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Our Christmas Symposium held at the Royal Society was, as always, well attended and very enjoyable. In addition to the wonderful science offered to us by an impressive line-up of speakers, the audience was also treated to a very striking illustration of how research can be translated into effective treatments for the devastating conditions that affect the nervous system. Mike Robins, the recipient of the BNA Award for Public Service, gave a dramatic and personal demonstration of how deep brain stimulation is alleviating the symptoms of his Parkinson’s disease. Mike made the point vividly that successfully translating research through to treatment can have a profound impact on the quality of people’s lives.

As we highlighted in the previous Bulletin, translational research is being promoted by the Wellcome Trust, through their newly initiated Masterclasses in Clinical Neuroscience. At that stage it was difficult to predict what the level of interest in running these courses from basic and clinical scientists would be. However, it was clear from the response to the first call that there is a lot of enthusiasm for the scheme, with considerable interest in having BNA as the partner learned society. Proposals were submitted for a number of different clinical conditions including motor neuron disease, stroke, traumatic brain injury and autism. We look forward to supporting the first round of Masterclasses and hope that the scheme will continue in order to enhance interactions between basic scientists and clinicians in a wide variety of clinical conditions.

By the time this Bulletin is published our National Meeting will be almost upon us. The core of the meeting is, of course, the extensive scientific programme of plenary lectures, symposia and poster viewing which the programme committee hopes will cover the interests of the majority of BNA members. However, there is a series of special events that should appeal to those also interested in the other activities the BNA aims to promote, including neuroscience teaching, winning grants and career paths for junior scientists. The Public Awareness of Science Group will host a café-bar discussion chaired by the Radio 4 presenter, Quentin Cooper. At the last national meeting in Brighton, the café-bar forum proved to be a great way of promoting lively debate while relaxing with a drink after a day at the meeting. Another special event has been organised to commemorate the 10th anniversary of European Dana Alliance for the Brain (EDAB) and will include discussions between neuroscientists and artists about how the two can interact. No doubt the free wine will help these discussions get under way. A free lunch should also be an added incentive to attend the AGM during the meeting and members are encouraged to come along if they have views about the BNA they wish to air. If you haven’t already registered for the meeting, you can always come along to Harrogate and do it on site.

I will be stepping down from the BNA Committee at the Harrogate meeting and this is my final contribution to the Bulletin. It has been a fun being on the BNA committee and I would like to thank past and present colleagues for making it one of the few committee meetings I actually looked forward to. I am delighted to hand over the tasks of introducing this wonderful publication and reporting on various BNA activities, to Colin Ingram, our new Honorary Secretary.

Dates for your diary: BNA events 2007

- **1st – 4th April, 2007:** 19th National Meeting, International Centre, Harrogate, North Yorkshire, in association with Neuroscience Ireland
- **9th May, 2007:** One Day BNA-Promemoria Symposium and Workshop: Functional Cellular Neuroimaging and Microscopy, at The Open University, Milton Keynes
- **27th June, 2007:** Controversial Issues in Neuroscience: Talking therapies – all in the mind?, a café-bar discussion at The Dana Centre, London, SW7
- **13th – 17th July, 2007:** IBRO World Congress, Melbourne, Australia
- **4th – 8th September, 2007:** 8th European Meeting on Glial Cells in Health and Disease, at Imperial College, London
- **26th September, 2007:** Controversial Issues in Neuroscience: Mind wars, a café-bar discussion at The Dana Centre, London, SW7
- **17th October, 2007:** One Day Symposium: ‘Bench to bedside in acute stroke: ‘Finding our way’ or ‘Lost in translation’?. University of Edinburgh
- **12th December, 2007:** The Christmas Symposium, at The Royal Society, London, NW1

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:** 1st June 2007

The BNA Bulletin is produced by Yvonne Allen in the BNA Conference Office, with assistance from Adam Koppel.

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

Bulleted Editor, BNA Conference Office, The Sherrington Buildings, Ashton Street, Liverpool L69 3GE

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

The British Neuroscience Association is registered as a charity (1103852) and as a charitable company (4307833)  ISSN 1475-8679
I’m actually not attending school at the moment – I’m taking some time out to get some real-world work experience and to concentrate on working with Pro-Test.

You have clearly mobilised much support for animal research. Do you feel satisfied? Is there more you would like to achieve? Is there an ‘end-point’ to your campaign?

I’m very glad with all that Pro-Test and other advocacy groups have achieved over the last year in the animal research debate, and I just hope that we are able to carry on spreading the truth. I don’t think that there is a real end-point where Pro-Test is concerned, but eventually I do hope to take a more hands-off role, so that I can engage in advocacy of other issues.

Do you have any regrets? How are you coping with the abuse from those opposed to your views? Has your family been involved too? Are they supportive?

I have no regrets, and the few offensive e-mails that I do get really don’t bother me. My family were initially quite worried about possible reprimals, but they’ve always been very supportive, and we all feel a lot safer now.

Is there anything you would like to say to BNA members in particular? How can the BNA help you?

I’d like to thank the BNA’s members for improving the health of this country in spite of not being given the respect and pay that they deserve, and I’d especially like to thank all the nurses who attended both our demonstrations. Currently, we don’t have any specific plans that we need help with, but please do keep supporting us, and if you wish to make a donation (always very appreciated) then please go to our website (www.pro-test.org.uk).

Good science communication is a collaboration, not a battle between press and academia. And researchers find that using the media gains wider recognition for their academic work, which in turn leads to international awareness, better research links with other international institutions, and ultimately gets them access to grant funding and collaborations.

Putting a Factor 45 sunblock on your baby’s skin when you finally get time for that much needed holiday in the sun seems a sensible precaution. But you may not know that you are probably using nanotechnology, and the cream may contain tiny mirror particles so small that they could pass straight into your child’s skin cells, with all sorts of unknown future health implications. If you feed processed and pre-prepared baby foods to your infant, do you check to see whether it contains genetically modified soya extracts, or possibly dangerous pesticide residues? And if you do check the labels and sources of these products, do you understand the science enough to know what risks you are taking with your child’s health?

I’d expect neuroscientists and other readers of BNA Bulletin to understand medical risks, pressure group hype, and the limited conventions of newspaper reporting well enough to make informed decisions about these types of concerns. But does the public have sufficient information? And do the politicians and grant bodies who decide on the funding and other resources which will allow effective neuroscience research to continue in the NHS and at academic institutions in the UK in the future understand your current problems and needs?

Of course, if you are a sophisticated reader of tabloids, our national daily newspapers, you will understand the convention of the question mark in my title. Apart from its apparent mission to test readers’ comprehension of English, it can contain vital information affecting our future lives and divide it into either cancer causing or curing, the Daily Mail has made one other great contribution to scientific debate – the question mark headline.

When a scientist writes ‘Does eating hedgehogs prevent migraines?’ then the answer is usually ‘Yes, our study seems to indicate so.’ But when the Daily Mail writes a headline such as ‘Is breakfast tea the cure for cancer?’ you can bet that the answer is ‘No’. Otherwise the headline would read ‘Tea is the cure for cancer’. I am indebted to my friend, former Mail writer and current Daily Telegraph consumer affairs editor, David Demens, for this succinct analysis and indicator of the completely diacritic gulf between ordinary public readers and the scientific community.

So is neuroscience likely to become as controversial as stem cell research or GM foods in the near future? – No, probably not. But are your future medical advances in our understanding of drug and alcohol addiction, amnesia, Parkinson’s and obesity likely to be misinterpreted by the public, media and alternative medical practitioners? – Yes, very likely.

So what can we do to make sure that the public (and funding bodies, concerned relatives, nurses, government ministers and all the other meddlers and legitimate tax paying members of our society) understand the implications of scientific research so clearly and so accessibly that neuroscience gets the credit and support it so obviously deserves and needs?

Public mistrust has driven an explosion in scientists’ efforts to communicate their work in the last twenty years, along with a hunger from the public, industry and government to understand them. If we, the taxpayers, are paying for the work, then we have a right to know what is being done in our names.

Our physicists, chemists, biologists and other science experts have had to learn to communicate better if they are not to lose even more public confidence, faced with outrage and protest from pressure groups and the public over health scares, pollution and personal safety issues. Newspapers, radio and television have also had to find journalists who can understand and interpret jargon and the highly technical reports which often contain key findings. You might expect that government and industry would resist any attempts to make the scientists’ work understandable, especially since investors and decision makers are a focus of the pressure groups’ anger. However, British and European politicians and senior scientists have realised that, if society is to benefit from new types of jobs and ways of working using mobile telephones, the internet and all the other modern technologies, and gain the full benefits which science, technology and medicine can deliver for society, then people need to understand science better.

Which means engaging us in dialogue, not simply telling us after decisions have been made.

At the same time, businesses and industry have realised that, if they want shareholder confidence,
Another New Year has arrived. I hope that it brings you all the important things you seek and few of those that you do not.

From a political point of view I fear that the latter will not be true. The discussions about the future of the RA have now reached a critical point. The momentum towards the proposal of abolition of peer review panels and the introduction of a metrics-only-based RA continues. This change is supported strongly by many of your employers! External to Government, the main supporters of the metrics only approach are University Vice-Chancellors and The Academy of Medical Sciences. All other “academies”, including The Royal Society, The Royal College of Chemistry, The Institutes of Physics and Biology, and – of course – The Biosciences Federation are strongly opposed to the abolition of peer review panels. We want these panels maintained and we want them informed by robust metrics including those relating to output.

The main argument for change is to reduce costs – including those costs associated with time. We agree that strenuous attempts should be made to implement clear and substantial reductions in the bureaucracy associated with the RA and believe that this is one of the most important contributions that can be made to improve the evaluation of the quality of the data fed into the formula.

‘The BSF holds the view that it is potentially dangerous to rely on an algorithm for activity as critically important as the RA. We think it essential that there is some wise evaluation of the quality of the data fed into the formula.’

Second, because the BSF thinks that a metrics-based formula approach will disadvantage some areas of the Biosciences. We are particularly concerned about those sorts of disciplines where research is truly excellent but grant income is low and outputs may be relatively sporadic.

Research in Systematics is an example where these anxieties are relevant.

Third, and following from the previous point, the BSF thinks it likely that Vice-Chancellors will inevitably move to support the proposals of the Biosciences Federation most suited to whatever algorithm that emerges. These areas will, of course, “do well”.

And finally, and personally, because I have had too many computer generated, non-existent Bank managers based on incorrect information or a “mistake”. I have always managed to receive an appropriate level of charges reimbursed. I doubt that you will get (many) apologies out of the RA!

What can you do about this situation? Well, of course you can continue to support the BSF and I would welcome your ideas about how costs can be reduced effectively and peer review panels maintained. Some of you could also start an interesting discussion with your employer!

There are quite a few issues emerging that will have an effect on your professional lives. By the time that you read this, I will have met with a Task Group of our Fellows on the response to a paper published by the Research Councils on Peer Review and our response will be on our web site. If you haven’t seen the Research Councils’ proposals, you might like to download rucuk.ac.uk/research/peer/efficicien ypp.htm . I don’t wish to prejudice our response to these proposals, but I am 100% confident that we will not be 100% supportive – and nor will you!

I am anticipating a busy year. However, I want all the activity to be reactive. A proactive position, taken at the right time, can often be more influential than “fire fighting”. Ideally, I or Jaspal or one of the issues where we should trigger debate to come from the Member Organisations. If you have thoughts or ideas that you want to address in the next year or so please let us have them via your Council.

We are quite pleased by the number of “hits” our jobs link page received during 2006. You may remember that this was a new initiative for us and is aimed to provide a resource for postdocs. I write “quite pleased” because we are fully aware that all web sites can be improved. If you – or junior colleagues not members of the Society – have a bright idea that you may have got in mind, you can contact our office. I don’t promise to pursue them all, but I do promise to “cherry pick” the very best for consideration!

Dr Richard Dyer
Chief Executive,
Biosciences Federation
welcome@bioscifed.org
www.bfs.ac.uk
Sophie Buglass completed an intercalated degree in Neuroscience last summer at the University of Leeds, deservedly gaining first class honours after an exceptional performance in her examinations and thesis. For her final year project, she investigated the modulation of calcium homeostasis by hypoxia and p-amyloid to explore possible mechanisms of cell death in Alzheimer’s disease. Described by her supervisor, Chris Peers, as ‘one of the best students I’ve had the pleasure to supervise’, Sophie produced publication-quality data in less than eight weeks. She has now returned to her medical course but feels the insight she has now gained into neuroscience has broadened her career prospects immensely such that she might return to the laboratory bench again one day. She’d be very welcome!

Karen Luyt was also an exceptional student, notaverse to winning prizes and medals during her PhD, and publishing a number of papers in quality journals for her outstanding research. Supervised by Elek Molnar at the University of Bristol, Karen investigated the cellular and molecular mechanisms of white matter injury in the immature brain, concentrating in particular on the identification and function of metabotropic glutamate receptors and GABA receptors in oligodendrocytes, implicated in the cell death, proliferation and differentiation of these cells. Identifying their presence and receptor sub-type might offer the possibility of pharmacological intervention to mitigate the effects of premature birth on myelination, Karen hopes.

Since returning to her consultant’s position in neonatal medicine, she feels the experience of her PhD has greatly enhanced her understanding of white matter development and injury in the immature brain, and hopes to see translational research directing clinical management strategies one day. Her qualifications in both clinical neonatal medicine and basic neuroscience are an increasingly essential requirement, she feels, for a successful translational approach.

So, heartfelt congratulations from the BNA to both Sophie and Karen! But we should also mention two close runners-up: Holly Griffiths, a first class student at the University of Manchester, for the Undergraduate prize; and Amos Fatokun, another outstanding PhD student, at the University of Glasgow. Their nominations gave the judges much angst in their decision-making but also much reassurance in the quality of undergraduate and postgraduate teaching and research in the UK.

The BNA Awards, 2006

The BNA Award for Public Service was presented to Mr. Mike Robins in recognition of his tireless work in promoting the value of animal research in benefiting human health. “I owe my quality of life to this small device,” said Mike Robins, pointing to an electronic controller in his jacket pocket. He switched it off and on his right hand began to shake violently and uncontrollably. Mr. Robins developed Parkinson’s disease in his early fifties and, for eight years, his condition worsened until he could no longer feed or dress himself. Thanks to the successful treatment using deep-brain stimulation, his life has changed beyond recognition. “Now I can have a proper conversation, go out on my own, and drive to work,” he said. “Every morning I wake up and marvel that I no longer shake.”

Both awards were presented by Professor Richard Frackowiak at The Royal Society in London, on the occasion of the annual Christmas Symposium. This was the last function Richard Frackowiak would undertake for the BNA as he now retires from the presidency and Graham Collingridge takes up this challenging role.

Congratulations to our BNA prize winners for 2006: Sophie Buglass (Undergraduate prize) and Karen Luyt (post-graduate prize), closely followed by runners up Holly Griffiths and Amos Fatokun.

Where have all the SFN abstract slots gone?

SNF has changed the allocation practice for slots. In 2006 FENS was appointed as the unique distributor of slots for entire Europe. The total number of slots that FENS distributed in 2005 was 419. Only PhD students and postdocs were eligible. Taking into account the fact that, especially the smaller, financially compromised countries, the Executive Committee of FENS decided to distribute the slots according to the following scheme:

1. Category I: Societies with 100 or less members: 123 slots
2. Category II: Societies with 20 to 1000 members: 120 slots
3. Category III: Societies with 1001 and more members: 126 slots

41 slots remained at the disposal of the Executive Committee.

363 slots have been distributed (every eligible applicant received a slot).%2

was still a proportion of the entire allocation unused.

Upon request, the FENS office released the figure (above) to describe the ‘slots’ that the ‘Executive Committee’ of FENS allocated for the Atlanta meeting last year. Clearly, BNA members would be wise to still apply (even if they do not necessarily meet all the criteria) and request to go on a waiting list to receive one of the ‘leftovers’ this time round.

BNA NATIONAL COMMITTEE: NOMINATIONS SOUGHT

Nominations are now invited for election to the BNA National Committee for TWO vacancies that arise this autumn.

Nominations should be proposed and seconded by extant BNA members and sent to the BNA Office (y.allen@bna.org.uk) by 31st July 2007. Members of the BNA Committee perform a vital role in influencing the goals and ambitions of this vibrant society. Would you like to contribute for the next three years? Informal enquiries are always welcome (y.allen@bna.org.uk; tel 0151 794 8449).

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Professor Colin Ingram (Honorary Secretary) c.c.ingram@ncl.ac.uk
Dr Stefan Przyborski (Treasurer) stefan.przyborski@durham.ac.uk
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The BNA committee 2007

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Yvonne Allen with Duncan Banks (left) and Peter Woolfsons at the BNA stand in Atlanta last year. The BNA exhibits at SFN meetings every other year to promote the society on the world stage and say ‘hello’ to members, past and present, and to tout for new ones. It is still a sad fact that many more BNA members go to the American meeting than support their own national meeting, or even the biennial FENS gatherings.

In 2005, the Society for Neuroscience decided to change the way it distributed sponsored abstracts to other neuroscience societies that may have implications for the future funding of these to BNA members. Although the BNA was one of the first societies to negotiate this ‘deal’ whereby BNA members could present as non-members at the SFN annual meetings, many other national societies were then also keen to claim a similar allocation. It was fast becoming a chaotic mess so, to simplify the procedure, SFN decided to give a (still generous) allocation instead to FENS to distribute to constituent FENS members on its behalf. BNA members still wishing to obtain one of these are now requested to contact the FENS office directly. However, the FENS Council then decided to impose its own rules and regulations on their distribution, such that priority goes to students and early career post-docs only, disproportionately to smaller societies and to poorer countries. The outcome of this was that, although BNA members fulfilling the criteria appear to have been awarded sponsored abstracts with no problem, there

SNF could no longer offer the ‘slots’.

In recent years, a number of BNA members have commented on a corresponding drop in the SFN abstract slot allocation. As a result, the BNA is now considering ways to increase its profile at SFN meetings. This will involve increased BNA exhibition and opportunity for members to present their work. This year’s BNA Award for Outstanding Contribution to British Neuroscience went to Professor Horace Barlow FRS, a fellow of the Trinity College in Cambridge, for his lifelong contribution to the research into the mechanisms of visual perception. His pioneering work that studied neuronal activity using simple cell recordings has been instrumental to our understanding of visual inhibition, the process whereby a neuron firing in response to one group of retinal cells can inhibit the firing of another neuron, which allows perception of relative contrast. In 1961, he published a seminal article in which he addressed the issue of the computational properties of the visual system. This and his subsequent work have laid the foundations for the burgeoning field of computational neuroscience.
Drugsfuture – can BNA members help?

The BNA regrets that it must raise the annual subscription fee from 1st March, 2007, for all members by a modest £5 per year, to reflect inflationary increases in its operational costs over the last year that, in many cases, have risen by nearly 10%. Unfortunately, we now have to ask for 100p per week from everyone to help us maintain and improve the service we can offer. This means the annual subscription for full members paying by direct debit will be £39 per annum, and the student fee will be £35.

Please remember that this fee also includes your membership subscriptions to FENS, IBRO and the Biosciences Federation that the BNA pays on your behalf – four for the price of one! And some of these subscriptions rose by a staggering 200% this year! So, younger members especially should remember to include membership of all these societies as well on their CVs.

The benefits of BNA membership now include:

- (1) FREE admission to many events throughout the year including ‘One Day Symposia’ and the ever popular Christmas Symposium
- (2) Reduced registration fees (up to 30%) to the National Meeting
- (3) Regular BNA Bulletin and other relevant mailings
- (4) Regular ‘BNA Email Alert’ service
- (5) Student prizes, and bursaries for attendance at BNA annual meetings
- (6) FREE on-line access to European Journal of Neuroscience
- (7) Concessionary (SIN membership rate) registration fees and sponsored abstract forms for Society for Neuroscience annual meeting (now handled by FENS)
- (8) FREE advertising in the BNA Bulletin and on the BNA Website
- (9) FREE Inclusive membership of the Federation of European Neuroscience Societies (FENS), the International Brain Research Organisation (IBRO) and the Biosciences Federation (BSF).

We do hope you agree that this is tremendous value for money and that you continue to support as many of our events as possible.

For further information on any of these benefits, contact: membership@bna.org.uk

Engaging the public down under

The Manchester Science Group (www.manchesterscience.blogspot.com), comprising lecturers Dr Ellen Poliaff (School of Psychological Sciences, University of Manchester) and Dr Stuart Allan (Faculty of Life Sciences, University of Manchester) and Science Communicators Dr Ermina Ochu and Dr Michelle Lockwood, will be running a series of public engagement activities at the IBRO World Congress of Neuroscience in Melbourne, July 12-17 2007.

The group were invited to submit a proposal to the Local Organising Committee and this was accepted. The proposed events build on existing activities developed by the group over the last couple of years, and include a ‘Brain Discovery Stand’ in Federation Square, one of Melbourne’s most popular public spaces (www.fedsquare.com). The group will also be hosting an interactive pub quiz, ‘You Know it Makes Sense’, which has run successfully at Cafe Scientifique events in Manchester and Nottingham. A poster will be presented as part of the main congress where the group will share with the other delegates their experiences of developing and delivering public events for diverse audiences.

If any members of the BNA are attending the IBRO Congress and are interested in taking part, even for a few hours, in any of these activities then please contact Stuart Allan (stuart.allan@manchester.ac.uk).

PLUS – Neuroscientists are invited to participate in our European Dana Alliance of the Brain DAY IN THE LIFE project, where scientists give the public an insight into their lives. Check the blog or email: mansci@ googlemail.com for more details.

The AMS is concentrating on three main areas of concern about future drug use.
- (a) Cognition enhancers.
- (b) Future legal and illegal recreational drugs.
- (c) Drugs for mental health.

It is asking for detailed submissions on the issues these topics might raise over the coming 20 years. If you would like to discuss, as an individual or for an organisation, start by taking a look at the guidelines, which are at www.acmedsci.ac.uk. The AMS will report to government by the end of 2007.

In addition to seeking the opinions of experts such as the members of the BNA, the study is also gathering views more widely.

Public engagement

January 31 saw the launch, at the Dana Centre in London, of Drugsfutures, an innovative consultation occurring both online and in person. The aim is to get an idea of the future developments from both experts and a wide range of the public. Managed by the OPM (Office for Public Management) with partners including the British Association for the Advancement of Science, it is running until the end of March.

There is a range of ways to get involved. One is by invitation only. Defying the insights of Alexei Sayle, who says that nobody should be able to run a workshop unless they are engaged in light engineering, we are running some workshops to which you might be invited to reflect the idea of the “public” in the sense of a sample of individuals recruited to match the population of Science as a whole) to discuss and debate the issues. At large. But we will also be talking to other people who are experts in some aspect of drug use. They include groups such as young people, drug users, and people who care for others with mental health problems.

Each of these groups will be asked to explore a specific aspect of drug use. They will be helped along the way by a background note on the future possibilities, including a scenario for future drug use, that is intended to help their thinking without railroading it. We will also be inviting some experts to report to events, to provide further information.

Each workshop will focus on one of these five following themes:
- Drugs and the law
- Drugs and society
- Drugs and young people
- Drugs and mental health
- Drugs for a smarter brain

During the workshops, people will be asked to explore topics questions such as the regulation and control of drugs, including the balance between regulating addiction via the health system or via criminal justice. For example, how far should the use of cognition enhancers be allowed to go? Should they be illegal for anyone who does not have a demonstrable clinical need for them? Should they be compulsory for anyone who runs a nuclear power station, flies a plane or drives a bus? What about job interviews? If you use a cognition enhancer to look clever at the interview, will you feel obliged to take it once you get the job?

A related set of issues will arise when Drugsfutures considers our emerging knowledge of neuroscience and genetics. We are starting to find genuine genetic markers to susceptibility to addiction, confirming the centuries-old wisdom that drunkenness runs in the family to a degree that social settings alone cannot explain. At the same time, we are able to test whether an individual expresses gene combinations that make them susceptible to addiction.

One issue we shall explore with the participants will be the implications of consciousness will be with dangerous high levels of drug susceptibility? He or she might become a problem gambler, a heroin user, or a heavy smoker, depending what influences they are exposed to. But it is hard to imagine locking them away from all possible exposure to potential addiction. Almost as tricky is the advice to give people with a low susceptibility to addictive harm. Can they try any behaviour they like with impunity?

Previous OPM work for the Foresight project showed that the public is less panicked about the issues raised in this project, by the possibilities of drug use than one might imagine. They often think that people have a right to try drugs out, and would be reluctant to see people vaccinated against addiction even if it became technically feasible.

To ensure the sample we need, the workshops will not be public events. But Drugsfutures has an online life in which we hope you will participate. At www.drugsfutures.org.uk. There you can join an online consultation where you can register painlessly and then let us know what you think.

Also at that address you will find the Drugsfutures Blog, where you can join in discussions of topical issues to do with addiction and treatment. You will need to register separately for the blog. We would welcome your comments, questions or suggestions for themes to be discussed.

The team would very much welcome your participation in Drugsfutures and we look forward to your first contribution.

By Martin Ince
Science writer and editor of the Drugsfutures Blog
Drugsfutures@martinince.com

ANNUAL GENERAL MEETING 2007

The BNA will be holding its Annual General Meeting this year during the 19th National Meeting in Harrogate:
1.00pm, Tuesday, 3rd April, 2007, Conference Suite, Harrogate International Centre.

All members are invited to attend
The Launch of the European Coalition for Biomedical Research (ECBR)

The ECBR, with a current membership of 42 scientific institutions from 19 countries across the EU, representing 44,000 scientists, held its inaugural meeting in Brussels on November 8th 2006. It elected an Executive Group (Prof. Edith Olath, Chair, Dr Mark Matfield, General Secretary, and three Executive Members, Prof Peter Janssen, Dr Duncan Banks, and Prof. Christine Giudicelli), and adopted a Manifesto setting out concerns about the proposed revision of the EC Directive 86/609 which regulates the use of animals in research across EU member states. The website (www.ecbr.eu) provides ongoing updates on activities and links to member organisations.

**Background**

The ECBR was initiated by EBRA specifically to coordinate response to the revision of the EC Directive 86/609. This revision was proposed in a report from the Environment Committee in December 2002, which set up a Technical Expert Working Group drawn from European professional bodies (e.g. EBRA, EFPIA, FELASA), but excluding representative from Patient groups. The Expert Group planned to draw up a report by the end of 2003, but this was delayed for a year by EU elections. A Swiss company, Pregnos, was then commissioned in 2004 to assess the impact of the proposals, and mounted a hastily prepared consultation, which attracted only 66 replies, followed by a long internet questionnaire sent to experts, plus requests for views from the general public. The questionnaire/document provided a clear indication of what might be in the final revision, while the ECBR supports many of the objectives, the factual mistakes and the bias of some of the consultation document prompted the ECBR to draw up its manifesto to raise particular concerns and to suggest changes in wording. The consultation timetable deciding out the Draft Revision of Directive 86/609 include delivery of the final Prognos Opinion in November, joint inter-service consultation in December 2006, leading to release of the Draft legislation early in 2007 under supportive German presidency of the Council.

Adoption of the revised directive will depend on agreement of the final version by all three European legislative bodies: the Commission, the Parliament and the Council. The rounds of consultation between these bodies and the Environmental Committee will afford vital opportunities for ECBR members to lobby and consult with relevant members to enhance their understanding of the critical issues involved.

**Why should the ECBR be concerned about the revised directive?**

The ECBR supports legislation to improve animal welfare and the harmonisation of welfare practice across the EU. However, current evidence suggests that the revisions may include legislation which could be detrimental to biomedical research, without achieving increased welfare benefits, or promoting the 3Rs. Problematic proposals include:
- A ban on first generation bred non-human primates (NHPs).
- Extension of cover to invertebrates (cephalopods, decapods).
- Increased regulation of transgenic animals and xenotransplantation.
- Extension of cover to fetal and embryonic forms.
- Extension of cover to animals killed for tissue.

Further possible revisions include provisions that are effectively in place in several EU countries (including the UK) and which the ECBR would seek to clarify and promote:
- Compulsory cost/benefit analysis
- Ethical review process
- Minimum animal/technician ratio
- Standardised pain/suffering assessment
- Standardised procedures for analgesia
- Specified methods for euthanasia (ban on CO2)
- Implementation of the 3Rs
- Regulations for use of animals in education and training.

Although the details of the draft amendments to Directive 86/609 have not been released, the ECBR is taking proactive measures:
- To alert scientists to the possible negative impact of some of the proposals.
- To inform EU legislative members about potential implications in terms of increased costs and administrative burdens without achieving improvements in animal welfare.
- To suggest amendments to the proposed revisions of Directive 86/609 in its Manifesto.

The ECBR Manifesto

The Manifesto was finalised at the launch meeting and can be seen in full on the website.

The key elements include the following issues:
1. Inclusion of ‘recital’ statements to emphasise the importance of freedom of research for scientific enquiry.
2. Importance of harmonisation of national controls on animal experimentation across EU member states.
3. Euthanasia
   - All animals to be killed by a competent person using a humane method.
   - Animals bred for tissue should not be included in the scope of the Directive.
   - Ban on the use of CO2 for euthanasia is not justified.
4. Authorisation
   - The ECBR supports the proposed system for authorisation and ethical review, but wants time limits and avoidance of duplication in the process to be clearly specified, as follows:
     - A deadline of 60 days for completion of local and national authorisation, to start from the date that projects are submitted to the local ethical review process.
     - A statement that the review process must not duplicate any of the project assessments made by the local ethical review body.
5. Caging and welfare standards
   - The Council of Europe Convention ETS123 has recently revised standards for caging and welfare that member states must adopt, at an estimated cost of over one billion Euros for upgrading. This will cause problems especially for academic institutions which will need time to raise funding. The ECBR proposes that the Directive should allow:
     - A minimum of 10 years before institutions are required to comply with ETS123 standards.

5. Transparency

The proposal that all relevant non-confidential information from the authorisation process be made public would involve huge administrative and legal costs. The ECBR proposes that transparency would be more effectively and efficiently served by:
- Publication of a summary of the research councils in easily understood language (‘lay summary’).

6. Non-Human Primates (NHPs)

- The proposed ban on use of first generation (F1) purpose-bred NHPs is based on the erroneous view that most NHPs are F2. Currently, only New World NHPs, constituting 13% of research use, are F2+ stock. Most EU research (87%) uses F1 Old World NHPs, and F2 animals are not available. Welfare would better be served by improving the breeding conditions, rather than setting up long-term breeding colonies, which breeders are not prepared to undertake. The ECBR proposes that:
  - The ban on use of F1 NHPs should be lifted.
  - The EU should set up a system for inspecting NHP suppliers, and approving their breeding and conservation practices.
  - NHPs should only be obtained from EU approved suppliers.

7. Multiple sites

- To avoid duplication and conflict the ECBR proposes that where projects run across several sites:
  - Ethical approval obtained from any one institution should be accepted by the other institutions involved.
  - Training in order to facilitate communication between laboratories and harmonise training standards the ECBR proposes that the Directive should change the EC to set up an Ethical Review Group to:
    - Set up training standards and curricula for member states.
    - Require member states to adopt and mutually recognise these standards and curricula.

**What happens next?**

The draft Directive is expected to be issued in April 2007. The EC has already (Jan 18) issued a working document which has incorporated several of the suggestions in the ECBR Manifesto. This document is confidential, but in general terms there are still issues to resolve, for example:

- Frequency of project reporting to ethical review committees.
- Use of non-human primates.
- Training requirements.
- Funding for research on alternative approaches.

Therefore, the ECBR will continue to work to publicise the manifesto, and inform EU administrators and legislators about the issues.

The overall strategy involves:
- Enlarging the coalition and forming alliances with other interested bodies.
- Keeping ECBR members and allies informed.
- Targeting MEPs and convincing them to put down amendments which reflect ECBR proposals.
- Lobbying MEPs and members of the Commission and Council to support these amendments.

What can individual ECBR members do?

- Send a message (Fax and email) to your MEP.

**The problem**

- The amendment

**Arguments for the amendment**

The coordination provided by the ECBR will be much more effective than lobbying by individuals or single associations. As Mark Matfield commented ‘the larger the coalition, the more effective it can be’. Working together we can achieve EU legislation that will enhance the value of care for experimental animals, without imposing undue increases in costs and administration. Improved welfare will enhance the quality of the science that results.

By Duncan Banks and Helen Hodges (dbanks@open.ac.uk; hodges@kcl.ac.uk)
RDS NEW ZEALAND
UNDERSTANDING ANIMAL RESEARCH IN MEDICINE WINTER 2006

Understanding Animal Research in Medicine


The RDS: Defending the use of animals in research and testing

The use of animals in research has been in the news frequently in the past year, with the People's Petition earlier in 2006 to the more recent publication of the Weatherall report in December supporting the use of non-human primates in research of biomedical or medical importance. Indeed, as neuroscientists, you know all too well that animals are still necessary in medical and scientific research and need to be aware of the arguments in favour and against as well as the current status of the debate.

The Research Defence Society (RDS) is the leading UK organisation that represents doctors and scientists in the debate concerning experiments on animals. It recently commissioned an opinion poll of GPs that showed 96% of female doctors agree that animal research has made an important contribution to many medical advances. The results were announced by Health Minister, Andy Burnham, in October last year.

RDS is the only organisation which brings together the academic and commercial sector to work on policy, representation and communications. RDS engages in dialogue with all interested parties and comments publicly on any issue as it relates to the use of animals in research.

RDS believes that research using animals should be well regulated, conducted humbly and only when there is no alternative. Not all medical research needs to use live animals - useful results are also obtained by using computers, studying cells and tissues, and some studies that are done on patients and human populations. RDS provides the research community in context to explain when animals need to be used.

RDS would like to see a time when replacement, refinement or reducing of laboratory animals is no longer required, at least in many areas of research. However, society has unmet medical needs and there are gaps in our knowledge. RDS considers that current technical and scientific limitations mean that full replacement is unachievable in the foreseeable future.

The RDS was founded in 1969 by Dr Stephen Paget, at a time of intense public interest in medical research and animal welfare. Its comprehensive website contains information on animal welfare, the number of animals used in research, the types of animal and the research areas in which they are used. The number of animal experiments has halved over the last 30 years and is now roughly stable as the increasing use of alternative methods has compensated for reductions in the use of wild-type strains. The RDS lists some of the key medical benefits derived from animal research over the past century and also the benefits for animals that resulted from the use of laboratory animals. It also has a recently-introduced hot topics and policy section that addresses current issues.

Richard Dyer, Chief Executive of the Biosciences Federation, receives an OBE

The British Neuroscience Association would like to congratulate Richard Dyer on the receipt of an OBE in the Queen’s New Year Honours List. Richard receives the award for services to biology, particularly his contribution to the Babraham Institute and Babraham Research Campus.

Richard Dyer joined the Babraham Institute in 1974 as a neuroendocrinologist, becoming Head of Department in 1986. His distinct scientific contributions were on understanding how specialized nerve cells in the brain regulate hormone production and thereby control the female reproductive cycle. In 1986, he was awarded the Annual Medal of the UK Society for Endocrinology and, in 1987, the Medal of the Polish Physiological Society. In 1994, he was appointed Director and led the Institute through a period of great change.

In 2005, just before his retirement as Director, the Institute was highly praised for the excellence of its research and scientific training in an independent assessment for the BBSRC, the Institute’s main sponsoring Research Council. Richard Dyer’s vision of an integrated biotechnology campus, with researchers from both the academic and commercial ends of the biotech spectrum working in close proximity, has been realised. The “Babraham Research Campus”, with its Biobusiness Park, is now the UK’s most active location for start-up and emerging biotech companies, with another building opening in late 2007 which already has multiple expressions of interest.

Dr Dyer is now Chief Executive of the Biosciences Federation, an umbrella organisation representing the UK’s biological expertise and providing independent opinion to inform public policy and to promote the biosciences. He is also Vice President of the European Science Foundation and continues as a member of the Babraham Bioscience Technologies Ltd Board.

Dr John Bicknell, former Acting Director, said: “I am delighted that Richard’s contribution to the Babraham Institute and its conception of the Babraham Research Campus has been recognised. I believe Richard was the prime mover in bringing the Institute to its current, highly successful state as a vibrant international research centre for discovery biology in the 21st century with its promise and potential for applications in biomedicine. This award to Richard is a truly deserved tribute from which his colleagues at the Institute will take great pleasure.”
The Genes to Cognition (G2C) Programme ([www.genes2cognition.org](http://www.genes2cognition.org)) is a systematic integrative research program that bridges basic and clinical neuroscience and was initiated by support from the Wellcome Trust. G2C is a consortium of scientists primarily based in the UK, studying synaptic molecules and their role in behaviour. The G2C Programme collects and integrates data in the areas of psychiatry, human and mouse psychology, cellular neurophysiology and cell biology, proteomics and biochemistry, molecular biology, human and mouse genetics and genomics.

As neuroscientists, we seek to tackle one of the great scientific challenges - understanding the mechanisms of human behaviour - as well as help relieve the enormous burden of neurodegenerative diseases on our community. Lessons learned from the study of cancer and cell growth have told us that there are far more molecules, cell biological processes and, ultimately, disease types than ever expected. Importantly, these insights have emerged not from one technique or investigator but from integrating a diverse range of studies. There is no reason to suppose that the biology of brain diseases will be any less complex.

In several areas of biology it is now clear that large scale projects with publicly available data and distributed resources make an important contribution alongside traditional individual projects and collaborations. Large-scale projects, through economy of scale, can expedite progress and remove the need (and cost) for many basic experiments in specialist laboratories. For example, we no longer need to perform in situ hybridization to document the basic expression pattern of genes in the mouse brain because of the Allen Brain Atlas; we no longer need to manually clone and sequence a piece of genomic DNA from humans, mice and other species because of genome projects.

It is very early days for large scale projects in neuroscience. One type of program is where a single methodology is extensively employed (e.g in situ hybridization). Another type of program is where multiple technologies or areas of study are integrated. Systematic programs that link basic and clinical neuroscience may be particularly useful to a broad sector of the neuroscience community.

G2C scientific strategy

The central theme of the G2C project is the study of multiprotein complex, called NRC (NMDA Receptor Complex) or MASC (MAGUK Associated Signaling Complex), found at excitatory synapses in the mammalian brain. These complexes were isolated from mouse brain and found to have a surprisingly large number of proteins (~180). Over 50 of these have been implicated in human diseases. In experimental animal models such as the knockout mouse or drug studies there have been ~50 genes reported to alter the properties of synaptic plasticity and forms of behavioural plasticity. These behaviors include learning and memory, pain, visual and somatosensory plasticity amongst others. The NRC/MASC set of proteins is clearly very important for human diseases and animal models of those diseases. G2C scientists are conducting a systematic study of mutations and polymorphisms in mouse and human genes encoding postsynaptic proteins, and exploring how these genes influence a broad range of phenotypes - especially cognition.

Modular organisation of the consortium

The consortium has a modular architecture where different modules include specific scientific disciplines or activities (see Box 1). Details of people involved with these modules can be found on the G2C website. These modules provide a natural way for collaborators to join the program.

The connection between mouse and human genetics is central to the strategy. In brief, the human genetics involves clinical investigators interested in diseases of the brain (e.g. cognitive disorders, mental retardation, schizophrenia, bipolar disorder) and normal cognition (e.g. cognitive ageing and individual differences). Human DNA samples are sequenced and analysed for the NRC/MASC genes and variants identified. Because of the extensive information on these molecules in the G2C program from basic science studies the human genetic variants can be rapidly evaluated. Thus, there are several complimentary aspects to the collaboration between clinical and basic scientists.

The study of the genes in mice typically involves the generation of knockout mice and examination of their behaviour (e.g. learning and memory tasks, neuropathology and electrophysiology studies). The data and all reagents are made available to collaborators and widely distributed. One important vehicle for distribution of data is the G2Cdb.

G2Cdb: an integrative databases for synaptic biology

The G2C program has created an integrative database (G2Cdb) that links multiple databases (see Box 2). We are creating a comprehensive database of all mouse knockouts that have been studied in synaptic plasticity. Similarly we have built a knockout mouse behaviour database. We aim to make these databases repositories for published data (curated manuscripts), data generated in the G2C program as well as place for data submission directly by external groups. There is a linked database on the human genetics and disease affecting synaptic proteins. This in turn is linked to a further database on synaptic proteomics.

Education and Training in G2C

Scientific research into the basis of behaviour and disease is of great interest to lay people. We recognize the importance of education on all aspects of the research program and rather than develop educational material after the research has been completed we are developing that material from the outset. The major collaborator in the educational program is the DNA Learning Centre at Cold Spring Harbor (www.DNALC.org). They are developing an education website and materials for schools and colleges called ‘G2C Online’. This website will contain extensive information, videos and interviews that informs on all aspects of the G2C research program.

Participating in the G2C program

The G2C program welcomes new collaborators. The interactions, sharing of information and reagents through the program are proved to be very helpful in speeding progress. Using the modular framework of the program provides a simple way to identify connections. There are also training opportunities for students and scientists wishing to learn new methods. Send any enquiries directly to Sieth Grant (sg@sanger.ac.uk) or through the website contact our collaborators.

By Sieth Grant (email: sg@sanger.ac.uk)

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Box 1: Research modules

Human: Psychiatry & Psychology
Clinical studies
Sample collection
RNA analysis
Mouse studies: Creation of mutants
Molecular: RNA and proteomics
Neurobiology: Neurophysiology
Electrophysiology
Behaviour

Box 2: Data resources

Database: G2Cdb
Mouse genetics of synaptic plasticity
Mouse genetics of behaviour
Human genetics of synaptic proteins
Synapse proteomics
GLIAL CELLS in health and disease

The VIIIth European Meeting
Imperial College, London
4th to 8th September, 2007

An international meeting that will examine neuron-glial interactions in development, health and disease, and the role of glia in stem cell biology and regeneration. Imperial College is one of London’s largest academic venues, located in the heart of the museum and cultural district.

There will be nine plenaries, twenty-one symposia, lively themed poster sessions, an exhibition and a full range of social events.

PLENARY LECTURERS:

- Dwight Bergles (Maryland, USA)
- Ron McKay (Washington, USA)
- Patrick Charnay (France)
- Marie Fibin (New York, USA)
- Helmut Kattenmann (Berlin, Germany)
- Pierre Magistretti (Lausanne, Switzerland)
- Peter Bregby (Edinburgh, UK)
- Bill Richardson (London, UK)

SYMPOSIA:

- Neuronal-glial signaling in oligodendrocytes and neurogenetic disease
- Glial regualation of chronic pain
- Functional role of Bergmann glia-purkinje cell signaling
- How do glial-axonal interactions impact the organization of the node of Ranvier?
- Neuroinflammation: a two-edged sword
- Transcriptional control of differentiation in myelinating cells
- Glia in spinal cord injury and regeneration
- Mechanisms of myelination
- Pannexins: an alternative pathway for cell-cell communication
- Diverse regulatory roles for glutamate receptors at the tripartite synapse
- The role of astrocyte dysfunction in epilepsy
- The molecular pathology of myelination

ABSTRACT DEADLINE: 1st May, 2007
Further information: www.eurogliacell.org • Enquiries: Secretariat +44(0) 1850 143 681
Organised by the UK Glial Cell Club, in association with The British Neuroscience Association

www.eurogliacell.org
We have all heard about migraine. And with more than five million migraine sufferers in the UK alone, you would know at least a few of them. However, do we know about migraine as a disease? The answer is probably not very much. It is not in the least surprising, as, unless we or someone in our household suffers migraine, we are unlikely ever to witness the extent of a full-blown migraine attack. This has, in the past, prevented the broad social acceptance of migraine as a severe and very disabling disorder. In this short review, I shall briefly describe the clinical features, the recent research on currently available genetic models of migraine.

Clinical Spectrum and Epidemiology

Migraine is an episodic neurovascular disorder that affects approximately 6-8% of men and up to 25% of women in the general Western population. It is estimated that approximately 12% of the general population have 18 migraine days per year, which poses a substantial burden on the affected individual and society. Within the European Union, the annual cost associated with migraine exceeds €6 billion. The World Health Organization, therefore, ranks migraine amongst the twenty most disabling disorders. Since 1988, migraine has been defined by diagnostic criteria established by the International Headache Society and is commonly grouped into migraine without aura and migraine with aura. As such, a migraine attack can consist of up to three phases: 1) the prodrome, with symptoms preceding the headache and suffered by about one-third of migraine patients; 2) being studied, however, not generalised to other genetic markers; 3) the characteristic severe, unilateral (one-sided) and often pulsating headache that can last anywhere between hours and days. Typical symptoms suffered during the prodromic phase include retention of fluids, craving for certain types of food and mood changes. This phase signals the onset of a full-blown migraine attack. Those suffering with migraine will experience an aura phase. The migraine aura is characterised by neurological symptoms, which can vary and include visual disturbances (seeing dots, flashing lights, or blind spots), auditory hallucinations, or speech impairments. The migraine headache associated with an attack takes the shape of a severe, unilateral throbbing pain occurring around the eyes and temples. The headache is accompanied by nausea and increased sensitivity to light (photophobia) and/or sound (phonophobia).

Migraine Pathophysiology

The migraine headache appears to result from the activation of the trigeminal system, consisting of the meningeal and superficial cortical blood vessels, which are innervated by the trigeminal nerve. Projections of the trigeminal nerve through the brain stem (specifically the trigeminal nucleus caudalis) activate higher order centers in the brain. A series of carefully conducted experiments both in the rodent and human brain have led to the now generally accepted hypothesis that migraine aura arises directly from a phenomenon termed cortical spreading depression (CSD). CSD is characterised by a slowly propagating wave of strong neuronal depolarisation across the cortex that is followed by a long-lasting neuronal suppression. Once CSD reaches the visual cortex, the ensuing neuronal silencing results in the characteristic visual aura symptoms. Specific medication for migraine is available. However, only about 50% of migraine patients respond satisfactorily to the drugs. The design of effective and prophylactic migraine treatments is hampered by our lack of detailed mechanistic knowledge on how migraine attacks are initiated. It has been suggested that CSD that may be an initial migraine trigger, and recent animal experiments indeed provide some evidence for a potential link between CSD and migraine attacks. Specifically, crotamiton, an antihistamine, was shown to activate the trigeminal system and evoke changes in the meninges and brainstem consistent with the development of headache pain. However, direct evidence for such a causative relationship between CSD and trigeminal activation is still lacking in humans.

Migraine Genetics

Migraine (both with and without aura) shows a strong genetic component and is thought to be of multifactorial origin. However, to date no direct genetic component could be shown. It is generally assumed that a genetic pre-disposition reduces trigger thresholds for migraine. However, as knowledge of the nature of migraine triggers and how these act has increased, research efforts have focused on a severe and very rare inherited form of migraine: familial hemiplegic migraine (FHM). FHM is characterised by attacks of migraine with aura, associated with an often transient (halo-sided body paralysis during the attack). FHM is generally considered a valid model for the more common forms of migraine, especially since FHM patients frequently suffer attacks of ‘common’ migraine. Three distinct genetic loci for FHM have been identified to date, all resulting in dysfunction at the synaptic level (Figure 1).

Mutations in the CACNA1A gene, encoding the alpha-1 subunit of neuronal Cav2.1 calcium channels, are associated with FHM1. These channels are expressed widely in the nervous system, where they are directly involved in the release of neurotransmitter molecules from synaptic nerve terminals. Familial hemiplegic migraine results from a Bloom syndrome for glutamate receptor GluR2. This syndrome is defined by an opening of Cav2.1 to open and to mediate an influx of calcium ions into the synaptic. These calcium ions cause a migraine attack to be accompanied by a loss of function of the protein (FHM1 and FHM2), Modified from...

Figure 1A. Mutations in all three known loci for FHM result in increased levels of the neurotransmitter glutamate, resulting in increased glutamate release from the pre-synaptic terminal (FHM1 and FHM3), or reduced clearance of glutamate and K+ ions from the synaptic cleft by astrocytes (FHM2). As a result, FHM brains are more susceptible to cortical spreading depression (CSD), which underlies migraine aura and is a potential migraine trigger 

Within the European Union, the annual cost associated with migraines exceeds €6 billion. The World Health Organization, therefore, ranks migraine amongst the twenty most-disabling disorders.

Knock-in (KI) mice carrying the human CACNA1A R1202 mutation (a single amino-acid change from arginine to glutamine in the Cav2.1 channel) do not show any neurological or anatomical phenotype and appear healthy. However, electrophysiological recordings of neurotransmitter release both in the central and the peripheral nervous system showed significantly enhanced neurotransmitter release.

Cerebellar granule neurons isolated from brains of R1202 KI mice have increased neuronal calcium currents. At the peripheral nervous system, CACNA1A R1202 KI mice have increased evoked and spontaneous neurotransmitter release under conditions similar to those occurring in the brain during CSD (i.e. low extracellular Ca2+ and high K+ levels). These changes in neurotransmission have been demonstrated to be functional, resulting directly from altered amino-acid properties of the Cav2.1 channel, and not originating from e.g. morphological changes.

The hemiplegic migraine KI mouse model (carrying the serine to leucine amino-acid acid change at position 218) has been generated and is currently widely used. However, no genetic model for either FHM2 or FHM3 are available yet. Taken together, FHM1, R1202 KI mice and other transgenic FHM KI mice can serve as useful models to investigate migraine pathophysiology and will be instrumental in discovering migraine triggers and testing novel therapeutic approaches.

Conclusion and Outlook

The identification of FHM-associated mutations in genes encoding two ion channels and an ion-transporting ATPase has increased our understanding of the pathophysiology of these conditions and defined a molecular basis for migraine, on which to focus research efforts. A further boost has come from the generation of genetically sensitised mouse models, which are proving to be very valuable in the study of the key pathophysiological processes underpinning the disorder. These new experimental systems will aid research efforts into the nature of migraine triggers and the increased sensitivity to them in migraine patients. These insights will be instrumental for developing in particular novel prophylactic migraine therapies.

Acknowledgements:

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The author is European Molecular Biology Organization post-doctoral fellow and trainee of the Michael Smith Foundation for Health Research.

By Simon Kaja (kaja@msl.ubco.ca)

Links: The Migraine Trust (www.migrainetrust.org)

(See page 22 overleaf for references)
A summary of neuroprotective and Aβ-associated degenerative pathways at the cholinergic synaptic terminal. Activation of α7 nicotinic acetylcholine receptors by nicotine activates the PKA/AMPK pathway which protects neurons from oxidative toxicity. Aβ oligomers upon Ni-DHATs to activate MAPK/ERK pathways resulting in cell death. Several major surviving used in the treatment of AD reduce the breakdown of ACH by acetylcholinesterase (AChE), thereby elevating the quantity of ACh available to activate nAChRs. One of these, galantamine, can also act directly on nAChRs to evoke the neuroprotective pathways. For clarity, α7 nAChRs are shown on the presynaptic neuron only; although most brain α7 nAChRs are thought to be presynaptic, they can be located postsynaptically at certain synapses. Note that mammalian neuron is known to act primarily through glutamate receptors, there is also evidence that it also has actions at ACh receptors.

Nicotinic acetylcholine receptor loss

Brain nAChRs are ligand-gated ion channels consisting of five subunits that form a central, cationic channel which opens in response to acetylcholine binding. In the brain, nAChRs are generated from α (α2-10) and (β2-4) subunits. The 3 most important brain receptors are composed of α7, α4β2 and α3β4. As well as being the subject of extensive studies on the development of AD for the following reasons: 1) the most vulnerable neurons in AD appear to be those expressing high levels of α7 receptors (indeed, treatment with the α7 antagonist [9] of and NACHRs and some of their associated proteins change in AD; 3) nicotine and acetylcholinesterase (AChE) inhibitors currently used for treatment of AD can protect cultured neurons from amyloid toxicity via nAChRs [1, 2]; 4) Aβ binds with high affinity to α7 nAChRs [40]; and 5) polymorphisms of the Aβ peptide linked to AD [41]), it is clear that AD involves loss of cholinergic neurons in the brain [11, 33] as well as an overall reduction in NACHRs [32-34] and that different subunits are involved. However, results are regulated in AD in a specific manner [18], although there are conflicting data on the details of the subunit- and tissue-specificity of these changes.

Direct actions of Aβ on nAChRs

Aβ oligomers that do not protect against nAChRs are known to be constitutively functional. Aβ oligomers activate nAChRs with increased sensitivity to nicotine stimulation. Nerve:41:701-710

Aβ binds with high affinity to α7 nAChRs [40]; and 5) polymorphisms of the Aβ peptide linked to AD [41], it is clear that AD involves loss of cholinergic neurons in the brain [11, 33] as well as an overall reduction in NACHRs [32-34] and that different subunits are involved. However, results are regulated in AD in a specific manner [18], although there are conflicting data on the details of the subunit- and tissue-specificity of these changes.

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elevated hypophysiotropic tau protein [59], but it is unclear whether this increase in FYN contributes to hyperphosphorylation of tau or is a protective response to it. In extracts of human AD brains, soluble FYN increases with cognitive severity [10], and in neonatal 7E6 AD mice, no FYN or JAK2 block the neuroprotection against Aβ toxicity of therapeutic acetylcholinesterase inhibitors [41]. However, FYN may also play a role in Aβ toxicity. Indeed, Aβ activates both FYN and the P63 kinase [47], while germline knockout of FYN is neuroprotective in mice [6, 25]. More research is needed to explore the complex roles of this potential therapeutic target in AD and neuroprotection.

One receptor, two opposite outcomes

How can nACHRs mediate both the toxic actions of Aβ and the protective actions of nicotine? Perhaps this is some way in which these ligands operate different signaling pathways. The simplest explanation might be that Aβ’s antagonist actions block the therapeutic effect of nACHR activation. Setting aside the controversy over the actions on nACHRs of Aβ, this explanation is unlikely to offer a full explanation because Aβ alone evokes the ERK/MAPK signaling cascade through nACHRs. Nicotine activates the ERK pathway but via a different route to Aβ, involving PKA [4]. Thus, α7 receptors appear to be differentially coupled to different downstream signaling pathways depending on which ligand is bound and, in the case of Aβ, on the aggregation state and time of exposure. Further studies are required to establish the functional balance of signaling cascades can determine the survival of neurons.

nACHRs and calcium signaling

The nACHRs may provide a link between Aβ and disruption of calcium homeostasis, which is also thought to play a part in AD. The α7 subtype may be of particular relevance since it is much more permeable to calcium than the α3 and α5 nACHRs. Acute application of Aβ to the human neuroblastoma cell line results in a rapid increase in intracellular calcium ions in dependence upon both α3/7 and α7 nACHRs. This calcium signal arises from three sources: influx of extracellular calcium through voltage-gated calcium channels from intracellular stores and calcium influx through the α7 receptors. It has been shown that the α7 receptors, but not the α3/72, specifically trigger calcium release from intracellular stores, and calcium influx through the α7 receptors. This means that α7 receptors must have a direct function in generating the calcium signal.

Conclusion: nACHRs as a route to new therapies

While it is clear that Aβ kills neurons and nicotine protects them against Aβ toxicity, much remains to be resolved to unravel the mechanisms by which death or survival is the outcome. Intracellular signaling initiated by Aβ and nicotine is complex and involves much cross talk between different signaling pathways, arguing for a systems-based approach to understanding precisely how nicotine or Aβ can determine a cell’s fate. Such a task could be facilitated by the deployment of mutant supressor and RHA screens as well as the ease of transgene production, afforded by invertebrate model genetic organisms [6, 7, 8, 20, 27]. Identifying new components of these pathways offers the prospects of new targets for therapeutic intervention. In addition, because α7 receptors are present in human lymphocytes, AD-related alterations in expression of the receptor and key associated protein genes in these cells may form the basis of a biomarker for early detection of AD or evaluating progression of the disease and responsiveness to drugs [21].

References

SCIENTIFIC WRITING PRIZE

General Category – 2nd Prize: Genes for alcohol use turn up in drunk worms andCheapate flies

By Rebecca Poole
(R.L.Poole@bristol.ac.uk)

Rebecca Poole graduated with a degree in Biology from Southampton University in 1999. She stayed at Southampon to study for a PhD, in Plant Pathology and, in 2003, joined the Functional Genomics group at Bristol University to investigate genetic factors that influence bread making quality in wheat. Rebecca enjoys the challenge of science communication and currently volunteers for the Bristol and Bath branch of the British Association for the Advancement of Science.

Inebriated worms and drunken flies are helping researchers pick the genetic locks that drive some of us to drink. At Southampton University, scientists are busy studying the wriggling of worms in alcohol. The worms in question aren’t the familiar earth worms you dig up in the garden, “they are natural soil dwellers like earth worms”, says Prof Holden-Dye, “but these worms are much smaller. They are only just visible to the naked eye”. C. elegans are in fact just over 1 mm long. Somewhere way back on the path of evolution, they went their way and we went another direction for researchers, however, these worms behave in much the same way as any of us after one too many, “What’s been previously observed by other scientists is that worms become overexcited in alcohol, but then as the amount of alcohol increases they get sluggish”, says Prof Holden-Dye. Other researchers are using fruit flies instead of worms to demonstrate the same effects. Fruit flies positively love a drink it seems, perhaps not that surprising considering their fondness for rotting fruit. Scientists measure how unsteady on its feet a drunken fruit fly is by watching how quickly it tumbles through an ally filled device, the “inebriometer”. The drunken the fly, the more quickly it emerges out of the bottom.

So what is it exactly that scientists are hoping to learn by observing drunk worm worms and flies? “There is considerable evidence that some worms are better at holding their drink than their others, essentially there is variation as to how quickly they get drunk,” says Prof Holden-Dye, “other areas are good at building up tolerance to the effects of alcohol; worms that have become tolerant are more resistant to the effects of alcohol after more than one exposure”. The same is seen in flies. It has been known for some time that these two factors, initial sensitivity to alcohol and tolerance, might be linked to the development of alcohol abuse problems in the general population. “This definitely isn’t the full story”, says Prof Holden-Dye, “but they are obviously important factors that we can look at in worms and other organisms like fruit flies and that might say something about how we deal with alcohol. We still don’t really know that much about how alcohol acts on our brains”.

The Holy Grail is to find genes that are tied to how the brain is affected by alcohol and those which may play a part in making some of us more likely than others to develop a dependency problem. The human brain is jaw-droppingly complex with billions of neurons, the specialised cells that comprise the brain and nervous system, and trillions of synapses, the junctions between neurons that act as communication gateways. It performs tasks of unimaginable complexity in the blink of eye. Frankly, our brains stick two fingers up at even the most sophisticated of computers we have today. By comparison, C. elegans has a relatively reserved 302 neurons, each one of which has already been exquisitely mapped by scientists. Do, so we cantially all more some organisms are Nature’s gift to those in the genetics business. In much the same way as it’s advisable to learn your alphabet before you start on the great works of Shakespeare, scientists are starting their search for interesting genes in worms and flies. So far this approach is proving fruitful. Cheapate (does what it says on the tin, a Cheapate fly gets drunk very quickly) and Hangover are two genes that have been identified in fruit flies and numerous others have wriggled their way into the spotlight in worms. Excitingly, some of these genes are also known to be at least partly responsible for governing how these organisms respond to certain stresses, adding credence to the long held belief that stress and drug and addiction behaviours are linked in all of us. The hard task now is to pin down exactly what these genes and others like them do, so we can begin to unravel how alcohol really works it magic or wrecks its havoc on our brains.


Kate Holden-Dye obtained a BSc in Biochemistry and is now finishing off a PhD at the University of Bristol in the School of Medical Sciences. Her PhD research is on the viability of an integral membrane protein.

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Researcher Category – 1st Prize: Scientists reveal that autism and hyperactivity have the same cause

By Kate Holden-Dye

Although Dustin Hoffman gave one of the most famous portrayals of autism in Rainman, his co-star Tom Cruise’s hyperactive performance on Oprah Winfrey’s sofa more recently may also be a good depiction, if recent science is to be believed. Amazingly one in three individuals with autism are hyperactive and inattentive, a condition known as ADHD (attention deficit hyperactivity disorder).

Perhaps a lead role involving both autism and ADHD would be too ambitious even for Dustin, but off-screen, autism and ADHD are closely linked. Both conditions begin in childhood and are associated with differences in the brain. It might be, however, that brain differences do not cause autism or ADHD, but arise as a consequence of living with autism or ADHD. On the other hand, genes that cause a part – but until now we didn’t know whether the same genes cause autism and ADHD. That is why my colleagues and I at the Institute of Psychiatry carried out a study on autism and ADHD in over 6000 pairs of twins. No study until now has had the scope to tackle this issue. TEDS (the Twins Early Development Study) included identical twins, who share all their genes, and fraternal twins, who share half their genes.

Double trouble
We compared how alike one twin’s level of autistic behaviours were with the other twin’s amount of ADHD behaviours. If the same genes cause both autism and ADHD it is expected that in identical twin pairs, who share all their genes, the level of autistic behaviours in one twin and the amount of ADHD symptoms in the other twin will be the same. Less similarity between autistic and ADHD behaviours would be expected in fraternal twins because they do not share all their genes. This is what we found.

The results showed that at the genetic level, autism and ADHD weren’t so different. It became clear from our findings that more than half the genes for one were also influencing the other.

Symptom-specific effects
Of course, it is not that simple. A complication is that both autism and ADHD consist of several different types of symptoms. Odd social interaction, communication problems and obsessive and repetitive behaviours are all part of autism, and ADHD includes inattentiveness and hyperactivity. Earlier work by our group has shown that the different autistic symptoms are caused by mostly different genes. So as well as just looking at the overlap between autism and ADHD as a whole, we needed to look at overlap between the separate symptoms.

In this next stage, we found that it was the communication difficulties in autism that were caused by the same genes as ADHD. In contrast, the obsessive and repetitive behaviours showed very little overlap with ADHD.

As Professor Robert Plomin, a co-author on the study and the deputy director of the Social Genetic and Developmental Psychiatry centre, commented, “It’s startling that there appears to be greater genetic overlap between autistic communication difficulties and ADHD than there is genetic overlap within autism itself”. In other words, children who seemingly appear genetically to have much more in common with children with inattention and hyperactivity than with children with autism are likely to be more common in males than in females. That, says the professor, is an important question for future research.

By Angelica Ronald

After completing her undergraduate degree in Experimental Psychology in 2000 at the University of Bristol, she spent a year in advertising selling snack food. Yearning for a more academic life, she returned and did her PhD at the Social Genetic and Developmental Psychiatry Centre at the Institute of Psychiatry, London, on the causes of children’s social development and cognitive ability. Her thesis focused on the causes of autism spectrum conditions. She is currently working as a postdoctoral researcher on genetic risks to autism and related conditions.

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DBS is extensively used to treat different types of movement disorders, most commonly the tremor (a repetitive, involuntary movement of a body part) associated with Parkinson’s disease. Parkinson’s disease is a degenerative disease, and occurs due to the loss of a particular type of brain cells which can contain a chemical called dopamine. Dopamine is extremely important in the part of the brain which controls movement (the motor system), and without it patients may develop a tremor, and may eventually become unable to initiate movement.

Such problems of the motor system are thought to occur due to abnormal electrical activity in the brain. This is because brain cells communicate with one another using electrical signals. DBS is able to treat such problems by one or two electrodes being surgically implanted in specific areas of the patient’s brain, and an electrical current being applied through these electrodes. This arrangement is shown in Figure 1, where we can see the electrodes implanted, and wires leading to the battery powered stimulator (a device similar to a pacemaker) which is implanted in the chest. The electricity injected during DBS can then disturb the abnormal electrical signals in the patient’s brain, and ease their tremor. At present, one in 500 people suffers from Parkinson’s disease, and every year 10,000 people are newly diagnosed with it. Since DBS was pioneered over a decade ago there have been over 35,000 implants worldwide, and the estimate is that as many as 80% of people who receive this treatment will experience a reduction or complete suppression of their often disabling symptoms. The decision to allow a patient to undergo this surgery depends on a number of factors, and is usually made only after trying the non-surgical option of drug treatment to replace the lost dopamine.

And yet, although DBS is widely used and successful at achieving therapeutic benefits, in a precise way in which the injected electrical current affects the electrical activity of the brain is not fully understood. The difficulty is that although we can produce accurate images of where the electrode is inside the brain, as shown in the MRI scan in Figure 2, there is no way that we can see or measure exactly how the current spreads in tissue, and how this current is interacting with the brain’s own electrical signals. Another way to try to understand what exactly is going on in the human brain during DBS is to use mathematics. As part of a team at Imperial College London, I am interfacing the clinical research undertaken by my colleagues, with the development of 3-dimensional computational models of the implanted electrode and the surrounding area of brain. Simple models, like the one shown in Figure 3, can be used to visualise the electric field created around the, and then the, electrode. These computational models can then be used to study how the injected current interacts with the surrounding brain tissue.

The goal is to use mathematical modelling to better understand how the current influences the brain’s activity and predict how to use this procedure more effectively. Our computational results from theoretical models explains the difference in the electric fields created by two commonly used stimulation approaches, and therefore can help doctors to better target the abnormal activity that exists as a result of disease. The final challenge will be to use such computer models within routine clinical practice in order to predict the best settings for the current applied to each individual patient, and as when they require the intervention.

As the use of this procedure spreads to new ailments such as epilepsy, depression, and bipolar disorder, the number of patients who may benefit from the procedure will also increase. But in order to understand more about how the electrical current is achieving the observed effects, theoretical research hand in hand with clinical research needs to be undertaken.

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Highly Commended - Changing the face of our lives: how our innate interest in faces can change the choices we make

Faces are important to people. They are strongly linked with our sense of identity. Anyone who has been watching the news lately will be aware of the surgical pioneering work into full face transplants. These are not without risk: patients undergoing transplants will have to take immunosuppressant drugs throughout their lives to prevent their bodies from rejecting the new facial tissue. Nevertheless, people unlucky enough to have suffered facial damage are willing to take the risk. So, why are faces so important to us?

Studies have demonstrated that looking at faces produces greater brain activity than looking at strings of letters or textures. Furthermore, newborn infants appear to pay greater attention to faces than to arbitrary objects. Such evidence has prompted researchers to suggest that our interest in faces is innate.

If indeed we are predisposed to focus on faces, it may be for good reason. If we were unable to identify others as friend or foe, we would quickly run into trouble. People suffering from prosopagnosia, the inability to recognise faces, do encounter such difficulties. Dr Brad Duchaine of the Institute of Cognitive Neuroscience explains: “Imagine failing to recognise your boss in the elevator or walking right past your boyfriend. Even worse, imagine picking up the wrong child at daycare or failing to recognize yourself in mirrors or phones. These sorts of incidents occur regularly for people with face recognition problems, and not surprisingly lead to serious social problems.”

So we may be predisposed to pay attention to faces because this confers a social advantage. Indeed, it’s possible that faces guide us in deciding whom we can and cannot trust. Research by psychologists in Canada has demonstrated that we are more likely to trust individuals whose facial features are similar to our own. This is possibly because we use facial resemblance as a cue to detect kin and are hardened to cooperate with family. Furthermore, scientists in New Zealand found that we are disposed to remember the faces of individuals who cheat in “social contract” games more accurately and recalling them and returning it when promised. Naturally, remembering cheats is important if you wish to avoid them in the future.

But why do we trust individuals with symmetrical faces? For example, a symmetrical face is thought to indicate good health, and therefore “good genes”, which ought to be desirable in a potential mate if we hope to produce healthy offspring. There can be a conflict of interests for women however, since masculine characteristics indicate good genes, but more feminine features convey a caring personality – one more likely to invest in rearing children. Research has found that generally, young women prefer men with slightly feminised features, but that when their fertility is at its peak, a masculine face is more attractive.

Our innate interest in faces is used by advertisers to sell products. Research from the Center for Consumer Marketing has shown that a smiling face on an advert can lead consumers to a positive viewpoint towards the company using the advert, making them more likely to patronize the company and to recommend them to others. Faces really are important. They help us to decide who to trust, whom to mate, even what products or companies to trust. Those who are unable to recognise faces can suffer for it. Those who have lost their faces feel lost without them. Not even faces it seems should be taken at face value.

By Gillian Pepper gillianpepper@gmail.com

Gillian has a BSc in Zoology with Evolution and Ecology from the University of Liverpool, where she hopes to return to further study in 2007. Since graduating in 2005, Gillian has completed a variety of work experience projects related to science communication, including work with the Science Media Centre, BBC Focus Magazine and Newton’s Apple, and has also spent four months in India working as a volunteer. She is now one of the UK co-ordinators for Yearoutindia, a company that sends volunteers to do charitable work at various sites in southern India.
Highly Commended: The real cause of obesity: addicted to food

By Flora Devlin

Telling obese people to ‘just eat less’ is the equivalent of advising a chronic heroin addict to ‘cut down a bit’, say scientists.

According to research carried out at New York’s Brookhaven National Laboratory, obesity is literally an addiction to food. The findings may offer clues to why current strategies to combat obesity are failing. The condition is as much a psychological problem as a physical one and should be treated accordingly, scientists urge.

It has previously been shown that drug addicts and alcoholics have fewer receptors for dopamine, a neurotransmitter associated with feelings of pleasure and satisfaction, than non-addicts. The Brookhaven team, led by Professor Gene Jack Wang, has discovered that obesity causes the same kind of change in brain chemistry. The results imply that obese people consume more food to stimulate dopamine reward circuits that ‘pleasure’ endorphins in the brain, just as addicts feel compelled to take drugs to obtain a high. If you find this hard to believe, think about the feeling when you devour that first mouthful of chocolate.

In the experiment, the brains of 10 severely obese people and 10 individuals of normal weight were examined. In the obese subjects, dopamine receptors were injected with a radioactive chemical tag, made to bind to the dopamine receptors. Positron Emission Tomography (PET) was used to pick up the radioactive signals, the strength of which indicates the proportion of dopamine receptors. The obese group were found to have significantly fewer receptors. The study further revealed that there is an inverse relationship between weight and the number of dopamine receptors. That is, the more obese the individual, the fewer their dopamine receptors.

The advice given to obese people on the NHS Direct website is ‘Try not to overeat – listen to your body and stop when you’re full.’ However, in an obese person, there may be an overabundance message from the dopamine receptors in the brain saying, ‘carry on eating!’

Whether the observed differences in brain chemistry determine obesity or are a result of obesity is unclear. ‘It’s possible that obese people have fewer dopamine receptors because their brains are trying to compensate for having chronically high dopamine levels, which are triggered by chronic overeating,’ said Professor Wang.

‘However, it’s also possible that these people have low numbers of dopamine receptors to begin with, making them more vulnerable to addictive behaviours including compulsive food intake.’ This question is a current area of investigation.

This research revolutionises our understanding of obesity. The focus needs to shift away from ‘which diet’ to the question of how to tackle food addiction. One possibility is prescribing drugs that artificially alter dopamine levels. However, these drugs are highly addictive and would only be appropriate when a person’s weight is at a proportion of their optimal level. A better alternative is exercise. Not only does it have the direct physical effect of weight-reduction, but it also provides the all-important dopamine high.

So what is my point? Stop feeding the ever-expanding diet industry and get the nation on a bike.

Source:
Brookhaven National Research Laboratory www.bnl.gov
By Flora Devlin (floradevin@hotmail.com)

Aging Research – the new dynamics

New Dynamics of Ageing (NDA) Research Programme was launched on 1st November, 2006, at the Queen Elizabeth Conference Centre, London. This multi-disciplinary research initiative aims to improve the quality of life in later years by funding ‘the largest and most ambitious research programme mounted in the UK.’

NDA is the result of five government departments, seven charities and 26 councils. The programme is the UK’s largest ever investment in research into the biology of ageing.

The NDA initiative has already identified five projects for funding, and The Launch Meeting was treated to an impressive round up of progress to date:

• Sara Arber (University of Surrey) has gathered together six academic partners in six disciplines for work on optimising the quality of sleep of the elderly in care homes, and will work with four other academic partners to use of blue light, and involve relatives and residents associations.
• Ruth Hancock (University of Essex) is engaged in modelling the needs of old people up to 2030. This comprehensive project will recruit government departments (e.g. Pensions Policy Unit, Census Office), health services, industrial partners...
MEETING REPORTS

Genes and Synapses: New insights from studies on Invertebrates

ONE DAY SYMPOSIUM 8th November, 2006, Oxford, UK

Research on invertebrate organisms has already made outstanding contributions to Cellular Neuroscience, providing access to uniquely identifiable neurons, sometimes of large diameter, making them well suited to the application of electrophysiological and biochemical studies on neural signaling mechanisms and the integrative physiology of neural networks. Invertebrate neuroscience has been further empowered by the sequencing of the first animal genome for the nematode Caenorhabditis elegans and development in that same model organism of gene knockdown by RNA interference. UK-based research takes advantage of invertebrates, continues to be strong and 85 neuroscientists participated in a lively one day RNA Meeting (8 lectures and 25 posters) at St John’s College in Oxford on November 8th, 2006, organised by Professor Emmanuel (MRC FGU Oxford), Lindy Holden-Dye (Southampton) and Mark Darlison (Nottingham Trent), in collaboration with Sam Potts and Yvonne Allen in the BNA Office.

This meeting demonstrated, yet again, the strengths of invertebrates as model organisms. They offer easy-to-manipulate genetic tools to pinpoint gene functions underlying complex behaviours. Having a short life cycle and simple nervous systems, invertebrates such as the worm C. elegans are readily amenable to forward and reverse genetic screens to correlate gene activity with certain behavioural characteristics. Genetic manipulations, such as gene overexpression or deactivation using knockdown by RNA interference, are relatively simple and, in the case of C. elegans, have even been performed on a genome-wide scale. Thus, many aspects of neurobiology, including genetics, biochemistry and electrophysiology, can be readily studied in invertebrates providing an excellent first step in the study of gene function.

Mário de Bono showed how the worm continues to be an excellent model for establishing the neural circuitry involving foraging behaviour and the important role played by oxygen sensing. Also deploying the worm, Lindy Holden-Dye reported on new studies showing how neuropeptides regulate important aspects of behaviour. Work on another important genetic model organism, Drosophila melanogaster, was well represented. Mary O’Connell described RNA editing in the fly nervous system and showed how this can add greatly to the functional diversity in voltage-gated and ligand-gated ion channels. Mario Zito described one neural axial images depicting dendritic development and connectivity in the fly embryonic nervous system. Michael O’Shea described a fascinating example of natural antisense regulation of NOS and its role in memory formation. David Shepherd described one example of what is a growing area: the use of invertebrate models to study aspects of human neurodegenerative disorders by modelling tautopathies in Drosophila.

Andrew Jones and David Sattelle reported on a combination of functional diversity in nicotinic acetylcholine receptor families, taking advantage of the new invertebrate genome currently emerging (bee, mosquito, fruit beetle as well as additional fly and nematode genomes). Richard Baines described exciting work on the regulation of neuronal excitability via Pumilio dependent control of a sodium channel gene. Steve Nunnish brought us back to the worm at the end of the day demonstrating the regulation of neurotransmitter release by GTases. Finally, Robert Walker, a pioneer in invertebrate neuropharmacology and a passionate advocate of such work in the UK, explored some of the common threads in current research and speculated on some key areas where work on invertebrates can contribute in the immediate future.

It emerged that invertebrates can be used to study not only basic neuronal signalling, but also more complex phenomena that underpin developmental plasticity. A large cohort of other post-graduate students and we attended and listened to a variety of excellent talks, ranging from developmental and biochemical studies, accompanied by some beautiful images and descriptions of elegant scientific techniques. This friendly and informal meeting provided students especially with a great opportunity to network, compare experimental approaches and share their enthusiasm. For this, we thank all the speakers and poster presenters, and above all, the organisers and the BNA.

By Zara Luedtke (Southampton) and Michael Brierie (Oxford)

Butterflies of the Soul: The BNA Christmas Symposium
The legacy of Golgi and Cajal: past, present and future

By Jane Qiu

14th December, 2006
Royal Society, London

The year 2006 marks the 100th anniversary of the first Nobel Prize for Physiology or Medicine, which was shared by Camillo Golgi and Santiago Ramón y Cajal for their key contributions to our understanding of the nervous system. Golgi discovered a new histological staining method that allows neurons and their processes to be distinctly labelled. By using this revolutionary technique, Cajal’s meticulous studies of the entire nervous system, coupled with the Neuron Doctrine, were established. The BNA’s annual Christmas symposium was held to commemorate their outstanding achievements in neuroscience. Jane Qiu reports.

The symposium, chaired by Richard Frackowiak of University College London, got underway with a presentation by Javier DeFelipe of the Institute of Cajal, Madrid. He gave a historical overview of research that led up to Golgi’s and Cajal’s discoveries and hypotheses, many of which are still largely relevant to neuroscience to this day. In the 1860s, scientists already suspected that there were many types of cortical neurons that are different in their size and morphology. It was thought that the network of continuous nerve branches is crucial for the function of the nervous system, whereas the cell body serves only to provide nourishment — a hypothesis called the Reticular Theory. It was not until 1873, when Golgi discovered his “reaction nerve” (“black reaction”), it was possible to conduct detailed studies of the nervous system.

Cajal discovered this important method in 1887 and made a series of discoveries in the following few years. In contrast to the Reticular Theory, he proposed that neural networks were equipped with both sensory and motor connections. He divided neurons into two categories: multipolar and unipolar. Multipolar neurons were connected by synapses, while unipolar ones provided sensory and motor connections.

The following speakers presented their areas of research, highlighting how the scientific insights of Golgi and Cajal have had a significant impact. Alain Prochianz, of the École Normale Superieure in Paris, focused on the role of a family of transcription factors called homeoproteins in the spatial and temporal regulation of neural development. He showed that the expression of the homeoprotein Pax2 induces the development of the eye in zebrafish, and how a gradient of homeoprotein Engrailed is established along the rostrocaudal axis of the tectum or the target field of retinal projection. This gradient is crucial for Mauthner cell specification and retino-tectal topography: temporal retinal axon project to the tectal regions with low levels of Engrailed expression; nasal retinal axons have the opposite preference.

This is confirmed by in vitro studies which show that Engrailed repels growth cones — a notion that was put forward by Cajal in

Future (stage 2) programmes start with funding for a year to form networks (national and international) between researchers to establish a basis for collaborative research which will subsequently form the platforms for full grant applications.

The ‘Silver Revolution’
The UK research councils have demonstrated commitment to research on ageing. The ESRC’s ‘Growing Older’ programme (launched in May 1998, which funded 24 projects was the direct forerunner of the NDA initiative, whilst the MRC’s life cycle approach ensures the needs of ageing receive specific, if more limited, attention. However, it will take a massive shift in research effort and public awareness to push through a major paradigm shift in which the elderly can participate fully in all aspects of life, instead of being marginalised. The NDA initiative will certainly work towards achieving an independent and healthy life for the elderly. However, this will crucially depend on the full involvement and participation of the elderly themselves, to create and sustain momentum.

By Helen Hodges
Emeritus Professor of Psychology
Institute of Psychiatry, London

Muscle cells of the nematode Caenorhabditis elegans labelled with green fluorescent protein, courtesy of Michael Brierie, MRC Functional Genetics Department.
1909 – of temporal axons but also attracts that of nasal axons. Dr Prochnitz went on to demonstrate the role of another homoeoprotein OTx2 during the critical period of visual development in early- or late-developing axons in the binocular visual cortex of mice coincides with the transfer of OTx2 between neurons from the dorsal thalamic to the visual cortex. This is of particular interest, as it specifies the timing of the critical period. Manipulating the expression of OTx2 by gain-of-function or RNA interference resulted in shifting and could not be effectively compensated by the loss of function of other OTx2-related genes.

The third speaker Thomas Klaussberger, who holds a position as the MRC Anatomical Neurophysiology Unit, Oxford University, and an honorary position at the Centre for Brain Research in Vienna, demonstrated how single neurons contribute to global activity in the hippocampus. Although Cajal and his contemporaries had noted the myriad of neuronal types with distinct morphology, the diversity of neuronal cell types is not fully appreciated until the advances in molecular biology and electrophysiological recordings. As Dr Klaussberger explained, the proper functioning of the cerebral cortex depends on neural networks formed by projection neurons and interneurons that primarily use the neurotransmitters glutamate and GABA, respectively.

Interneurons have an important role in modulating cortical output and plasticity. In the basic hippocampal circuitry, for example, the principle cells are innervated by 14 types of GABAergic neurons, which themselves are innervated by 4 types of interneuron-specific cells. Dr Klaussberger illustrated the anatomical details of such connections and how various GABAergic interneurons with differing patterns of involvement in communicating with different parts of the brain. He concluded that different classes of interneurons evolved because distinct subcellular domains of the GABAergic synapse become fully appreciated until the advances in molecular biology and electrophysiological recordings. As Dr Klaussberger explained, the proper functioning of the cerebral cortex depends on neural networks formed by projection neurons and interneurons that primarily use the neurotransmitters glutamate and GABA, respectively.

The topic of the final talk, presented by Michael Coleman of the Babraham Institute in Cambridge, was axonal degeneration. One type of axonal degeneration was first observed by Waller in 1850 as a result of damage to the nerve fibres of the lateral column of the sciatic nerve. He noted that “it is particularly with reference to nervous disease that it will be most desirable to extend these researches, and that the results of their labours will be of great importance, which was later coined as Wallerian degeneration. He was also a well-known pioneer in the field of immunology and his team showed that the “Wallerian degeneration” was due to trauma, injury, and degenerative processes. In 1913, Cajal published a book titled “Degeneration and Regeneration of the Nervous System”, in which he detailed many histological drawings and his hypotheses. Dr Coleman remarked that “there is little to observe in fixed, wild-type tissue that Cajal did not already report” and, indeed, many researchers have often ended up “reinventing” his discoveries.

However, the development of novel, powerful experimental approaches has allowed new functional insights into the role of the axonal degeneration process. In the last decade, the degeneration process is delayed to 2–3 weeks, has been used to show that both physical injury and a blockade of axonal transport trigger a protracted axonal death programme. The Wg, which is expressed in the embryonic axonal projection, is a key signal in the regeneration process.

In the next presentation, Antoine Triller, also of the Ecole Normale Superieure in Paris, discussed surface trafficking of neurotransmitter receptors between synaptic and extrasynaptic membranes. He explained that the number of such neurotransmitter receptors at synapses, which partly determines synaptic strength, is controlled by dynamic interaction with intracellular scaffold proteins. Most receptors are recruited and transported to the synapse only from non-synaptic locations, and the process of receptor trafficking into and out of synapses is regulated during development and by plasticity. Novel insights into this area of research have been facilitated by the advent of semi-quantitative imaging tools because these novel nanomaterials enable measurements at the single-molecule level with high signal-to-noise ratio.

Dr Triller showed that the scaffolding protein gephyrin is crucial for the assembly and the dynamics of mGluR6-containing receptor clusters in the synaptic and non-synaptic membranes by connecting the cytoplasmic domains of receptors to cytoskeletal systems. This allowed the group to define the role of gephyrin in regulating the lateral diffusion of neurotransmitter receptors in and out of the synapse. In addition, this dynamic behaviour is regulated by intracellular calcium concentration and by the cytoskeleton in response to synaptic activity. Intriguingly, lateral diffusion of neurotransmitter receptors is also regulated by the length of the spine neck as this spine morphology, which is in turn, varies with plastic processes.

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However, the development of novel, powerful experimental approaches has allowed new functional insights into the role of the axonal degeneration process. In the last decade, the degeneration process is delayed to 2–3 weeks, has been used to show that both physical injury and a blockade of axonal transport trigger a protracted axonal death programme. The Wg, which is expressed in the embryonic axonal projection, is a key signal in the regeneration process.

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VSO is an international development charity that works through volunteers. Our vision is a world without poverty in which people work together to fulfill their potential. We bring people together to share skills, creativity and learning to build a fairer world. VSO welcomes volunteers from an ever increasing range of countries, backgrounds and ages. National agencies in Canada, Kenya, the Netherlands, the Philippines and India recruit volunteers from many different countries worldwide. This international approach allows us to combine and learn from a rich variety of perspectives. In all the countries where we work, VSO is represented by a Programme Office. Staff and volunteers in our Programme Offices work together with local partner agencies, and increasingly with the people whose interests VSO aims to serve, to agree a programme of development priorities in their country and region.

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University of Edinburgh, Doctoral Training Centre

PhD studentship: 4 YEAR PhD IN NEUROINFORMATICS and COMPUTATIONAL NEUROSCIENCE

This is a 4 year programme with a strongly interdisciplinary character and is ideal for students who want to apply their computational and analytical skills to problems in neuroscience and related fields. The first year consists of courses in neuroscience and informatics, as well as projects based in experimental labs. The first year is followed by a 3 year PhD project. The PhD project is commonly done in collaboration with one of the many departments and institutes affiliated with the DTC.

The DTC programme is made up of 3 themes:
1) Computational and Cognitive Neuroscience.
   Computational, mathematical, and experimental studies of information processing in the nervous system.
2) Neuromorphic Engineering and Robotics.
   Artificial sensor perception, neuromorphic modelling, spiking computation, and neurorobotics.
3) Data Analysis and Systems.
   Imaging data analysis using machine learning, Bayesian methods, and neurally inspired software.

Edinburgh has a strong research community in these areas and leads the UK in creating a coherent programme in neuroinformatics. Edinburgh has been voted as ‘best place to live in Britain’, and has many exciting cultural and student activities. Students with a strong background in either computer science, mathematics, physics or engineering are particularly welcome to apply. Motivated students with other backgrounds will also be considered.

About 8 full studentships are available to UK students and a small number of EU students.

The stipend is about 12,300 GB pounds per annum.

Applicants from outside the EU will need to provide their own funding and evidence thereof.

Full info and application forms can be obtained from:
http://www.anc.ed.ac.uk/neuroinformatics. • E-mail: neuroinformatics-phd@inf.ed.ac.uk
Contact: Mrs Pat Ferguson • Phone: (44) 131 650 3090 • Fax: (44) 131 650 6899
Address: School of Informatics, 5 Forrest Hill, Edinburgh, EH1 2QL, Scotland, UK
Applications received by March 30th, 2007 will receive priority treatment.

University of Glasgow, Division of Clinical Neuroscience

PhD studentship

MRC funded studentship in pre-clinical imaging in neuroscience (4 years)

Stroke is a major killer and can cause significant disability in survivors. Specific treatment options are currently limited (thrombolysis within 3 hours or aspirin). The time window for acute neuroprotection therapy depends on the length of time injured but potentially salvageable tissue (penumbra) survives in each patient. Magnetic Resonance Imaging (MRI) techniques improve diagnostic accuracy, and offer the opportunity for physiological brain imaging. This project will involve the development and validation of a new MRI technique to identify penumbral tissue in the ischaemic brain using established rodent stroke models, imaged in a state-of-the-art 7T small animal MR scanner.

The 4 year MRC funded PhD studentship, will be available from 1st October 2007 with a stipend of £12,300 per annum. Applicants should hold or expect to gain a first or upper second class honours degree in a biological or biomedical science or related field.

Eligibility requirements for MRC studentships are listed in the Studentship guide - (http://www.mrc.ac.uk/Careers/Studentships/Informationforstudents/index.html)

For further information contact Professor I Mhairi Macrae (m.macrae@udcf.gla.ac.uk) Tel 0141 330 6978, Division of Clinical Neuroscience, Wellcome Surgical Institute, Garscube Estate, Glasgow G61 1QH, UK.

Applicants should submit a CV including e-mail addresses of 2 referees.

A closing date has not yet been set. Applications received by March 30th, 2007 will receive priority treatment.
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