



**Thalamostriatal  
projections  
revisited: new  
questions and  
answers**

**Scientific**

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● The sixth FENS Forum in Geneva (12-16 July) proved again to be a great success. This event continues to be Europe's largest neuroscience event – over 5000 registered, including nearly 500 from the UK alone, exceeding the numbers that attended in Vienna in 2006. An exciting programme delivered nine plenary lectures, 11 special lectures, 56 symposia, about 3500 posters and 240 oral presentations – surely enough to have satisfied everyone's scientific appetite. The BNA provided thirty bursaries that enabled PhD students and young post-docs to present posters at the meeting, many for the first time.

● If you were unable to travel to Geneva, we hope that you will certainly make a date to attend the 2009 BNA National Meeting (Liverpool, 19th-22nd April) – get this in your diaries now! The call for symposia produced some excellent proposals that the committee has wrestled to get down to the number that can be accommodated by the programme. The scientific programme is now available on the website ([www.bna.org.uk/bna2009/](http://www.bna.org.uk/bna2009/)) and includes for the first time some workshops and satellite meetings.

● During the spring, many BNA members were involved in events for Brain Awareness Week and you are encouraged to start thinking ahead to events for next year (16-22 March 2009) as these often take some considerable time to organise. If you want any advice or help, please contact the EDAB office. Many BAW events involved bridging the science-art divide and this theme continued on the 16th April with an evening event at the Whitworth Art Gallery, Manchester entitled "The Art-Science Divide – where does brain science fit in?" At this event, BNA President Graham Collingridge hosted a public discussion on the 'two cultures' led by Nancy Rothwell (Manchester), Mark Lythgoe (London), Erinma Ochu (Manchester) and Lizzie Burns (Oxford) – (see page 34 for report).

● During 2007/8, The Wellcome Trust has piloted a series of Masterclasses in Clinical Neuroscience, an initiative to bring together basic researchers and clinicians to tackle key clinical issues with the aim of promoting translational research. The

BNA has been co-hosts of two of the three awards. The first of these on 'The Future of the Restorative Neurosciences in Stroke Rehabilitation' was coordinated by Richard Greenwood and John Rothwell (Institute of Neurology) and held last September. The second, which was coordinated by Kevin Talbot (Oxford) and Ammar Al-Chalabi (King's College, London), addressed 'Controversies in Motor Neuron Disease Research and Practice' and took place on 21-23 May. This explored all aspects of the pathology, therapeutics, clinical care and future research directions in understanding this disease.

● Can I encourage our PhD and post-doctoral members to think about contributing to the Young Neuroscientists Day which will be held in Cardiff soon in October? These events have proved to be very valuable opportunities for researchers who are new to the field to have the chance to present their data and to network with others at a similar stage. If you would like to get involved in this event or consider hosting a similar event in future years, please contact Vanessa Davies or Anne Cooke (see page 13 for further details).

● The National Committee is always open to suggestions from the membership about events that they would like to see organised or suggestions for ways that we can better serve the neuroscience community. Please feel free to make those suggestions, even if you do not feel you have the time to get involved in implementing them. Remember the BNA is only as good as its membership.

● Finally, can I draw your attention to important changes to the administration of our membership database. Since 1st April, the database, including collecting subscriptions, has been managed by Portland Customer Services (PCS), a wholly owned subsidiary of The Biochemical Society. This will enable the BNA Committee to concentrate on managing our other activities, such as meetings, symposia and other events and publications. Further information on this change can be found on page 11).

### Front cover:

Electron micrograph of an axon terminal (highlighted in blue) of an identified parafascicular thalamic neurone forming synapses with two dendritic shafts and a dendritic spine in the striatum. Overlaid is a digital reconstruction of the soma and dendrites of a juxtacellularly-labelled parafascicular neurone. See *Scientific Review*, pp15-17.

### DATES FOR YOUR DIARY: BNA EVENTS 2008 / 2009

● **22nd October, 2008:**  
Young Neuroscientists' Day,  
at the University of Cardiff

● **25th November, 2008:**  
'Out of body experiences'  
A public cafe-bar discussion  
at the Dana Centre, London, SW7

● **17th December, 2008:**  
BNA Annual General Meeting,  
at The Royal Society, London SW1

● **17th December, 2008:**  
The Christmas Symposium,  
at The Royal Society, London, SW1:  
'The meaning of sleep: 21st Century  
thinking'

● **19th – 22nd April, 2009:**  
BNA 20th National Meeting,  
The Adelphi, Liverpool

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

DEADLINE FOR SUBMISSION OF ITEMS FOR THE NEXT BULLETIN: 15th December, 2008.

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

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## A skills shortage in the biosciences – what can we do about it?

**Richard Dyer**  
Chief Executive, Biosciences Federation

There are frequent reports and comments about the shortage of skills in the biosciences: shortages that are important and potentially damaging to the prosperity of our country. However “skills” do not exist in some semi-independent context. It is always necessary to define what the “skills” are needed for, and this can produce conflicts for those responsible for the delivery of our bioscience skill base.

The first skill that we all need is the skill to be a good and productive citizen. In a knowledge driven economy, scientific skills should be part of the skills portfolio of as many citizens as possible, even though they do not themselves pursue a career in science. For me, it is highly desirable that we have more citizens who understand the scientific method, who appreciate the difference between probabilities and absolutes and who make decisions on the basis of evidence and not Luddite prejudice. With this training, public discussion about climate change, biodiversity or disease will be better informed and there will be greater understanding of the contribution that practicing scientists are making to the debate. In time, the public trust in scientists, which is already quite good, might improve further. The knowledge driven economy demands a scientifically literate population. Delivery of this essential skill is an important responsibility of our schools and universities.

However, more usually, a skills shortage is used to describe a more specific problem than the generic need to have science as part of our everyday cultural base. The BSF, together with the ABPI, published a report earlier this year entitled “*In vivo* sciences in the UK: sustaining the supply of skills in the 21st century” (the report is available at [www.bsf.ac.uk](http://www.bsf.ac.uk)). One of our recommendations is that a small number of Masters Programmes could be introduced to help alleviate a shortage that is already with us and is having important effects in the pharmaceutical sector. We propose thirty-six dedicated

studentships for this Programme for each of the next three years. This is an important area and yet the solution involves really small numbers: *in vivo* skills are definitely not required in all life science graduates. Of course, practical skills are very definitely required because most science and most biology are intensely practical subjects.

There are many other areas of the biosciences where skills are being lost and yet the solution needs relatively small numbers of practitioners. Take for example the field of systematics and taxonomy. There is no doubt that we are losing the capacity to identify precisely some of our native species – for example, lichens. Yet we need really expert individuals in this area today perhaps even more than in the past: we cannot monitor the effects of climate change on our flora

‘The knowledge driven economy demands a scientifically literate population. Delivery of this essential skill is an important responsibility of our schools and universities’.

and fauna unless we can identify species correctly. Perhaps we will end up relying on the “gifted amateurs” who already contribute much in this area – but in this case the academic subject will be lost.

The production of modest numbers of high level experts in many areas of the biosciences is predominantly the responsibility of our universities and, to a lesser extent, the Research Councils. I write “lesser extent” because some disciplines – for example taxonomy – can be internationally excellent without relying on large grants. And this leads to a second problem. Much biology today is rightly “big science” – big grants and big teams. The business of running a University means that these big science teams are financially more attractive than those individuals virtually grant free. Furthermore, individuals without grants are likely to find it difficult to meet the

charges that Open Access brings. The result, of course, is that there is real pressure on systematics and taxonomy (and many other minority skills) as a profession. However, the country needs these skills.

Clearly the skills landscape is complex and varied. The question to face is whether or not the delivery of highly specialised skills can continue to be left to the vagaries of the market place. This essay is not leading to a conclusion that, for example, all universities with a life science degree have Masters Programmes for *in vivo* skills, or that all plant science departments have top level taxonomic skills. That would be absurd! But the question to answer is how we produce those experts that the country requires – and in sufficient numbers.

Not everyone will like the last sentence. Some will have a wider view, especially in the context of their own expertise. But that can be left to the market place. What we need is confidence that the UK will have the full portfolio of bioscience skills that will be essential if we are to maintain our strong global position in this area. These are skills that would be difficult to “buy in” if our own skill base was lost.

What is needed is top down management, coupled with inducements, in order to build a few excellent teams in minority subjects that are nonetheless essential. Let funding be ring-fenced and Universities/Institutes compete for the money to provide leadership in these areas. This is not a new idea: it happens often. For example, if you want capital equipment for structural biology from the BBSRC you have to apply from one of about ten universities. What is new is the argument that this should be done to sustain skills – and there is the key word. Any initiative must be sustainable in the long term. These are not arguments for five years and then the money can be recycled into some other project. These are arguments for a generation – and, sadly, as a consequence they will not seem very dynamic where it matters!

# SPOTLIGHT ON FENS SCHOOLS

## NEUROSCIENCE EDUCATION PROGRAMMES SUPPORTED BY FENS - *a closer look*

Mike Stewart, Professor of Neuroscience at the Open University is a member of the **FENS Schools Committee**. Here, he reviews the involvement of FENS in neuroscience education through the schools programmes, **NEUROTRAIN**, and **PENS** (the Programme of European Neuroscience Schools). In addition, within the Federation of European Neuroscience Societies (FENS), there is a programme called **NENS** (Network of European Neuroscience Schools) which represents graduate schools and programmes across European countries that offer Master's, MD and doctoral degrees in neuroscience.

A major aim of the Federation of Neuroscience Societies (FENS) since its inception in 1998 has been to enhance education in Neuroscience, and to train students and young investigators through a schools programme spread across Europe and the FSSU. Funding is provided for these schools (though may be supplemented by other resources) but applicants must bid for resources and the process can be very competitive.

The **NEUROTRAIN** project aims to provide a standard platform for neuroscience training in Europe by offering a series of four events from 2006 - 2008 to implement a training system standardised coherently in relation to structure, programme frame, patients perspectives, industrial aspects, complementary skills, event management, selection of high-quality scientists, topics and tutors, and evaluation after events to enable continuous improvement. NEUROTRAIN is supported by the European Commission, Research Directorate General, Marie Curie Conferences and Training Courses, Contract No. MSCF-CT-2005-029703. For more information see <http://neurotrain.fens.org>

**PENS**, the Programme of European Neuroscience Schools, is a FENS - IBRO collaboration. This programme, aimed to train students and young investigators throughout Europe, brings together educational activities previously sponsored by FENS through its Schools Committee and by IBRO's Regional Committees for Europe: Western Europe Regional Committee (WERC) and Central and Eastern Europe Regional Committee (CEERC).

**Student selection:** Student applicants (which is a term that includes post-docs) are selected on the basis of their research record, e.g. how many publications the student has, conferences attended, the relevance of their research topic to the school, and references provided by their supervisors. There are usually many more applicants than places available and selection also examines the geographical location of successful applicants to ensure that no particular country is over-represented. Effort is also made to ensure the participation of students from central and eastern European countries (some of whom suffer from the added complication of needing to obtain visas). Costs for students are usually kept to a minimum and there are bursaries for students from central and eastern European countries to provide help with travel and subsistence. The locations are held in attractive geographical locations and the schools include a mix of lectures and practical sessions. There is time for social activities, which are designed to encourage interaction between students. As a follow up to the previous schools, FENS has established a Schools Alumni and there was a special Alumni symposium at Geneva with speakers chosen from amongst those who have attended a past school. In addition, there was an Alumni party in Geneva at a very attractive location in the city, to which Schools *Alumni* were invited to apply to attend.

**For organizers,** PENS provides funds to support high-quality Schools and Courses on a wide range of important topics in the Neurosciences. Particular attention is given to proposals from the

membership that encourage an active involvement of the students and the teachers during the entire event. The overall goals are to:

- increase the quality of Neuroscience education in Europe.
- decrease gaps between different European neuroscience curricula and between Europe and the rest of the world, while maintaining regional research priorities.
- increase the mixing and collaboration of young European neuroscientists.
- create a network of alumni and teachers capable of enhancing scientific collaboration and the establishment of international research projects within Europe (e.g. The Alumni Programme).
- alert scientists from the graduate student to the young faculty level to the research possibilities offered by laboratories in Europe and outside (e.g. publicizing the Network of European Neuroscience Schools (NENS) and IBRO's International Registry of Neuroscience Programme).
- increase the visibility of European neuroscience educational programmes and their role in and outside Europe.
- assist the development of Neuroscience outside of Europe by providing opportunities in Europe for the training of promising students who intend to return to their home countries (e.g. the present IBRO-FENS Fellowships programme, as well as the travel grants offered to students accepted to the European schools).

The programme provides full or partial support for the following educational activities in all of Europe:

### **Lecture-based PENS-Blackwell Summer School.**

In 2008, PENS will sponsor one lecture-based Blackwell Summer School. Minimum duration of the School is 1 week. PENS will provide a budget of up to 40.000€.

The PENS-Blackwell Summer School is intended for about 40 doctoral students and young scientists who have sufficient scientific background and experience to fully benefit from the course. The format of this lecture-type school is similar to the PENS-Hertie Winter School. Registration fees for the students (covering also lunch and lodging) must not exceed 300€.

### **Lecture-based PENS-Hertie Winter School (Tirol, Austria).**

Scheduled for the winter season 2008/2009, this school takes advantage of local arrangements and organization established in previous years. Hence, applications from neuroscientists only have to focus on the Scientific Programme. The duration of the School is one week. The daily schedule includes 4-5 daily lectures of 40 minutes each with an additional 20 minutes for discussion and 3 poster sessions. The School accepts 40 students and young scientists who provide evidence of sufficient scientific background and experience to benefit fully from the course.

The budget is administered by Professor Alois Saria who serves as the local organizer. Total travel costs for teachers must not exceed 10.000€.

# SPOTLIGHT ON FENS SCHOOLS

## **PENS - Partially Supported Schools.**

In collaboration with local and partner organizations, PENS may support a limited number of lecture-based or practical schools in Europe by providing each up to 20.000€. Applications for this school category should include a scientific programme and information on the proposed location and facilities. Minimum duration of the School is one week.

The number of participants should not exceed 40 students and young scientists. The money granted by PENS should be used primarily to enable the participation of students with few resources. Selection of students will be entrusted to the school organizers, in accordance to PENS Guidelines, with final approval by the PENS committee.

## **PENS Visiting Lecture Team Programme (VLTP).**

European Research Centres may request a visit by a team of 4-5 experts to cover one or more specific topics in Neuroscience. PENS will help to set up the team and pay the travel costs, whereas all local costs are carried by applicants. Average duration of the visit is 3-5 days.

## **PENS Open Format Schools.**

PENS also encourages proposals for categories of schools and courses not specified above but fitting the overall guidelines. Minimum duration is one week.

**The Deadline for Submissions to hold a school is normally in July in the year before the schools take place**

**Selection Procedure:** Proposals are reviewed by the PENS Committee and the final selection announced by 1st November in the year preceding the schools. During the review process, applicants may be contacted by the PENS Committee with suggestions for modifications of the proposal. Below is the list of schools that were selected for 2008:

1. April 27 - May 5, 2008 - Saint Petersburg, Russia  
PENS Partially Supported School. **Models in neuroscience: turning experiments into knowledge**
2. August 2-24, 2008 - Frankfurt am Main, Germany  
PENS-Blackwell Summer School **Theoretical Neuroscience and Complex Systems**
3. September 7-27, 2008 - Lausanne & Geneva, Switzerland  
PENS Training Center **Imaging Brain Function: From Synapses to Networks**
4. September 7-27, 2008 - Bordeaux, France, PENS Training Center  
European Synapse Summer School
5. September 13-20, 2008 - Bangor, Wales  
PENS WICN Summer School **The Neuroscience of Memory: Methods and Concepts to Investigate Our Internal Representation of the World**

## **The Network of European Neuroscience Schools (NENS)**

NENS is a formal structure within the Federation of European Neuroscience Societies (FENS). NENS was founded in 2003, and represents over 130 graduate schools and programmes across 30 European countries that offer Master's, MD and doctoral degrees in neuroscience.

NENS offers a basis for communication between European neuroscience graduate programmes, that creates a basis for mutual support. Specifically, we have the following goals:

- the promotion of the European higher education area in the field
- assisting in generating quality standards in neuroscience programmes
- encouraging and supporting mobility among graduate students and teachers
- increasing choices and opportunities for graduate students
- improving the cooperation among current and future European scientists
- generating new and significant knowledge in the field
- laying the basis for obtaining consortium funding at national and EU levels

NENS offers a yearly **annual general meeting** where coordinators and directors of NENS member schools and graduate programmes can come together to discuss common issues and dilemmas that we face in optimising neuroscience graduate education, engaging in state of the art research, and recruiting talented students to our programmes. Advice and exchange of experiences in terms of grant acquisition, identification of grant application partners, discussions of recruitment strategies, credit pointing, and quality control are key areas of discussion. NENS members are given the opportunity to talk about their programmes and experiences, and give feedback to NENS as to the kind of support needed.

NENS offers **stipends for graduate students** who would like to gain methodological or practical experience in the laboratory of another NENS member school. Grants are targeted at graduate students at the Masters level or early phase of the doctoral studies, that wish to acquire key new skills for integration into their research work. Funding of up to 1,000 € can be acquired. Only students of NENS members' schools are eligible to apply. Calls are regularly announced on the NENS website.

With over 130 members schools and programmes, representing at a conservative estimate over 5,000 neuroscience graduate students and about 2,500 teachers and senior researchers, NENS offers a powerful voice and lobby at the European level.

NENS states that *"Our shared experiences and the establishment of a tradition of mutual support both in terms of neuroscience education and research, means that each school can optimise its quality, recruitment potential and output"*.

As a whole this renders Europe an extremely attractive basis for completing neuroscience degrees at the graduate level, and pursuing postgraduate careers on the European continent.

In addition, NENS boasts the most comprehensive online source of neuroscience graduate school information in Europe.

In joining NENS, you can:

- Become part of NENS neuroscience graduate programme directory and avail of the opportunity to advertise your programme to a huge international readership
- Advertise vacancies and announce educational events at your institution to an international user base via the NENS website
- Expand your professional and personal networks across the European neuroscience community
- Identify cooperation partners within other neuroscience graduate programmes
- Benefit from exchange of methodological know-how between NENS members
- Take part in the NENS Annual Meetings and meet Neuroscience coordinators from all over Europe.
- Gain access to training stipends for your graduate students
- Receive our monthly NENS Newsletter with up-to-date information on the community and in-depths reporting on member programmes

## **How to register with NENS**

Do you offer a structured Master's or doctoral degree programme in the neurosciences? To register with NENS, simply go to our online platform, register on the website, fill in a questionnaire and add your neuroscience programme or school to the directory. That's it! We are very much looking forward to welcoming you within the NENS community.

## **If you are a student**

As a student you can make use of all our web services. You have the possibility to search the programme directory, identify Master's or PhD programmes of interest, find out about training opportunities in our member programmes and schools, and read the monthly newsletter. What's more, you can get into contact with other students and programme officers via the Discussion Board.

**For further information contact the NENS Office on [nens-office@rub.de](mailto:nens-office@rub.de)**

## BNA 20th National Meeting - an invitation to all our members

I am sure you are all now aware that our next biennial meeting will be held in Liverpool (19th – 22nd April, 2009) and we are delighted to be using for the first time the recently re-furbished conference facilities at The Adelphi. This is a unique and historic venue that now offers spacious conference facilities in addition to its other grand rooms and restaurants. Built in the same year as the *Titanic*, it still boasts a complete replica of the liner's smoking room. *Well worth visiting!*

Liverpool is a fascinating city, particularly now as it basks in its re-emergence as one of the most significant, stylish and cultured UK cities. It is also currently enjoying 'European Capital of Culture' status, a testament to the confidence with which Liverpool has re-vamped and re-vitalised itself. We are confident that this new venue for us will attract the largest delegation ever to our meeting.

However, it is the core scientific programme that is most instrumental in attracting you all. To this end, we can assure you that the Programme Committee has worked extremely hard in recent months to generate an exciting, topical and eclectic array of seven world-class plenary speakers, 20 symposia and over 50 themed poster sessions. For the first time, we are also planning accompanying workshops and satellite meetings to further add to the appeal. The full programme of speakers and events is now available on our website ([www.bna.org.uk/bna2009/](http://www.bna.org.uk/bna2009/)), but a summary can be found on page 12. With an exciting range of peripheral events and social gatherings as well (yes, there'll even be a Magical Mystery Tour and a few other Liverpoolian surprises thrown in too!), we hope you will agree that this will be a wonderful celebration of (mostly) UK-based neuroscience and decide to support your national meeting next year. See you in Liverpool!

**Yvonne Allen**  
*Executive Secretary*

**Nicola Gilmore**  
*Conference Administrator*

## BNA Committee 2008

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*g.l.collingridge@bristol.ac.uk*

**Professor Colin Ingram (Honorary Secretary)**  
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**Dr Yvonne Allen (Executive Secretary)**  
*y.allen@bna.org.uk*

## BNA member becomes Secretary General of the Saudi Society for Medical Education

Ismaeel M. Bin-Jaliah has been recently elected as the Secretary General of Saudi Society for Medical Education (SSME). Dr Bin-Jaliah is an Assistant Professor of Neurophysiology and the Director of Medical Education Center at King Khalid University in Abha, Aseer, Saudi Arabia.

## Nominations for the BNA Committee now sought!

How involved would you like to be in the activities of the BNA? Would you like to shape our future for the next few years? If you have enthusiasm, drive and lots of big ideas and initiative, then why not stand for election? A brief CV and a few words about what you could bring to the BNA should reach the BNA Office ([y.allen@bna.org.uk](mailto:y.allen@bna.org.uk)) by

**1st December, 2008 deadline**

**We are currently seeking to enlarge the committee by FOUR in order to help with the expanding role of the committee, so why not come and help us?**

**For further information, please call  
Yvonne Allen (0151 794 5449)**

## Brain Science Writing Prize - where are the past winners now?

In 2005, Yvonne Allen and Penny Fidler hatched an idea over a glass of wine (or two) to introduce a new prize into the BNA's repertoire – The National Brain Science Writing Prize. In collaboration with EDAB and At-Bristol, the competition has now blossomed into a popular annual event attracting more and more entries each year. Here, Eleanor Barrie, herself a prize winner in its inaugural year, and now a freelance public relations and science communicator, catches up with other past winners to see if their prizes spawned new careers.

It's time to write about the brain – the National Brain Science Writing Prize, 2008, was launched on 10th March to coincide with Brain Awareness Week. This year, the competition ran in partnership with Focus magazine (in addition to its long-standing sponsors), who will be publishing the winning articles on their website. The competition is a chance for researchers and the general public to try their hand at communicating the wonders of brain science, and to see their work published. But what about the past winners of the prize? Where are they now? And did winning inspire them to go further in science communication?

I caught up with some of the winners of the 2005 and 2006 competitions, and found that all of them had caught the science communication bug. Will Davies, who won first prize in the researcher's category in 2005, is now an RCUK Fellow working on sex-linked genes. "As an RCUK Fellow, I have the opportunity - and am strongly encouraged - to communicate my research," he says. "Winning the National Brain-Science Writing Prize has given me the confidence and skills necessary to undertake this task."

Jim Stone, highly commended in 2005, also benefited from taking part. "My main objective was to write a clear account of the Baldwin effect, which is a controversial, and often misunderstood, topic within evolutionary biology. I wrote the essay over a rare child-free week-end when my wife took our two children off to visit relatives," he says. "Writing the essay had the side effect of clarifying my own thinking, and convinced me that it should be possible to demonstrate that learning accelerates evolution." This led to the publication of a paper in PLoS Computational Science - "Distributed

Representations Accelerate Evolution of Adaptive Behaviours" – in August 2007.

Rebecca Poole (2006 winner) and Martin O'Neill (2005 runner-up) have also gone on to do more science writing. Rebecca thinks that winning the prize gave her the confidence to write more. "I am now working part-time in research to pursue writing further," she says. Martin was shortlisted for the *Daily Telegraph Young Science Writer Competition* last year. "I intend to continue writing about science and, of course, I will be submitting another entry for this year's National Brain Science Writing Prize," he says.

Another winner has applied her flair for science communication to new media. Gillian Pepper, highly commended in 2006, recently launched her own website, *Science Policy and Communication Information – a Directory*:

([http://gpepper.bizland.com/DIRECTORY\\_HOME.html](http://gpepper.bizland.com/DIRECTORY_HOME.html))

"I hope that in time, it will develop into a full and useful directory for all those interested in science in society organisations and their activities, and also hope that it will be a helpful guide to those looking to work in the field," she says.

The competition has clearly been a useful springboard for these past winners, and this year's should bring the same benefits to a new group of talented writers. If you'd like to be one of them, then start thinking - what do people need to know about brain science, and how can you convey it in an interesting and original way? The deadline has now passed for 2008, but there will be another competition announced later this year. Good luck!

By Nell Barrie ([eleanor.barrie@googlemail.com](mailto:eleanor.barrie@googlemail.com))



## 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 2008).

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 31st OCTOBER 2008 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](mailto: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 2008
- Any supporting material including undergraduate dissertation/thesis, or a report on any research the undergraduate has carried out.
- A statement of career intentions.

NOMINATIONS SHOULD BE MADE BY 31st OCTOBER 2008 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](mailto:y.allen@bna.org.uk)

## BNA awards

John O'Keefe and Lord Sainsbury

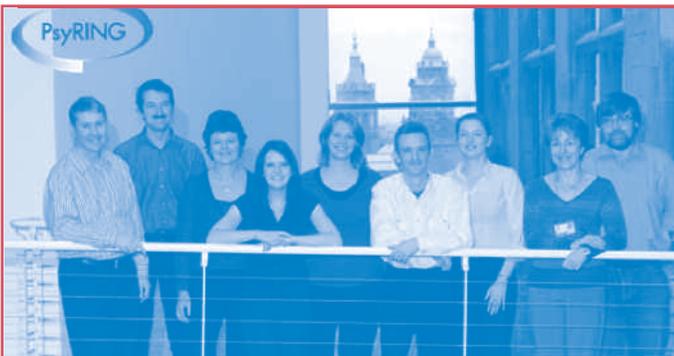


Graham Collingridge presents to John O'Keefe

At the Christmas Symposium each year, the BNA awards two special honours: one for Outstanding Contribution to British Neuroscience, the other for Public Service. Our deserving awardees this time were Professor John O'Keefe FRS (left) and Lord Sainsbury respectively, both of whom have contributed to our discipline in distinctive ways.

Many BNA members will already be familiar with the pioneering work of John O'Keefe on hippocampal cells that respond selectively to the animal's spatial location, so called 'place cells'. This work then spawned the Cognitive Map Theory that is still one of the dominant theoretical paradigms in the study of hippocampal function.

Less familiar will be the contribution that Lord Sainsbury has made to science, not only in his ministerial role in government for many years, but also in his generous charity donations. He is widely known for his chairmanship of the huge supermarket chain, but fewer are aware of his genuine interest in neuroscience since his undergraduate studies in psychology. Unable to receive the Award himself through illness, Dr Sarah Caddick, his advisor for neuroscience, was present instead to thank the BNA on his behalf. She assured us that he was both honoured and delighted to be selected and that the plaque would hold a prized position among his collection.



## New Psychiatric Research Institute opens in Glasgow

PsyRING (the Psychiatric Research Institute of Neuroscience in Glasgow) is a new joint institute between the Universities of Glasgow and Strathclyde and NHS Glasgow.

The Institute has operated for the past decade, under the name of YRING, in an exclusive collaboration with Mitsubishi Pharma Co, one of Japan's leading pharmaceutical companies. YRING developed and employed sophisticated genetic, molecular, cellular, systems level and behavioural neuroscience approaches, alongside an integrated clinical programme, to discover and develop novel treatments for schizophrenia. Targets and drugs identified through this work are progressing for drug research and development.

Building upon the skills and success of YRING, and the support of Scottish Enterprise, PsyRING provides a range of translational drug screening, development and clinical services to companies and other collaborators active in the development of drugs in the psychiatric and neurological sector worldwide. These activities are combined with a strong academic research programme aimed at increasing understanding of the causes of major psychiatric disease and speeding up the process of drug development.

A symposium to launch PsyRING, was held in the University of Glasgow in March, 2008. The symposium, entitled "New developments in the understanding and treatment of Schizophrenia" was attended by some 100 delegates

including representatives of major pharmaceutical companies, neuroscientists and clinicians. Presentations provided an overview of the activities of the PsyRING team in the previous ten years of collaboration with Mitsubishi Pharma as well as presentations of their future plans and activities across the areas of preclinical and clinical development of drugs for psychiatric disease. Keynote lectures provided by Professor Paul Harrison (University of Oxford) and Professor Douglas Blackwood (University of Edinburgh) allowed attendees to gain an insight into the latest research into genetic factors in schizophrenia.

The symposium provided an exceptional opportunity for experts in the field of schizophrenia research and treatment to discuss emerging trends in drug discovery for the disease.

PsyRING has already attracted over £1million of contracts and collaborations with a number of organisations active in the field, including Mitsubishi Tanabe Pharma Co., the Translational Medicine Research Collaboration (TMRC) and GlaxoSmithKline.

**To learn more about PsyRING and its activities contact Professor Judy Pratt, Professor Brian Morris or Professor Robert Hunter ([busdev@psyring.co.uk](mailto:busdev@psyring.co.uk)). The Institute's web site can be found at [www.Psyring.co.uk](http://www.Psyring.co.uk)**



## John O'Keefe awarded the Gruber Prize, 2008

The BNA was delighted to hear that our awardee for 'Outstanding Contribution to Neuroscience' last year, Professor John O'Keefe, has this year won the prestigious Gruber Prize for his seminal work on the neural basis of complex cognitive functions in freely moving animals. He will receive this prize on 16th November, 2008, during the annual meeting of the Society for Neuroscience in Washington, DC, and will then deliver the *Peter and Patricia Gruber Lecture*.

Dr Sten Grillner, at the Karolinska Institute in Sweden and Chair of the Gruber Foundation's Neuroscience Selection Advisory Board, said: "John O'Keefe's astounding discovery [of place cells] explains how the brain makes us find the way from point A to B along a tortuous and complex path. We then need to remember a sequence of different places to pass – all in appropriate order. Each place cell serves as a sign-post that tells us how far we have reached along the path."

He added: "The ability to remember the path to any important location, spatial navigation, is an indispensable property of the nervous system of practically all animals, without which there would be chaos. It also tells us about key aspects of learning which may have critical importance in understanding human disorders such as memory loss."

*John O'Keefe was also awarded the FENS EJN prize this year.*

Commenting on Professor O'Keefe's award, Professor Ed Byrne, Dean of UCL Biomedical Sciences and Head of the UCL Medical School, said: "Professor John O'Keefe's major discovery of the hippocampal cells that underpin spatial navigation and memory is one of the seminal discoveries of modern neuroscience. John follows a tradition of great scientific discovery in neuroscience at UCL and is a worthy companion for his illustrious forebears."

Among Professor O'Keefe's current research interests is the application of his extensive knowledge of place cell behaviour and hippocampal spatial function to the study of diseases of memory, in particular Alzheimer's disease. He and his colleagues have recorded hippocampal units in a mouse model of Alzheimer's during a spatial memory task, finding deterioration in the spatial information content of place cells in older transgenic mice, which correlated with the animals' impairment on the memory task and also with amyloid plaque burden in the hippocampus – a neuropathological sign of Alzheimer's.

Professor O'Keefe said: "We think that this will be a good model for the study of the development of the disease and for assessment of potential treatments. A failing memory is one of the earliest signs of Alzheimer's and we hope to identify the underlying brain pathologies through their effects on place cell memory function."



## Congratulations!

The BNA Undergraduate and Postgraduate Prize competition was as popular as ever, attracting a worthy number of excellent nominations that were, as always, so difficult to choose between. But two winners clearly shone through eventually: **Ros Langston** and **Richard Hickman**.



**Ros Langston** completed her PhD thesis at the University of Edinburgh, under the joint supervision of Dr Emma Wood and Professor Richard Morris. During this time, the main focus of her research was to examine the putative neurobiological mechanisms underlying episodic-like memory in the laboratory rat. '*Episodic memory in humans is the phenomenon whereby one remembers unique events from one's past and their spatiotemporal aspects in vivid detail, automatically recalling rich contextual information about a particular event. This type of memory is impaired early in Alzheimer's disease and also in human amnesic patients with damage to the medial temporal lobe area of the brain, which includes the hippocampus*', she said. Ros went on to study the contribution of the hippocampus to memory for unique events in the rat, using behavioural tasks based on paired associate learning and novelty exploration paradigms, and combined these with temporary pharmacological or permanent neurotoxic inactivations of the hippocampus. '*The results demonstrated a specific role for the rat hippocampus in tasks designed to model aspects of human episodic memory. Such tasks provide useful tools for further investigation of the neural substrates of episodic memory and the establishment of links between clinical and animal studies*', she concluded.

Ros is now a Bettencourt post-doctoral fellow in Trondheim, Norway, working with Edvard and May-Britt Moser at the Kavli Institute for Systems Neuroscience & Centre for the Biology of Memory. This lab is world-renowned for its expertise in recording single neurons in the brains of awake, behaving rats, a technique Ros was keen to add to her repertoire. She is now changing direction (slightly) and currently studying the

ontogeny of spatial navigation in the rat. '*The aim of my project is to see where in the brain the first spatial correlates of single neuron firing appear, where does the spatial map in the brain originate? And how are the spatial firing properties of cells in the hippocampus and entorhinal cortex affected by early experience?*' Collaborative studies with Dr Jamie Ainge (St Andrews) and Drs Francesca Cacucci and Tom Wills in John O'Keefe's lab at UCL are starting imminently as Ros continues to carve a fascinating career in neuroscience, eventually back in the UK, she says.

**Richard Hickman** is an exceptionally talented intercalated medical student who graduated last summer with first-class honours in neuroscience at the University of Birmingham. His research dissertation investigated the phylogenetic difference in scarring and regeneration in the injured central nervous system between rat and fish, under the watchful eyes of Professors Martin Berry and Ann Logan in the Molecular Neuroscience Group. For this work and exemplary exam results, he was awarded the intercalated Biological Science Prize (formerly the Arthur Thompson Trust Prize) from the Medical School. Now he has the prestigious BNA Undergraduate Award to add to his collection.

Having returned to his medical studies, Richard now wishes to pursue his neuroscience interest further through research, during or after his foundation year posts.

**The BNA wishes both Ros and Richard much success in their flourishing scientific careers and congratulates them whole-heartedly on their fine achievements.**

## Career structure in the Biosciences - what can the Biosciences Federation do?

I am quite often asked why the Biosciences Federation (BSF) doesn't 'do something' about the career structure for research bioscientists. More often than not, the questioner is thinking only about the public sector, and especially the career structure for postdocs in universities. I usually answer by asking what exactly the questioner thinks the BSF could do and the response is nearly always rather vague.

Action can only follow an analysis of the problem. In many ways, the situation is well understood, but it does require stating. In the public sector, the modern biology that has raised so many expectations is usually conducted by large teams funded by significant amounts of external money. The team may consist of one tenured senior member of the academic staff, perhaps a more junior member of the academic staff and maybe a dozen people on fixed term contracts. In most institutions, there will be few, if any, opportunities for the short term staff to join the faculty.

However, they may not all wish to become a university academic. The majority may be postdocs but they will have a range of career aspirations. Some postdocs will have a predominantly technical role. They fill positions that used to be occupied by staff that had completed vocational training, which may have culminated in an HNC, and who became treasured technicians with a tenured post. These positions have largely disappeared. And with them stability in essential expertise. Sometimes, probably too often, promising areas of research are closed down because a postdoc leaves and his or her critical skills cannot be replaced.

Other postdocs do not aspire to become team leaders. They have seen the pressure that arises when teams are maintained on grants and want a different 'work life balance'. Although they may want nothing more than a 'first lieutenant' role, many in this cohort are truly excellent scientists. When I was in Bristol, there were tenured university posts of Research Associate and Senior Research Associate. These positions also have largely disappeared.

Finally, some postdocs are truly driven by their research and strongly promote their work at meetings and elsewhere. They are conscious of citation metrics and identify the route for a research career. Many of this smaller cohort succeed.

All of this is well known. I write about it briefly, not to indicate a yearning for a golden age (which it was not!), but to emphasise that there are different career paths in research for public sector bioscientists and that separate structures are needed for each. But that is only the beginning, honesty is also needed. How many group leaders really state explicitly that a postdoc is in effect a technician? How many think that their responsibility is discharged by finding another postdoc position for someone who would be better off doing something else – perhaps running a pub!? How many are truly delighted when the ambitious, successful

postdoc begins to overshadow them? How many suggest that their postdocs should join a contract research organisation and not think about being an international star? How many acknowledge openly that the biosciences cannot continually expand and, therefore, not all postdocs will get jobs in the area?

So what does 'do something about careers' actually mean? Certainly, I believe it is possible to 'do something'. Whilst at Babraham, we created two career paths for postdocs: one for potential team leaders, and one for team players. Entry to both paths was very competitive. The potential team leaders were funded by the Institute for two years and had to get a significant grant within this time – preferably a prestigious personal Fellowship. Astonishingly, virtually all were successful. There was no promise of a tenured post but all became very much better equipped to find one. The team players had to have needed generic skills and the ability to refresh them; they also had to be excellent scientists. This very successfully opened a much needed career path for some and provided stability in the essential expertise that the organisation needed. But, of course, this cost money and is not something that many other organisations were/are prepared to do.

Let us focus on the last sentence for a moment. Babraham was (is) not cash rich. The Institute decided to reduce the scope of its activities in order to improve the scale. The issue of 'scale and scope' is not systematically addressed in this country. Universities do not have to teach all subjects, or, indeed, undertake research in any. Some universities do not hesitate to reorganise schools and close subject areas in order to improve the structure and financial strength of the organisation. Perhaps the argument should be made more strongly that human capital is the greatest asset of all and that 'scale and scope' issues apply very strongly to staff at all levels.

So what can the BSF do? Currently we are engaged in working with others on identifying skills shortages – both current and anticipated, both vocational and generic. This work holds promise of important outcomes. But I would be delighted if we could also look at the career question in a potentially constructive way in order to make generic recommendations. Please write to me if you have a view about the constructive way forward.

**By Richard Dyer,**  
**CE, Biosciences Federation**  
**(richard.dyer@bsf.org.uk)**

## Portland Customer Services take over the management of BNA membership



Most of you are aware by now that Portland Customer Services (PCS), a wholly owned subsidiary of The Biochemical

Society, has been managing the BNA membership database since April this year. If you haven't been contacted by them about renewing your membership, you soon will be. It's a case of 'three strikes and you're out' now, I'm afraid – if you do not renew after your third reminder, then we assume you no longer wish to be a member.

The BNA Committee is confident that maintenance of our database is now in expert hands and will receive professional attention at all times from the 'team'. Rhonda Oliver, the Managing Director, said:

*"Portland Customer Service (PCS) is delighted that the BNA has chosen our professionalism, software and systems to carry out their membership fulfilment. We are looking forward to developing an excellent working relationship with the BNA and demonstrating our commitment to providing the highest level of customer service to their members."*

We do hope all members agree with our decision, and feel content that their enquiries or concerns about membership are dealt with courteously and professionally by PCS at all times.

**The contact details for membership matters are now:**  
**bn@portland-services.com, or telephone 01206 796351.**  
**Just ask for BNA!**

# CALL FOR ABSTRACTS

## 20th National Meeting

### The Adelphi, Liverpool, 19-22 April, 2009

An eclectic blend of the best neuroscience, supported by over 50 themed poster sessions, peripheral events and full social programme. In addition, there will be an exhibition displaying the latest equipment, reagents, literature and techniques

#### PLENARY LECTURERS

**Bob Burgoyne** (*Liverpool*) ● **Dick Passingham** (*Oxford*)

**Nancy Rothwell** (*Manchester*) ● **Elizabeth Gould** (*Princeton, USA*)

**Andrew Parker** (*Oxford*) ● **Malcolm Brown** (*Bristol*) ● **David Porteous** (*Edinburgh*)

#### SYMPOSIA

- Extending the hippocampal memory system: beyond the fornix
- Steroid hormones and neuroprotection: is it all good news?
- Structure-function studies in ionotropic glutamate receptors
- GABAA receptors, cortical function and psychiatric disease
- Molecular and functional properties of human stem cell-derived neurons in vitro.
- Neural basis of drug addiction
- G-protein coupled receptor trafficking and neuronal function (provisional title)
- Novel gene regulation mechanisms in neuroscience and psychiatry
- Between hope and despair: sleep and circadian dysfunction in neurological disorders
- Mechanisms of cortical circuit function and development: insights from the barrel cortex
- Prion paradigm: lessons for neuroscience
- Neuron-glia interactions in plasticity and pathology
- Mechanisms of synaptic transmission: insights from model organisms

- Activity dependent mechanisms in the development and plasticity of sensorimotor systems: towards understanding and treatment of cerebral palsy.
- Frontal lobe interactions during learning and decision-making
- Making sense of basal ganglia and cerebella neuroscience: a computational modelling approach
- Brain connectivity: from structure to function
- 5-HT systems in psychiatric disorders
- Recent advances in the biology of myelination
- New insights into stress and synaptic plasticity

#### WORKSHOPS

- Brain Connectivity Workshop: Dynamic Causal Modelling
- Analysis of Structural, Diffusion and Functional MRI Data
- Translational approaches in drug discovery and development
- Beyond the bench: engaging the public in brain science

#### SATELLITE

- Glutamate Receptors – The Long and Winding Road

**ABSTRACT DEADLINE: 31st JANUARY, 2009**

[www.bna.org.uk/bna2009/](http://www.bna.org.uk/bna2009/)

[bna2009@liv.ac.uk](mailto:bna2009@liv.ac.uk) +44 (0)151 794 6440

## Postgraduate Symposium – Young Neuroscientists Day 2008

Following the fantastic success of the Young Neuroscientists' Day 2007 (YND07), we are pleased to announce that a similar event will take place again this year in Cardiff on 22nd October, 2008, at University Hall Conference Centre.

This year, the programme will include:

- hugely popular poster sessions (places for 150 posters)
  - 5 themed talks
  - guest speaker (Dr Emma Robinson)
- plenary speaker (Dr Sarah-Jayne Blakemore, UCL)

---

**PLUS, we will be running 14 MINI-SYMPOSIA.** These will give thirty delegates the opportunity to each give a 10 minute talk on their work (selected from submitted abstracts). We strongly encourage you to submit abstracts, regardless of experience or stage in your career - this is a valuable chance to present YOUR work to your peers in a friendly environment!! (chance to practice before SfN or the BNA National Meeting too!)

Topics for the mini-symposia that you can present in include:

- Neuroimaging
- Behavioural Neuroscience
- Genetics
- Brain Plasticity and Repair
  - Visual Neuroscience
- Cognitive neuroscience
- Developmental Neuroscience
- Systems Neuroscience
- Cellular Neuroscience
- Molecular Neuroscience
- Computational Modelling
  - Bioinformatics
- Neurobiology of Disease
- Clinical/Applied Neuroscience

YND08 is for everyone in the early stages of their career who is interested in neuroscience - post-docs, PhD students, or those at a similar level in their lab-based or clinical research career.

FULL DETAILS AND REGISTRATION

[www.youngneuroscientistsday.com](http://www.youngneuroscientistsday.com) or [www.cardiff.ac.uk/cnc](http://www.cardiff.ac.uk/cnc)  
Or contact Vanessa Davies ([daviesvj@cardiff.ac.uk](mailto:daviesvj@cardiff.ac.uk))

## CHRISTMAS SYMPOSIUM, 2008

1.00pm – 5.00pm, Wednesday, 17th December,  
The Royal Society, 6-9 Carlton House Terrace, London, SW7

### THE MEANING OF SLEEP: 21st CENTURY THINKING

*Chairs: Graham Collingridge (Bristol) and Bruno Frenguelli (Warwick)*

Dr. Jozsef Csicsvari (Oxford)

*Reactivation of Cell Assemblies in Sleep: Insights into Memory*

Dr Simon Archer (Surrey)

*Sleep, genes and circadian rhythms*

Dr Paul Reading (South Tees NHS Trust)

*Seized by somnolence: the science of narcolepsy*

Dr Jenny Morton (Cambridge)

*When the Golden Chain Breaks: Sleep and Neurodegenerative Disorders*

Dr Peter Naish (Open University, Milton Keynes)

*'Look into my eyes and go to sleep'...but do we?*

Professor Simon Williams (Warwick)

*The Politics of Sleep: Problems, Policies and Prospects*

**Tickets are FREE for BNA members but must be ordered in advance. BNA members may bring guests to this popular annual event and everyone is invited afterwards to join the BNA Committee for a 'seasonal' reception.**

**Contact: [events@bna.org.uk](mailto:events@bna.org.uk), or tel: 0151 794 5449.**

## Controversial Issues in Neuroscience

6.30pm, TUESDAY, 25th NOVEMBER, 2008,  
at The Dana Centre, 165 Queens Gate, London SW7

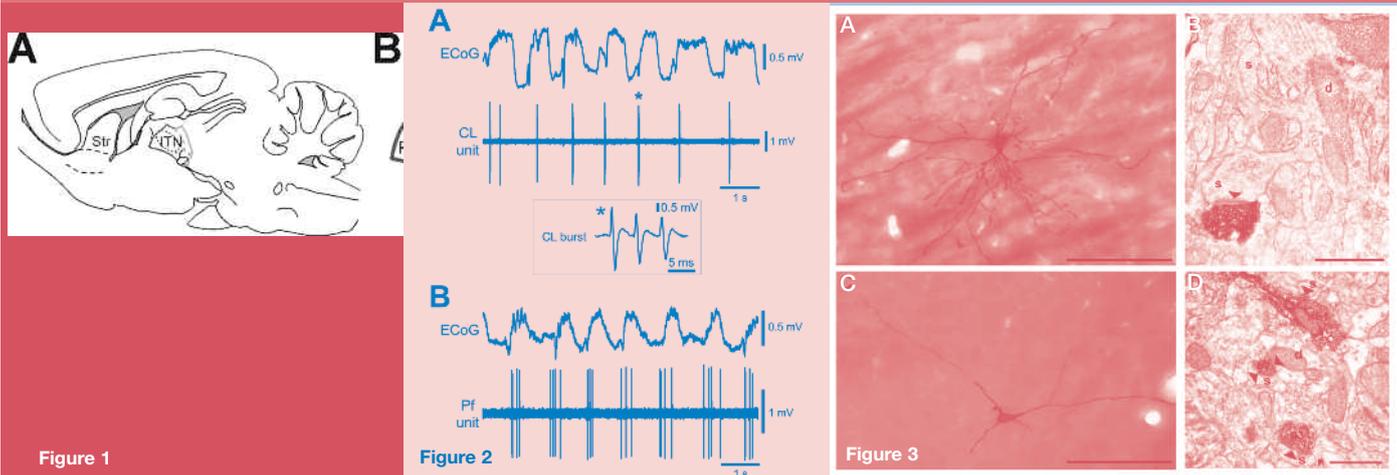
### Out of body experiences

Join us for a lively café-bar discussion on this timely and controversial topic that will examine the myths and reality behind these extraordinary and commonly reported experiences. Speakers will include clinicians, neuroscientists and patients who will share anecdotes and explanations.

**This event is FREE to BNA members.  
For tickets, contact: [tickets@edab.org.uk](mailto:tickets@edab.org.uk)**

## Dissecting the thalamostriatal pathway

**CAROLYN LACEY** was a very deserving winner indeed of the BNA Postgraduate Prize, 2007, for her outstanding PhD thesis supervised by Peter Magill and Paul Bolam in the MRC Anatomical Neuropharmacology Unit in Oxford. She is now at Stanford University, California, continuing to investigate the complex anatomy of the thalamus. Here, she describes the intricacies of the connections between the thalamus and striatum and their functional significance, and how her work questions established beliefs.



**Figure 1:**

**A.** Schematic representation of a sagittal section of a rat brain the level of the rostral and caudal components of the ITN (red and green, respectively) and the striatum (Str). **B.** Schematic of some of the ITN, delineating the central lateral (CL), paracentral (PC), parafascicular (Pf) and ethmoid (eth) nuclei. The mediodorsal (MD) nucleus of the medial thalamus is also shown. Adapted from Paxinos and Watson (2007).

**Figure 2:**

**Activity of identified CL and Pf neurones during cortical slow-wave activity.** **A.** Extracellular activity of a typical CL neurone firing bursts of action potentials (a typical burst is denoted by an asterisk and shown in the boxed inset) in time with cortical slow-wave ("sleep") activity, as shown in the electrocorticogram (ECoG). **B.** Extracellular activity of a typical Pf neurone firing single action potentials in time with the cortical slow-wave activity.

**Figure 3:**

**A.** Juxtacellularly-labelled CL neurone with typical 'bushy' somatodendritic characteristics. Scale bar = 100  $\mu$ m. **B.** Axon terminal of the CL neurone shown in A forming an asymmetric synapse (arrowhead) with the head of a dendritic spine (s) emerging from a dendritic shaft (d) of a presumed MSN in the striatum. Scale bar = 0.5  $\mu$ m. **C.** Juxtacellularly-labelled Pf neurone with typical 'reticular-like' somatodendritic characteristics. Scale bar = 100  $\mu$ m. **D.** Three axon terminals of a Pf neurone establishing synapses in the striatum. Two terminal boutons (b1 and b3) each form asymmetric synapses (arrowheads) with dendritic spines (s), and another bouton (b2) forms an asymmetric synapse (arrowheads) with a dendritic spine (s) and a dendritic shaft (d). Scale bar = 0.5  $\mu$ m.

Scale bar = 100  $\mu$ m. The complete digital reconstruction of this neurone is shown in the cover illustration. **D.** Three axon terminals of a Pf neurone establishing synapses in the striatum. Two terminal boutons (b1 and b3) each form asymmetric synapses (arrowheads) with dendritic spines (s), and another bouton (b2) forms an asymmetric synapse (arrowheads) with a dendritic spine (s) and a dendritic shaft (d). Scale bar = 0.5  $\mu$ m.

### Thalamus: The sensory gateway

The thalamus is often thought of as a chief integrative gateway between the incredibly diverse stimuli of the external world and the most complex of internal environments, the brain. It thus comes as no surprise that the thalamus is intimately involved with many sensory, motor and cognitive processes in the brain. The largest division of the thalamus, the dorsal thalamus, is comprised of a number of distinct subregions, which are often referred to as "relay" nuclei due to their acknowledged functional roles and their massive reciprocal connections with two major forebrain structures, the cerebral cortex and the basal ganglia (Jones, 1985). Important components of this relay system are the intralaminar thalamic nuclei (ITN), which lie within the internal medullary lamina of the thalamus, close to the midline (Fig. 1A). The ITN are key intermediaries in the continuous dialogue between cortical/basal ganglia structures and a rich variety of subcortical regions that also process externally- and internally-generated information. Thus, the ITN integrate information from many different brain regions, before passing it on to their main targets via the thalamocortical and thalamostriatal pathways. In part because of the widespread connectivity of the ITN with these (and other) structures, it has been suggested that the glutamatergic neurones of the ITN together form an homogeneous, integral component of the so-called 'ascending reticular activating system' that underlies arousal, wakefulness and sensory perception.

### Intralaminar thalamic nuclei

The ITN are divided into rostral and caudal components in mammals (Fig. 1). The rostral ITN include the central medial nucleus (CeM), the paracentral nucleus (Pc), and the central lateral nucleus (CL). The caudal ITN are made up of the ethmoid nucleus, centre median nucleus (CM) and parafascicular nucleus (Pf). The latter two are often referred to as one entity; the centre median-parafascicular complex (CM-Pf). The CM is more developed, and easier to distinguish from Pf, in primates as compared to rodents, and thus, in rats, the CM-Pf is commonly referred to simply as 'Pf'. There are two types of projection or relay neurone in the ITN, at least when defined on the basis of somatodendritic geometry (Scheibel and Scheibel, 1967; Deschênes et al., 1995; 1996). Neurones in the rostral ITN possess the classical thalamic 'bushy' morphological characteristics, whereas those in the caudal nuclei are 'reticular-like' (that is, their dendritic architecture is similar to that of neurones of the reticular formation). Bushy-type neurones have radiating, profusely branching dendrites, whereas reticular-like dendrites are longer with fewer branches.

### Bimodal activity of thalamic neurones

The functions of neurones in ITN and other thalamic relay nuclei are assumed to be mediated by two distinct activity modes – 'tonic' or 'bursting' – according to the requirements of ongoing information processing (Sherman, 2001; Llinás and Steriade,

# SCIENTIFIC REVIEW

2006). These two modes of firing are typical of thalamic neurones recorded in vivo, and are dependent on vigilance state (Sherman, 2001; Llinás and Steriade, 2006). The convention is that the burst mode (two or more conventional action potentials fired in quick succession) occurs only when the membrane potential is relatively hyperpolarised, and is prevalent in the thalamus during slow-wave (“sleep”) activity when excitatory input is rhythmically suppressed. In contrast, the tonic mode (single action potentials) occurs when the neurones are relatively depolarised, during waking for example (see review Steriade et al., 1993). Each mode of activity is achieved by a distinct combination of synaptic inputs and intrinsic membrane properties (see Destexhe and Sejnowski, 2003). It has been hypothesised that the burst mode may enhance the reliability of information flow between thalamic neurones and their targets, and is well suited to induce plasticity at thalamostriatal and thalamocortical synapses (Lisman, 1997), as well as acting as a “wake-up call” for salient changes in the external environment (Sherman, 2001). Conversely, the tonic firing mode may have a more subtle effect on target neurones, providing a mechanism for more linear input-output relationships (Sherman, 2001).

## The thalamostriatal pathway in function and dysfunction

As compared to other thalamic nuclei, the ITN provide the most extensive innervation of the basal ganglia, most notably the striatum (Groenewegen and Berendse, 1994; Smith et al., 2004). The ITN neurones are key mediators of ascending subcortical influences on the basal ganglia and are ideally placed to directly update the striatum on information exchanged between thalamus and cortex. However, the functional roles played by the thalamic inputs to striatum are not clearly understood. In one important study, Matsumoto et al. (2001) proposed that the thalamostriatal pathway has two major roles: to supply the striatum first, with “attention-gated multimodal sensory information” and, secondly, with “context-dependent signals of behaviourally significant events”. In other words, thalamostriatal inputs provide information on sensory events of behavioural significance, and are likely to be important for arousal, attention, orienting and action selection (Kimura et al., 2004; McHaffie et al., 2005).

Of course, to fully appreciate the roles executed by the thalamostriatal pathway, one must first consider the functional organisation of the basal ganglia. The basal ganglia are a group of highly interconnected subcortical nuclei involved in a number of processes, such as motor, associative, cognitive and limbic functions. The basal ganglia are also the site of the primary pathology in several movement disorders, such as Parkinson’s disease and Huntington’s disease. The striatum is the principal input structure and the largest of the basal ganglia nuclei. It is composed of GABAergic medium-size densely spiny projection neurones (MSNs) and four types of interneurone (Bolam et al., 2000). Striatal MSNs integrate information from a wide variety of afferents (predominantly the cortex and the thalamus) and convey this complex information to ‘downstream’ targets within the basal ganglia. According to the direct/indirect pathways model of information flow through the basal ganglia, cortical input to the striatum is processed and subsequently transmitted

to the output nuclei of the basal ganglia via two routes; either directly from the striatum to the output nuclei or indirectly via the globus pallidus and subthalamic nucleus (De Long, 1990). The consequences of activation of the direct and indirect pathways are functionally opposite in the target regions of the basal ganglia, such as the thalamus, and imbalances between

‘Understanding the fundamental physiological and anatomical characteristics of the ITN and their projections to the striatum is critical to dissecting the functional influence of the thalamus on the basal ganglia, and the role of the basal ganglia as a whole’.

the two pathways contribute to various hypokinetic and hyperkinetic disorders (DeLong, 1990). Even though the classic indirect/direct pathways model has been critical for understanding and predicting function, as well as dysfunction, it

is often conceptualised as a closed cortico-basal ganglia-thalamocortical circuit, and as such, neglects the role of the input to the striatum from the ITN. In short, it is difficult to reconcile the thalamostriatal system with current models of basal ganglia function (DeLong, 1990; Smith et al., 1998). It is likely, however, that the ITN have important roles in basal ganglia physiology and pathophysiology. The ITN may relay sensory information to the motor-related cortices and the basal ganglia to assist in neural processes underlying the initiation, guidance, or termination of motor responses under appropriate behavioural conditions. A deficit in this sensory transmission could adversely influence motor function and thus contribute to movement disorders. Thus, understanding the fundamental physiological and anatomical characteristics of the ITN and their projections to the striatum is critical to dissecting the functional influence of the thalamus on the basal ganglia, and the role of the basal ganglia as a whole.

The CL and Pf nuclei are prototypical examples of rostral and caudal ITN, respectively, and their glutamatergic neurones exert influences on widespread cortical and subcortical targets. A factor perhaps limiting our complete understanding of the roles of these two nuclei, and the thalamostriatal pathway in general, is that the rostral and caudal ITN are often grouped together in schemes of the functional organization of (thalamo)cortical and basal ganglia circuits (Llinás et al., 1998; Smith et al., 1998). Several lines of evidence suggest, however, that CL and Pf neurones have dissimilar intrinsic properties and/or synaptic connections, raising the possibility that these nuclei might play distinct roles in modulating striatal and cortical activity. First, the dendritic architectures of CL and Pf neurones differ, implying divergent integrative properties (Deschênes et al., 1996). Second, tract-tracing studies have shown that, in the striatum, axons emanating from CL preferentially synapse with dendritic spines, whereas axons from Pf tend to synapse with dendritic shafts (Smith et al., 2004).

## Defining the cellular substrates of the thalamostriatal pathway

To define the functional roles played by CL and Pf neurones, it is critical to understand their physiological modes of operation in vivo, with due consideration of intrinsic physiological and morphological properties. The overall objective of my original thesis research was to define, and correlate, the physiological and morphological properties of ITN neurones, principally those in CL and Pf, as well as the synaptic connections they establish in striatum. Although the ITN have been historically thought of as having similar properties and functions, our recent findings

have demonstrated that identified neurones of the rostral and caudal components of the ITN have fundamentally different firing properties *in vivo*, somatodendritic architectures and connectivity at the level of the striatum (Lacey et al., 2007). Using a multidisciplinary approach, we have demonstrated that neurones of the rostral and caudal ITN provide functionally distinct inputs to the striatum. We carried out recordings of single CL and Pf neurones in anaesthetized rats and, after physiological characterization, we juxtacellularly labelled the neurones with a tracer, Neurobiotin. The juxtacellular recording/labelling technique is powerful because it enables one to selectively label the same neurone that you have extracellularly recorded from and thus unambiguously identify and morphologically characterize the recorded neurone (Pinault, 1996). Using this technique, we were able to precisely define the location of the recorded neurones within in the CL or the Pf, and, more importantly, we could correlate the somatodendritic characteristics, axonal projection patterns and synaptic connectivity of a labelled single neurone with its *in vivo* physiological properties (Lacey et al., 2007). The results of our studies show that CL and Pf neurones are different at several functional levels. First, CL neurones, but not Pf neurones, engage in burst firing modes during slow-wave (sleep) activity (Fig. 2), which is a stereotypical property of thalamic relay neurones (see above). Thus, CL and Pf neurones operate as typical and atypical thalamic neurones, respectively. In addition to differences in physiological properties of neurones in these two nuclei, the morphological properties and synaptic connectivity were distinct (Fig. 3). We confirmed that CL and Pf neurones had strikingly different dendritic architectures; the former exhibited dendrites typical of thalamic relay neurones (Fig. 3A), but the latter did not (Fig. 3C). The study also revealed that the axons of identified CL and Pf neurones established synaptic connections with different targets in the striatum: these neurones target, on average, dendritic spines and dendritic shafts, respectively (Fig. 3B and D). Importantly, Pf neurones, but not CL neurones, exhibit a clear heterogeneity with respect to their postsynaptic targets in striatum. Thus, single Pf neurones can innervate both dendritic spines and shafts, or exclusively innervate dendritic shafts, or selectively innervate dendritic spines. Furthermore, a single axon terminal of a Pf neurone could simultaneously establish synapses with

both dendritic spines and shafts (see cover of this issue). The selective innervation of distinct domains of the somatodendritic membrane of MSNs is likely to have different influences on target cell activity, although how and to what degree this influences striatal output is not yet understood.

### The thalamostriatal pathway: a new outlook

The results of these studies have further clarified the fundamental physiological and anatomical attributes of the rostral and caudal ITN neurones and their projections to the striatum. Although the ITN are commonly considered as functionally homogeneous, our work has directly demonstrated that the fundamental properties of CL and Pf neurones differ and they provide different temporally-patterned inputs to distinct striatal targets. One important implication of these data is that the field should re-evaluate the dogma that dorsal thalamic relay neurones are homogeneous in their firing properties, given that in our study Pf neurones do not express the typical operational principles of thalamic relay neurones. Moreover, because of the multiple differences in the physiological and anatomical characteristics of CL and Pf neurones alone, the ITN should no longer be collated into a broad category of “the thalamostriatal pathway”, with a common mode of operation, for the sake of conceptual convenience. This new information has far-reaching implications for our understanding of both the thalamocortical and thalamostriatal pathways (and other subcortical brain areas), and future studies should perhaps be dedicated to dissecting out other potential differences between the rostral and caudal components of the ITN and their projections.

### Acknowledgements

*The author wishes to extend her warmest thanks to her thesis supervisors, Professor Paul Bolam and Dr. Peter Magill, both of whom more than generously devoted their time and energy to successfully getting her through the D.Phil. Her thanks also go to everybody at the MRC Anatomical Neuropharmacology Unit, Oxford. The author would also like to extend special thanks to Ben Micklem for help with figures and for designing the cover illustration. This work was funded by the Medical Research Council UK. During her D.Phil., the author was also supported by travel awards from The Guarantors of Brain and The Keble Association, and the Faith Ivens Travel Grant (Keble College, Oxford).*

### References

- Bolam JP, Booth PAC, Hanley JJ, Bevan MD (2000) Synaptic organisation of the basal ganglia. *J Anatomy* 196:527-542.
- DeLong MR (1990) Primate models of movement disorders of basal ganglia origin. *Trends Neurosci* 13:281-285.
- Deschênes M, Bourassa J, Parent A (1995) Two different types of thalamic fibers innervate the rat striatum. *Brain Res* 701:288-292.
- Deschênes M, Bourassa J, Doan VD, Parent A (1996) A single-cell study of the axonal projections arising from the posterior intralaminar thalamic nuclei in the rat. *Eur J Neurosci* 8:329-343.
- Destexhe A, Sejnowski TJ (2003) Interactions between membrane conductances underlying thalamocortical slow-wave oscillations. *Physiol Rev* 83:1401-1453.
- Groenewegen HJ, Berendse HW (1994) The specificity of the 'nonspecific' midline and intralaminar thalamic nuclei. *Trends Neurosci* 17:52-57.
- Jones EG (1985) *The Thalamus*. New York: Plenum Press.
- Kimura M, Minamimoto T, Matsumoto N, Hori Y (2004) Monitoring and switching of cortico-basal ganglia loop functions by the thalamo-striatal system. *Neurosci Res* 48:355-360.
- Lacey, C.J., Bolam J. P. and Magill P.J. (2007). Novel and distinct operational principles of intralaminar thalamic neurons and their striatal projections. *J. Neurosci.* 27: 4374-4384.
- Lisman JE (1997) Bursts as a unit of neural information: making unreliable synapses reliable. *Trends Neurosci* 20:38-43.
- Linás R, Ribary U, Contreras D, Pedroarena C (1998) The neuronal basis for consciousness. *Philos Trans R Soc Lond B Biol Sci* 353:1841-1849.
- Linás RR, Steriade M (2006) Bursting of thalamic neurons and states of vigilance. *J Neurophysiol* 95:3297-3308.
- Matsumoto N, Minamimoto T, Graybiel AM, Kimura M (2001) Neurons in the thalamic CM-Pf complex supply striatal neurons with information about behaviorally significant sensory events. *J Neurophysiol* 85:960-976.
- McHaffie JG, Stanford TR, Stein BE, Coizet V, Redgrave P (2005) Subcortical loops through the basal ganglia. *Trends Neurosci* 28:401-407.
- Paxinos G and Watson C (2007) *The Rat Brain in Stereotaxic Coordinates*, 6th Ed, Elsevier Academic Press, San Diego.
- Pinault D (1996) A novel single-cell staining procedure performed *in vivo* under electrophysiological control: morpho-functional features of juxtacellularly labeled thalamic cells and other central neurons with biocytin or Neurobiotin. *J Neurosci Methods* 65:113-136.
- Scheibel ME, Scheibel AB (1967) Structural organization of nonspecific thalamic nuclei and their projection toward cortex. *Brain Res* 6:60-94.
- Sherman SM (2001) Tonic and burst firing: dual modes of thalamocortical relay. *Trends Neurosci* 24:122-126.
- Smith Y, Bevan MD, Shink E, Bolam JP (1998) Microcircuitry of the direct and indirect pathways of the basal ganglia. *Neuroscience* 86:353-387.
- Smith Y, Raju DV, Pare JF, Sidibe M (2004) The thalamostriatal system: a highly specific network of the basal ganglia circuitry. *Trends Neurosci* 27:520-527.
- Steriade M, McCormick DA, Sejnowski TJ (1993) Thalamocortical oscillations in the sleeping and aroused brain. *Science* 262:679-685.

Although perhaps not famed for its Neuroscience research, there is a large and growing Neuroscience community at Warwick which spans many disciplines including biology, sociology, psychology, economics and art history. In this article Mark Wall and Kevin Moffat (Biological Sciences) give an historical overview and current day perspective on Neuroscience research at Warwick.

Figure 1

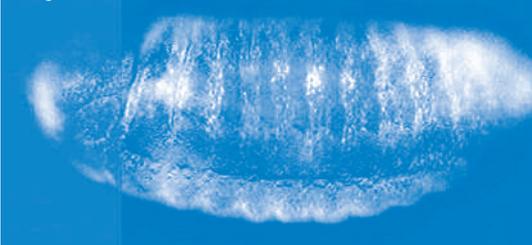


Figure 2

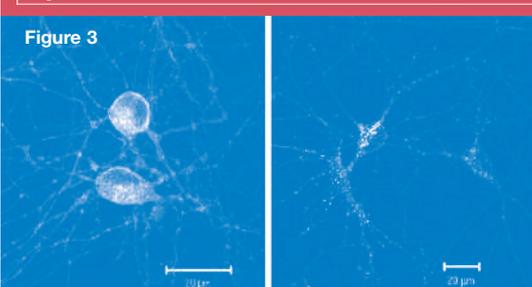


Figure 3

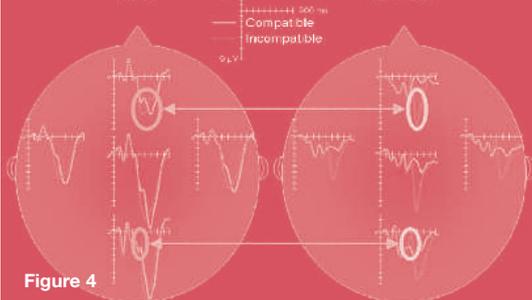


Figure 4

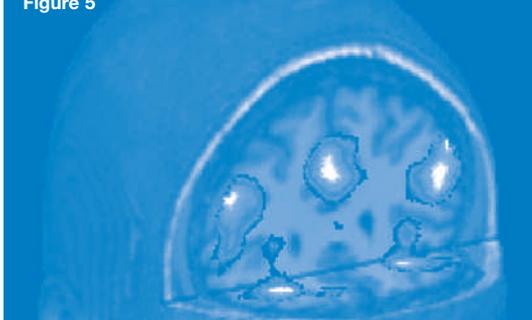


Figure 5



## Neuroscience in Biology

Within the Biological Sciences Department (<http://www2.warwick.ac.uk/fac/sci/bio>) the first groups to have an interest in Neuroscience took a developmental approach. In the mid 1980s, **Liz Oliver-Jones** and **Hugh Woodland** developed a bank of monoclonal antibody markers for studying development in the frog, *Xenopus laevis*. In particular, they had an interest in the formation of ectoderm (neurectoderm). Subsequently, **Oliver-Jones's** laboratory has published a number of papers on the analysis of genes involved in early neural development. More recently, she has collaborated with **Nicholas Dale** investigating NTPDases and the regulation of eye development (see below).

**Cahir O'Kane** (1988-1993) had developed the technique of enhancer-trapping in *Drosophila* in the laboratory of Walter Gehring at the University of Basel. At Warwick, Cahir's laboratory developed a number of enhancer-trap markers for developing neural structures in the fly. This rapidly led to the publication of a description of the embryonic development of the peripheral nervous system in *Drosophila*. With the arrival of **Kevin Moffat**, first as a post-doc in the O'Kane lab in 1990, subsequently appointed as a Lecturer in 1994, Warwick was quick to collaborate on the use of second generation enhancer-traps, first developed by Brand and Perrimon at Harvard University. This technique allowed for the control of gene expression in marked cells during development. They quickly built a bank of "GAL4 lines" or "drivers" with defined expression control in the central nervous system of both the developing and adult fly. Many of these lines are still used widely in the fly neurobiology community, for example, GAL4 drivers expressing in the mushroom bodies of the brain (an area involved in olfactory processing) and in the giant fibre circuit (involved in visual escape behaviours). To go with the expression system, the Warwick *Drosophila* groups developed new tools to analyse neural function in the fly: The first attempts to analyse cell shape via transgenic markers; toxicigenic ablation via transgenic Ricin-A chain; toxicigenic neuronal inactivation via transgenic tetanus toxin-A chain.

Kevin Moffat's group began to analyse the development of the *Drosophila* adult giant fibre neurons, using the markers and tools he had developed in the O'Kane laboratory. His group was able to describe the complete development of the giant neurons. More recently, his group have identified a number of new genes involved in the development of adult neural circuitry: short-stop, ken and barbie, arouser (Figure 1 - Ribbed appearance of *arouser* expression in *Drosophila* embryo) and slowmo. The development of the genetic tools has also led the Moffat laboratory to use *Drosophila* for the study of neurologically important genes. They have recently published on the analysis of the human torsin dystonia homologue in the fly, describing for the first time neurodegenerative phenotypes associated with loss of this type of protein. Similar studies are now being continued with collaboration with Bruno Frenguelli on an ART funded project analysing the hyper-phosphorylation of tau in the well established *Drosophila* Alzheimer's models.

The arrival of **Richard Baines** in 2001 led to the introduction of a combination of genetic and electrophysiological approaches in *Drosophila*. Richard had developed patch clamping techniques of identified embryonic neurons in *Drosophila*. The fly group at Warwick was thus able to make progress on the contributions of specific transcription factors to motoneuron electrical properties. Since Richard's move to Manchester, collaboration has continued with Kevin Moffat and the Luschnig laboratory, University of Zurich. Together they have described a translational control mechanism to regulate expression of the voltage gated sodium channel gene, *paralytic*.

## The formation of the Neuroscience Group

In 2000, Ted Pridgeon, a retired Lincolnshire farmer living in nearby Leamington Spa, generously endowed a Chair of Neuroscience at the University of Warwick. The first and current occupant of this Chair, **Nicholas Dale**, started to establish Neuroscience as a serious discipline within the Department of Biological Sciences. Thus Nicholas Dale and Mark Wall, the first two appointments, joined Kevin Moffat to form a nascent Neuroscience grouping.

The establishment of a graduate entry medical school at Warwick, initially jointly with Leicester in 2001, gave the opportunity to make further appointments in Neuroscience. This led to the recruitment of David Spanswick, Kevin Lee, Peter Stanfield (group leader of the Molecular Physiology group) and Richard Baines (see above). Neuroscience research at Warwick has now entered a second phase of expansion. Firstly, there have been recent appointments to the experimentalists within Biological Sciences –notably Bruno Frenguelli, Yuriy Pankratov and Sonia

Correa. This gives the Neurosciences at Warwick critical mass, especially in the area of purine-mediated signalling, with others in the Department entering this field, notably the developmental biologist Liz Oliver-Jones through collaborations with Dale. Secondly, there have been appointments of computational neuroscientists in other Departments such as Jiang-feng Feng in Computer Sciences, Magnus Richardson in Systems Biology and additional members of Biological Sciences have begun Neuroscience projects (Teresa Pinheiro).

Nicholas Dale's current work revolves around studying signalling by ATP and adenosine in a variety of physiological and developmental contexts. These include how the brain detects CO<sub>2</sub>, particularly in the context of respiratory chemoreception; the function and role of hypothalamic tanycytes; mechanisms of adenosine release in the preoptic areas contributing to the homeostatic control of sleep; and the control of eye development in the early frog embryo. In addition, Nick continues to develop biosensor technologies: making sensors smaller and more sensitive and for a wider range of analytes, such as glutamate and D-serine; and optical nanosensors to allow detection of transmitter release around specific structures.

**Mark Wall** joined the Neuroscience Group in June 2000 as a Warwick Research Fellow. His major interest is the cerebellum and he has investigated how GABA and glutamate synaptic transmission change during postnatal development. In particular, investigating synaptic and extrasynaptic transmission at Golgi cell-granule cell synapses and mossy fibre-granule cell synapses. More recently, he has collaborated with Dale and investigated the release of adenosine following activation of parallel fibres. This adenosine release is both calcium and action potential dependent and thus is probably by exocytosis. The lack of detectable ATP suggests that adenosine could be directly released (*Figure 2 - Adenosine release occurs in cerebellar slices Trace from an adenosine (ADO) biosensor placed on the surface of the molecular layer of a transverse cerebellar slice from a P23 mouse. An ATP biosensor was inserted into the molecular layer close to the ADO sensor. Stimulation (at arrows, 20 Hz, 5 s) in the molecular layer leads to adenosine release (detected by the ADO sensor) but no detectable ATP release*). He is continuing this work investigating the mechanism of adenosine release and how it changes during postnatal development. He is also collaborating with Frenguelli and Pinheiro investigating protein aggregation and cerebellar degeneration (see below).

**Peter Stanfield** joined the University of Warwick in 2001. Peter works on potassium channels of the inward rectifier and tandem pore families – channels that set the resting potential of cells, including those of the nervous system. He works with patch clamp and molecular biological methods to investigate how channel function is related to its structure. Collaborations are: within Warwick, with Jianfeng Feng and his laboratory; with Mike Sutcliffe (Manchester) for computational chemistry, building structural models, and with the Department of Physiology, University of Debrecen, Hungary, on potassium channels of neurones of the auditory pathway and elsewhere.

**David Spanswick's** (Warwick Medical School) main research interests are neuronal electrical synapses in health and disease, central autonomic control of organ, body and cardiovascular homeostasis in health and disease at the level of the hypothalamus. These interests are related in that electrotonic coupling is an important feature of autonomic sympathetic preganglionic neurones (SPN) and the SPN are the model for health and disease that his group has previously focused on. David uses electrophysiological, anatomical and molecular approaches in collaboration with colleagues both overseas and within the UK.

**Dawn Collins** joined Biological Sciences as a temporary lecturer in 2003 and was appointed to Associate Professor in Neurobiology in Warwick Medical School in 2006. Dawn's interests include the electrophysiological correlates of anxiety and stress-related behaviour and emotional drive. Employing both *in vitro* and *in vivo*

behavioural techniques, her current research includes: investigations into the role of gap junctions in neuronal oscillations and patterning within the fear circuitry; investigations into alterations in plasticity in amygdalo-hippocampal pathways underpinning emotionally related behaviours using a novel non-noxious model of conflict and (with Spanswick) investigation of the emotional component underlying the drive to feed.

**Bruno Frenguelli** joined the Neuroscience Group in August 2007. His interests in the release and role of the purines in seizure activity and ischaemia complement the existing strengths in purinergic signalling in the group. In this regard he currently has three PhD students investigating: the modulation of the nucleotide pool after *in vitro* metabolic stress; the trafficking of adenosine receptors in models of seizure activity and the role of P<sub>2</sub> (ATP) receptors in seizures. (*Figure 3 - Agonist-induced trafficking of adenosine A1 receptors. Left panel, hippocampal neurones with a homogenous and uniform distribution of A1-GFP fluorescence. Right panel shows discrete punctae after 1 hour exposure of parallel sister cultures to adenosine, consistent with intracellular trafficking. The implications of adenosine receptor trafficking for seizure activity is a major strand of the Frenguelli lab's research program. A1-GFP constructs courtesy of Dr Tim Palmer, Glasgow University*). Magnus Richardson (Systems Biology) and Bruno are exploring the potential for seizure prediction in *in vitro* models of epilepsy through a combination of empirical experimentation and mathematical modelling, whilst with Kevin Moffat, Bruno is investigating *tau* hyperphosphorylation in *Drosophila*. With Teresa Pinheiro and Mark Wall, Bruno is utilising organotypic cerebellar slices as models of proteinopathy. In addition, he collaborates with Professor Richard Morris (University of Edinburgh) on the synaptic tagging and capture hypothesis, a potential mechanism by which "flashbulb" memories are encoded. Bruno retains strong links with his previous institution (the University of Dundee), in particular with Drs Alex Doney, Andrew Irving and Calum Sutherland, co-supervisors on three of the current PhD projects.

**Yuri Pankratov** joined Warwick in September 2007. Prior to joining Warwick, Yuri worked on the mechanisms of synaptic transmission in the hippocampus and neocortex with particular focus on P<sub>2</sub>X and NMDA receptors. His current research interests are: the properties and function of astroglial NMDA and P<sub>2</sub>X receptors; the neuron-glia communications in the neocortex, and the role for ATP receptors in synaptic plasticity and development.

**Sonia Correa** has recently joined Biological Sciences as a Warwick Research Fellow. Her research interests are centred on the trafficking of transmembrane proteins involved in synaptic plasticity and related pathological disorders. As trafficking and phosphorylation of certain proteins are associated events during plasticity, she is primarily interested in the role of mitogen-activated protein kinase (MAPK) pathways in long-term depression (LTD). In mature neurons, the MAPK signalling pathways can be activated by glutamate receptor stimulation, but very little is known about the identification of direct MAP kinase substrates, which is crucial to understanding the contribution of different signalling pathways to synaptic plasticity. Using a "chemical" protocol to induce LTD in the hippocampus, Sonia will be using different proteomic approaches combined with mass spectrometry to look for possible substrates of the p38 MAP kinase cascade in the induction of LTD.

Research led by **Teresa Pinheiro**, a structural biologist by training, focuses on the molecular mechanism of prion conversion and other amyloidogenic proteins involved in brain degenerative diseases, such as Alzheimer's and Parkinson's. Jointly with Mark Wall and Bruno Frenguelli, she is developing new tools and tissue culture models to study the susceptibility of different brain cells to amyloid protein aggregates, and identify the cellular mechanism and early molecular markers of neurodegeneration. Teresa is the Warwick Convenor for the Midland Alzheimer's Research Trust (ART) Network and Warwick University hosted the ART Network's annual meeting on the 10th June this year.

**The Systems Biology Centre**

**Georgy Koentges** is Co-Director of the Systems Biology Centre (<http://www2.warwick.ac.uk/fac/sci/systemsbiology>). Georgy is interested in how programmes of cellular behaviour in the embryo are orchestrated by transcription factor networks. He studies these networks using state-of-the-art technologies of functional genomics and conditional transgenesis. His work focuses on two developmental systems: the neural crest and the developing brain.

The neural crest is an embryonic tissue which forms the majority of structures in the face. Georgy is interested in how and when fates are decided in neural crest mesenchymal stem cells and cartilage/bone progenitors and how information about the shape of craniofacial structures is encoded. This has bearings on the origins of cancers as well as degenerative diseases such as rheumatoid arthritis, in which the same molecular pathways are activated again later in life. To this end, he uses and develops new tools of conditional gene activation/inactivation by Cre- or Flip-recombinases in transgenic mice.

Georgy is also interested in the molecular patterning events that govern the development of the accessory olfactory system, which is dedicated to the perception of pheromones in mammals. Neurons in the so-called vomeronasal organ (VNO) are excited by exposure to pheromones and are connected to so-called mitral cells in the accessory olfactory bulb. Using gene-targeting approaches, Georgy has mapped projections of VNO neurons to mitral cells by genetically tagging cells expressing a single receptor. This revealed stereotypic projection patterns, raising the hypothesis that specific areas in the brain (ie the accessory olfactory bulb) compute specific pheromones that are sensed by specific sub-types of receptors

**Theoretical Neuroscience**

**Magnus Richardson** joined the Warwick Systems Biology Centre as an RCUK Fellow in September 2006. He is a theoretical neuroscientist working closely with electrophysiologists studying cortical microcircuitry. His principal interests are the development of experimentally verified models of different classes of cortical pyramidal cells and interneurons, as well as the modelling of dynamic and stochastic properties of central synapses.

**Yulia Timofeeva** joined Warwick in January 2007 as an RCUK Academic Fellow in the Department of Computer Science (Computational Biology Group; <http://www2.warwick.ac.uk/fac/sci/dcs/research/compbio/>) and the Centre for Complexity Science ([http://www2.warwick.ac.uk/fac/cross\\_fac/comcom/](http://www2.warwick.ac.uk/fac/cross_fac/comcom/)). Her research interests are in the area of theoretical neuroscience and in particular the application of principles from biophysics and nonlinear dynamics to the modelling and study of neural systems. The general aim of her current research is to unravel some of the design principles by which dendritic machinery is used for information processing. Together with Prof Stephen Coombes (University of Nottingham), Yulia has just established a new UK Mathematical Neuroscience Network ([mathneuronet.org.uk](http://mathneuronet.org.uk)) funded by the EPSRC.

**Jianfeng Feng** (Computer Sciences) is interested in complex phenomena arising from biological systems (neuroinformatics and bioinformatics). His current interests include computational neuroscience, neural computation with applications to vision engineering problems, bioinformatics including microarray data processing and proteomics, neuroinformatics, in particular, multi-unit *in vivo* recordings, stochastic and deterministic dynamical systems, Biological control and optimal control, including control of Parkinson disease.

*There are two major computational neuroscience symposiums at Warwick in the near and more distant future: in December 2008, "Computational Neuroscience", organised by Jianfeng Feng; and in May, 2010, "Dendrites, Neurones, Networks", organised by Magnus Richardson and Yulia Timofeeva.*

About 4 years ago, **Robert MacKay**:

(Maths; <http://www2.warwick.ac.uk/fac/sci/maths/>)

was stimulated by discussions with Nick Dale to study the control of breathing rhythm. He currently has a final year Masters student investigating Prof Jack Feldman's (UCLA) data on the pseudo-random sequence of inspiration/expiration patterns in opiate-treated rats. He also has a current PhD student investigating principles by which the controlling ganglia produce synchronised bursting in a robust yet controllable way. Robert has also begun collaborating with Magnus Richardson and David Spanswick on electrically coupled neurones.

**Psychology**

The **Cognitive NeuroScience** (<http://www2.warwick.ac.uk/fac/sci/psych/research/conscience/>) group is interested in studying the links between perception and action. Their aim is to better understand how so-called 'controlled' (or voluntary) processes are instantiated by structures in the nervous system and by their automatic functions, and how so-called 'automatic' (or involuntary) processes are controlled by structural, intentional, and environmental factors. **CoNSci** is housed in a custom-build lab suite, comprising eight labs (five of which have separate control rooms), a central reception and waiting area, and a dedicated electrode placement and cleaning room. Equipment includes polygraph facilities for integrated multi-modal electrophysiological and psycho-physiological recordings, three medium-density EEG (electroencephalography) sets for precision ERP (event-related brain potentials) studies (*Figure 4 - Cortical potentials recorded in the Cognitive NeuroScience Lab*), and one high-density EEG, in addition to standard equipment for measuring response speed, accuracy, or force. The team, at present consisting of **Friederike Schlaghecken**, **James R. Tresilian** and **Elizabeth A. Maylor**, specialises in the investigation of behavioural and electrophysiological correlates of control mechanisms in the human brain. Study interests range from research into the on-line control of movement parameters, to low-level inhibitory control of pre-potent response tendencies, to top-down, high-level cognitive control processes in young and older adults. They are part of Warwick's **Centre for Cognitive and Neural Systems** ([http://www2.warwick.ac.uk/fac/cross\\_fac/cogsys/](http://www2.warwick.ac.uk/fac/cross_fac/cogsys/)), which aims to strengthen interdisciplinary research links between departments. Within this context, they are currently investigating, together with **Jianhua Yang**, **Evor Hines**, **Daciana Iliescu**, and **Mark Leeson** from the Department of Engineering, new methods for the analysis of large electrophysiological data sets, particularly in the context of human cortical activity associated with cognitive control processes.

**Warwick Manufacturing Group**

**Gemma Calvert** has recently been appointed as the Chair of Applied Neuroimaging and will be based in the new Digital Laboratory of the Warwick Manufacturing Group (WDL; <http://www2.warwick.ac.uk/fac/sci/wmg/>). Her research focuses on helping companies understand how the brain responds to products, their packaging, and the influence of advertising and marketing messages. Using fMRI in conjunction with a range of other techniques including psychophysics, eye-tracking, electroencephalography (EEG) and magnetoencephalography (MEG), the Applied fMRI group at the WDL will be elucidating the mechanisms behind purchasing and financial decision-making, as well as monitoring the implicit processes that influence and guide human behaviour (*Figure 5 - This figure illustrates the brain areas within the frontal lobe that were more activated when subjects viewed television advertisements compared to the surrounding daytime television programming. These include areas involved in executive functions (e.g. decision-making) bilaterally, the anterior cingulate (attention) and orbito-frontal cortex (involved in coding the rewarding properties of a stimulus)*). The group is also working closely with other members of the WDL to provide information concerning human brain function to guide the development of efficient visualisation graphics, virtual-reality platforms and optimal web-based security systems.

Neuroscience at Warwick extends to a variety of other departments, summarised below.

#### Warwick Medical School

(<http://www2.warwick.ac.uk/fac/med/>)

**Matthew Broome** was appointed Associate Clinical Professor of Psychiatry at Warwick in November 2006. His interests focus on the formation of delusions and the onset of psychotic illness. His work has largely involved using neuroimaging techniques together with those of cognitive neuropsychology. Previous studies have examined formal thought disorder using fMRI, cortical thickness in schizophrenia, reasoning biases linked to the formation of delusions and working memory and executive function in a high risk group for psychosis. Since moving to Warwick, he has developed collaborations with Alan Chalmers of the Digital Laboratory and is hoping to collaborate in neuroscience research to investigate the functional role of proteins linked to the genes for schizophrenia.

#### Chemistry

(<http://www2.warwick.ac.uk/fac/sci/chemistry>)

**Martin Lochner** is interested in the chemical and site-specific modification of ligand-gated ion channels. In particular, working towards attaching fluorescent tags near the agonist binding site of the serotonin 5-HT<sub>3</sub> receptor. He aims to achieve this by using designed and chemically synthesised modification reagents and post-photoaffinity labelling techniques. Martin also has an interest in purinergic signalling. One of his planned projects concerns the synthesis of highly selective inhibitors of E-NTPDases. This family of enzymes is considered to be a key player in extracellular nucleotide (e.g. ATP) hydrolysis and thus limits their action on P<sub>2</sub> type receptors.

#### Engineering

(<http://www2.warwick.ac.uk/fac/sci/eng/>)

**Julian Gardner** is researching CMOS sensors; biomimetic electronic noses; chemical microsensors; chemical microsystems; electronic tongues; biomedical engineering; and pattern recognition.

**Nigel Stocks** was originally appointed as a Warwick University Research Fellow in Engineering in 1995. His general area of interest is stochastic nonlinear systems and, in particular, information transmission/processing in nonlinear systems. This in turn has led to an interest in the theoretical aspects of neural population coding (these systems are of course highly nonlinear and stochastic). Currently, Nigel has two Neuroscience projects: 1) The discovery of an effect termed suprathreshold stochastic resonance (SSR) in neural populations and 2) the introduction of noise, at the neural level, into cochlear implants to improve the temporal neural coding of speech signals (with Robert Morse, Aston).

#### Sociology

**Simon Williams'** recent research has focused on sleep and society, including a recently completed interdisciplinary seminar series on sleep and society (<http://www2.warwick.ac.uk/go/sleepandsociety>) and a project on representations of sleep science and sleep medicine in the news. He is currently researching developments in both sleep and wakefulness promoting drugs and was involved in a recent public debate on these topics, to coincide with the Wellcome Sleep and Dreaming Exhibition. Williams is co-founder of the new neuroscience and society group at Warwick:

(<http://www2.warwick.ac.uk/fac/soc/nsw>), funded through Warwick's Institute of Advanced Studies:

([http://www2.warwick.ac.uk/fac/cross\\_fac/ias](http://www2.warwick.ac.uk/fac/cross_fac/ias)), which brings together the social, basic and clinical neuroscience communities at Warwick, and which recently hosted a very successful visit by Prof Gary Lynch (UC Irvine) on the topic of cognitive enhancers (<http://www2.warwick.ac.uk/newsandevents/audio/?podcastItem=braindrugs.mp3>). Simon has recently hosted a symposium at the British Sociological Association conference 'Social Worlds/Natural

Worlds' at Warwick on 'Society, Self and the Neurosciences'.

**Steve Fuller** is the UK partner of an EU Framework 6 project on 'The Knowledge Politics of Converging Technologies', which concerns the impact of the emerging research synergies in nano-, bio-, info- and cogno- sciences and technologies. He is also interested in the implications of the neurosciences on the humanities, especially historical inference and philosophical definitions of humanity.

#### History

The Wellcome Centre for the History of Medicine at Warwick (<http://www2.warwick.ac.uk/fac/arts/history/chm>) has a number of staff with research interests in Neuroscience. These include:

**Mathew Thomson** is researching the history of psychology and psychiatry in 20th century Britain, including his recently published book *Psychological Subjects: Identity, Culture, and Health in Twentieth-Century Britain* (Oxford, 2006).

**Ingrid Sykes** is a Wellcome Postdoctoral Fellow, working on blindness and sound in 19th century France: a project which is utilising neuroscientific research on perception of sound.

**Claudia Stein** has organised a Summer School (7-11 July 2008) which will explore the history of medical imaging from the Renaissance to present times:

(<http://www2.warwick.ac.uk/fac/arts/history/chm/activities/summer-school>). This included a session on the many challenges that neuro-imaging presents to the understanding of ourselves as human beings.

#### Art History

(<http://www2.warwick.ac.uk/fac/arts/arthistory/>)

**Paul Smith** is currently developing a theory of representation by using ideas from neuroscience, and transformational generative grammar, to show how drawings and paintings have a syntax.

#### Economics

<http://www2.warwick.ac.uk/fac/soc/economics>

**Jonathan Cave** has been developing models related to the economics of both recreational and cognitive-enhancement drugs. This research, conducted with colleagues at the University of York and the Rand Drug Policy Research Centre, considers the neuroscientific (neuroeconomic) aspects of how decisions relating to drug use, progression, recovery, etc. are made. This has implications for both individual choice behaviour (e.g. risk assessment, cognitive framing, habituation, etc.) and for societal impacts (network formation and contagion, social learning and mediation of effects).

#### Institute of Education

<http://www2.warwick.ac.uk/fac/soc/wie/>

**Nick Lee** is an expert advisor to Department of Children, Schools and Families 'Beyond Current Horizons' programme, scoping relations between learning and technology in the medium term future. He is researching pharmacological and technological means of enhancing children's learning with colleagues from Warwick.

**Alan Prout** was Director of ESRC programme on the Future of Childhood. He has written widely on childhood and technological/pharmaceutical developments. He is an expert advisor to DCSF 'Beyond Current Horizons' Programme.

The rich tapestry of neuroscience-related work at the University of Warwick, driven by a deep appreciation of the importance of these disciplines in modern society, together with support from the University at the very highest levels, has created an environment in which Warwick neuroscience can branch out into clinical, social, moral, cultural, philosophical, applied and economic arenas. This will be enormously valuable in both raising the profile of neuroscience at Warwick and in the future development of these initiatives.

## Brain Awareness Week, 2008

During the second week in March earlier this year, many BNA members in a number of fine institutions were involved in creating exciting activities for young and old alike to enjoy that introduced them to the workings of the brain. Below are brief accounts of some of their adventures together. If you are interested in participating next year, then please do contact the European Dana Alliance for the Brain (EDAB) for further advice and information ([edab@which.net](mailto:edab@which.net)).

### Brain Awareness Week in Bristol



Are you in touch with your senses? This year **Sensational Neuroscience** was the theme that linked Bristol's contributions to Brain Awareness Week (BAW), when Bristol's neuroscientists joined forces – together with its newest member, 'SAM' – to talk to the public about the wonderful world of the brain.

Bristol has an extensive and active neuroscience community united by the umbrella organisation 'Bristol Neuroscience' (BN). Coordinated by BN's facilitator Dr Anne Cooke, a team of forty plus students, researchers and professors developed an exciting variety of activities for BAW, all designed to explain some of the complexities of the brain and communicate their passion for neuroscience.

The fun started with 'Science Alive' in Bristol's busy shopping arcade in the centre of town. 'Science Alive' is a two day event organised by the University of Bristol to mark National Science and Engineering Week. The event's director, Kathy Sykes, Professor of Science and Society at the University of Bristol, described how 'Science Alive' enables University researchers to take science to the people of Bristol, giving them first hand experience of "some of the astonishing research that's happening on their doorstep".

The highlight of the neuroscience stand was BN's newest member, SAM, the 'Sensory Anatomical Man'. Perhaps rather rudimentary and unfriendly at first glance, nervous shoppers and children agreed, after encouragement, to shake SAM's hand, watching as this triggered a signal, marked out in lights, travel up his arm and activate his sensory cortex.

SAM, however, had more than one trick up his sleeve. If, instead of simply shaking his hand, you gave his finger a good strong squeeze, he pulled back his hand in response to the 'painful' pinch, demonstrating an automatic withdrawal response – also causing many visitors to give a jump of surprise in turn! SAM's designer Dr Emma Robinson, from Bristol's Department of Physiology and Pharmacology, was delighted with his inaugural

performance and indeed he seemed to get the ultimate seal of approval as 'pretty cool' (male aged 10).

After meeting SAM, there were many other brainy activities to choose from. Taking on the challenge of the Stroop Test – a classic demonstration of inhibition by top-down processing – was very popular. Visitors battled it out to reach top place on the Stoop Test leader board and be in with a chance of winning a squeeze stress brain. Building a neuron from scratch using pipe cleaners proved, as always, to be a brilliant way of explaining the building blocks of the brain. From here, a chance to see the real version under the microscope evoked interest with "wow come and check this out [dad]!" From neurons to anatomical regions – jigsaw puzzles and models of the brain were used to help explain different structures, their associated functions, and how these communicate to help us interact with the world around us.

Stickers stick in the mind as well as on jumpers; specially made BN and BAW stickers, plus pencils and certificates, were given to children to strengthen their memories and the facts learnt from the BN stands. For slightly older and more interested teenagers and adults, further information leaflets and books such as 'It's Mind Boggling' and 'Brain Facts' donated by The Dana Brain Foundation, and BNA's 'Neuroscience – Science of the Brain', were extremely helpful in opening a wider window into brain research.

Having warmed up nicely at *Science Alive*, the 'Sensational Neuroscience' exhibition and team then relocated across town to award-winning 'Explore @t-Bristol' science centre. Here, researchers and SAM spent the week running similar activities, some of them adapted to suit younger minds, introducing neuroscience to well over 2000 of the next generation of potential scientists.

In summary, much fun and brainy facts were on offer during Bristol's BAW, proving a success for visitors and researchers alike. However, at both Science Alive and @t-bristol, it was the

# SCIENCE AND COMMUNICATION



direct contact with 'real scientists' that people seemed to value the most. Teachers commented it was one of the 'best' science events they had attended, 'mainly because of the great interactions between scientists and kids', making a visit to the BN stands 'educational and inspiring'. Reinforcing this message, Dr Anne Cooke commented that, '*Taking brain science to a wider audience is an essential part of being a neuroscientist*' and BAW gives 'researchers the opportunity to 'introduce [people] to the endlessly fascinating science of the brain'.

Indeed, the enthusiasm of all the neuroscientist volunteers was fantastic, and credit should go to all those who helped develop,

organise and take part in both events. We are also very grateful to the Federation of European Neuroscience Societies for their BAW grant, The Dana Alliance for the Brain and BNA for educational materials, and for the support of the University of Bristol's Applied and Integrated Medical Sciences Centre for Excellence in Teaching and Learning (AIMS CETL).

**BN is already cooking up plans for something even bigger and better to mark BAW 2009.... Hope to see you in Bristol next year!**

**By Claire Durant, University of Bristol**

## Brain Awareness Week in Leeds



On Wednesday 12th and Thursday 13th March 2008, the Faculty of Biological Sciences (FBS) at the University of Leeds hosted around one hundred 15-17 year old students from five schools in the Yorkshire region for **Brain Awareness Week**. Each day the visitors followed a similar timetable (a lecture, a demonstration area/lunch, a practical class and a debate to end the day). The visitors were looked after by undergraduate neuroscience students wearing distinctive "I am a brainy guide" pink T-shirts!

On Wednesday, visitors first heard from Professor Brian Robertson who reviewed the history of neuroscience and his contribution to the study of the role of ion channels in the brain. During the demonstration, visitors wandered around a large

number of displays from neuroscientists from FBS, the Faculty of Medicine and Health and St James's Teaching Hospital. After lunch, students attended their chosen practical class which included a nerve conduction velocity experiment where students drew the course of the median nerve on their arm and then stimulated the nerve and recorded EMG activity in the thumb. In other classes, students recorded action potentials from neurones in the snail brain! One group of school students had the rare opportunity to tour a research laboratory which was also

exhibiting the art work of Jim Patterson (Duncan of Jordanstone College of Art and Design, University of Dundee), who has a Wellcome Trust 'People' award in collaboration with Prof Brian Robertson to make artworks around the theme of ion channels important in brain function. To end the day, students attended a lively debate on careers in neuroscience, organised by Dr Susan Deuchars.

On Thursday, visitors started their brain awareness journey by listening to Professor Jim Deuchars talking about the vagus nerve, and hearing the now infamous vagus nerve song.... After the demonstration and lunch session, visitors attended their chosen practical class and then finished their trip with an ethics debate organised by Dr David Lewis.

All of our visitors got a thorough insight into the workings of the brain and the fun of doing science at university. We are grateful to the Federation of European Neuroscience societies for funding the event in conjunction with FBS, University of Leeds. All our visitors also received a number of free gifts, some from FENS and a neuroscience guide generously supplied by the BNA.

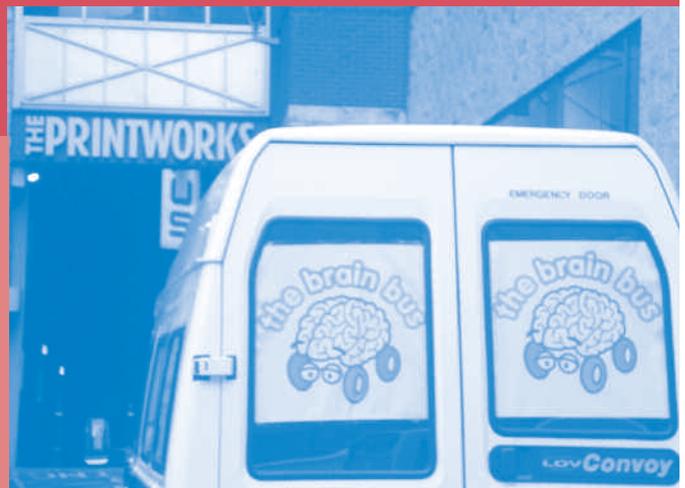
**By Dr Neil Morris, University of Leeds**

## Brain Awareness Week in Manchester



Right  
The Brain Bus visits  
The Printworks in city  
centre Manchester

Left  
Mirror drawing proves  
too easy for these  
passers by at The  
Printworks



Having secured funding from RCUK and The DANA Foundation, Stuart Allan and Ellen Poliakoff set-off round various venues in the Greater Manchester Area on their 'Brain Bus' during Brain Awareness Week 2008.

Seven different venues were visited over a two-day period and people aged 8 through to 88 were engaged with the

various brain-related activities. Twenty young researchers from the University of Manchester helped to crew the Brain Bus at various stages.

Overall the whole project was a great success, with rave reviews from the many participants. Hopefully, therefore, the Brain Bus will ride again in 2009!

## Brain Awareness Week in Newcastle

Susan Aldworth (left) and Fiona LeBeau (right), in front of 'The Self as a Shadow Puppet' series, inspired by their collaboration.



For members of Newcastle's Institute of Neuroscience, Brain Awareness Week not only provides the opportunity to communicate something of our science to members of the public, but also provides the stimulus to get engaged in cross-disciplinary activities outside of our usual line of research. **BAW2008** was no exception.

The first of this year's main events was an exhibition of works by the London-based artist Susan Aldworth held at the Sandford Goudie Gallery in the Customs House, South Shields. Entitled 'Scribing the Soul', the exhibition was the culmination of a year-long collaboration between Susan and neuroscientist Fiona le Beau, whose work on neuronal oscillations provided the inspiration for six new works. Throughout the year, Susan had spent a number of periods in Fiona's laboratory where the study of the neural circuitry underlying intrinsic brain rhythms is investigated using a combination of electrophysiology and imaging techniques. The new views that Susan gained, together with inspiration from their conversations on scientific and perceptual aspects of consciousness, led to the series of new etchings entitled 'The Self as a Shadow Puppet', which were exhibited alongside work from Susan's seven-year journey into neuroscience. Over the five weeks that the exhibition ran, a wide variety of people were able to view the works

and gain a new perspective on the relationship between the brain and what makes us ourselves ('the soul').

The second main event was an interdisciplinary symposium open to the public entitled 'Drawing on Consciousness' that was held in Culture Lab at Newcastle University on Friday, 14th March. Hosted by Culture Lab Director Sally Jane Norman and by Institute of Neuroscience Director, Anya Hurlbert, the symposium brought together about 130 people from the community and university, including fine arts students, physicians, lawyers, musicians, engineers, and philosophers. The theoretical psychologist Nicholas Humphrey (London School of Economics) spoke vividly on the survival benefits of consciousness and the deep pleasure of the 'thick moment' of sensation, a pleasure which resonated throughout the afternoon (1) in poetry reading by text artist, poet and playwright Valerie Laws who challenges the boundaries of science, art and literature, (2) in the perspective drawings of visual artist Richard Talbot,

and (3) in the dialogue between the audience and discussion panelists David Clarke (music theorist), Elaine Perry (a neuropathologist with a deep interest in consciousness and the effects of medicinal plants), and Sinead Murphy (philosopher). Visual images of brain rhythms, fluorescently-dyed neurons, neurosurgical procedures, and kaleidoscopic memories from Susan's exhibition helped the participants to cross the disciplinary divide and understand what consciousness means to others.

The symposium helped to draw out a common understanding of what consciousness is and how it is expressed, and to explore common beliefs about

consciousness as an entity, whether it is physical, psychological, or elusive. As well as these two main events, a public lecture by Mark Lythgoe on the search for Einstein's brain was also scheduled for this week. Unfortunately this was cancelled at the last minute when power failure on the East Coast rail line left Mark stranded for eight hours with dwindling lap top batteries and supplies of refreshment. Perhaps for Mark and his fellow travelers, this also provided a moment to reflect on the way the world can impact on our consciousness. Many thanks Network Rail.

**By Colin Ingram, Institute of Neuroscience, University of Newcastle**

## Brain Awareness Week in Southampton

*Joanne Bailey (far right) with Deji Asuni and Tracy Newman*

In early March this year, a group of enthusiastic volunteers from Southampton University took on the task of promoting neuroscience to the general public, from junior school children to grandparents. Our aim was to strike up a passion for neuroscience in the potential researchers of tomorrow – not a completely straightforward task! For many people, the brain is a mysterious structure that is needed for life and occasionally malfunctions leading to neurodegeneration, such as Alzheimer's or Huntington's Disease.

To promote the brain as an exciting structure that can be studied and understood, we designed various interactive games all with brain related prizes. One game, 'label your own brain cap', used silicon swimming caps with all the major brain regions printed on it; The children had to name each region and describe its function and, in so doing, helped raise their awareness of where each brain region is in their heads. All the answers were available on posters on the surrounding display along with information about what a neuroscientist does and what cells the brain is comprised of.

The diligence and precision with which some of the children labelled their brain hats was outstanding, truly a very motivating sight, but whether they were motivated by the thought of winning a walking brain, a brain mould, or a growing brain I cannot be sure! The hat task also provided much amusement throughout the day as various helpers modelled the hats and helped to promote our cause.

Agarose and jelly brains made from brain moulds were used to illustrate what a whole brain looks like. The agarose brain injected with red food colouring produced a fantastic slimy brain that almost lasted the whole day despite being poked and prodded by small children eager to put their hand all the way through it to see what it feels like.

Manipulating 'play doh' into the shape of either an astrocyte or a neuron proved to be another popular interactive game for the visitors. Children and parents first viewed the cells



under a light microscope before being set the task of moulding the play doh in a Petri dish into one of the two different cell types. I have never seen so many pink, brown, green and blue neurons perfectly sculpted with a myelin sheath encased axon and tiny little sausage roll shaped dendrites! 150 neurons and astrocytes were carefully formed and handed over with great pride to be displayed on the boards behind the stand.

Overall the day was a great success; maximum fun was had by both participants and helpers alike. The children were involved in the tasks and consequently appeared to be really enthused and interested in the function, structure and health of the brain. We hope that some will be inspired to pursue neuroscientific research and help us to progress in our learning and understanding of brain function and dysfunction and tackle the increasing problems of neurodegeneration.

Many thanks all the people that supported and helped to make the day fun, interesting and successful, in particular Tracy Newman, Deji Asuni and Catherine Cowen, and to everyone that helped out on the stand during the day.

**By Joanne Bailey, University of Southampton**

## Publicising the FAST campaign to raise stroke awareness in Southampton City Primary Care Trust



**Suspect a stroke?  
Act FAST. Call 999.**

**F**  
**A**  
**S**  
**T**

**Facial weakness**

Can the person smile? Has their mouth or eye drooped?

**Arm weakness**

Can the person raise both arms?

**Speech problems**

Can the person speak clearly and understand what you say?

**Test all three symptoms**

Stroke is a medical emergency.  
By calling 999 early treatment can be given  
which can prevent further brain damage.

Stroke helpline 0845 3033 108 www.stroke.org.uk



The Stroke Association Rehabilitation Research Centre at the University of Southampton (<http://www.stroke.soton.ac.uk>) holds a five-year programme award (2004-2009) from The Stroke Association. While the main focus of the Centre is research into 'Recovery and Rehabilitation after Stroke', its role also includes finding new and innovative ways to disseminate research findings as well as supporting the work of The Stroke Association by raising stroke awareness.

The current research programme consists of a longitudinal follow-up study and a series of feasibility studies. The longitudinal study evaluates patients after stroke at regular intervals from stroke onset till three years post stroke. Sub-studies include looking at the effect of infection post stroke on outcome, examining levels of activity after stroke through activity monitoring, and evaluating quality of life post stroke by means of a qualitative approach. The feasibility studies explore (1) balance and balance retraining early after stroke, (2) functional electrical stimulation during weight bearing activities, (3) strategies to avoid falls post stroke, and (4) implementation of a self-management programme for people after stroke.

In addition to publishing and presenting research findings, the Centre is also organising a conference with the aim to 'make the evidence work for patients and their families'. The conference aims to make scientific research findings accessible to academics, clinicians and people affected by stroke, by bringing together key people and leading researchers in the field of rehabilitation to present current insights into the rehabilitation of stroke, discuss possible implications for clinical practice, and identify future goals for research: (<http://www.neurorehab2008.soton.ac.uk>)

The Stroke Association Rehabilitation Research Centre was awarded a grant to organise an event during Brain Awareness Week (10th-16th March 2008). The grant was donated by the DANA Foundation (<http://www.dana.org/>) via the Federation of European Neuroscience Societies (<http://fens.mdc-berlin.de/>). It was decided to raise stroke awareness by organising (1) a poster and leaflet campaign to all surgeries within Southampton City PCT and (2) a free information afternoon for members of the public and stroke survivors where

presentations by members of our team would be held on the topic of stroke, stroke prevention, stroke symptoms, and stroke rehabilitation.

To raise stroke awareness, we chose to use the 'Stroke is a Medical Emergency' and FAST campaign developed by The Stroke Association. This campaign was launched on 6 October 2005 and its main aims were (1) to raise awareness of the symptoms of stroke and if you suspect a stroke to call 999 and (2) to improve the emergency response to stroke, by ensuring that diagnosis and treatment happen as quickly as possible. Key messages of the campaign were (1) stroke should be treated as a medical emergency to ensure the best patient outcome, and that healthcare services should be appropriately organised and (financially) supported to ensure that this can happen; (2) you can tell whether someone is having a stroke or Transient Ischemic Attack (TIA) by using **FAST** – **F**ace, **A**rms, **S**peech **T**est; and (3) if you suspect someone is having a stroke, act FAST and call 999. The 'Stroke is a Medical Emergency' campaign has been successful in terms of raising awareness of stroke and the symptoms of stroke, achieving specific policy objectives and driving stroke up the political and health agendas. It won the Healthcare and Medical Research Category at the prestigious UK Charity Awards in 2006.

But what is the scientific value of FAST? 'Does FAST capture enough stroke?' is a question Kleindorfer and colleagues asked in a recent publication in *Stroke* (2007;38:2864-8). They assessed the percentage of stroke/TIA patients identified by the FAST message by examining presenting symptoms of 3498 stroke/TIA patients presented to an emergency department. The FAST message was able to identify a high percentage of stroke and TIA patients (88.9%), although it performed much better for ischemic stroke

(8.9% missed) and TIA (8.2% missed) than for hemorrhagic stroke (30.6% missed).

Kleindorfer et al. also compared the presenting symptoms of the stroke/TIA patients between the FAST message and the 'suddens' symptoms. The 'suddens' is the current public message adopted by the American Heart Association and lists five stroke warning signs; (1) sudden numbness or weakness of the face, arm or leg, especially on one side of the body; (2) sudden confusion, trouble speaking or understanding; (3) sudden trouble seeing in one or both eyes; (4) sudden trouble walking, dizziness, loss of balance or coordination; and (5) sudden, severe headache with no known cause. With the latter more extensive list of symptoms, it should not come as a surprise that of the 3498 stroke/TIA patients, 11.1% had presenting symptoms not included in the FAST message, whereas 0.1% had presenting symptoms not included in the 'suddens'. Of interest is the symptom 'numbness' which is not part of the current FAST message supported by the Stroke Association but included in the original FAST message published by Kothari et al. (*Ann Emerg Med* 1999;33:373-8). Without numbness, the percentage of missed stroke/TIA patients increased significantly from 11.1% to 16.8%.

Successfully raising public awareness of any medical condition which requires emergency services is of course not solely dependent on the sensitivity of the message but must also consider how easy the message can be remembered by the public. With that in mind, the FAST message seems to have a clear advantage over the 'suddens' list of symptoms but this remains to be proven since to the best of our knowledge, no research in this field has been reported. However, based on the study by Kleindorfer et al., including numbness as a sign of stroke in the FAST

message seems favourable as it increases the sensitivity of the instrument significantly. Finally, research could also provide answers as to how the public can be made better aware of the signs and symptoms of stroke. Music seems an innovative way, as the

Massachusetts Department of Health developed an animated video clip for the FAST campaign which can be found on YouTube

(<http://www.youtube.com/watch?v=YHzz2cXBIGk>). Look it up. FAST!

By Dr Geert Verheyden, Roberts Fellow – Neurosciences, University of Southampton, and Dr Dorit Hyndman, Senior Research Fellow, University of Southampton Address for correspondence: [G.Verheyden@soton.ac.uk](mailto:G.Verheyden@soton.ac.uk)



## Pro-Test March On Oxford

Saturday 9th February, 2008

Seeing groups of people marching out on protest is a common sight in large cities. However, many of these groups are campaigning for awareness of plights around the world that it is not always possible to do something about. Not often are such groups marching in the name of science, in the name of something that can progress, be changed and significantly affect the lives of people in Britain and the world over.

**Pro-Test** was founded by Oxford-based Laurie Pycroft, a 16-year-old school leaver, in 2006, as a counteractive group to SPEAK. SPEAK is an animal rights demonstration group that opposes the construction of the new medical research laboratory in Oxford. **Pro-Test** was created to show the opposite view: that animal research is necessary (for now at least) to further advances in medical research, and to protest against the violent approach often used by animal rights protesters using only pacifist methods. True to form, this pacifist attitude was demonstrated fully by **Pro-Test** during their most recent rally on the 9th February, 2008.

This rally, **Pro-Test's** third, was the first to be held for 20 months – the second rally was held in June, 2006, and the month of this most recent rally was on the 2-year anniversary of **Pro-Test's** first. Despite the weather being on **Pro-Test's** side (a beautiful, clear, not-too-cold late winter morning), turnout was not as buoyant as at the first protest (800 turned up to the first **Pro-Test** march), with approximately 200 marchers. Nevertheless, the crowds were cheerful and clearly passionate about the cause. While many signs had been brought by the **Pro-Test** committee to be distributed amongst the supporters, some had brought their own - one particular sign declaring 'walking again thanks to animal research'. Many also bought the supportive custom-made **Pro-Test** t-shirts that were on sale throughout the march at £5 each.

The march began on Broad Street at 12 noon, before moving up Holywell Street to South Parks Road (the location of the new laboratory) and then working back round to Broad Street, finishing at approximately 2pm and including stops for speeches. As well as hearing from people who have directly benefited from animal research, such as Kevin Elliott, a member of the public who is heavily



involved in **Pro-Test**, speeches were also made by the founder of **Pro-Test**, Laurie Pycroft, and the organisation's co-president, Tom Holder. The marchers were also treated to statements from Oxford University and the current government, as well as speeches from scientists such as Tipu Aziz, and politicians such as Evan Harris (Liberal Democrat MP for Oxford West and Abingdon).

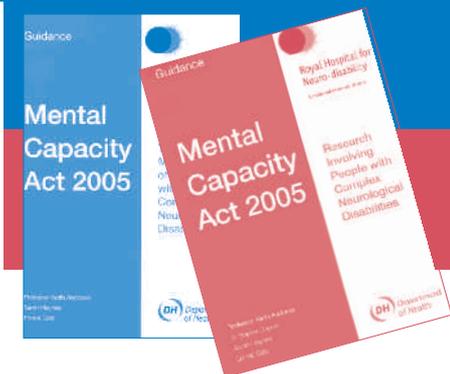
Evan Harris' speech, which took place on Broad Street towards the start of the march, was one of the afternoon's great highlights. Harris gave a coherent, rousing and sincere speech that appealed greatly to the crowd's sensitivities, and he held his own marvellously when his speech was interrupted by the aggressive shouts of a lone animal rights protestor. Harris responded by not only lauding the protestor's right to protest but also by suggesting (half dryly and half sincerely) that the protestor, and anyone sharing his sentiments, obtain a 'Do Not Treat' card, freely available online, declaring that, as someone against medical testing on animals, he was not to receive any treatment that had been formulated in this way, which (as he

pointed out) excludes virtually everything except homeopathy and the laying on of hands.

With the animal rights sympathiser having been escorted away by the police without incident, the march continued in the same cheerful, relaxed and celebratory vein in which it began. With so much having been accomplished by **Pro-Test** since its foundation, the emphasis was more on celebrating what has been achieved so far by researchers, and on support for their continued work. There was also an emphasis on debunking myths perpetrated by animal rights supporters: contrary to popular belief, being **Pro-Test** does not mean not caring about animals. Rather, all of the scientists who spoke at the march spoke of how the treatment of the animals concerned (mostly rodents) is of the utmost concern, and of how animal research also helps animals in terms of veterinary medicine.

While the chants used during the march were only intermittent and relatively makeshift, making for perhaps less of an impact than the organisers had hoped for, the **Pro-Test** supporters were in incredibly good spirits, no doubt fuelled in part by the beautiful sunshine catching Oxford's unmistakable architecture. Finishing at Broad Street again, the band of supporters had by this point drawn several spectators. Overall, despite the lack of attendance as compared to **Pro-Test's** first march, the peaceful nature of the event very much reflected **Pro-Test's** general ethos. This is an ethos that **Pro-Test** continues to move forward with: that, despite the march being over, there is still much to do in terms of school talks, press releases and general support of the work done by researchers and contractors – and, of course, the planning of the next march.

By Bianca Simmons, Lady Margaret Hall, Oxford



## MENTAL CAPACITY ACT – two publications for help and guidance

The Mental Capacity Act was implemented on 1st October, 2007, to cover all decisions made, or actions taken, on behalf of people lacking capacity to make those decisions for themselves.

The Institute of Neuropalliative Rehabilitation, the academic section of the Royal Hospital for Neuro-disability (RHN), has been commissioned by the Department of Health to develop two sets of guidance for the implementation of the act: 'The Management of People with Complex Neurological Disabilities' and 'Research Involving People with Complex Neurological Disabilities'.

The Royal Hospital for Neuro-disability is an independent national medical charity based in Putney, south west London. Much of the hospital's work is in post-acute specialist rehabilitation for adults with complex neurological disabilities incurred through accidents or strokes as well as treatment and long-term care for people with neurodegenerative conditions, including Huntington's disease and multiple sclerosis.

As such, these two sets of guidance have been drawn up based upon the experiences of staff at the RHN and are intended to assist

and encourage further research into the field. Both booklets are seen as comprehensive insights into all the relevant provisions of the Mental Capacity Act and provide practical measures into ways to take forward best practice and research projects.

**The two titles are available for order for £7.50 each from the Institute of Neuropalliative Rehabilitation on 020 8780 4500 ext 5140 or: [institute@rhn.org.uk](mailto:institute@rhn.org.uk).**

## News of latest research on Alzheimer's disease attracts crowd to University conference

Relatives and carers of people with Alzheimer's disease joined charity fundraisers at a one-day conference at the University of Southampton earlier this year to highlight research being carried out into the condition.

They heard talks on laboratory work from Professor Hugh Perry and Dr Amrit Mudher and clinical perspectives from Professors Clive Holmes and James Nicholl. Areas covered included an analysis of how the disease develops, the importance of inflammation in the brain, why fruit flies are used in research, whether a successful vaccine against Alzheimer's is imminent and how common infections can hasten the progress of the condition.

Dr Mudher talked about the work that is being carried out in her and Professor Shepherd's laboratories which attempts to model aspects Alzheimer's Disease and Huntington's Disease in the fruit fly *Drosophila*. Simple model organisms like *Drosophila* enable the study of early pathogenic events that underlie neurodegenerative diseases at the level of single cells. *Drosophila* has been used as a model organism to study various biological processes for the last 70 years and as a result there is a wealth of experimental, and particularly genetic, tools that make it a highly experimentally tractable model organism. The findings from the flies modelling aspects of Alzheimer's Disease flies suggest that neuronal dysfunction (in the form of axonal transport and synaptic defects) precedes the formation of pathological hallmarks or overt neurodegeneration. Current projects are concerned with unravelling the molecular basis of the neuronal dysfunction in these flies, and screening drugs that may ameliorate these

effects and thus have some therapeutic value.

Professor Perry spoke about the effect of peripheral infections on the progression of chronic neurodegeneration in a model of prion disease. His work highlights an interplay between a peripheral inflammatory response perhaps as a consequence of an infection and the chronic innate inflammatory response in the brain. The impact of the systemic inflammation serves to exacerbate the ongoing neurodegenerative processes in this model.

Professor Clive Holmes followed on from Professor Perry and presented results that test Professor Perry's findings in human patients. His data demonstrate that peripheral infections (such as the common cold or flu) in Alzheimer's Disease patients appear to further compromise their cognitive status to a very significant extent. This correlates with the levels of circulating cytokines in these patients' blood after the infection. These findings have important implications for the care of Alzheimer patients and imply that early and effective management of peripheral infections may be critical for the preservation of cognitive abilities during the course of the illness.

Professor James Nicholl finished the session by discussing his work on the clinical trials of a vaccine for Alzheimer's Disease. This vaccine targets Abeta peptide, the building block of amyloid plaques which are one of the hallmarks of this disease. Professor

Nicholl's research shows that vaccination results in almost complete removal of these plaques from the brains of treated Alzheimer's patients. Further investigations have revealed that the removal of plaques is mediated by the phagocytic cells of the brain, the microglia. The current work is geared towards understanding how this treatment influences the cognitive abilities of treated patients.

Professor David Shepherd, Head of the School of Biological Sciences, said the aim of the Neuroscience Information Day was to showcase the comprehensive nature of research underway at Southampton. 'Our work extends all the way from the laboratory bench to the clinic; both scientists and clinicians take part in this research. Much of our work is financed by charities and we wanted to let them know how we are spending the money.'

**By Dr Amrit Mudher, University of Southampton**

*The event was organised with the Alzheimer's Society and the Alzheimer's Research Trust. James Winkworth from the city branch of the Alzheimer's Society said: 'This was an excellent opportunity for people interested in the disease and those directly affected to gain extra knowledge about this very impressive cutting edge research.'*

*Further information about this event including sound clips from each of the presenters can be found on: <http://www.sbs.soton.ac.uk/research/neuroinformationday.php>*

# The Christmas Symposium 2007

at The Royal Society, London, 17th December, 2007

## *The Ageing Brain: from basic mechanisms to public policy*

*The BNA Christmas Symposium of 2007, chaired by Raj Kalaria and Helen Hodges, certainly brought up a topic which all of us will find of personal interest. What happens to our brains as we age? And perhaps more importantly, what can we do about it?*



*Helen Hodges (far right) and Raj Kalaria (second left) with speakers: Peter Coffey, Carol Brayne, Robin Morris, Doug Turnbull and Eric Karan.*

There is one certainty in life, and that is that death will surely come to all of us. We can attempt to change our outer appearance through cosmetic surgery but we have little understanding of what is going on inside us, particularly when it comes to the brain. This symposium brought together leading researchers in the field to try to give us a multi-faceted, holistic approach to dealing with pathologies affecting the brain as it ages.

**Doug Turnbull**, School of Neurology and Psychiatry in Newcastle, started the proceedings by demonstrating that brain ageing, and related disorders, result from a power supply issue. (I know what you're thinking, but the problem here isn't as simple as unplugging the power supply, waiting 30 seconds, and trying again. The problem here is mitochondrial). Turnbull focussed on Parkinson's disease; he told us that between 75 and 84 years of age, the likelihood of suffering from Parkinsonism was 29.5% and this rose to a huge 52.4% in those aged 85 and above. Thus, Parkinson's disease, its mechanism and method of treatment, is of particular interest to over half the population who reach 85 years of age.

Turnbull explained that, in a recent study, mice with defective mitochondrial DNA polymerase showed signs of premature ageing. Through further work using PCR studies, he found that the mutations in mitochondrial DNA increased with age. He explained that age is the major key factor that leads to deficiencies in mitochondria of neurons in the substantia nigra. This then leads to neurological diseases such as Parkinson's and Alzheimer's Diseases. He also reported that exercise, and some of the compounds which can be found in red wine, were a way of 'recharging the batteries.'

**Robin Morris**, Institute of Psychiatry, Kings College London, then switched the focus to Alzheimer's disease. He told us about the changes which occur in the white matter of the brain as we age. He explained that the risk of hypertension increases, and this leads to disruption of white matter structures, which in turn affects our behaviour.

He described the increasing risk of hypertension leading to a disease called Small Vessel Disease (SVD), where the deposits of homogenous glossy hyaline thicken blood vessel walls and leads to leukoaraiosis, or abnormal diffusion of white matter, which has been shown to cause Alzheimer's disease.

Morris conducted a study comparing brain function in Alzheimer's Disease patients versus a group of community volunteers using techniques such as 'trail-making.' Trail-making requires the subject to connect a series of jumbled numbers in the correct order. As the complexity was increased, for instance by introducing a selection of alphabetical letters as obstructive elements, the patients found it very difficult to connect the numbers. This showed the failure of executive function - our ability to think, prioritise and manage our time. In memory tests, however, the patients showed less impairment when compared to the community volunteer controls.

Morris expounded on Diffusion Tensor Imaging (DTI), a technique based on Brownian motion used to measure white matter integrity. The basis of the technique is that the architecture of an axon bundle, surrounded by myelin sheath, usually aligns in a particular direction facilitating the diffusion of water along it. If, however, the bundle of axons is disrupted, the motion of water around the brain area will become isotropic, or of no particular direction. This can be used to indicate tract damage.

There was a particularly interesting question asked by Dr Morris: “What is normal ageing and to what extent is it inherently pathological?” He himself had started research in the field at the humble age of 20 years; and with all due respect, he is no longer of that so tender an age. As he grew older, research findings proliferated, but their significance and relevance diminished. Alas, scientific progress has never been rapid or linear.

The next step would be to conduct longitudinal studies which would help with prediction, treatment and risk measurement of the disease. He further suggested that we need to think about ageing at least by the time of middle age, and strategies for prevention mainly reside in the areas of increasing exercise, improving diet, and cognitive-based training techniques.

**Eric Karan** was the third speaker, visiting us from the pharmaceutical company, Eli Lilly., and sharing with us the development of understanding of Alzheimer’s Disease, from its initial categorisation to what we know now.

Karan explained that, whilst Alzheimer’s disease could be implicated by signs of dementia, of which it is a major cause, definite diagnosis can only be given at post-mortem. An indicator during life is the mini mental-state exam (MMSE) which involves simple questions such as what time it is, the current date and analysing the response to simple instructions. The score achieved gives a sign as to the severity of the disease.

From an anatomical viewpoint, one could see that the hippocampus deteriorates and amyloid plaques develop. The volume of brain tissue depreciates by 2.2% each year; and, concomitantly, the oxygen use of tissues which still remain also decreases. Functional MRI has been key in allowing this type of study.

In our current understanding, there are two major anatomical aspects that are visible in the disease – plaques and tangles. The plaques are formed by aggregation of A $\beta$ 42 protein, an amyloid precursor; the neurofibrillary tangles are caused by *tau* protein, which exists in forms phosphorylated to different degrees. This protein usually binds and unbinds with the cell cytoskeleton and modulates its stability. However, the protein can aggregate abnormally in the hyperphosphorylated disease state

The genetic indication of the disease is the APP gene. When it is present, there is A $\beta$ 42 amyloid plaque development, and 100% penetrance is seen with the gene. However tau protein related tangles are always present. The relationship between plaques and tangles and their specific/relative contribution to Alzheimer’s disease is still a mystery.

Another confusing matter is that there are mice models with brains inundated with such plaques and yet they show no signs of Alzheimer’s disease. Apolipoprotein E (APOE) isoforms which interact with the A $\beta$ 42 protein are currently in development in search of treatment.

The treatments which have been tried include acetylcholinesterase (AChE) inhibitors such as rivastigmine and donepezil, but these only have temporary benefits. As

drug potency increases, side effects become more pronounced. NMDA receptor antagonists such as Ebixa (mentanin) have also been used.

Karan explained that the ideal approach would be multi-therapeutic, dealing with the disease appropriately at different stages. Through the pathogenesis and induction of the disease, there would be the first stage of intervention which would try to delay the onset of the disease. Then, as symptoms were detected, there would be symptomatic treatment to alleviate and modulate the problems associated with the disease. As the disease progresses further, risk tolerance for measures of intervention increases greatly and, therefore, patients and their families are willing to undertake treatments which have greater risk associated with them.

Current research revolves around antibody studies for treatment of CNS diseases; anti-inflammatory drugs such as Flurizon have been implicated and undergoing further study.

**Professor Ian Philp**, the National Director for Older People, was the next speaker, and he propounded a fresh, proactive approach towards helping older people. His top tips were three: dance (stay active), get a dog (communicate), and go to church (interact with people). All of these are forms of positive neural stimulation and so, of course, you might have your own way of doing these, say, playing badminton, getting a cat, and going to the mosque.

Professor Philp highlighted the importance of uniting policy and practice in dealing with ‘frailty’. He went on to correct the three myths that the government don’t care, that nothing can be done, and that we don’t need specialists. The NHS spends £42 billion on older people and £8 billion of that is on social care. Yes, he agrees, ‘its not rocket science’, it’s actually far more complex!

We need to recognise the problems before diagnosing with a disease label. Our workforce is not skilled to deal with the issues that face people with dementia, most assistants have only three days of training.

Professor Philp took us through the development of problems in three stages and what the service response should be to them. First, the general population should be helped with partnerships for health and well-being. At the second level, as early problems such as a single age-related conditions develop, our primary health services, social care and specialist support should intervene. Then, at the third level, as needs become more complex, a multi-disciplinary specialist approach would be best to help sufferers maintain comprehensive control of all aspects of their lifestyle. It is important to appreciate that being able to maintain good health, independence, general well-being and not being a burden on anyone is key to our satisfaction.

The five key ingredients for a health service re-design would be: 1) early intervention after incidents of falling, confusion, feet problems, reports of poor visibility etc; 2) streaming to specialist care; 3) early supported discharge rather than trying to sort everything in hospital; 4) multidisciplinary

assessment; 5) partnership and integration with the community as a whole including improved housing and family connection.

Such major changes would not be disproportionate in attempting to cope with what has been described as one of the greatest challenges of science.

**Peter Coffey - Director, The London Project to Cure Blindness** - then introduced a new area to the discussion, he talked about vision as a major biological marker of ageing. The focus of his talk was age-related macular degeneration (AMD). AMD is a pathology which affects 25% of people over the age of 60. The major problem, from which the name is derived, is the deterioration of the macula, an area in the fovea which contains the highest concentration of rods and cones in the eye. This results in loss and/or distortion of vision, symptoms might include, for instance, deformed writing. Common procedure used to detect AMD is Amsler's chart. This consists of a straight line grid with a central black dot. The patients are asked to concentrate on the black dot and then describe or draw what they perceive to be the lines of the grid. Whilst a person with normal vision would see a straight line grid, people suffering from AMD describe or show distorted lines due to the disruption to their vision.

There are two types of AMD - dry AMD and wet AMD. Dry AMD is most common, accounting for 90% of cases, and results from fatty deposits lying between the neural cells and photoreceptor cells in the retina. These are highly disruptive once they encroach on the macula region. Wet AMD occurs in the remaining 10% of cases, and results from bleeding of blood vessels in the eye. The retinal pigment epithelial cells (RPE) are affected and many of the photoreceptors in the region die.

The London Project is exploring transplantation of patients' own peripheral retinal cells (from the lower visual field). These cells are taken and slipped under the neural retina. The eye is allowed to return to function, held in place using heavy eye oil which is later removed. This operation takes 2-3 hours and has three stages and is, therefore, not feasible globally on the scale that it is required. The whole macula with a diameter of about 1.5mm cannot be covered as it would require too much of the patients' cells.

Other options under investigation include using embryonic stem cells. Corneal-linked stem cells have already been used for acid burns, and even those from mice embryos worked.

The technique of developing cells for usage requires only 3 stem cell lines (i.e. not endless amounts needed). Embryonic stem cells, when left, spontaneously pigment to become the RPE cells that are needed. This resulted in a rather unusual discovery - after throwing away the cells for four years thinking that they were becoming contaminated, the lab came to realise they were becoming the very cells they were trying to develop!

Human embryonic stem cell-derived (hESC-derived) RPE cells are encouraged to pigment by melanosomes, and they themselves usually phagocytose debris in their normal form.

Introduction into the AMD patient's eye could help with treatment. The photoreceptors might also be hESC-derived and it is also possible to develop these from the RPE cells. Furthermore, Vitamin A treatment of RPE cells causes neuralisation to opsins and rhodopsins which form the basis of the neural retina.

Our final guest was **Professor Carol Brayne, Public Health Medicine at Cambridge University**, who spoke about the epidemiology and policy that surrounded the matters of the ageing brain. She described to us the MRC study that had been started in the early 1991-2001 by her group. From their findings, they hoped to find the distribution and determinants of disease and health in the UK population.

The study was novel in that it looked at health issues from a public perspective - the effects of differences in personality, education and social class. Improved education seemed to increase the risk of disease by only 6%, and similarly social class seemed to bear little risk. The key factor when discussing social class is that those of a higher social class, with arguably healthier diet and lifestyle, generally live longer and are, therefore, more likely to reach an age when dementia and other such illnesses might affect them. Interestingly, those who reported themselves in poor health had 3.9 times more risk of having Alzheimer's disease, but perhaps this reflects the effect of a negative resolve more than quality of healthcare. The study also highlighted the way in which men and women were affected differently. Women generally lived longer with disease compared to men, 4.6 years and 4.1 years respectively.

One of the tests used in the study was the GMS, or geriatric mental state examination. The key focus of the test is for the people to self-rate their health, to self-report physical health, whilst comparing this to their actual medical record. Although the statistics were of limited value (for instance, the number of participants fell from 13,000 to 3,000 during the time period), there was still no doubt of the usefulness of the study. Perhaps the drop out rate highlights the importance of the study itself, because this was most likely due to the effects of frailty. Professor Brayne reported that 700,000 people live with dementia in the UK, with an average of 168,000 new cases per year.

Comparison with other countries is very difficult, especially as the life expectancy is often lower than the major onset of dementia, at around 85 years. None the less, such population studies allow us to make reasoned predictions for the situation in coming years and allow a medium by which to evaluate current policy and determine future policy.

And as we leave the symposium, we should all go away with a message. I certainly went away inspired for the future, with a better understanding of the need to make a difference with science. Age-related diseases are complex, nothing is yet certain, there is a lot to be determined, and yet there is always hope for a cure. Ringing in my ear is the need for social inclusion, and that, whilst we wait to find a cure for a disease, we can at least improve the lifestyle of the frail elderly by showing them respect and practical assistance.

**By Tausif Hussaini, PhD student, University of Bristol**

## Encephalitis – the broader spectrum: rare forms of encephalitis

22 January, 2008, London

The Encephalitis Society started out 15 years ago as a fairly modest support group in response to the very limited help available for people, and their families, who had been affected by encephalitis. Since then, it has expanded its activities very substantially and is the only resource of its kind in the world, providing evidence-based information, education and support services. The Society has also supported and funded a number of research studies and is currently involved in a large scale collaborative study of the outcome of encephalitis with the University of York. The society organizes an annual seminar, which this year had as its topic some of the less familiar varieties of encephalitis.

Professor Tom Solomon from the new Liverpool Brain Infections Group ([www.liv.ac/braininfections](http://www.liv.ac/braininfections)) opened the meeting with a presentation on *Encephalitis in the Global Village*, which highlighted the threat of emerging viruses. He has worked extensively on Japanese encephalitis in Vietnam and, although still a rarity in the UK, this is actually one of the more important brain infections on a worldwide scale. There are anything from 35,000 to 50,000 cases each year with a 30% mortality and 30% of survivors left with significant neurological sequelae.

It has a varied neurological profile which, as well the more familiar features of encephalitis, such as fever, headache, confusion, seizures, raised ICP and coma, may involve acute movement disorders with Parkinsonian mask-like faces, orofacial dyskinesias, choreoathetosis, rigidity and tremor. The Japanese encephalitis virus can also attack anterior horn cells, leading to presentation with a polio-like ascending flaccid paralysis. Dengue is another mosquito borne flavivirus which can cross the blood-brain barrier to produce an encephalitic illness in a proportion of infected patients. Human enterovirus 71 (HEV71) was isolated from the stool of a child with encephalitis in California in 1969. After sporadic cases and small outbreaks of HEV71 infection worldwide in the 1970s and 1980s, there was a large and severe outbreak in Sarawak in 1997 with 34 deaths in 2628 reported cases. Neurological involvement included aseptic meningitis, encephalitis and acute flaccid paralysis. Since then there have been further outbreaks in Southeast Asia and Australia.

Although these illnesses have tended to be viewed in this country as exotic rarities, the ease and speed of international travel and the effects of climate change are making awareness of them increasingly relevant – a reality brought home by the appearance of West Nile fever in New York City.

*Fungal infections of the CNS* are mostly familiar to us in the UK as something seen in on a relatively small scale in immunocompromised patients. However, as Dr William Hope, Infectious Diseases Physician and Senior Research Fellow, The University of Manchester emphasized, they actually represent a major problem from a global perspective. *Cryptococcus neoformans* is a leading cause of AIDS-related deaths in sub-Saharan Africa and *Aspergillus* is a major source of morbidity and mortality in immunocompromised patients, with an associated mortality of 40-50%. The expenditure on antifungal drugs worldwide is astronomical – billions of dollars – and rising. Dr Hope's presentation emphasized that the key to understanding

the pathological process in cerebral aspergillosis is the recognition that *Aspergillus* is angiotropic and angioinvasive. He also reviewed the under-recognized but quite common condition of neonatal haematogenous candida meningoencephalitis, in which there is widespread involvement of the CNS with *Candida*.

The second theme of the meeting was the role of the immune system in the pathogenesis of encephalitis. Oxford has been a leading centre in the characterization of *voltage gated potassium channel antibody encephalitis* and Professor Angela Vincent from the Weatherall Institute of Molecular Medicine reviewed the work of their group. VGKC antibody-associated limbic encephalitis occurs in both men and women. It is an adult-onset condition seen in people from 30 to over 70 years of age, with an acute or subacute onset of memory loss, seizures, personality change and occasionally more florid psychotic features, with high signal in the hippocampi on MRI. Associated malignancies are uncommon and immunological treatments with intravenous immunoglobulins and steroids may produce significant clinical improvement. What was particularly interesting is that this seems to be an expanding phenotype. VGKC antibodies may be linked predominantly to seizures or atypical psychosis occurring in isolation, with some indication that immunosuppressive treatment may be helpful. There has been a suggestion that a proportion of patients with adult onset temporal lobe seizures with hippocampal sclerosis may actually have a history of a previous encephalitic illness with evolving MRI changes, raising the possibility that untreated limbic encephalitis may be a causative factor in some cases. So what started out as something of a relatively small print curiosity, may turn out to have much broader implications for epileptology and neuropsychiatry.

Dr Ian Hart, Consultant in Neurology and Neuroimmunology from the Walton Centre in Liverpool, developed the theme of *autoimmune encephalitides*, dealing with Hashimoto's encephalitis, Rasmussen's encephalitis and paraneoplastic encephalitis.

He emphasized the practical clinical point that, while these are all rare conditions, they are not that rare and need to be remembered in the differential diagnosis. Looking for antibodies in the blood is useful and can help make the diagnosis. They need to be thought of sooner rather than later, since immune treatments may be helpful in individual patients if they can be started early enough, before brain cell death and permanent disability has developed.

The meeting ended with a fascinating presentation from Professor Gavin Giovannoni from Barts and the London on *Encephalitis Lethargica*, which in contemporary neurology is defined as an acute or sub-acute encephalitis with at least three of the constellation of basal ganglia involvement, oculogyric crises, ophthalmoplegia, obsessive-compulsive behaviour, akinetic mutism, central respiratory irregularities and somnolence or inversion of the sleep-waking cycle. There is evidence of an inflammatory process in the basal ganglia, brainstem and hypothalamus and it looks like it may be one of a spectrum of autoimmune CNS disorders, characterised by anti-basal ganglia antibodies associated with recent streptococcal infection.

The encouraging message from this seminar is that the future for encephalitis research in the UK looks bright, with the very active involvement of several different research groups of international standing. It's doubly encouraging that the Encephalitis Society is able to convene meetings like this one, to make sure that the practical benefits from this new knowledge will reach a wide audience as quickly as possible, helping improve the care of people with encephalitis both in this country and on a more global scale.

By Dr Steve White and Ava Easton, Encephalitis Society

## Dangerous sports: boxing clever?

11th March, at The Dana  
Centre, London, SW7

*A public café-bar discussion, chaired by Gaetan Lee (Science Museum), and involving Mark Burford (Cityboxer, London), Peter Dangerfield (ring-side medic, University of Liverpool), Mike Loosemore (English Institute of Sport) and Daniel Sokol (medical ethicist, St George's Hospital, London). Yvonne Allen describes the evening.*

Call me an 'old softie' if you want (and many do), but I always thought there was something distinctly unsavoury about placing men in a roped enclosure and watching them bash each other about until one collapses, either with exhaustion or severe concussion. And this in the name of 'sport'? However, despite bristling with prejudice, I tried to go with an open mind and a sense of curiosity (one always does) to the Dana Centre last March, prepared at least to finish the evening better informed and less bigoted than when I arrived (one always is).

So, imagine, here I am, glass of merlot in one hand, bag of Tyrell crisps in the other (for, yes, it is that kind of establishment), waiting to be convinced or otherwise that boxing is a noble sport and that the BMA is up its own...err...nether regions in wanting it banned.

The evening begins with the speakers introducing their professional interest in the sport and stance they are coming from. From this, it is clear, perhaps a little disappointingly, that we are not going to have much of a punch-up here tonight as they were all supportive of the sport continuing (though for different reasons). It also became apparent that amateur and professional boxing are two different 'animals'; the amateur game is highly regulated, has fewer rounds and heads are protected – the emphasis being as much on skilful defence as much as aggressive attack. Conversely, all conceded that the professional game is much more overtly aggressive, the end-point being ideally a 'knock-out', the opponent falling 'punch-drunk' and (invariably) bleeding in an exhausted heap, for matches can be anything up to 15 rounds. Moreover, the professional game can be infiltrated by rather unscrupulous 'promoters', and the stakes are indeed high, with huge sums of money lost or won in such a short space of time. It is little wonder the mafia took – and still do take – quite an interest.

But let's return to the point: is boxing clever? On the positive side, we are told that boxing is a great work-out. You have to exercise virtually every muscle in your body so the health benefits from this extreme cardiovascular experience are immense. Moreover, the sport is classless and cheap, anyone can join in. Indeed, youngsters who are failing in the academic stakes can gain high esteem for their prowess in the ring instead. The sport is very fair, for opponents are carefully matched for weight, size and skill, and it is highly regulated – witness the proverbial attention of the medical profession at the ringside and beyond. Finally, it is claimed that boxing can channel aggression away from the streets. Indeed, many boxers insist the sport 'rescued' them from a life of crime though, statistically, this is hard to verify, of course, and is largely anecdotal.

Fine then. The sport seems healthy, clean, safe, fair, noble and socially responsible, so why on earth is the BMA trying to ban it? The BMA, of course, is concerned medically with the long-term brain damage of repeated blows to the head, and there are certainly some high-profile examples (Mohammed Ali, for one) that would support their case. However, the panel

were adamant that boxing injuries are far less common than other sports (such as rugby, horse-riding, skiing, racing – the list goes on) and there are virtually no fatalities (at least in the amateur game). So the medical case grows weaker and more suspect. We are only then left with the *moral* case instead: can it be right that men can be encouraged to punch themselves silly egged on by a baying crowd? How can this sit comfortably in a society where GBH is a criminal offence and smacking children is wrong? OK, conceded, other sports are more dangerous. But in no other sport is there the actual *intent* to do harm, is there?

Not surprisingly, at this point, the discussion moved on to women, children and old people. Many in the audience (and some of the panel now) did have more difficulty with the concept of women fighting, though no-one was prepared to suggest it should be specifically banned – no-one dared! The age constraints of 11-34 years for the amateur and professional game alike virtually deny the middle-aged to elderly and the very young from participating, so we can be ageist but not sexist, it seems. But there are more reasons, of course, why these groups are more vulnerable. Brain injury can be exacerbated in older brains because sub-dural spaces are wider, making vessels more vulnerable to rupture, for instance; the older brain is also more sensitive to dehydration; and women should have pregnancy tests before fighting, it was suggested, because of potential risks to the unborn child. It was generally agreed, however, that the risks were low and that the danger of developing breast cancer from blows to the chest (yes, really!) was a bit of a myth.

At this point, it was a member of the audience who now moved the discussion on to white collar or 'city boxing', as it's called, an activity that first emerged among the professional classes in New York City, and was originally designed to alleviate stress of a lunchtime. Relatively new and far less regulated, it was not surprising that the panel were a little more uneasy about its existence alongside its long-established mentor.

Finally, out of interest, someone asked if there had ever been any precedent for banning boxing in other countries. Yes, was the answer, most notably Sweden, but it was re-introduced there in the 1980s after careful consideration of the physical risks that were, eventually, agreed to be minimal.

And so the evening drew to a close, and I was left much wiser and a little less condemning of boxing as a sport. I now understood the clear distinction between the amateur and the professional game, I was more convinced that boxing is no more dangerous than a bout on the rugby field, and I had been persuaded that it has a useful social role to play, especially for those unable to aspire to greater things in other ways. Its participants, often less educated and articulate than the mighty intellectuals of the BMA, are clearly disadvantaged when arguing their case. No fair contest then – unlike a bout of boxing (ha!).

## The Art-Science Divide – where does brain science fit in?

Whitworth Gallery, Manchester,  
16 April 2008



Lizzie Burns enthuses the 'Brain Modellers'.



From left: Erinma Ochu, Graham Collingridge, Nancy Rothwell and Mark Lythgoe.

Earlier this year, the BNA was successful in acquiring funding from EDAB and the MRC to host a public event that would address a topical issue in neuroscience. The BNA had decided that it was time to re-examine the 'two cultures' - art and science - to see if some common ground could be found. Expounding their views were Dr Mark Lythgoe, Professor Dame Nancy Rothwell, Dr Erinma Ochu and Dr Lizzie Burns. The result was a lively debate, chaired by Graham Collingridge, that revealed opinions are still as diverse as ever. But it was certainly a fun event, finishing yet again with a touch of creative brain modelling, as always a most enjoyable finale. Nell Barrie describes the evening's talks below.

This event centred around the art-science divide. Each speaker gave a 15-minute presentation on their view of the divide, and after each talk the audience was invited to ask their own questions. After the talks Dr Lizzie Burns, led a brain modelling workshop which demonstrated just how successfully art and science can be combined.

The event was very popular, with around 70 guests attending. Around half of this number stayed for the brain modelling workshop. The atmosphere was fun and informal and guests were enthusiastic in asking questions and participating in the brain modelling.

### Dr Mark Lythgoe

Mark introduced the original CP Snow lecture that first described the "two cultures" of art and science. He believes there is a divide between art and science, but posed the question of whether the difference is as great now as it was when Snow gave his famous lecture in 1959.

He then took a light-hearted look at one key difference between artists and scientists – dress sense! Mark pointed out that the clothes worn by students in the art department of a university are obviously different from those you'll see in the engineering department.

He suggested that perhaps the difference is down to a tendency for scientists to be more *systemising*, while artists are more *empathising*. A typical "systemiser" will tend to be driven to understand systems, for example being fascinated with how machines work. On the other hand, artists tend to be more empathising, driven to understand other people's thoughts and emotions. He suggested that people may in

fact be born with these predispositions. However, Mark bucks the trend himself because he feels that, although he's a scientist, he's an empathiser at heart.

Mark finished by saying that while he does believe there are some differences between a typical "arts person" and a typical "science person", it is these different kinds of people that work together to enable society to create new ideas.

### Professor Dame Nancy Rothwell

Nancy began her talk by saying that she is worried by the way the education system in the UK divides students into artists or scientists. She explained that she believes it's better to have a mix of systemisers and empathisers in all disciplines. She traced the art-science divide back to the formation of the Royal Society in 1660. The Society made a distinction between nature and what it called the "colours of rhetoric", meaning that the way nature is described and portrayed can sometimes mask the true facts.

Nancy went on to look at the differences between science and art. While science is based on hypotheses and evidence, art is perhaps less rigorous, she argued. But she also pointed out that some scientists don't like this rigour, quoting T.H. Huxley's opinion that the "tragedy of science" is "the slaying of a beautiful hypothesis by an ugly fact".

She argued that although there are differences between art and science, there will always be an overlap. Some disciplines combine the two – for example, music is an art but is very mathematical, and archaeology and choreography also combine artistic and scientific skills. She pointed out that many Nobel-prize winning scientists have emphasised the importance of creativity and inspiration in their work, and quoted David Lloyd George: "you can't cross a chasm in two small jumps", demonstrating that great leaps in scientific knowledge rely on creativity.

She said that scientists shouldn't be portrayed as *uncool nerds*. This is dangerous because it will drive people away from science, and gives an unfair picture of what science and scientists are really like. But she also ended by saying she believes it's vital for scientists to think broadly.