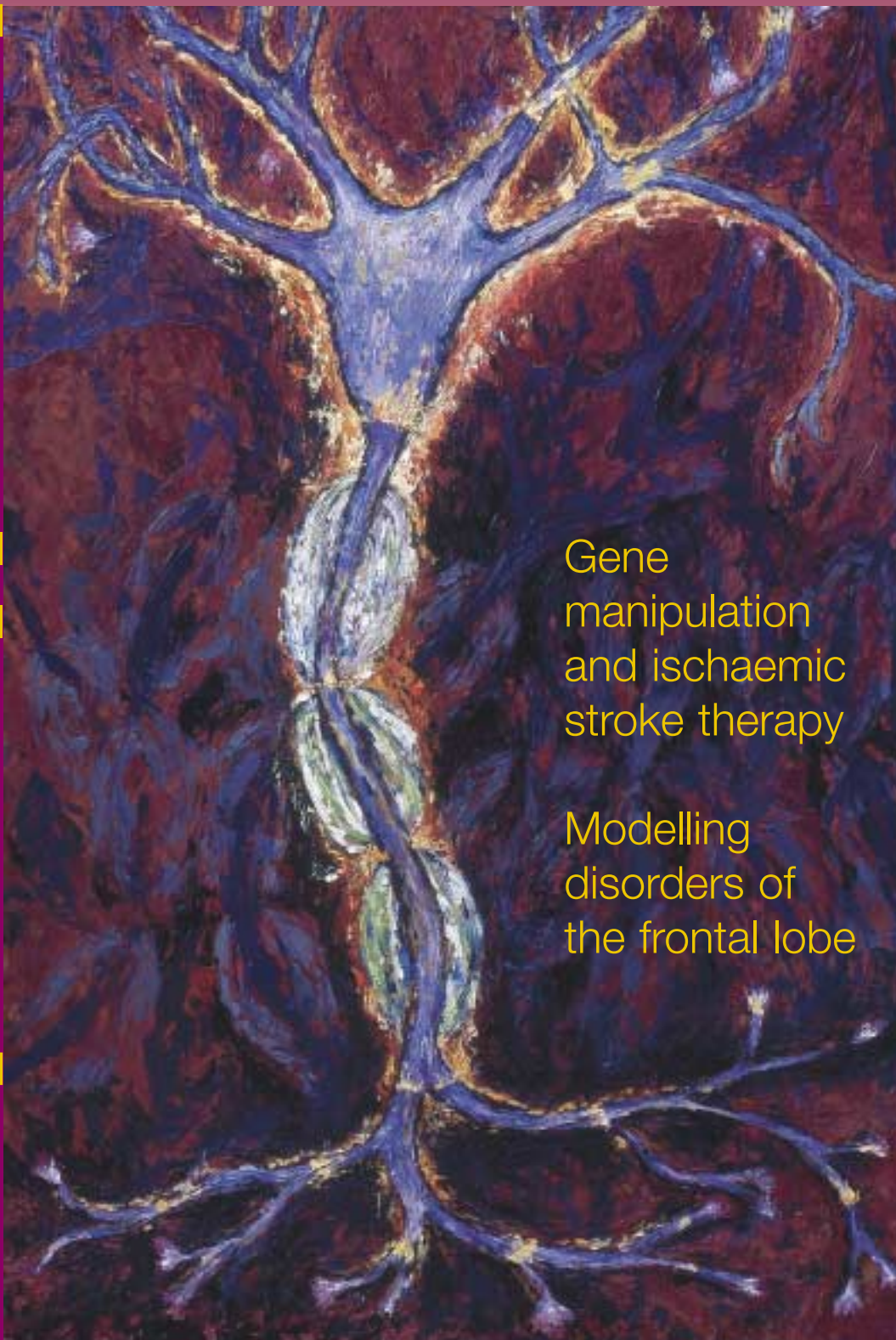


# Quarterly



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● We are delighted to announce that Graham Collingridge has accepted the invitation of the committee to become President of the BNA in January, 2007. Graham is Director of the MRC Centre for Synaptic Plasticity at the University of Bristol and a Fellow of the Royal Society. However, he hardly needs introducing to the majority of our members, being a long-time supporter of the BNA, as well as its predecessor, the BRA. Our current President, Richard Frackowiak will "hand over the reigns" to Graham at the Christmas Symposium in London on the 14th of December this year after which Graham will remain President until 2010. (see 'Interview', pages 4/5)

● BNA membership is now consistently over the 2000 mark. As we've highlighted before, the BNA has a high proportion of student members - currently 31% of the membership are in this category. Our proportion of student members is greater than the majority of scientific societies and, due to the very modest membership fees that we charge them, this brings with it a significant financial challenge. However, the BNA is wholeheartedly committed to attracting student members recognising that they often remain full members of the society after completing their postgraduate degrees. The ongoing commitment to our student members is reflected again this year in our support for the Postgraduate and Early Career Symposium, 13th - 14th September. The event will be hosted by committee member Vincent O'Connor and colleagues at the University of Southampton. If you are one of our student members, this event is a great opportunity to start building networks with your peers for the future. And as well as the science, the Symposium includes a short workshop on 'media training', focusing on the role of the media in communicating

science. There will also be a session for students to discuss fellowships and grant applications for post-doctoral research with staff from the leading grant awarding bodies.

● One of neuroscience's founding fathers, Santiago Ramon y Cajal was giving out advice to young scientists more than a century ago in his book "Advice for a Young Investigator" published in 1897. Whether his advice would be relevant to our student members nowadays is open to question. However, what's not in question is the scientific legacy that Cajal left for modern neuroscience. It seemed fitting, therefore, that we should use the Christmas Symposium this year to commemorate the contribution of Cajal and Golgi to modern neurobiology in the centenary year of the award of their Nobel Prize. As is customary at this event, the 2006 awards for "Contribution to British Neuroscience" and "Public Service" will be presented by our President, Richard Frackowiak. We are delighted that these will go respectively to Horace Barlow and Mike Robins.

● It's a while since I reminded members of a way in which they can make their subs go further for BNA. If you sign up for *Gift Aid*, it means that for every pound of your membership fee the BNA gets an extra 28p from the Inland Revenue. This means more money in our coffers for supporting local group activities, one-day symposia and student bursaries! If you haven't already signed up, please send in the form available on the BNA website under the Members" Pages. You know it makes sense!

● **13th - 14th September, 2006:**

Postgraduate and early career neuroscientist symposium and workshop in media training: University of Southampton

● **27th September, 2006:**

Controversial Issues in Neuroscience: 'Criminal behaviour - nature or nurture?' A café-bar public discussion at the Dana Centre, London, SW7

● **8th November, 2006:**

One Day Symposium:  
'Genes and synapses: new insights from

invertebrates'.

St John's College, University of Oxford

● **14th December, 2006:**

Christmas Symposium:  
'The Legacy of Cajal and Golgi',  
The Royal Society, London

● **1st - 4th April, 2007:**

19th National Meeting, International Centre,  
Harrogate, North Yorkshire, in association with  
Neuroscience Ireland

The British Neuroscience Association Newsletter is published regularly and distributed to over 2,000 members of the BNA. The views expressed in the newsletter are the authors' own and are not necessarily the opinion of the BNA committee.

**DEADLINE FOR SUBMISSION OF ITEMS FOR THE NEXT NEWSLETTER: 1st OCTOBER 2006**

The BNA Newsletter is produced by Yvonne Allen in the BNA Conference Office.

Please send any items for inclusion in the next newsletter to:

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**Tel: 0151 794 5449 / 4943 ♦ Fax: 0151 794 5516 / 5517 ♦ email: newsletter@bna.org.uk**

# INTERVIEW



Earlier this year, Professor Graham Collingridge FRS was invited by the BNA Committee to become President after the retirement of Richard Frackowiak in December, 2006. To our delight, he said he felt honoured to accept. He also willingly agreed to be interviewed for BNA Bulletin about this impending role, his hopes and aspirations for the BNA during the next three years of his presidency and beyond. He also muses on the future of neuroscience in the UK but has one overriding message to BNA members. Support our national meeting! Below, he tells you why.

'I am a strong believer that modern neuroscience is best progressed by a multi-disciplinary approach, one that merges the traditional disciplines. The BNA is perfectly poised to be the society to represent the interests of individuals who share this multidisciplinary spirit'.

**Graham, you are very well known in the neuroscience community but for those who may be less familiar, can you tell us a bit about yourself?**

I did my undergraduate degree in Pharmacology at Bristol during the 1970s and then a PhD at The School of Pharmacy in London, with John Davies. After a couple of post-docs, first in Vancouver and then in Sydney, I returned to Bristol as a lecturer, in the Department of Pharmacology. I left briefly to be the Head of the Pharmacology Department in Birmingham in the early nineties, but returned to Bristol, where I joined the Department of Anatomy. Here, I was Head of the Department before establishing the first Medical Research Council (MRC) Centre in 1998. I am still the Director of the MRC Centre for Synaptic Plasticity. I also retain ties with Vancouver where I am a Visiting Professor at the University of British Columbia.

**And about your work? What inspired you?**

During my undergraduate degree in Bristol, the emphasis was very much on neuroscience. The department was full of inspirational individuals, including Ray Hill, Dick Evans, Kanti Bhoola and Alex Livingstone. Professor Jimmy Mitchell was the Head of Department and was very much instrumental in creating such a stimulating and conducive environment for doing science. I did my research project with Peter Keen and this inspired me to become a research scientist. The experience of practical lab work was a major factor in this decision. Frankly, I am concerned that, with the increase in student numbers nowadays, we are unable to give them all this unique and special insight into scientific enquiry. Many undergraduate students have to do library-based projects as there are not enough supervisors to go around and budgets are tight. This is a very unfortunate position.

What else has inspired me? The answer is the science itself. Over the last few decades, neuroscientists in the UK have been responsible for some of the most important and influential discoveries in the discipline. Two have greatly influenced me. One of these is Tim Bliss' seminal work on long term potentiation (LTP). His discovery and characterisation of LTP has considerably enhanced our understanding of the molecular basis of learning and memory. The other is Jeff Watkins' discovery that glutamate is the brain's principal excitatory neurotransmitter, and his subsequent identification

of, for example, the NMDA receptor. Most of my scientific career has built upon these discoveries by trying to understand the role of glutamate receptors in LTP.

**You have accomplished so much - but is there anything you would still like to achieve?**

I would like to understand better how glutamate receptors are altered during LTP and to start to gain more insights into how aberrant LTP contributes to disease.

**How would you best describe the role of the BNA?**

I was an enthusiastic member of the former Brain Research Association (BRA) so I have been committed to this society for quite some time. I am a strong believer that modern neuroscience is best progressed by a multidisciplinary approach, one that merges the traditional disciplines, such as Anatomy, Biochemistry, Pharmacology and Physiology. The BNA is perfectly poised to be the society to represent the interests of individuals who share this multidisciplinary spirit. I think it admirably embraces this ideal in its ambition to become an important 'umbrella' organisation for all facets of neuroscience in the UK. In particular, the BNA meetings are wonderful for bringing many disciplines together under one roof. Increasingly, we are seeing a move towards systems-led disciplines, as evidenced by the huge success of the American Society for Neuroscience annual meeting. Also, the MRC and Wellcome Trust have neuroscience boards, not grants panels based on traditional disciplines. The BNA is, therefore, a society of major importance to neuroscientists in the UK and will, I believe, become increasingly more and more so. I see younger scientists readily embracing the multidisciplinary approach. This is the society for them and for us more established neuroscientists.

**Do you think the BNA is achieving its objectives? Is there room for improvement?**

Yes and no. The approach is absolutely right; there is nothing I would change. The BNA is providing an excellent forum for young scientists. There is a good blend of activities throughout the year, and the society is generous with its bursaries for FENS and BNA meetings. As a founding member of the European Dana Alliance for the Brain, I am particularly pleased to see so many collaborative ventures with EDAB. Public engagement in science is something I am passionate about and I think the BNA's activities in these areas have been first rate. I also

welcome the good interactions with major pharma and the biotech industry - though maybe there could be more input from this crucial sector that depends so much on the strength of the UK's neuroscience base.

But there is always room for improvement in any activity. I would say that the BNA's national meeting could be better attended, for sure. Given the numbers engaged in neuroscience in the UK, and the strength of the discipline, I think there could be better support from this community, just to reach that critical mass at the meeting. I know people like its small(ish) size - it is friendly and informal as a consequence - but it should be larger to become more effective. There are some big groups in this country that never go. It would be one of my goals and ambitions as President to try and engage more of these scientists and increase their participation in this excellent forum.

**So do you have any other ambitions as President?**

From what I've said already, you won't be surprised to hear that I think my overriding ambition would be to get the national meeting better recognised for what it is. This is a first class gathering and an excellent showcase for the very best of neuroscience, primarily in the UK, of course. But there is always a fantastic array of international speakers too.

I would also like to think that I could contribute to getting the BNA even more secure financially. It operates on a shoe-string. Of course, these two ambitions are not mutually exclusive. If more members supported their national meeting, then that support could be ploughed back financially into the society to allow its core activities to grow.

**Have you any thoughts about the BNA's relationship with FENS? With SfN?**

I have always been very supportive of FENS. I am impressed by the way the former European Neuroscience Association (ENA) has been transformed into FENS. Clearly, ENA wasn't working, but FENS has been such a phenomenal success, with about 5-6,000 now regularly attending its meetings. It has become a major player in the neuroscience global community, and deservedly so. I like the alternating, biennial arrangement - one year FENS, the next year our national meeting. With Richard Morris, a former BNA president, about to become president of FENS, this can only mean good things for the relationship between BNA and FENS.

But SfN? Of course, their annual meeting, the enormity of it, means that it will always be a main meeting on the neuroscience circuit. BNA will always be complementary to the much larger scale SfN has to offer. Nonetheless, I would hope to see more neuroscientists in the UK looking first to BNA as the 'must attend' meeting, with FENS occupying the alternate year, and a trip across the pond once in a while to attend SfN.

'I think my overriding ambition would be to get the national meeting better recognised for what it is. This is a first class gathering and an excellent showcase for the very best of neuroscience'.

**Is it important to remain a committed and supportive member of the Biosciences Federation?**

The Biosciences Federation does things that BNA simply couldn't do alone, given our size and capabilities. It has political clout more than anything because it collectively represents a huge proportion of the biosciences community, so it's the right voice

for us to gain access to these higher echelons. I am perfectly happy with the BNA remaining a committed member.

**Do you have any general thoughts about the future of neuroscience in this country?**

Clearly, it's a discipline that is here to stay, and will undoubtedly increase in importance, especially since many of the major diseases afflicting mankind are diseases of the brain. These will become even more of a problem with an aging population and, thus, an increasing prevalence of these often age-related disorders. Fortunately, the government is at last realising this too. There is likely to be increasing resources directed at the major disorders, such as dementia. Whilst unfortunately I do not think that the UK will invest in basic research at the level seen in the US, I think that things will get better. If nothing else, our government recognises the importance of a *knowledge economy*. Slowly, we can recover from disastrous cuts in research funding that the UK suffered in the 1970s and 1980s. This adversely affected the science base in general and the growth of neuroscience, particularly in expensive areas such as molecular biology. By comparison to then, I think the outlook is much healthier.

Neuroscience also benefits from being inherently fascinating. People will always be curious about the brain. Topics like consciousness, learning and memory, stress and emotion will always drive this curiosity. So, the future for neuroscience in the UK is excellent.

**Finally, do you have any particular message you would like to send our members as your presidency approaches?**

I would like to implore them, again, to support our national meeting! This should really be *the* event for everyone to go to. A quality, multi-disciplinary meeting, on home territory is an excellent opportunity to engage with our own neuroscience community and is the basis for excellent research in the UK.

*The BNA National Meeting will be held in Harrogate, 1st to 4th April, 2007. Full programme details can now be found on the BNA website ([www.bna.org.uk](http://www.bna.org.uk)). See page 12 in this issue of BNA Bulletin for a summary of the programme. Graham Collingridge will be delivering a key-note plenary lecture at this meeting. His work has inspired many artists, including Dr Lizzie Burns, University of Oxford, whose painting, 'Neurone', is featured on the front cover.*

## Open access: one size does not fit all



**Jane Qiu** is an associate editor for Nature Reviews Neuroscience. She joined the magazine after six years of post-doctoral research on myelin biology and nerve regeneration, first at the City University of New York and then at King's College London. She is also a freelance science writer, and has contributed to Nature, The Economist, The Irish Times, BioMedNet, and the Science Museum's Dana Centre. In this essay, she applauds the value and ideal of the open-access model, but maintains that the existence of a variety of publishing systems is crucial for best serving the scientific community and the public alike.



'It is irrefutable that production of reliable, high-quality information comes with a cost. It is, therefore, a question of who should pay for the validation and dissemination process'.

In May this year, American senators John Cornyn and Joseph Lieberman introduced a bill that would make a voluntary National Institutes of Health (NIH) policy mandatory and extend it to every major federal research agency, from the National Science Foundation to the Department of Defence. If the bill is passed, it will be compulsory for federally funded scientists across all disciplines to make their accepted papers freely available online within six months of publication. This is declared by some as a victory of the open-access movements, leaving others fear that the bill will have damaging effects on the scientific publishing industry.

The problem of access to published research was first brought to light by the crisis in university journal budgets. There are some 24,000 peer-reviewed journals, publishing around 2.5 million articles each year. Spiralling price rises mean that libraries are spending more money to subscribe to fewer journals. This has led people to question the justification of publishers to charge universities for access to the research results their scientists help to produce. Meanwhile, some advocates argue that the public should not have to pay to read the results of the scientific research which it has, through its taxes, financed.

The campaign to promote open access to scientific literature - making it free for anyone to read - has led to the climatic launch of the Public Library of Science (PLoS) Biology in October 2003, followed by PLoS Medicine a year later. The aim of the publisher PLoS is to show that open access can work by competing head-on for the best research papers with today's top scientific and medical journals, such as Nature, Science, Cell and The New England Journal of Medicine.

Few people would disagree, in principle, with the ideal of a subscription-free utopia. The slogans such as "Free for all" are irresistibly seductive. However, accessibility to information is only one of the several output measures in publishing. Other parameters, such as the quality of information and absolute communication equity, are equally paramount. It is irrefutable that production of reliable, high-quality information comes with a cost. It is, therefore, a question of who should pay for the validation and dissemination process. Employing highly qualified and well trained editors to sift through hundreds of manuscripts is an expensive business. The more editorial input a journal provides, such as editing texts and graphics, the more expensive it becomes. Traditionally, publishers recoup these costs by charging for access to the final product. PLoS turns this 'reader-pays' model on its head and charges a 'dissemination fee' of US\$1,500 to the authors of accepted papers.

In support of this 'author-pays' publishing model, some wealthy funding agencies, such as the Wellcome Trust in the UK and the US-based NIH and Howard Hughes Medical Institute (HHMI), have agreed to provide its grantees with the funding to cover open-access dissemination fees - in the case of the HHNI, around US\$3,000 for each of its researchers in 2004. Such generous financial endorsements are admirable. In reality, however, many less well-off funding agencies may not be able afford this additional cost. More importantly, not all researchers are funded by handsome research grants. In almost every field, there are many scientists doing outstanding research who are not part of any large, federally funded project. Who pays the dissemination fees for these people? This issue becomes even more poignant for researchers in developing countries. Editors at PLoS suggest that authors who are unable to pay won't have to. A fair policy, perhaps. But its journals will not be able to survive unless the majority of authors are able to pay, which is probably not the case in many disciplines and in most developing countries.

Some propose that universities and institutions will pay the dissemination fees. But how will universities decide which areas of research to support? The BioMed Central, a UK-based open-access publisher established in 1999, has introduced a scheme that might help to resolve this difficulty. Under this scheme, universities and institutions pay a flat fee to cover the publication charges for all their scientists - an author-pays equivalent of the reader-pays site licence. Payments for publication under any membership schemes is likely to have to come from the library budget, so the open-access publishing model effectively puts the crisis back onto the shoulders of the researchers, and will not ultimately solve the problem of university journal budgets. In addition, many universities and institutions, especially in developing countries, may not be capable of helping their researchers to pay for their publications.

It seems likely, therefore, that some scientists will not be able to publish their results because they cannot afford the dissemination fees, resulting in an unintended distortion in the publishing culture. Each publishing model - be it reader-pays or author-pays - has trade-offs. But one must realise that the trade-offs are not symmetrical. When a scientist does not have a subscription, he can nonetheless get information about the article from the abstract or by requesting a copy of the paper through various channels. When a scientist does not have the funds to publish an article, the results will never appear as part of the permanent literature - an utterly ludicrous prospect with unthinkable long-term consequences.

Apart from this affordability problem that will heavily impinge on researchers worldwide, many people question whether the open-access model is affordable for publishers. PLoS is heavily subsidised by the generous US\$9 million grant from the Gordon and Betty Moore Foundation. The crucial question is, therefore, will it survive when the money runs out? Many

publishers think that US\$1,500 per article is far from enough to cover the costs of producing a journal of the highest quality. Some feel that this estimate is low by four- to six-fold.

As the PLoS journals become more successful and receive more and more submission, the author-pays model gets more difficult to sustain, which is referred to as the "PLoS' growing pains" by Donald Kennedy, the editor-in-chief of *Science*. That is because it costs almost as much to reject a paper responsibly as it does to accept one. The higher the rejection rate, the larger becomes the expensive budget that must be met by the fixed revenue from author fees. The rejection rate in the best journals, such as *Nature*, *Science* and *Cell*, is over 90% of submitted manuscripts, making the editorial costs per published article very high.

Judging from other open-access publishers, the picture of financial sustainability is not terribly rosy. For example, the BioMed Central has not moved into profit after seven years of business, and is not expected to do so for sometime. A journal that is losing money or lives on the margin of losing money will have little editorial independence, no matter how lofty its initial editorial ambitions might be. Even if open-access publishers are able to break even, it is unlikely that they will have sufficient revenues to promote technological innovations necessary for long-term development of the industry.

Open access is an interesting and innovative business model. PLoS has made an impressive start and should be congratulated. Many traditional publishers have responded by launching new open-access journals or by allowing their articles to be freely available a certain amount of time after publication. Some previously reader-pays journals have adopted a hybrid system, in which researchers can choose to pay the dissemination fee and, as a result, their papers will be freely available. The growth of the open-access movement and the publishers' response to it reflect the fact that market forces will, in the end, lead to a variety of models, each well suited to particular disciplines.

The shift in gravity triggered by the open-access movement has undoubtedly put a stop to excessive rises of journal prices, which is a hugely progressive achievement. But let's not get carried away. Governments and funding agencies should continue to allow the market dynamics, as well as the freedoms generated by the internet and the more relaxed view of copyright, to drive innovation and determine which publishing models can best serve the needs of researchers and consumers of research information. Laws aiming to enforce free public access to research papers will result in a wholesale change to open access and cause unforeseen distortions in the practice of scientific publishing. Ultimately, diversity is the key to all success. One size does not fit all.

By Jane Qiu,  
Nature Reviews Neuroscience (J.Qiu@nature.com)

## Unlocking the secrets of brain and body at the University of Nottingham



before birth but can 'programme' the brain and body for the rest of a child's life, scientists believe.

Other researchers will look at the way the brain matures during adolescence. In one of the studies, for example, their aim is to recruit up to 300 local children over a five-year period and use MR imaging to build up a picture of the developing brain, kidneys and other organs.

Professor Tomas Paus, Director of the *Brain and Body Centre*, and one of the leading researchers in the field, said: "The ultimate goal is prevention of disorders of the brain and the body.

"If you know what leads to a particular disorder - such as depression or obesity or hypertension - and if you can detect it early on during adolescence, you can come up with strategies that can prevent it.

"For example, if we learned through our research that certain individuals are more likely to develop cardiovascular complications associated with obesity if they have a particular genotype, and were exposed *in utero* to cigarette smoking, then, in the future, we could target those individuals with personalised drugs to improve their long-term health."

The centre is equipped with state-of-the-art equipment to investigate the interaction between brain and body, including:

- Three Magnetic Resonance Imaging scanners - to study internal organs of humans and animals
- Imaging Analysis Suite - for analysis of MRI data
- EEG Lab - to measure brain activity
- Transcranial Magnetic Stimulation equipment - to stimulate parts of the brain
- Cardiovascular suite - to measure blood pressure and cardiovascular reactivity

- Psychological testing suite - for study and observation of children and adolescents

- Functional genomic laboratory - to study genes and their function

Professor Paus added: "What is unique about the centre is the close interaction and integration of the two systems: the brain on one side and the body on the other. That will make a big difference because, in the past people, have tended to work in isolation: neuroscience and cardiovascular health have been separate.

"There's no other research centre in the UK that is really integrating the two sides to the extent that we are."

The University already has a very strong background in magnetic resonance imaging. In 2003, Professor Sir Peter Mansfield was awarded the Nobel Prize for Medicine for his groundbreaking work in the field of MRI.

Professor Sir Colin Campbell, Vice-Chancellor of the University of Nottingham, will welcomed guests to the inaugural celebratory event that included excellent talks from Professor Tomáš Paus, Director, Brain and Body Centre, University of Nottingham; Dr Leslie Ungerleider, National Institute of Mental Health, Bethesda, USA; Professor Timothy Aitman, MRC Clinical Sciences Centre, Imperial College London; Professor Trevor Robbins, University of Cambridge; Professor Anna Dominiczak, University of Glasgow; and Professor Richard Frackowiak, Wellcome Department of Imaging Neuroscience, London.

**For further information, contact Professor Tomas Paus, Director of the Brain and Body Centre, on +44 (0)115 951 5362, [tomas.paus@nottingham.ac.uk](mailto:tomas.paus@nottingham.ac.uk); or Media Relations Manager Tim Utton in the University's Public Affairs Office on +44 (0)115 846 8092, [tim.utton@nottingham.ac.uk](mailto:tim.utton@nottingham.ac.uk)**

A new centre at The University of Nottingham will carry out world-leading research into the human brain and body in a bid to unlock the secrets of obesity, hypertension, depression and addiction.

Equipped with the latest technology for monitoring brainwaves, imaging the body's vital organs and studying the role of genes, the *Brain and Body Centre* will help to improve the health of future generations.

The £4m centre will build on The University of Nottingham's international reputation in genetics, medicine and neuroscience, using cutting-edge magnetic resonance (MR) techniques for which the University is a globally acclaimed leader.

By using a unique approach that looks at the human brain and body in tandem, scientists hope their work will lead to new discoveries relevant to disorders of the brain - such as addiction or depression - and of the body, such as obesity and hypertension.

Experts from the USA and all over the UK gathered at University Park on March 29 for the official launch event and a mini-symposium of distinguished speakers.

Research projects at the centre will look in particular at the environmental and genetic factors that shape the brain and can have life-long effects on the health of the body. Some environmental factors - such as maternal smoking during pregnancy - occur



## The new Institute for Neuroscience in Manchester - a major £40 million investment gets underway

The formation of a new university in Manchester in October, 2004, provided a unique opportunity to bring together internationally recognised neuroscientists from the former Victoria University of Manchester (VUM) and the University of Manchester Institute of Science & Technology (UMIST) (both RAE 5\* groupings in UoAs 5 and 11) with complementary research interests, and to integrate them with clinical neuroscientists. These scientists have expertise and interests ranging from theoretical and computational neuroscience, through molecular and cellular studies of the nervous system, to research on animals, normal volunteers, and patients with major diseases of the nervous system.

Neuroscience in the Faculty of Life Sciences (FLS) covers several inter-related research themes, which highlight the multi-disciplinary nature of the current neuroscience research in Manchester, and range from Integrative Neurobiology and Behaviour, Molecular and Cellular Neuroscience, and Systems Neuroscience. There are 37 principal investigators (including 6 fellows), 42 post doctoral researchers and 36 postgraduate students in FLS, and this group has been further

strengthened by the recent appointment of three RCUK academic fellows and lectureships in Neuroscience, plus appointments in the related areas of Anatomy and Integrative Vertebrate Biology. Our strategic aim to expand further is highlighted by current recruitment to lectureships in neurobiology and neuron/matrix interactions, and a GSK Chair in neuroscience.

The Centre for Clinical Neuroscience is a cross-faculty initiative based within the Faculty of Medical and Human Sciences (FMHS), and with a goal to improve health, healthcare and knowledge through high-quality research in clinical and cognitive neuroscience. The Centre is complemented by colleagues at Hope Hospital whose interests include neurodegeneration and neuroplasticity, pain, stress and mood disorders and cognition, language and psychosis. Meanwhile, the Faculty's Neuroscience and Psychiatry Unit studies abnormal brain mechanisms which underlie common mental illnesses such as schizophrenia and depression.

There are plans to integrate basic and clinical activities through the Institute for Neuroscience that is to be based in a new building that is currently under construction. This state-of-the-art facility,

which represents a £40M investment, will be jointly occupied by FLS and FMHS neuroscientists, and its open plan design aims to promote effective collaboration.

Neuroscience in Manchester is also strongly represented at both undergraduate and postgraduate level with several degree programmes available, including BSc degrees in both Neuroscience, and Cognitive Neuroscience and Psychology. Furthermore, the new MNeuroSci programme, which is the first four-year undergraduate Masters in Neuroscience in the UK, enables students to undertake a major research programme in their final year of study. In addition, a Masters course in Computational Neuroscience will begin this autumn.

Indeed, the future looks good for neuroscience in Manchester as scientists will be able to work in a dynamic and exciting environment that will advance the University of Manchester as being a major contributor to cutting-edge research in neuroscience.

*By Dr Catherine Lawrence, RCUK Research Fellow, and Dr Simon Merrywest, Research Business Manager, Faculty of Life Sciences, Manchester.*

[catherine.lawrence@manchester.ac.uk](mailto:catherine.lawrence@manchester.ac.uk)

## Leaving a legacy - your gift for the future

Remembering a charity in your will provides a lasting legacy to your support and commitment

If you are considering making a will, and would like to make a difference to the future of neuroscience research in this country, then please consider leaving a legacy to the British Neuroscience Association

**Here are some of the examples of what your legacy could help to create:**

- A special lecture, either at the national meeting, or a public venue
- A special symposium devoted to a particular research area
- A prize for excellence in researching a special topic
- Student bursaries to attend selected meetings, symposia or events

If you have already made a will, it's sensible to review it regularly. You can include a legacy to the British Neuroscience Association with a simple addition of codicil. All donations are exempt from inheritance tax because the BNA is a registered charity (1103852).

**What to do next?**

Please contact Yvonne Allen in confidence:

**Dr Yvonne Allen**

BNA Executive Secretary, BNA Office, Sherrington Buildings, Ashton Street, Liverpool L69 3GE.

**Tel: 0151 794 5449 Fax: 0151 794 5516 Email: [y.allen@bna.org.uk](mailto:y.allen@bna.org.uk)**

### HAVE YOUR CONTACT DETAILS CHANGED?

The website can help!

BNA members move around a lot, it seems! Sadly, many of them forget to tell us and mail and email messages are returned undelivered. The new website is fully interactive and allows you to check your membership number and contact details at the click of a 'mouse'. Simply look at the Members' Pages and follow the instructions.

So have you forgotten to tell us about a recent move? Has this newsletter been forwarded on to you? Are you planning on changing your address soon? Do you know other members who are not receiving our communications? Get in touch with the BNA Office now ([membership@bna.org.uk](mailto:membership@bna.org.uk)) or get onto the website!

[www.bna.org.uk](http://www.bna.org.uk)

## GiftAid it!

### Don't let the Chancellor have any more of your money!

Many members are already helping us enormously with this scheme, so much so that we have already earmarked a lot more money for our bursary scheme next year to allow our students to attend the BNA National Meeting in Harrogate and other meetings of affiliated societies. But we could do better! The BNA can collect an extra 28p for every pound that you give us in subscriptions if you sign the 'Gift Aid' form obtainable from the website ([www.bna.org.uk/docs/giftaid.doc](http://www.bna.org.uk/docs/giftaid.doc)). Can you help us? We are sure we can spend it more wisely than the inland revenue! To qualify, you must be paying your subscription to the BNA privately and be a resident UK taxpayer.

This article will be the first of a series to keep you informed about the activities of the Biosciences Federation and what it plans to do in the future. As the first of a series some introductions seem appropriate!

## The Biosciences Federation: what is it doing and where is it going?



Richard Dyer

The Biosciences Federation (BSF) was established in 2002 and since then has acted to influence national policy and strategy in biology-based research - including funding and the interface with other disciplines - and in school and university teaching. In practice, the BSF has the capacity to bring together the strengths of 41 Member Organisations and 42 other organisations that are affiliated members. This represents a cumulative membership of more than 55,000 scientists covering the full spectrum of the biosciences from physiology, biochemistry and microbiology to ecology, taxonomy and environmental science.

The second brief introduction is to me! I became Chief Executive of the BSF on the 1st of January this year. I was previously the Director and Chief Executive of The Babraham Institute and before that I was very active in neuroendocrine research. Currently, I remain a Vice President of the European Science Foundation.

You may wonder what attracted me to the BSF following my retirement from Babraham. The answer is simple. I fundamentally believe that the BSF has a very important role and it is in the interest of the biosciences to ensure that the role is delivered effectively. Since taking up my appointment, this view has been substantially reinforced. Why?

The answer has many strands. First, there is a great deal happening with the potential to have a major impact upon our professional lives. Active research workers think first and foremost about funding and their research group - and that is entirely appropriate. However, funding, and the priorities that are often associated with research allocations, are amongst the most easily identifiable areas where it is important to express views to Government and other opinion formers. There currently seems to be a Competitive Spending Review every other year, and the outcome of this review determines Research Council budgets and the money available for grants, studentships and capital equipment. In recent reviews, the biosciences have fared well but all expect that the 2007 Review will be tough. Strong arguments will need to be presented if the biosciences are to continue to flourish. Of course, the Research Councils are currently working on their inputs to the Review, but it is also important that organisations like the BSF contribute to the width and the intensity of the debate. For Chemistry, Physics and Engineering, there will be powerful participation from the Royal Society of Chemistry, the Institute of Physics and the various engineering academies. These are very effective organisations and the BSF was established to provide an equally effective voice for the biosciences. It is important that this aim is realised; it is an ambitious aim because the BSF currently has rather limited financial resources.

And there is much that needs to be done! Currently, in addition to thinking about the Competitive Spending Review, the BSF should be providing evidence to enquiries on Research Council Institutes, the NHS research/MRC merger, the House of Lords enquiry into the reasons for the drift away from science A Levels, the way that the British Library will store data in the future and much more! It can't all be done. Some responses will require research and all will have to be first-class if they are to be influential. And we are influential - on several occasions this year the BSF has been asked to follow up a written response by attending the Science and Technology Committee at Westminster to answer questions that arise from our input. You should not expect less. Some Societies have told me that they can deal with these matters through their own policy group (which is sometimes just a single person). Frankly, I don't believe it and don't think that they fully understand the scale of what is needed, or the excellence and effectiveness of, for example, the Royal Society of Chemistry. Today, the Government believes that Chemistry is in the middle of a severe crisis (partly true, but entirely true for synthetic organic chemistry) and that everything is fine in the biosciences (partly wrong). The biosciences seem fine because numbers of students have increased in recent years. However, this fact masks the relative decline in students taking the core subjects on which much of modern biology now depends.

I have emphasised that the BSF needs to respond to all enquiries that may impact upon the health of the biosciences. One can describe this as reactive mode. However, the BSF also needs to operate in a proactive mode. This requires horizon scanning and input into the debate at a very early stage - certainly before a committee seeks "evidence". How is this to be done? The answer is in the word 'scanning'. The BSF needs to follow what is being said in Parliament and then provide direct, unsolicited input to committee chairs or individual parliamentarians. We are working to make these contacts.

The proactive mode is especially important in the context of Europe. Without attention to this, one can find that an idea appears, seems to go underground and then suddenly seems to reappear as a fait accompli.

where no discussion is possible. Let me give you a relevant example. You will know that there has been a debate about a European Research Council (ERC). You will not have heard much about it in recent months. You may even think that this idea will not come to fruition. The facts are that the budget for Framework Programme 7 will be increased by 40% to E54bn for seven years. The debate in coming months will be about how this money is partitioned and, from the evidence of previous Programmes, not now about the budget envelope. At least E7bn is earmarked for the new ERC - I anticipate the final

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figure will be higher but not by more than 50%. Therefore, the ERC will have a budget of a little more than a billion Euros a year to distribute in response mode to scientists in 25 countries and from all science disciplines, including the Humanities and Social Sciences. The budget will be only about two thirds of that administered by the new MRC. There will be no just retour: last year ERC meant European Research Competition in some quarters.

This all leads to an obvious problem. How can the ERC retain credibility if the rejection rate for excellent applications is very high because the total funds are inadequate? The answer, of course, is to find a way of restricting applications. How this is to be done is still the subject of debate and discussion. However, one idea that is almost certain to prevail is that around 30% of the available funds should be restricted to 'young investigators'. I think that this is a good idea. However, it will not be implemented without significant agitation in this country unless 'young' is defined carefully. The problem is created by the different ages across Europe at which individuals obtain their PhD. It is quite easy to imagine a scenario where a 'young'

German scientist of 40 can apply as a 'young investigator' but a scientist of 32 from the United Kingdom would be excluded. It is on matters like this that the BSF also needs to be active.

How will we judge success? It will be the case that we will see some of our ideas implemented. This is already happening. But, of course, it will also often be the case that we will be unable to claim sole ownership of the ideas. For me, there will be two criteria for success. The first is that the BSF will be approached directly for its views - perhaps even in confidence by a senior official or member of the Government. Examples of this are occurring. The second is that you, the member, think that by working together through the BSF your interests are well represented and that, partly because of action taken by the BSF, the biosciences continue to flourish.

Hmm! I seem to have taken on quite a demanding job!!

By Richard Dyer  
(rdyer.bsf@physoc.org)

## The National Neuroscience Writing Prize: 2006

Could you engage the public in neuroscience? Do you want to tell the world about your research? Well, now's your chance! As part of its commitment to public awareness of science, the BNA has joined forces with 'Your amazing brain' website and The European Dana Alliance for the Brain (EDAB) to find the best brain communicators in the country.

We're looking for a newspaper-style science article of around 650 words on the subject of brain science.

**There are two separate prizes, each worth £250:**

- For the best article on any area of brain science.
- For the best article describing your own area of research in a

neuroscience-related subject.

**The closing date is 31st October, 2006.** Winning entries will be published in the *BNA Bulletin* and more widely in the public domain.

**For more details, go to [www.bna.org.uk/writingprize](http://www.bna.org.uk/writingprize) or [www.youramazingbrain.org/writingprize](http://www.youramazingbrain.org/writingprize)**



## POSTGRADUATE AWARD

A prize of £500 will be given to the best Post-graduate applicant who has completed a Ph.D/ D.Phil. thesis in the year prior to the award (by October 2006).

The prize requires that work is completed and the thesis has been submitted and approved, even if not formally awarded, by the deadline.

**The following will be required:**

- Nomination from the student's supervisor
- External examiner report or recommendation
- Abstract of the thesis
- Statement from the student highlighting the importance of the work in the thesis (in no more than 300 words).

**NOMINATIONS SHOULD BE MADE BY 1st OCTOBER 2006 TO:**

DR YVONNE ALLEN, BNA EXECUTIVE SECRETARY,  
THE SHERRINGTON BUILDINGS, LIVERPOOL L69 3GE  
TEL: 0151 794 5449 | FAX: 0151 794 5516  
EMAIL: y.allen@bna.org.uk



## UNDERGRADUATE AWARD

The area of study for this award (£250) will be broad, including not only neuroscience *per se*, but also subjects where a large part of the degree comprises neuroscience.

The following will be required:

- Nomination by the Course Tutor, Course Supervisor or Head of Department
- Evidence of success including marks of student in final exam summer 2006
- Any supporting material including undergraduate dissertation/thesis, or a report on any research the undergraduate has carried out.
- A statement of career intentions.

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# 19th National Meeting

- in association with Neuroscience Ireland  
Harrogate, North Yorkshire, 1st - 4th April, 2007

A celebration of neuroscience to mark the 10th anniversary of the BNA! An eclectic programme exploring the very latest findings in:

- neurodegenerative diseases ● addiction
- learning and memory ● neural signalling
- cortical development ● neuroimaging

### PLENARY LECTURERS

**Graham Collingridge** (Bristol, UK)  
**Salvador Moncada** (London, UK)  
**John Lowry** (Conway, Ireland)  
**Edvard Moser** (Oslo, Norway)  
**Yves Barde** (Basel, Switzerland)  
**Helen Mayberg** (Atlanta, USA)  
**Joe LeDoux** (New York, USA)

### SYMPOSIA

- The Neuropathology of Autism: recent advances in understanding neurochemical mechanisms
- Ubiquitination dependent regulation of synaptic development and plasticity
- Neuroreparative approaches using stem cell biology
- A role for inflammation in neuro-degeneration: Where do we stand?
- Cannabinoids: fate, food and fear
- Purines in physiology, plasticity and pathology
- Circadian rhythms in the brain
- Sleep and Anaesthesia: common mechanisms?
- Synaptic Origamy: protein folding at the synapse
- Emotion and Cognition: anatomical substrates and therapeutic targets
- Subcellular and proteomic approaches to dissect neuronal signalling pathways
- From cell-cell recognition to memory formation
- Alcohol: molecular and cellular mechanisms of intoxication, tolerance and addiction
- Multi-sensory Processes
- Alzheimer's Disease: current therapies and progress on the development of drugs to slow disease progression
- Discovering drug effects through functional brain imaging
- Hippocampal neurogenesis in mood disorders and their treatment.
- Basal Ganglia subcortical connections: exploring the brainstem.
- Thalamocortical development
- New mutant models for neurodevelopmental and neurodegenerative disorders

There will also be over 50 themed poster sessions, a full exhibition, several peripheral events and a lively social programme.

Registration opens 1st October, 2006. Abstract deadline – 31st January, 2007  
Bursaries will be available for student members of the BNA

Further information: [www.bna.org.uk](http://www.bna.org.uk) email: [bna2007@bna.org.uk](mailto:bna2007@bna.org.uk) tel: 0151 794 4943/5449

# 13th - 14th September, 2006: University of Southampton

This year's symposium for young neuroscientists, or those in the early stages of their careers, will include a short workshop on 'media training' that will focus on the role of the media in communicating science. It will also incorporate practical techniques and advice on how to engage and handle media exposure. Such a course will serve as a timely insight into the media world, but will also be very useful for those wishing to improve their communication skills in general. The course will be led by a team of experts that will include Elaine Snell (Snell Communications), Myc Rigglusford (Walnut Bureau) and Huseyin Mehmet (Imperial College, London). There will also be the opportunity at the end of the day to consult with representatives of the major grant awarding bodies about funding for future research careers before relaxing at the evening reception. The next day, students will be encouraged to present their work (platform or poster) at a special neuroscience symposium that will also feature a special plenary lecture from Professor Hugh Perry (University of Southampton), coordinated by Vincent O'Connor.

The registration fee (£50 for BNA Members; £75 non-members) will include all refreshments, lunches and evening reception, and all documentation. Accommodation will be available in local Halls of Residence, £38 per night, with en-suite facilities and full English breakfast.

For further information: [events@bna.org.uk](mailto:events@bna.org.uk). Tel: 0151 794 4943/5449.

Registration open now! ([www.bna.org.uk](http://www.bna.org.uk))

**ABSTRACT DEADLINE: 31st JULY, 2006**

# Controversial Issues in Neuroscience

6.30pm for 7.00pm, Wednesday, 27th September, 2006  
at The Dana Centre, 165 Queens Gate, London, SW7

## Criminal behaviour - nature or nurture?

Join us for a lively café - bar discussion between scientists, lawyers, ethicists and the public on the purported influence of genes over criminal behaviour.

Chaired by Nick Ross (BBC). Speakers will include Steve Jones (UCL), Tony Maden (ICL) and Annie Bartlett (St Georges, London).

Tickets are FREE but must be ordered in advance:  
contact [events@bna.org.uk](mailto:events@bna.org.uk), or tel: 0151 794 4943/5449.

## One Day Symposium

### Genes and Synapses: new insights from studies on invertebrates

Wednesday, 8th November, 2006, at St John's College Oxford  
Chaired by David Sattelle (Oxford) and Lindy Holden-Dye (Southampton)

#### Speakers:

- |   |   |
|---|---|
| <b>Mathias Landgraf</b> (Cambridge)<br>'Dendritic development in the Drosophila CNS - neural maps and connectivity'                                   | Pumilio-dependent control of a sodium channel gene'   |
| <b>Mario de Bono</b> (Cambridge)<br>'Navigating the soil environment by a blind worm: O <sub>2</sub> sensing and the evolution of foraging behaviour' | <b>Lindy Holden-Dye</b> (Southampton)<br>'Neurotransmitters and regulation of C. elegans pharynx and feeding behaviour'                                 |
| <b>Andrew Jones</b> (Oxford)<br>'Acetylcholine receptor gene families - molecular and functional diversity'   | <b>Mark Darlison</b> (Nottingham)<br>'Insights into the evolution of inhibitory ion-channel receptors from studies on the genome of Ciona intestinalis' |
| <b>Mary O'Connell</b> (Edinburgh)<br>'RNA editing in Drosophila: two nervous systems for the price of one'  | <b>David Shepherd</b> (Southampton)<br>'Modelling in Drosophila human neurodegenerative diseases'   |
| <b>Richard Baines</b> (Warwick)<br>'Regulation of neuronal excitability through   | <b>Michael O'Shea</b> (Sussex)<br>'Natural Antisense Regulation of NOS - Role in Memory Formation'  |

Posters on all aspects of Invertebrate Neuroscience are welcome.

Tickets will be FREE for members of the BNA and will include refreshments, lunch and evening reception (non-members, £65; student non-members, £30).

For further information and ticket reservations, contact: [events@bna.org.uk](mailto:events@bna.org.uk)  
or tel: 0151 794 4943/5449.

The Christmas Symposium: 2006

## The Legacy of Golgi and Cajal: past, present and future

1.00pm - 5.00pm Thursday, 14th December, 2006,  
at The Royal Society, 6 - 9 Carlton House Terrace, London, SW1

A symposium to commemorate the contribution of Golgi and Cajal to modern neurobiology upon the centenary of their Nobel Prize

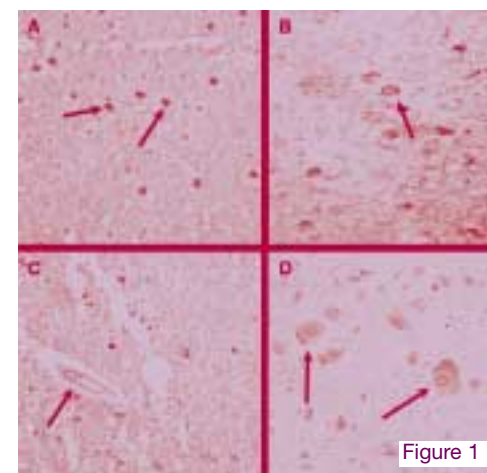
CHAired BY RICHARD FRACKOWIAK (LONDON) AND PAUL BOLAM (OXFORD)

#### Speakers:

**Javier De Felipe** (Madrid), **Alain Prochiantz** (Paris),  
**Thomas Klausberger** (Oxford), **Annette Dolphin** (London),  
**Antoine Triller** (Paris), **Michael Coleman** (Cambridge)

## Gene and protein expression after ischaemic stroke: a microarray-based study

Dr Nick Mitsios is currently a research associate in the School of Biology, Chemistry and Health Sciences at Manchester Metropolitan University. He describes here the work he completed for his PhD thesis that was supervised by Dr Mark Slevin, Manchester Metropolitan University, and subsequently awarded runner-up status in the annual BNA Post-Graduate Prize competition. Several novel findings emerged that offer important information about gene changes after stroke. He also highlights the importance of the penumbra, the dysfunctional but potentially viable area adjacent to the infarct, that could be manipulated to improve treatment.



'Novel data derived from this study could significantly improve our understanding of the death-promoting and survival pathways responsible for governing the pathology of ischaemia and pinpoint potential targets for drug discovery'.

Figure 1. P-JNK localization (visualized with VECTOR RED) in TUNEL-positive cells (visualized with DAB) from penumbra (arrows - A). Active caspase-3 staining (visualized with DAB) in TUNEL-positive cells (visualized with VECTOR SG) with the morphological appearance of neurons (arrow - B) and blood vessels (arrows - C) from infarcted regions of the tissue. Cdk5 localisation (visualized with DAB) in TUNEL-positive cells (visualized with VECTOR SG) with the morphological appearance of neurons from penumbra (arrows - D).

Stroke is a major cause of death and disability and current therapies are unsatisfactory. So far, clinical trials based on molecules identified following analysis of stroke progression in animal models, have generally failed to improve recovery after stroke in man. Significant differences in gene activation between animal models of middle cerebral artery occlusion (MCAO) and stroke in patients may explain the failure of these strategies. However, current awareness of the pathophysiological events after stroke suggests that treatment could be improved by manipulation of gene and protein activation, particularly in the penumbra, the dysfunctional but potentially viable area adjacent to the infarct, where blood flow is higher than a neuronal disabling concentration<sup>1</sup>.

Therefore, more detailed studies examining cell specific protective mechanisms after stroke in humans are required. Moreover, it is important to identify proteins which could be exploited to design novel treatment modalities. Previous studies have demonstrated stability of mRNA in human post-mortem brain tissue and concluded that post-mortem brains are a valuable resource for differential gene and protein expression studies<sup>2</sup>. However, the number of studies using human tissue has been limited by the virtual impossibility of obtaining post-mortem tissue without considerable delay.

As a first step towards formulating a sound scientific basis for future investigations, the present study was designed to investigate the changes in gene and protein expression after stroke in humans. Recent advances in DNA microarray technology have provided tools to investigate the expression of thousands of genes in a single hybridization experiment. In cerebral ischaemia,

this approach has been used to reveal important molecular events using animal models. In this study, microarray technology has been utilised for the first time to identify global changes in gene regulation in post-mortem tissue from 12 patients who survived for 2 - 37 days after suffering from stroke. Novel data derived from this study could significantly improve our understanding of the death-promoting and survival pathways responsible for governing the pathology of ischaemia and pinpoint potential targets for drug discovery.

Gene expression was studied at three different time-points after disease onset, which gave a good overview of early (first week after stroke), medium (up to 3 weeks after stroke) and late (more than 3 weeks after stroke) changes in expression. The results showed that 98 genes were upregulated and eight were downregulated in a pool of brain samples taken from penumbra plus infarct of the four patients who survived from 2 to 6 days after stroke, corresponding to 9% of the represented probe sets. One hundred and two genes were upregulated and eight were downregulated in a similar pool taken from patients who survived from 9 to 20 days after stroke (9% of the represented probes) and, finally, 10 genes were upregulated and 14 were downregulated in a pool of patients who survived from 26 to 37 days after stroke (2% of the represented probes).

This study has identified a number of molecules that could be targeted in future efforts to provide strategies against post-ischaemic brain injury<sup>3</sup>. Several novel findings emerged, offering important information about gene changes after stroke, most of which have not been previously described after stroke in man and only a minority of them were known to be induced by ischaemia. A number of growth factors<sup>4</sup>, apoptotic<sup>5</sup>,

neuroprotective, angiogenic and pro- as well as anti-inflammatory molecules have been detected and a full functional characterization of the differentially expressed genes and proteins is essential. Although their exact functions and cellular expression after stroke needs further clarification, hypotheses on their role and significance in the framework of stroke pathophysiology will be discussed.

Studies in rodent models of brain ischaemia have demonstrated the altered expression of genes that control apoptosis. There is, therefore, evidence for the involvement of apoptotic proteins in animal models of stroke but very limited studies with human tissue and, although interruption of the apoptotic cascade decreases cell death in animal models, whether programmed cell death contributes to stroke in humans is less well established. Here, the altered expression of key pro- and anti-apoptotic proteins provides evidence for the activation of apoptotic pathways in human stroke tissue.

JNK is a regulator of cell survival and death in a number of neural and non-neural systems *in vitro* and its activation has been associated with induction of, or protection from, apoptosis. Recent evidence has suggested that activation of JNK may play an important role in promotion of neuronal cell death. JNK1 protein was increased, phosphorylated, and translocated to nuclei in the rat brain after ischaemia, while in an animal model of stroke, JNK phosphorylation was seen in neurons undergoing apoptosis<sup>6</sup>, and phosphorylated-JNK (p-JNK) colocalized with TUNEL-positive neurons after cerebral ischaemia in mice<sup>7</sup>.

Consistent with these data, the present study has confirmed the proposed key role for JNK phosphorylation in apoptotic cell death after stroke by demonstrating increased expression and phosphorylation of both JNK1 and 2 in patients who survived from 3 to 26 days after stroke and phosphorylated-JNK (p-JNK) co-localization in TUNEL-positive nuclei of cells with the morphological appearance of neurons from infarct and penumbra regions (Fig 1A). Because of the key roles that JNK signals play in the cross-talk between multiple cell death pathways, JNK is an attractive target in the context of stroke where excitotoxicity, oxidative stress and apoptosis may converge. So far, inhibition of JNK activity has resulted in permanent protection against transient ischaemia, and JNK inhibitors are reportedly successful up to 6 hours after ischaemic onset in experimental rat and mouse models<sup>8</sup>. Therefore, inhibition of JNK activation might become an appropriate therapy for patients suffering from stroke in the future.

Cell death following ischaemia may be due to cellular necrosis or apoptosis, as the outcome of an ischaemic insult is different in the ischaemic core and the penumbra. Several reports have shown that apoptosis participates in the deterioration of brain injury after cerebral ischaemia and caspase-3 has a central role in mediating apoptotic neuronal death in animal models of

brain injury and ischaemic stroke, although conflicting data with respect to its presence and causative role under ischaemic conditions have been reported. The biochemical events leading to neuronal death in penumbra are generally more subtle and there is much debate and considerable controversy as to whether this type of cell death represents a classical form of caspase-3 mediated apoptosis. Moreover, limited information is available on caspase-3 activation after brain ischaemia in man, since a fairly recent analysis of post-mortem samples from stroke patients has failed to reveal an apoptotic morphology<sup>9</sup>.

Active caspase-3 was found within cells showing features of apoptosis, and more than half of the active caspase-3 labelled cells were TUNEL-positive after MCAO in the mouse, suggesting the importance of caspase-3 activation to ischaemia-induced apoptosis in brain<sup>10</sup>. Both nuclear and cytoplasmic localisation of active caspase-3 was observed in neurons after ischaemia, and active caspase-3 was evident in neurons and microglia throughout the infarcted core in the rat at all times examined<sup>11</sup>. However, caspase inhibition only partially protects against ischaemic damage, suggesting the involvement of caspase-independent pathways after stroke<sup>12</sup>. Here, active Caspase-3 levels were upregulated in penumbra and infarct of patient samples and positively correlated with JNK2 phosphorylation levels in infarct. Active caspase-3 expression was not demonstrated in contralateral tissue but was dramatically increased in neurons from grey matter infarct and penumbra of patients surviving from 3 to 26 days after stroke. Strong active caspase-3 staining was also seen in TUNEL-positive cells with the morphological appearance of neurons and blood vessels from infarcted regions of the tissue (Fig. 1B & C). These results have highlighted the importance of caspase-3 activation in ischaemia-induced apoptosis and provided evidence for caspase-3 activation in cells undergoing ischaemic cell death in man.

Neuronal cell death after brain ischemia may also be associated with activation of cyclin-dependent kinases (Cdk). Cdk5 is a unique member of the Cdk family, not involved in cell cycle events, but expressed primarily in the central nervous system and mainly in neurons. Previous studies have suggested that apoptotic or necrotic death of neurons after brain ischemia may be associated with activation of cyclin-dependent kinases and growing evidence suggests that deregulated CDK5, which is not involved in cell cycle control, rather than cell cycle relevant members of the CDK family, promotes neuronal death. Although other neurological diseases have been studied, little has been published on the expression of Cdk5 and the other cell cycle proteins after brain ischaemia in man. Cdk5 may indeed have a role in the events associated with neuronal response to ischaemic injury, as demonstrated by a postischemic increase in Cdk5 activity in the rat brain following ischemia<sup>13</sup>, while strong Cdk5 and p35 (activator of Cdk5) immunoreactivity was detected in neurons after MCAO in the rat<sup>14</sup>. Weishaupt et al. showed that Cdk5 activates

neuronal cell death pathways upstream of mitochondrial dysfunction and demonstrated that inhibitory activity against Cdk5 confers neuroprotection and may promote functional long-term rescue of injured neurons<sup>15</sup>.

The present study has demonstrated that Cdk5 was upregulated in penumbra and infarct in the majority of patient samples examined, this upregulation being most prevalent in patients surviving up to one week after stroke. An increase in the number of Cdk5, phosphorylated Cdk5 (p-Cdk5) and p35 positive neurons, astrocytes and microvessels occurred in samples from patients who survived from 3 to 29 days after stroke<sup>16</sup>. Staining of neurons became irregular and clumped in the cytoplasm, and nuclear translocation occurred. New evidence has also been provided for an association of Cdk5 with apoptosis after stroke, as Cdk5 colocalized with TUNEL positive neurons (Fig. 1D) and p-Cdk5 was found in the nucleus of active caspase-3 stained cells. Cdk5 is also involved in modulation of cell growth and survival in non-neural cells. Sharma et al. were first to demonstrate that Cdk5 was highly expressed in proliferating endothelial cells (EC) and suggested that it may have a role in the regulation of EC proliferation, apoptosis and angiogenesis<sup>17</sup>. Immunohistochemical data from the present study have shown that Cdk5 stained microvessels co-localised with TUNEL-positive cells, suggesting that Cdk5 upregulation may also be associated with EC apoptosis after stroke.

The normal conformational isoform of cellular Prion protein (PrPc) may also play an important role in cellular function in the central nervous system. Recent findings have suggested that PrPc may have neuroprotective properties and its absence contributes to an increased susceptibility to oxidative stress or apoptosis-inducing insults. Bounhar et al. have proposed a role for PrP

against Bax-mediated neuronal apoptosis and showed that PrPc potently inhibits Bax-induced cell death in human primary neurons, while further data have supported the proposed role for PrPc in the neuroprotective adaptive cellular response to hypoxic injury: Prp mRNA was upregulated during hypoxia and PrPc immunoreactivity accumulated within neurones in the penumbra of human and rodent brain, while the infarct size in PrP-null mice was greater than in wild-type<sup>18</sup>.

Data from the present study have supported the proposed role for PrPc in the neuroprotective adaptive cellular response to brain ischaemia and extended its potential role to humans. In agreement with previous experimental data, an increase in PrP mRNA and protein levels in infarct and penumbra of patients who survived up to 6 days after stroke has been noted, with strong staining observed mainly in neurons and blood vessels. Thus, PrPc may be involved in the regulation of ischaemia-induced neuronal cell death early after stroke in humans. In summary, the results of the current study represent novel data that have demonstrated the altered expression of several pro- or anti-apoptotic proteins in human stroke tissue, suggesting an apoptotic response to ischaemia in human brain and activation of the apoptotic pathway after the induction of ischaemic stroke in man. As there is increasing evidence that several neurodegenerative diseases (including stroke) involve activation of an apoptotic cascade, advances in clarifying the molecular mechanisms of apoptosis-regulating proteins may reveal strategies for pharmacological intervention in these conditions.

**By Nicholas Mitsios  
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## Response conflict, prefrontal cortex and dopamine: a rat model of Stroop-like performance

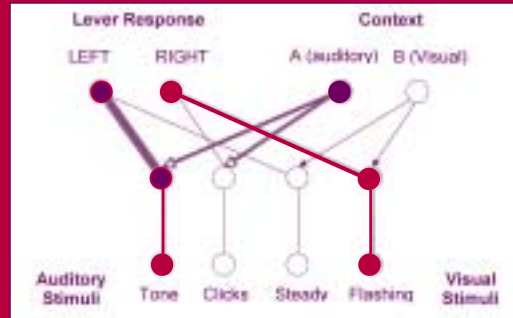


Figure 1: Basic architecture of computational model (after Cohen and Servan-Schreiber, 1992); bottom-up activation from a (sensory) input layer is indicated in red; top-down modulation by contextual units is indicated in purple. Trial represents presentation of a Tone + Flashing light incongruent compound cue in Context A. Presentation of tone and flashing light cues promotes activation of competing pathways leading to left and right lever presses, but additional top-down activation from the auditory cue context, A, biases responding towards left lever presses appropriate to the auditory tone cue.

Dr Josephine Haddon is currently a post-doctoral fellow in Professor Simon Killcross's laboratory in the School of Psychology, University of Wales, Cardiff. Her PhD thesis, supervised by Simon Killcross, was a runner-up in the prestigious BNA Post-Graduate Prize competition and describes how the performance of rats in a novel context-dependent bi-conditional discrimination paradigm closely reflects the response competition seen in human cognitive paradigms such as the *Stroop* task. This provides, she argues, an important tool for understanding the neurobiological processes underlying such tasks. It can also provide insight into behavioural anomalies seen in patients with disorders of the frontal lobe who fail to use contextual information appropriately.

In everyday life, we have to learn to perform particular actions in the presence of specific stimuli or events. For instance, we have to remember to add milk when making a cup of tea, but not when making a cup of coffee. However, sometimes it is necessary to override the common or usually performed behaviour in order to respond appropriately - when making coffee for a friend we may have to add milk. Thus, a mechanism, or set of mechanisms, is necessary for responding to be controlled by different cues in different situations or contexts. In order to achieve this flexibility in our behaviour, we need to learn about events in a manner specific to particular contexts, and to use this information to govern responding at a relevant point in time. This modulation of performance by contextual, or task-setting information, has a pervasive influence on human behaviour, ranging from the use of task-instructions to guide effortful, goal-directed responding, to the implicit or incidental control of behaviour (e.g. habitually smoking cigarettes when in a social context but not otherwise), and is thought to be especially important in situations when there is conflict between different actions or responses (Cohen, Braver & O'Reilly, 1998; Miller & Cohen, 2001). Moreover, this contextual modulation of behaviour has been implicated in a wide variety of everyday situations from the formation of episodic memories (Burgess, 2002; Butler & Rovee-Collier, 1989; Chun & Phelps, 1999) to relapse in drug addiction (Shaham, Shalev, Lu, de Wit, & Stewart, 2003).

Failure to utilize contextual information often leads to inappropriate or impulsive behaviours and an inability to co-ordinate one's actions to achieve a goal. This kind of impairment is classically seen with patients with disorders of the frontal lobe (Miller & Cohen, 2001) including patients with Parkinson's disease and schizophrenia (Cohen & Servan-Schreiber, 1992; Braver, Barch & Cohen, 1999). In particular, patients with schizophrenia are severely impaired on a number

of cognitive tasks involving response conflict such as the continuous performance task (Rosvold et al., 1956) and the *Stroop* task (Stroop, 1935, MacLeod, 1991). In the *Stroop* task, participants are required to read the word or name the colour of the ink the word is printed in. The stimuli comprise either congruent (i.e. the word GREEN in green ink) or incongruent (i.e. the word GREEN in red ink) word-colour combinations. In order to successfully complete this task, participants must respond to the task-relevant stimulus attribute whilst ignoring the distracting, task-irrelevant, attribute. The ability to respond according to the relevant stimulus attribute is especially important when the aim of the task is to name the colour of an incongruent colour-word compound, as participants are required to inhibit the dominant tendency to read the word, resulting in a greater number of errors and longer latencies to respond (MacLeod, 1991; Stroop, 1935). Both frontal and schizophrenic patients have been reported to have difficulty in performing the *Stroop* task, displaying increased reaction times and errors compared to normal controls, especially when they are required to select the sub-ordinate, but task-appropriate, colour naming response over the dominant tendency of word reading on incongruent trials (Cohen & Servan-Schreiber, 1992; Perret, 1974).

Using knowledge and understanding from current research in human cognitive neuroscience, we have developed a novel context-dependent bi-conditional task in rats which is analogous to the *Stroop* task in humans. In this task, contextual cues are used to govern choice responding when animals are presented with audiovisual compounds that provide conflicting response information (Haddon, George, & Killcross, submitted; Haddon & Killcross, 2006; Haddon & Killcross, in press). Animals were trained on two lever press tasks, one auditory and one visual, learnt in the presence of different environmental cues (checked and spotted cage contexts). For example, in the

checked context rats received presentations of the auditory cues (tone or clicker) during which different lever presses (left or right, respectively) led to food pellet reward. Similarly, left and right lever presses led to reward in the presence of visual cues (steady and flashing light respectively) in the alternative spotted context. Following training on these two tasks, rats were presented with novel combinations of the training cues (i.e. tone & steady light, tone & flashing light, clicker & steady light, and clicker & flashing light), in each of the training contexts, and allowed to choose between the different responses (left and right). These test compounds were composed of elements that dictated the same lever press responses (e.g. tone & steady light, and clicker & flashing light), or different lever press responses (e.g. tone & flashing light, and clicker & steady light) during training, termed *congruent* and *incongruent* compounds respectively. In the case of the congruent compounds there was no ambiguity. Both the tone and steady light dictated a left response, and both the clicker and flashing light dictated a right lever choice. However, response choice to incongruent cue compounds was ambiguous (i.e. the tone dictated a left response, but the flashing light dictated a right response). Responses during these incongruent compounds were defined as correct according to whether they had previously been trained in the test context. That is, using the example above, in the checked context responding should be dictated by appropriate choice with respect to the auditory cues, regardless of the visual element of the compound, whereas in the spotted context, responding should be dictated by appropriate choice with respect to the visual cues whilst ignoring the irrelevant auditory element.

Using this procedure, we demonstrated that the contextual cues came to control responding, such that in normal animals the context was able to control performance during incongruent stimulus compounds. Hence, this procedure can be viewed as reflecting aspects of the *Stroop* task in humans (Stroop, 1935; MacLeod, 1991). The *Stroop* task requires that task instructions are used to disambiguate conflicting response information provided by incongruent colour-word combinations; in the rat task, contextual cues disambiguate conflicting response information provided by the audiovisual compounds. In further experiments, we demonstrated that, following asymmetric training on the two biconditional discrimination tasks (in which one discrimination was "over-trained" relative to the other "under-trained" discrimination), similar response competition and interference effects were observed in rats compared to those observed in human participants performing the *Stroop* task. Rats demonstrated increased interference from over-trained stimulus elements when required to produce the context-appropriate but under-trained response to incongruent compounds. This increased interference from the over-trained cues manifested as increased incorrect responses and

decreased correct responses (Haddon, George & Killcross, submitted; Haddon & Killcross, in press) and is consistent with observations of increased difficulty in naming the colour of incongruent colour-word combinations in humans (Stroop, 1935; MacLeod, 1991).

In further studies, we have demonstrated that performance of this context-dependent biconditional discrimination task depends on the functioning of the prefrontal cortex (Haddon & Killcross, 2005; 2006; Marquis, Killcross, & Haddon, submitted), paralleling findings with the *Stroop* task in humans. Both pre-training excitotoxic lesions (Haddon & Killcross, 2005; 2006), and reversible inactivation (Marquis, Killcross, & Haddon, submitted), of the prefrontal cortex resulted in a selective impairment in responding during incongruent, but not congruent, compounds; rats were unable to use the contextual cues to disambiguate the response conflict induced by incongruent compounds. These findings are consistent with results from both neuropsychological and neuroimaging studies in humans (Perret, 1974; Cohen & Servan-Schreiber, 1992; Carter et al, 1998; 2000; Botinivick et al, 1999; MacDonald et al,

2000), and are in agreement with models proposing a role for the prefrontal cortex in the ability to maintain and use goals to direct behaviour, especially in situations of response conflict (Miller & Cohen, 2001).

'Failure to utilize contextual information often leads to inappropriate or impulsive behaviours and an inability to co-ordinate one's actions to achieve a goal. This kind of impairment is classically seen in patients with disorders of the frontal lobe including patients with Parkinson's disease and schizophrenia'.

The successful development of this novel paradigm has allowed for a direct, and more detailed, examination of the underlying neurobiology and neurochemistry involved in the behavioural control of response competition in Stroop-like tasks than is currently possible with human neuroimaging and neuropsychological studies. Consequently, the use of this procedure will contribute to our understanding of the disruption to cognitive function seen with a number of neuropsychological disorders including schizophrenia. Researchers have suggested that the use of contextual or task-setting cues to govern responding is dependent upon dopamine function within the prefrontal cortex, and dysfunction of dopamine modulation has also been implicated in the pathology of schizophrenia (Cohen & Servan-Schreiber, 1992; Weinberger, 1988). Although recent research has suggested a role for dopamine in the use of conditional information to guide behaviour (Dunn, Futter, Bonardi & Killcross, 2004) little research has examined the locus of action of these systemic drug effects. With this in mind, we have recently used the context-dependent bi-conditional task to examine the modulation of response conflict by prefrontal dopamine. Following training on the auditory and visual tasks, rats received infusions of either a control substance (artificial cerebro-spinal fluid, aCSF) or the D1 dopamine receptor agonist SKF-38393 (SKF) into the prelimbic region of the prefrontal cortex and responding to congruent and incongruent compounds was recorded. Overall, boosting prefrontal dopamine receptor activation by directly infusing SKF resulted

in improved performance during incongruent compounds (in which response conflict is high) but impaired performance during congruent compounds (in which response conflict is low). Moreover, the performance of individual animals following SKF infusion was found to be related to their baseline performance following aCSF infusion. More specifically, negative linear correlations were observed between baseline performance and the change in performance following SKF infusion during both congruent and incongruent compounds. Animals demonstrating poor baseline performance showed improved performance following SKF infusion; in contrast, animals demonstrating good baseline performance showed poorer performance following infusion of SKF. Although a correlation between baseline performance and performance change following SKF infusion was evident during both congruent and incongruent compounds, the effect was more marked during incongruent performance.

In addition to supporting previous work indicating a role for prefrontal dopamine in the use of contextual cues to resolve response conflict, the discovery of a relationship between baseline performance and subsequent performance following SKF infusion is also consistent with the inverted-U hypothesis that relates efficiency of cognitive performance to the level of D1 receptor stimulation (Arnsten, 1998; Zahrt, Taylor, & Arnsten,

1997). According to this hypothesis, in rats with lower baseline performance, dopamine activity within the prefrontal cortex is sub-optimal and so can be boosted by infusion of the D1 agonist to near optimal levels, resulting in improved performance. In contrast, in rats with higher baseline performance, dopamine activity within the prefrontal cortex is already optimal, and so increasing dopamine activity by D1 agonist infusion produces too much activity and leads to a deterioration in performance.

To summarise, we have demonstrated that the performance of rats in a novel context-dependent bi-conditional discrimination paradigm closely reflects the response competition seen in human cognitive paradigms such as the *Stroop task*, and so provides an important tool for understanding the behavioural and neurobiological processes underlying such tasks. Furthermore, we have shown that this paradigm is highly sensitive to both prefrontal cortex manipulations and prefrontal dopaminergic function, both of which are thought to be dysfunctional in patients with schizophrenia (Kraepelin, 1950; Levin, 1984; Cohen & Servan-Schreiber, 1992), and, as such, this paradigm will be of importance in the assessment of preclinical agents in treating the cognitive impairments seen in this disorder.

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# FOCUS ON NEUROSCIENCE DUBLIN



BNA Bulletin continues its 'Focus on...' series of articles that explores major neuroscience centres, this time giving the floor to Dublin. This couldn't be more apt and timely as Neuroscience Ireland launches itself formally this year with an inaugural meeting in Cork in September. Moreover, the BNA National Meeting next April will be held in association with NI, recognising the important contribution Ireland is making to our discipline. So times are definitely riding high for Irish neuroscience, and with increasing government support and enthusiasm, neuroscience research will stay high on the political agenda. Ian de Souza, a postdoctoral researcher in the Applied Neurotherapeutics Research Group at University College Dublin, was invited by BNA Bulletin to describe what's going on in Dublin these days. It makes impressive reading.

Researchers conducting neuroscience in Dublin have interests that cover the entire breadth of the field from studies at a cellular level right through to animal models and patient-based neuroscience. I will take you on a journey through Dublin focusing on the larger concentrations of neuroscientists located at University College Dublin (UCD), Trinity College Dublin (TCD), The Royal College of Surgeons in Ireland (RCSI) and Dublin City University (DCU).

At University College Dublin, neuroscience researchers are located primarily within the Conway Institute. Neuroscience is a major research theme within the School of Biomolecular and Biomedical Science and there are twelve principal investigators. To give an indication of the scale of research, this group has published 62 papers and attracted over 20 million in research funding from domestic and overseas sources in 2004-2005. Current research ranges from the study of learning and memory at the molecular, cellular and behavioural levels to analysis of the molecular basis to neurodegenerative diseases and the development of neurotherapeutics. A broad range of neurobiological tools is used to investigate brain function in state-of-the-art laboratories.

The *Applied Neurotherapeutics Research Group (ANRG)* is a research cluster involving three principal investigators from UCD, one from TCD and the pharmaceutical firm Wyeth. The ANRG is focused on building a research and development initiative to provide a new generation of drugs to be used in the treatment of brain illness. This most complex human endeavour focuses on a largely untapped resource of drug targets - the molecular and cellular events that relate gradual drug change of brain circuits to modified behaviour. This is an increasingly important issue in modern drug development as most, if not all, drugs used to treat psychiatric and neurological illness take weeks, if not months, to elicit their beneficial effect. Researchers

at UCD are also recognized internationally for their contribution towards understanding mechanisms of synaptic transmission, neurotransmitter transport, detection of neurotransmitters, regulation of G-protein coupled receptors in the CNS and amyloidogenic protein aggregation.

Moving into the city centre, Trinity College is probably the most well known of Dublin's universities. Neuroscience activities here are co-ordinated under the umbrella of *Trinity College Institute of Neuroscience*. Trinity College Institute of Neuroscience (TCIN) is Ireland's first purpose-built research institute to advance the frontiers of neuroscience. This interdisciplinary research institute opened in July 2005, and consists of a unique niche of over 30 principal investigators conducting research in areas spanning molecular/cellular to clinical/translational neuroscience. In addition to the intensive research activities in TCIN, the institute also runs a highly successful undergraduate degree in neuroscience, and a four-year Health Research Board-funded integrated Ph.D. programme. In addition, a one-year M.Sc. in Neuroscience will be introduced in October 2006. The building infrastructure of TCIN consists of 3,500 sq. metres of dedicated research space, and is one of the few such centres in the world to be established from the start with a truly interdisciplinary programme. In TCIN, scientists from such fields as genetics, physiology, biochemistry, pharmacology, neurology, psychiatry, psychology, microbiology and physics collaborate in addressing the most pressing problems of our time - how to foster and maintain the best functioning of the human brain.

The noble purpose of the institute is: "To advance understanding of key human brain functions through an internationally unique research interaction of molecular, cellular and cognitive neuroscience with neurogenetics, and applying

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this knowledge to the characterisation, diagnosis and treatment of the range of neuropsychiatric, neurological and age related brain disorders."

## Key scientific strengths are as follows:

**Brain plasticity and memory:** Scientists at TCIN are to the fore worldwide in uncovering the molecular bases of synaptic plasticity, revealing how learning and memory occur and how declines might be reversed in neurodegenerative diseases. Studies focus on normal ageing in tandem with neurodegeneration, and significant strides are being made in distinguishing between the processes of normal ageing and disease. Stress, for instance, has profound effects on the memory centres of the brain, and several investigators at TCIN are approaching analysis of this from several perspectives.

**Genotype-phenotype studies:** Fundamental research into the genetics of brain function is another major strength of TCIN, and the interdisciplinary ethos has manifested itself in major research projects between molecular geneticists, psychiatrists, neurologists and psychologists. Links are now actually being made between molecules and brain function as a result of imaginative interdisciplinary collaborative work. Progress has been made in identifying genes that result in altered behaviour in disorders such as attention deficit disorder and schizophrenia.

**Imaging the brain:** With new state of the art high field magnetic resonance imaging (MRI), scientists at TCIN can now reveal the brain systems involved in cognitive processes, attention, memory and emotions and study dynamic changes that occur in diseases such as schizophrenia, cognitive impairment and Alzheimer's disease. The underlying science of imaging the functioning brain is intellectually intensive and the mechanics of performing the work extremely challenging, necessitating the development of cutting edge techniques in MR physics applications. These imaging techniques allow the TCIN scientists to study the effects of drugs, such as cocaine and cannabis, on function and cognitive processes in the brain, an area of research where TCIN scientists have international collaborations. The imaging centre at TCIN also houses a 7Tesla animal MRI scanner to facilitate imaging in animal models of CNS disease.

Also in the city centre, located on St. Stephen's Green, is *The Royal College of Surgeons in Ireland*. Over the past decade, this international Medical School and Research Institute has enjoyed rapid expansion, with neuroscience now constituting the largest research front. Here, neuroscience researchers work in a number of areas including:

**Mutant models of neuropsychiatric disorders:** Mutants with targeted gene deletion or transgenesis allow study of the functional roles of genes associated with risk for disease and targets for drug action. Research in Prof John Waddington's group involves phenotypic characterisation following deletion of dopamine receptor subtypes and mutation for genes, such as neuregulin and COMT, that have been associated with risk for schizophrenia. A particular interest involves phenotypic

effects in behavioural and psychopharmacological models of psychotic illness.

**Craniofacial dysmorphism and brain dysmorphogenesis:** The brain and face develop in exquisite embryological intimacy, such that early disruption to brain development is accompanied by craniofacial dysmorphism. Research in Dr Robin Hennessy's group is applying 3D laser surface imaging and geometric morphometrics to resolve facial shape changes and asymmetry in neuropsychiatric disorders of early developmental origin as indices of brain dysmorphogenesis. The group has a particular focus on the developmental pathobiology of schizophrenia and bipolar disorder.

**Morbidity and mortality in psychosis:** Schizophrenia is a life-shortening psychotic illness of uncertain origin, with the vast majority of patients dying from natural causes such as cardiovascular disease. Dr Jogin Thakore's group has found that untreated first episode patients with schizophrenia are at a high risk of cardiovascular disease. In addition, the group and its collaborators are trying to establish reliable electrophysiological brain markers for schizophrenia and to determine if they are genetically determined.

**Apoptotic pathways and nerve cell injury:** Defects in apoptosis pathways have been implicated in neurodegenerative, ischemic and neurooncological disorders. Research in Prof Jochen Prehn's group is focused on the role of mitochondria and Bcl-2 family proteins in nerve cell injury. The Bcl-2 family of proteins contains pro- and anti-apoptotic proteins that regulate the mitochondrial pathway of apoptosis. The group aims to identify mechanisms of apoptosis and BH-3-only protein activation *in vitro* and *in vivo*, and its therapeutic interference.

**Seizures, signalling pathways and cell fate:** Research in Dr David Henshall's group is focused on understanding the signaling pathways that are activated in neurons after a seizure that culminate in either death, survival or neuroplastic changes. Particular interest is on the role of apoptosis-regulatory proteins of the caspase & Bcl-2 families, death receptor signaling and 14-3-3 proteins, and their potential therapeutic relevance. The group combines an array of experimental models together with translational material from epilepsy patients.

Leaving the city centre and moving towards the north, research in neuroscience continues at Dublin City University (DCU), primarily in the *International Centre for Neurotherapeutics (ICNT)*. This is a newly-constructed, state-of-the-art and well-funded Centre undertaking research into the biochemical mechanisms of communication in the nervous system, especially synaptic transmission. This purpose-built multi-disciplinary Centre was established to develop novel treatments for certain neuronal disorders due to hyper- or hypo-activity of nerve terminals. The research is funded by Science Foundation Ireland (SFI), Allergan Inc. and the U.S Government. The ICNT team is presently made up of 15 staff led by J. Oliver Dolly, SFI Research Professor of Neurotherapeutics, whose area of expertise encompasses many aspects of Molecular and

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Cellular Neurobiology. Research efforts are focused on identifying and structurally characterising proteins responsible for the fundamental process of quantal release of transmitters, and its indirect regulation by voltage-sensitive K<sup>+</sup> channels which control the excitability of nerve endings. Major aims include deciphering the molecular basis of abnormalities in synaptic transmission, and using the resultant information to develop novel treatments for the associated disease symptoms.

**Therapeutics effective in correcting the symptoms of over-active cholinergic nerves:** Fundamental research carried out by this group on the selective and potent inhibition of transmitter release by botulinum neurotoxins has underpinned their successful and worldwide clinical use in treating human dystonias, spasticity and other movement disorders, as well as autonomic neuronal abnormalities of secretory glands (e.g. hyper-hydrosis, -salivation and lacrimation etc.), over-active bladder (e.g. in spina bifida, spinal cord injuries and multiple sclerosis) and gastrointestinal tract (e.g. pyloric sphincter). Current efforts are devoted to developing second generation homologues and tailoring their functional properties for novel therapies, using established protein engineering techniques. Also, information is being sought on the molecular triggers for nerve sprouting and synapse remodeling induced by blockade of acetylcholine release due to cleavage of SNAP-25 by botulinum toxin A. Special attention is being devoted to deciphering the signaling for the eventual retraction of these neurites, in relation to the extraordinary duration (many months) of therapeutic benefit it offers. Likewise, individual steps of exocytosis are being deciphered and the functional domains identified by overcoming the toxin's inhibition of exocytosis by expressing recombinant variants of SNAP-25.

**K<sup>+</sup> channels as novel targets for developing drugs to treat neuronal abnormalities:** Several years of work on neuronal K<sup>+</sup> channels have been devoted to elucidating their oligomeric/primary structures and characterising the genetic defects in these proteins in certain human channelopathies. This group were the first to show the global 3D structure determined for K<sup>+</sup> channels purified from brain, highlighting the presence of 4 channel-forming  $\alpha$  subunits and 4 auxiliary  $\beta$  proteins.



**LEFT**  
Orlova, Dolly *et al.*  
*J. Mol. Biol.* 326, 1005-1012 (2003)

**RIGHT**  
Model of bacterial KcsA channel, highlighting the ion selectivity filter and residues required for external and internal blockers. Doyle *et al.*, *Science* 280, 69 (1998)

Such molecular definition of hetero-tetrameric subtypes in normal and diseased brain, coupled with their reconstruction by recombinant means, are providing authentic targets for drug refinement/development. This has been achieved by tandem linkage of the genes encoding different constituents of neuronal voltage-activated K<sup>+</sup> channels (Kv). Subsequent expression of

these proteins on the surface of mammalian cells generates channel tetramers with pre-defined combinations and stoichiometries of  $\alpha$  subunits which mimic the subtypes found in human brain. Similar protein engineering can produce a unique K<sup>+</sup> channel that appears in demyelinated axons from patients with multiple sclerosis, and those containing identified mutations (e.g. inherited channelopathies in children). By these means, existing K<sup>+</sup> channel drugs are to be tested for capacities to act discriminatively on one of the normal or abnormal K<sup>+</sup> channel subtypes, with the eventual goal of being able to raise the excitability of under-active nerves. As the high-resolution crystal structure of one mammalian K<sup>+</sup> channel has recently been published, use of the co-ordinates for the mouth of its ion filter ought to aid the design of selective blockers which, in the longer-term, might prove effective in normalising synaptic transmission in certain neurons in diseased states. Other investigators in DCU's School of Biotechnology carry out research into neuropeptidases.

Space limitations preclude me from mentioning all the individuals involved in neuroscience in Dublin and I have focused, for the most part, on basic research. Hopefully I've managed to give you a flavour of the neuroscience community here which you can see is a very research-active. The great concentration of internationally recognised neuroscientists has fostered several enduring and fruitful collaborations across the city and beyond. I've had the good fortune to have worked in neuroscience research at RCSI, TCD and now at UCD and I think Dublin is a great place to be involved in neuroscience. All this important research would not be possible without the main funders of neuroscience research in Ireland; Science Foundation Ireland, The Health Research board, Enterprise Ireland, The European Union, The Wellcome Trust and the NIH. Significant infrastructural funding has also come from the Higher Education Authority and The Programme for Research in Third Level Institutions.

Our neuroscience community in Dublin is further enhanced nationally by important neuroscience research taking place at other Universities in Cork, Galway, Maynooth and this year marks the inaugural conference of Neuroscience Ireland which takes place in University College Cork on the 21st and 22nd September 2006. We are also delighted to be collaborating with the BNA in the next in their series of excellent national meetings.

Finally, I would like to acknowledge John Waddington and Jogin Thakore (RCSI), Tom Connor (TCD) and Oliver Dolly (DCU), without whose assistance this article would not have been possible.

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For more information, consult the following websites:  
[www.ucd.ie/sbbs/research/neuroscience.htm](http://www.ucd.ie/sbbs/research/neuroscience.htm)  
[www.ucd.ie/neurotherapeutics](http://www.ucd.ie/neurotherapeutics)  
[www.tcd.ie/neuroscience](http://www.tcd.ie/neuroscience)  
[www.dcu.ie/icnt/index.shtml](http://www.dcu.ie/icnt/index.shtml)

## TALKING TO THE MEDIA: WHY AND HOW

by Andrew King

The Science Media Centre (SMC) is an independent organisation located at the Royal Institution in London, which was set up a few years ago in order to provide an interface between science and the news media. It was established largely because so few scientists were willing to engage with the media. The most important role of the SMC is to act as a press office, supplying journalists with information or arranging interviews with appropriate scientists when science-related stories hit the headlines. The SMC also provides media training and runs several events each year aimed at providing more general advice for scientists when talking to the media, either on matters relating to their own research or on topics such as the use of animals in biomedical research.

The most recent News Media Event took place on 16th May 2006. This was extremely well attended and included presentations from people working in different aspects of the news media, a university press officer and from two scientists with experience in dealing with the media. Not surprisingly, great emphasis was placed on the value of effectively communicating science to the general public. The great majority of what members of the public know about scientific research is provided in one way or another by the media, so it is vitally important that news journalists and editors receive accurate, interesting and well-explained information when they need it.

By definition, news stories almost invariably have to be put out quickly. One of the main problems encountered by the SMC and by university press officers is that queries from journalists often need responses within a matter of minutes. If scientists are not available to respond this quickly, it is inevitable that the media will seek alternative and possibly less well-informed sources. Consequently, the SMC has established a database of scientists willing to speak on topics that are likely to feature in the news and is very keen to add to this database.

The representatives from the media stressed that they also wish to hear about new, interesting research. Sometimes this is achieved through press releases made by scientific journals. But in other cases, it requires the scientist to be proactive in alerting the press office of his/her university or funding body about novel findings that are likely to have more general appeal.

The most entertaining part of the session was provided by the

writer and broadcaster, Vivienne Parry, who outlined the 'dos and don'ts' of dealing with the media. Besides appreciating that the media operate to strict deadlines, the key points she made were to think about the audience - is the interview for the *Sun* newspaper or *BBC Newsnight*? What is the key message? Be honest, brief, passionate about the research, and use clear, everyday phrases (remember that you are not addressing your peers). Of course, this requires a certain amount of preparation and, in the case of TV interviews, some care over choice of clothing. Vivienne also stressed the importance of looking at the interviewer to avoid appearing untrustworthy and, in the case of radio interviews, of not moving around or using paper notes.

This was followed by a question-and-answer session with representatives from BBC Online, ITN News, *The Guardian* and *The Daily Express*. Given the tight timescale of most news stories, some concern was expressed by members of the audience about the possibility of mistakes being made by journalists. The journalists stressed that the primary aim was to put out stories containing accurate information. It was pointed out that scientists frequently decline to comment because the topic in question is not their area of research. The journalists responded, however, by pointing out that scientists are usually a lot more expert than they are.

The event concluded with presentations by Allan Pacey and John Henry, who spoke about their own experiences in dealing with the media. They argued that scientists have a responsibility to communicate with journalists. Although this can become a big commitment, it can also be very rewarding.

Overall, this event provided a valuable insight into how the media obtains and prepares science-related news stories and will hopefully encourage scientists to make themselves available for comment via their press offices or even to undertake media training. We are fortunate in the UK that the media often - though certainly not always - employs specialist science reporters. The journalists are, therefore, generally on the side of the scientist. The various activities of the SMC will undoubtedly play a vital role in promoting the work and views of the scientific community to the news media and, therefore, in helping to improve the public's perception of the importance of science.

By Andrew King  
Professor, Department of Physiology,  
University of Oxford

If you would like to know more about the work of the Science Media Centre, or would like to register your willingness to speak on scientific issues, then please contact Claire Bithell at the SMC ([CBithell@ri.ac.uk](mailto:CBithell@ri.ac.uk)) or Yvonne Allen at BNA ([y.allen@bna.org.uk](mailto:y.allen@bna.org.uk)).

## FACT FILE

### Did you know that:

- 84% of people find out about science from TV programmes, news and documentaries
- more than half the population have no science qualifications whatsoever
- 75% of people think scientists should listen to what ordinary people think

- 2 out of 3 women feel ill-informed about science
- 86% of the population think science makes a good contribution to society
- 96% of people think children should be taught science
- 30 years ago, BBC Horizon had an audience of 400,000; today, that figure is close to 2 million

Source: The Wellcome Trust 'Public Engagement' Conference, Manchester, April, 2006

## PUBLIC ENGAGEMENT - YOU KNOW IT MAKES SENSE!

Funded by The Wellcome Trust Value in People Award and The University of Manchester.



Dr Ellen Poliakoff collaborates with fellow neuroscientist Dr Stuart Allan and science communicators Dr Erinma Ochu and Dr Michelle Lockwood as the *Manchester Science Group*. Here, she describes some of her recent experiences developing and working on two public engagement projects about the brain and the senses.

We were invited some time ago to deliver a *Café Scientifique* talk at the University of Manchester's *Café Muse*. This is part of the UK-wide *Café Scientifique* network and, typically, the monthly sessions consist of academics talking about their research, whilst the audience has a cup of coffee, a beer or a glass of wine. The talk is then followed by an opportunity for the audience to informally quiz the academic.

We agreed to run a session about the brain and senses and decided to attempt to innovate the format for our session, making it more interactive for the audience and more distinct from a typical academic talk. Going along to a previous talk at *Café Muse* confirmed our approach. We found that it was hard to see the PowerPoint slides being projected onto one wall of the café, hard to hear what was being said, and hard to feel involved if you were far from the speaker.

Therefore, back in December, we began to brainstorm what we might do to overcome these issues. Erinma and Michelle came up with the idea of using a pub quiz format, which has, after all, already evolved to run within a noisy café or pub environment. We decided to include both questions and hands-on demonstrations in a six round format, one for each of the classic five senses and an extra round for the additional senses. I worked with Michelle to develop these. We settled on questions with a choice of three possible answers, as well as a few true-or-false type questions, so that everyone, regardless of prior knowledge, would have a chance of getting the questions

right. As well as including some more basic questions, we also tried to link the senses to more the more typical pub quiz domains of general knowledge (e.g. *The strong linkage between smell and memory is called the....? A Tolstoy Effect; B Proust Effect; C Dickens Effect*) and politics (*Which vegetable is George W Bush Senior claimed to have an aversion to? A Carrots; B Brussel sprouts; C Broccoli*).

An essential step was holding a trial quiz a week before the real event with a hastily assembled group of colleagues and friends (complete with wine and crisps) in order to try out our questions and to give our quiz master - actor Barry Sloane - the chance for some practice. We quickly realised that we needed to cut the number of questions, which was really useful to know, even if it did mean losing my favourite true-or-false question (*'At the end of the Beatles' song "A Day in the Life", an ultrasonic whistle, audible only to dogs, was recorded by Paul McCartney for his Shetland sheepdog' - true or false?*). It also meant that we could try out alternative demos. For instance, for demonstrating unusual taste combinations, we opted for chilli-chocolate rather than caviar with chocolate. Even after this, there were still a few more practical problems to solve - how would we distribute the demos to the teams, how would the audience know what to do, and how would we move quickly between rounds of questions?

On the night, quiz master Barry - dressed in a blond wig and frilly shirt - read out the questions and I was the demo-master who gave out the instructions. Stuart and Erinma moved between the tables handing out the demos and adding up the final scores, while Michelle worked behind the scenes controlling the sound and playing music to signal the start of each demo. Over eighty people came along to the event and split into ten teams. Initially, some of the regular *Café Scientifique* visitors seemed slightly perturbed by the new format. However, once they had their name stickers on, most of the teams quickly relaxed and become quite talkative. Indeed, some people commented that they had been coming to *Café Scientifique* for a long time but this was the first time that they'd ever spoken to other people. The feedback that we got was encouraging too, for example "Will keep talking about this for weeks" and "entertaining and educational". It was also great fun to help run the event and, although being demo-master was very different to giving a talk, there were close links between the material in the quiz and my lectures to first year students on perception and the senses. Indeed, I was even able to add my favourite Paul McCartney question to the start of my first year lecture on hearing!

We had also agreed to present our session at the Nottingham *Café Scientifique* two weeks later (it was almost a tour!) The room layout at the Wax Café in Nottingham was even more challenging - long and thin with very small tables. This meant that it was impractical for us to distribute the demos table-to-table, so instead we packed all the demos into red cardboard boxes and instructed the teams about what to take out. More

than seventy people packed into Café Wax and formed 11 teams. The crowd in Nottingham were even livelier than Manchester, perhaps helped by the later start time of the event.

No sooner were we back from Nottingham than it was time to think about our upcoming trip to the Edinburgh Science Festival in April. The format was a short play, followed by table-top demos based around the five senses. We began to discuss what demos to use for each sense. Our task was to find something to fit into less than six minutes that would allow the audience to learn by discovery (rather than by presenting dry facts) and, if possible, to link it to some research being carried out at Manchester University. We spoke to various academics whose research links to the senses, including Jeanette Hobbs from the Faculty of Life Sciences who researches taste and Liz Orton from the MRC hearing group. Liz suggested demonstrating the hearing screening test used on newborn babies and offered to come up to Edinburgh with us. Stuart spoke to Dr Matthew Cobb from the Faculty of Life Sciences about demos for smell. He suggested using smells - like motor oil - to evoke memories and showing that most people can tell the difference between two alcohols with only one carbon atom difference in structure. In the meantime, Erinma was working with actors Vicky Brazier and James Scales to develop the script for the play - based around Little Red Riding Hood visiting her psychiatrist Dr Lupine.

All too soon, I found myself ironing tablecloths in Edinburgh and about to feature in the first performance of 'You Know it Makes Sense'. The audience of thirty sat around five round tables - the brightly coloured tablecloths and flowers gave it a 'cabaret' feel. If the pub quiz had seemed a big step away from a typical academic talk, this was a leap even further. I was volunteered to introduce the start of the show, before being interrupted by Dr Lupine (the psychiatrist). This was definitely the closest that I've come to acting in many years, but James, who played Dr Lupine, made it easy for me to look surprised by genuinely surprising me by changing the timing of his entrance in every performance! The play showed that things are not always what they seem and led into the second half where the audience could trick and challenge their senses. At first, we had planned that the audience would move from table to table, but then decided it would be simpler for the scientists to move instead, carrying their equipment in the aforementioned red cardboard boxes. We had five scientists from the University of Edinburgh to help us. I presented the size-weight illusion as part of

"touch"- a larger object feels heavier than a smaller object of the same weight (in our case, tomato soup cans). I had a hard act to follow because, for most of the audience, we came after the "taste" activity, which involved working out the difference between English and Irish Cadbury's Dairy Milk (not all public engagement demos have to include chocolate, but it helps!) Again, Michelle used music to move us on and to make sure we didn't run over our allotted time at each table. Sitting at the tables with the audience certainly stimulated conversation, as Stuart found out when one lady told him a particularly memorable story about the smell of lavender being used to mask the smell of the decomposing body of her downstairs neighbour!

Sitting back at my desk in Manchester, what can I conclude from my experiences? The quiz and drama formats were certainly engaging and novel for the audience. Looking through the feedback cards from the events, the phrase "not what I expected" appears almost as often as "fun" and "enjoyable". The interactive approach did entail more preparation than the traditional "scientist lecturing to the public" approach, but has left us with a resource that can be adapted and updated. Indeed, one quiz participant suggested that we could use a version of the quiz with school children. And for me, taking part in something different meant that I returned to my day-to-day research and teaching duties with a renewed sense of enthusiasm.

Funded by The Wellcome Trust Value in People Award and The University of Manchester.

**For all Manchester Science Group Events check...**  
<http://www.manchesterscience.blogspot.com/>

We are looking for London-based neuroscientists to volunteer for *You Know it Makes Sense* at The Dana Centre in October 2006. To get involved, please email: mansci@googlemail.com

#### Answers

1. True - Paul McCartney did include the whistle!
2. The strong linkage between smell and memory is called the Proust Effect.
3. George W Bush Senior is claimed to have an aversion to Brussels sprouts.
4. Dairy Milk made in Ireland tastes different to Dairy Milk made in England due to the use of different milk powders and flavouring levels used by each factory. There is some disagreement about which tastes nicer!

It produces a range of materials, and organise numerous events for children (Key Stage 1 to 4) and for the general public under the project title 'Science for All'. *Science for All* also provided research, consultancy and the development of customised science communication presentations and activities for external clients.

It would be its goal to extend these activities to the biomedical field as well, particularly neuroscience. The SCU, working together with the BNA, is therefore keen to hear from graduates who might like to explore this possibility.

For further information, please contact: Dr Dominic Dickson, Department of Physics ([dominic.Dickson@liv.ac.uk](mailto:dominic.Dickson@liv.ac.uk)) or Dr Yvonne Allen, BNA ([y.allen@bna.org.uk](mailto:y.allen@bna.org.uk)).

## SCIENCE FOR ALL AT THE SCIENCE COMMUNICATION UNIT, THE UNIVERSITY OF LIVERPOOL

The Science Communication Unit (SCU) exists alongside the Department of Physics' experimental physics research groups to provide the expertise and infrastructure to promote our subject and our research to the widest possible range of audiences.

## Development and Plasticity of the Human Cerebral Cortex

**2nd FENS/IBRO International Summer School Zadar-Zagreb, Croatia 25th September - 4th October, 2005**

An article recently published in *Trends in Neurosciences* (Aguayo et al, 2005) stated that there is a chronic under-funding of basic neuroscience training in Europe. This sparked a joint venture by FENS and IBRO to promote and build greater strength in the brain sciences by organising schools and courses that will train Europe's future neuroscientists.

In September 2005, Croatia became one of the latest venues to host one such FENS/IBRO International School. A total of 28 young scientists, representing more than 17 countries, descended on the beautiful Croatian coast for a programme comprising nine days of lectures, with two days of practical courses, aimed at exploring the latest research on the human cerebral cortex. Albert Aguayo (IBRO president) and Ivica Kostovic (Director of the CIBR) opened the school at the stunning seafront town of Zadar, which was to provide an inspiring backdrop for the initial seven-day lectures element of the programme. The invited

faculty comprised numerous leading neuroscientists from several countries, including Pasko Rakic (Yale, New Haven), Yehezkel Ben-Ari (INSERM, Marseilles) and Giorgio Innocenti (Karolinska Institute, Stockholm), who each gave special evening lectures at Zadar University.

In Zadar, the gathered faculty covered an extensive range of topics, giving talks on subjects including neurogenetic events in the human cerebral cortex (proliferation, migration and cell lineages); synaptogenesis, development of dendrites and formation of thalamocortical, corticocortical and monoaminergic connections; genetic and molecular mechanisms of regionalisation and cortical area specification; molecular patterning of cortical neurons; neurophysiology of the immature human cortex; characteristics of early cortical networks; development and plasticity of hippocampal circuitry and signalling molecules; development of working memory and executive functions in non-human primates and in normal and dyslexic children; neuroimaging of cortical development; neuronal imaging of the human foetal brain; DTI mapping of human brain connectivity; vulnerability in cortical development; animal models of developmental pathologies; plasticity and recovery repair of cortex and neurodevelopmental outcome after perinatal damage; neuroprotection in early life; generic vs. species-specific features of human neocortical evolution.

In order to foster meaningful scientific exchange between the faculty and students, each student had the opportunity to

present his or her current research through a short seminar or poster presentation. This atmosphere of open intellectual exchange was embraced further as both faculty and students resided in the same hotel, facilitating their interaction.

Following the intense lecture-based element of the course, the group relocated to the historic and cultural heart of Croatia: the 900-year old capital city of Zagreb. The practical course was held at the Croatian Institute of Brain Research (CIBR), part of the Zagreb Medical University. Founded in 1990, the CIBR is a hugely impressive, newly constructed building and forms the centre-piece of this dynamic institution. All were impressed by the state-of-the-art facilities, which included newly renovated laboratories and a fine infra-structure, complete with a magnificent double spiraling marble staircase, built to represent the DNA double helix.

Highlights of the practical course included hands-on laboratory work and an insight into magnetic resonance imaging of the human fetal brain; 3D reconstruction of fluorescence labeled neurons with confocal microscopy and NeuroLucida; stereology using the Stereo investigator system; single cell electrophysiological recording; multiple immunocytochemical labelling techniques; in situ hybridisation; electron microscopy; confocal microscopy. It was concluded with a tour of the vast Zagreb neuroembryological collection.

Of course, the scientific event wouldn't have been complete without a social element thrown in! The highlight was a boat trip to the Kornati Islands, an archipelago of more than 1000 islands which make up one of Croatia's most prized National Parks. There was a further inland trip to the Plitvice Lakes. In true Croatian style, the Gala dinner included a plentiful array of local fine wine and traditional food specialties from the region, topped off with a wine-tasting competition and dancing. Many firm friendships were established and some of us have already held a reunion at the Society for Neuroscience meeting in Washington last autumn. Indeed, a further small-scale scientific meeting is planned to take place in London and Oxford in March 2006.

I can safely say that the entire course was a resounding success, being stimulating and inspiring, both scientifically and socially, and I highly recommend that other PhD students and post-docs apply for future courses of this nature. Everyone was impressed by the exceptional organisation, and in a country with such a firmly rooted university tradition, it was not surprising to see that study and research in neuroscience has assumed a new, greater priority. This perception was reinforced further on my recent visit to the CIBR, where its Director, Prof Kostovic, informed me of a new and exciting initiative to further promote the development of neuroscience in Croatia. Further details of upcoming FENS/IBRO International Schools can be found at [www.ibro.org](http://www.ibro.org) or <http://fens.mdc-berlin.de/schools>.

**By Hana Ross**  
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(left to right): Hana Ross (Oxford), Kenneth Kwan (Yale), Michael Baratta (Colorado)



Christopher Pryce (left) with Paul Harrison

From left: Colin Ingram, James Winslow, Michael Barnham (Dean of Life Sciences), Jolanta Opacka-Juffry, Charles Marsden, Danielle Champagne, Chris Pryce, Cecilia Essau

## EARLY LIFE STRESS: BEHAVIOURAL AND NEUROBIOLOGICAL CONSEQUENCES.

**BNA One-Day International Symposium: 5th April, 2006, at the Whitelands College, Roehampton University, London.**

On a sunny April morning in the beautiful grounds of Whitelands College, it was difficult to believe anyone could think about 'stress' but this long overdue international symposium endeavoured to do just that! Sponsored and organised in collaboration with the BNA, Roehampton University played host to a number of leading delegates from across the research field of early life stress. With increasing epidemiological evidence highlighting the importance of the early postnatal period in human development and how negative stimuli during this sensitive time can increase the long-term risk of developing psychiatric disorders, the effects of early life stress has become a crucial hot topic for neuroscience. The symposium session was chaired by Christopher Pryce (Zurich) and Colin Ingram (Newcastle), who, with a total of eight speakers, provided an inspiring insight into the topic. A brief commentary of each speaker's contributions follows.

**Dr. Christopher Pryce** from the Laboratory of Behavioural Neurobiology, Swiss Federal Institute of Technology (ETH, Zurich) discussed the long-term effects of early life environmental manipulations. In particular, his group has focused on the chronic effects of early deprivation studies in rodents and primates, and their potential as a model for depression. Interestingly, he has shown in progressive ratio studies of reinforcement, rats previously subjected to early deprivation had significantly reduced motivation to obtain reward, the effect of which could be reversed by fluoxetine. He also reported alterations in spontaneity/ exploring behaviours, progressive ratio tasks, and family specific changes in acute hormonal responses and receptor expression in response to early life deprivation in the marmoset. His research suggests the use of early environmental stress can provide psychoneuroendocrine models of depression.

**Professor Paul Harrison**, head of the Molecular Neuropathology Group (Oxford) gave a comprehensive overview of the neuropathology of mood disorders with reference to the current clinical definitions and treatment available. He reviewed MRI and fMRI results for bipolar disorders that indicate a reduction in the size of the cingulate cortex and hippocampus, the reduction related to the number of episodes and duration suffered. Post mortem results suggest a reduction in the number and density of glia in key brain areas (anterior cingulate, dorsal lateral prefrontal cortex, amygdala), a reduction in both astrocyte and

oligodendrocyte markers and a decrease in neuronal density and size in areas such as the paraventricular nucleus. He highlighted the need for consistency in sampling due to cellular heterogeneity in areas such as the cingulate cortex, which have led to contradictory findings.

**Dr. Danielle Champagne** from the University of Leiden (Holland) described how natural variation in the pup-dam maternal relationship of mice and rats may infer the development of behavioural and endocrine responses to stress in the adult offspring. She described her group's novel observation that pups nurtured by dams that display naturally high licking and grooming behaviour have reduced acetylcholine and corticosterone expression in response to stressful stimuli, suggesting an improved feedback regulation of the hippocampus-pituitary axis (HPA) and a blunted response to stress. Excitingly, differences in the expression of corticosterone releasing factor (CRF) mRNA in prominent HPA areas (paraventricular nucleus, central amygdala, locus coeruleus) were observed between pups reared by high licking mothers and low licking mothers suggesting 'experience-dependent' plasticity.

**Dr. James Winslow** from Washington (USA), overviewed features of current primate models for psychiatric illnesses focusing on the model of adverse rearing through maternal separation. He discussed the importance of the hormones oxytocin and vasopressin and their suggested roles in social recognition and learning. Interestingly, it has been observed that offspring subjected to nursery rearing have fewer affiliative forms of behaviour and a reduced level of oxytocin in their cerebrospinal fluid. Maternally-reared offspring showed an increase in social contact behaviour and social buffering of stress responses in comparison to nursery-reared animals, which lacked social competence. In startle response tests, nursery-reared primates showed an enhanced fear potential, which was corrected by a chronic treatment of fluoxetine.

**Professor Colin Ingram** from the University of Newcastle discussed potential mechanisms for early life programming of stress and anxiety responses. He described the fascinating model of early life infections, which works by challenging the immune system with an injection of endotoxin in pups 3 to 5 days post partum. Behavioural stress testing in adult animals treated with endotoxin showed significant increases in the number of basal corticosterone pulses in comparison to non-treated animals. Upon challenging the animals with white noise, endotoxin-treated rats showed a greater plasma corticosterone response and higher levels of anxiety. He also shared with the symposium his work on the disruption of parental care and its long-term consequences, revealing that rats subjected to early maternal separation had greater anxiety responses in the elevated plus maze, and his group's on going work to elucidate what underlies these changes in anxiety levels at a molecular level.

**Dr. Jolanta Opacka-Juffry** from the University of Roehampton (host and co-organiser) described early life deprivation as a neurodevelopmental model of depression. She gave a comprehensive overview of depression as a disorder of neuroplasticity, where neurochemical imbalances are implicated in the pathophysiology of mood disorders, and where morphological changes have been seen at the level of dendritic atrophy, synaptic atrophy and neuronal loss. Her group has been investigating the long-term neurobiological effects of early life deprivation in rats. The density of glial fibrillary acidic protein (GFAP)-active astroglia was reduced in the limbic system of early deprived rats. The mean total lengths of primary astrocytic processes were also found to be significantly reduced in the CA1 area of the dorsal hippocampus. She also reported a tendency to reduced 5HT1A receptor binding in early derived rats versus non-handled controls. These novel results suggest changes in the integrity of astroglia in brain regions implicated in stress-related mood disorders.

**Professor Charles Marsden** of the Institute of Neuroscience (Nottingham) presented work on the behavioural and molecular consequences of early life adversity. He noted the interesting observation that, whereas adult male rats who endured maternal separation show a significant alteration in the latency time to leave the closed arms of an elevated plus maze when compared to controls, the female rat subjected to the same protocol did not, suggesting gender differences in relation to current stress models. He also presented some exciting results related to the animal model of isolated rearing. Weaned rats housed alone compared to those housed in groups, displayed a structural loss of hippocampal synapses, increase in striatal dopamine (DA) and

serotonin (5-HT) function, and loss of DA and 5-HT function in the hippocampus and prefrontal cortex. Isolated rats also showed an altered response to restraint and footshock stressors, and novel object discrimination, although the later was only observed in male isolated rats.

**Professor Cecilia Essau**, an expert in child psychopathology from Roehampton University reviewed the course and outcome of anxiety disorders in adolescents. Anxiety disorders are the most prevalent of mental disorders with almost 30% of adults meeting the clinical criteria during their lifetime. Early onset of anxiety disorders during childhood or early adolescence is associated with risk of developing other mental disorders later in life. In a seven-year follow up study, gender differences emerged around the age of 15, with females suffering from more than one anxiety/ mental disorder. She reported the startling results that 22% of those with anxiety disorders in the first trial had additional disorders in the follow up trial. She also highlighted the need for standardised diagnostic interviews to disclose the true nature of anxiety disorders.

The day came to an end with an active general discussion, where the need to close the research gap between clinical research displaying the prevalence of females with anxiety disorders and animal studies where male subjects are normally used was strongly highlighted.

**By Lisa Wells**

**Lisa Wells is a PhD student jointly supervised by Dr Jolanta Opacka-Juffry (Roehampton) and Professors Ian Kitchen and Susanna Hourani (University of Surrey, Guildford).**

## Controversial Issues in Neuroscience: *Deep Brain Stimulation*

**A café-bar discussion at The Dana Centre, 165 Queens Gate, London, SW7 on Wednesday, 15th March, 2006**

One of the most fascinating things about public discussions at the Dana Centre is that you never know whom you might get to sit next to. On the occasion of 15th March, I find myself talking to 'Peter', a patient of Marwan Hariz, with whom he exchanges warm glances as Marwan joins the other panelists to discuss **Deep Brain Stimulation (DBS)**. Imagine that. I was indeed honoured to hear a real-life account of a surgical procedure that had, erstwhile, had only existed for me in academic journals or, increasingly, in glossy magazines, such is the attention this technique is now attracting. And there was much more of this come.

*'We are reminded that it is still very much a procedure to alleviate symptoms - it is by no means a cure.'*

But first, we are being addressed by our chair, Mary Baker, President of the European Parkinson's Disease Association, who remarks that mankind is the only species to have doubled its life expectancy in less than a century. Neurodegenerative diseases, as a consequence, have become the most challenging as we strive to live these longer, quality lives. She presides with her usual eloquence and panache as she invites Oxford neurosurgeon, Tipu Aziz, to introduce DBS and its procedures.

It is not a 'new' technique as such, Tipu says, for the idea that electrodes in the brain can control behaviour has been around for some time. With advancing understanding of the neuropathology and neurochemistry behind PD, it was inevitable that stimulation of the brain regions involved, in particular the sub-thalamic nucleus (STN), should start to have therapeutic appeal. At the

same time, lesional surgery, such as bilateral thalamotomy, though often successful, was fraught with unpleasant side-effects and was, frankly, becoming quite dangerous. Hence, the 1990s saw the advent of DBS, with wires inserted and devices implanted that meant the STN could be 'turned off' or, at best, 'turned down' at will.

Tipu Aziz now operates on at least one PD patient a week, though his concern is growing for the 20% of patients that respond to neither drugs nor surgery. Interestingly, such drug-resistant patients do respond to pedunculopontine nucleus (PPN) stimulation, a region of mounting importance, clearly, in basal ganglia and brainstem functional connectivity.

There are still technical problems, of course, for wires can break, batteries are rather large, haemorrhaging is still a problem in a small percentage of cases. So the future will see rechargeable batteries, smaller devices, programmable pacemakers and new and/or multiple targets, Tipu confidently projects. Whatever, the technique remains an amazingly powerful weapon in the growing armoury designed to combat this distressing and alarmingly prevalent disease.

At this point, we are privileged to bear witness to a poignant demonstration by Mike Robins, an early patient of Tipu Aziz, of life before and after DBS. With the device turned on, he is lucid, vivid and calm recounting the tremor he developed over 10 years ago that Tipu was eventually able to bring under control; with the device turned off, he is swiftly debilitated by violent, uncontrollable shaking, so much so that his son leaps to help him stabilise his hand sufficiently to find the 'on' switch again. Amazing, truly amazing. We are all appreciating the short break in the proceedings that now ensues while we assimilate this experience.

Marwan Hariz, Head of Functional Neurosurgery Unit, UCL, resumes the discussion and is telling us about other movement disorders he treats with DBS, notably dystonia. Here, the pallidum is the target, but he reminds us that it is still very much a *procedure* to alleviate symptoms - it is by no means a *cure*. We

do not even know how it works, so how can it ever be more than palliative? But these issues do not concern Amy Westall and her father, Martin, who is now describing to us his experiences of coping with a severely dystonic child, eventually confined to a wheelchair, but who, since 2003, now leads a virtually normal life after Marwan was able to control her dystonic spasms.

Inevitably, we are now concluding the evening talking, yet again, about NHS budgets and priorities in the health system. Neurologist Patricia Limousin informs us these are expensive treatments, involving a huge team of highly skilled specialists ranging from neurologists, who select suitable candidates for surgery in the first place, to the psychologists, speech therapists and nurses who are involved in the post-operative care. But Peter next to me is now telling me that, only a year after his DBS, he is able to hold down a job after many years on invalidity benefit. So what's more expensive - a lifetime on benefits, or surgery that brings an able and intelligent human being back contributing to

society again? Sadly, our policy makers and budget holders do not always see the wider picture. They should come to the Dana Centre more often, clearly.

**By Yvonne Allen**  
BNA Executive Secretary

*Professor Tipu Aziz will be speaking at the BNA National Meeting, 1-4 April, 2007, in Harrogate. See [www.bna.org.uk/harrogate\\_07.htm](http://www.bna.org.uk/harrogate_07.htm) for further details. Mike Robins will receive the BNA Award for Public Service this year, to be presented by Richard Frackowiak at The Royal Society, 14th December, 2006, during the annual Christmas Symposium.*

*The series of 'Controversial Issues in Neuroscience', in collaboration with EDAB, continues at The Dana Centre with an exploration of the ways genes might influence criminal behaviour. 'Criminal behaviour - nature or nurture?' will take place on Wednesday, 27th September. See page 13 for further details.*

## NEURODEGENERATIVE DISEASES: FROM BENCH TO BEDSIDE

A BNA sponsored symposium at the Association of British Neurologists Spring Meeting, Friday, 21st April, 2006, at The Grand Hotel, Brighton.



From left: John Collinge, Maria Spillantini and Anne Rosser

Scheduling a symposium for Friday afternoon at the end of a long and tiring three day meeting was, surely, tempting fate. In addition, the weather was warm and sunny, a pleasant respite from an otherwise inclement spring. Brighton, with its quaint shops and Bohemian café society, beckoned. Nevertheless, an impressively large audience stoically remained in the deeper recesses of this, the grandest of 'Grand Hotels', and they were not to be disappointed. For the joint ABN-BNA symposium on

underway involving over 60 patients, about half of whom are placebo controls. This is yet to report and, under a recent EU tissue directive, has briefly suspended activity. Hence, Anne Rosser was keen to point out that any definitive answers would take several years to come. However, although primary foetal tissue implants were currently the 'gold standard', she was optimistic about the potential development of alternative donor tissues such as engineered cell lines, xenografts and stem cells. Embryonic stem cells had most potential, she felt, though directing neuronal differentiation to the appropriate phenotypic end-point was her main concern. But would these ever provide a 'cure'? Probably not, they will only ever *slow* progression. Should we be implanting pre-clinically? Probably yes, but the science is not there yet, she warned.

**John Collinge** (London) then concluded the afternoon by discussing prion disease, how different it can be from conventional infectious conditions. There are no antibodies since it is host-derived, for instance, and it is under strong genetic control. He spoke of the public health issues such as the long, silent incubation periods and sub-clinical infection, and the resistance to conventional sterilisation. Finally, he spoke optimistically of transgenic models such as the PrP null mice that neither propagate prions nor develop pathology. At first glance, they seem completely protected, but the prion titre reaches the same level as normal mice eventually.

Therapeutic approaches, he went on to describe, are most likely to involve the development of antibodies and vaccines. Early studies with anti-PrP monoclonal antibodies in mice have shown long term survival with peripheral but not CNS prion disease. Research into prion immunotherapeutics has been frustrating, overcoming the blood-brain barrier is now a key challenge. Alternatively, the development of rigorous clinical trials for the safety and activity of quinacrine, for instance, will also occupy researchers seeking as yet elusive prevention and alleviation.

In summary, therefore, three illuminating talks concluded in highly cautious mode. There was agreement on the need for a realistic, open perspective and long-term strategy. Equally, there was accord that 'first generation' therapies are not a cure; at best, they can be expected to delay progression. The 'second generation' may prove more hopeful. This is indeed the next challenge.

**By Yvonne Allen**  
BNA Executive Secretary

*Symposia on neuroreparative approaches using stem cell biology, and current therapies for slowing disease progression in Alzheimer's disease will feature as part of the 19th BNA National Meeting, to be held in Harrogate, 1st - 4th April 2007. See page 12 for further details, or consult the website ([www.bna.org.uk](http://www.bna.org.uk)) for the full scientific programme and regular updates on all the activities.*

'*Neurodegenerative Diseases: from bench to bedside*', chaired by Graham Venables and Richard Frackowiak, analysed some of the latest laboratory findings and candidly discussed their clinical potential.

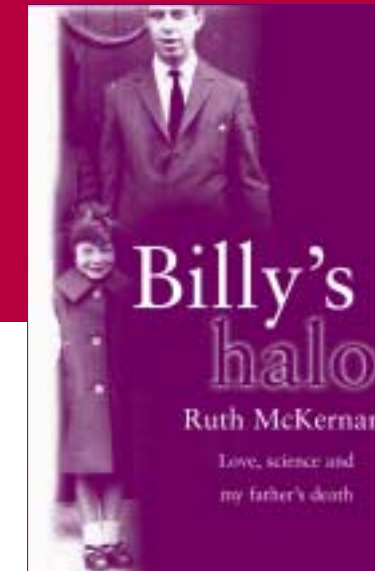
**Maria Spillantini** (Cambridge) explored *tau* and  $\alpha$ -synuclein's involvement in the pathogenesis of neurodegenerative diseases, in particular the use of transgenic mouse models to elucidate their role. They are also being successfully deployed to analyse future therapies, such as AChR agonists, kinase inhibitors, gene therapy, stem cells and anti-inflammatory drugs. Interestingly, P301S mice (*tau* mutant model) showed prolonged longevity and slowed progression of motor neuron loss after ibuprofen. However, in all these studies, Maria Spillantini was adamant that they are far from a cure, and even further from halting the disease process entirely.

Likewise, **Anne Rosser** (Cardiff) was equally as cautious. She spoke of the technical difficulties of cell replacement therapies in general and, in particular, of problems with their evaluation. Clinical assessments have been rather poor to date but are nowadays becoming much more rigorous. One of the longest ongoing studies (Creteil, France) has involved a 10-year follow-up and showed most patients stabilised for at least six years but then deteriorated. However, the sample size was small so unreliable; instead, a huge multi-centre UK study (Cardiff, Cambridge, Manchester, Aberdeen, Belfast, and Hammersmith) is now

## Billy's Halo: Love, Science and My Father's Dream

By Ruth McKernan

Published by Doubleday,  
March 2006,  
Hardback, 320pp, ISBN:  
0385608551



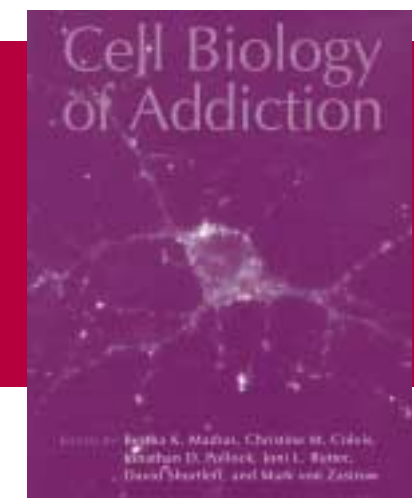
**T.W. Robbins.**  
Professor of Cognitive Neuroscience,  
University of Cambridge

*Billy's Halo* is a unique book. Ruth McKernan is well known to us as a former head of the late-lamented Merck, Sharp and Dohme Neurosciences Centre at Terlings Park (she's now doing something similar at Pfizer) and an international authority on amino-acid receptors and their therapeutic potential. In this beautifully written and conceived work, she movingly describes the serious illness under intense care of her self-made, businessman father Billy, his subsequent recovery, but his ultimate succumbing to cancer.

Interwoven with her reminiscences of life as the proud daughter of Billy, are fascinating descriptions of her own experiences, first as a graduate, then post-doctoral scientist and, ultimately, employee of big Pharma. But the key features of the book, prompted by meditations about her life events, are succinct and lucid vignettes of scientific themes such as the neural basis of emotional memory, stem cells, the sense of smell, infectious disorders, consciousness, laughing, functional neuroimaging and the neuroendocrinology of stress. Her ambitious aim is thus to introduce the general reader to biological research in its most relevant contexts and manifestations. In this, she succeeds amazingly well. The book is a model of how to engage the public with science whilst providing insight into a professional scientist's life and work. She shows the world that scientists, too, have feelings, and that they can sometimes transcend the literary limitations of high impact scientific journals. Highly recommended.

## Cell Biology of Addiction

Edited by BK Madras, CM Colvis, JD, Pollock,  
JL Rutter, D Shurtleff and M von Zastrow;  
Published by Cold Spring Harbor Laboratory Press,  
January 2006  
Hardback, 465pp, ISBN 0879697539



This book has evolved from a course presented at Cold Spring Harbor Laboratory over the period 2001-2005. It claims to provide readers with an intensive overview of the fundamentals, state-of-the-art advances and major gaps in the cell and molecular biology of drug addiction within the broader context of neuroscience. Overall, it fulfils these claims. The wide coverage is reflected by the topics being presented into five component parts: Genetics, Development and Drug Abuse, Cell Biology and Pharmacology, Synaptic Plasticity and Addiction, Systems Analysis of Drug Abuse. The chapters on 'Imaging' appear to have been erroneously included in the genetics sections. In general, the layout of the chapters is clear with inclusion of a description of goals and an abstract. The illustrations are patchy in part but satisfactory overall.

The diverse topics covered include the 'endocannabinoid system', the 'COMT genotype in psychiatric disorders', 'Imaging the addicted brain' and 'functional genomics and proteomics of drug abuse'. The chapter on endocannabinoids provides basic information on the metabolism of endocannabinoids, although the relationship with this system and other drugs of abuse, particularly the well-established link with the opioid system, would also have been beneficial to include. The article on COMT focuses on linkages for alcoholism and schizophrenia. The chapters on imaging provide a useful overview of the technologies available and the elegant studies that have been

performed to probe dopamine dysfunction in the addicted brain. Chapters on genetics and genomics cover gene mapping approaches, use of transgenic animals and genomics using microarray expression analysis. Inclusion of the recently introduced technology of localised gene manipulation to probe gene function in specific brain regions would have completed this section. Nevertheless, the reader is given a creditable overview of the basis of these advanced technologies and their application to addiction research.

To summarise, this book provides a very good overview for PhD students and those just entering the field. The established expert will also glean useful information, given the diversity of topics covered which are generally presented in a highly readable fashion. One critical issue that is not adequately discussed is the relationship between the cellular biological processes affected by addictive drugs and the multiple behavioural facets that they evoke. Clearly, these are important issues to address in the future and the reason why many of us are stimulated to research this challenging field.

**Judith Pratt,**  
Professor, Physiology and Pharmacology,  
University of Strathclyde

## The VIIIth EUROPEAN MEETING ON GLIAL CELLS IN HEALTH AND DISEASE

4th to 8th September, 2007, LONDON

The BNA is pleased to announce that it is collaborating with the UK Glial Cell Club to organise the 2007 European Glial Cell meeting at Imperial College, London, located in the heart of the museum and cultural district of the city.

The European Glial Cell meetings have provided an international focus for scientists interested in neuro-glia interactions since they started in 1994. The 2007 London meeting will deal with the biology of glial cells in development, health and disease, in addition to general issues in developmental neurobiology, stem cell biology and regeneration. It will offer:

- nine plenary lectures
- over twenty symposia
- extensive poster sessions

The Call for Symposia is now open and proposals should be submitted by email to Professor Kristjan Jessen (k.jessen@ucl.ac.uk) by 15th July, 2006.

**Full instructions can be found on the website:**  
<http://www.euroglialcell.org>

Other important dates:

- Registration and submission of abstracts opens **1st October, 2006.**
- Abstract deadline will be **30th April, 2007**
- Booking deadline for low cost accommodation at Imperial College and University College, London, student halls of residence will be **31st July, 2007.**

There will also be an exhibition and a full social and partners' programme of events to enjoy.

**For regular updates and all further information, consult the website:**

<http://www.euroglialcell.org>

## Autism: Art and Music 17th September, 2006,

at West Road Concert Hall, Cambridge.

The Autism Research Centre, Cambridge, is hosting a fundraising concert and art exhibition entitled 'Autism: Art and Music' to take place on 17th September, 2006, at West Road Concert Hall, Cambridge. This concert of music, exhibition and auction of visual art consists of work solely by people on the autistic spectrum.

**For more information, look on the website, at**  
<http://www.arc-conference.com>,  
or telephone 01234 328330,  
or email [sally@arc-conference.com](mailto:sally@arc-conference.com)



## Neuroscience Ireland Inaugural Conference

(incorporating an Independent Meeting of the Biochemical Society entitled: "Neurological disorders: molecules, mechanisms and therapeutics")

**Devere Hall, University College  
Cork, Ireland**

**21st - 22nd September, 2006**

### Local Organising Committee:

Kieran McDermott (Chair), Justin McCarthy, Yvonne Nolan, Cora O'Neill, (all UCC)

### Programme Committee:

Kieran McDermott (Chair), Tom Connor (TCD), Justin McCarthy (UCC), Yvonne Nolan (UCC), Cora O'Neill (UCC), Billy O'Connor (UCD)

2005 has seen the formation of the official Irish neuroscience organisation, Neuroscience Ireland, at a time when research in the area of neuroscience within Ireland is dramatically increasing. This research activity is spurred by a rise in the numbers of neuroscience investigators in Irish universities, hospitals and research institutes, as well as increased success by neuroscience researchers in attaining state and industrial funding.

The inaugural conference of Neuroscience Ireland will formally launch the Society. The focus of the meeting of Neuroscience Ireland is to bring together for the first time all researchers working in neuroscience in Ireland (north and south) and also to attract the participation of some of our expatriate researchers currently working abroad. The scope of the meeting will be broad to include all aspects of neuroscience. We hope that you will attend to make this a successful and enjoyable inaugural meeting!

### Plenaries Lectures:

**Professor Ferdinando Nicoletti (Rome)  
Dr Antoine Triller (Paris)**

The Registration deadline is 20th July 2006.

### Information:

For further information please contact any member of the local organizing committee at [neuroscience2006@ucc.ie](mailto:neuroscience2006@ucc.ie). Kieran McDermott may also be contacted directly at [kmcd@ucc.ie](mailto:kmcd@ucc.ie) or 021 4902247/4902246.

**Full details are also on the website:**  
[www.neuroscienceireland.org.ie](http://www.neuroscienceireland.org.ie)

## Ted Honderich, a speaker at the BNA Christmas Symposium last year, provide's proof of the force of philosophy in thinking about right and wrong in the world now

Humanity, Terrorism, Terrorist War is a new book that thinks with its readers about the question that comes before all others about terrorism, its causes, the war in Iraq, and what is to come. That is the question about which the world actually disagrees, the bottom-line question of right and wrong. The book makes its way to judgements on what others merely declare to be necessary or unacceptable.

The terrorist attack of 9/11 is condemned by the argument of the Principle of Humanity that it can only be the end and the means that justifies the means. The arguments for the Iraq war, a terrorist war, are subjected to paralysing analysis. As for such terrorist attacks as that of 7/7 in London, their true enemies have not been Blair and Bush, who are in effect their friends. There is no other book like this.

"Ted Honderich makes a powerful case that "an easy answer is wrong," so that to find the right answer, or the least unacceptable, will be anything but easy. His inquiry explores some of the most painful and controversial issues of the day. It merits, and will reward, careful reflection." Noam Chomsky

**For more information:**

**Alison Silver, Trade Marketing Executive, 020 7922 0909, [asilver@continuumbooks.com](mailto:asilver@continuumbooks.com)**

## Homepage4Science is buzzing

THE FIRST PIXEL PAGE FOR THE SCIENCES IS BASED ON THE MILLIONDOLLAR HOMEPAGE CONCEPT AND ALLOWS SCIENTISTS TO PROMOTE THEIR OWN WEBSITES.

Within less than a month of its inception, the Homepage4Science ([www.homepage4science.com](http://www.homepage4science.com)) has generated a real buzz in the scientific community. An "easy find" display has separate areas for Vendors of Science Products and Services, Academic Societies, Publishers and Jobs. Companies can buy advertising pixels online; each one has a short description and a link to their website.

The feature that has captured everyone's imagination is the 'free' area where individual scientists or academic groups can place pixels free of charge. These 'free pixels' remain active for 45 days, after which time they can be renewed. They are being used for a range of purposes, with many scientists putting links to their personal web pages on their university website. Others are using their pixels to advertise forthcoming conferences, university courses, research group websites or even whole departments. Several charitable organisations have taken pixels and there is even an entry from the Whisky Appreciation Society of Aquaculture, based in the University of Stirling!

The brilliant pixel page concept was started by Alex Tew, a student at the University of Nottingham, to fund himself through University. His idea was pixel advertising that links through to homepages - his web site at [www.milliondollarhomepage.com](http://www.milliondollarhomepage.com) has recently sold its millionth pixel. The finished page is somewhere between an online advertising hoarding and internet installation art.

**Proceeds from the sale of commercial pixels on the Homepage4Science support the i-kode.com™ service ([www.i-kode.com](http://www.i-kode.com)) that is committed to reducing the waste associated with unwanted scientific direct mail.**

- All pixels placed on the Homepage4Science must meet our Acceptable Use Policy (AUP, see [www.homepage4science.com/FAQ.html](http://www.homepage4science.com/FAQ.html) for details).
- All users placing pixels (free or paid-for) must provide an email address for security and administration purposes. However, this is not passed to any third party.
  - Pixels are selected in blocks of 100 (10 x 10 pixels).
  - Paid-for pixels cost \$1 each, with a minimum purchase of 1 block (100 pixels). These expire after 1 year, but can be renewed.
  - There is no limit on the number of paid-for pixels that an organisation can buy, subject to meeting the terms of our AUP.
  - Scientists are able to take a maximum of 10 blocks in the free area and these pixels expire after 45 days, after which time they can be renewed or replaced, also free of charge.

## i-kode.com™ FINALISTS IN THE 2005 DTI / INTERFORUM E-COMMERCE AWARDS

### ENVIRONMENTAL RECOGNITION FOR SERVICE TO REDUCE SCIENTIFIC JUNK MAIL

Ikon Informatix Ltd, the company behind the i-kode.com™ online service that helps life science researchers take control of their mail, was recently recognised for its contribution to the environment by reducing scientific junk mail. The company was selected as a finalist in the Environmental section of the ICT Innovators Award category in the prestigious DTI / InterForum 2005 E-Commerce awards. These awards recognise best practice in the development of information and communication technologies (ICT) by UK business and public sector communities and are open to all sizes of organisations from small business to large enterprise and the public sector.

Susan Sinclair, founder Director of Ikon Informatix, attended the award dinner and was impressed with the calibre of her fellow finalists. "Even though we didn't win" she said, "we can feel proud to have been in such company and we feel honoured to receive this recognition of our work to reduce waste."

The i-kode.com™ service is available at [www.i-kode.com](http://www.i-kode.com). It saves time and reduces waste. Scientists can quickly and easily manage their interaction with the Vendors, Academic Societies and Publishers who send scientific direct mail. They can add themselves to or remove themselves from mailing lists and even request removal from all scientific mailing lists. When a scientist moves, it only takes a minute to update their information with all their selected organisations, making it less likely that mail will continue to be sent to their old address to be thrown away.

Every year between thirty and fifty million pieces of scientific mail are sent to people who have moved. That represents over \$150m worth of waste. In addition, over 50% of all marketing mail is thrown away unread. The cost of handling and disposing of this unwanted mail is of increasing concern to universities and research organisations. But, what is junk mail to one scientist may be important new product information to the person in the next lab. The i-kode.com service now makes it possible for scientists to be selective in the mail they receive.

- Strict procedures are enforced to ensure the confidentiality and security of personal data stored on the i-kode.com™ system.
- Scientists' details are only passed to those organisations that the individual scientist has selected.
  - The i-kode.com™ service is not a mailing list.
- Other features of the service allow vendors to be more targeted in the type of mail that they send, so the scientist is more likely to receive information about products or services that are of relevance to them.
- The i-kode.com™ service allows colleagues, lab managers or departmental secretaries to pass on details of scientists who have left. These are incorporated into a monthly 'gone-aways' list that is provided to i-kode™ Partners so that they can remove the names from their mailing lists.
- The i-kode.com™ service was featured in the Spring issue of the British Neuroscience Association newsletter, circulated to the association's 2000 members early in 2005.

## University of Manchester

Funded PhD Studentship starting  
September 2006

**The association between febrile seizures and temporal lobe epilepsy and the role of inflammation.**

Prolonged febrile seizures in children have important clinical implications because of their proposed link with temporal lobe epilepsy, the most common and intractable epilepsy syndrome in adults. Frequently this syndrome is also accompanied by brain damage in the hippocampus. However, the precise link between prolonged febrile seizure, hippocampal damage and temporal lobe epilepsy remain controversial. The pro-inflammatory cytokine interleukin-1 plays a key role in many neurodegenerative conditions, including epilepsy, and has also been implicated in the pathophysiology of febrile seizure. This suggests that interleukin-1 or other inflammatory mediators may have a prominent role in linking prolonged febrile seizure to temporal lobe epilepsy.

This Epilepsy Research Foundation ([www.erf.org.uk](http://www.erf.org.uk)) funded PhD aims to test this hypothesis. This will be achieved by using a recently described experimental model of temporal lobe epilepsy, where recurrent seizures are produced by combination of a focal cortical lesion and induction of hyperthermic seizure. Using this approach a series of experiments will be performed to characterise cytokine expression and to establish whether genetic or pharmacological inhibition of interleukin-1 signalling can reduce the appearance of recurrent seizures. Should this be the case then these findings may reveal novel therapeutic strategies for the prevention of temporal lobe epilepsy.

This studentship is open to UK/EU applicants who have, or expect to obtain a 2:1 or first class honours degree in a relevant subject.

Further information can be obtained by contacting  
**Further Information**

**Dr Stuart Allan.**  
Email: [stuart.allan@manchester.ac.uk](mailto:stuart.allan@manchester.ac.uk).  
Tel: 0161 275 5255.

Application forms can be obtained from:  
<http://www.ls.manchester.ac.uk/postgraduate/howtoapply/>  
or by contacting the  
Faculty of Life Sciences, Graduate Office  
(email: [pg.lifesciences@manchester.ac.uk](mailto:pg.lifesciences@manchester.ac.uk);  
Tel: 0161 275 3883).

Applications with two letters of reference  
should be returned to:

The Graduate Office,  
Faculty of Life Sciences  
The University of Manchester  
Oxford Road  
Manchester  
M13 9PL.

## University of Manchester

Funded PhD Studentship starting  
September 2006

**'Systemic and central mechanisms of host defence responses'**

The host defence response is critical for the survival of organisms and for their recovery from injury and infection, but can also be highly detrimental if activation is sustained or inappropriate. The response includes not only local tissue changes and activation of the immune system, but also a diverse range of physiological changes many of which are mediated by the central nervous system. The cytokine interleukin-1 (IL-1) is a pivotal mediator of local tissue responses, and systemic and CNS aspects of the host defence response. However its sites, mechanisms of action and mediators, and particularly the relationship between peripheral insults and CNS events are not fully understood.

This PhD project will investigate the actions of IL-1 systemically and in the brain on the host defence response and identify the mechanisms of communication between the periphery and the brain.

The project is in collaboration with UCB Celltech (BBSRC CASE award) and the student will benefit from complementary approaches and powerful research tools available at the two organisations (such as knock out mice and highly specific anti cytokine antibodies). S/he will combine the use of in vivo approaches in rodents with molecular and cellular techniques. This will include the opportunity to profile in detail the expression of cytokines, both peripheral and central, during the host defence response using the most up-to-date techniques, including microarray and luminex.

This studentship is open to UK/EU applicants who have, or expect to obtain a 2:1 or first class honours degree in a relevant subject.

Further information can be obtained by contacting  
**Dr Stuart Allan** ([stuart.allan@manchester.ac.uk](mailto:stuart.allan@manchester.ac.uk)).

Application forms can be obtained from:  
<http://www.ls.manchester.ac.uk/postgraduate/howtoapply/>  
or by contacting the  
Faculty of Life Sciences, Graduate Office  
(email: [pg.lifesciences@manchester.ac.uk](mailto:pg.lifesciences@manchester.ac.uk);  
Tel: 0161 275 3883).

Applications with two letters of reference  
should be returned to:

The Graduate Office,  
Faculty of Life Sciences  
The University of Manchester  
Oxford Road  
Manchester  
M13 9PL.