Issue No. 70
Spring 2014

BNA Bulletin

THE VOICE OF BRITISH NEUROSCIENCE TODAY

Guided by the light

Optogenetics and fruit fly behaviour

Networking opportunities

Brain imaging and schizophrenia

PLUS:

Synaptic plasticity

Hoarding disorder

Zebrafish nerve regeneration

Babies' social brain development

BNA
British Neuroscience Association

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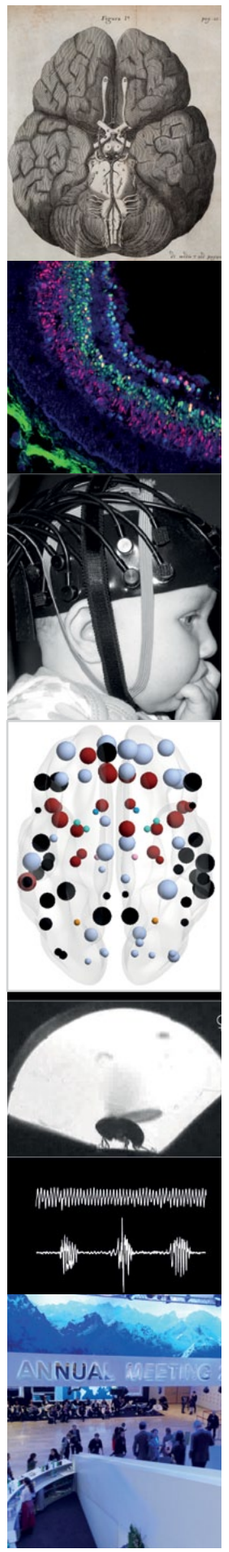

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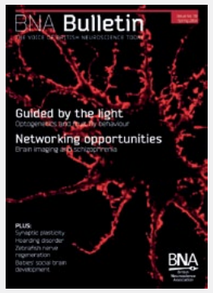

Cover: Visualising kainate receptor distribution in hippocampal neurons.

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Message from the President

Dear BNA Members

We started 2014 with a bang when we announced that the BNA2015: Festival of Neuroscience will take place in Edinburgh on 12–15 April 2015. It will be held at the Edinburgh International Conference Centre, EICC, in the centre of that glorious city. Narender Ramnani, who organised the immensely successful 2013 Festival at the Barbican, will again lead in 2015. The call for proposals generated a flood of great ideas for symposia and plenaries which will showcase some of the best neuroscience.

What makes it a Festival is the public programme of events as well as the science conference, so we are collaborating with the Edinburgh International Science Festival to produce an array of events and activities for the public that explore the brain. If you have ideas and would like to get involved, contact the BNA's CEO, Elaine Snell (elaine.snell@bna.org.uk).

We already have a full year. There will be a symposium on 'Optogenetics: controlling the brain with light' on 3 April at the University of Oxford (see page 13). Gero Miesenböck, a winner of the 2013 Brain Prize, will deliver the plenary lecture. He will also give a public talk at the Museum of the History of Science the evening before. In partnership with the Biochemical Society, a two-day symposium on 'Astrocytes in health and neurodegenerative disease' will take place in London on 28–29 March (see page 12).

We are delighted that Ruby Wax and Colin Blakemore – both Patrons of the BNA – will be 'in conversation' at the Sheldonian Theatre in Oxford on 4 June 2014. The conversation between them will be a fascinating insight into Ruby's personal experience of depression and Colin's knowledge of the neuroscience underlying mental illness. Details are on page 7.

Our Local Group Representatives continue to actively promote the BNA, organising seminars, symposia and public activities. We are grateful to them for all their hard work. If you are not already in touch, you'll find a list of local groups on our website.

This is the Year of the Brain, a Europe-wide initiative – and it's going to be an exciting year for the BNA!

Russell Foster, President

BNA2015 for Edinburgh

Edinburgh will be the location of BNA2015: Festival of Neuroscience, due to be held on 12–15 April 2015.

Following the great success of BNA2013 at the Barbican in London, a similarly ambitious event will be organised at Edinburgh International Conference Centre.

Further details will be announced in due course, but BNA2015: Festival of Neuroscience is likely to include around 50 symposia and workshops and a range of internationally recognised plenary speakers. The BNA will again be partnering with other learned societies to deliver a comprehensive scientific programme with an outstanding public engagement element. See **www.bna.org.uk/festival2015** for further details.

Brain Awareness Week

Multiple activities are taking place across the UK during 10–16 March 2014 to mark Brain Awareness Week, an initiative organised by the Dana Alliance for the Brain.

MakeBelieve Arts, for example, will be taking their 'Journey to the Centre of the Brain' project, supported by the Arts Council and Wellcome Trust, to primary schools across the south of England. Several universities, including Nottingham and Leicester, are organising open days of talks and hands-on activities.

Brain Awareness Week is a global campaign to increase public awareness of the progress and benefits of brain research. See **www.dana.org/BAW/** for details of this year's events and how to get involved in next year's initiative.

The European Year of the Brain

The European Brain Council has pledged to make 2014 the European Year of the Brain. More than 200 organisations, commercial, academic, charitable and political, have pledged to support the Year of the Brain in Europe in 2014. Numerous luminaries, including BNA President Russell Foster, Colin Blakemore and Richard Morris, have also lent their support to the initiative. Further details can be found at **bit.ly/LFXTPi.**

Secretary's Report

Dear Colleagues

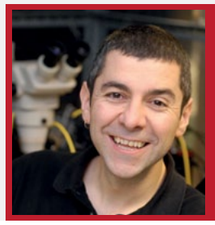
Yes – it's official: the BNA2015: Festival of Neuroscience will be held in – cue drum roll – Edinburgh! Programme planning is well underway, with around 50 symposia and eight plenary lectures in the pipeline. The scientific programme will be just as excellent as it was in London last year. And, like 2013, a major public engagement programme is also being assembled to run in parallel with the main conference. Make a note in your diaries of 12–15 April 2015 for what promises to be another neuroscience spectacular from your BNA.

As you might expect, we've also been very busy with other things. From the ever-popular Christmas symposium, featuring music and the brain, to co-sponsored meetings with the Biochemical Society and Oxford Neuroscience on astrocytes and optogenetics, respectively, the BNA is pushing the agenda of topics of interest to our members. Furthermore, public engagement continues apace with two of our high profile Patrons, Ruby Wax and former BNA President Colin Blakemore, in conversation later this year in Oxford.

Never an organisation to neglect its members, your views were once again shared with BNA Council during the Local Group Rep forum held the day after the Christmas Symposium. A very useful exchange of opinions and ideas suggested more ways in which the BNA can reflect the needs and aspirations of its community. Key points included greater student involvement and the potential to introduce both lay and undergraduate membership categories. This would tap into the terrific general interest in neuroscience and a new neuroscience careers leaflet aimed at school students and undergraduates, which will be available soon on the BNA website.

As always, BNA HQ is very keen to hear from you, our members. This can be done through your Local Group Rep, any Committee or Council member, or the BNA Office.

If you do contact the BNA Office, you will probably receive a response from Cecilia Sheen (cecilia.sheen@bna.org.uk). Cecilia is covering for Louise Tratt, who is taking maternity leave. We send Louise our best wishes at this exciting time.



Bruno Frenguelli, Secretary

BNA Council and National Committee

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Gary Gilmour (Eli Lilly & Co): Corporate Representative
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Cecilia Sheen (BNA): Executive Officer

Supporting our members

The BNA's support for **Thelma Lovick** enabled her to win her employment tribunal case against the University of Birmingham.

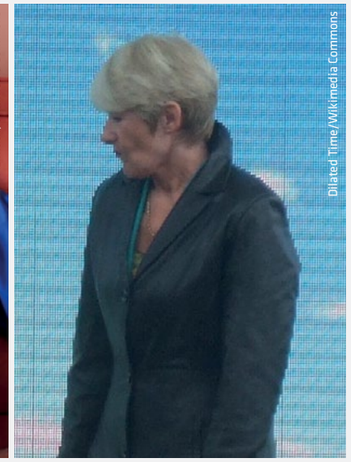
Dr Lovick, a long-standing member of the BNA, was dismissed from the university for a technical infringement of the Animals (Scientific Procedures) Act 1986. The BNA helped Dr Lovick through a university hearing and appeal processes and, when these were unsuccessful, supported her through an employment tribunal, which threw out the case against her in September 2013. One of the criticisms of the university was that it had not taken account of the experts the BNA and others had made available through the process. Dr Lovick has since taken up a position at the University of Bristol.

Standing up for science

David Nutt, former President of the BNA, has been awarded the 2013 John Maddox Prize for Standing up for Science. The prize recognises courage in promoting science and evidence on a matter of public interest, in the face of difficulty and hostility.

The award, a joint initiative of the science journal *Nature*, the Kohn Foundation, and the charity Sense About Science, reflects Professor Nutt's commitment to evidence-based debate about drug regulation, often in the face of political opposition. The award is named in honour of former *Nature* editor, Sir John Maddox.

Azimuth/Wikimedia Commons



Dilated Time/Wikimedia Commons

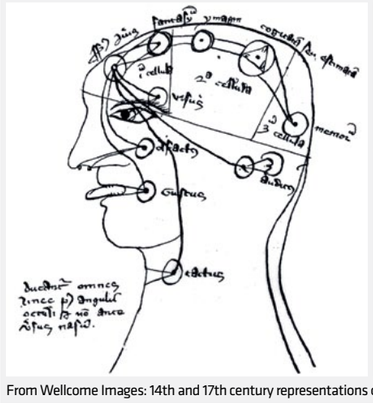
Colin Blakemore and Nancy Rothwell, two leading scientists identified by the Science Council.

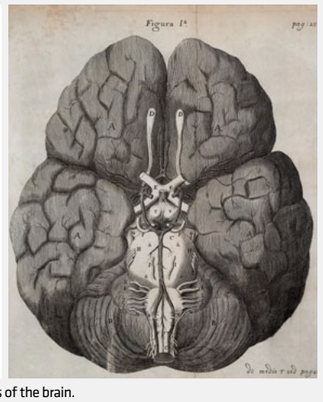
The hot 100

The Science Council has attempted to dispel the notion that there is a single type of scientist, identifying ten leading scientists – including some familiar names – in ten categories.

The list is aimed at groups such as the government, media and the public who may equate the term 'scientist' only with long-gone luminaries or those making landmark discoveries. The list emphasises that there are many different types of scientist, each making important contributions to wider scientific endeavours. Categories cover teaching, entrepreneurship, policy-making and communication, as well as discovery.

The 'investigator scientist' category includes both **Uta Frith** and **Nancy Rothwell**, while 'communicator scientists' include **Colin Blakemore** and **Hannah Critchlow** of Naked Neuroscience fame. Health psychologist **Marie Johnstone** (Aberdeen) is named as a 'developer/translational' scientist, as is artificial intelligence specialist **Sir Nigel Shadbolt** (Southampton) and psychologist **Andy Young** (York). **Max Headley** (Bristol) is recognised as a 'policy maker' scientist for his work on animal use in research. The full list can be found at **bit.ly/1auYWHA.**





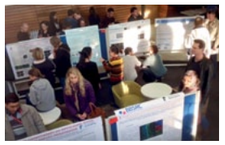
From Wellcome Images: 14th and 17th century representations of the brain.

Wellcome Images

All out-of-copyright historical Wellcome Images are being made freely available under the Creative Commons Attribution (CC BY) licence, enabling them to be used and manipulated freely, for commercial or personal purposes, as long as the original source is acknowledged.

The 100,000 images include numerous historically important images of the brain and nervous system. High-resolution files can be downloaded directly from **http://wellcomeimages.org**

Events



Neuroscience@ Nottingham

On 11 December 2013, Nottingham neuroscientists gathered for the annual Neuroscience@ Nottingham Poster and Lecture Day.

More than 50 posters presented neuroscience research from across the University of Nottingham's Schools of Life Sciences, Bioscience, Psychology, Physics, Mathematics and Medicine, and the MRC Institute of Hearing Research, covering topics ranging from cellular neuroscience to cognitive and clinical neuroscience. Guest speaker **Joanna Wardlaw** (Edinburgh) gave a fascinating overview of her multidisciplinary translational research programme on vascular disorders of the brain.

Postgraduate poster prizes were awarded to Beili Shao (Division of Clinical Neuroscience, Stroke Group) and Sorley Somerled (School of Psychology, Behavioural Neuroscience Group), for their excellent research and presentations on the effects of hyperglycaemia on cerebral barrier function and on the role of prefrontal cortex in the hippocampal learning behaviour translation, respectively.

Oxford Neuroscience Symposium

The fifth Annual Oxford Neuroscience Symposium will take place on 26 March 2014. As well as a wide range of local speakers, the Symposium will also include a guest lecture from **Francesca Happé** (Institute of Psychiatry) on autistic spectrum disorders.

UCL Neuroscience Symposium

The 2014 UCL Neuroscience Symposium will take place on Thursday 19 June at the Institute of Education. The symposium is only open to members of the UCL Neuroscience community and invited guests. The day's programme will be announced shortly.

Barts Neuroscience

Queen Mary and Barts and the London (QMBL) Neuroscience Society organised a one-day Barts Neuroscience symposium on 12 February 2014. The student-led event featured a stellar lineup of speakers, including **David Nutt**, **Daniel Wolpert** (Cambridge), **Richard Frackowiack** (Lausanne), **David Clayton** (QMUL) and **Nick Fox** (UCL). The meeting also included a poster competition open to undergraduate and graduate students, and practical skills workshops.

Edinburgh lecture online

The Edinburgh Neuroscience 2013 Public Christmas Lecture can now be enjoyed online. In their presentation, 'Folding and unfolding: the molecular origami of dementia', **Richard Knight** and **Jean Manson** cover the misfolding of key brain proteins, how they lead to disease, and how a better understanding of misfolding may ultimately lead to new treatments. The lecture can be viewed at **bit.ly/1gUK6OF**.

Glasgow Neuroscience day

The 5th Glasgow Neuroscience day, held at the University of Strathclyde, took place on 17 January 2014. A keynote address on imaging pain was given by **Irene Tracey** (Oxford).

Cambridge Neuroscience Seminar

The 26th Cambridge Neuroscience Seminar, 14 March, sponsored by the BNA, focuses on 'Brain science and mental health'. The Seminar features plenary lectures from **Mark Johnson** (see page 18) and **Trevor Robbins**, with an evening public plenary lecture by **Michael Owen** (Cardiff) on 'Genes, brains and psychiatry'.

Bristol brains

Researchers at Bristol have taken their 'Brain Box Challenge' to more than 1000 primary school pupils.

The Brain Box Challenge is a hands-on practical workshop, helping pupils in years 4–6 understand what the human brain looks like, how scientists study it, how it differs from those of other animals and how it controls our behaviour. Organised by Dave Turk, the initiative has been running since October 2012, and in September 2013 his department received the STEM University Department of the Year award for Bristol, Bath and Somerset from STEMNet. See **bit.ly/1kPPloA** for more.

Rowling clinic

The Anne Rowling Regenerative Neurology Clinic at the University of Edinburgh was formally opened by Her Royal Highness, The Princess Royal in October 2013. The centre is named after the mother of author J K Rowling, who provided a £10m donation. Anne Rowling died from multiple sclerosis in 1990. See **http://annerowlingclinic.com/** for more about the centre.

Nudge–it

John Menzies and **Gareth Leng** (Edinburgh) have been awarded an €8.9m EU Framework Programme 7 (FP7) grant for an international collaborative study of the determinants of food choice. 'Nudge-it' will bring together an interdisciplinary team of dozens of scientists from 16 institutions across six European countries, the USA and New Zealand. The aim is to better understand decision-making in food choice and to build predictive models to contribute to public health policy.

Brain injury award

David Menon (Cambridge) and **Andrew Maas** (Antwerp) are leading a £25m Europe-wide investigation into the causes of and treatments for traumatic brain injury. Data will be analysed from more than 5000 patients recruited from across Europe, providing detailed insight into the scale of such injury in Europe, differences in treatment and best practice in identification and treatment. The investigation is part of the International Traumatic Brain Injury Research initiative, running in the USA, Canada, and elsewhere.

A platform for dementia

The MRC has launched the UK Dementias Research Platform (UKDP) to promote the use of population cohorts in dementia research.

The UK has outstanding strengths in population cohorts, including the 500,000-strong UK Biobank cohort. As cohort members age, the prevalence of dementia and neurodegenerative disease increase. Physiological and other data collected by the cohorts may provide insight into the development of such conditions (or protection against them). Findings could feed into early detection and development of new treatments.

The UKDP, which will cover 22 cohorts and two million participants, is intended to be a public–private partnership, with GSK already pledging its support. Five-year funding of £5m has been awarded to a team led by John Gallacher (Cardiff), with an executive team of investigators from Cambridge, Edinburgh, King's College London, Imperial College London, UCL and Swansea. A £650,000 feasibility study, funded by the MRC and the NIHR, is intensively characterisating 24 pre-clinical Alzheimer's disease patients, to try to identify early biomarkers of disease. The project is being led by Simon Lovestone (Oxford and King's College London) in collaboration with the Imanova brain imaging partnership. See **bit.ly/1dBeSfu** for more on the UKDP.

Dementia funding

The ESRC and NIHR have awarded £20m funding for six dementia research programmes designed to slow or prevent the development of dementia and improve the quality of life of dementia patients and their carers.

The 'Neighbourhoods and Dementia' programme, led by **John Keady** (Manchester), will explore what makes a 'dementia-friendly neighbourhood'. The 'Promoting Independence in Dementia (PRIDE)' study, led by **Martin Orrell** (UCL), aims to identify how social and lifestyle changes can reduce the risk of developing dementia and disability.

Gillian Livingston (UCL) is leading a 'Managing Agitation and Raising Quality of Life' programme, while **Martin Knapp** (London School of Economics and Political Science) will be developing a tool to identify the future needs of dementia patients and their carers. The 'Living well with Dementia' study, being led by **Linda Clare** (Bangor University), will examine the factors that help dementia patients maintain their quality of life. Finally, 'Seeing what they see', led by **Sebastian Crutch** (UCL), will focus on posterior cortical atrophy, which particularly affects vision.

Leonard Wolfson Centre opens

The Leonard Wolfson Experimental Neurology Centre at UCL has been formally opened. Funded by a £20m award from the Wolfson Foundation, the Leonard Wolfson Centre has been set up to improve understanding of neurodegenerative diseases and to provide facilities in which experimental therapeutics can be tested in humans (see *BNA Bulletin 66*, Autumn 2012).

Wikimedia Commons

Messing with your head: Kylie Minogue.

Music and the masses 1

A new 'citizen science' project aims to identify what makes a song so catchy. Launched at the Manchester Science Festival, #Hooked asked celebrities and members of the public to nominate their favourite catchy tune. A poll of 700 people concluded that 'I Can't Get You Out of My Head' by Kylie Minogue was the catchiest ever. Wellcome Trust Engagement Fellow Erinma Ochu and computational musicologist John Ashley Burgoyne aim to analyse the selected songs to try to find the roots of their catchiness.

As well as a simple 'name-that-tune' game for the web, the team hopes to provide insight into the aspects of music that appeal to the brain, potentially feeding into musical therapies for neurodegenerative or other conditions. See **bit.ly/19zk44c** for more.

Music and the masses 2

The MRC is launching a mass participation study to assess whether listening to loud music is contributing to increased hearing loss in the UK population.

Around 1 in 6 people have some form of hearing loss, sufficient to cause difficulties with communication, with numbers rising by some 12 per cent over the past 20 years. Listening to amplified music could be contributing to this increase.

Michael Akeroyd from the MRC Institute of Hearing Research and colleagues are asking people to go online, describe their listening habits and take a short hearing test. The results should reveal any correlations between past listening habits and current hearing difficulties. The test can be taken at **www.100yearsofamplifiedmusic.org/.**

More games

Four new games have been added to the Great Brain Experiment app, a 'citizen science' project using mobile phone games to gather information on psychological and cognitive tests. Developed by a team at the Wellcome Trust Centre for Neuroimaging and White Bat Games, the new games will test decision-making, performance under pressure, hearing ability and use of information to make predictions (see *BNA Bulletin* 69, Autumn 2013). See **www.thegreatbrainexperiment.com**

Wellcome Trust Investigators

Neuroscientists again feature in the New Investigator and Senior Investigator awards recently announced by the Wellcome Trust:

New Investigators

Christopher Petkov (Newcastle): Neuronal mechanisms for extracting communication signals and signalling sequences: From animal models to humans.

Senior Investigators

Jonathan Clarke (King's College London): Cellular and molecular regulation of early brain development.
Leon Lagnado (Sussex): Synaptic computation in the visual system.
Walter Marcotti (Sheffield): The development and function of the mammalian auditory circuitry.
Kate Storey (Dundee): Cellular and molecular mechanisms regulating neuronal differentiation in embryos and adults.

Royal Society fellowships

Neuroscience features in several fellowship projects recently funded by the Royal Society.

Royal Society University Research Fellowship

(providing potential leaders with the opportunity to build an independent research career):

- **Brian Patton** (Oxford): Imaging deep tissue neural processes with nanodiamond.

Newton International Fellowship

(sponsored by the Royal Society and the British Academy):

- **Sungho Tak** (South Korea to UCL): Dynamic causal modelling for near-infrared spectroscopy.
- **Rafael Pineda Reyes** (Spain to Edinburgh): Kisspeptin neurones: linking reproduction with behaviour.
- **Takao Sasaki** (Japan to Oxford): From individual cognition to collective intelligence.

Dorothy Hodgkin Fellowship

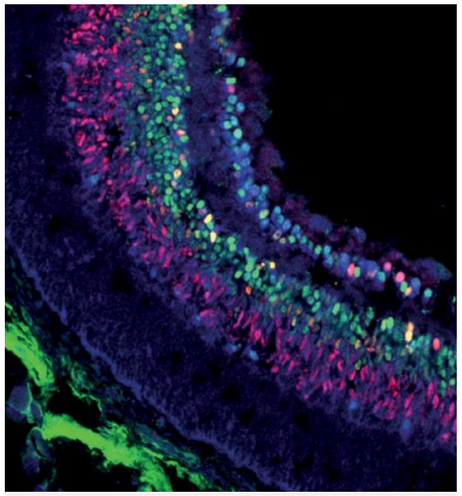
(helping early-career researchers who require a flexible working pattern progress to a permanent academic position):

- **Sebastian Cachero** (Cambridge): Transynaptic labeling of neural circuits in *Drosophila*.

Charles Fernyhough's *Pieces of Light: The New Science of Memory* was runner up in 2013 Royal Society Winton Prize for Science Books. Described by Ian Sample in the *Guardian* as "utterly fascinating and superbly written", the book focuses on reconstructive aspects of memory, combining science and memoir.

Neuroeconomics accolade

Timothy Behrens (Oxford) has received the 2013 Young Investigator Award from the Society for Neuroeconomics for his work on brain function in decision-making (see *BNA Bulletin* 68, Summer 2013). Professor Behrens shared the award with Daphna Shohamy from Columbia University in New York.



Retinal section, by Sasha Woods.

Art of science

Neuroscience made a strong showing in Bristol's annual Art of Science competition, with Sasha Woods one of the runners for this beautiful retinal section. The winning images were turned into a 2014 calendar. Winning entries can be viewed at **bit.ly/1cDol2n.**

Louisa Gross Horwitz Prize

John O'Keefe has been awarded Columbia University's 2013 Louisa Gross Horwitz Prize, alongside **Edvard Moser** and **May-Britt Moser**. Professor O'Keefe, Director of the Sainsbury Wellcome Centre for Neural Circuits and Behaviour at UCL, was recognised for his landmark work on spatial maps within the hippocampus.

Gabbay Award

Gero Miesenböck (Oxford; see page 20) is one of this year's recipients of the Jacob Heskel Gabbay Award in Biotechnology and Medicine. The award, created by the Jacob and Louise Gabbay Foundation, recognises scientists in academia, medicine or industry whose work has outstanding scientific content and significant practical consequences in biomedical sciences.

Neuroscience research may find application in the classroom.

Neuroscience in education

The Wellcome Trust and the Education Endowment Foundation (EEF) have launched Education and Neuroscience, a £6m fund to support collaborations between educators and neuroscientists to develop and evaluate neuroscience-based educational interventions.

A better understanding of brain function, and how students learn, offers the prospect of improved teaching methods. Indeed, an online survey of teachers carried out by the Wellcome Trust found that many teachers were optimistic about the ability of neuroscience to improve future teaching practice. However, some supposedly 'scientific' innovations, such as the belief in different learning styles and commercially developed interventions such as Brain Gym, have little evidence to support them.

To support the initiative, the EEF and Wellcome Trust have carried out a literature review, examining the impact of educational interventions based on neuroscience, surveyed teachers and parents to understand their perspectives, and approaches they are already using, and commissioned a series of articles from neuroscientists (see the Wellcome Trust's ThInk blog, **http://thinkneuroscience.wordpress.com/).**

See **bit.ly/LfhW6n** for further details. The deadline for the first round of applications is 6 May 2014.

Authentic Biology in schools

Students from five secondary schools presented the results of academic research they had undertaken at a symposium featuring BNA President Russell Foster and Lord Winston.

The students have been participating in the Wellcome Trust's 'Authentic Biology' initiative, which teams up schools with nearby universities enabling students to carry out genuine experimental research. Supported by a Wellcome Trust Society Award, Authentic Biology was piloted by Dave Colthurst at the Simon Langton Grammar School for Boys, who worked with researchers at the University of Kent on a project focused on myelin basic protein. The scheme has now been extended to five schools, linked to the Universities of Bristol, Sheffield and Southampton and Queen Mary, University of London.

The results form the research projects were presented at a second annual Authentic Biology Research Symposium on 4 November 2013. The Kent collaboration also hopes to publish its results in an academic journal.

News in Brief

Neuroscience at Davos

Cambridge neuroscientist **Barbara Sahakian** joined world leaders and other dignitaries at the Davos World Economic Forum in January. Every year, leading thinkers from business, politics, academia and other sectors gather at Davos to discuss how to improve the state of the world. The theme of this year's meeting was 'The Reshaping of the World: Consequences for Society, Politics and Business'. Professor Sahakian was a discussion lead in sessions on the neuroscience of leadership, performance-enhancing technologies and redefining ageing. See **page 31** for more.

FENS on film

Budding film-makers might like to enter a video competition being run by FENS in association with the FENS Forum, 'Jump the FENS', to be held in Milan 5–9 July 2014. €750 prizes are available for there categories – protocol videos, educational presentations and for humorous entries. Entrants must include at least one PhD or postdoctoral student registered for the FENS Forum. The closing date for entries is 30 April 2014. Further details can be found at **www.jumpthefens.eu/video-contest.html**

Music all in the mind

The Christmas Eve edition of BBC Radio 4's *All in the Mind*, presented by Claudia Hammond, drew inspiration from the BNA Christmas Symposium. The 30-minute programme featured speakers from the symposium – hear the results at **bbc.in/1cp3ejp.**

Naked neuroscience

David Nutt joined Hannah Critchlow for a special Christmas Naked Neuroscience podcast. Professor Nutt chose some of his favourite neuroscience stories from 2013, featured alongside items of laughter and addiction. The November 2013 podcast was a more sombre affair, 'Bombing the Brain' examining the impact of war on mental health and the potential for brain enhancement and brainwashing. Podcasts can be downloaded from **bit.ly/12NaQuZ.**

Writing on the brain

PhD student **Scott Armstrong** (Imperial College London) won the 2013 Max Perutz Science Writing Award for his article 'Saving the brain from itself'. He received a prize of £1500 and his essay was published in *Times Higher Education*.

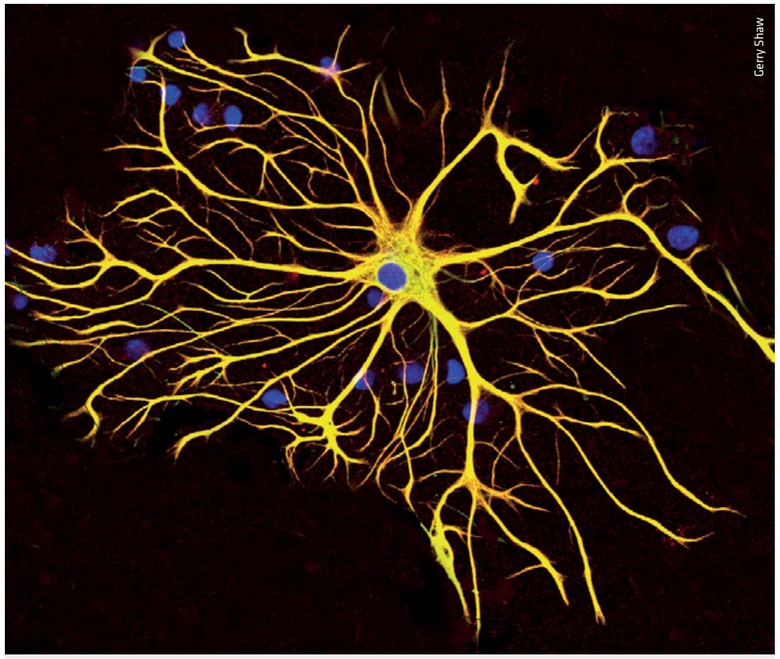
Astrocytes in health and neurodegeneration

The BNA and Biochemical Society have joined forces to organise an international conference on astrocytes and their role in health and disease, to be held on 28–29 April 2014.

Astrocytes, the most abundant cell in the human brain, have traditionally been viewed as 'support cells' and given significantly less attention than neurons. Recent years have seen a resurgence of interest in astrocytes and other glial cells, with the growing realisation they not only contribute to normal brain function but also play significant roles in brain disease. The joint BNA–Biochemical Society conference, featuring speakers from the UK, Continental Europe and the USA, will cover emerging research in these areas, with a particular focus on neurodegeneration.

The biochemical mechanisms underlying the development and progression of most neurodegenerative diseases remain unknown. It has become increasingly clear that signalling between glia and neurons influences the progression of neurodegenerative diseases. Research in this area has traditionally focused on microglia, considered to be the major immune cell in the brain. However, in the past few years, deficits in the function of astrocytes are increasingly recognised to be associated with neuronal loss in motor neuron disease, Alzheimer's disease and some rare lysosomal storage disorders.

In addition, there is now substantial evidence that astrocytes regulate normal neuronal activity and connectivity, playing important roles in basal synaptic transmission and long-term potentiation. Major research efforts are ongoing to understand the signalling pathways by which astrocytes and neurons communicate, and the mechanisms by which astrocyte–neuron interactions are disrupted in neurodegenerative diseases.



An astrocyte grown in tissue culture.

The 'Astrocytes in health and neurodegeneration' conference brings together leading researchers investigating the role of astrocytes in health and astrocyte dysfunction in neurodegenerative diseases. As well as relatively well-studied neurodegenerative conditions such as Alzheimer's disease and motor neuron disease, it will also provide a forum for researchers working on lysosomal storage disorders, including rare neurodegenerative diseases of childhood such as the neuronal ceroid lipofuscinoses. Topics include:

- Astrocyte–neuron interactions
- Astrocytic signalling pathways
- Energy metabolism and astrocytes
- Neuroinflammatory responses of astrocytes
- Astrocyte dysregulation in brain injury, Alzheimer's disease, lysosomal storage disorders, and motor neuron disease.

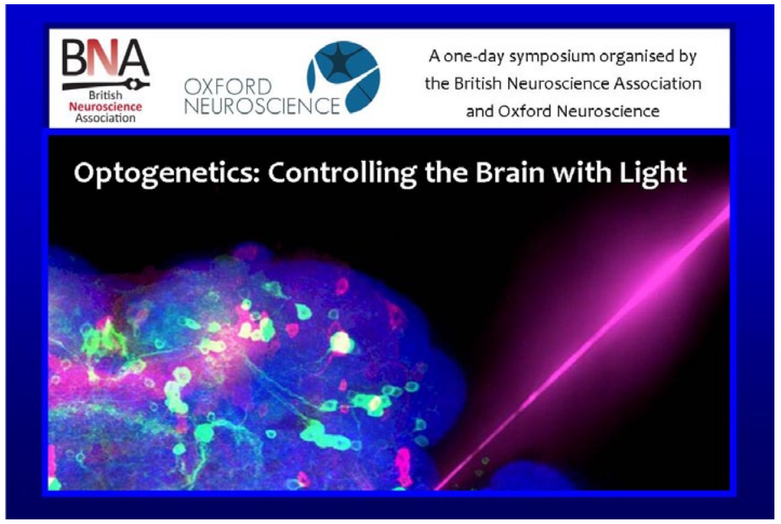
Speakers include:

- **Alexei Verkhratsky** (Manchester)
- **Andrey Abramov** (UCL)
- **Dmitri Rusakov** (UCL)
- **Mark Sands** (University of Washington, USA)
- **Michael Sofroniew** (University of California Los Angeles, USA)
- **Milos Pekny** (University of Gothenburg, Sweden)
- **Nicola Allen** (Salk Institute, USA)
- **Pamela Shaw** (Sheffield)
- **Pierre Magistretti** (University of Lausanne, Switzerland)
- **Siddharthan Chandran** (Edinburgh)
- **Vladimir Parpura** (University of Birmingham Alabama, USA)
- **Yuriy Pankratov** (Warwick)
- **Jon Cooper** (King's College London)

Plenary lectures will be given by Michael Sofroniew (University of California Los Angeles, USA) and Alex Verkhratsky (Manchester).

The conference will take place at the UCL Institute of Child Health on Guilford Street in Central London. Conference sponsors include Portland Press Ltd, Biochemical Society Transactions and ASN Neuro, and proceedings will be published in *Biochemical Society Transactions*.

BNA members can benefit from reduced registration rates. Full details of the conference can be found at **bit.ly/1eFNJsc**



Optogenetics: controlling the brain with light

A one-day symposium on optogenetics, organised by the BNA and Oxford Neuroscience, will showcase some of the ways in which this powerful new technique is being used to study nervous system function.

In 2013, Gero Miesenböck of the University of Oxford and five other researchers were awarded the prestigious Brain Prize 2013, endowed by the Grete Lundbeck Foundation, for their development of optogenetics. To mark this achievement, the BNA and Oxford Neuroscience have teamed up to organise a one-day symposium, 'Optogenetics: controlling the brain with light', to be held on 3 April 2014, which will showcase how groups in the UK and elsewhere in Europe are using the technology to explore neural function.

The symposium has been designed to give graduate, postgraduate and other early-career researchers a sense of how optogenetics can be used to address biological problems, and to inspire them to think how they might apply the technology in their own studies.

Optogenetics provides a powerful way to selectively activate (or inhibit) groups of neurons in living, behaving organisms. First reported by Professor Miesenböck in 2002 (see page 20), it relies on genetic methods to express a light-sensitive ion channel (nowadays typically channelrhodopsin, originally identified in algae) in specific subsets of neurons. A light signal can then be used to stimulate neural activity in these specific neurons.

The technology has distinct advantages over conventional methods of electrode-based stimulation. For a start, it is possible to work with large numbers of cells – far more than would be possible with electrode-based approaches. In addition, genetic control elements are used to limit the expression of the light-sensing mechanism to specific cells in a population, without each individual cell needing to be identified in advance. Furthermore, the technique is far more flexible than electrode-based methods – precise neuronal control is possible even if a behaving animal moves around.

These technical advantages have opened up multiple new opportunities to identify neural circuits and to probe their properties in living organisms. In recent years, the technology has been refined and widely adopted worldwide. The symposium will hear how researchers have used optogenetics to address biological problems in a range of experimental model organisms. Speakers include:

- **Ole Paulsen** (Cambridge): Using optogenetics to probe left–right asymmetry of hippocampal memory
- **Stephanie Cragg** (Oxford): Illuminating the gatekeepers of dopamine transmission
- **Vincent O'Connor** (Southampton): Guiding light to feeding behaviour in *C. elegans*
- **Claire Wyart** (Paris): Dissecting spinal circuits underlying sensory motor integration with light in a small vertebrate
- **Alexander Gourine** (UCL): Studying the function of vital circuits using optogenetics
- **Sergey Kasparov** (Bristol): Application of opsin-based actuators to study astrocyte-to-neuron communication
- **Dimitri Kullmann** (UCL): Optogenetics for closed loop control of neural activity.

A plenary lecture will be given by keynote speaker Gero Miesenböck, Director of the Centre for Neural Circuits and Behaviour at the University of Oxford, who will be introduced by Colin Blakemore (School of Advanced Study, University of London). The symposium will be chaired by BNA President Russell Foster. Sponsorship has been provided by the International Brain Research Organization, Laser 2000, Tracksys Microscope Services Ltd, CoolLED and Laser Quantum. Full details of the symposium can be found at **bit.ly/1hhL9c5.**

Ruby Wax in conversation with Colin Blakemore
Wednesday 4 June, 19.00-20.30
Sheldonian Theatre, Oxford

Join TV personality Ruby Wax in conversation with Colin Blakemore. This discussion will explore the many ways in which neuroscience has come to play such an integral part in Ruby's life and career. We also learn how she overcame depression, and find out how a neuroscientist views mental illness from Professor Blakemore. A thoroughly insightful evening not to be missed. Details will be on the BNA website shortly.

Hitting the right notes

Thanks to the ubiquitous carols (and, inevitably, Slade), the musical brain was the appropriately seasonal theme of the 2013 BNA Christmas Symposium, held in partnership with the Sainsbury Wellcome Centre at UCL.

In a richly varied programme, Maria Chait (UCL) opened proceedings with a fascinating insight into how the brain's auditory system can detect patterns in sound – an ability fundamental to the appreciation of music. Not only are we remarkably quick at detecting patterns in series of notes – typically by about the fourth note in a repeating pattern – but we also seem to do so automatically. These pattern-recognition skills, suggested Dr Chait, may have evolved to enable us to predict what is coming up and to rapidly spot deviations from expectations.

Katie Overy, Director of the Institute for Music and Human and Social Development in Edinburgh, brought an interdisciplinary perspective to the day. One of her main interests is the 'rhythmic brain' and the curiously powerful effects of regular rhythms or beats. Rhythmicity appears to have a powerful influence on the body, while many human behaviours show striking rhythmicity (including clapping, as readily demonstrated by audience participation). Perhaps, Dr Overy speculated, the power of beats may have deep-seated roots, as a mechanism for coordinating group activities or promoting pro-social behaviour.

Lauren Stewart at the Christmas Symposium.

One of music's most striking qualities is its ability to trigger strong emotional responses in listeners – a power instinctively exploited by film-makers and others. Alan Watson (Cardiff) discussed the brain systems involved in these responses, particularly emotional brain networks. Given its lack of any clear evolutionary purpose or advantage, it is curious that music taps so powerfully into emotional and reward pathways, and is capable of generating such pleasing and even intense emotional responses.

Lauren Stewart (Goldsmith's, University of London) focused on an unusual condition, congenital amusia. People with this condition, she suggested, cannot make sense of music; they cannot recognise familiar tunes and may even find music unpleasant to listen to. She has recruited a group of Londoners with characteristics of congenital amusia, finding intriguing evidence that their difficulties may not be a simple perceptual abnormality – their tonal perception skills are generally near-normal– but may actually reflect a lack of awareness of these skills. Hence congenital amusia may be a meta-cognitive rather than perceptual deficit.

In a break from academic presentations, Peter Todd described the Alzheimer's Society's 'Singing for the Brain' service, in which trained musicians run regular workshops for people with dementia and their careers. Based on 'old-time' songs, the stimulating and hugely enjoyable sessions provide a boost to both memory and wellbeing.

Finally, Jason Warren (UCL) explained how neurodegeneration can have highly specific effects on musical perception and appreciation. The composer Ravel, for example, who probably suffered from frontotemporal dementia, became unable to express his musical ideas in later life. Brain imaging is now revealing the neuroanatomical correlates of highly specific deficits in musical cognition in different patient groups. More generally, he suggested that music may have evolved as a mechanism for communicating complex mental states, supporting the remarkable social cognition skills of humans.

Uta Frith receiving her award.

Jane Haley with Russell Foster.

During the symposium, presentations were also made to the year's BNA award winners – Uta Frith (contribution to neuroscience), Jane Haley (public understanding of neuroscience), Rumana Chowdhury (postgraduate award; see page 32) and Elina Jacobs (undergraduate award; see page 32).

As well as the stimulating scientific presentations, participations were treated to virtuoso violin playing during intervals by Jinpo Xiang, a sixth-form student from Newcastle under Lyme. And during post-talk mince pies and wine, entertainment was provided by the Rhapsody in Bluegrass ensemble, Kelly Jakubowski and Steven Lyons. The highlight of the day, though, may have been BNA President Russell Foster's Christmas cracker jokes – some of which, fortunately, have been captured for posterity in the *Guardian's* feature on scientists' favourite jokes **(bit.ly/1bBRB89).**

Speakers at the BNA's Neuroscience Summit.

Neuroscience Summit

The BNA has published a report of the Neuroscience Summit, held at the Royal Society in April 2013, outlining some of the ways in which the BNA can play its part in tackling the huge challenges posed by disorders of the brain and nervous system.

The Neuroscience Summit, a joint venture between the BNA, the European College of Neuropsychopharmacology (ECNP) and the European Brain Council (EBC), brought together neuroscientists, leaders from research councils, industry and patient organisations to take stock of UK neuroscience and how it can best address the health and social consequences of brain disorders. It was supported with a grant from the Federation of European Neuroscience Societies (FENS).

As outlined in an analysis commissioned by the EBC, brain disorders are responsible for an enormous health and economic burden in Europe – amounting to some €800bn every year. At the same time, technological advances and a greater understanding of the brain are opening up new opportunities for interventions. A key challenge is how to ensure this potential is realised to the benefit of the citizens of Europe (and beyond).

The summit heard presentations from the EBC's Mary Baker and Sharmila Nebhrajani of the Association of Medical Research Charities on public and patient involvement in research. John Perry, John Williams and Melanie Welham provided a funders' perspective, from the Medical Research Council, Wellcome Trust, and Biotechnology and Biological Sciences Research Council, respectively. Industry views were represented by Jackie Hunter of OI Pharma Partners and Gary Gilmour of Lilly UK. Colin Blakemore and David Nutt brought an academic perspective, while Richard Morris and Trevor Robbins helped to draw out the day's conclusions. The summit was introduced by BNA President Russell Foster and chaired by BBC Radio's Quentin Cooper.

The importance of the subject was underlined by messages of support from both the Prime Minister, David Cameron, and the Minister of State for Universities and Science, David Willetts.

A number of key themes emerged from the meeting. Patients were seen to have a potentially vital to play throughout the research process, from feeding into policy-making and priority-setting to advising on research protocols and grant applications. In the research arena, there was widespread support for more emphasis to be put on interdisciplinary research and collaboration – between disciplines and across institutions.

Russell Foster outlining the BNA's vision.

There were also calls for greater interactions between academia and industry, recognising the complementary skill sets in the two sectors. Industry has retreated from the field and more needs to be done to entice additional commercial investment. Nevertheless, significant efforts are being made, particularly through industrial–academic consortia and partnerships to tackle difficult problems collaboratively. Sharing more information in the public domain and 'open innovation' approaches can avoid duplication of efforts, promote coordinated, concerted efforts to understand disease mechanisms, and accelerate drug development processes.

Even so, more needs to be done to promote interdisciplinary and cross-sectoral working. More ways to encourage and reward working in partnership need to be developed, and career paths for young scientists to reflect contributions to team working as well as individual achievement. Other incentives may be needed to encourage further industrial investment, while the European regulatory framework needs to be re-examined to ensure that unnecessary regulation does not slow down the development of new medicines.

The discussions and themes have been refined into a series of action points. The BNA is now working on how these action points can best be taken forward. The aim is to ensure not just that the UK retains its position as one of the world leaders in neuroscience research but also that this intellectual potential is fully exploited to help those affected by debilitating and deadly brain disorders.

A copy of the Neuroscience Summit report can be downloaded at **bit.ly/1crbSgU**.

The evolution of translational CNS medicines research

Developing medicines for CNS conditions is even harder than non-CNS drug development, but there are reasons to be optimistic, says **Alan M Palmer**.

Alan M Palmer.

Traditionally, scientific research has been categorised as either fundamental, driven by scientific curiosity (and without any obvious practical value), or applied – designed to solve practical problems. Fundamental and applied researchers occupy different worlds, possess distinct cultures and respond to different drivers. In the medical domain, this makes it difficult to translate fundamental research results into practical applications that enhance human health and well-being. To help bridge this gap, the concept of translational research was proposed in 1968 and has led to the concept of 'translational medicines research' (Ref. 1).

From knowledge to medicine

The essence of translational medicines research is the efficient and effective conversion of biomedical knowledge into new medicines. It encompasses all research activity from fundamental biology to a marketed drug (Fig. 1). Key aspects of this process are: (1) understanding the biological basis of human disorders (to permit the discovery of a tractable molecular target for drug discovery); (2) lead generation and optimisation (the 'hit' molecules that bind to the molecular target are subjected to a battery of tests to assess whether they are likely to be safe and effective in humans); and (3) clinical testing, to meet the safety, quality and performance standards laid down by regulatory authorities (Ref. 2).

Wikimedia Commons

Developing CNS medicines is a challenge.

Translational medicines research is an increasingly important aspect of neuroscience, particularly as 13 per cent of the global burden of disease is attributable to mental, neurological and substance abuse disorders, greater than both cardiovascular disease and cancer (Ref. 3). This burden will increase substantially, as the number of people in the world aged over 65 years is set to rise sharply and the incidence of many brain disorders (e.g. Alzheimer's disease, stroke and Parkinson's disease) increases exponentially after age 65.

However, developing therapies for disorders of the brain is notoriously difficult. CNS drugs take on average 35 per cent longer than other new prescription medicines to complete clinical trials and receive regulatory approval (Ref. 4). CNS drug candidates are also less likely than their non-CNS counterparts to become medicines. As a result, several pharmaceutical companies, including AstraZeneca, Pfizer, GSK, Merck and Sanofi, have substantially reduced their CNS drug discovery and development efforts in the UK and overseas.

In an attempt to discover and develop approaches to improve the speed, efficiency and effectiveness of CNS R&D, a Translational CNS Summit was held in London on 22–24 October 2013, organised by Hanson Wade (Ref. 5). A number of encouraging themes emerged:

- **Target identification:** The development of new drugs for CNS disorders has been hampered by poor knowledge of underlying pathophysiology. However, molecular genetic data are now helping to change this situation. For example, genome-wide scans are revealing mutations and rare copy number variants that (rarely) cause or increase the risk of a CNS disorder. Such data can lead to the creation of mouse models that can be used to facilitate the discovery of new drug targets (Ref. 6).
- **Animal models of CNS disorders:** The predictive validity of animal models of CNS disorders is generally poor. For example, despite the tremendous advances in transgenic animal technology (especially for research into Alzheimer's disease), the success rate for CNS drug candidates in clinical development has not increased. However, the use of automated systems (including touchscreen technologies) to analyse rodent behaviour, coupled with the use of rodents genetically modified to reflect risk genes for particular CNS phenotypes, is likely to generate animal models with better predictive validity (Refs 7, 8).
- **The use of biomarkers in clinical studies:** A biomarker can be defined as a biological variable that has a statistically significant relationship with parameters of disease states or the activity of a drug or drug candidate. They have great value in clinical trials. They allow for more homogenous patient populations in clinical trials through patient selection and stratification, and potentially significantly smaller sample sizes. They also provide opportunities to track disease progression, and hence the impact of medicines, over convenient timeframes (Ref. 9).

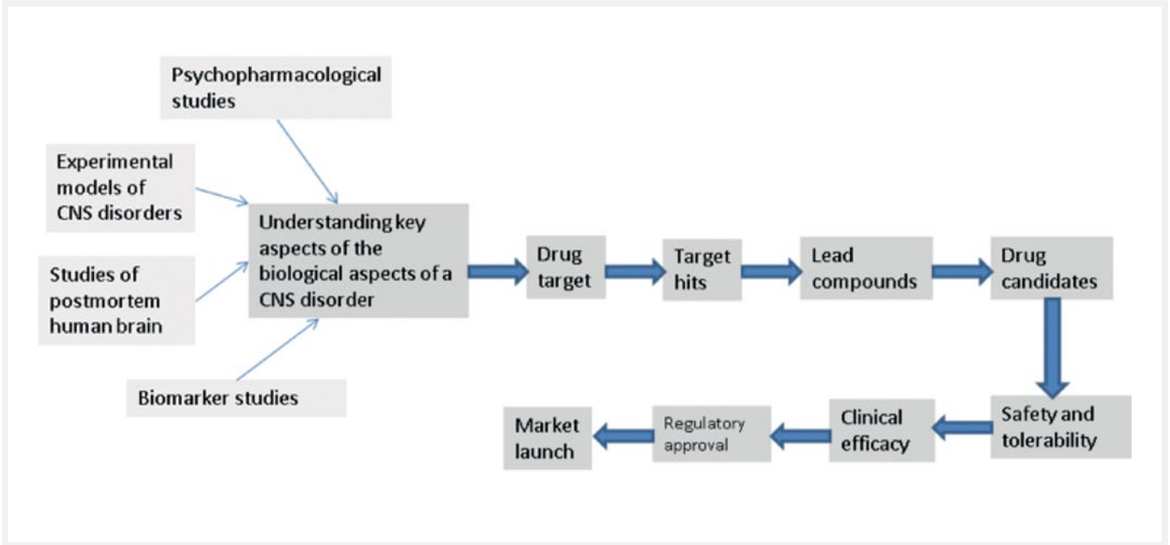


Figure 1. The components and process of translational medicines research.

Future prospects

CNS translational medicines research is in the midst of major change. Unfortunately, UK medical charities, which account for one-third of all public expenditure on medical and health research, typically exclude medicines research companies from applying for funding. By doing so, they are rejecting the very organisations – biotech companies – with the know-how to translate research into tangible patient benefit.

Important exceptions are Cancer Research Technology and the Wellcome Trust. These world-leading organisations illustrate what can be achieved outside of traditional pharmaceutical business constructs, particularly for early stage translational medicines research. New public–private partnerships are also evolving where risks and resources are shared among several participants. Good examples include the Division of Signal Transduction Therapy in Dundee and the Structural Genomics Consortium in Oxford.

Translational research funding is also available from organisations such as the National Institute for Health Research and the Technology Strategy Board, as well as from new European funding vehicles, such as Horizon 2020 (nearly €80 billion of funding available over 7 years) and the Innovative Medicines Initiative (IMI). IMI is a joint initiative between the European Federation of Pharmaceutical Industries and Associations and the European Commission. With a budget of €2 billion, it is driven by industry through the identification of bottlenecks to which research can contribute solutions and research areas of common interest that reduce drug development times and costs. An example is the Pharma-Cog project, which aims to develop and validate new tools to test candidate drugs for the treatment of the symptoms of Alzheimer's disease, as well as compounds that slow disease progression.

These and other translational medicines research initiatives (including MRC Technology) reflect a new paradigm for medicines research, based on open and integrated partnerships with wider stakeholder involvement (Ref. 10). With individuals from industry joining their ranks, universities will play an increasingly important part in this process. Academic drug discovery is now well established in the USA, as illustrated by bodies such as the Academic Drug Discovery Consortium, which has 98 member universities across North America (www.addconsortium.org). Similar trends are likely to be seen in the UK.

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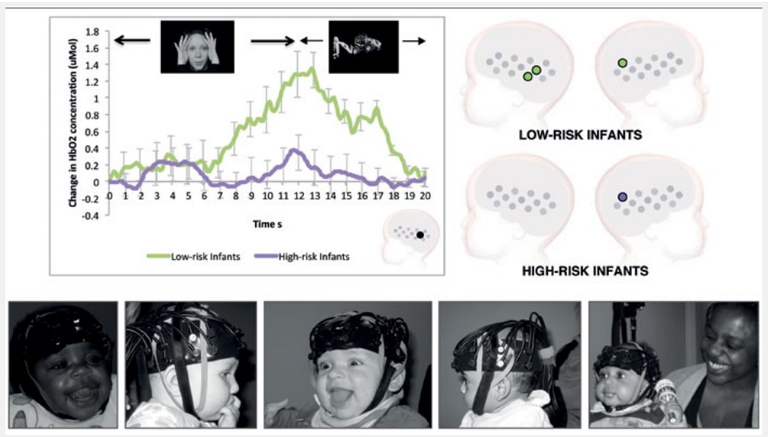
Alan M Palmer *is a neuroscientist and entrepreneur. Currently he is a visiting Professor at UCL and the University of Reading; Life Science Entrepreneur in Residence at the University of Bristol; a director of Cerebroscience Ltd, MS Therapeutics Ltd and One Nucleus Ltd; and non-executive director of Neuro 360 Ltd and the BNA.*

Inside a baby's brain

A new imaging technology is shedding light on social brain development in babies – and revealing remarkably early abnormalities in infants at risk of autism.



NIRS has revealed differences in the brain responses of infants at risk of autism to social stimuli.

The biological roots of autism remain poorly understood. In part, this reflects how difficult it is to study in early infancy, says **Mark Johnson** an MRC scientist at Birkbeck, University of London: "The surprising thing is, for the first year to 18 months, it's not been possible to use any behavioural markers to predict autism at age 3; rather, they seem to look fairly typical in terms of their overt social behaviour. Looking at neural or brain function measures is turning out to be more informative."

To aid such work, Professor Johnson has established the British Autism Study of Infant Siblings (BASIS), a national network facilitating the study of infants at risk of autism. Children with elder siblings with autism are themselves at significantly greater risk of developing the syndrome.

In 2012, Professor Johnson and colleagues used EEG and eye-tracking technology to show that abnormal responses to social stimuli – faces – at around nine months of age was associated with diagnosis of autism at age 3. However, although convenient, EEG has limited spatial resolution. For the past decade or so, Professor Johnson has been working with Clare Elwell in UCL's Faculty of Engineering to adapt a form of optical imaging, near-infrared spectroscopy (NIRS), for use with infants. NIRS detects the same bloodflow signatures as fMRI but, crucially, with more simple, cheaper and portable equipment.

Even so, developing detector caps for young infants was a technical challenge. Professor Elwell and Professor Johnson worked side by side to develop the technology and the scientific questions it could address. The power of the new approach was confirmed in 2013, with the striking discovery that, in response to social stimuli, babies at risk of autism as young as 4–6 months showed abnormalities in the social brain areas of the temporal cortex known to be defective in older children and adults with autism.

At this stage, points out Professor Johnson, it is not possible to say whether these are early indicators of later autism, as the children have not yet reached the age of clinical diagnosis. But if they are, NIRS may ultimately have value as a diagnostic tool (or at least a method to identify those at significant risk of autism).

Not all infants at risk go on to develop autism, however, suggesting that environmental inputs might be compensating for innate vulnerabilities. "There's quite a lot of interest in what those compensatory factors might be," says Professor Johnson. "If you can understand them, you might have a better chance to develop new interventions." Professor Johnson has been involved in a trial of an intervention designed to enhance parents' social interactions with their babies, the results of which are due to be published later in 2014.

The work may also shed more light on the developmental mechanisms of autism, says Professor Johnson: "There's still a big debate about whether these young babies have problems because they have some sort of social brain network problem, or whether social stimuli are more spatiotemporally complex, and thus some more widespread cortical synapse problem is revealed better by social stimuli."

Recently, Professor Johnson has even applied NIRS to newborns – in collaboration with colleagues in Italy, where mothers typically stay longer in hospitals than in the UK. This work established that activity in social brain areas fired up remarkably rapidly. "Only a few hours of social interaction is enough to get these cortical systems tuned up," says Professor Johnson. Over the first few days of life, social brain activity increased, correlating with the levels of social stimuli babies received.

The combination of engineering development and science underpinning NIRS has been highly productive, says Professor Johnson: "We've been able to train up PhD and postdoctoral researchers who are experienced in both the infant psychology, the neuroscience side, and the medical physics side. It's been very successful." The approach has now been adopted by more than 20 groups worldwide: "It's spreading fast so it shows there's a real need for it."

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Extreme hoarding

A surprisingly large number of people accumulate possessions so excessively that their lives are severely affected – victims of the newly defined 'hoarding disorder'.

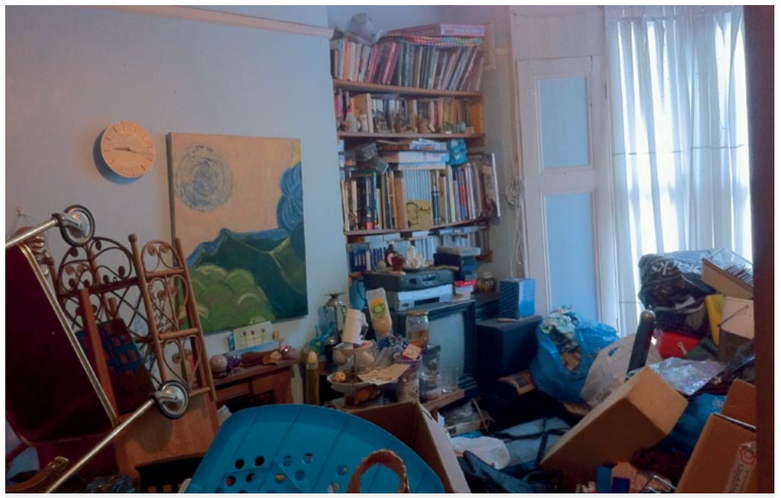
David Mataix-Cols is a specialist in obsessive-compulsive disorder (OCD) and related conditions. Although the condition can be treated reasonably well, he noticed that one group of patients responded suboptimally: "About 15 years ago I discovered, by chance, that patients who have OCD and also hoard don't respond so well to conventional evidence-based treatments for OCD. And that triggered a number of studies to try to understand why."

His subsequent work, carried out at the Institute of Psychiatry, and other studies showed that, although excessive accumulation of possessions can be a consequence of OCD, most hoarders were quite distinct from other OCD patients – in terms of symptoms and behaviour, brain activity, and genetics. Dr Mataix-Cols and others proposed that 'hoarding disorder' was a distinct clinical entity, a classification now written into the psychiatrist's diagnostic bible, DSM-5, and also likely to be included in the WHO's ICD-11 guidelines. "It's now globally recognised as a bona fide separate entity," says Dr Mataix-Cols.

He is keen to stress that the diagnosis does not pathologise 'normal' behaviour, such as collecting. "There might be some superficial similarities with the hobby of collecting. Many healthy people do this, and it's a highly pleasurable and very social activity. That is in sharp contrast with hoarding disorder, which involves extreme difficulty with parting with possessions." Accumulation of objects, and an inability to discard them, ultimately has a significant impact on people's lives: "The end product is severely cluttered living spaces, to the extent that they are no longer usable." The condition is socially isolating and distressing for patients and their families.

A cluttered living space is not necessarily indicative of hoarding disorder, points out Dr Mataix-Cols: "It could be the end product of dementia or schizophrenia or other severe mental disorders or even the consequences of a brain lesion." These possibilities need to be excluded before a diagnosis of hoarding disorder can be made.

As well as showing that hoarding disorder is distinct from OCD, and that the diagnostic net does capture normal collecting behaviour, Dr Mataix-Cols has carried out population-based work to estimate its prevalence. Initial questionnaire-based surveys have suggested a prevalence of 2–5 per cent; more recent home- and interview-based research puts the figure at around 1.5 per cent.



The living space of a typical person with hoarding disorder.

Nevertheless, he adds, very little is known about the condition: "These are early days: it's a new disorder, we're only just beginning to understand it." It has been linked to some behavioural traits, such as indecision, procrastination and, perhaps oddly, perfectionism. Some preliminary brain imaging studies have pointed to possible involvement of the ventromedial prefrontal cortex, cingulate cortex and limbic structures. Twin studies suggest a moderate level of heritability.

Its environmental origins are also obscure. "We know there is a very high level of self-reported trauma," says Dr Mataix-Cols. It might be expected that material deprivation when young might be a risk factor: "But that doesn't seem to be the case. These patients were not worse off as children in terms of material possessions. So that intuitive link does not seem to hold."

Interestingly, although patients are typically diagnosed in middle age, this might be the end point of a much longer process: "If we ask them, when did this problem start, almost invariably they say 'in my childhood'. That's why we started looking at childhood populations to try to understand the origins or seeds of what will later become problematic." Indeed, a survey of adolescents found that significant numbers, around 2 per cent, already reported problems discarding possessions.

Dr Mataix-Cols recently moved to the Karolinska Institute in Stockholm, Sweden, and plans to continue working on hoarding disorder. As well taking advantage of the excellent twin registries in Sweden to study its epidemiology, he hopes to uncover more about its biological mechanisms, while better treatments for patients are also an important priority: "No one knows what to do with them; they're very hard to treat."

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Gero Miesenböck

The sweet smell of success

The first to develop 'optogenetic' approaches for neuroscience, Gero Miesenböck is now using the technology to probe the neural circuitry of fruit flies, particularly that underlying olfactory-guided behaviour.

One of the most significant technological advances of the past decade, optogenetics allows for extraordinarily precise manipulation of neural activity. Rather than just observe neural activity, neuroscientists can now intervene, assessing how stimulation (or inhibition) of specific neurons affects neural circuitry and the behaviour of living organisms. In a series of landmark publications, **Gero Miesenböck** at the University of Oxford has demonstrated the power of the new technology and how it can be applied to address critical biological questions.

Optogenetic control grew out of studies using genetic modification to visualise neural activity. Hippocampal neurons were engineered to express a protein that was stored in synaptic vesicles and lit up after exocytosis. "That was the very first genetically encoded reagent designed specifically to look at activity in the nervous system," recalls Professor Miesenböck. In particular, it established the principle of using genetics to target and study specific neural cell types.

Useful though this was, the extension to light control of neural activity was a game-changer, and Professor Miesenböck can recall the precise moment when inspiration struck: "It was the weekend, I'd taken a long walk and come back home and started reading a novel I was absorbed in at the time. Then suddenly I thought, wouldn't it be amazing if one could use light to control a specific genetically targeted cell type in the intact brain."

Unbeknownst to Professor Miesenböck, a similar thought had occurred to Francis Crick, who had speculated about the possibility in a paper published in late 1999. "I became aware of that article because he cites one of my earlier papers on genetically encoded imaging probes, and I received a citation alert via email. I read that paper and was stunned to see the importance Crick attached to the 'far-fetched' possibility of using light to control genetically targeted neurons, a possibility we were already working on it."

The connection led to a fruitful correspondence: "I wrote to Crick to say we were doing these experiments and he sent back a very encouraging letter saying, 'I'm surprised and delighted you're already doing this, please keep me posted about how your experiments progress'. Which is what I did."

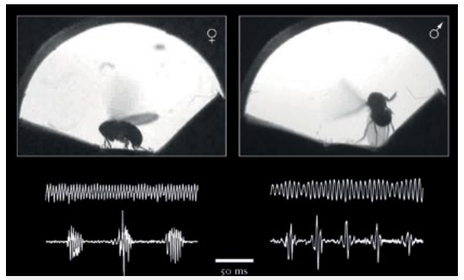
In January 2002, Professor Miesenböck published a paper showing that the approach was feasible, and sent Crick a preprint: "Once again he replied quickly saying he was excited to see that the system worked and that he looked forward to seeing how the field would develop."

The impact of the 2002 paper took time to be felt, says Professor Miesenböck. "I think it was a slow burner. Several people have told me that when they saw it they ran to their supervisors and said 'have you seen this?' but overall it developed very slowly."

That all changed in 2005: "The second paper, in *Cell* in 2005, where we actually controlled the behaviour of a fly, that started to stir people's imagination. It got a lot of attention, also in the lay press – some of it quite crazy 'mind control' stuff. But that paper showed what really might become possible." A significant boost, he adds, was the subsequent adoption of channelrhodopsin, creating a single-component and more efficient system: "That was a catalyst of the whole field taking off."


The set up for implanting memories in flies.

"TO APPROACH BIOLOGICAL SYSTEMS WITH THE MINDSET OF AN ENGINEER CAN BE VERY FRUITFUL."



Optogenetics can make female flies sing like males.

To show how optogenetics could be used, Professor Miesenböck turned to sex. Fruit flies display highly stereotyped sex-specific courtship behaviours. The genetics of sex determination and control of sex-specific morphology were well established, but how nervous system function drove sex-specific behaviours was much less clear.

In 2005, it was discovered that the products of the *fruitless* gene, which come in male and female forms, were critical controllers of sex-specific behaviour. But *fruitless* is active in just 2 per cent of neurons, and these 2000 or so neurons of male and female flies looked very similar. "Optogenetics was the obvious tool to get at that question," says Professor Miesenböck. "It was a wonderful opportunity to show off the power of the technique. It would have been unimaginable to control a large and dispersed population of cells in an intact behaving animal with electrodes."

Using optogenetics, he was able to switch on the circuit dedicated to male-specific courtship in females, causing them to display male-specific behaviours: "They started to sing as if they were trying to woo another female."

The implication was that the adult fly brain is to a large degree built in a 'unisex' manner, with only a few master regulatory nodes flipping activity between male and female behaviour. "Which I think is a very economical and elegant solution to what's a very complex problem, namely how to build male and female nervous systems. Wiring up a brain is probably the most difficult developmental problem evolution has had to solve, and if you had to find two separate solutions for males and females that would complicate things further. If you build a unisex brain first, at a relatively late stage in development you can just set a few switches and get male- or female-specific behaviour. I find that quite appealing."

Professor Miesenböck went on to use optogenetics to implant a new olfactory memory. "Olfaction has always played a significant role as most of the behaviours we study are influenced by odour inputs," he points out. Pheromone detection is important in sexual behaviour and memory for olfactory cues is critical to food seeking. "So it's important to understand how odour information is represented in the brain."

Recent work has revealed how flies can discriminate between similar smells: "We found there is a surprising mechanism where you have parallel excitatory and inhibitory lines innervating a brain region where odour discriminations are made. Inhibition helps to separate overlapping odour representations."

Interestingly, says Professor Miesenböck, this idea is present in the artificial intelligence literature, with suggestions that inhibitory signals can provide input gain control to enhance the ability of 'perceptrons' to discriminate input patterns. "It was striking to find an implementation of this idea in the brain of the fly."

These studies, and the cellular engineering underpinning optogenetics, emphasise a key theme of his research. "Engineering concepts and physical principles should play a much larger role in biology and neuroscience in particular," he says. "To approach biological systems with the mindset of an engineer can be very fruitful."

This theme permeates throughout the Centre for Neural Circuits and Behaviour, established by Professor Miesenböck late in 2011 with funding from the Wellcome Trust and the Gatsby Charitable Foundation. Experimentalists, engineers and theoreticians are using the fly to understand how neurons act in concert to drive behaviour. Flies, he suggests, are an ideal model, being easy to work with, cheap and with powerful genetics, and none of the regulatory overhead associated with vertebrates. "Although we sometimes joke that if our centre succeeds, and we show how evolved the cognitive abilities of fruit flies are, we might actually shoot ourselves in the foot!"

Optogenetics remains core to the Centre's work, though he is keen to stress that it is just a tool: "It is one method in an arsenal of many. We use it when we can use it productively. I'm dismayed when I get applications from potential graduate students saying they would like to work on optogenetics. I think they are putting the cart before the horse. What always has to be the ultimate motivation is to solve a biological problem, not to apply a technique."

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Jack Mellor

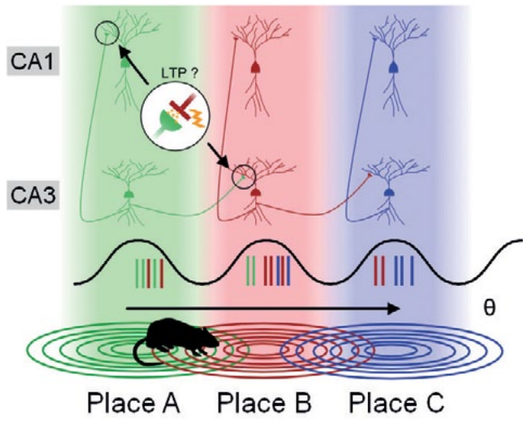
Plasticity: from synapse to network

While the molecular mechanisms of synaptic plasticity are gradually being unravelled, a further challenge will be to understand their effects on neural circuits.

Synaptic plasticity has long been conceived as the neural basis of learning and memory. Ever since the first demonstrations of long-term potentiation (LTP) more than 40 years ago, researchers have searched for the cellular mechanisms that cause the properties of a neuron to change following stimulation. **Jack Mellor** at the University of Bristol, recent recipient of a Wellcome Trust New Investigator Award, has spent much of his career exploring these mechanisms of synaptic plasticity. Now, though, he is shifting his focus to understand how they influence neural circuits responsible for key neurobehavioural phenomena such as memory.

After a PhD at the MRC Laboratory of Molecular Biology in Cambridge with Andy Randall, Dr Mellor's first postdoctoral appointment enabled him to spend two years in the USA – working with Roger Nicoll at the University of California San Francisco – and a final year in John Isaac's lab at Bristol. After an MRC Career Development Fellowship, he secured a permanent academic position at Bristol.

"My background is as a synaptic physiologist," he explains. "Right now we study hippocampal networks and synapses and how they function." And although synaptic plasticity lies at the heart of his work, he is now looking at wider issues: "We've moved towards also thinking about what plasticity means to the function of the network."



Theta rhythms in the hippocampus provide a mechanism for encoding of spatial trajectories in the hippocampus. From Sadowski *et al.*

With its well-established roles in memory formation and spatial navigation, and well-described neural architecture, the hippocampus is an excellent model in which to address these kinds of question. "What we've become interested in is how the hippocampus actually encodes memories," he says. In the context of spatial memory, that means understanding the coordination of 'place cells' – hippocampal cells that fire when an animal is in a specific spatial location. It is has been suggested that synaptic plasticity could arise if place cells responsive to similar locations were synaptically connected (and, indeed, that the degree of plasticity would reflect how close locations were, providing a way to encode spatial distances).

With John Isaac, Dr Mellor was able to show that this did indeed happen. By transposing place cell activity from freely moving rats into hippocampal slices, he was able to show that LTP could be induced but only when place cells had coincident firing fields. "We're now moving on to think about how that plasticity might enable place cells to be wired up to maintain or encode an engram or memory from that group of cells within the hippocampal network."

Acetylcholine: the key to memory?

Notably, induction of LTP in place cells was dependent on raised levels of acetylcholine. This neuromodulator has a critical role in hippocampal function, and is an area of growing interest in Dr Mellor's lab.

This strand of work has important translational implications, particularly for the development of cognitive enhancers to treat memory deficits. Acetylcholine levels fall during early stages of Alzheimer's disease, and components of the acetylcholine system have been widely targeted as a strategy for boosting or maintaining memory: "The only treatments we currently use for the cognitive deficits in Alzheimer's disease are the cholinesterase inhibitors, and no one really knows how or why they work," Dr Mellor points out. "There's an idea they boost the amount of acetylcholine in the cortex and the hippocampus. If that is the case, we might want to understand more about what acetylcholine is doing to those networks to cause those effects."

Moreover, current treatments are not very effective and have significant side-effects, so there is significant potential to develop better, more

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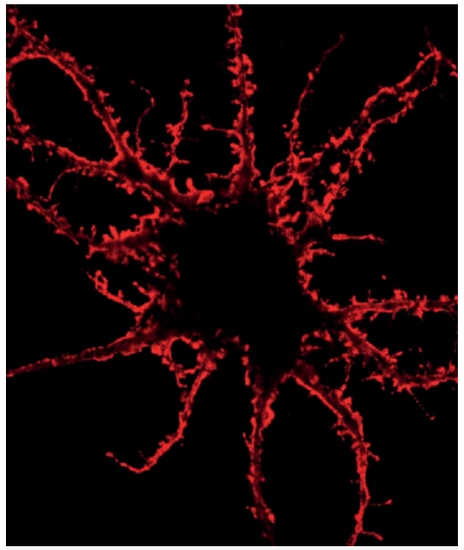
"IF WE CAN UNDERSTAND HOW ACETYLCHOLINE HAS ITS EFFECTS... THEN WE WOULD HOPE TO BE ABLE TO SAY THIS IS THE TARGET YOU OUGHT TO GO FOR."



Visualisation of kainate receptors in hippocampal neurons.

selective approaches. Dr Mellor has established collaborations with industrial partners, Lilly and GSK, and hopes his work will have practical spin-offs: "If we can understand how acetylcholine has its effects, which specific receptors it targets to improve the function of that hippocampal network, then we would hope to be able to say this is the target you ought to go for."

A key question, he suggests, will be the nature of acetylcholine receptors expressed on hippocampal cells. He and others have begun to identify routes through which activation of different receptor subtypes can influence plasticity. A major challenge now is to integrate these disparate findings: "Quite a lot of work has already been done on which receptors are expressed on which cell types and what the functional effects of those receptors are. What were trying to do is put that together into an integrated network model."

Hence, the lab has a growing interest in computational models: "We've been developing our approach to computational modelling for a while and we're at the stage where we have some really good models being built at the moment, and the predictions they make can be really exciting."

Standing up for kainate

Another strand of Dr Mellor's research focuses on kainate receptors which, he argues, have been unjustly neglected: "They're always seen as the poor cousins of the other more famous ionotropic glutamate receptors, AMPA and NMDA receptors. There is a perception they do the same thing as AMPA receptors but weaker and they're not nearly as exciting as NMDA receptors, because they don't appear to have the same function in terms of synaptic plasticity. They have also suffered from a lack of pharmacological tools to isolate their functions. So they tend to get a bit sidelined."

Nevertheless, he points out, because they appear to play a more modulatory role in synaptic and cellular function, they may prove better targets to manipulate circuit behaviour. They are also highly conserved and have recently been linked genetically to several human diseases: "So they must be really important for something."

As well as showing how they can influence the excitability of pyramidal cells, Dr Mellor has become increasingly interested in their developmental role. They appear to play a significant part in wiring up the developing nervous system, particularly the hippocampus. Abnormalities in this development could have long-term consequences: "If you have disruptions to the wiring up of neuronal networks in development, that is likely to be important in certain neurodevelopment disorders. We think kainate receptors and the control of their functional expression may be important for this."

With Jeremy Henley, Dr Mellor has also been examining the cell biological mechanisms that control trafficking of kainate receptors to and from the neuron cell surface. This work has identified a key role for phosphorylation and addition of the ubiquitin-like 'SUMO' polypeptide, SUMOylation, in intracellular trafficking. A further collaboration with Jonathan Hanley is examining intracellular proteins regulating AMPA receptor trafficking during synaptic plasticity and under ischaemic conditions where changes to AMPA receptor expression influence excitotoxicity. Such studies will continue to provide molecular insight into how the properties of individual neurons and synapses are controlled. An additional challenge will then be to integrate this knowledge to understand how networks of neurons can work together to achieve the mysteries of memory and learning.

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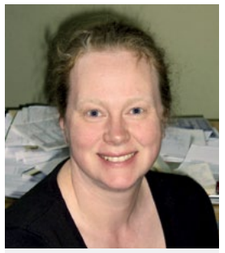


Catherina Becker

The remarkable regenerating fish

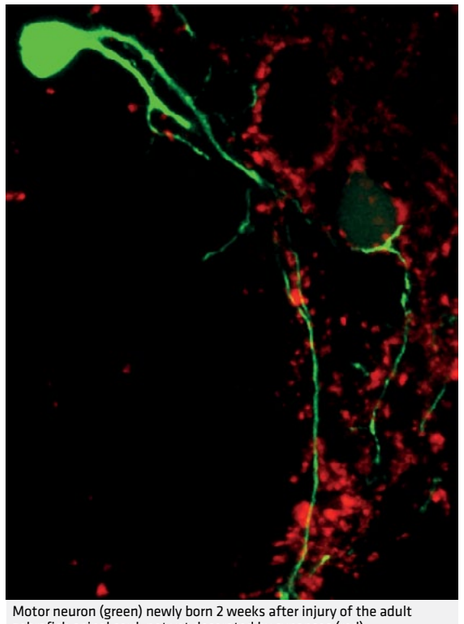
Zebrafish can rapidly repair a severed spinal cord. A better understanding of how they do so may suggest ways to enhance human nerve regeneration.

Catherina Becker, based at the Centre for Neuroregeneration in Edinburgh, has long been fascinated by the ability of amphibians to regrow body parts. For the past 20 years, however, it is the zebrafish, a more convenient experimental model, that has been her main focus. It too shows remarkable powers of recovery, and Professor Becker's group has begun to identify the molecular mechanisms underpinning this regenerative capacity.

"Frogs and salamanders, especially salamanders, are fantastic regenerators, but rather iffy to keep in the lab," says Professor Becker. "As zoologists, you can do fantastic things like breed them out of season by putting them into the vegetable compartment of your own fridge to mimic winter." Her mother was not so keen on her bringing work home, and amphibians also have experimental drawbacks: "They do not lend themselves well to, say, genetic or high-throughput studies. Each individual is quite precious as you've bred them yourself and raised them to adulthood, which takes over a year."

So, on moving to the Swiss Federal Institute of Technology in 1994, Professor Becker turned to zebrafish, establishing a model for spinal cord regeneration in collaboration with her husband and co-investigator Thomas Becker. In mammals, spinal cords are essentially unable to regenerate, but a paralysed fish with a severed spinal cord will typically recover within six weeks: "Most of them will swim as if nothing has happened," says Professor Becker.

"That obviously is a very interesting phenomenon," notes Professor Becker. "You're taking an adult nervous system and damaging it, and the anatomical recovery is not 100 per cent but the functional recovery is." Furthermore, zebrafish are easy to grow and to manipulate genetically, and are amenable to all kinds of studies from the cellular and molecular through to the behavioural: "That's what's really neat about the fish. It offers us this whole spectrum of approaches."



Motor neuron (green) newly born 2 weeks after injury of the adult zebrafish spinal cord, not yet decorated by synapses (red).

Development and regeneration

One key theme of Professor Becker's work is the seemingly close connection between development and regeneration. Many of the processes that build a fish in the first place are also used in repair after injury. Hence insight into developmental processes may also provide clues to regeneration.

Her main interest has been regrowth of motor neurons, spinal neurons driving the muscular contraction required for swimming. In 2008, now in Edinburgh, she showed that, after spinal cord lesion, progenitor cells in the spinal cord switch from making glia to motor neurons. These new cells integrate into existing circuitry, underpinning regain of function.

In terms of mechanisms, a key role is played by the developmental morphogen sonic hedgehog. Hence, the adult fish nervous system appears to maintain a class of progenitors, or stem cell-like cells, capable of being activated by sonic hedgehog and generating new motor neurons.

One suggested reason for the lack of spinal cord regeneration in mammals is high levels of Notch signalling – Notch is thought to play a key role in cellular decision-making between proliferation and differentiation. Notch signalling is also enhanced after spinal cord lesion in zebrafish, but apparently not to levels that shut off new neuron production completely. Hence regeneration may depend on Notch levels being neither too high nor too low – or in the 'Goldilocks zone' as Professor Becker puts it.

Recently, Professor Becker and colleagues have identified a key factor driving regeneration after spinal injury – dopamine. During development, growth of brainstem neurons needs to be integrated with the generation of motor neurons along the body axis. Descending axons of dopaminergic neurons in the brain play this key role during development, and also during regeneration. Acting through the dopamine D4a receptor and the hedgehog pathway, brainstem dopaminergic neurons promote motor neuron development at the expense of interneurons.

"THAT'S WHAT'S REALLY NEAT ABOUT THE FISH. IT OFFERS US THIS WHOLE SPECTRUM OF APPROACHES."

Regeneration and neurodegeneration

Such studies have drawn attention to the importance of factors such as Notch, hedgehog signalling and dopamine in nerve regeneration. But fish are also providing insight into a related area, neurodegeneration.

Oddly, the relevance of zebrafish to neurodegeneration featured in the recent Spider-man reboot, *The Amazing Spider-Man*. Dr Curtis Connors, aka the Lizard, is missing a right arm and keen to translate experimental work on limb regeneration. On a school trip to his lab, Spider-Man's alter ego, Peter Parker, highlights the direction Connors is taking: "A person gets Parkinson's when the brain cells that produce dopamine start to disappear. But the zebrafish has the ability to regenerate cells on command. If you can somehow give this ability to the woman you're talking about, that's that. She's…she's curing herself."

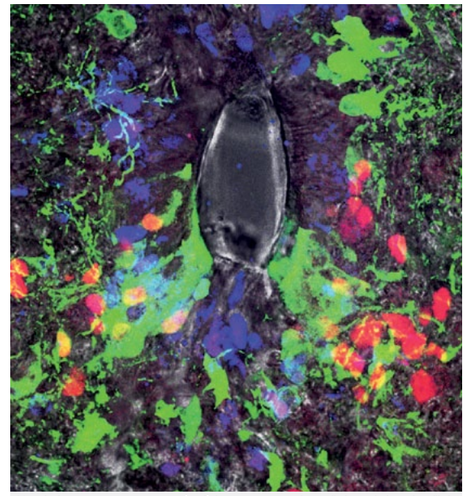
A screen for genes involved in motor neuron differentiation triggered Professor Becker's interest in a lectin-like protein, chondrolectin. Coincidentally, Kevin Talbot in Oxford and others implicated chondrolectin in the death of motor neurons in spinal muscular atrophy (SMA), a form of motor neuron disease. In fish, chondrolectin seems to have a role in axon pathfinding, but collaborative work with Professor Talbot suggests it may also be involved in cell survival. Notably, boosting chondrolectin levels rescued the SMA phenotype in zebrafish.

Professor Becker, Professor Talbot and Professor Tom Gillingwater in Edinburgh are continuing to explore the cellular and developmental phenotype of chondrolectin-deficient fish. In addition, a drug screen is being undertaken to identify compounds able to rescue the motor neuron deficits and generate potential therapeutic leads.

In other studies, zebrafish will be used to assess the neuroprotective effects of compounds developed by a local biotech firm, Antoxis. Complementing work on human patient-derived cells (led by Tilo Kunath), the work on fish will reveal whether the compounds actually have a protective effect on motor neuron function.

Returning to the original biological phenomenon, it remains unclear why fish have such powers of regeneration. "It's very hard to imagine an evolutionary advantage," says Professor Becker. In the wild, an animal with a severed spinal cord is unlikely to survive the six weeks required to regain swimming abilities. Perhaps, she suggests, the mechanisms help to repair minor damage incurred during daily life. Whatever the explanation, understanding how zebrafish achieve what mammals cannot may ultimately point the way to much-needed therapies.

Zebrafish, a valuable model for regeneration research.



Newly born motor neurons (red) in a cross section of the adult zebrafish spinal cord, some labelled with BrdU (blue); spinal progenitor cells and oligodendrocytes (green).

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Lena Palaniyappan

Networking opportunities

Studies of the brain's folding patterns, and other forms of structural and functional brain imaging, are providing new insight into schizophrenia – and suggesting possible new strategies for intervention.

It has long been hoped that brain imaging will ultimately impact on psychiatric practice. According to **Lena Palaniyappan**, an academic psychiatrist at the University of Nottingham, that day is fast approaching, with brain imaging moving from a descriptive to a mechanistic understanding of mental disorders.

After his medical degree in India, Dr Palaniyappan undertook postgraduate medical training in Nottingham and Newcastle. He is now a Wellcome Trust Clinical Research Fellow in Translational Neuroimaging in Psychiatry, and is interested in the use of brain imaging – structural and functional – to understand conditions such as schizophrenia.

"One of the most robust findings in imaging is loss of grey matter in patients with schizophrenia," he points out. "My question was, is this just simple loss of grey matter? Do people lose chunks of grey matter tissue, or is anything else happening on the surface of the brain? For example, is it thickness that is lost or the folding pattern of the brain, or is it the surface area that is shrinking? What exactly is happening?"

Conventional morphometric structural imaging techniques provide insight into volumes but little else. Instead, Dr Palaniyappan turned to surface-based morphometry, which takes 3D brain images and converts them into a two-dimensional sheet of cortex, allowing features such as thickness, surface area and brain folds to be examined. "When we looked at it, all sorts of changes were happening in the brain in schizophrenia, but the most striking was the reduction in the complexity of the brain folds."

The brain's primary folds (gyri) and furrows (sulci) are common to all, and form the basis of standard brain atlases. However, smaller-scale secondary sulci show more variability. Notably, the brains of people with schizophrenia showed distinctive gyrification abnormalities, mostly reduced complexity of folding. "This is important, as many of the folds we have in the brain, the gyrifications, these are decided very early in life. By around two years of development, most gyrification is complete."

The findings thus point to an early origin for these brain abnormalities in patients. "Although the story of schizophrenia being a neurodevelopmental disorder has been bubbling for a while, there's no convincing proof," notes Dr Palaniyappan. To his concern, some have argued that it is a neurodegenerative condition. "So looking at folding patterns gave an idea that maybe a significant proportion of what we see in grey matter is not simply a result of degeneration – a lot of it has probably happened very early in life, even before the age of two."

The implications of these findings are significant. They suggest good places to start looking to understand mechanisms of disease. And if cell death is not the cause, there may be more potential to exploit the brain's innate plasticity in treatment.

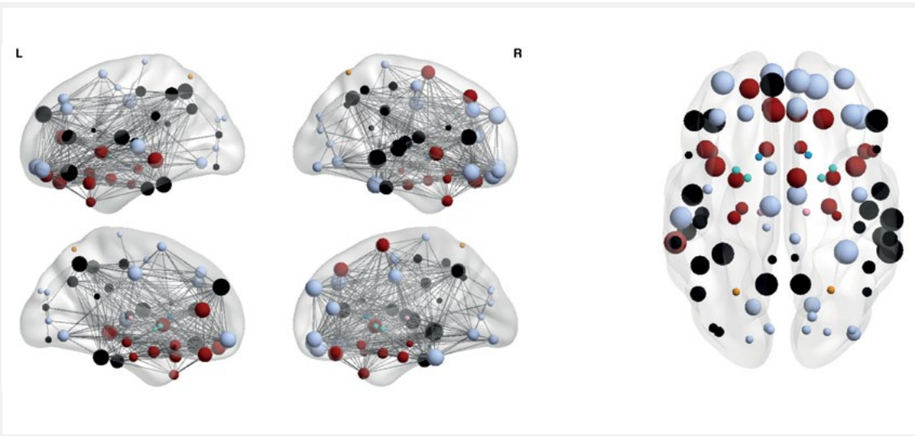
Dr Palaniyappan has gone on to show that gyrification abnormalities appear to have biological significance. Notably, with Paola Dazzan and Robin Murray at King's College London, he has discovered a correlation with treatment response – those with the most striking gyrification abnormalities showed poorest responses to anti-psychotic treatments. In addition, in patients suffering a psychotic episode, abnormal gyrification was greater in schizophrenia than bipolar disorder patients. This makes sense, he suggests, as bipolar disorder is not thought to be a neurodevelopmental condition.

Hence, brain imaging could help to characterise patients early in disease. Illness trajectories and treatment response profiles are remarkably heterogeneous in psychotic disorders. With novel imaging approaches, it may therefore be possible to provide some guidance to patients on the likely course of their disease, and also to give clinicians some clues to the likely response to treatment in psychosis.

Making connections

A key question remains – what is the cause of the gyrification abnormalities in schizophrenia? Although he stresses it is speculative, Dr Palaniyappan points to animal studies showing that early damage to white matter pathways in rodents leads to altered gyrification in adults. "This is maybe what is happening in schizophrenia, even before the age of two. Possibly there are some lesions in the white matter tracts which are not immediately visible but in adult life they produce this disturbed folding patterns."

This way of thinking emphasises the importance of neural circuitry in schizophrenia – and here Dr Palaniyappan has uncovered tantalising evidence of a possible mechanistic basis for the diverse and troubling symptoms of the disease.



Graphs based on volumetric patterns in schizophrenia. The nodes indicate specific brain regions while edges indicate the relationship between two regions.

His focus was drawn to the insula, one of the most highly folded parts of the brain and one showing significant folding abnormalities in schizophrenia. "So we thought, let's look at how this region is connected to the rest of the brain – let's see if it's different in people with schizophrenia compared to healthy controls."

This time he turned to functional imaging, applying Granger causal modelling techniques to understand functional connectivity between areas of brain activity. The key test was to examine activity while the brain was in 'idling mode' – when the distinctive 'default mode network' is typically active. When the brain needs to attend to an external stimulus, the default mode network shuts down and activity boots up in a 'central executive network' embedded in the prefrontal cortex. These transitions are triggered by a 'salience network' centred on the insula, a brain mechanism thought to be responsible for switching between internally and externally focused attention.

Dr Palaniyappan and colleagues discovered a striking reduction in salience network connectivity to the executive network in people with schizophrenia. "And, interestingly, the amount of reduction directly predicted how unwell the patients were. The clinical severity and the functional ability of the patients were very much related to the reduction in connectivity between the insula and the frontal cortex."

These findings, he suggests, make sense of the diverse and puzzling symptoms of schizophrenia: "The clinical features of schizophrenia are very diverse and don't immediately appear to be connected with each other. But you can explain a lot of them using this simple model, that there is a switch in the insula and that this switch doesn't function effectively – people don't switch between the internal and external world effectively."

"...ALL SORTS OF CHANGES WERE HAPPENING IN THE BRAIN IN SCHIZOPHRENIA, BUT THE MOST STRIKING WAS THE REDUCTION IN THE COMPLEXITY OF THE BRAIN FOLDS."

Furthermore, they point to a specific pathway that could be targeted in treatment. Several possible approaches could be envisaged to boost activation of the salience network, including neurofeedback ('brain training'), neurostimulation (transcranial magnetic stimulation or transcranial direct current stimulation), pharmacological interventions or through cognitive approaches such as mindfulness – or, indeed, a combination of methods.

Dr Palaniyappan is currently involved in a trial using magnetic stimulation on normal volunteers: "If we find signals strong enough to suggest that insula can be modulated by focused magnetic stimulation of frontal cortex, we will then try this on a clinical population, patients with psychosis or depression." Other studies are aiming to get at the neurochemical basis of defective network activity, and the possible involvement of glutamate and GABA signalling.

Dr Palaniyappan's work forms part of a wider Centre for Translational Neuroimaging in Mental Health at Nottingham, led by Peter Liddle. Brain imaging is non-invasive, quick and feasible even for acutely affected patients. It is, he suggests, close to giving clinicians useful information about individual patients. In the meantime, it is also generating vital information about the mechanisms underlying these devastatingly complex conditions.

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The legend of the Black Horse (revisited)

Robert Balazs and Edward H Reynolds

Within 50 years, the BNA has grown from a few dozen scientists to a large and flourishing organisation. It is timely to recall the foundation of the Brain Research Association (BRA), which later became the BNA, especially as a legend has arisen that the BRA was founded in 1968 by a group of London-based neuroscientists meeting informally in a pub, the Black Horse, between 1965 and 1968 (Refs 1–3). This legend is factually incorrect and we wish to set the record straight based on documented evidence and our own experience (Ref. 4). One of us (R.B.) was one of the four founding members of the Black Horse group.

Derek Richter (1907–1995) was Director of the multidisciplinary MRC Neuropsychiatry Research Unit from 1955 until his retirement in 1971. Among several international contributions to neuroscience, he was a founder member and served on the first Council of the International Brain Research Organisation (IBRO) in 1960. In that capacity he and fellow Council member Donald MacKay first wrote to 29 neuroscientists throughout the UK on 6 July 1967 enquiring about the possibility of establishing a national BRA, such as then existed in the USA, USSR and Japan. Only five respondents opposed the idea.

Richter convened and chaired a meeting at the National Hospital, Queen Square, London, on 23 February 1968, which unanimously agreed to establish the BRA and elect an Organising Committee (OC). Richter conducted a postal ballot and eight members of the OC were elected from different neuroscientific disciplines according to IBRO principles. The OC first met on 9 May 1968 and invited Richter to attend. Richter outlined how the BRA had been formed and the Committee elected. The Committee thanked Richter for the major part he had played in founding the BRA. At the first AGM of the BRA on 7 May 1971, when the Constitution was approved, Richter proposed the vote of thanks to the Officers.

The above are the documented facts. But in their account, Abi-Rached and Rose have written Richter out of the story. Instead they claim incorrectly that the BRA started as a group of like-minded scientists who met at the Black Horse and "from the London discussion group we became the BRA". The Black Horse group was set up in 1965 by four neuroscientists including Rose and one of us (R.B.) to promote discussions and exchange of ideas between London-based neuroscientists in a friendly and congenial environment. The meetings were informal and academic. There were no minutes and there was no political agenda. The group did not, as Abi-Rached and Rose claim, organise conferences, workshops or courses. The latter activities were all begun by the newly formed BRA, as the minutes confirm. This does not diminish the contribution of the members of the Black Horse group to the subsequent work of the BRA.

The legend of the Black Horse appears to be based on frail memories, inadequate historical research and perhaps some degree of wishful thinking. Rose, who was not elected to the OC of the BRA, but was later co-opted, was not one of the founders of the BNA as stated in the BNA Bulletin, but he was a founding father of the Black Horse group. Richter, who was a member of both the Black Horse group and the BRA, was the major founder of the BRA and thus the BNA.

Robert Balazs *is an Honorary Senior Research Associate, UCL;* **Edward H Reynolds** *is a Consultant Neurologist and Honorary Senior Lecturer, King's College London.*


BNA British Neuroscience Association

bulletin

The voice of British neuroscience today

INTO THE BRAINS OF BABES
How a bundle of cells develops a sense of self

BAD SCIENCE and other things that frustrate Ben Goldacre

PMS & PROZAC Could pills prevent pre-menstrual syndrome?

THE LEGEND OF THE BLACK HORSE

OR HOW THE BNA CONTRIBUTED TO THE BIRTH OF NEUROSCIENCE OVER A PINT IN A LONDON PUB

Joelle M. Abi-Rached, Anne Cooke and Steven Rose

Joelle Abi-Rached', a History of Science PhD student at Harvard, and Steven Rose, well-known researcher, broadcaster, author, political activist and one of the founding fathers of the BNA, recount how its birth marked a key moment in time for neuroscience worldwide

Free love, the moon landing, and the assassination of John F. Kennedy all mark the 1960s as a decade of change. And significant change was also afoot in the long history of brain science for, in the 1960s, a new type of interdisciplinary science gained an official name: neuroscience.

During the mid-1960s this 'London Black Horse Group' actively promoted neuroscience in the UK, organizing conferences and workshops, acting as a lobby group, promoting new courses, degrees, centres and chairs in the neurosciences and gradually engaging in the ethical and social implications emerging from this new field of research.

Neuroscience first saw the day of light under the name of the 'Neurosciences Research Program' or NRP. Founded in 1962 by American biophysicist Francis O. Schmitt, the NRP was predecessor to the American Society for Neuroscience, the world's largest organisation dedicated to neuroscience today.

It wasn't until three decades later, in 1996, that BRA became the British Neuroscience Association. The linguistic mutation from 'brain' to 'neuroscience' is an illuminating moment in the history of the BNA (and brain research more broadly) for it reflects the rise of neuroscience in both scientific and popular imaginations. Indeed the new century, on the cusp of which this mutation took place, was heralded as 'the century of neuroscience'.[1]

In Britain, meanwhile, the first organisation that could lay claim to being dedicated to neuroscience was the Brain Research Association (BRA) formally founded in London in 1968. Although not, yet, neuroscience by name, the BRA shared the ethos of the American NRP, namely to promote multidisciplinarity and collaboration across the brain sciences.

And now? Fifteen years on, the BNA is again making significant change. Outwardly this can be seen in the new logo. As for more... come to Harrogate 2011 to find out!

Yet the BRA came from very humble beginnings. It started as an eclectic group of like-minded scientists – not yet neuroscientists – who would gather at the Black Horse pub in Rathbone Place, London, to discuss topics that cut across different disciplines in brain science (see box).

1 Joelle has written the much fuller, fascinating account: From brain to neuro: the BRA and the making of British neuroscience, 1965-1996 in the Journal of the History of the Neurosciences. jabi@fas.harvard.edu

2 Kandel, E.R. 1999. Biology and the future of psychoanalysis: a new intellectual framework for psychiatry revisited. Am J Psychiatry 156(4): 505-24; Jacob, F. 1998. Of Flies, Mice and Men Cambridge, Mass, Harvard University Press.

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People

BNA British Neuroscience Association

It was back in the dark ages of the mid 1960s. The word neuroscience was almost unheard of – we were neurochemists, neurophysiologists, neuroanatomists, scattered through the various departments of the London colleges. We were well used to the technical seminars in our own specialist departments, each on a highly specific microdetail of some brain process, structure or molecule. But somehow the grander picture – the reason why we had chosen to study brains and not livers or toenails – was lacking.

Soon similar groups took off in other university cities, and from the London discussion group we became the BRA. Our informality was only marginally affected when the much lamented Pat Wall joined us, just back from the US in protest against the Vietnam war and the controller of a small grant intended to foster communication amongst neuroscientists.

A group of us – some half dozen postdocs and young lecturers – decided we could do something better. Between us we assembled a mailing list of all the brain scientists and departments in the London area and called a meeting to plan a London-wide seminar series. The idea would be that we would choose a broad topic such as memory, or pain and invite three or four speakers from different disciplines to approach it each from their own perspective. There were to be two rules; eschew technical jargon so that disciplinary divides could be bridged; and no professors or heads of department so we would not feel intimidated.

Of course we became more established, though we fobbed off an attempt to turn us into a subsidiary of the International Brain Research Organisation. But we knew we had finally become respectable when a group of younger women published a spoof article in New Scientist proposing a rival outfit to the BRA, with the acronym JOCKSTRAP.

If I remember rightly the first meeting was held in a lecture theatre in UCL, where it was immediately apparent that we needed a third rule – to meet in a more convivial place. We chose a meeting room in a pub in Rathbone Place just off Oxford Street, with beer on tap, and the meetings grew wings and flew.

In due course the young postdocs and lecturers became professors in their turn, and in even due-er course grew old and retired.

Our legacy is the BNA. Sarté!

FOUNDERS OF THE BLACK HORSE GROUP
Steven Rose — John Dobbing (1922-99) — Robert Balázs
LATER JOINED BY:
Chris R. Evans — Patrick (Pat) Wall

THE BLACK HORSE

Top right: the BNA logo old (l) and new (r)
Right: The Black Horse pub in Rathbone Place, London, where the seeds of BNA were sown.

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The original *BNA Bulletin* article.

Reply from Joelle M Abi-Rached, Steven Rose and John Lagnado

Balázs and Reynolds' wish to honour Derek Richter is understandable on several levels, including personal ones (Richter found a job for Balázs when he left Hungary after the abortive revolution of 1956), but in this context unsustainable. Two of us were original members of the Black Horse group. A third, the late Herman Bachelard, wrote an account of those early days in the *BNA Bulletin*:

"[...] in researching this short history, two of the founders (John Lagnado and Steven Rose) both confirmed that Derek Richter had not been a founding member as he had suggested in his memoirs (*Life in Research*, Stuart Philips, 1989). What actually happened was that, a year or so after the beginnings of the Black Horse Group, Derek Richter (towards the end of 1968), as a UK representative of the International Brain Research Organisation (IBRO), suggested that it become affiliated with IBRO as the Brain Research Association (BRA). This was agreed and the group then broadened to include neuroscientists from outside London, and an informal organising committee... was established..." (Ref. 5).

In her account, Abi-Rached (Ref. 2) argued that the BNA – and hence its predecessor, the BRA – could be viewed as a "more formal prolongation of the Black Horse meetings", emphasising the vital role played by other like-minded scientists who, beginning in the 1960s started to think about the brain in interdisciplinary ways. Neuroscience was in the air. The term appeared in 1963 in the title of the official bulletin of a new initiative, the Neurosciences Research Program (NRP), founded a year earlier by MIT biophysicist Francis O Schmitt. Rose was one of the only four British scientists among 136 participants at the NRP's first 'Intensive Summer Program' in 1966 in Colorado. It was this and earlier NRP activities that inspired him to bring together the group that initiated the Black Horse meetings in 1965.

The role of the diverse and enthusiastic group of scientists who initially met at the Black Horse (many of whom became, and remain, BNA members) should not be trivialised. Five of the eight members of the first BRA committee were from the Black Horse group (Rose chose not to stand due to pressure of other commitments). John Dobbing and Chris Evans were elected joint secretaries, and Pat Wall was the BRA's first chair. In addition, not only was the London group the backbone of the BRA, it was its engine and a model to emulate. The minutes of the first meeting of the BRA (9 May 1968) state: "This informal group with approximately 200 members might well form the nucleus of the London branch of the new Association" (Ref. 6). The second meeting (19 September 1968) describes the increasingly growing informal network of the Black Horse group as the model for other burgeoning groups of the BRA. Hence Bachelard is correct to state that: "The London group remained the most active with regular meetings taking place either at the pub or, increasingly, at Queen Square" (Ref. 5).

To reiterate arguments already mentioned in letters exchanged in the *Journal of the History of the Neurosciences* (Refs 2–4), Richter certainly helped expand the Black Horse group into a formal organisation that could represent UK interests on the IBRO but his role was 'catalytic' rather than foundational. To describe him as the 'founding father' of the BNA is another legend that needs to be deconstructed, if not for the appreciation of the many scientists who took part in the making of neuroscience in the UK (Balázs included), then for history's sake.

Joelle M Abi-Rached *is MD, MSc, PhD candidate in History of Science at Harvard University;* **Steven Rose** *is Emeritus Professor of Biology at the Open University and Emeritus Professor of Physick at Gresham College London;* **John Lagnado** *is Honorary Archivist, the Biochemical Society (UK).*

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4. **Balazs R, Reynolds EH.** Derek Richter, the British Brain Research Association, and the Legend of the Black Horse. *J Hist Neurosci.* 2013;22:199–207; 212–4.
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Ruth McKernan CBE.

A day at the Palace

Ruth McKernan's career has taken her to San Diego and to senior positions in some of the world's biggest pharmaceutical companies – as well as to a seat next to Sir Bradley Wiggins at Buckingham Palace.

In 2013, Ruth McKernan, chief scientific officer of Neusentis, a unit within Pfizer, was awarded a CBE in The Queen's Birthday Honours. The award recognised her work in business and innovation.

The CBE came out of the blue: "I was at work and my husband called me and said 'there's a letter here from the Cabinet Office, do you want me to open it?' My immediate thought was, 'Oh God what have I done now?'" In fact, the letter was an enquiry to see if she would be interested in accepting the honour, should it be offered.

She answered in the affirmative, and in December 2013 made the trip to SW1A: "Having my husband drive through the gates of Buckingham Palace with my kids in the car was exciting," she recalls. Colleagues were similarly swept along: "People at work were very excited for me and had a necklace made, which they commissioned, with neurons on the front of it."

The day itself provided an opportunity to meet high achievers from all walks of life.

"I sat next to Bradley Wiggins so had a nice chat to him. It was quite interesting because he seemed to think he'd done nothing special and I had. And I was thinking, 'yeah but Bradley, I can't even ride a bike…"

Indeed, she ended up rubbing shoulders with all kinds of high achievers: "It was interesting to talk to people from all different walks of life, where their colleagues and peers think of them as the best in their discipline. It was an honour, and I was and still am very excited by it."

From a scientific family – her father, Billy, was a biochemist – Dr McKernan studied pharmacology and biochemistry at King's College London before a PhD at the Institute of Psychiatry, looking at the mechanism of action of antidepressant drugs. After postdoctoral work at the University of California San Diego, she returned to the UK to join Merck.

"I'd always been interested in medicines, and how to make medicines, particularly in psychiatric and CNS disorders," she explains. "There's a huge gap in how people are treated. I'm sure there are much better drugs to be made."

She spent 17 years at Merck, rising from junior scientist to head of site, and establishing her reputation with work on subtype-specific drugs for GABA receptors. From Merck in Harlow, she transferred to Pfizer in Sandwich, before the company's reorganisation in 2011 enabled her to establish the Neusentis unit in Cambridge, bringing together work on stem cells and regenerative medicine as well as pain and sensory disorders.

Interestingly, she also took time out from Merck to work for the *Independent* as a science writer, winning an award for best series of articles in a broadsheet newspaper. "After that, I wrote a book, *Billy's Halo*, which was shortlisted for the MIND book of the year (it didn't win but it was nice to go the party)." The book is an unusual mix of science and personal reflection, centred on her father, Billy, a life-threatening bout of septicaemia and his eventual death. Still keen on communication, time pressures are currently inhibiting further forays into print: "I have an idea for another book, which might get written when I retire."

Now, the challenges of developing new medicines for pain and other conditions, as well as a multitude of other work, such as helping to establish a Catapult Centre to support the development of cell therapies, and sitting on various high-level boards, more than fill her time. She is excited by the potential of stem cells, both as therapies but also as tools to understand disease processes and the effects of drugs. She also believes that genetics and intensive phenotyping, as well as electronic health record and epidemiological data, are generating exciting opportunities for more targeted 'precision medicine'.

While some pharmaceutical companies have withdrawn from CNS conditions, Dr McKernan believes the great strides being made in understanding such conditions will eventually tempt industry back. "I see that as a temporary lull. Where science leads pharma companies will follow."

She finds refuge from helter-skelter daily pressures in the garden. Here, she suggests, the tranquility provides scope to make sense of the weekly information overload: "Sometimes you just need that quiet time to reassimilate and reprioritise. I find it very therapeutic."

A short piece **Ruth McKernan** *wrote for the Guardian reflecting on her father's illness and eventual death can be found at* **bit.ly/1gDtkUH**

Every year, world notables gather at Davos.

Davos in mind

At the recent World Economic Forum in Davos, **Barbara J Sahakian** had an opportunity to convince world leaders of the importance of neuroscience to global wellbeing, brain health and wealth.

Amongst the thrill of seeing many heads of states and the glitz associated with Davos was the excitement of realising that governments around the world have finally got it! They finally understand that there is no greater financial or societal challenge than the impact of mental health disorders.

Dementia, depression and other neuropsychiatric disorders destroy mental capital and wellbeing. One in four of us will suffer from a mental health disorder at some point in our lives. Alzheimer's disease, schizophrenia, depression and mania all have associated cognitive symptoms. It is these problems with attention, memory, decision-making, planning, problem-solving and impulse control that compromise our ability to work and create difficulties in activities of daily living. Absenteeism and 'presenteeism' at work for those with depression, and institutional care for those with dementia, constitute major financial problems for global productivity.

Neuropsychiatric disorders often go undetected and untreated, so early detection and treatment are key. We can stop these debilitating disorders from becoming chronic and lifelong. Enhancing cognition through pharmacological and other means, including good nutrition, exercise, education and 'serious games', will be essential.

It is encouraging that governments realise that they need to promote good brain health across the lifespan. This will create resilience in individuals and a flourishing society. Since 75 per cent of mental illnesses start before the age of 24 years, it is important that we detect and treat them in young people.

Governments need to consider mental health as every bit as important as physical health. A commitment to neuroscience and mental health will ensure good mental capital and wellbeing for all members of society. It is a win–win situation, since new discoveries and treatments will generate new businesses and aid the economy, while also reducing healthcare costs and burden to society.

At Davos, there was much neuroscience discussion that ranged from very basic science, such as the Human Brain Projects, both US and European, to understanding the effects of poverty on the brain in children and healthy ageing.

Guang-Zhong Yang, Lady Gwen Borysiewicz, Barbara J Sahakian and Sir Leszek Borysiewicz.

Important sessions covered how we might, through new developments and technology, promote new discoveries that could impact on both mental health and wealth development. For example, much new technology, including optical imaging and computing, is being invented for the Human Brain Projects, discussed by Allan Jones (Allen Institute, Seattle), Thomas Insel (National Institute of Mental Health, Bethesda) and Henry Markram (Lausanne). Much of this will be applicable in businesses, including those using large databases, and biotech companies.

In addition, in one of my own sessions, facilitated by *Nature* Editor Philip Campbell and introduced by surgeon Lord Darzi, there was extensive discussion of robotics and games for cognitive training. And the potential for theory of mind in robots was discussed in the session moderated by Lord Rees, former President of the Royal Society. All these sessions generated much lively discussion with the audience – mainly business leaders, government officials and the media.

Both science and technology and higher levels of cognitive abilities and education are linked to increased prosperity (e.g. increased gross domestic product). Furthermore, investment in mental health has provided substantial economic benefit in the past, and should continue to do so in the future.

Let's hope that Davos has even greater contributions from neuroscience and mental health in 2015.

Barbara J Sahakian *is Professor of Clinical Neuropsychology at the Department of Psychiatry and MRC/Wellcome Trust Behavioural and Clinical Neuroscience Institute, University of Cambridge. She is also the author (with Jamie Nicole LaBuzetta) of Bad Moves: How decision making goes wrong, and the ethics of smart drugs (Oxford University Press, 2013).*

Q&A: Rumana Chowdhury

Clinician scientist Rumana Chowdhury (UCL) won the BNA's Postgraduate Award 2013.

Q: What did you discover in your research?
A/ The neurotransmitter dopamine declines as part of the normal ageing process. My research used a variety of techniques to examine how this loss of dopamine might affect human cognition in older age. I found that reinforcement learning and episodic memory could be improved by giving older adults a drug to increase dopamine levels. I used MRI to show that these effects were related to the structural integrity of the dopamine system and functional activation in dopamine target regions including the nucleus accumbens and hippocampus. The importance of this work is that it brings together the biological, structural and functional changes in the ageing brain to provide a novel perspective on the critical contribution of dopamine to individual differences in learning and memory.

Q: What did you think when you heard you'd won the BNA award?
A/ I felt very excited! It is a real honour for the BNA to recognize my doctoral work. I am also grateful to my supervisors, Professor Emrah Duzel and Professor Ray Dolan, who guided my work and were a constant source of inspiration.

Q: What are your long-term plans?
A/ I plan to pursue a career as an academic neurologist, dividing my time between research and clinical work. In my future research, I intend to examine neural networks underlying cognition and how these networks break down in ageing and neurological disorders such as Alzheimer's disease. I hope that this line of work will provide a deeper understanding of cognitive dysfunction and provide a basis for developing therapies for people with memory problems.

Q: What advice would you give to a young researcher?
A/ Keep asking questions! And stay positive – there are lots of ups and downs in research, but it's worth it in the end when you discover something meaningful.

Q: What do you enjoy doing outside science and medicine?
A/ I'm a keen musician. I play the piano and guitar and love watching live music.

Q&A: Elina Jacobs

Elina Jacobs (Edinburgh) won the BNA's Undergraduate Award 2013 for her dissertation 'Imaging myelination *in vivo* using zebrafish'.

Q: What did you discover in your research?
A/ I did my research in David Lyons's lab at the Centre for Neuroregeneration under the supervision of Tim Czopka. The lab uses zebrafish as a model to understand the development of myelination in the CNS, and the first thing I discovered was what an amazing model organism the zebrafish is for neural development. Zebrafish embryos are completely transparent, and being able to look down the microscope at a living organism and see its developing CNS shine in different colours thanks to fluorescent genetic markers captivated me throughout my project.

Q: What did you think when you heard you'd won the BNA award?
A/ I was ecstatic, of course! And it gave me a confidence boost as well – if I can achieve an award by doing what I love, then hopefully that means that I'm on the right track by aiming for a research career.

Q: What are you doing now?
A/ I'm at UCL on the Wellcome Trust four-year Neuroscience PhD Programme. I am currently doing my first rotation in Sarah-Jayne Blakemore's group at the Institute of Cognitive Neuroscience. After having looked at development in a model organism, I wanted to know what it's like to do human neuroscience and learn more about human brain imaging techniques. It's been a steep learning curve since my background is mostly in biology, but I'm really enjoying it!

Q: What are your long-term plans?
A/ I like the idea of an academic career since that would allow me to combine research and teaching, I have worked as a tutor for school kids before and really enjoyed it. I've been lucky to have some great teachers and mentors, and I'd like to do the same for others.
In terms of what research I'd like to do, I am fascinated by the interaction of nature and nurture and how they affect mental health. I want to understand how genetic and developmental predispositions combine with every-day life stressors, and how that can lead to mood disorders like depression.

Q: What do you enjoy doing outside science and medicine?
A/ I enjoy playing piano and singing, dancing salsa, and I love travelling.

Obituary

Colin Ingram
(1960–2013)

It is with profound sadness to reflect on the loss of Professor Colin Ingram. Colin was a scholar, a genteel man, a teacher and a friend. He passed away unexpectedly at home in Newcastle on 15 December 2013.

An accomplished neuroscientist, Colin was the founding Director of the Institute of Neuroscience (IoN) at Newcastle University. Colin came to Newcastle from the University of Bristol in July 2000, appointed to the Chair in Psychobiology in the School of Neurology, Neurobiology and Psychiatry. He subsequently served as Head of the School (2006–08), which transformed into the IoN in 2008. Until his death, he shared this role on a rotating basis with Anya Hurlbert. He led the expansion of the IoN, which has grown to be one of UK's largest neuroscience groups, with a focus on research in rodents, primates and humans. More than a third of our academics are clinicians, spanning disciplines of neurology, clinical neurophysiology, neurosurgery and psychiatry, underpinning translational neuroscience and the Wellcome Trust Centre for Translational System Neuroscience, initiated by Colin.

Colin made significant contributions to our understanding of the hypothalamo-pituitary axis (HPA) and corticosteroid neurobiology. During his PhD studies at the Babraham Institute (1982–86), he made some of the first recordings of electrical activity and membrane ion currents in pituitary cells. He was particularly interested in how variations in corticosteroid secretion might alter HPA activity to trigger certain psychiatric disorders associated with stress, anxiety and depression.

Remarkably, he also successfully managed two other creativities: one was in neurotechnology, with a view to developing novel approaches that can be applied to the development of neuroprosthetic devices (e.g. retinal implants and cortical neurochips); the second was in neuroinformatics, grid-based analysis and databasing facilities (the CARMEN e-science platform, developed through EPSRC funding and currently supported by the BBSRC) for neurophysiological data.
As a consequence, Colin had a key role in the development of neuroinformatics in the UK and he chaired the Data Sharing programme of the International Neuroinformatics Coordinating Facility.

With incredible drive, determination and dedication, he took serious interest in wide-ranging aspects of neuroscience in Newcastle. As Director of the IoN, he was perceptive and had vision to advance the neurosciences beyond the North-East. As well as developing collaborations with the RIKEN Brain Science Institute in Japan, last November Colin led an impressive group to establish various projects with scientists and clinicians at the I-NK Institute of Neuroscience in Kolkata, India. I regret I missed this exciting venture because of my own outreach obligations in Nigeria and Rwanda. Colin achieved all these prodigious successes through his resilience and convivial personality, persuading people to work together and always looking for the best in colleagues around him.

I believe the BNA owes him particular thanks. Colin played a significant part in the BNA for over a decade: he was first elected to the national committee in 2001, subsequently served as Treasurer (2004–07) and finally as Honorary Secretary (2007–11). While I had the privilege to work with three successive Presidents (Colin Blakemore, Nancy Rothwell and Richard Frackowiak), Colin gave the best of himself under four BNA leaders (Richard Frackowiak, Graham Collingridge, Trevor Robbins and David Nutt) – he was one of few BNA stalwarts who wore different hats within the organisation. His sincerity, wisdom and thoughtful approach were the hallmarks during his years of dedication to the BNA. Many will miss Colin and his infectious wide smiles. He is survived by his wife Christine Ingram, and children, Alex, Miles and Rachael.

Raj Kalaria *(BNA National Committee 1998–2000; Honorary Secretary 2000–04) is Professor of Cerebrovascular Pathology (Neuropathology) in the Institute for Ageing and Health, Newcastle University, Newcastle upon Tyne NE4 5PL.*

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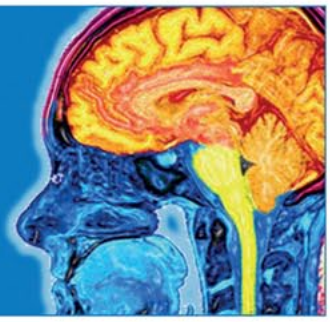

Once again the BNA is joining forces with learned partner societies to host **BNA2015: Festival of Neuroscience** from 12-15 April 2015 at the Edinburgh International Conference Centre.

The Festival of Neuroscience is a unique event. It incorporates all aspects of neuroscience and brings together clinical and non-clinical researchers together - biochemists, pharmacologists, anatomists, developmental biologists, physiologists, immunologists, oncologists, psychiatrists and psychologists.

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For more information visit www.bna.org.uk/festival2015

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