'Family history may be an additional tool for predicting which children will go on to develop a lifelong disorder,' said Professor Moffitt.

The majority of the original 1,000 Dunedin participants are still taking part in the study – even though 60 per cent have since emigrated elsewhere. 'They are now scattered all over the world,' said Professor Moffitt. A team

based in New Zealand keeps in touch with them, and every time a follow-up takes place, they are flown home and spend a day being assessed by different groups of researchers. 'There are lots of interviews, assessments and tests,' she said. 'They come in and go from room to room, which are staffed by different research teams.' Those behind bars are either escorted to the assessment venue, or sometimes researchers visit them in prison.

The Moffitt/Caspi team is now preparing for the 2010 follow-up. This time their assessments will include a new set of genetic measures – they want to compare the length of telomeres, stretches of DNA at the end of chromosomes that protect the genetic information that sustains a cell, and stop the chromosome ends from fraying. But each time the cell divides and the DNA replicates – to grow new skin, blood or bone, for example – the telomeres become shorter. When they are too short, the cell can no longer divide and becomes inactive or dies. Studies elsewhere have shown this process to be associated with cancer and ageing. 'It's not yet known if shorter telomeres are a sign of ageing, or contribute to the ageing process,' said Professor Moffitt. 'What we want to find out is if shorter telomeres are related to the stressful life experiences of the men with persistent antisocial behaviour, and whether they have something to do with the accelerated ageing we started to see at age 32.' ■

# Neighbours' role in next generation

Where you live and what your neighbours are like can be hugely influential on whether children develop antisocial behaviour.

Professors Terrie Moffitt and Avshalom Caspi set up a second birth cohort with the support of the Medical Research Council here in the UK in 1997, this time using twins to help them study the role environment and genetic factors have in the development of antisocial behaviour.

The *Environment Risk Study* is tracking 1,100 pairs of twins born in 1994 and 1995 to a representative sample of families in England and Wales – from the richest of the rich to the poorest of the poor. Researchers have visited them in their homes at age five, seven and 10 – and are just finishing an assessment at age 12.

A recent study with colleagues at Harvard University in the USA looked at the effect of neighbourhood attitudes on the behaviour of children in this sample. Twenty close neighbours of each of the participating

families were approached and asked to fill in an anonymous questionnaire measuring 'social cohesion' – would they get involved in a campaign to save a local amenity?, would they intervene to help stop trouble on the streets?, for example.

'We found the weaker the social cohesion, the more likely kids were to have antisocial behaviour, regardless of their individual circumstances, or of what was going on in their own homes and families,' said Professor Moffitt.

Strongly united neighbourhoods in deprived areas that share the same values and supportive attitudes had lower levels of antisocial behaviour. But the analysis of information collected from more affluent areas showed that social cohesion had no effect on how children behaved.

The study was part of the *Social Contexts of Pathways in Crime (SCOPI) Network*, a five-year Economic and Social Research Council research programme which aims

to achieve a better understanding of how young people become involved in crime.

'It seems the willingness of neighbours in poorer areas to look out for each other and intervene when trouble arises can have a potentially protective effect on a child's development,' said Professor Moffitt. 'This is a significant relationship in deprived neighbourhoods and policies designed to build and enhance a community could make a real difference.'

The *Environment Risk Study*, run under the umbrella of the IOP-based *Twins Early Development Study* (TEDS), is assessing the participating twins at key times in the development of antisocial behaviour – before and after they join primary school, before and after they join secondary school, and then at 16 and finally at 18. At each follow-up, the child's behaviour is assessed with the help of parents and teachers. ■



Rehan Jamil

# Why improving parenting skills can help children's life chances



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Improving the skills of parents can make a real difference to the antisocial behaviour of children. Research by Child and Adolescent Psychiatrist Professor Stephen Scott and colleagues has shown that the right programmes, delivered by skilled practitioners, can help steer children away from the path that is likely to lead to a life of crime, unemployment and loneliness.

'Research in the IoP's MRC Social, Genetic and Developmental Psychiatry (SGDP) Centre by Professor Terrie Moffitt has discovered that children who display antisocial behaviour tend to carry on in the same way throughout life,' he said. 'There is a really high risk of offending, drugs, violent behaviour, limited and unsatisfactory relationships, unemployment and social exclusion.'

Now the government has invested £10 million a year for three years to launch a new Parenting Academy based at King's College London. Its remit is to train professionals who work with parents, and to develop and test support packages that can really make a difference to both

individual families and the communities in which they live. The Academy, officially called the National Academy for Parenting Practitioners, was launched at the end of 2007 and is a collaborative venture between the IoP at King's, the Family and Parenting Institute, and Parenting UK, an umbrella body that brings together organisations

**'The new Parenting Academy will train professionals who work with parents and develop and test support packages that can really make a difference'**

providing services to parents. Professor Scott is its research director and almost half the money is to be invested in research aimed at developing and trialling practical, easy-to-deliver programmes that really work for families, including those that are hard-to-reach, and foster families.

The foundations of the Academy were laid nearly a decade ago by a series of research projects carried out by Professor Scott and the team of researchers based at

the IoP who are part of the King's Parenting Unit. Both his research and his clinical work at South London and Maudsley NHS Foundation Trust's Conduct Problems Clinic and Adoption and Fostering Clinic led him to believe that evidence-based parenting interventions were worth investing in, that they could change behaviour patterns for the benefit of the individual child and society.

'Until about 20 years ago, treatment was always directed at the child,' he said. 'Various therapies were based on the thinking that there must be something deep inside the child, that you needed to get to the bottom of what that was. But these therapies didn't seem to improve behaviour.'

Research at the SGDP Centre and elsewhere has shown that temperament and genes do play a part in antisocial behaviour. But studies have also illustrated that family factors, and the way children are brought up, play a major role: children with antisocial behaviour often live with high

levels of criticism and hostility from their parents, for example.

In the early 1990s, inspired by parenting programmes developed in the USA, Professor Scott ran a controlled trial to see whether a group parenting programme could make a difference to antisocial behaviour in children aged three to eight years. The children involved had been referred to child and adolescent mental health services because their behaviour was so severe. 'They were completely disobedient at home, kicking and stealing, fighting, lying, refusing to go to bed, sticking compasses into people at school,' said Professor Scott.

The research team dubbed English accents onto one of *The Incredible Years* videotape programmes developed by Carolyn Webster-Stratton, Director of the Parenting Clinic at the University of Washington, which had

**'SPOKES made parents feel more competent, their children's antisocial behaviour decreased while concentration increased'**

proved highly successful in trials there. The group of parents met for two-hour weekly sessions over a period of three months: the programme covered play, praise and rewards, setting boundaries and handling misbehaviour. Participating parents also discussed their own child's behaviour and were supported while they practised alternative ways of managing it. The therapists came from a range of disciplines and were trained to lead the sessions.

And at the end of the trial, the behaviour of children of parents who had been part of the group had improved. 'When we followed the families up a year later, there were still gains,' said Professor Scott. 'This was the first trial in Europe of this kind of thing, carried out by regular clinicians, not specialists, and it worked. The programme had an effect on the competence of parents, and it was the toughest and most difficult cases whose behaviour improved the most.'

Next, the team members turned their minds to the concept of early interventions – work to address the behaviour of young children before patterns became established and more difficult to challenge. In addition to parenting styles, risk factors identified for persistent antisocial behaviour throughout life include lack of concentration and symptoms of attention deficit hyperactivity disorder, and difficulties reading and learning at school.

Working with Educational Psychologist Professor Kathy Sylva at Oxford University, another trial began, this time based in eight primary schools in Lambeth in south London. *The Supporting Parents on Kids Education in Schools* (SPOKES) intervention was designed to improve parenting skills, antisocial behaviour, concentration and reading ability. Teachers and parents of children in reception class and year 1 were asked to fill in questionnaires to help the research team identify children who

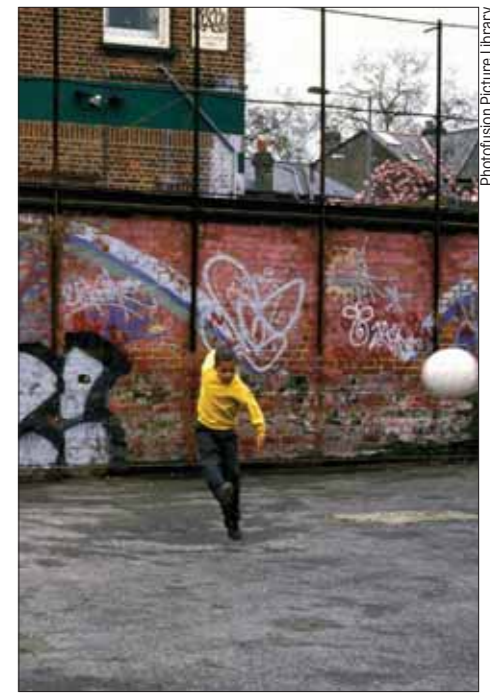
had problems, and their parents were invited to join a group which met for three terms at their child's school. In the first term, there was a relatively intensive 12-week *Incredible Years* programme; in the second term, the group work focused on how parents can help children to read; and the third term covered problem-solving and how to help resolve disputes without violence and aggression.

'The group met for a total of 26 weeks and most parents stuck at it,' said Professor Scott. 'Three-quarters came to the majority of sessions – it was impressive how committed they were.' And once again, the trial proved successful: parents felt more competent, their children's antisocial behaviour decreased while concentration increased, and their reading age went up by six months. 'This trial suggested again that an intervention with parents could improve a child's life chances,' he said. A five-year follow-up of the group is currently being undertaken to see if the intervention has made a difference in the long term.

Then came the UK government's RESPECT agenda, a cross-department strategy to tackle bad behaviour and nurture good, to work towards a society where antisocial activity is rare. Professor Scott joined the RESPECT taskforce, and at the same time started lobbying for the need for some sort of parenting centre to promote evidence-based interventions, and to make sure those leading the programmes were well-trained. 'What we know from our studies is that the skill of the practitioner working with the parents really counts,' he said. 'Having filmed group sessions during our research, we discovered that the least skilled therapists had no effect at all, and possibly made the children worse.'

His campaigning was successful: in January 2006, the then Department for Education and Skills (now the Department for Children, Schools and Families) announced plans to set up such a body and the consortium of King's College London (the IoP), the Family and Parenting Institute, and Parenting UK successfully competed against other bids to take plans forward.

Over recent years, there has been a rapid increase in self-help books, reality TV programmes offering advice, government initiatives like SureStart, voluntary schemes and support groups, all aimed at giving parents the help they need to raise their children well. Professor Scott says much of this support is simply not effective in changing behaviour. The task of the Academy, based on the Strand in central London, is huge: to reach organisations and individuals working with parents and disseminate information about programmes that are proven to work. One of the plans is to develop a very visible web presence, an authoritative site for both practitioners and parents, offering a seal of approval to



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successful programmes that have been tried and tested.

The research arm of the Academy will include four trials of interventions: family therapy based at home for teenagers with antisocial behaviour; a wider trial of SPOKES; *Fostering Changes*, a support programme for foster parents developed by Professor Scott's team; and a programme developed to engage and help hard-to-reach families. In addition, the research team will be looking

**'The aim is to help all parents raise their children to be happy, healthy, safe, ready to learn, and to make a positive contribution to society'**

at programmes already in use that have not yet been evaluated. The team will investigate what skills are needed by people working with parents, and find the best possible training methods. And they will develop ways of measuring parenting – both 'good' and 'bad' – and ways of gauging the success of professionals working in the field.

In the longer term, the Academy plans to give parents the knowledge and support they need to bring up children in the best way they can – through the media, through publications, through schools and through health services. The aim is to help all parents raise their children to be happy, healthy, safe, ready to learn, and to make a positive contribution to society, said Professor Scott.

All this, he said, makes economic sense too. Another study carried out by the King's Parenting Unit showed that the public cost for individuals aged 28 who had displayed antisocial behaviour when they were 10-years-old is up to 10 times higher than for their peers. The costs mount because of crime, extra educational provision, foster and residential care, and state benefits. ■

# Missing link in the search for genes?

The search for specific genes that contribute to mental health problems has not been as fruitful as some scientists expected when they first started to study the human genome. A new area of research is now exploring what makes genes switch on and off: controlling mechanisms 'above the genome' called epigenetic factors, which determine the function and expression of the genes. And one of the first studies in this field at the IoP will concentrate on changes to these controlling mechanisms in the womb that may make children more susceptible to developing attention deficit hyperactivity disorder (ADHD).

'In the past, we have concentrated on looking for specific genes and how they interact with environmental factors in our search for the causes of mental health problems. While this research has produced some interesting findings, we are still a long way from discovering those causes,' said Dr Jonathan Mill, who heads a new team in the MRC Social, Genetic and Developmental Psychiatry (SGDP) Centre which is dedicated to epigenetic studies of psychiatric disease. The DNA sequence is in fact very stable, he said, and neither it, nor environmental influences, simply explain behavioural differences between individuals: 'you can often find identical twins, who share exactly the same genes, who are raised in a similar way, but who have real differences in behaviour and development,' he said. 'One may have ADHD for example, and the other may not.'

Our epigenetic profile – factors that essentially tell genes to stop or go – could be the missing link in the quest to understand why the same set of genes lead to mental illness in one person and not in another. 'We want to find out how and why factors controlling gene expression are influenced by the environment,' he said.

**'Our epigenetic profile could be the missing link in the quest to understand why the same set of genes lead to mental illness in one person and not in another'**

DNA methylation is a chemical modification process that regulates the expression of genes throughout life by attracting methyl-binding proteins that alter the physical structure of the genome. Epigeneticists think that too much or too little DNA methylation, along with other changes that affect the structure of the chromosomes, can lead to long-term changes in gene expression.

Epigenetic research in the field of cancer has shown, for example, that genes that produce proteins whose job it is to stop



Jenny Matthews

he said, when cell replication and growth are at their busiest during bursts of developmental change: gestation, puberty and menopause, for example.

In ADHD then, previous research has shown children of mothers who smoke and drink alcohol during pregnancy are more likely to develop the disorder.

Dr Mill is looking for different patterns of DNA methylation in the brains of rats exposed to nicotine and alcohol pre-natally who then go on to develop symptoms of ADHD. Sophisticated techniques in the SGDP Centre's laboratories allow researchers to study samples of DNA and analyse patterns of DNA methylation across the genome.

This research is being carried out in collaboration with colleagues at the IoP, and in Brazil and Norway. Dr Mill is planning to

**'Children of mothers who smoke and drink alcohol during pregnancy are more likely to develop ADHD'**

expand this line of study to look at the effects of diet and toxins on DNA methylation during gestation and the development of not just ADHD, but also other psychiatric illnesses.

It's still early days, and all the research is currently being carried out with rats. At the moment, they are searching for changes to the epigenetic profile in brain cells, but it may be that different patterns of DNA methylation could be detected in other tissues. If changes were detectable in blood, for example, researchers could then easily measure epigenetic differences in humans.

Proving that smoking and drinking during pregnancy changes DNA methylation and gene expression to make children more vulnerable to developing ADHD would have a clearly preventative benefit, he said. But in future, if epigenetic factors are proven to be instrumental in the whys and wherefores of the development of an illness, scientists could potentially develop ways of altering the DNA methylation process and re-adjusting gene expression to help prevent or cure psychiatric problems.

Scientists also think it's possible that epigenetic profiles can be passed down through the generations, that parental methylation marks may be inherited by their children or grandchildren. 'If that were the case, it would shatter existing ideas about inheritance,' said Dr Mill. 'If you could inherit a change in gene expression caused by the environment independently of the DNA sequence, it would mean the environment of one generation could affect the health of future offspring.'

tumours growing have been suppressed because they have been over-methylated. The products of other genes that promote tumour growth have been over-expressed as a result of under-methylation.

So the question Dr Mill and others working in this emerging arena want to answer is: what influences the DNA methylation? It seems that lifestyle and life circumstances are crucial.

'We think that epigenetic factors like DNA methylation can be changed by both the environment and random events in cells,' he said. 'So we think things like diet, medication, hormones and radiation, for example, can affect the amount of DNA methylation and the physical structure of the chromosomes.' Psychosocial factors also have a part to play: one Canadian study showed that young rats who weren't cared for affectionately by their mothers had altered DNA methylation around genes linked to coping with stress.

'We also think that once DNA has been epigenetically modified, these changes are passed on in the body as cells replicate. So if changes occur in the womb, for example, gene expression may be altered for the rest of your life and make you more susceptible to developing certain illnesses, even though the genetic sequence itself is not mutated.' Epigenetic changes are most likely to occur,

# Separating the triad of autism traits

People are currently diagnosed with autism when they have a triad of traits – impaired social ability, difficulties with communication, and restricted and repetitive behaviour. But are all three characteristics inextricably linked? Dr Francesca Happé thinks not: studies of people with autism and their relatives over almost two decades have led her and her colleagues to believe each of the three features of autism are caused by largely independent genes, are associated with different brain regions and are related to different cognitive characteristics.

A Cognitive Psychologist, Dr Happé has spent some 20 years trying to work out why people with autism view the world so differently. 'People with autism have striking social difficulties,' she said. 'They find it hard to recognise other people's thoughts and feelings. At the same time, they have superior cognitive processing in terms of eye for detail. We have been looking at the underlying causes of these different aspects of autism, searching for a parsimonious explanation, but try as we might, we have been unable to find one.'

So instead of continuing to search for a single cause of autism, they are now trying to understand more about what causes the three individual characteristics, and why they co-occur. To this end, Dr Happé and her IoP colleague Professor Patrick Bolton have launched the largest ever community-based twin study of the autism spectrum with the help of 300 families who are part of the IoP-based *Twins Early Development Study* (TEDS). Using information gathered from TEDS families, Dr Happé, Dr Angelica

Ronald and colleagues have already found a considerable number of children who have difficulties in only one area of the autistic 'triad.' What's more, the comparison of the development of identical and non-identical TEDS twins when they were aged seven and eight suggests that, while each different aspect of the triad is highly heritable, separate genes contribute to each individual trait. 'It looks as if largely independent genetic influences operate on the three different traits,' said Dr Happé. 'If this is correct, the search for

**'Research suggests separate genes contribute to each individual trait'**

genes "for" autism may be far less effective than searching for genes affecting, for example, social skills specifically, or those contributing to rigid and repetitive traits.'

This conclusion has been supported by other studies that illustrate how individual traits run in families of people with autism – close family members often share just one of the triad of traits, to a lesser or greater degree. 'Many fathers of children with autism in particular show the same sort of focus on detail, rather than the bigger picture,' she said, 'and social difficulties can also be found in family members who may not show an eye for detail.'

If the theory is correct, she says, many individuals may possess one characteristic of the triad, but do not meet the diagnostic criteria for autism. 'There may be people who have pretty poor social skills, but have no problems with communication, or people

who are able socially, but have rigid and repetitive behaviour.'

The new Medical Research Council-funded twin study seeks to find out more about the causes of the triad's individual traits as well as their interaction in autism. Two hundred of the participating families have at least one twin with a diagnosis on the autism spectrum. 'We will be visiting families and interviewing them about symptoms and current functioning, asking about childhood illness and other health problems in order to identify environmental factors that may have played a part, and undertaking cognitive testing of the twins to look for different psychological processes that underpin the triad traits.'

The TEDS twins are now aged between 12 and 14. 'Because we have information about them that families and teachers gave when they were younger, we will be able to check back for precursors to the development of the characteristics during the early years,' she said. The researchers will eventually use the information they gather to help search for genetic, environmental and cognitive influences underlying each of the individual features.

'What we want to do is to understand how the triad hangs together in autism,' she said. 'Most importantly, as we abandon the search for a single cause for autism and increase our understanding of the three distinct characteristics, we may need to abandon the search for a single "cure" for autism, and instead tackle the individual traits of the triad.'

**'When I found out I was pregnant in 1998, I was over the moon,' says Angie Perks. 'Then I had a scan, which confirmed that I was having twins. At 37 weeks, I gave birth by C-section to Kylie, who weighed 5lb 9oz, and then Thomas who was 6lb 3oz.'**

'By 14 months, Kylie was walking and talking. At 18 months, Thomas finally began to walk, but he never played with his twin sister and wasn't talking, so I asked my health visitor, who was also concerned about him. She got in contact with the Child Development Centre and a lady came to see us. Penny came to our house to watch Thomas. I remember he was sat on the floor lining his bricks in a row and making sounds. She sat writing in her book, then she looked at us and said, "I think Thomas may have autism." I actually had an idea that she might say that as I had looked on the internet and came across this website which explained to me



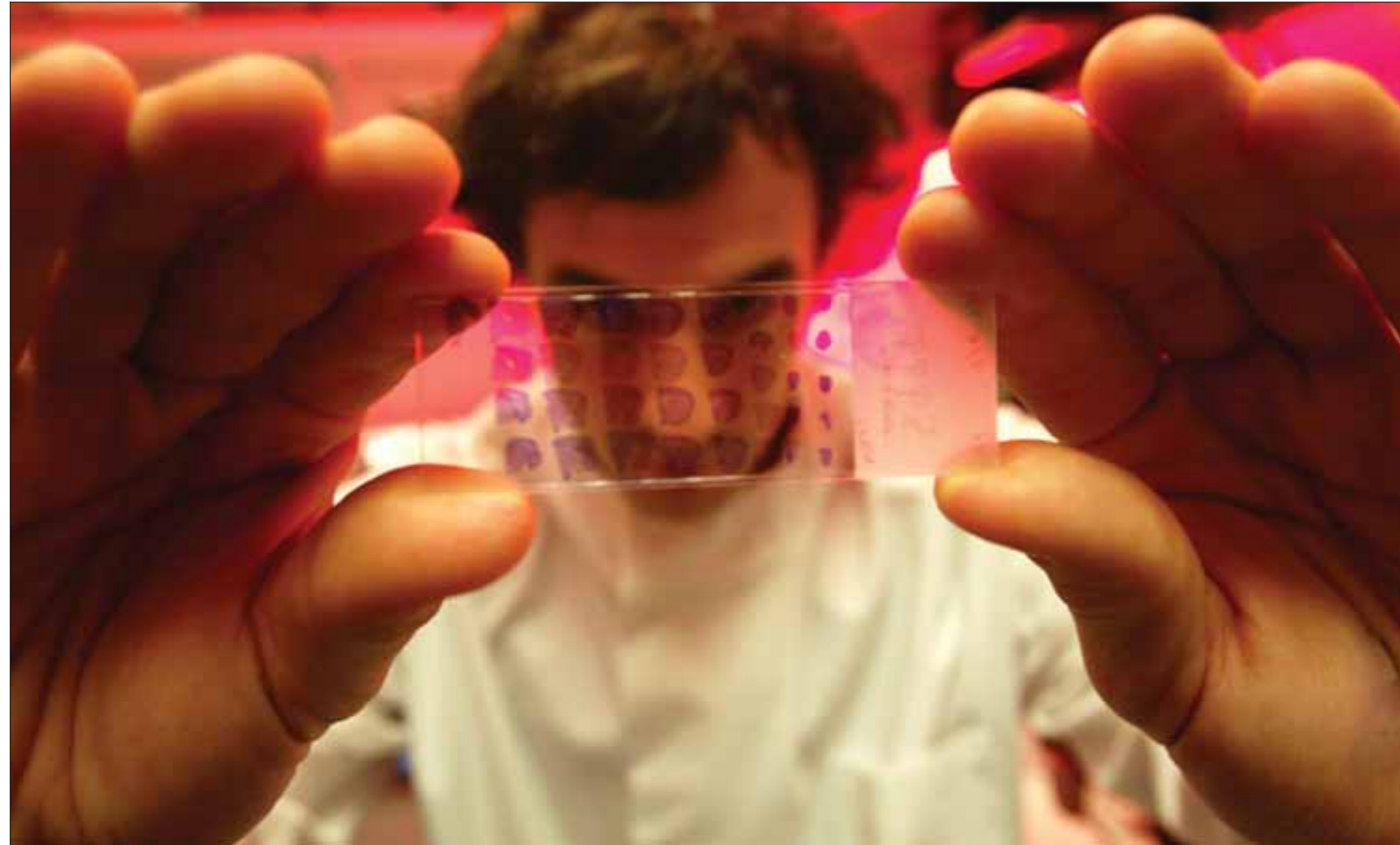
Photos courtesy of Angie Perks

what the symptoms were. After an assessment at hospital, Thomas was diagnosed with severe autism. The twins are now nine, and Thomas is still non-verbal and still in nappies. He can be destructive and it is sometimes hard work looking after him and making sure Kylie doesn't lose out. My mum helps a lot and Kylie has now started going dancing and has some shows coming up, though Thomas won't be able to sit through them.

'Thomas goes to a really good special school and they write me a letter every day to say what he's done as he can't tell me. He loves his routine and he stays in his room for hours and hours. Kylie is his big sister and always will be. When other children ask her about her brother, she tells them he's got autism and what that means. Children can be cruel, and if they don't understand, she doesn't want to know them.

'People don't realise they are twins because they are nothing alike at all. They look different and they have completely different personalities. I used to be really upset at the stares that Thomas would get, but now I just take no notice. People just see him as a naughty boy. They really don't understand about autism, and they certainly don't understand why one twin can have it and the other not.'

# Brains yield clues in the quest to find a cure for Batten disease



Rehan Jamil

At least 10 children born in Britain every year will be diagnosed with Batten disease. These children will become blind, have seizures that become increasingly more severe, lose the ability to walk, speak and feed themselves and will then die. Scientists have known for some time that inheriting two mutated genes from parents who are carriers prompts the progressive deterioration of the brain and nervous system. But they still don't fully understand what effect the mutations in these genes have, and how this causes the devastating symptoms.

Batten disease, or neuronal ceroid lipofuscinosis (NCL), is a collective name for at least 10 different disorders in which the lysosomes, tiny waste disposal units inside every cell, stop working. As a result, the cells become full of waste material and then die. The many types of NCL are all genetically different, have similar symptoms, and start at different ages. Infantile Batten disease, for example, starts when a child is between six months and two years old: a diagnosis means inevitable death in mid-childhood. Children with juvenile Batten

disease have no symptoms at all until they are aged between five and nine but will die at any time between late teenage years and early adulthood.

## **'Painstaking study of sections of brains affected by Batten disease yields clues about the early stage of the disease that are vital for developing treatments'**

There are at least 50 other similar rare disorders where lysosomes malfunction and fill with waste products: altogether, one in every 7,000 children will have one of these genetic diseases. At the moment, there is no known cure for most of them, and research teams around the world are working together to understand more about the process of the diseases, and to develop treatments that can save children's lives.

One of those teams is based at the 10P: the Paediatric Storage Disorders Laboratory (PSDL) is in the MRC Centre for Neurodegeneration Research and the dedicated, newly-equipped, state-of-the-art facility is led by Dr Jon Cooper. While some research teams are trying to understand the

role of genes and the proteins they produce, and others work to develop therapies, the PSDL is concerned with what happens inside the brain.

'For a long time, people thought the waste build-up inside the cells was the key to understanding the disease,' said Dr Cooper. 'Our work has led us to believe this is really a by-product of Batten disease and there are other, more crucial events, that happen within the brain. These events may be different in each form of NCL.'

For many years, scientists have known very little else about Batten disease except that it is inherited, that waste material collects inside cells, that the brain progressively shrinks as neurons die, and that the retina degenerates, leading to blindness. Even though separate genes have been identified for most types of Batten disease, some of them still remain a mystery. There are two types of Batten disease genes – one sort that should make an enzyme to consume the waste material inside the lysosomes, and others whose roles remain unknown. These include CLN3, the mutated version of which leads to the juvenile type of Batten disease. 'We don't

know what the proteins made by these genes should normally do, let alone what happens when they go wrong,' said Dr Cooper. One study with colleagues elsewhere in King's College London is using fruit flies to investigate what the CLN3 protein normally does in the brain. 'We can do simple but powerful genetic tricks in these fruit flies to help answer this mystery,' said Dr Cooper.

In the PSDL, the research team is studying the brains of sheep, another species that naturally gets Batten disease. 'We have found out that some brain cells are far more vulnerable than others,' he said. 'It seems immune responses within the brain that start long before brain cells start to die are important, and it is also clear that the synapses, through which brain cells talk to one another, are also targeted early in the disease, and are re-arranged before they too are lost.'

The researchers have discovered that most forms of the disease start deep inside the brain, rather than on its surface in the cortex. 'Although the cortex is severely affected by the end of the disease, we have found that the neurons start dying in the thalamus, right in the middle of the brain,' said Dr Cooper. 'The thalamus is like a general post office where information of all kinds is sorted. It receives this information and sends it to the right places. We've discovered that the thalamus is the epicentre of the disease – so it's a bit like an earthquake spreading upwards to the cortex.' The PSDL team has found too that glial cells in the brain seem to play an important role. 'Star-shaped astrocytes,

which control the environment around brain cells, become active particularly early and we are working to understand if this is a positive or negative event,' he said. And working with colleagues at the University of Rochester in the US, the PSDL has shown that there is an autoimmune response in one form of Batten disease. Numerous types of autoantibodies –

## **'One in every 7,000 children will have one of these genetic diseases. At the moment, there is no known cure for most of them'**

that instead of protecting against infection can attack – have been found in brains affected by the juvenile disease, getting in through a leaky blood-brain barrier. 'If these autoantibodies directly contribute to the disease, this could be something we could block,' he said.

All this work involves painstaking study of sections of brains affected by Batten disease in order to yield clues about the early stages of the disease that are vital for developing treatments.

Transplanting human neural stem cells is one hypothetical treatment: either to replace dying neurons or to be a source of enzymes that are missing in some forms of NCL. The PSDL has been involved with the work leading up to the first clinical trial of human stem cell treatment for infantile and late infantile Batten disease, now being carried out at Oregon Health and Science University in collaboration with Stem Cells Inc in the USA. Other research is focusing on treatments that would replace missing

enzymes in the lysosomes; that would give a new copy of the faulty genes; or that would break down the build-up of waste material in the cells. But for any of these treatments to be successful, scientists must first understand the nature of the neurodegeneration.

'By finding out about the processes inside the brain in each form of Batten disease, we now have landmarks to measure how successful new treatments are by studying the effect they have – do they slow things down, or even stop them?', said Dr Cooper. 'All the new information we are finding out is telling us a great deal about how the disease attacks the brain and will help us to target therapies to where they can be most effective in halting the relentless progress of the disease.'

The PSDL also work closely with charities that support families of children with Batten disease – the Batten Disease Family Association (BDFA) here in the UK and the Batten Disease Research and Support Association in America. Both charities have given financial support to the PSDL's work, and Dr Cooper is an advisor to, and sometimes spokesperson for, the BDFA. Keeping families informed of progress in research is a high priority for him and the laboratory organises regular open days for these families.

'Sadly, a diagnosis of Batten disease is currently a death sentence,' he said. 'I hope we are gradually moving towards the day when these children will get the chance to have a future.' ■



Photofusion Picture Library

The Batten Disease Family Association website is at [www.bdfa-uk.org.uk](http://www.bdfa-uk.org.uk)

# Developing and testing sometimes controversial treatment programmes

People with chronic fatigue syndrome (CFS)/ME (myalgic encephalomyelitis) are often ill for a very long time. In addition to the chronic, disabling fatigue, symptoms can include headaches, short-term memory problems, pain in the joints, disturbed sleep and difficulty with concentration. About half of people with CFS/ME are unemployed, and those who are in work have 10 times more sick leave than other general medical outpatients.

CFS/ME has been an enigma to researchers and doctors for more than two decades since it first emerged as an illness: the symptoms are still medically unexplained, there is no specific test, and diagnosis is by exclusion – when the profound fatigue is not caused by anything else. The research effort in this field has concentrated on treatments aimed at reducing the fatigue and helping patients reclaim their lives, but treatment programmes for CFS/ME have attracted controversy over the years, the choice between rest and activity sometimes being at the core of the debate.

The National Institute for Health and Clinical Excellence (NICE) Guidelines for CFS/ME recommend cognitive behaviour therapy (CBT) and graded exercise therapy (GET), both of which encourage patients to become active again. Some patients have expressed concern, however, that GET and CBT may make their symptoms and disability worse. Now the largest ever trial of treatments

**‘CFS/ME has been an enigma to researchers and doctors for more than two decades’**

for CFS/ME is underway. Funded by the Medical Research Council, the five-year PACE (*Pacing, graded activity and cognitive behaviour therapy: a randomised evaluation*) trial compares different types of treatment with the help of 600 volunteer patients, in the care of six different specialist clinics. The trial will provide evidence to either reassure or confirm patients’ doubts about the efficacy and negative effects of CBT and GET, and will include the first scientific evaluation of pacing – or APT (adaptive pacing therapy) – the treatment of choice for many patients. Pacing is based on the concept of an organic disease, and is about balancing activity and rest to help manage CFS/ME. It is supported by patient organisations like the UK charity Action for ME, which is involved in the trial.

One of the collaborators in PACE is the Chronic Fatigue Research and Treatment

Unit based at the IoP, jointly run with King’s College Hospital, and headed by Professor Trudie Chalder, who says she thinks people’s beliefs may have an important part to play in the recovery process. ‘No-one knows what causes CFS/ME, though we do think some viruses can give people an increased risk of developing it, and that a period of stress and over-activity may somehow be involved.’

Clinical experience and previous research has now prompted Professor Chalder and the Unit’s team to search for common patterns of beliefs amongst patients which they think may hinder recovery, including a fear that exercise or activity may make symptoms worse, and a dwelling on, and catastrophising of, their symptoms. ‘Beliefs and attitudes towards illness are important in many conditions, both physical and mental,’ she said. ‘It is possible that a fear of the danger of activity and exercise may inadvertently perpetuate the symptoms of CFS/ME.’

Shifting beliefs that may make recovery more difficult is one of the aims of the cognitive behaviour therapy used within the Unit. ‘CBT for CFS/ME encourages people to build up activity and establish a sleep routine, and tackles beliefs like “I can’t get better” or “this will make my symptoms worse”.’ Over recent years, Professor Chalder has adapted this therapy and developed a family-based cognitive behaviour programme as a treatment for children and young people, aged 11 to 18. For them, the consequences of CFS/ME are dire, impacting on their education and on their physical and social development as a result of long periods out of school.

An initial trial of the therapy, which involves the whole family at each session, showed it to be very successful. Six months after the therapy had ended, 83 per cent of the young people were back at school 75 per cent of the time, felt less fatigued, were more socially adjusted, less depressed and less fearful of exacerbating their symptoms. ‘The pilot showed family-based CBT, which encourages them to start doing things again, helped them to rebuild their lives,’ she said. The Unit has run a bigger trial, comparing family-focused CBT with psycho-education sessions, giving the same sort of messages. The young people have been followed up a year later to see which treatment has been more effective: the results are still being analysed.

All sorts of treatments have been advocated for CFS/ME over the years: a review of the scientific literature by the Unit team found

evidence that showed CBT and GET – involving an individually-designed home exercise programme – to be beneficial, but insufficient evidence to support the use of antidepressants, dietary supplements, prolonged rest, homeopathy, evening primrose oil and other alternative therapies.

The NICE Guidelines, published in August 2007, say there is not yet enough evidence to judge whether pacing makes a difference. Hence the PACE Trial, which seeks to find out not only whether treatments work, but why they work for some people and not for others. All participants – who will be randomly allocated to CBT, pacing, GET, or specialist care (followed by treatment of their choice) – will be assessed 10 weeks

**‘A fear of the danger of activity and exercise may inadvertently perpetuate the symptoms’**

after treatment, then again at six months and finally after a year. The IoP’s Centre for the Economics of Mental Health is analysing the cost-effectiveness of all the treatments.

Meanwhile other research projects in the Unit here are trying to understand more about the psychological mechanisms involved in CFS/ME in order to hone and develop treatments. Recently, members of the team carried out a brain scanning study, comparing the activity of neural circuits of people with CFS/ME and healthy volunteers while they completed tasks testing working memory and concentration, problems with which are reported by patients.

Both groups performed equally well on the tests, but the brains of people with CFS/ME ‘lit up’ in a different way to the brains of the healthy group. ‘The differences in the activation of the working memory network could be for a number of reasons,’ explained Professor Chalder. ‘The results of the CFS/ME group are similar to those seen in previous research when sleep-deprived healthy adults perform similar tasks. Many patients with CFS/ME have disturbed sleep, so the differences may be as a consequence of that.’

It could also theoretically be because more effort was involved in the tasks by those with CFS/ME, who characteristically are extremely conscientious and have high expectations of themselves, she said. Investigating common characteristics in patients and the role they potentially play in the development and maintenance of CFS/ME is a future area of research. ■

Rehan Jamil



## Those with stressful jobs more likely to be depressed

High-pressure jobs with high-demand workloads and tight deadlines are twice as likely to lead to depression and anxiety. Research based on information given by nearly 1,000 32-year-olds shows that young people who experience stress at work have double the risk of developing symptoms of depression and anxiety disorder than young people with less demanding jobs.

The research team, based in the MRC Social, Genetic and Developmental Psychiatry Centre at the IoP, ruled out the possibility that other factors – like a previous history of mental illness – had a part to play.

The link between stress at work and mental ill health was made in an analysis of information collected in the longitudinal *Dunedin Multidisciplinary Health and Development Study* based in New Zealand, which includes a cohort of 1,000 men and women who regularly give information about their health and lives.

Fourteen per cent of working women and 10 per cent of working men had had a first episode of depression or anxiety at age 32. Forty-five per cent of these new cases of depression and anxiety were attributable to stress at work. ■

**and...**

The IoP’s Professor of Psychology David Clark has been campaigning alongside Lord Richard Layard at the London School of Economics and Political Science for more trained therapists to treat the one in six people who have depression or chronic anxiety in the UK. They were among the signatories to *The Depression Report*, published in 2006 and calling for wider access to evidence-based psychological treatment, in particular cognitive behaviour therapy. The Report said only a quarter of people with depression or anxiety received any kind of treatment – and the only barrier to helping them was lack of investment in services.

In 2007, Health Secretary Alan Johnson announced a government decision to train and employ 3,600 new therapists by 2010/2011.

# Can GP-based care for the mind also help benefit heart disease?

Can treating the mind also help the heart? A package of work funded by the UK government's National Institute for Health Research aims to find out more about the link between depression and heart disease – and whether treatment from GP-based nurses could help save lives at risk from coronary problems.

There is some evidence to show that depression worsens the cardiac prognosis, said Professor André Tylee, who is leading the *Up-Beat* research programme: scientists think depression may exacerbate the symptoms of heart disease because of biological mechanisms associated with the inflammatory response of the immune system and the hormonal stress response system. Twenty per cent of people with heart disease also have depression, double the rate of people without heart problems.

What's more, depression is associated with a 50 per cent increase in the costs of long-term medical care for conditions such as heart disease, stroke and diabetes – depression has a knock-on effect on diet, lack of exercise, lack of compliance with self-care regimes and other behaviour that can contribute to worsening of symptoms, said Professor Tylee.

The five-year research plan starts with an information-gathering exercise that will inform the development of a 'stepped' treatment programme for depression that could be given by practice-based nurses. Nurses already regularly see patients with heart conditions to monitor their physical symptoms, such as cholesterol and blood

pressure, so it makes sense for them to care for patients' mental health at the same time, said Professor Tylee.

The information-seeking first stage will include tracking 800 patients with heart disease recruited from three south London GP practices for four years to find out about symptoms and treatment, detailed interviews with 50 patients randomly selected from this cohort, and interviews with GPs and practice nurses.

**'People with heart disease are twice as likely to get depression as other people'**

'We want to find out what professionals currently do, how they treat someone who has both conditions,' said Professor Tylee. 'Do they treat the depression differently? – do they say it's understandable that because you've had a heart attack you've become depressed, for example, and then not treat the depression as rigorously as they should? We'll also be able to find out about how they feel about different treatment options, which will help us develop the trial treatment.'

The new treatment will be tested in a clinical trial involving up to 20 group practices in south London, recruited through the Greater London Local Research Network. Professor Tylee said the programme will involve stepped care tailored to individual patients – starting with self-help materials and advice about diet and exercise through to medication and psychological treatments. Practice nurses will be trained to deliver the programme and the results evaluated by following up some 180 patients, half registered with GPs where the treatment is being trialled and half continuing to see their GP and practice nurse as usual.

If it makes a difference, the treatment could be made widely available at GP surgeries across the country.

'We know that people with heart disease are twice as likely to get depression as other people,' said Professor Tylee. 'What's more, a lot of people with heart trouble may be depressed and not know it – and the depression is probably making their heart disease a lot worse. We want to find out about that, and what we can do about it. If we treat the depression, can we improve the heart as well as the mind?' ■

# Old age not as good in France, Italy and Spain

Older people living in France, Italy and Spain are more likely to be depressed than their peers living in Sweden, Austria, Denmark, Germany, Switzerland, Greece and The Netherlands.

The differences were revealed by SHARE (*Survey of Health, Ageing and Retirement in Europe*), an ongoing European Commission-funded study which is gathering information about the health and wealth of people as they grow older.

The SHARE team includes researchers from the participating European countries: the IoP's Professor Martin Prince leads on mental health issues.

Twenty-two thousand people in the 10 countries, on average aged 65, were interviewed in their homes. Those living in France, Italy and Spain had the highest depression scores and were more likely to report loss of interest, pessimism and lack of enjoyment than older people in the other participating countries. They were also less well-educated than older people elsewhere and performed less well on cognitive tests.

Researchers think national social and economic policies affecting older people could help to account for the differences in symptoms of depression between countries. ■



Mother & Baby Picture Library

# Depression linked to early birth

Treating depression during pregnancy could prevent thousands of premature births each year, says Dr Veronica O'Keane, who specialises in perinatal psychiatry: a study carried out by Dr O'Keane and her colleagues showed that mothers-to-be who are diagnosed with depression are more likely to give birth before 37 weeks.

The study measured the stress hormones in pregnant women and found those with depression had higher levels, and were more likely to deliver their babies earlier or prematurely: babies born before 37 weeks are more likely to die in the first few weeks of life, and are at risk of developing lung disease, cerebral palsy, blindness or deafness. The researchers think increased stress hormones somehow prompt early birth.

Babies born to depressed mothers were more likely to have higher levels of stress hormones themselves: tests on two-month-old babies showed those whose mothers had been depressed during pregnancy produced higher levels of cortisol when they were given routine inoculations. 'These higher levels may mean children will be more prone to developing depression themselves in later life,' said Dr O'Keane.

'Depression is more common during pregnancy than after birth, but mothers who suffer depression during pregnancy receive virtually no support from doctors.'

The small study involved 25 pregnant women who had a diagnosis of major depression, and 35 healthy women. Three of the women with depression gave birth before 37 weeks, and all gave birth on average three days earlier than the other group. ■

# Anorexia and autism share personality traits

When Professor Janet Treasure likened anorexia to Asperger's syndrome in *The Times* newspaper, many people with the eating disorder responded in agreement. 'I have struggled with anorexia in varying degrees of severity for the past 10 years,' wrote one correspondent to the *timesonline*. 'A few years ago I began to notice how many similarities the illness has with autism /Asperger's, and was so struck by the sheer number that I actually wrote down a list of them.'

A number of shared personality traits and similarities in the thought processes of people with anorexia and people with autism have been highlighted by the research team led by Professor Treasure and her colleague Professor Ulrike Schmidt in the Section of Eating Disorders at the IoP. They think that these ways of mental processing may be inherited and somehow make someone more prone to developing anorexia.

'People with anorexia tend to be perfectionists, have obsessive compulsive traits and worry about mistakes,' said Professor Treasure. 'They concentrate on detail rather than the bigger picture, and find it difficult to change rules they have set themselves once they have fixed them in their brain. These are personality traits shared by people with autism and we are now investigating whether some of them may be caused by inherited anomalies in the neural networks and brain mechanisms responsible for information processing.'

A major tranche of research is being undertaken to discover whether any of the similarities in information processing could be 'endophenotypes' of anorexia – genetically influenced characteristics present in an individual and their close family members that may have no direct relation to the eating disorder. Researchers theorise that certain endophenotypes – particular styles of thinking, for example – may make people more susceptible to developing one of many mental health problems. It may be that eating disorders, autism spectrum disorder, attention deficit hyperactivity disorder (ADHD) and obsessive compulsive disorder all share some endophenotypes, which could challenge current thinking that these are all separate, unrelated disorders.

Identifying endophenotypes is important, says Professor Treasure, because it could help unravel the genetic conundrum of anorexia: searching for the genes

involved in these individual characteristics could be a much easier task than hunting for specific 'anorexia' genes.

'We know that anorexia is heritable,' she said, 'but finding the genes involved is very difficult. There may be dozens and dozens that contribute to its development, and these may interact with each other, and interact with brain chemistry, brain structure and the environment – social pressure and culture, for example – in a plethora of ways.'

'Because the genetic basis of an individual endophenotype is less complicated and less complex, identifying them can help us break down different mental illnesses into parts that are easier to understand. So once we have identified an endophenotype, we can look for genes that contribute to its presence, which may in turn contribute to the development of anorexia.'

**'We know that anorexia is heritable, but finding the genes involved is very difficult'**

A series of projects funded by charities, European grants and NHS money has already led the field in the search for candidate endophenotypes. The next stage is to investigate traits researchers think to be potential endophenotypes. They are doing this with the help of people with anorexia and their families who are willing to complete puzzles that throw light on their thought processing styles, have scans which show what's going on inside their brains, and give samples of their DNA for analysis. Correlating all this information will enable researchers to conclude whether certain characteristics are indeed endophenotypes – these include what scientists call 'impaired set shifting', 'weak central coherence' and 'weak Theory of Mind'.

Set shifting is the ability humans have to swap between different tasks or mindsets. Previous studies have shown that people with anorexia and their close family members have difficulties with set shifting, which means they find it hard to multi-task, deal with change, and tend to be rigid and inflexible in their thoughts. Because this trait is found in family members who do not have an eating disorder, researchers think it fulfils some of the criteria of an endophenotype.

Weak central coherence is a principal characteristic of the way people with autism

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## and...

The *Up-Beat* research programme is funded by one of six programme grants made to South London and Maudsley NHS Foundation Trust in 2007 by the National Institute for Health Research. The total amount of UK government money awarded was £12 million and all six programmes aim to increase understanding of mental health problems and to develop new treatments. Academics from the IoP are the chief investigators on each of the programmes: the other five focus on treatments for people with anorexia; treatments for people with intellectual disabilities and mental health problems; improving the physical health and decreasing cannabis use in people with severe mental illness; reducing stigma and discrimination; and improving inpatient care.

spectrum disorder think, and refers to an information processing style where there is a tendency to concentrate on the minutiae rather than the bigger picture. 'Excessive attention to detail is an enduring personality trait found in people with anorexia,' said Professor Treasure. 'In terms of the illness, people are so focused on the detail of maintaining their eating behaviour that they are unable to see the bigger, severe consequences that the anorexia has on their lives.' Some of the research already carried out is showing that people with anorexia fare less well in tests that demand global strategies, but excel in tasks that require bias to detail.

And 'Theory of Mind' (ToM) refers to social cognitive abilities that help humans engage in complex social interaction and to recognise emotion in others. ToM is impaired in people with autism and recent studies are highlighting poor social communication skills and small social networks in people

with eating disorders. The underlying neural networks that lead to difficulties in registering emotions may be one of the endophenotypes for both anorexia and autism, suggested Professor Treasure.

Discovering cognitive characteristics, which may or may not be endophenotypes,

**'Thinking styles can be an obstacle to patients getting better – gaining weight doesn't change the way you think'**

can, very importantly, influence the development of better psychological treatments for anorexia that are tailored to particular styles of thinking. The research team is already designing experimental new treatments with the help of their increased knowledge.

'Thinking styles can be an obstacle to patients getting better – gaining weight doesn't change the way you think,' said

Professor Treasure. 'We want to develop treatments that address the mechanisms inside the brain that help cause or prolong the illness, and moderate the thought processes that might contribute towards problems.' So finding out how people think and learn can lead to treatment tailored to their specific style, treatment that, for example, tackles perfectionism or inflexibility. One small study has already shown that people did better on tasks measuring set shifting ability after cognitive remediation therapy that specifically targeted the way they think rather than the contents of their thoughts.

As new treatments are pioneered, there will be long-term studies to measure their success. In 2007, the UK Department of Health's National Institute for Health Research awarded £2 million to help translate new understanding about anorexia into treatment. ■

## Therapy to change thinking styles

Consultant Clinical Psychologist Dr Kate Tchanturia started working in the Eating Disorders Service run by South London and Maudsley NHS Foundation Trust (SLaM) 10 years ago and at first found it a challenge to help. 'Patients who are admitted to a ward are extremely ill, physically weak and extremely unmotivated. The last thing they want to do is to talk about their eating when they are like this,' she says.

'I started to get interested in how people with anorexia processed information, and wondered if there were any underlying thought processes to their extremely rigid eating behaviour.' She put together a battery of tests to measure cognitive abilities that could be used in research looking for evidence of common styles of thinking among people in the acute stages of the illness, then in people who had recovered, and later, in collaboration with other members of the Eating Disorders Service team, in close family members.

After almost a decade of observing and researching a rigid mindset that kept patients with anorexia on the path towards starvation, she has piloted specially-designed cognitive remediation with inpatients. The 10 45-minute sessions, which start shortly after admission, are not designed to be a cure, or even to tackle life-threatening eating behaviour. What they do is address thinking styles that help keep people trapped in anorexia and may contribute to its development in the first place. By changing the way they think, she said, patients may be more likely

to go on to engage in psychotherapies that focus on what they are thinking about – food and eating.

The data are still being analysed, but all of the 30 patients who participated in the pilot are now willing to continue with psychological work around their core symptoms. And it seems as if the cognitive remediation has had an effect on their thought processes: measures completed at the end of the 10 sessions show the styles of all participants has shifted,

**'The therapy is not designed to be a cure or even to tackle life-threatening eating behaviour. What it does is address thinking styles that keep people trapped in anorexia'**

indicating a move towards less inflexibility in their thoughts and less attention to detail.

The cognitive remediation sessions, run by volunteer therapists supervised by Dr Tchanturia, are a starting point in the process of therapy, she explains. Food and eating don't play a part: instead individuals are asked to complete a series of puzzles and games that help them think about how they are thinking, and whether that style helps or hinders them. After the last session there is an exchange of letters about the process, and those written by both patients and therapists are being analysed to help measure the success of the pilot. The feedback is good, she said, with patients particularly liking the fact that they did not have to speak about their eating disorder during the sessions. 'The sessions

themselves didn't feel like "therapy" sessions,' said one, 'but kind of one-to-one workshops. It was so nice that there was no connection to the eating disorder and that I was able to concentrate on other aspects of me.'

The next step is a bigger trial of cognitive remediation for inpatients, to be carried out in collaboration with Stanford University in the USA. At the same time, Dr Tchanturia and her colleagues are looking at ways of incorporating and testing the success of cognitive remediation in outpatient treatment services run by SLaM, and running workshops for health professionals in the field wanting to find out more.

'The pilot study is promising, but there is a long, long way to go,' she said. 'The real challenge is to formulate and incorporate cognitive remediation into the whole treatment package, to work out how to put it into practice.'

'This has generated a lot of interest around the world. It shows how professionals and families in different countries are all desperate to find something that can help. We know that family therapy is very good for adolescents, but there is no medication that helps and even though different sorts of psychotherapy can be successful, there is a group of patients who don't get better despite therapy, and many still relapse. Processes of thinking may play a part in this. Cognitive remediation before treatment begins may simply help move people on. ■



## Home-based support and training for carers

When someone has anorexia, the whole family can be put under immense strain. Watching someone you love starve themselves is terrifying and extremely stressful: carers have to deal with difficult behaviour, stigma and shame, anger, guilt and self-blame. What's more, they may struggle to get the professional help or information they need, says Gill Todd, Clinical Nurse Leader in the Eating Disorders Service at South London and Maudsley NHS Foundation Trust (SLaM): research into eating disorders at the IoP is closely interwoven with these clinical services.

It's not surprising that the atmosphere at home can become tense, and that hostile and critical comments sometimes spill out, she said. Yet negative emotions like these can inhibit recovery from anorexia: research has shown that the positive support of families can be crucial in the recovery process.

'Carers need both emotional and practical support from their network of family and friends, and also from professionals,' she said. 'The skills they need at home are similar to those needed by professionals working on specialised units.'

Successful three-day workshops developed by the Eating Disorders research team offer carers just that – relevant information and the chance to develop skills they can use to manage better at home, give appropriate care and at the same time reduce their own levels of distress.

Now the research team is testing ways of making that training available

to carers, wherever they live, through a DVD package and on the internet. Both the DVDs and website are based on the successful workshops but can be worked through in carers' own time, at their own pace.

Both illustrate the communication, assessment and motivational skills carers need to help reduce the symptoms of anorexia, and to cope better with caring – how to support people at meal times, for example, how to facilitate weight gain and re-establish healthy eating, how to manage crises and conflict, and how to assess and manage risk. Information is also included about the use of the Mental Health Act, the role of different health professionals, and about NHS and voluntary services.

The five-DVD package comes with a manual giving theoretical and practical information and 100 carers are currently helping the research team test what difference it makes to them and the person they are caring for.

The web-based programme – developed in collaboration with beat (formerly the Eating Disorders Association), Dr Chris Williams from the University of Glasgow, Media Innovations and patients and carers – is being tested both off and on line by families of people with anorexia who are being treated at SLaM's Eating Disorders Service. This is a small preliminary study, which will inform the development of a larger trial to test the efficacy of the programme. ■

**'Caring for a loved one with an eating disorder is a frightening and stressful experience,' says Pam Macdonald, whose daughter had anorexia. 'Looking back on that bleak journey still evokes strong memories of a long, dismal tunnel littered with countless pitfalls.'**

'A major uncertainty was my own role in the process. Quickly discarding those initial feelings of guilt as futile, I nevertheless desperately craved information on how to react to the present situation. I wanted knowledge and guidance on how to react to the alien that had invaded my daughter's body. I needed to know that I was handling the situation in a way that was conducive to a healthy outcome. In my search for these answers, I stumbled across Professor Janet Treasure's work in skills-based learning for carers of those with eating disorders.'

Pam is now working on the project that is testing the effectiveness of a package of DVDs offering this training to carers, wherever they live, for her PhD.

'The DVDs and manual illustrate motivational techniques and strategies used to manage common problems that arise frequently when caring for a loved one,' she says. 'Animal analogies encourage carers to consider their own unique responses to the symptoms, and the possibility that some of these may be maintaining or even aggravating the symptoms. Safely tucking my offspring in the maternal pouch may have worked when she was aged six, but perhaps kangaroo-type behaviour wasn't entirely beneficial to the healthy emotional development of a 16-year-old.'

'I strongly believe that this type of family research and the tools taught are desperately important in supporting someone with an eating disorder.'

beat (formerly the Eating Disorders Association) offers information and support to people with eating disorders and their carers. Visit [www.b-eat.co.uk](http://www.b-eat.co.uk)

### and...

[www.eatingresearch.com](http://www.eatingresearch.com) is a website developed for families and friends of people with eating disorders by the research team at the IoP and staff at South London and Maudsley NHS Foundation Trust's Eating Disorders Service. The site offers up-to-date information about research into the causes of anorexia, bulimia and other eating disorders, details of projects developing new and better treatments and projects designed to support carers. There are pages about how to volunteer to participate in research, as well as news and events listings.



## Writing may help bulimia

Can writing about thoughts, feelings and moods for a short period each day make a difference to the symptoms of bulimia?

Previous studies have shown that therapeutic writing can make a positive difference to both the physical and emotional health of people who are not well. Structured writing tasks are already used in the treatment programme at the Eating Disorders Outpatient Clinic run by South London and Maudsley NHS Foundation Trust at the Maudsley Hospital and are being piloted elsewhere with patients who have cancer, asthma, cystic fibrosis and HIV.

Now a study seeks to find out if therapeutic writing could be beneficial for people who are binge eating and vomiting but who are not receiving any treatment.

Instructions will be sent by email, as will questionnaires designed to measure the effects of the task on the symptoms of bulimia and emotional well-being. 'People with bulimia are often too ashamed of their behaviour

to seek help and the anonymity of email may help to overcome the potential issues of shame and embarrassment,' said student Clinical Psychologist Olwyn Johnston who is carrying out the study. 'This research will explore why therapeutic writing leads to improvements in some people's health, and also look at why it may work for some people and not for others.'

Previous research has shown that psychological factors play a role in the development of bulimia: people may have low self-esteem, difficult family and social relationships, and may be lonely or depressed. Some people have had traumatic life experiences and the bulimia is an outlet for their emotions, helping them to cope with life.

Ninety people are being recruited to help with the study: half of them will be asked to write about everyday things rather than their emotions to find out whether it is the act of writing itself or the content of the task that makes a difference. ■

**My first proper seizure was when I was 17, just after I had passed my driving test,' says Nicola Bryant, who is now 35 and an accountant. 'I was in the office but I don't really remember very much about it because when my epilepsy became very bad, it wiped out loads of my memory.'**

'That first seizure was totally unexpected, and I carried on having them, with no real warning, until 2000, when I had brain surgery to remove scarring that the doctors thought was causing them. I'd been on medication, which was helping to control the seizures, and I took a year off work and went to Australia. When I came back in 1997, I tried to come off the tablets, but then my epilepsy went haywire. I had a lot of seizures – I would lose consciousness and be wiped out for two days at a time. It was impossible to work and my whole life was messed up, everything went horribly wrong. I had to give up my job and my house in London and move back in with my parents in Oxfordshire so my mum could look after me.'

'The surgery removed the scar on the left side of my brain. I don't know why the scar



Photo courtesy of Nicola Bryant

was there: it might have come from an accident I had when I was young and fell on my head, or from accidents I had when I used to horse ride.

'The operation made a real difference. It didn't stop the epilepsy, but the seizures came a lot less often and were a lot less severe. After the surgery, I was prescribed a new drug and the seizures stopped altogether. The last one I had was in 2001. Every year I ask to come off the tablets, but it's recommended that I stay on them: it's not worth risking losing my job, my driving licence, my memory. There's no telling if the epilepsy has definitely gone.'

'But thanks to the surgery and the medication, I have been able to rebuild my life. I'm working again – though when I was ready to return to work and started going for interviews, I was turned down for a couple of jobs when I mentioned my epilepsy – and am studying to finish my qualifications. Last year I ran the London Marathon for the National Society for Epilepsy, which has really helped and supported us. My memory is not brilliant and there are large parts of my life that I can't remember. Sometimes I get frustrated, irritated and a bit upset because it is really hard to remember simple things like routes to places. I have to take the pills every day but I am just so thankful not to have the seizures. ■

# Seeking to create an implant to revolutionise epilepsy treatment

Seizures experienced by people with epilepsy strike when millions of neurons in the brain 'fire' simultaneously. This unexpected electrical over-drive can produce many different symptoms – convulsions, blank staring, visual or other sensory disturbances, jerking arms and legs, for example. Mood, memory, behaviour, movement and consciousness can all be affected because the abnormal patterns of electrical activity disrupt function in the area in which they start, and sometimes spread to different parts of the brain.

A major tranche of research at the IoP seeks to learn how to predict when the repetitive bursts of electricity will occur, and ultimately work out ways of stopping them in their tracks, thus preventing a seizure from happening.

Scientists currently don't know what prompts the electrical disturbance that results in a seizure happening at any particular time. 'For some people, it's connected with lack of sleep,' said Professor Mark Richardson, who is leading the research programme, boosted in 2007 by a £1 million donation from John Paul Getty III. 'Some women get them according to the time of their menstrual cycle, and strobe lighting can precipitate seizures. It looks like there are multiple factors involved, and what they are, and why they cause the disturbance, is uncertain.'

**'In the UK, one in every 131 people has epilepsy. Each year, 1,000 people die as a result of accidents, or the seizure itself'**

What the research is concentrating on, then, is measuring the patterns of the electrical signals emitted from neurons to search for warning signs. 'If we can identify what happens leading up to a seizure, we could then develop and design some sort of device that constantly tracks electrical activity, recognises the warning signs, and then stops the seizure before it starts by stimulating a return to a normal pattern. An implant such as this could revolutionise treatment of epilepsy,' said Professor Richardson.

Anyone can, out of the blue, have a single seizure at some point in their life: a diagnosis of epilepsy is given when that seizure is not an isolated incident. Epilepsy can arise as a result of head injury, brain tumour, stroke or illness, or be genetically inherited. Seizures are usually quite short,

lasting for a few minutes, but they can continue for hours, days, and sometimes, but very rarely, weeks. They can start at any age, and tend to go into remission after a few years: studies in developing countries show that epilepsy often stops without any treatment.

In the UK, one in every 131 people has epilepsy and each year 1,000 people die as a result of accidents during a seizure – the most common being drowning in the bath – or the seizure itself. 'Some seizures switch off the brain mechanisms that control breathing and heart rate,' said Professor Richardson.

'The unpredictability of when the seizures will occur is a sword of Damocles hanging over patients' heads, he said. 'You try to live a normal life, but you live in fear of what might happen.'

Much of his team's research is carried out with the help of patients from all over the country, referred to a specialist clinic at King's College Hospital. Researchers monitor the electrical signals that allow neurons to communicate by stimulating them and measuring their response through electrodes implanted in the brain, or by non-invasive TMS (transcranial magnetic stimulation): this technique generates electrical stimulation by focusing an alternating magnetic field over a patient's scalp.

'What we do is measure the firing of nerve cells in response to stimulation and analyse how it changes over time. We know that in a seizure, lots of nerve cells are stimulated to fire. What we find is if you stimulate cells, you can see a slow change in the increase of their excitability: there is a bigger response from the neurons each time. The theory is that this response gets bigger and bigger, and then a seizure occurs.' Researchers also measure the passive electrical activity of the brain via EEGs (electroencephalograms), hooking electrodes to the scalp, allowing them to analyse the change in signals leading up to seizures.

The first choice for current treatment is medication that dampens down electrical activity throughout the brain, and can make people feel sedated or unsteady. For the majority of patients, drugs are successful and often only need to be

used pending natural remission. For the 20-30 per cent of people who don't respond to medication, surgery can be a cure, and constant mild electrical stimulation that seeks to regulate the electrical activity of the brain is a possibility if an operation is not feasible. The stimulator is a device like a pacemaker, attached to the vagus nerve in the neck.

'Surgery can be a cure if we can pin down in which part of the brain the seizures start, and if that part of the brain can be safely removed without detrimental effect,' said Professor Richardson.

To help assess the suitability for surgery, electrodes are routinely implanted in the

**'The unpredictability of when seizures will occur is a sword of Damocles hanging over patients' heads'**

brain to measure electrical surges and thus discover the area where seizures start. Once in place, they can be used for research tracking electrical activity in response to electrical stimulation, measuring the neurons' responses in a very detailed way.

And uniquely outside the USA, the IoP team is using tiny microwires inserted through these electrodes to record detailed electrical activity of individual brain cells. 'This will allow us to understand much more not only about epilepsy, but also about normal brain function,' said Professor Richardson. 'If the neurons we are monitoring are in an area of brain involved in a seizure, we can look at their excitability both before and afterwards. But we can also find out the way they fire when people are doing normal activities – like memory tests, or moving. This will help us understand more generally about how neurons encode thoughts and actions, and how different parts of the brain talk to each other while doing different tasks.'

'What we hope to do is to pull information from different measurements together and find the common patterns which indicate a seizure is about to occur,' he said. 'If we can find them, the next step is to start developing an implant that would be able to spot them and immediately kick-start the brain back into normal patterns. It would be a high-tech solution, but there is the potential for something like this to be put into clinical practice within a decade. ■

**The National Society for Epilepsy** provides information and support to people with epilepsy, and care for people with epilepsy through medical and residential services. Visit [www.epilepsynse.org.uk](http://www.epilepsynse.org.uk) to find out more about the organisation.

# New technologies discover genetic variations behind learning ability

Reading ability has been found to be highly heritable in the largest study of twins ever carried out in the UK, and based here at the MRC Social, Genetic and Developmental Psychiatry Centre. 'What we think is that the genes involved are generalist, and contribute not just to reading, but also to language skills, maths and science ability, and general cognitive ability,' said Research Professor Robert Plomin.

TEDS (*Twins Early Development Study*) tracks the genetic and environmental influences on the development of 15,000 pairs of twins born in England and Wales in 1994, 1995 and 1996 and is supported by the Medical Research Council. Research carried out with the help of the twins' families has consistently illustrated that heritable factors are at least as influential as environmental influences.

'Given our studies have proven the substantial heritability of learning abilities, it makes sense to look for the genetic variations responsible,' said Professor Plomin, who set up TEDS. 'We think many genes contribute to reading ability, but that each gene has only a small effect, which makes them hard to find.' So researchers are now using new and more sophisticated DNA techniques in a bid to identify them.

Professor Plomin and his colleagues studied the DNA of a group of TEDS children identified by tests and teacher assessments as having reading difficulties at age seven, and the DNA of a group identified as being higher achieving readers, to look for DNA differences between the two groups.

They used 'microarrays', a slide the size of a postage stamp that can assess hundreds of thousands of DNA differences throughout

**'The point of all this is working towards the time when we will be able to predict problems and intervene early'**

the whole genome – all the hereditary material encoded in the DNA that includes traditional genes but also billions of other DNA sequences. For this reason, such studies are called 'genome-wide association scans'.

And in the first genome-wide association scan of reading, supported by the US National Institute of Child Health and Human Development, they found 10 variations in the DNA sequence that were different in the two groups and therefore associated with individual differences in reading at age seven. These DNA variations are called SNPs – single nucleotide

polymorphisms. Three of them were not in traditional genes and the next challenge for researchers is to find out what influence those other DNA sequences may have.

A second study of TEDS children using microarrays was the first genome-wide scan for differences associated with general cognitive ability, also previously proven in family and twin studies to be highly heritable, and a major factor in predicting how well children fare in the education system and job market during later life. The research team looked for differences between one group of children who had scored highly on tests measuring general cognitive ability – verbal, spatial and memory skills as well as processing speed – when they were aged seven, and another group who did less well. This time they found six SNPs.

'A genome-wide scan is better than focusing on a small number of candidate genes,' said Professor Plomin, 'and we will be developing this work in future. There is so much else in the genome other than traditional genes that has an effect that we don't know about.'

'The point of all this is working towards the time when we will be able to predict problems and intervene early to stop the problems rather than waiting until it is often too late to help.'

'Identifying the genetic influences will help us develop new ways of thinking about effective education – to understand that children create their own experience within the educational process partly because of their genetic propensities.'

'If you simply put lots of money into schools, people still don't understand that the kids who learn faster are the ones who will profit the most. Our studies have shown that not only aptitude, but also appetite to learn are inherited. More money just increases the differences because the best take advantage and the poorer performing ones don't. What we need to do, therefore, is to target the children who are more likely to be at risk: therefore understanding more about genetic and environmental influences is crucial.'

'One of the most important things we have learned so far is that "abnormal" is "normal", that there are no learning disabilities, just a low end of a normal distribution of learning abilities. In other words, low performance in reading, writing, maths and science is simply the extreme of the same genetic and environmental influences that operate in everyone. ■



## Lessons from the trenches are of relevance to today's conflicts

Mild traumatic brain injury (MTBI) is being dubbed the 'signature' injury of the Iraq and Afghanistan conflicts. But Professor Edgar Jones in the King's Centre for Military Health Research says this is not a new disorder: its symptoms – amongst them headache, dizziness, irritability, amnesia and poor concentration – are similar to those of shell shock in World War I.

In a historical review of the World War I 'signature' injury that baffled doctors at the time, he suggested that 'hard-won lessons' from nearly a century ago have relevance today. Professor Jones said that head wounds and concussion were common battle injuries in both the 1914-1918 war, and in Iraq and Afghanistan. What's more, the military context is similar: the recent conflicts became wars of attrition, just as the one at the beginning of the last century did.

Shell shock caught the popular imagination and attention of the media then, he said, just as MTBI has done today. But without modern investigative techniques and knowledge, the British army struggled to understand and treat shell shock properly.

In World War II, the term 'shell shock' was banned by British authorities worried about another spate of hard-to-treat casualties: but military personnel continued to report headache, dizziness, fatigue and other similar symptoms. This time, they were described as 'postconcussional syndrome'.

Shell shock was initially thought to be a neurological disorder, caused by head injury or exposure to toxic substances, but subsequent research suggested that psychological factors contributed to its symptoms. 'It may be that labels such as shell shock reduce stigma and encourage people to seek help,' said Professor

Jones. 'On the other hand, they may divert attention from more easily treatable disorders such as depression and post traumatic stress disorder,' he said. And labels themselves can affect prognosis – studies have shown that strongly held negative beliefs can help perpetuate symptoms.

US army personnel returning from Iraq and Afghanistan are being diagnosed with MTBI, though to date fewer British soldiers have reported symptoms. 'US personnel have a range of symptoms that also meet the criteria for post traumatic stress disorder,' he said.

'There are dangers not only in assuming that MTBI is novel, but in characterising it solely as an organic injury. The evidence of the last two World Wars is that brain injury often arises in a context of psychological distress, requiring us to consider the physical but also the mental health of those with concussive injuries. ■





## Lengthy tours of duty affect health

Public debate has raged about whether UK armed forces have been 'overstretched' by simultaneous operations in Iraq and Afghanistan.

But research has shown that UK Ministry of Defence *Harmony Guidelines* designed to safeguard against excessive deployments are mostly working well. However, when they have been violated, there has been an increase in mental health problems.

And if a tour of duty has continued for longer than expected, individuals are much more likely to report increased use of alcohol and symptoms of post traumatic stress disorder afterwards.

A research team from the King's Centre for Military Health Research collected information about the frequency and duration of deployments from 5,500 regulars in the army, navy and air force over a three-year period, and compared that with information given about their mental and physical health.

They found that personnel who had had tours of duty lasting for 13 months or more were more likely to report mental ill health and problems at home. The *Harmony Guidelines* differ for each of the services, but for the army equate to a maximum 12 month deployment within three years.

'We showed guidelines on maximum length of deployment are sensible for the sake of both an individual and their families,' said Professor Simon Wessely, Co-director of the Centre. 'The guidelines aren't often broken, but if they are, there is an effect on mental health.'

The number of deployments within the past three years made no difference to people's psychological well-being: many who had been deployed on several occasions within the three years had been sent for short periods of time. The intervals in between each tour of duty may act as a buffer against the development of psychological symptoms, said Professor Wessely. ■

## No repeat of 'war syndrome' in Iraq

The war in Iraq has not taken its toll on the health of the armed forces serving there in the same way that the 1991 Gulf War did. A team of researchers from the King's Centre for Military Health Research has shown there has been no increase in psychological problems among those who took part in the invasion of Iraq in 2003, when compared to those who were deployed elsewhere.

The *Health and Well-Being Study* started soon after the end of Operation Telic 1, as the initial invasion of Iraq was called. The research team tracked – through questionnaires and interviews – more than 10,000 members of the armed forces and compared the experiences of those who had been in Iraq with those serving elsewhere.

'The first analysis of the information showed there has been no "Iraq War syndrome",' said Professor Simon Wessely, Co-director of the Centre which is jointly run by the IoP with the Department of War Studies in the sister School of Social Science and Public Policy at King's College London.

'About 20 per cent of those coming back from Iraq showed symptoms of common mental health problems – stress, poor sleep, unhappiness, worry, anxiety. But that figure is lower than in the general population. We also found, not surprisingly, that people were more likely to have subsequent problems if they had been in combat, exposed to enemy fire, or handled dead and wounded colleagues.'

Overall levels of mental health problems in the UK armed forces were lower than media reports suggest, and also lower than those experienced by US forces, he said. 'Rates of post traumatic stress disorder among US personnel returning home were considerably higher and there are many reasons for this. They were doing more fighting and taking more casualties. US military personnel sent to Iraq were younger with less experience of deployment and were more likely to be reservists. They also served there for at least twice as long.'

The team from the Centre had previously carried out extensive research into the health of armed forces who fought to liberate Kuwait in the 1991 war. The research had shown veterans of the Gulf War were twice as likely to be fatigued, have chest pains and other unexplained symptoms, and twice as likely to develop a psychiatric disorder as services colleagues who were not involved. Seventeen per cent of all UK service men and women who served in the campaign believed they had Gulf War syndrome as a result of being there. These health problems first started to be reported some three years after the conflict had ended, however.

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'Whilst the findings from Iraq are encouraging, it is premature and ill-advised to say there will be no longer-term health consequences of the war,' said Professor Wessely, 'and it's important to continue to monitor changes over time.' All participants in the original *Health and Well-Being Study* are being contacted again, and a new group of armed forces personnel have been recruited to boost the numbers of individuals giving information about their experiences to 20,000. This is now the biggest ever study of the health of the armed forces, is funded by the UK Ministry of Defence, and includes personnel who have been deployed more recently on military operations in Afghanistan.

'Originally, it was anticipated that Iraq was going to be a short, limited conflict, but things haven't turned out as expected,' said Professor Wessely. 'There has been counter insurgency and peace enforcement duties, and we want to find out what effect this has had on people's health. Because operations in Iraq have become prolonged, a health effect may become apparent with time. The possibility of a delayed effect cannot be ignored.'

Between January and June 2003, about 46,000 UK service personnel were deployed to Iraq for Operation Telic 1. Since June 2003, UK forces have continued to be deployed in south-eastern Iraq and neighbouring areas, and by the end of 2005, 100,000 UK military personnel had served there.

### 'Reserve troops in Iraq experienced more mental ill health than regulars'

Members of the Territorial Army and other reserve troops who were sent to Iraq experienced more mental ill health than regulars who were deployed there.

The study found reserve troops who had served in Operation Telic 1 were more likely to have depression and anxiety, and twice as likely to have symptoms suggestive of post traumatic stress disorder than their full-time colleagues who were on active duty.

'Regulars are constantly with their peers and can wind down and share experiences with each other,' said Professor Wessely. 'Reservists return to civilian life after only a couple of days of demobilisation and become an individual again. They are no longer part of a unit and are instead spending time with family, friends and work colleagues who may have little understanding of their experience.'

'On return from the invasion of Iraq, they also no longer had access to military medical services. Any health problems they had would have been dealt with by the NHS, and the number of NHS doctors with experience of the military is small.' When the results of this research were published, the government immediately revised its policy: military health services are now available to reservists who have been demobilised since 2003. ■

## Beliefs about signals may trigger symptoms



Rehan Jamil

Reports of electromagnetic sensitivity – symptoms like headache, nausea and tingling caused by electrical devices – have increased dramatically in Britain over recent years. It is estimated that four per cent of people in the UK have these medically unexplained problems when near power lines or mobile phone masts, or when using computers and mobile phones, for example.

The Mobile Phone Research Unit at the IoP carries out a programme of research to find out more about reported symptoms of sensitivity to both mobile phone signals and other electromagnetic fields. The work is supported by research grants from the UK Mobile Telecommunications and Health Research programme.

And so far, the studies have found that people who report symptoms when using a mobile phone do not react any differently to genuine or sham signals in testing sessions.

One study carried out by the Unit showed that 63 per cent of participants who said they reacted to mobile phones believed a signal to be present when in fact it wasn't. These sham signals triggered symptoms in the same way that mobile phone signals did during the testing sessions, carried out under 'double blind' conditions, when neither the researchers nor the participants knew whether signals were really being transmitted.

'We found no evidence to indicate that self-reported sensitivity to mobile phone type signals has a biological basis,' said James Rubin from the Unit, who led the research. 'This is in line with the results from the majority of previous studies testing for electromagnetic sensitivity – that there is no difference in the severity of the symptoms elicited by active or sham exposure to electromagnetic fields.'

But if an electromagnetic field does not cause the symptoms, what does? Dr Rubin thinks the problems may be the result of a 'nocebo' phenomenon – an ill effect caused by the suggestion or belief that something is harmful. 'Psychological factors could play a part,' he said.

Another explanation is that chronic illness or another health problem might cause the symptoms. A study carried out by the Unit compared the health of 71 people who reported sensitivity to mobile phones with the health of 60 people who experienced no problems. Nineteen of those sensitive to mobile phone signals also had symptoms triggered in the presence of other electromagnetic fields. Those who reported the greatest electrosensitivity also experienced greater depression and worse general health, and were more likely to worry about things like tainted food. ■

## Understanding more about depression and Parkinson's disease

More than a third of people with Parkinson's disease have depression or low mood. But doctors often find it hard to recognise it because many of the symptoms are similar to those of Parkinson's itself – and when it is diagnosed, treatment is not necessarily the best it could be, says Professor Richard Brown who is based in the MRC Centre for Neurodegeneration Research. Antidepressants tend to be prescribed, but there have been no long-term studies to find out how effective they are for patients already taking medication for Parkinson's.

'Because it's difficult to assess, depression in people with Parkinson's can be under-diagnosed or misdiagnosed,' he said. 'Patients themselves may fail to recognise symptoms as depression because they overlap with the symptoms of the disease. Or they may be

### 'If depression is diagnosed, doctors currently rely on antidepressants, but their effectiveness has not been tested'

reluctant to raise depression with their doctor, believe it's to be expected, or think it's irrelevant when they and their doctors are concentrating on managing their physical symptoms. They may also be reluctant to take more drugs on top of their already complicated treatment regimes.

'But evidence suggests depression in Parkinson's disease is associated with a greater disability and cognitive impairment, with reduced quality of life and even increased mortality. If a patient has depression, it is also more likely that their family care-givers will be depressed or distressed,' he said.

Now Professor Brown is leading a large Parkinson's Disease Society-funded study to find out more about the nature of depression experienced by patients: the results will be a springboard for future research on treatments specifically tailored to the needs of people with Parkinson's. 'The most limiting factor in finding the best treatments is our inadequate basic knowledge of the condition itself,' he said. 'Until now, no large-scale or long-term studies have been carried out.'

At least 500 people with Parkinson's are being recruited to the study through hospital-based neurology or care of the elderly services in London and south-east England, Newcastle

and the north-east of England, Liverpool and north Wales.

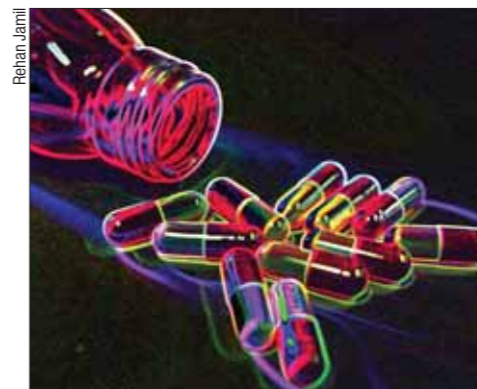
They will be interviewed about their general health, their Parkinson's symptoms and management of them, and they will be assessed for symptoms of depression and other mental health problems. Each participant will be interviewed once a year for five years, to allow researchers to find out what happens to those who are depressed, and if and when depression develops in those who are not depressed at the beginning of the study.

'We want to find out if there is more than one type of depression, why some people become depressed and others don't, why some recover while others remain chronically depressed,' he said. 'This will also help us understand more about how depression in Parkinson's should be assessed and diagnosed. At the moment, we are unable to effectively identify which patients are depressed, let alone which ones are at risk of becoming so.'

'If depression is diagnosed, doctors currently rely on antidepressants, but their effectiveness has not been tested in clinical trials,' he said. 'We need more research into other approaches to treatment as an alternative to medication, and we can only do that when we know more about the nature, causes and consequences of depression in Parkinson's.'

The study of *Mood States in Parkinson's Disease* is being carried out in collaboration with Newcastle University and the University of Liverpool.

About 10,000 people in the UK are diagnosed with Parkinson's disease each year: symptoms on average first appear when a patient is older than 50, although one in 20 people diagnosed is aged under 40. ■



Rehan Jamil

**Amanda Osborne was 28 when she was diagnosed with Parkinson's eight years ago. 'I had been ill for a few years – I was very tired all the time, my legs hurt a lot, I had terrible fatigue.** When I first went to see a neurologist, he said I probably had ME. I went back to work, but had more time off, and then my hands started shaking. When I went back to the neurologist, he referred me on to Charing Cross Hospital where they diagnosed Parkinson's. When the doctor first told me, I was glad to have a name for what was wrong. But then it hit me later, and I was shocked and just stayed in bed for while.

'Charing Cross put me in touch with a Parkinson's nurse, and I rang her, and she put me in touch with the Younger Parkinson's Network, a volunteer group within the Parkinson's Disease Society. I went with my mum on a weekend away organised for younger people who had Parkinson's and first of all, when I saw wheelchairs in the foyer, I thought: "oh no"... and I kept staring at everyone. Then there were talks by doctors, and I started talking to the people there, and as I found out more, it was easier. I joined the national committee for the Younger Parkinson's Network and did that for six years.

'I had to finish work (at Barclays Bank) in 2001 on health grounds.

'I'm on medication for the Parkinson's – I take tablets four times a day, and I have learned how to manage it. I'm 36 and single and should be going out in the evening, but if I'm very tired, it triggers the dyskinesia – the involuntary moving – and I hate doing that in public.

'If I'm tired and anxious, I can get the shakes, so I do have to pace myself. The other day I pruned a rose bush and the next day my hand wouldn't move.

'I had a bad bout of depression when I was about 20, and went on antidepressants at the time.

'I think Parkinson's and depression are linked. I get good days and bad days. I see the consultant every six months and he can tell what frame of mind I'm in. He prescribed me with antidepressants which I take in addition to the Parkinson's medication.

'When I'm down, I can be really horrible but there's nothing I can do about it. I don't cry a lot, but I do dwell on things, and little things really get to me.

'If I'm stressed, or get worked up, or worry about being ill, I can get very miserable. Sometimes I hate myself – I'm on my own and I've got a horrible illness. I saw a counsellor for two-and-a-half years and I think that did me good.

'I accept the depression though. When it comes I know it will pass again. I think it's all part of the course of the illness. '

**The Parkinson's Disease Society** supports people with Parkinson's, their families, friends and carers, and funds research into the progressive neurological condition. Visit [www.parkinsons.org.uk](http://www.parkinsons.org.uk)

# Communication with friends and family vital in aftermath of tragedy

Ordinary people are very resilient and generally don't need professional help to cope with tragedy and disaster if they haven't been directly involved or affected. That's the view of Professor Simon Wessely, Professor of Epidemiological and Liaison Psychiatry, informed by various studies, the most recent of which surveyed Londoners' reactions in the wake of the July 2005 tube bombings.

Working with MORI (Market and Opinion Research International), a team of researchers from the IoP carried out a random telephone survey to find out how the terrorist attacks had affected the emotional well-being of people who had read about or seen TV footage of the carnage. The Home Office-funded survey took place 10 days after the bombing and finished a few days before the second failed attack on the transport network.

Thirty-one per cent of the 1,010 people interviewed said they were very distressed, 55 per cent felt they were in danger and 58 per cent feared for the safety of their family and friends. Thirty-two per cent said they planned

to travel less on public transport and would cut down on visits into central London.

But six months later, a follow-up telephone survey of the same people found the level of distress had dropped considerably.

Those who remained seriously worried and concerned were the ones who had had difficulty contacting family and friends on the day, said Professor Wessely. Following the bombings, this stressful experience had been exacerbated by the mobile phone networks' inability to cope.

'The surveys showed that in the aftermath of a tragedy, people want to talk to family and friends, to mobilise their own social networks, and therefore in emergencies, communication is important and should be encouraged,' he said. 'Instead of telling people not to use their phones, we should be saying "keep it short."

'There have been similar findings in Israel where population surveys have shown the vast majority of people find checking on the whereabouts of their family and friends to be a helpful coping strategy after an attack.'

The first survey showed that 71 per cent of those interviewed had spoken to family and friends about the attacks. Less than one per cent had sought professional help and only 12 people said they needed it.

'The theme running through this is that people don't crack up, and psychological help for everyone from mental health professionals is not necessary. Resources should therefore be concentrated on the small number of people who do need it.

'Our research has shown that it was the same with population reactions in the Blitz – people's morale does not collapse. But some things have changed since then – in our more individual-focused world of today, we tend to forget that when bad things happen, we are supposed to feel bad. Unlike during the Blitz, nowadays all of us have almost instant media exposure to people in severe distress, and so feel the need to "do something". Hence the knee-jerk response to send in the "trained counsellors". It makes us feel better, even if the research shows it does little good for those directly affected.' ■

# Cognitive behaviour therapy can help lay traumatic memories to rest

Cognitive behaviour therapy (CBT) has been much in the news over recent years and has been recommended by the UK National Institute for Health and Clinical Excellence (NICE) as an effective treatment for all sorts of mental health problems. The umbrella of CBT embraces a wide range of treatments, however, and the ones that work best are those designed specifically to address the particular symptoms of a disorder or problem.

Professors David Clark and Anke Ehlers have done just that, developing and evaluating treatment programmes for people with panic disorder, social phobia, and people with post traumatic stress disorder (PTSD).

Both psychologists say this targeted approach leads to the very best results: the research they have carried out to test the efficacy of their programme of CBT

for PTSD, for example, shows that 75 per cent of people no longer have the diagnosis after treatment and a further 15 per cent improve, but don't get fully better. Work is now underway to investigate ways of helping people with remaining symptoms further.

'There are a lot of different techniques and versions of CBT for PTSD,' said Professor Clark. 'Some look at stress management, for example, but the most effective versions are trauma-focused. The NICE review of PTSD treatments has shown that you really have to tackle the trauma directly, otherwise the outcome won't be as good. The problem is that working with the memory of the trauma is painful, and patients will not be able to go through with treatment if the work is not done in a sensitive way. But it can be done.'

Their first step in developing a CBT programme for a particular problem is to find out why people aren't getting better naturally. 'Most people, for example, recover from anxiety without the need for treatment. They are able to work out themselves that their thoughts are unrealistic, that they are over-estimating how much danger there is. So in the first instance, we carry out detailed interviews with patients to discover what prevents their thinking from self-correcting.'

For PTSD, they needed to study the characteristic all-consuming intrusive memories that haunt an individual, flashbacks that make it feel like the assault, accident or disaster is happening to them time and time again.

'A sizeable number of people cope with trauma by themselves,' said Professor Clark.



'After a trauma, it's normal to have intrusive memories that cause distress, but it's natural for those memories to wane over a period of time. It's a similar process to getting over the loss of a loved one. The natural course is towards recovery.'

In PTSD, Professors Clark and Ehlers think something goes wrong with the processing ability of memory, making it impossible for individuals to put the traumatic experience behind them.

One of the planks of the CBT programme they have developed is based on the premiss that individuals are unable to 'elaborate' their memories of the event – to process them as something that has happened in the past and store them, rather than constantly experience them. 'People with PTSD actually feel their memories as if they were present reality,'

said Professor Clark. 'If they felt as if they were going to die during the trauma, they feel as if they are going to die every time the memory comes. What we do is to try to help them elaborate that memory by making it connect in their minds with the information "I didn't die" and "I am still alive" here in the present.'

**'People with PTSD actually feel their memories as if they were present reality'**

People with PTSD also often have very negative thoughts about themselves and their own capabilities. 'People blame themselves for what happened, or think they didn't do the right thing, or feel shame because they didn't resist an attack, or guilt because they didn't stop what happened,' said Professor Ehlers.

'People's view of themselves can change, they may seriously worry because they start to believe they are not as able, competent, good or kind as they thought they were.' These self-doubts and faulty beliefs can seriously affect the way people lead their lives.

The therapist's role is once again to help the patient find a more balanced perspective, to help an individual search for evidence to show them that their behaviour was all that could be expected of them in the circumstances.

'If after a terrorist attack someone feels guilty because they think they should have done more to help others, we explore the reasons why they could not do more – they were in shock, or injured, for example, or were already helping other people and could not be in two places at the same time. We may also ask other people what they would have

done in the same situation and feed their answers back to the patient,' said Professor Ehlers.

Tackling the triggers of the intrusive memories is another important aspect of the therapy. Smells, sounds or things in the environment that are seemingly unrelated can suddenly and unexpectedly prompt the realistically vivid images, said Professor Ehlers, and detective work is sometimes called for to make the link so an individual can understand why that is happening. 'If someone were involved in a road traffic accident at night, and the last thing they saw was the glare of headlights, they might be sitting in the garden and suddenly feel terrified because the sun unexpectedly breaks through the clouds. This sort of trigger, that isn't at all obvious, might make them think they are "going mad",' said Professor Clark.

The CBT programme Professors Clark and Ehlers' team has developed stretches over three months, with 12 90-minute weekly sessions. Professor Ehlers and her colleagues have recently been testing the success of a programme with the same number of hours condensed into a week: the idea is to offer a shorter treatment for people whose memories impinge so much that their lives seem about to implode because of the resulting anger, fear, nightmares and lack of sleep. The Wellcome Trust-funded trial is being carried out in collaboration with Oxford University's Department of Psychiatry, and results from a pilot study are promising.

Professors Clark and Ehlers first started developing CBT for PTSD following accidents,

violent crimes, attacks and disaster in the 1990s. More recently, they have successfully used the programme to help victims of terror.

The Omagh-based Northern Ireland Centre for Trauma and Transformation (NICTT) was set up in 2002 to offer CBT to people who had PTSD as a result of civil conflict in earlier decades: some people referred there were still experiencing vivid, intrusive memories from

#### 'CBT is an effective treatment for PTSD related to terrorism for both civilians and people in the military'

40 years ago. The whole Centre was set up as a controlled trial, the results of which have proved that CBT is an effective treatment for PTSD related to terrorism for both civilians and people in the military.

'Some of the people referred to the Centre were multi-traumatised and had been victims of terrorism several times,' said Professor Clark. 'Many had tried previous therapies that had been unsuccessful.'

In addition to its continuing caseload, the Centre now has the remit to train other therapists in CBT for PTSD throughout Ireland. Professor Clark continues to be the Clinical and Research Advisor there.

The experience gained in Omagh was invaluable when the team from South London and Maudsley NHS Foundation Trust's Centre for Anxiety Disorders and Trauma teamed up with Professor Chris Brewin at University College London and other trauma centres in the capital to offer therapy to people directly affected by the tube bombings on July 7 2005.

The service was set up in the immediate aftermath and everyone known to the police and accident and emergency services was contacted and sent a questionnaire, which screened for symptoms of PTSD: those who needed help were offered quick referral for a two-year period. 'This two-year outreach programme was necessary because sometimes more severe or complex cases take longer to come forward for treatment,' said Professor Ehlers. People could also self-refer to the screening team and all GPs in the capital were sent information about the service.

Different centres used their own form of CBT: here at the Centre for Anxiety Disorders and Trauma, the Clark/Ehlers model was used. In total, some 200 people received treatment, and improvement in symptoms was measured at the end of each session to enable a future analysis of its success.■

#### and...

Research into the psychological consequences of war, political violence, torture and natural disaster is undertaken in collaboration with the Istanbul Centre for Behaviour Research and Therapy in Turkey. Dr Metin Basoglu is both Head of the Trauma Studies Research Group at the IoP and founder and Director of the Centre. The research focuses on developing effective treatments for survivors of mass trauma who have post traumatic stress disorder, and to promote the evidence-based treatment to disaster-struck countries around the world.

## Public unperturbed by polonium

When former Russian spy Alexander Litvinenko died from polonium 210 poisoning in London in November 2006, the public were not overly worried about the possible effects of the radioactive substance on their health, even though traces were discovered in the heart of the capital.

An analysis of a telephone survey of 1,000 Londoners carried out by a research team from the IoP concluded this was because people assumed the death was an act of espionage rather than an act of terrorism, and because they were re-assured by information about the minimal risk to public health issued by the UK Health Protection Agency (HPA). Only 12 per cent interviewed thought they might be in danger: those who did mostly believed the contamination was targeted against the wider public rather than an individual.

Polonium 210 must be ingested or inhaled to cause harm and the HPA continually stressed

the risk to the general public was low. The Agency briefed the press on an almost daily basis and similarly updated its website. Seventy-one per cent of those interviewed by phone said they knew there was no risk unless they had spent time in a contaminated area, and 80 per cent felt the HPA's response had been appropriate.

Members of the public who had been in a contaminated area were advised to telephone NHS Direct, and many received follow-up calls from the HPA. People who were potentially at risk were offered a urine test. The research team also carried out in-depth interviews with 86 people who had been in places that had been contaminated. 'Most were satisfied with the contact they had had with the HPA,' said James Rubin who led the research.

'The polonium incident caused limited public concern about potential health risks. This is partly due to the public's perception



Getty Images

of the incident as a "spy story" and partly due to successful communication about low risk. It's important in similar incidents to give members of the public access to detailed, comprehensible and relevant information about any risk they might have been exposed to.■

## How do ingredients of cannabis induce symptoms of psychosis?

What does cannabis do to the brain and how does it contribute to the symptoms of psychosis? Some 50 healthy volunteers are helping researchers find out more about the effects of the drug on both the chemistry of the brain and their thoughts in a series of laboratory-based projects.

The links between cannabis and schizophrenia have regularly hit the headlines for the past couple of years. IoP researchers have already shown that people who have a pair of one type of the 'COMT' gene are more likely to develop schizophrenia if they smoke cannabis regularly during teenage years, and that people with psychosis who continue to smoke cannabis can make their symptoms worse.

Now Dr Paul Morrison is exploring the acute effects of cannabis on the brain, giving each of his volunteers an injection of pure, synthetic THC, the psychoactive ingredient of cannabis that produces the 'high'. He is then scanning their brains and asking them to describe how they feel while having the equivalent to a joint of street-strength skunk cannabis in their system. 'The idea is to explore how THC produces the symptoms of acute psychosis,' he said.

And he's found that about 40 per cent of the volunteers get symptoms of psychosis during the two hours they are under the influence of the drug. 'Some people have delusions, for example, believing their minds are being read, and some feel that something else is controlling their movements and thoughts,' he said. 'Some are no longer aware if they are merely thinking or are actually speaking out loud.' There is no marked change in the behaviour or perception of the other 60 per cent: a few are really bored, he says, while the others feel completely in control but altered in a way 'that's very enjoyable'.

Each of the volunteers in this study have SPET (single-photon emission tomography) scans at University College Hospital in central London, before and after the injection, to measure what's happening to the dopamine systems in their brains. Scientists studying schizophrenia think disturbance of this chemical neurotransmitter is somehow instrumental in psychotic mental states. Dr Morrison's research team is then correlating the experiences of the volunteers with the activity of the dopamine receptors. All volunteers are also giving a sample of their DNA to allow researchers to find out which types of COMT genes they have.



Rehan Jamil

'By comparing the information from the scans with the descriptions of what the volunteers are feeling, we will find out if the activity of dopamine is related to the temporary psychosis experienced by some. We will also be looking to see if those people who did experience symptoms of psychosis share the same types of COMT genes,' said Dr Morrison. This work is to continue in future with PET (positron emission tomography) scanners at St Thomas' Hospital, which give more information and better images of the brain's chemistry.

A second project is looking at the effects of THC on attention, memory and reasoning. Following the injection, volunteers are asked to carry out pencil and paper tests designed to measure these cognitive abilities, and once

#### '40 per cent of volunteers get symptoms of psychosis during the two hours they are under the influence of the drug'

more to talk about how they are feeling. The research team wants to find out if those people who experience transient psychosis while the drug is in their system also have difficulties remembering and concentrating.

And another group of healthy volunteers is soon to have an EEG (electroencephalogram) while under the influence of THC. This test measures and records the electrical activity of the brain, and involves electrodes being

attached to the head and hooked by wires to a computer. This will allow researchers to see if there are any changes in the normal pattern of communication between brain cells when the volunteers are asked to do a simple task like tapping with one finger or saying 'ah'.

'We want to find out whether THC has an effect on the synchronised firing of neurons needed to make something happen in our bodies. If there is an effect, it might explain why sometimes people don't know if they have spoken something or just thought it, the apparent disconnection between the will to do something and actually doing it, and knowing that you have done it, which we usually experience as one event,' said Dr Morrison.

THC is one of more than 60 molecules found in the cannabis plant: another molecular candidate for inducing altered behaviour is CBD, which reduces anxiety. Dr Morrison and colleagues are about to start work on similar information-gathering projects to assess this molecule's effect on the brain, injecting a synthetic version, then scanning, testing and talking to healthy volunteers.

At the same time, they are designing a tool that accurately measures the symptoms of short-term psychosis caused by cannabis alone, informed by the volunteers' descriptions of how they are feeling. To date they have been using existing measures designed for people with schizophrenia.■

# Insight from brain scans helps hone the use of antipsychotic medication

The majority of people with schizophrenia are, at some time after diagnosis, prescribed antipsychotic drugs, medication given not to cure, but to alleviate the symptoms of psychosis – hallucinations, delusions, agitation and confusion.

No one fully knows, however, how the family of drugs used as antipsychotic medication achieve their effects. Just as scientists do not yet have a complete picture of what happens inside the brain to cause the symptoms of psychosis, they do not yet have a full understanding of the mechanisms of antipsychotic drugs, also called neuroleptics.

There are about two dozen different types of antipsychotic medication, all of which alter the levels of chemicals inside the brain. The first were used in the 1950s and both this original generation of drugs (called typical antipsychotics) and a second generation used since the 1990s (atypical) can cause side effects in a significant number of patients. These include drowsiness, muscle stiffness, a dry mouth, shaking, restlessness, increased appetite, blurred vision and sexual difficulties, and are often one of the reasons why people stop taking their medication.

Understanding more about how and where the medications interact with the natural chemicals inside the brain can help doctors refine dosages and use existing drugs in a more effective way, with fewer resulting side effects.

Researchers already know that the abnormal production of too much of the brain chemical dopamine can lead to hallucinatory experiences, delusions and disordered thoughts. The chemical structure of antipsychotic medication allows it to bind with dopamine receptors and block their function. It seems that

## 'Scientists do not yet have a full understanding of the mechanisms of antipsychotic drugs'

by stopping the transmission of dopamine from one nerve cell to another, the drugs dampen these symptoms.

But does the medication stand in the way of other neurotransmitters, in addition to dopamine? Which receptors do they block, and in which parts of the brain? Do the drugs block too many receptors?

Are some receptors they bind linked to other receptors in different parts of the brain? And why is it that antipsychotic medication has no effect at all on some people?

Professor Shitij Kapur, newly-recruited Psychiatrist and Neuroscientist at the IoP, is working with volunteer patients, brain scans and funding from the Medical Research Council to find the answers to the many hows, wheres and whys about antipsychotic medication. It's a continuation of work previously carried out when Professor Kapur was Chief of Research at the Centre for Addiction and Mental Health in Toronto, Canada, looking at the role of brain receptors and neurotransmitters like dopamine, and how these are affected by the drugs. He and his team have shown that most antipsychotics, both old and new, block dopamine D2 receptors, one type of the group of receptors involved in the transmission of the chemical around the brain, but to different degrees in different patients.

D2 receptors are used in different pathways in different parts of the brain for different functions. 'One of the questions we want to answer is which D2 receptors, in which

regions of the brain, are the most critical for ameliorating the symptoms of psychosis,' said Professor Kapur.

Interfering with dopamine transmission in some areas of the brain can help to alleviate the symptoms, but blocking the transmission in other pathways can result in side effects. Blocking D2 receptors in areas of the brain involved in motor movement, for example, can lead to tremors and involuntary muscle movements. Professor Kapur and his team's research has shown that some drugs also block D3 receptors, but never D1 and D4. What effect then does that action have on the symptoms of psychosis, and what unwanted symptoms does it cause?

'We also need to find out the amount of medication we need to use,' he said. 'We have already observed that if you block 65 per cent of the dopamine system, people get relief from hallucinations and delusions. But if 80 per cent or more of the system is blocked, people get stiffness or tremors. They also report a subjective dysphoria – they say they feel like a "zombie". So while the existing drugs can improve the symptoms of psychosis, if too many receptors are blocked, it seems the more negative side effects a patient has. This has important implications for the prescribed dosage.'

Another finding emerging from this work has challenged the perceived wisdom that antipsychotic medication doesn't start working for up to three weeks. With the help of scores of patients and the insight given by brain scans, Professor Kapur and his colleagues found that the drugs

have a chemical effect on the brain on the first day of taking them.

The brain imaging technique he uses is positron emission tomography (PET) and the ongoing IoP-based research is being carried out in collaboration with the PET Imaging Centre at St Thomas' Hospital on the South Bank in London. The Centre is part of both Guy's and St Thomas' NHS Foundation Trust and King's College London's School of Medicine, a sister School of the IoP.

## 'Ultimately, this research will allow the design of more effective medication'

PET scans illustrate the chemistry of our bodies, and can be designed to highlight one of the thousands of different neurotransmitters in the brain, and show its activity at any one time.

The scan involves the injection of a very small amount of a radioactive tracer designed to search and lock on to a specific chemical like dopamine. The scanner has cameras that detect the rays emitted from the radiotracers and turn them into electrical signals that are processed by a computer to generate images of different 'slices' of the brain. The greater the concentration of the chemical, the greater a signal it gives.

'We scan patients before they take the medication, and then again afterwards to measure the chemical effects in their brain of different dosages, different drugs and after different periods of time,' said Professor Kapur. 'At the same time, we keep records of their symptoms to find out whether the medication is making a difference, who gets better and

who gets side effects. We can then correlate this information to what is happening inside the brain.'

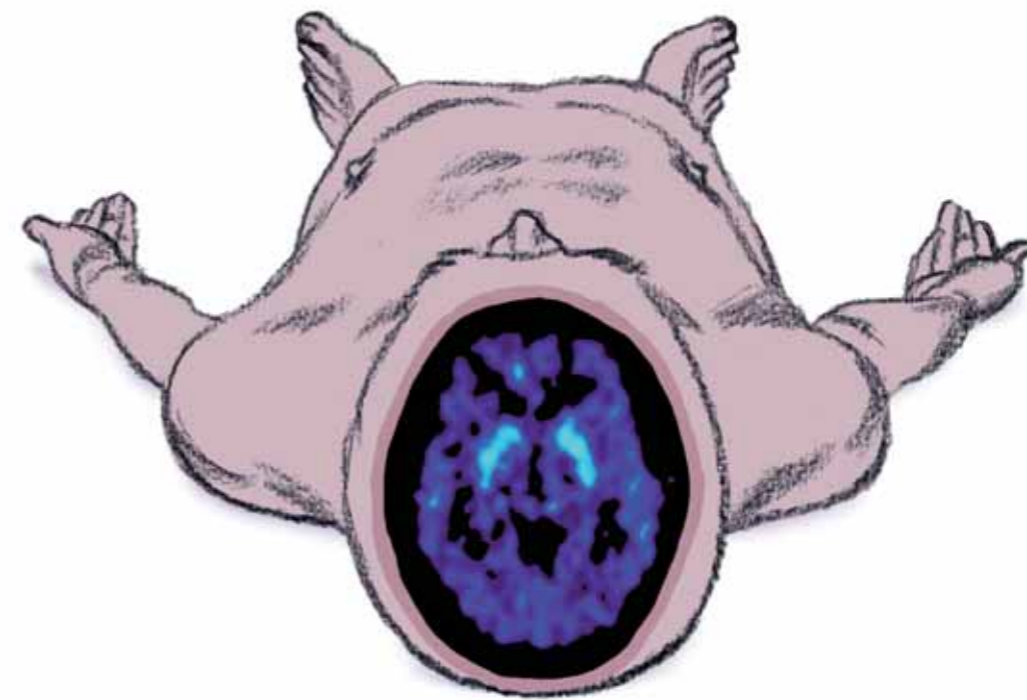
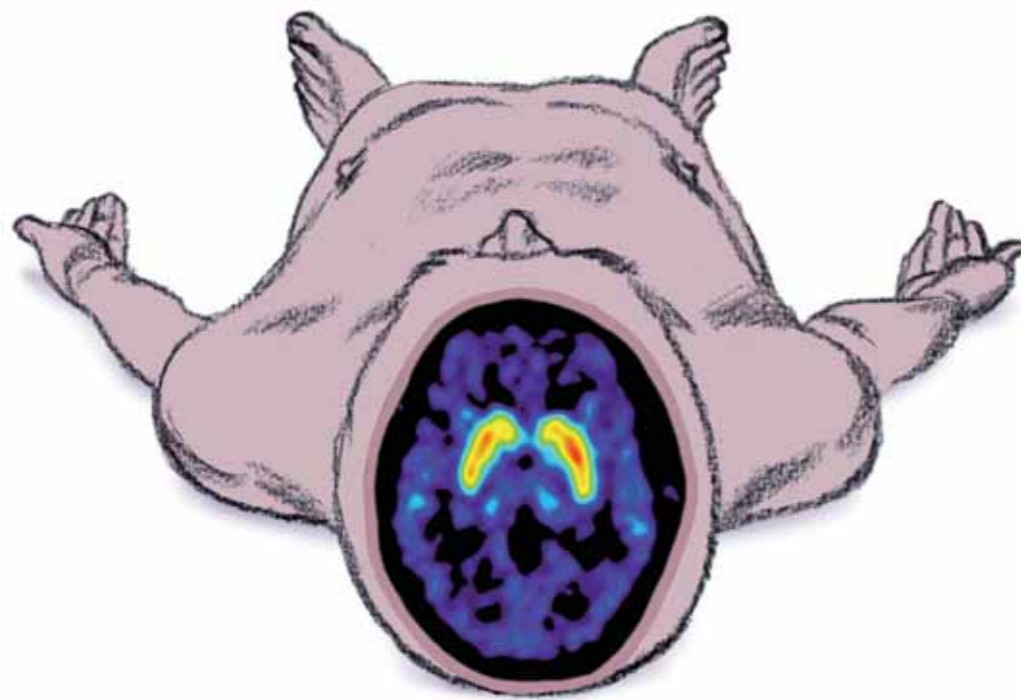
Listening to patients is as important as the metabolic information gleaned from the PET scans, he said. Their personal experiences are crucial to the research. Through this process the research team has learned that the medications don't simply eradicate the delusions and the hallucinations – they often help patients to detach themselves from the symptoms, to push them 'to the back of their minds'.

'All the research is about yielding information that allows us to refine the drugs, to allow better use of the medications currently available, and ultimately to design a totally new, more effective set of medications,' said Professor Kapur.

In the long term, then, increased knowledge about the neurochemical processes involved could lead to the development of more specifically targeted drugs that do the job they are designed to do, and that job only.

It may be that a new, third generation of antipsychotic medication will be designed to affect only, and very accurately, the levels of very specific chemicals in just the parts of the brain that are involved in creating the symptoms of psychosis.

As well as bringing direct benefits to patients, understanding how antipsychotic drugs work also gives greater knowledge about the chemical machinations of the brain that cause the symptoms of psychosis, helping to add more pieces to the jigsaw puzzle of how and why schizophrenia develops. ■



These PET scans show the level of dopamine neurotransmission inside the brain before and after treatment with the antipsychotic drug haloperidol. The first scan shows the level of dopamine transmission before drug treatment. The second scan shows how the medication blocks the D2 receptors, thereby decreasing the transmission of dopamine signals from one cell to another.

# Massive campaign to stamp out discrimination against mental illness



Peter Bush/NZ Rugby Museum

Former All Blacks player John Kirwan is one of a host of New Zealand celebrities who have spoken about their mental health problems in a series of TV adverts made for the national *Like Minds Like Mine* anti-stigma campaign.

England's biggest ever nationwide anti-stigma campaign in the field of mental health is to be launched in 2008, and the IOP is part of the consortium leading it.

Funded by the Big Lottery and Comic Relief, *Moving People* is the working title of the campaign which will involve thousands of service users up and down the country and aims to change attitudes that lead to discrimination against people with mental health problems in almost every aspect of their lives.

'The strong evidence is that an effective way to reduce stigma is through direct personal contact,' said Professor Graham Thornicroft, who has been involved for some years in a research partnership with

the national charity Rethink to find ways of combating stigma and discrimination, and works internationally in this field.

'Many people have strong, stereotyped views about mental illness, often formed in childhood. Direct contact with individuals means they can learn the truth, become more informed about the reality of mental illness and find out that people with mental health problems are people just like anyone else.'

Countless studies have highlighted people with mental illness reporting discrimination in work, marriage, parenting, relationships, housing, leisure and religious activities.

And yet Professor Thornicroft's research has shown that just two short sessions where service users talk about their lives and their

experience of discrimination can make a real difference to the attitudes of police and secondary school children. Now research from around the world is demonstrating how successful national anti-stigma campaigns can also be. A carefully orchestrated campaign in New Zealand, for example, says Professor Thornicroft, has led to a gradual improvement in public attitudes over the past 10 years, and has included a series of TV adverts which put the spotlight on celebrities talking about their experience of mental ill health.

*Moving People* will also include a media campaign, but only after a detailed consultation has been carried out with service users throughout England to shape its content and help develop a 'brand'. An international

advisory group will at the same time draw on experience from across the world to inform the campaign's on-the-ground activities, and the *Moving People* team will work closely with the UK government-funded SHiFT campaign, also challenging stigma and discrimination in England.

The IOP's role is one of evaluation: the consortium members charged with making *Moving People* happen are three charities – Mental Health Media, MIND and Rethink. Some of these organisations' existing local activities are to be immediately expanded to bring people with and without mental health problems together on a regular basis, with a focus on physical activity – from football to conservation projects.

## 'Many people have strong, stereotyped views about mental illness, often formed in childhood'

There will be periodic high-profile mass activity events like sponsored walks to both raise awareness and bridge the gap between those with mental health problems and those without. A programme of training in medical schools and teacher training colleges, led by service users, will aim to inform young professionals' views before they take the first steps on the career ladder: discrimination in education and even health services is well-documented.

The four-year project has £18 million worth of funding: 'an award of this scale is a once in a lifetime opportunity,' said Professor Thornicroft. He does not, however, underestimate the difficulties in 'changing knowledge, attitudes and, most importantly, behaviour.'

Since March 1993, the Department of Health has funded national surveys of public attitudes toward mental health. The most recent 2007 survey found that some attitudes have deteriorated over the last decade and that, in particular, the perceptions of danger posed by people with mental health problems have worsened.

Much of this deterioration may be to do with the way in which mental illness is portrayed in the media, said Professor Thornicroft.

'There is evidence that media coverage reinforces stereotypes and perpetuates misinformation. Previous research has shown that two-thirds of news items about mental illness are about risk, violence and threat. Fewer than 10 per cent of news stories are about service users, and people with psychosis are rarely interviewed or quoted: they are wrongly assumed not to be able to speak on their own behalf.' Part of *Moving People's* campaign will be targeted at the press, and the research team will be monitoring press cuttings, analysing the nature of coverage – sources used, balance, focus, language and tone.

The advantage of regular public attitude surveys is that they can measure trends over time. As well as using this information to help evaluate the overall success of *Moving People*, the IOP team will be finding out about the experiences of people with mental health problems, whether they find others' attitudes towards them actually do change, and whether that in turn has an impact on discriminatory practice. 'There's a difference in what people say when they are asked questions in a survey and how they behave in real life,' said Professor Thornicroft. 'Part of our evaluation will be to assess changes in the experience of discrimination and we will start with a baseline survey of 1,000 people in England using a scale we have developed to measure the discrimination they encounter. By repeating this survey over four years, we will be able to see if the campaign does affect the reality of everyday experience.'

The bottom line, he says, is that people with mental illness have as much right as everyone else to full citizenship, to have relationships and jobs. 'They should feel able to disclose their mental illness to potential employers and not fear doing so, as many currently do, and should be able to get full entitlements under the Disability Discrimination Act in the same way that people with physical disabilities do.'

Research has shown that employment can promote good mental health, but a diagnosis of mental illness counts against applicants for jobs. Only about 20 per cent of people with more

severe mental health problems are in work and many people with mental illness won't even apply for a job because they anticipate discrimination, he said.

*Moving People* will produce material specifically for employers, including guidance on how to implement the Disability Discrimination Act. The campaign team also plans to mount legal challenges to help highlight and change discriminatory policy. Educating employers about the reality of mental illness is crucial, said Professor Thornicroft. A survey carried out by the Shaw Trust showed that all 550 employers asked said none of their workforce had a mental health problem. But, statistically, 50 per cent of them are likely to be employing people with mental ill health, he said. 'The problem is, when companies believe these issues don't affect them, they are not interested in help with employment practices.'

He is made optimistic, however, by recent research from New Zealand, Scotland and Australia that shows outlooks can be changed, that stereotypical beliefs are not set in stone. 'We know we won't eradicate stigma and discrimination in four years,' he said. 'Think about kneeling buses for wheelchair users – it took 20 years to make them a reality after continued campaigning and advocacy. None of us involved in *Moving People* thinks the task will be complete within the time plan. This is the start of a long-term concentrated and persistent campaign.' ■

## 'Risk' from patients is based on anecdote

Local communities are often up in arms about the prospect of having a secure forensic psychiatric unit sited in their neighbourhood: so much so, they may mount legal campaigns against them, quoting risk of violence and criminal activity by patients.

But research has shown that this perception of risk is based on anecdotes alone, and that communities worry unnecessarily.

Secure forensic psychiatric inpatient units assess, treat and rehabilitate offenders with mental health problems. As part of their rehabilitation, patients are offered supervised and unsupervised leave from the units.

A study of four secure units, carried out by Professor of Forensic Mental Health Tom Fahy with West London Mental Health Trust, showed that over five years, there was only one conviction – and that was for a burglary, carried out more than five miles

away from the unit by a patient who had absconded. No patients were convicted of violent or sexual crimes during the five years. There were a number of incidents that were investigated by police but did not lead to a conviction – a patient with a history of arson was found not guilty of deliberately starting a fire in supermarket toilets, for example.

The research had set out to discover the true nature and level of risk posed by patients in medium secure units in the south-east of England. 'Our results clearly demonstrate medium secure units in this study did not have an impact on serious crime rates in the local communities,' said Professor Fahy. 'Acts of severe violence committed by patients on these units are rare, and even rarer in the vicinity of the units. Our findings show that the units do a good job in managing the risk that some patients in these units may pose.' ■

# Harnessing the power of neural stem cells to help repair brains

Finding ways to use neural stem cells to help repair the brain after a stroke or fix damage caused by disease is the main plank of the work of Professor Jack Price's laboratory in the Centre for the Cellular Basis of Behaviour (CCBB) at the IOP.

After a stroke, billions of brain cells die as the blood clot in the brain deprives them of oxygen. What follows is ongoing neurodegeneration as the dead cells, now unable to send signals to other parts of the brain, impact on other regions.

Working with neuroimaging scientists led by Dr Michel Modo and also based at the CCBB, the research team has found that engrafting just thousands rather than billions of neural stem cells can have an efficacious effect on both structure and function of the brain after a stroke.

Neural stem cells are 'multipotent' – they have the ability to become any of the specialised cell types found in the brain.

But the studies show that instead of straightforward replacing and rebuilding, the neural stem cells help the damaged brain to recover by somehow blocking the ongoing neurodegeneration.

'We simply don't know how they do that,' said Professor Price, a Professor of Developmental Neurobiology and Director of the CCBB. Finding out how that happens, and refining the process of engrafting neural stem cells in the light of that knowledge, is what his laboratory's programme of work, funded by the Charles Wolfson Charitable Trust, is all about.

'Originally, we thought stem cells would be regenerative,' he said. 'The idea was that if we put stem cells in, they would migrate through

## and...

The Centre for the Cellular Basis of Behaviour (CCBB) is based in the newly built James Black Centre next to the King's College Hospital campus. The £30 million building was opened in 2007 and is purpose-designed for scientists at both the IOP and King's College London School of Medicine. The CCBB is part of the IOP's Department of Neuroscience and its new laboratories, equipped with state-of-the-art equipment, will be responsible for almost doubling the amount of research carried out in basic neuroscience, helping to understand more about neurodegenerative and psychiatric diseases and to develop new treatments.

the brain tissue to where the damage lies and replace what's missing. But when we engraft stem cells, the proportion of tissue replaced is tiny. So we need to find out what the stem cells are doing to block the neurodegenerative process. Instead of replicating, are they turning into a different type of brain cell? Could they be inducing change in what's left? Are they secreting something?'

Another conundrum is why neural stem cells stored in the brain in a 'niche' don't galvanise to target damaged areas in the same way that engrafted stem cells grown in the laboratory do.

Even though scientists have known about niches of organ-specific stem cells in other parts of the body – in bone marrow, for example – for some time, the discovery of a niche of neural stem cells, lying against

## 'Neural stem cells have the ability to become any of the specialised cell types found in the brain'

the brain ventricle, is a relatively recent one. In the niche, the neural stem cells sit closely together with blood vessels branching into them.

Now a large project funded by the US National Institute of Biomedical Imaging and Bioengineering (NIBIB – part of the National Institutes of Health) *Quantum Grants Program* seeks firstly to understand more about the niche and how the stem cells and blood vessels interact, and then to copy its architecture in the laboratory. The idea is that the reconstituted niche could be implanted into a cortex damaged by stroke, providing both neurons and vascular cells to help with repair. The NIBIB *Quantum Grants Program* is designed to fund research for developing new technology for diagnosis, treatment and prevention, and Professor Price's team is collaborating with the Baylor College of Medicine in Houston, Texas on this, the first project to be funded under the programme.

'We think the niche environment is supportive, that the neural stem cells there have the potential to do things, but don't do them on their own, that the combination of neural stem cells and cerebral blood vessels is somehow important,' said Professor Price. 'What we want to do then is to recreate the niche in vitro and engraft it into the brain to see

what happens. It may be this is the way to make regeneration and replacement happen, as we've already discovered that stem cells alone don't do that,' he said.

Another project, funded by the Biotechnology and Biological Sciences Research Council and in collaboration with Nottingham University, is also concerned with developing a 'smarter milieu' for engrafted stem cells, which could help them better integrate. 'Experiments to date have involved injecting neural stem cells in a simple solution into the brain. But given we are trying to get these cells to integrate into the most complex tissue you can imagine, there must be a better way of doing it,' said Professor Price.

The team at Nottingham are materials engineers and, together with Professor Price's laboratory, they are trying to construct a matrix that resembles brain structure and will hold both neural stem cells and other components like proteins and growth factors. 'The artificial matrix will be a scaffold and we want to design it so that it will dissolve and disappear once engrafted,' he said.

All these experiments are at the moment carried out with rats and the help of neuroimaging techniques and behavioural tests to monitor the effects of the engrafted neural stem cells on the brain. Research of this kind is, however, bringing the concept of neural stem cell transplantation for human therapy closer to reality.

In future, neural stem cells manipulated in the laboratory could be used to help brains repair and recover not only after a stroke, but also in neurodegenerative conditions like Parkinson's disease, Alzheimer's disease and Huntington's disease.

But there are wider moral and ethical issues raised by the potential to harness the power of stem cells, said Professor Price. He is part of BIONET, a network led by the London School of Economics and Political Science and funded by the European Commission to consider the bioethical implications of stem cell research in an international context. 'In Britain, the use of human stem cells for research is strictly regulated, but many countries do not yet have explicit laws regulating human stem cell research,' he said. ■



Photo courtesy of Andy McCann

Andy McCann was 37, a PE teacher and assistant head teacher of a secondary school in south Wales when he had a stroke in the middle of an after-school class in the gym. The parent who was helping out happened to be a policeman, and had first aid training. He cleared the gym, called for an ambulance and Andy was taken to casualty, then admitted to hospital. 'The stroke was very violent,' says Andy, four years later. 'I suddenly collapsed and couldn't move or talk. While waiting for the ambulance, I was vomiting violently and starting to choke because I had lost my swallow reflex. I couldn't open my eyes because they were too light-sensitive. Strangely at the time I wasn't scared, it was an unreal experience and I disassociated from it.'

The diagnosis was made on the second day on the ward, following a CT scan that showed the part of the brain affected by the stroke was the cerebellum, at the back, responsible for muscle and movement co-ordination. 'The damage to the cerebellum matched the symptoms I'd shown,' he says. 'The speech deficit and inability to swallow were because I was physically unable to co-ordinate my tongue due to the damage caused by the blood clot.'

His speech came back relatively quickly and high doses of aspirin helped the clot to disperse. After eight days in hospital, he was discharged and his ongoing medical care transferred to a hospital nearer to his home in Cardiff. There, after numerous tests showed Andy was fit and healthy in every other way, his consultant guessed by a process of elimination that the stroke had been caused by vertebral artery dissection – a split in one of the vertebral arteries in the neck, leading to the back part

of the brain, which had bled and clotted over time. 'We don't know why it split – there have been reported cases of it doing so because of trauma, or sneezing, or even bending your head the wrong way,' says Andy.

The stroke was 'almost chance' and completely unexpected. 'There was no history in the family, I was very healthy, I was a keen sportsman, had played rugby in my youth and skied. I had competed in karate at international standard,' he says.

'I found having a stroke physically and psychologically a traumatic experience. It was difficult to continue to play sport and the consultant's advice was to give up teaching because of the potential stresses of the job. The Local Education Authority wanted me to retrain to another subject because of what the consultant had said, but I didn't want to do that after 17 years in teaching. PE was my love and subject. My career had been mapped out and suddenly it went pear-shaped. I was on Incapacity Benefit for two years, and in the early days thought that was it, that I was now unemployable.' But he became curious about why, physically, the stroke had happened and started a personal research project, which culminated in the publication of his book, *Stroke Survivor: A Personal Guide to Recovery*, in 2006.

'By then, I had started to take stock and think about my transferable skills and interests – sports psychology, stress management, for example,' he says. He trained and qualified as a Clinical Hypnotherapist and then set up a brand new training consultancy, which now offers 30 different courses about health, well-being and personal development tailored to the needs of different clients from the public, private and voluntary sectors. In January 2008, the business was nominated for a new business start-up award.

Andy also donates his time, giving talks about his experience at conferences and other events organised by the Stroke Association, the UK charity that funds research and supports patients and their families.

The biggest long-lasting deficits are fatigue and lower energy levels, he says. 'After a busy day or two, I feel more wiped out and have to pace myself. My speech will go a bit if I am very busy. My balance is not what it once was – you would notice nothing to see me walking, but I know it's not right. I'm much more aware of looking after myself now.'

# Analysing rising suicide in Taiwan

In Taiwan, 10 people in every 100,000 take their own lives: suicide is on the increase, and is now the ninth leading cause of death in the country.

Two PhD students, supervised by senior researchers at the IOP, are attempting to find out more about why people commit suicide or deliberately harm themselves – an important predictor of suicidal intent.

The first PhD research project is a study of people living in Nantou County where the Chi-Chi earthquake struck in September 1999, with a death toll of nearly 1,000. In the wake of the natural disaster, between 2000 and 2002, Nantou County had the highest suicide rate in Taiwan.

Dr Chin-Hung Chen is analysing information collected on a Suicide Register at the time to understand more about what prompted people to attempt – or succeed at – killing themselves. The Register was kept by a community mental health centre, set up for survivors of the earthquake by Taiwan's Department of Health. It contains records not only of deaths and attempts, but information gathered in interviews with those who did not succeed – about their intent, mental health and circumstances.

A second Taiwan-based PhD study is based in the Mackay Memorial Hospital in Taipei where between 40 and 50 people are admitted to the emergency department every month after attempting suicide or deliberately harming themselves. Chia-Yi Wu is interviewing 300 of them to try to trace any common warning signs, and to find out if they had tried to seek any sort of help before they had acted. If they did, she's asking what influence that help had; if they didn't, she wants to find out why not.

The results of both sets of research will help Taiwan health authorities develop policies designed to prevent suicide, and services to help people who may be contemplating it. The supervisors include Professor Martin Prince and Dr Rob Stewart: their team at the IOP undertakes community-based research around the world. They and their colleagues supervise many PhD students from overseas who carry out research in their home country, seeking to understand more about the causes of mental illness and evaluate culturally appropriate therapies and treatments, as well as to influence policy. ■

*Stroke Survivor: A Personal Guide to Recovery* by Andy McCann  
www.jkp.com/catalogue/book.php/isbn/9781843104100  
The Stroke Association, www.stroke.org.uk



## More people take own lives in hotter weather

As temperatures rise, so do the number of suicides in England and Wales.

Research led by the IoP's Dr Lisa Page and carried out in collaboration with the London School of Hygiene and Tropical Medicine looked at the relationship between temperature and suicide counts on a daily basis from the beginning of 1993 to the end of 2003.

Even though they found acts of suicide occurred most frequently in January, their analysis showed an overall increase on days when temperatures soared above 18°C.

For every one degree increase in mean temperature above 18°C, there was a 3.8 per cent rise in death by self-poisoning, and a five per cent rise in violent suicide.

More research needs to be carried out to discover why high temperatures affect daily suicide counts, said Dr Page. The team speculates that the most likely cause is a psychological one – previous studies have shown that people behave in a more aggressive, violent and less inhibited way

during excessively hot weather. The research team used information about the number of deaths due to suicide from the UK Office for National Statistics, and about daily temperatures from the Met Office.

They found that suicide increased by 46.9 per cent during a heatwave in 1995, but there was surprisingly no rise during similar weather in August 2003. This may be due to a period of very hot days a few weeks earlier, allowing people to adapt to higher temperatures, said Dr Page. If that is the case, a sudden soar in temperature could lead to a greater number of deaths than a gradual and sustained increase.

During the 11 years studied, there were 53,623 deaths as a result of suicide in England and Wales. The largest number of suicides took place on Mondays, with numbers declining as the week wore on. 1 January had the highest suicide count. The mean temperature was recorded above 18°C on 222 days. ■

## Enhancing the skills of school nurses

Depression during teenage years can lead to poor academic performance at school, social difficulties, and drug and alcohol misuse. Yet mental health problems during adolescence often go undetected and untreated, making them more likely to continue into adulthood.

Now a project led jointly by the IoP and the mental health charity Rethink is developing and testing a programme of training and a portfolio of resources for school nurses to help them offer appropriate help or a referral to

secondary school pupils who need it. If proved to be successful, the new training package will be available to more than 2,100 school nurses across the UK, mostly employed by the NHS, who work in state schools.

Two school nurses are involved with planning and shaping the QUEST project along with representatives from professional bodies – the Royal College of Nursing, the Community Practitioners' and Health Visitors' Association, and the School and Public Health Nurses Association.

Funded by the Health Foundation, the research is starting with a national consultation exercise: a survey of school nurses by post will make sure the training will be developed to meet their needs and suit the demands of the job. Rethink is charged with the creation of the programme, likely to involve workshops, web-based resources, printed material and DVDs, and sessions for teachers so they can spot and signpost pupils who may need support from school nurses.

A team of school nurses working for Sutton and Merton Primary Care Trust in south London will pilot the training which will then be evaluated with the help of schools nurses working for 13 primary

care trusts in the south of England, serving both inner city and suburban catchment areas. A randomised controlled trial, led by the IoP's Professor André Tylee, will gauge the success of the package by assessing and comparing the skills and knowledge of school nurses who have been trained with a group who have not yet attended workshops or accessed resources.

The UK Department of Health has recommended that school nurses be better trained to assess the mental health needs of pupils. 'Our starting point is to build the confidence and skills base of school nurses so they can detect mental health problems and provide necessary support and signposting,' said Professor Tylee. 'Some problems may require referral to specialist services, but for many problems, support, educational materials and interventions like guided self-help may be most appropriate.'

'Mental health problems limit young people's ability to cope, and to fulfil their potential during school years. They disrupt educational and social development and limit future achievement. School nurses are ideally placed to make a difference,' he said. ■

## Exploring minds of teenagers

Two thousand 14-year-olds from the UK, Ireland, France and Germany will take part in a pan-European collaborative project co-ordinated by the IoP which will help scientists understand more about the developing teenage mind.

The participating teenagers, recruited through schools, will complete a battery of tests designed to measure their attitudes and thinking styles, their mental health, their use of drugs and alcohol, and their behaviour. They will also give samples of their DNA and have MRI scans so researchers can correlate information about their brain structure, brain activity and genetic traits with their psychological profiles.

'Adolescence is a central point for development, and many mental health problems, including drug abuse, start during these years,' said the IoP's Professor Gunter Schumann, who is leading



the five-year IMAGEN project, which is funded by the European Commission.

Previous studies have shown the teenage brain to be particularly vulnerable to drugs and stress, and the idea is to identify both the psychological and biological factors involved in the processing of emotions, decision-making, risk-taking and behaviour at this time, as the brain prepares for adulthood.

'We aim to learn about biological and environmental factors that might influence mental health in teenagers and their subsequent mental health as they grow older,' said Professor Schumann. 'Ultimately, that knowledge will be used to help develop therapies and prevention strategies. The DNA samples and other databases we create will also be powerful resources for future investigations.'

The young people will carry out some of the tests focusing on personality and thinking styles at home on a computer. They will each visit a research centre once or twice, after school or at weekends, for interviews, brain scans and to give blood samples. Their parents or guardians will also be interviewed about themselves, and their child, and their teachers will be asked for information. Two years later, each of the original 2,000 will be interviewed again by telephone to find out if their attitudes and behaviour have changed.

The consortium behind IMAGEN is made up of leading experts in the field of genetics, behavioural and neuropsychological studies, neuroimaging, bioinformatics and biostatistics, from both the public and private sector. Part of the project is a huge investment in technology, so collaborators can easily share information. ■

**Veronique Black has been working as a school nurse since 1996. For the past four years, she's worked for Sutton and Merton Primary Care Trust. As well as supporting students, she works closely with teachers and parents: 'I go to most parents' evenings and have an appointment system where parents can arrange to see me,' she says. 'I also go to new parents' welcome evenings so parents know who I am and know how to make contact if they need help.'**

The brief of the team in which she works is to 'support the health of school age children and to support their families in dealing with health issues'. In Sutton and Merton, a typical caseload for a full-time school nurse includes one high school and three to four primary schools.

'We screen all five-year-olds in reception for height and weight, and send a health questionnaire to parents. We do further work with children where there is concern – about obesity, behavioural problems, asthma, epilepsy, for example – and work with teachers to make sure care plans are in place in schools.'

'School nurses are involved in immunisations at both primary and high schools – giving them in high school, and ensuring parents are fully informed about vaccinations and their children are up to date with them in primary schools. We work with the Child Protection Team and contribute to PHSE (Personal Health and Social Education) sessions.'

In addition, Veronique and her colleagues run confidential help and advice drop-in sessions in high schools, and also in the local Connexions Centre and sports centre. 'Often the teachers will refer a pupil to us,' she said. 'Sometimes parents contact us too if they are worried.'

Many of the young people who come to these sessions have behavioural or emotional problems, she says.

'The number of young people we are seeing with emotional and mental health problems is increasing. Self-harming has escalated dramatically, and there is more depression and anxiety. The clear-cut cases are easy – if we know we can help, we continue to see them on a regular basis. But there are some cases when we need to know whether we can realistically work with them, or whether we should refer them on. Sometimes you wonder if you are doing the right thing working with a pupil, or whether specialist services should be involved.'

Veronique and her colleague Belinda Shear are helping to steer the QUEST project. 'There is no doubt that more specific training around assessment and treatment is needed. This work will benefit school nurses and the young people they work with across the country.'

# Research and teaching of international renown

The Institute of Psychiatry (IoP), based in Camberwell, south London, is a School of King's College London and its *raison d'être* is two-fold – research and teaching, both in the field of mental health.

People who work at the IoP carry out research in order to have a greater understanding of mental health problems, diseases of the brain and how the mind works, and to then use that knowledge to develop effective treatments and services. They undertake this research using a range of methodologies and techniques – brain scanning; interviews with service users and their families; statistical analysis; proteomics (the study of proteins) technology; randomised controlled trials; and sophisticated machinery that studies DNA.

Their second mission is to equip the next generation of scientists and researchers with the skills they need to continue this work in future, through PhD study and taught programmes in different aspects of psychiatry, psychology and neuroscience. Turn to the inside back cover for a full list of programmes on offer.

The IoP is sited next to the Maudsley Hospital and both organisations are known throughout the world for their pioneering work. The Maudsley is run by South London and Maudsley NHS Foundation Trust (SLaM), the IoP's closest NHS partner: many of the IoP's staff work in SLaM's services and clinics, putting theory into practice and keeping in close contact with the service users their academic work seeks to serve. Service users are also involved in many projects as

researchers and advisors. A specialist Biomedical Research Centre in Mental Health, funded by the UK government's National Institute for Health Research, is based at the IoP and SLaM. It is one of 11 such Centres set up in April 2007, all located within University and NHS partnerships, to carry out 'translational research' that will help patients benefit more quickly from new scientific breakthroughs. The IoP (King's College London)/SLaM Centre partnership won the status through open competition: the successful 11 bids for Centre status were chosen by an independent panel of international experts.

The work of the IoP is also funded by the Higher Education Funding Council for England, grant-giving bodies like the Medical Research Council and the Wellcome Trust, the European Union, charities, organisations in the private sector and other UK government departments. Research teams bid successfully for some £130 million of funding for their work each year: the competitive bidding system operated by funding organisations ensures money available is awarded to the highest quality research. Ethics approval given either nationally or locally for every research study also guarantees the highest standards.

Many research projects are carried out in collaboration with colleagues in other King's College London Schools and at King's College Hospital NHS Foundation Trust; with other teams based in universities and mental health services around the UK and overseas; and with charities offering specialist support to service users and their families, as well as with private companies. ■



Rehan Jamil

## Sharing our knowledge

The Mental Health Knowledge Centre at the IoP aims to share the results of research with wider audiences. The Centre works collaboratively, for example, with the European Dana Alliance for the Brain to organise public events where IoP researchers join other professionals to speak about their work on a range of mental health problems.

[www.mentalhealthcare.org.uk](http://www.mentalhealthcare.org.uk) is a website for carers, families and friends of people with mental illness, developed by the IoP, SLaM and the mental health charity Rethink. It contains information about mental health problems and research news.

[www.eatingresearch.com](http://www.eatingresearch.com) has been developed by the eating disorders research team at the IoP. Many of the team also work in SLaM's Eating Disorders Service. The site contains comprehensive information about anorexia and bulimia, as well as resources for carers and health and education professionals.



Rehan Jamil



## More about us

■ The IoP is the Lead World Health Organisation (WHO) Collaborating Centre for Mental Health Research in Europe and part of an international network that carries out projects in support of the WHO programme on mental health.

■ *International Mental Health at the Institute of Psychiatry* promotes and undertakes collaborative work in developing and restructuring countries.

■ Two Medical Research Council (MRC)-funded centres are based here – the MRC Centre for Neurodegeneration Research, which investigates Alzheimer's disease, vascular dementia, motor neurone disease and other neurodegenerative diseases, both in the laboratory and through clinical studies; and the MRC Social, Genetic and Developmental Psychiatry Centre, which seeks to understand more about the effects of 'nature' and 'nurture'.

■ The King's Motor Neurone Disease Care and Research Centre is one of several in the UK funded by the MND Association. It offers clinical services at King's College Hospital and carries out research at the IoP.

■ The Sainsbury Centre for Mental Health is one of the IoP's academic partners. The Centre works to influence policy and practice, focusing on criminal justice and employment in the field of mental health.

■ The King's Centre for Military Health Research is jointly run by the IoP and the Department of War Studies in the sister School of Social Science and Public Policy at King's College London. The Centre's research team focuses on war and health, war and psychiatry, military personnel issues and social policy. Much of its work is funded by the UK Ministry of Defence.

■ The Cancer Research UK London Psychosocial Group, supported by Cancer Research UK, studies psychological and social aspects of cancer.

■ The MRC-funded *Twins Early Development Study* (TEDS), the largest study of twins in the UK, tracks the development of 15,000 pairs of twins and helps researchers find out about common disorders of childhood.

■ The Service User Research Enterprise (SURE) undertakes research to test the effectiveness of services and treatments from the perspective of people with mental health problems and their carers. SURE involves service users in a collaborative way in the whole research process: from design to data collection, through to data analysis and dissemination of results. It is one of the largest units within universities in Europe to employ people who have both research skills and first-hand experience of mental health services and treatments.

■ The IoP co-ordinates, along with the University of Manchester, the Department of Health-funded UK Mental Health Research Network (MHRN), a collaboration that supports large-scale projects and brings together service users, academics, doctors, nurses and therapists from around the nation.

■ The research arm of The National Academy for Parenting Practitioners, a government-funded collaborative venture between the IoP, the Family and Parenting Institute, and Parenting UK, is led by researchers here (see page 12).

■ The Centre for the Economics of Mental Health, which works in partnership with research teams here, elsewhere in the UK and across the world, evaluates the economic effectiveness of treatments and services to inform mental health policy making and the allocation of resources. It is the only centre of its kind outside of the USA.

■ The MRC London Brain Bank for Neurodegenerative Diseases provides research teams here at the IoP, and at centres across the country, with samples of brain tissue obtained, with consent, at postmortems. The Bank holds collections of brains affected by Alzheimer's disease, motor neurone disease and schizophrenia, as well as healthy brains.

Rehan Jamil



## Participate in our research

The research teams at the IoP rely on the help of about 5,000 volunteers a year who take part in their studies. *MindSearch* is a volunteer database supported by the IoP-based Psychiatry Research Trust. You can register your details if you are interested in participating in research studies by visiting [www.mindsearch.co.uk](http://www.mindsearch.co.uk)

# Dean Peter McGuffin writes:



Rehan Jamil

one of the things that makes the Institute of Psychiatry a wonderful place to work is that there is such a range of expertise that goes all the way across neuroscience and mental health research, from the social environment to the molecular and cellular basis of behaviour and disease.

What underpins all of these areas is a rigorous adherence to scientific method. One of the prime difficulties of studying psychiatric and neurological disorders is that, in life, the brain and the central nervous system are the body's most inaccessible organs. Historically this has meant that nervous and mental disorders have suffered more from mythologising than any other types of illness. There are still areas where the myth-making has not entirely ceased and the damage done by the alleged but spurious association between the measles, mumps and rubella vaccine and autism is one sorry example.

At the least, however, no one nowadays tries to assert, as was the case in my youth, that illnesses such as autism or schizophrenia are themselves purely social constructions or 'myths'. The disorders studied at the Institute do, however, still carry stigma and one of the areas highlighted in this research report is how stigma can be combated. Stigma is most often attached to disorders that appear frightening and about which little is known. All of the scientific endeavours described in this report are about understanding the causation of disorders or about making them tractable to treatment. I hope this report in itself will contribute to better public understanding that these are 'real', and no longer mysterious, illnesses. ■

As Dean, I have discovered that one recompense for the many tribulations of the job is that occasionally one really does get to have the last word. It is a particular pleasure to have that privilege in the context of this research report. Reading it, I am struck by the pace of progress in research here at the Institute of Psychiatry, King's College London. I first arrived at the Institute three decades ago as a senior house officer who already had earnest aspirations as a clinician researcher – although my own field, genetics, was then highly unfashionable. There was no such thing as molecular genetics in psychiatry and the modern era of brain imaging had scarcely begun. It is extraordinary to reflect on how things have changed. This report

is packed with advances in knowledge that have depended on the latest technologies in brain sciences that range from visualising the living, thinking brain to tracking down precise variations in genes and discovering the ways they interact with the environment. Moreover, one of the real strengths of the Institute is that all of these high-tech methods are being applied by scientists and clinicians working side-by-side, striving to discover ways of making things better for patients. Having said that, one can become dazzled by molecules and machinery, but many of the advances presented in this report depend on much less expensive but no less sophisticated tool kits such as those used by epidemiologists or cognitive behavioural therapists. Indeed,

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## To find out more

about the work of the Institute of Psychiatry,  
visit [www.iop.kcl.ac.uk](http://www.iop.kcl.ac.uk)

**Websites developed by the IoP  
for people with mental health problems  
and their carers include:**

[www.mentalhealthcare.org.uk](http://www.mentalhealthcare.org.uk)  
[www.eatingresearch.com](http://www.eatingresearch.com)

**To volunteer to take part  
in research at the IoP,**

visit [www.mindsearch.co.uk](http://www.mindsearch.co.uk)