University of BRISTOL
Elizabeth Blackwell Institute for Health Research

Bristol Neuroscience Newsletter

November - Decmber 2015

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Inside this issue:

What we do

The Bristol Neuroscience (BN) Theme makes full use of different techniques and approaches in our quest to understand the nervous system, from studying biochemical pathways to developing neurosurgical techniques, and from electrophysiology to animal behaviour – and everything in between.

BN enables members to collaborate and bring together complementary techniques. Topics as varied as synaptic plasticity, addiction, visual perception and pain are all studied in BN.

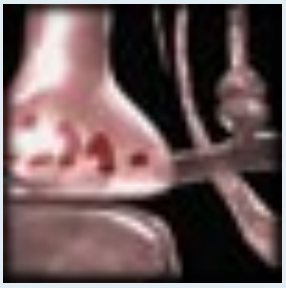
Combining our interdisciplinary strengths allows us to advance research and ensure BN can have the greatest impact on scientific, clinical, and real life questions in neuroscience today.

New Facebook page

The Theme recently opened a new Facebook account. Regular posts include information on funds and events which could be of interest to the wider BN community.

Please do join– see https://www.facebook.com/bristolneuroscience. We also have a Twitter stream followed by over 800 people on @BristolNeurosci. Thanks are extended to PhD candidate Rachel Harris for taking on the role of Social Media guru for Bristol Neuroscience!

Bristol Neuroscience Festival
18-19 March 2016



BNA 50th Anniversary Christmas Symposium

14 December 2015
9.00-21.00
King's College London
King's Building
Strand Campus
WC2R 2LS

EVENTS

Winter School: Neural Stem Cells
13-17 December 2015. Monte Bondone, Trento, Italy

Snapshots: 14 December 2015
14 December 2015, 13.00. Bridget Lumb (University of Bristol), Lecture Theatre 1, Chemistry

A screening of scenes from In the Real and discussion with the filmmaker
16 December 2015, 12.45. Conor McCormack (Artless Films), OS6, Oakfield House

3rd Caribbean Biomedical Research Days Conference
16-18 January 2016, 10.00. Bay Gardens Beach Resort & Spa, Rodney Bay, St. Lucia

Dementia HIT Clinical Research Showcase
19 January 2016, 11.00-17.00. Southmead Hospital

The social defeat hypothesis of schizophrenia: recent findings
16 February 2016, 12.45. Jean-Paul Selten (Maastricht University), OS6, Oakfield House

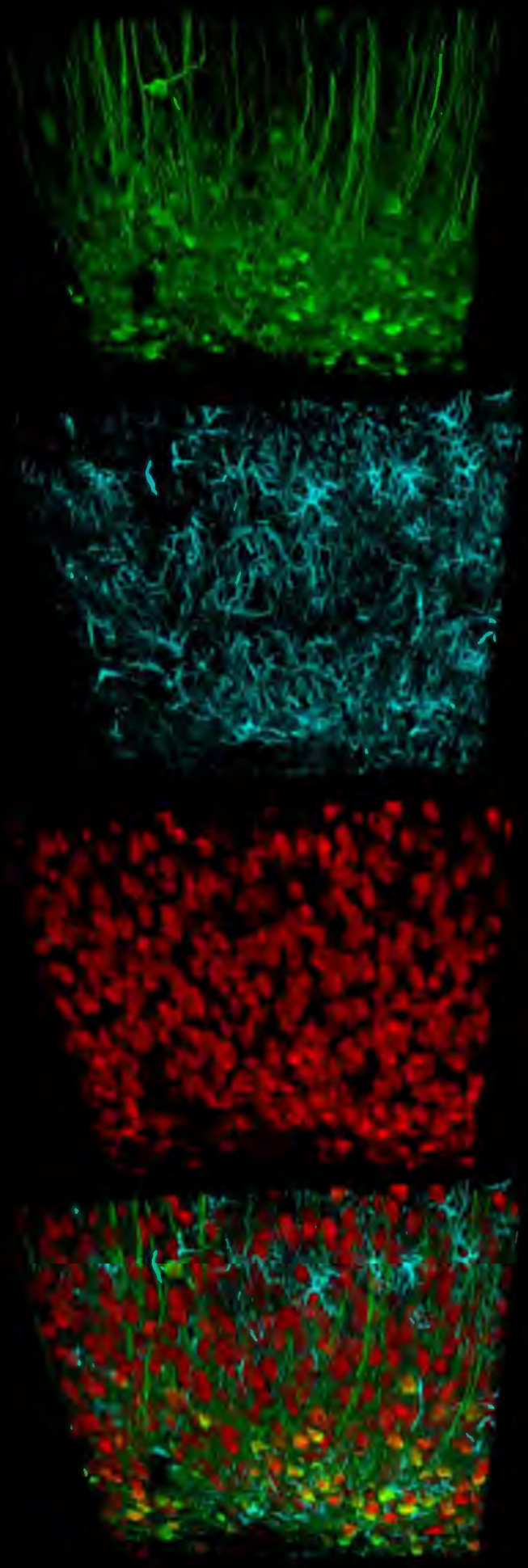
1st Instituto de Neurociencias PhD Student & Postdoc Meeting
18-19 February 2016. Manel Esteller (IDIBELL); Richard Morris (Edinburgh); Peter Scheiffele (Biozentrum); Andre Fischer (DZNE); David Dupret (Oxford); Thomas Klausberger (Vienna); Zafar Bashir (Bristol), Instituto de Neurociencias, Sant Joan d'Alacant, Alicante

Introduction to Research Grant Applications (Medical Faculties)
1 March 2016, 14.00-17.00. Zoe Holland (RED)

Ammar Al-Chalabi, Professor of Neurology and Complex Disease Genetics
10 March 2016, 14.00. Ammar Al-Chalabi (Professor of Neurology and Complex Disease Genetics, Director King's MND Care and Research Centre), OS6, Oakfield House

Brain Awareness Week 2016
14-20 March 2016

Surgical Trials Showcase 2016



'Brain mesh' – images of different types of stained cells in the cortex

Bristol's Festival of Neuroscience

Part of

BRAIN AWARENESS WEEK

Public exhibition and talks at the Wills Memorial Building University of Bristol

Queen's Road BS8 1RJ

18th – 19th March 2016

There will be interactive exhibitions and hands-on activities for all ages.

'Brilliant brains show' with At-Bristol.

Opportunities to meet scientists and discuss their work.
'Best of Bristol Neuroscience' lectures
School Brain Art competition
and much more....

Public Lecture by Prof Bruce Hood

"The Domesticated Brain: How the Changing Social Environment Turned Us into Children"

Victoria Rooms

Queen's Road, Queens Road
Bristol BS8 1SA

18th March 2016, 18:30-20:00

For more information: www.bristol.ac.uk/neuroscience/bnf

For enquires email: bnf-2016@bristol.ac.uk

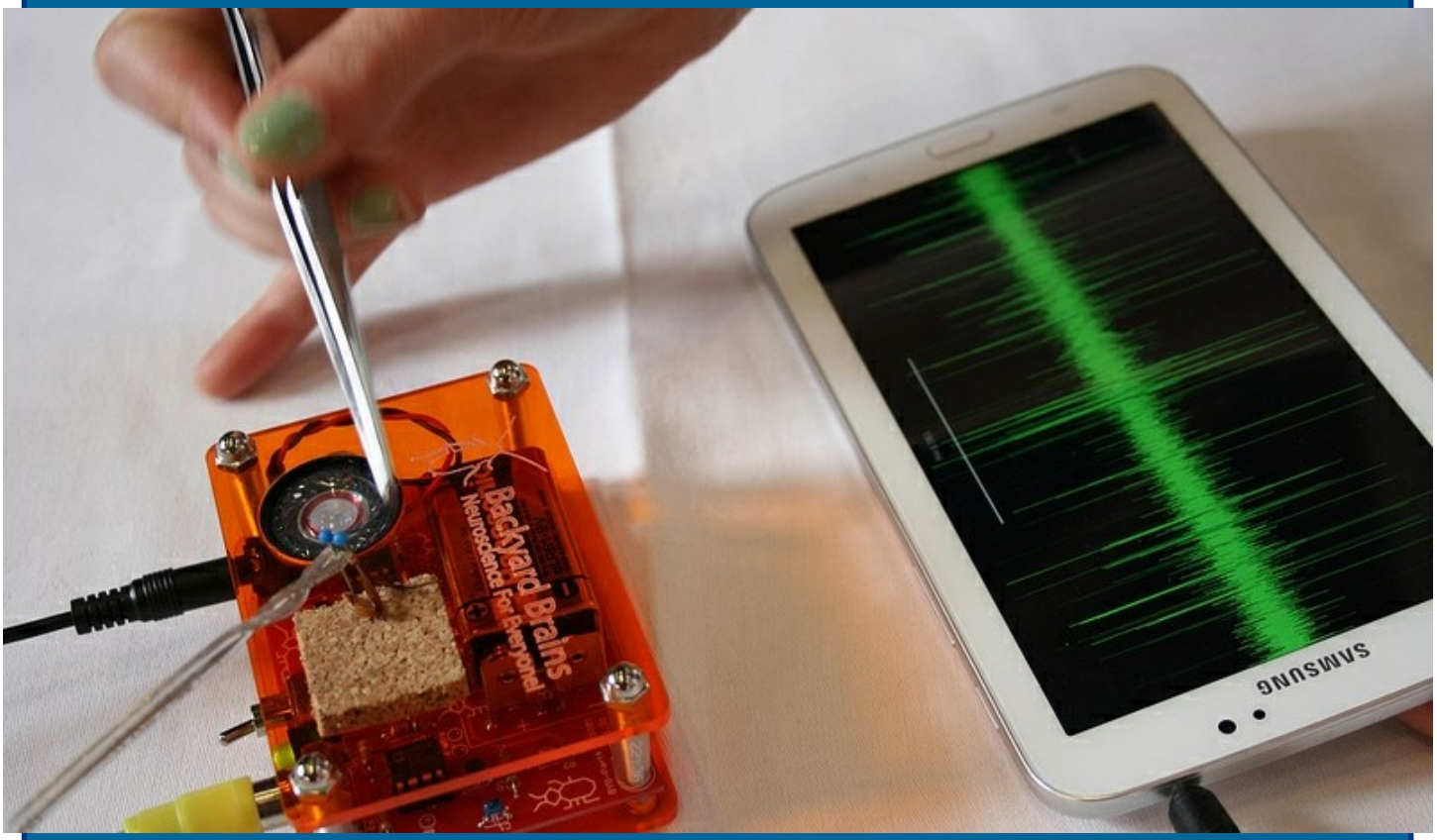
University of BRISTOL

bristol neuroscience

Bristol Neuroscience Festival 2016

part of Brain Awareness Week
18 - 19 March 2016
Wills Memorial Building

The festival is a two day public science event designed for all ages from primary school to adult. There will be exhibits, talks, hand-on activities and a Brain Art competition.



The organising committee are inviting contributions for:

Research Poster Displays: The aim is to engage the public in your state of the art neuroscience research. Please send a title and brief summary of your proposed display content.

Hands on activities: We're looking for suggestions for hands-on activities suitable for all ages.

Volunteers: If you're interested in helping out at the two day event please email your name and contact details.

Send proposed ideas and contact details to
bnf-2016@bris.ac.uk by 29 January 2016

18 March 2016, 9.00-17.00. M-Shed

Feel It Festival
October 2016

Philosophy of Psychiatry Reading Group
Fortnightly meetings from 6 November 2015 in the Philosophy Library, Cotham House. This semester's book is *Alien Landscapes? Interpreting Disordered Minds* by Jonathan Glover.

NEWS

- With collaborators from UCL and the Universities of Lausanne and Cambridge, Dr James Hodge has discovered that a protein, **Ionotropic Receptor 25a (IR25a), has a key role in entraining the brains of fruit flies to react to small changes in temperature**. The circadian clock is a timer that allows an organism to adjust their behaviour and physiology according to the time of day, which is controlled by changes in light and temperature. In experiments with fruit flies, the team discovered that IR25a is part of a pathway to the circadian clock that detects small temperature differences. This pathway operates in the absence of known 'hot' and 'cold' sensors in the fruit fly's antenna, which points to the existence of periphery-to-brain temperature signalling channels. They investigated whether flies lacking IR25a were able to synchronise their circadian clocks to temperature changes; results showed that, when temperature fluctuations were large, flies lacking IR25a could adapt. However, when the changes in the temperature range were small, the flies lacking IR25a could not adapt. *Our findings reveal a surprising complexity of how temperature signals reset the brain clock. Similar to what has been described for light resetting of the human and fly circadian clock, it seems clear that organisms do not rely on a single pathway, but employ multiple input routes for both temperature and light. This hints to the importance of accurate circadian clock synchronization with the environment, and future work will address how these different input signals are integrated in the brain clock*.

Drosophila was used to look at the circadian clock

Reference: Chen C, Buhl E, Xu M, Croset V, Rees JS, Lilley KS, Benton R, Hodge JJL & Stanewsky R (2015). *Drosophila* Ionotropic Receptor 25a mediates circadian clock resetting by temperature. *Nature*. Published online 18 November 2015.

- **Professor Neil Williams has been appointed the new Director of Strategic Alliances** for EBI, with the responsibility for implementing the University's new Strategic Alliance Framework in which they will develop productive strategic partnerships with pharmaceutical and biotechnology industries. Together with Director of Regional Health Partnerships Professor Lars Sundström, they will ensure that Bristol's environment and capability for health and biomedical research translation is fully optimised.

- **PI Professor Richard Apps and co-PI Professor Bridget Lumb** have been awarded £600k by the BBSRC to investigate the *Role of the*

NEWS

cerebellum in survival circuits activated by fear. The project has been funded for four years.

- **Professor Elek Molnár has been appointed as Biological and Medical Sciences Review Panel member** for the British Council Newton Fund Institutional Links, Researcher Links Travel Grants and Workshop Grants, and Newton-Al-Faradi Post-Doctoral Mobility Scheme

- **Dr Anja Teschemacher has been awarded a three year 'Science without Borders' PhD studentship** from September 2015. Awarded by the Ministry of Science, Technology and Innovation of Brazil, the project is entitled the *Role of signalling between astrocytes and central noradrenergic neurones in control of the cardiovascular system*.

University Policy on Open Access to research publications

Senate has approved a mandate for the institutional policy on Open Access to research publications, and this will take effect from 1 October 2015. Academics and research students are required to deposit, at the point of acceptance from the publisher, eligible research outputs in the institutional repository (Pure). The mandate is to ensure that all research outputs that will be submitted to the post-2014 REF are eligible, under new requirements from HEFCE. Further information about the mandate and help available. For the full policy please see the Institutional Policy web page.

- Dr James Hodge (Co-PI) together with Dr Katie Lunnon (PI), Professor Jonathan Mill and Dr Jonathan Brown (Exeter), Professor Nick Allen (Cardiff), Dr Vasanta Subramanian (Bath), and Professor Caroline Relton (Bristol) have been **awarded a GW4 accelerator grant** entitled *Harnessing CRISPR/Cas9 technology to develop new models of Alzheimer's disease*. They received £75k to complete the six-month project.

- **An investment of £150,000 on behalf of the Elizabeth Blackwell Institute** for Health Research, through its Wellcome Trust ISSF Award (match funded by the University of Bristol), will fund three new posts that will be openly available to help support all health and biomedical researchers across the University in their informatics needs. These posts will come into full effect in the early part of 2016, and will comprise:

i) A *Biomedical Research Computing Analyst* based in the Advanced Computing Research Centre who will enable researchers working with high throughput, multi-omic data and complex modelling to have enhanced access to the University's HPC and Research Data Facilities in order to generate, refine and optimise the research software they specifically need.

Congratulations are extended to Bridget Lumb, Professor of Systems Neuroscience, who has been made an Honorary Member of the Physiological Society

ii) A *Genome Informatician* located in the Life Science Building 'Omics Hub' with expertise in Galaxy software and who will support researchers analyse deep sequencing, RNA-seq and CHiP-seq

iii) A *Microscopy Image Analyst* based in the Wolfson BioImaging Facility in the Biomedical Sciences Building to help researchers with their image processing and analysis needs. Dr Stephen Cross has been appointed into this role and is expected to be in post on 1 February 2016.

- **Ant colonies are often referred to as superorganisms as they are both complex and co-operative**. The question asked by PhD student Thomas O'Shea-Wheller (pictured, right, with a colony of rock ants) was, to what extent do they actually behave as a single entity? To answer this, migrating ant colonies were subjected to differing forms of simulated predator attack. By targeting ants scouting at the periphery of colony activity, and workers within the very heart of the nest, they were able to show very different responses to predation depending on location. When scouts were removed, the foraging 'arms' of the colony were retracted back into the nest. However, when ants were removed from within the nest itself, the whole colony absconded, seeking asylum in a new location.

Our results draw parallels with the nervous systems of single organisms, in that they allow appropriate, location dependent, responses to damage, and suggest that just as we may respond to cell damage via pain, ant colonies respond to loss of workers via group awareness

Reference: O'Shea-Wheller TA, Sendova-Franks A, Franks NA (2015). Differentiated Anti-Predation Responses in A Superorganism. *PLOS ONE*. Published online 11 November 2015.

- Wellcome Trust Clinical Research Training Fellow and PhD student Anna Simpson (Tony Pickering/Nina Balthasar lab) was awarded first prize for *Corticotrophin-releasing-hormone neurons in the paraventricular hypothalamus: evidence for glucose sensitivity* and PhD student Stefan Hirschberg (Tony Pickering lab) was awarded third prize for *Re-Engaging Endogenous Pain Control: A Chemogenetic Strategy* in the **Poster Competition at the Bristol Doctoral College Festival of Postgraduate Research**.

- Professor Elek Molnár has been selected by the Directorate-General for European Parliamentary Research Services to participate in the **Member of the European Parliament (MEP) Scientist Pairing Scheme at the European Parliament**.

- **Professor Andy Levy's enthusiasm for creating medical and veterinary manikins and products has resulted in**

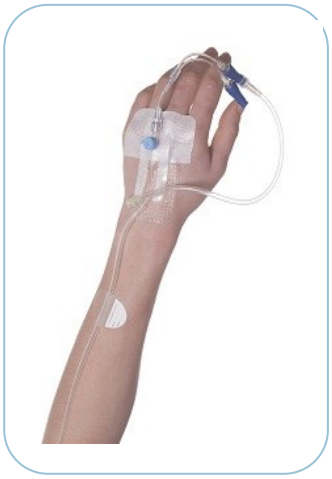
Bristol Biobank

The Bristol Biobank (funded by the David Telling Charitable Trust with stakeholders from the University of Bristol and University Hospitals NHS Foundation Trust) stores samples collected from patients and healthy volunteers for use in biomedical research. The samples form a biorepository to which researchers can apply for use in their research. The collection of a wide range of samples will provide a platform for research into complex conditions.

Researchers may request to deposit samples into the Biobank following the end of a NHS Research Ethics Committee approved study. Consent must have been taken using study specific documentation for the storage and use of these samples in research beyond the study. The team will also be happy to receive applications to deposit samples for specific projects you wish to set-up using Biobank permissions and documentation.

The Bristol Biobank is licensed by the Human Tissue Authority (licence 12512) to store human tissue for research and has ethics approval from Wales Research Ethics Committee 3 as a research tissue bank to collect and issue biomaterials for biomedical research across a range of therapeutic areas. If you are interested in finding out more about the opportunities of working with the Biobank please contact Manager Claire Matthews.

three designs being sold nationally and internationally. In 2009 he entered the UoB 'Bright Ideas' competition with an idea for a product that would keep intravenous (IV) lines in place without them kinking or dislodging from the patient. Having won, he then developed the idea. After five years of prototypes, local company P3 agreed to produce the finished product. Known as Tube Anchor (pictured right), it is currently being trialled on patients at Bristol Royal Infirmary. Along with the Tube Anchor, Andy also uses another of his creations, VibraTip on his hospital rounds. VibraTip is a pocket-sized device used for diabetic neuropathy and has recently been noted as having potential to improve the diagnosis of diabetic peripheral neuropathy by the National Institute of Health and Care Excellence (NICE).



- Professor Richard Apps, PI, with co-applicants, Professor Zaf Bashir, Dr Conor Houghton, Professor Stafford Lightman and Professor Krasimira Tsaneva-Atanasova (Exeter) have been awarded a £1.8M **Wellcome Trust Neural Dynamics four year PhD programme**. This will allow for three intakes (2016-2018) and will fund 12 students.

- PI's Professor Elek Molnár together with Professor Aniko Varadi (UWE), and Dr Kathleen Gillespie have been **awarded a three-year PhD Studentship** for C H Caygill from the University of West of England.

- Dr Jon Witton has been awarded an **Alzheimer's Research UK (ARUK) Research Fellowship** for £203,456 in the lab of Dr Mike Ashby (co-supervised by Prof Andy Randall) to study *Dysfunctional synaptic and neuronal network encoding in tauopathy-associated dementia* over the next three years.

- PhD student Caroline Phelps (supervisor Bridget Lumb) won a **poster prize at the British Association for Psychopharmacology** Summer Meeting. Her poster was on *Induction of neuropathic pain does not affect baseline attention but does influence attentional changes seen with gabapentin and amphetamine*.

- **Fiddler crabs are sensitive to the polarization of light across the majority of their eyes**, potentially allowing them to use polarization information for general visual tasks. Dr Martin How from the Ecology of Vision Group and colleagues studied wild populations of fiddler crabs on mudflats close to the Pacific entrance of the Panama Canal. A fiddler crab's body generates polarization contrast against the background which means that, when backlit by the sun, their claws and legs appear bright to any creature with polarization vision, including fellow members of the species. The researchers tested whether male crabs living in and defending burrows responded to approaching targets on the mudflat over distances proportional to the polarization contrast of the target; they found that male crabs responded to the approaching target as if it was a threat, thus provoking a sequence of typical defensive behaviours. Results show that these animals use their polarization vision to enhance contrast in their visual environment, thus increasing their ability to detect and respond to both fellow members of their species and ground-based predators.

Our results provide one of the first pieces of evidence for a function of object-based polarization vision under natural lighting conditions

Fiddler crab (*Uca stenodactylu*) Image © Martin How

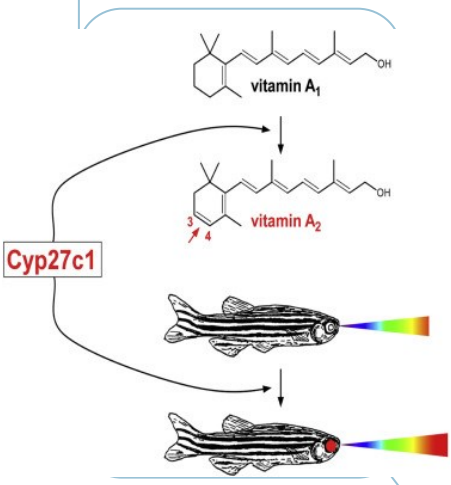
Reference: How MJ, Christy JH, Temple SE, Hemmi JM, Marshall NJ & Roberts NW (in press). Target Detection Is Enhanced by Polarization Vision in a Fiddler Crab. *Current Biology*.

- A study, co-authored by Dr Shelby Temple, Dr Martin How and Dr Nicholas Roberts, has finally solved the long-standing mystery of how certain vertebrate species adapt their colour vision to different environments. It found that a **cytochrome called Cyp27c1 converts vitamin A1 to vitamin A2 in zebrafish**

New translational research centre

The £5.3 million Translational Biomedical Research Centre (TBRC), currently under construction at Langford, aims to get research out of the laboratory and ensure patients worldwide can access ground-breaking treatments as quickly as possible. Funded by UoB, MRC and BHF, the centre's 'topping-out' was celebrated in September, led by the Centre's Director, Professor Raimondo Ascione.

TBRC will use experimental models relevant to human disease and anatomy and procedures will be tracked in living animals using non-invasive scanning techniques. This will help test new treatments to NHS standards while reducing the number of animals needed. It will operate under the One-Health concept for the benefit of people, animals and environment. This is a key development in the University's vision for a research culture that feeds directly and rapidly into tangible and lasting benefits for the health and welfare of humans and animals alike.



and toads, thus allowing the animals to red-shift their photoreceptor spectral sensitivity. This helps these and other animals to optimise their visual system as they shift between blue clear-water or terrestrial habitats and turbid freshwater habitats.

Reference: Enright JM, Toomey MB, Sato S-Y *et al*. (in press). Cyp27c1 Red-Shifts the Spectral Sensitivity of Photoreceptors by Converting Vitamin A1 into A2. *Current Biology.*

- Led by academics from Bristol, Cambridge, Queen's Belfast, and UCL and hosted by North Bristol NHS Trust, **a clinical trial will investigate if losartan**, a blood pressure drug that first became available in 1995, **can complement current treatments for Alzheimer's disease (AD)**. The researchers believe losartan can slow down the progression of AD by improving brain blood flow and altering chemical pathways that cause brain cell damage, brain shrinkage and memory problems in AD. The trial known as RADAR (**R**educing pathology in **A**lzheimer's **D**isease through **A**ngiotensin ta**R**geting), is hoping to recruit approximately 230 participants, together with a similar number of carers, from across the UK including sites covering the Tayside, Lothian, Grampian, Glasgow, Border and Lanarkshire areas, all of which are partners in the Scottish Dementia Clinical Research Network (SDCRN). The study is a double blinded placebo-controlled randomised trial. People with AD who have high or normal blood pressure can take part if they meet certain eligibility criteria and RADAR will use brain imaging to measure whether losartan reduces the rate of brain shrinkage that is known to occur in AD. It will also be using what are standard questionnaires on memory performance and quality of. Led by Professor Pat Kehoe, the team are using Join Dementia Research to help with recruitment to the study; this service allows anyone with and without dementia to sign up using basic demographic and health information and be matched to dementia research studies in their area.

- **A new Psychosis Health Integration Team (HIT)** has been approved. Led by Dr Sarah Sullivan, CLAHRC West/Centre for Academic Mental Health; Dr Simon Downer, Consultant Psychiatrist, Bristol Mental Health; and Dr Martin Jones, Chair of Bristol Clinical Commissioning Group, the HIT aims to hear the voices of people who experience psychosis, their families and carers, and those of staff in mental health services and other settings, in order to improve services across the city. It will focus on

Professor Elek Molnár has been appointed as an Expert Panel member in Brussels for the Horizon 2020 European Commission Framework Programme for Research and Innovation

eight aims:

- Improve employment opportunities
- Improve appropriateness and therapeutic value of hospitalisation
- Improve general (physical) health outcomes
- Better integration of care pathways
- Greater emphasis on the relationship with trauma
- Better engagement with people's networks from the outset
- More caring crisis response
- Improving staff health (the impact of working with people with psychosis)

- A free **Dementia UK public meeting** hosted by Professor Pat Kehoe took place on 20 July 2015. A series of short talks from clinicians and researchers included contributions from Dr Scott Miners, Dr Liz Coulthard, Professor Seth Love, and Catherine McKeever from Alzheimer's Research UK- these were followed by a Q&A session. Over 84,000 people in the South West are living with dementia and many more have loved ones with the condition. Events like this allow members of the public to get a better understanding of the effects of Alzheimer's and other dementias. Hearing from scientists and clinicians is great way to learn more about dementia and the progress being made towards finding a cure.

Research conducted by Rachel Perry, Professor Andy Ness and Dr Rachel Churchill concludes that there is insufficient evidence for the use of taking an Omega 3 fatty acid supplement in treating major depressive disorder. They gathered data from 26 randomised trials involving a total of 1,458 participants, which investigated the impact of giving an Omega 3 fatty acid supplement in a capsule form and compared it to a placebo. In one study, involving 40 participants, they also investigated the impact of the same supplementation compared to an anti-depressant treatment. The review found that whilst people who were given Omega 3 fatty acids reported lower symptom scores than people with the placebo, the effect was small and there were important limitations that undermined confidence in the results. The analyses showed that although similar numbers of people experienced side effects, more data would be required to understand the risks of taking Omega 3 fatty acids.

Reference: Appleton KM, Sallis HM, Perry R, Ness AR & Churchill R (2014). Omega-3 fatty acids for depression in adults. *Cochrane Database of Systematic Reviews*. 5 (CD004692).

- **Dr Sylvia Carter has received a 'Faculty of Biomedical Sciences Commendation' for achievement of an excellent PhD degree.** Her thesis, entitled *Signalling, Epigenetic and Gene Transcription Changes in the Rat Hippocampus Following Morris Water Maze Training*, described which signalling molecules are activated in hippocampal neurones when rats are trained to learn to find a hidden platform in the Morris water maze. She investigated how these molecules via so-called epigenetic processes produce changes in the expression of genes involved in learning and memory processes. Her work has increased our understanding of the molecular neurobiology underpinning learning and memory processes.

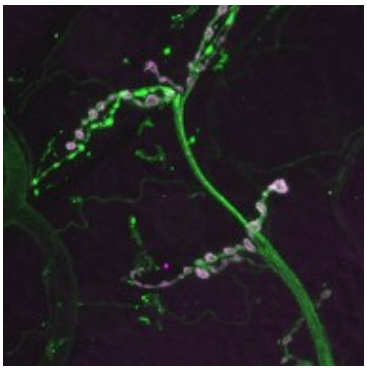
Dr Phil Clatworthy has been awarded the Stroke Association Thompson Family Senior Clinical Lectureship. The award will enable Phil to advance his research on vision in stroke alongside his clinical practice as Consultant Stroke Neurologist at North Bristol NHS Trust. Phil was awarded an EBI Early Career Fellowship in June 2014 to work on understanding brain plasticity and perceptual learning following brain injury with a view of developing individualised visual rehabilitation. This work is directed toward improving health using stratified (or personalised) medicine, a major priority area in medical research. His work focuses on rehabilitation of brain injury, and enhancement of recovery using pharmacological and non-pharmacological methods (e.g. non-invasive brain stimulation). There is also a strong neuroscience component in this research, aimed at understanding mechanisms underlying recovery and rehabilitation, which he has been developing with groups within the University. Phil is looking to develop a research group at UoB and welcomes enquiries from people interested in working in his research area– contact him on phil.clatworthy@bristol.ac.uk.

Follow Phil on his blog

Her research was conducted in the Neuro-Epigenetics Research Group and was supported by an MRC PhD capacity building studentship, the Integrative Pharmacology Fund of the British Pharmacological Society, and a BBSRC grant awarded to Professor Hans Reul.

- A new **national service called Join Dementia Research launched to help members of the public with and without dementia register their interest in participating in research**. Led by Dr Liz Coulthard it is funded by the Department of Health and delivered by NIHR in partnership with Alzheimer's Research UK, Alzheimer's Society and Alzheimer Scotland. The online and telephone service is the first of its kind in the UK; by signing up, volunteers agree to be contacted to take part in new studies getting underway in their area, from which point they can decide if they wish to take part. There are currently 39 research studies looking for volunteers through Join Dementia Research, including several studies running in the Bristol area. These include a clinical trial to investigate whether a blood pressure treatment could slow memory decline in people with Alzheimer's, as well as study investigating the earliest brain changes in the disease.

- Many of our everyday cognitive functions rely on communication between the hippocampus and prefrontal cortex. The mechanisms that lead to disruptions to the channels have been explored by Professor Zafar Bashir and his team. They studied two neurotransmitters, calledglutamate and dopamine, which work together in controlling normal transmission. They found that subtle **changes in the interplay of these transmitters completely altered the flow of information from the hippocampus to prefrontal cortex**. Overactivation of the D2 class of dopamine receptors led to suppression of the function of NMDA



receptors, which are activated by the neurotransmitter glutamate, at the synaptic connection between hippocampus and prefrontal cortex. This in turn leads to a marked disruption of communication between the regions. Findings demonstrate a mechanism for how a connection in the brain needed for complex mental tasks is disrupted in schizophrenic patients.

Reference: Banks PJ, Burroughs AC, Barker GR, *et al*. (2015). Disruption of hippocampal–prefrontal cortex activity by dopamine D2R-dependent LTD of NMDAR transmission. *Proceedings of National Academy of Sciences*. 112(35), pp. 11096-101

Cognitive Reading Group

Meet every Monday at 1pm in the Philosophy Department, Cotham House. Open to all, covers a broad range of topics. Each meeting will focus on a different paper (neuroscience, robotics, anthropology, psychology etc.) on a particular topic

contact

chris.burr@bristol.ac.uk

- Light polarization tells us the orientation in which the light waves are oscillating. **Humans can perceive the polarization of light with the naked eye using 'Haidinger's brushes'**, a subtle visual effect which appears like a yellow bow tie at right angles to the polarization angle. In an experiment originally used to test the visual abilities of octopuses and cuttlefish, Dr Shelby Temple and colleagues from the Ecology of Vision Group developed special filters to vary the percentage of polarized light from 0-100% and

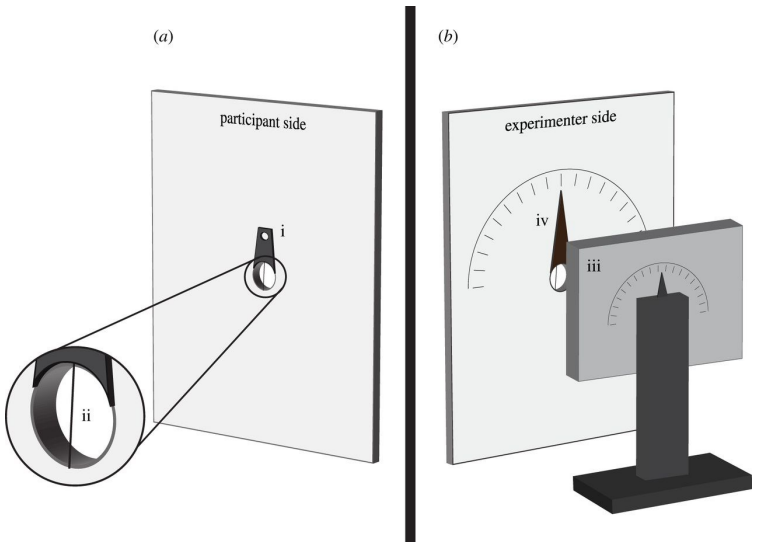


Photo caption: Experimental set-up for the alignment task designed to characterize the rotational dynamics of Haidinger's brushes. (a) Participants sat on one side of an opaque panel and used a handle (i) to rotate a thin piece of translucent monofilament fishing line (ii) until it was aligned with the long axis of the yellow component of Haidinger's brushes. (b) On the other side of the panel, the experimenter set the orientation of the modified LCD monitor (iii) that presented two alternating polarization orientations. One orientation was used to refresh Haidinger's brushes and the other was used for alignment; the latter was accompanied by an audible sound to inform the participant of which polarization orientation they should be aligning. The experimenter recorded the orientation set by the

participant using the position of a pointer (iv), which was also attached to the rotating monofilament line holder (ii).

tested the minimum percentage polarization at which Haidinger's brushes could be detected – among 24 people, the average polarization sensitivity threshold was 56%. The team also took the first measurements of the dynamics of Haidinger's brushes, confirming that some individuals would perceive a 'flip-flop' effect as the polarization angle is rotated. This shows that the cornea can dramatically affect how polarized light is received; as the optical properties of the cornea vary between individuals, this may partly explain why people often report their experience of seeing Haidinger's brushes quite differently. The ability to see Haidinger's brushes is associated with the organisation of carotenoid pigments in the macula. The risk of acquiring Age-related Macular Degeneration (AMD) has previously been correlated with low carotenoid pigment density– researchers are presently adapting their approach with the aim of developing a screening device to detect individuals at high risk of AMD, currently the leading cause of blindness in the developed world.

Reference: Temple SE, McGregor JE, Miles C *et al*. (2015). Perceiving polarization with the naked eye: characterization of human polarization sensitivity. *Proceedings of the Royal Society B.* Published online 1 July 2015.

- The protein Synapsin 1a plays a key role in regulating how synapses operate by regulating the amount of chemical transmission. SUMOylation is the process by which a protein called SUMO is attached to a target protein and modifies its function. Studying SUMOylation has shown that synapsin 1a is a target protein for the process. It has also been found that **mutation A548T in synapsin 1a, which has already been associated with autism and epilepsy, reduces synapsin 1a SUMOylation and interferes with its ability to function, causing impaired synaptic function that may contribute to neurological**

A large-scale review that evaluated the medical efficacy of cannabinoids across a range of conditions found there is moderate evidence to support the use of cannabinoids for the treatment of chronic pain and spasticity in patients with multiple sclerosis. The meta-analysis looked at results of different randomised-controlled studies involving more than 6,400 patients to investigate the benefits and side effects of the chemicals. They found there was only moderate-quality evidence to suggest cannabinoids may alleviate chronic neuropathic or cancer pain and muscle contractions or involuntary movements due to multiple sclerosis. There was lower-quality evidence to suggest that cannabinoids alleviated the symptoms of nausea and vomiting due to chemotherapy, weight gain in HIV, sleep disorders and Tourette syndrome. There was very low-quality evidence to indicate patients treated with cannabinoids showed improvement in anxiety, psychosis and depression. Cannabinoids were associated with a range of side of effects including dizziness, dry mouth, fatigue and confusion. The team did not find any clear evidence on the benefits or adverse effects from taking particular type of cannabinoids or its mode of administration.

Reference: Whiting, Penny *et al.* (2015). Cannabinoids for Medical Use: A Systematic Review and Meta-analysis. *The Journal of the American Medical Association*. 313(24).

disease. These results show the extent and how critical the role synaptic proteins regulated by SUMOylation play in neurological disorders. Importantly, they provide further evidence for SUMO modification of synaptic proteins in health and disease.

Reference: Tang L, Craig TJ & Henley JM (2015). Synapsin Ia SUMOylation is required to maintain synaptic vesicle availability and is reduced in a mutation linked to autism. *Nature Communications*.

The wiring diagram of the brain is so massively interconnected, we need to consider how even subtle changes in one part of the brain can cause trouble for other nodes of the circuit Matt Jones

- Down syndrome is the most common genetic cause of intellectual disability, and is triggered by an extra copy of chromosome 21. **Recent research has clarified which part of the brain's vast neural network contributes to problems in learning and memory in Down syndrome.** Using genetically engineered mice it was shown that increased expression of chromosome 21 genes disrupts the function of key brain circuits involved in learning and memory. Using microscopy, nerve cell recordings and maze testing, they found abnormal structure and function of synapses in the networks of the hippocampus. Dysfunction at the input synapses of the hippocampus propagates around hippocampal circuits in the mouse model, resulting in unstable information processing by place cells and impaired learning and memory. Over the course of a lifetime, even subtle impairments of this type will profoundly influence intellectual abilities. The study highlights the vulnerability of the hippocampus to increased expression of chromosome 21 genes. Therapies which aim to normalise the function of these disrupted networks may be particularly beneficial as part of the future treatments of Down syndrome.

Reference: Witton J, Padmashri R, Zinyuk LE *et al*. (2015). Hippocampal circuit dysfunction in the Tc1 mouse model of Down syndrome. *Nature Neuroscience*. 18, 1291–1298

- Researchers at Bristol can **recruit participants online** via Call For Participants, an advertising platform focused on bringing opportunities for taking part in academic research to the general public. A dedicated notice board will advertise surveys, interviews and other research studies. The company will also provide support and guidance on how to advertise research and communicate to the public. To post an advert go to https://www.callforparticipants.com/researcher.

GW4 Early Career Neuroscientist Day

Formerly the Young Neuroscientist event, the Early Careers Neuroscientist events bring post-doctoral and postgraduate researchers together for a full day of talks, posters and networking. Topics encompass all neuroscience fields from cell biology to cognitive psychology.

On Monday, 21 September we welcomed 116 delegates from across the UK to At-Bristol. We hosted 19 early career talks, 58 posters, 16 invited speakers and 8 exhibitors. A series of parallel sessions provided an invaluable opportunity to hear about Scientific Techniques, Academic Careers, Alternative Careers and Public Engagement, as well as the chance for early career researchers to present in a conference setting in one of four scientific themes.

Plenary speakers were Professor Adrian Harwood, Technical Director of the Neuroscience and Mental Health Research Institute, Cardiff University and Professor Anne Rosser, Professor of Clinical Neuroscience and Honorary Consultant Neurologist at the University Hospital of Wales, Cardiff. Oral and poster proceedings are available to download from the BN intranet site alongside a number of speaker presentations.

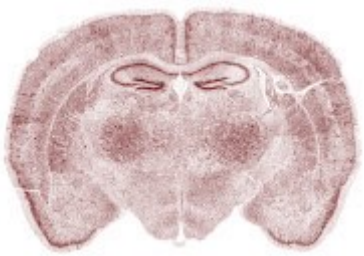
Congratulations to the **Prize Winners**:

Posters
4th: AK Simpson-*Corticotrophin-releasing hormone neurons in the Paraventricular hypothalamus: Evidence for glucose sensitivity and projection to autonomic relay areas*, University of Bristol
3rd: M Alsaqati–*Of mice and men: Level of endocytic proteins are altered with ageing in the brain*, Cardiff University
2nd: B Stevens-*Identification of the source of noradrenergic inputs to the BNST from the brainstem using a novel variant of canine adenovirus*, University of Bristol
1st: CA Hales-*Differential effects of acute treatment with ketamine and conventional antidepressants on a rodent judgement bias task*, University of Bristol

Oral
Developmental session: Adam Cunningham-*Developmental co-ordination disorder, psychopathology and cognition in 22q11.2 deletion syndrome*, Cardiff University
Cognitive session: Bonni Crawford-*Expectancies of social pain and pleasure are reflected in brain structure*, Cardiff University
Behavioural session: Emma Yhnell-*Using cognitive training as a therapeutic intervention in a kock-in mouse model of Huntington's disease*, Cardiff University
Cellular session: Haiyan An-*Modelling of cellular pathology caused by ALS-associated mutations in FUS gene by targeted genome modifications in cultured human cells*, Cardiff University

Thanks are extended to all **sponsors**, including: Primary sponsors Eppendorf and ThermoFisher Scientific**;** Industrial Sponsors: Promega, Lonza, Sigma-Aldrich, Roche, Proteintech, Zeiss, Merck-Millipore; Academic Sponsors: British Pharmacological Society, The Company of Biologists, F1000Research, Cardiff University School of Psychology, British Association for Psychopharmacology, University of Bristol School of Physiology and Pharmacology, Cardiff University School of Biosciences, Bristol Neuroscience, GW4, University of Exeter Medical School, Cardiff University Neuroscience & Mental Health Research Institute, University of Bristol School of Experimental Psychology, Cardiff University School of Medicine

ELIZABETH BLACKWELL FUNDING SCHEMES



Clinical Primer Scheme

Closing date: 11-Dec-15

The awards are aimed at Medical & Veterinary clinical graduates considering a career as a clinical academic but wishing to experience life as a researcher before deciding. They are designed to give outstanding early career clinicians the chance to experience a world-class research environment for the first time. Applications from suitably qualified clinical graduates are invited for six month biomedical research primer projects to be undertaken at the University of Bristol.

EBI Workshops Funding

Support for interdisciplinary workshops in health research at a new or emerging interface between two or more disciplines. Applications are reviewed on a rolling basis.

EBI Catalyst Fund

Pump priming awards can support the most promising and ambitious ideas across the widest interdisciplinary boundaries. These projects will be identified largely through the running of workshops to explore new possibilities and identify the big questions. Applications are reviewed on a rolling basis.

Returning Carers Scheme

UoB has introduced a Returning Carers' Scheme (RCS) to support academic staff across all faculties in re-establishing their independent research careers on return from extended leave (16 weeks or more) for reasons connected to caring - such as maternity leave, adoption leave, additional paternity leave, or leave to care for a dependant. The deadline for applications is 30 April and 31 October each year.

H2020: 2016-2017 Societal Challenges and LEIT Work Programmes published

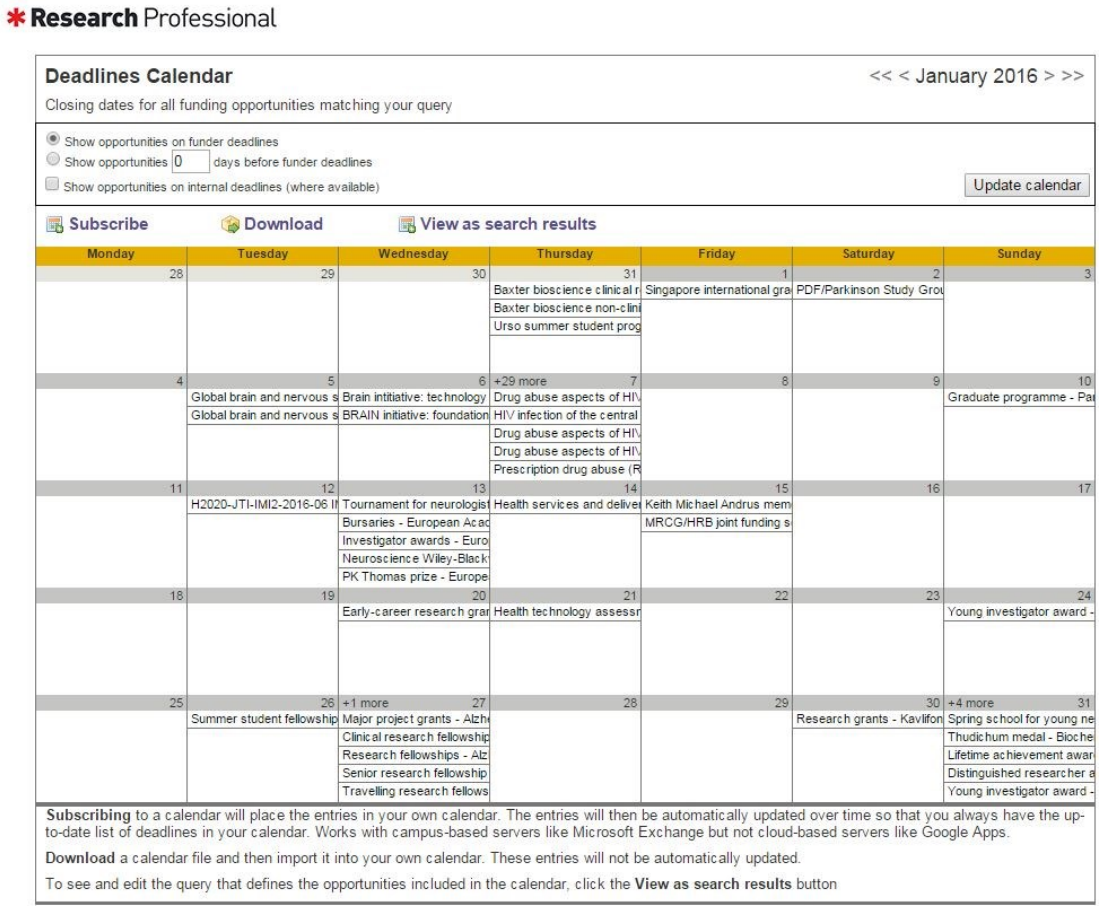
The Societal Challenge Work Packages reflect the policy priorities of the EC and address shared concerns across Europe. The challenge-based approach is expected to bring together resources and knowledge across different fields, technologies and disciplines. Topic areas include Health, Food Security, Energy, Transport, Climate, Security and Inclusive, Innovative and reflective societies. A minimum of three partners from three different EU countries are required for both Societal Challenges and LEIT proposals, with a variety of deadlines over the next two years (starting February 2016). If you are interested in discussing involvement in one of these calls, either as a lead or partner, or would like more details about what is available in your area of interest please contact Tiernan Williams.

FUNDING OPPORTUNITIES

Calendar of potential funding opportunities for Bristol Neuroscience

Set up via Research Professional (RP), a full calendar of funding opportunities for BN Research is available online. Subscribing to a calendar will place the entries in your own calendar, which will automatically update according to pre-specified search criteria. Staff and students have FREE access to Research Professional online from all computers on the University network. You can create your own personalised funding opportunity e-mail alerts by registering with RP.

Find out all about it on the RED website!!



Medical Research Council

Closing date: normal board deadlines apply Award amount: unspecified

The MRC have announced a highlight notice in *Neurovascular Ageing*, in which they hope to bring together the neuroscience and cardiovascular research communities. As this is a highlight notice, there is no ring-fenced pot of money, but applications in this area will be given suitable strategic uplift by the Boards. The highlight notice will be in place for a year.

The Wellcome Trust new Strategic Framework

Wellcome's new framework consists of three complementary approaches across science, research and engagement with society:

1. Advancing Ideas. Wellcome will continue to respond to great ideas and inspired thinking that address the fundamental health challenges of our time.
2. Seizing opportunities. Wellcome brings ideas together to make a big difference, providing intensive support that creates real change. They identify times when concerted intervention can accelerate progress towards better health. Priorities will evolve as new challenges arise, drawing on insights from a rich history of achievement and a network of experts from different disciplines around the world. Initial priorities include Science education.
3. Driving reform. Wellcome changes ways of working so more ideas can flourish, leading by example and campaigning for wider reform. Their record in areas like open access to research results, public engagement, and research careers has earned us the credibility to challenge ways of working, and to propose better alternatives. One area on which reform will concentrate is Science to health- insights most improve health when they are applied to diagnosis, prevention and therapy. They will work to improve intellectual property and translation systems so business and academia are encouraged to innovate for better health.

More information on the Wellcome Trust Strategy page.

Wellcome Trust
Four-year PhD studentship programmes

Closing date: none Award amount: stipend, fees, lab expenses, travel

Enable students to undertake in-depth postgraduate training at centres of excellence throughout the UK in the following biomedical research areas: developmental biology and cell biology; genetics, statistics and epidemiology; immunology and infectious disease; molecular and cellular biology; neuroscience; physiological sciences; structural biology and bioinformatics.

Guarantors of Brain
Brain entry scholarship

Closing Date: none Award amount: £60,000

Provides transitional funding support for early career clinicians. The aim is to provide transitional funding at entry from the early specialist training grades, prior to obtaining a research fellowship. Applicants must be eligible for, or be engaged in, neurology higher specialist training based in the UK.

Guarantors of Brain
Postdoctoral Fellowship

Closing Date: none Award amount: £60,000

This provides transitional funding support for early career clinicians. May be undertaken on completion of a higher degree and while waiting for a specialist registrar post, or at a later stage in training but before the completion of training.

The Avon Primary Care Research Collaborative (APCRC)
Research Capability Funding (RCF)

Deadline: 18-Dec-15 Award amount: unspecified

This call is open to NHS and Higher Education Staff across Bristol, North Somerset and South Gloucestershire working in Primary Care, Community Healthcare and Public Health. Funding can 'ring-fence' your time for up to a day a week for a year in order for you to focus on writing a high quality NIHR grant application.

National Institute of Mental Health
BRAIN initiative: foundations of non-invasive functional human brain imaging and recording – bridging scales and modalities (R01)

Closing Date: 06-Jan-16 Award amount: US$700,000

Support transformative discoveries that will lead to breakthroughs in understanding human brain function. The research objective is to advance our ability to accurately and precisely infer microscopic details of underlying anatomy and physiology in the human brain from the more limited data available from non-invasive functional brain mapping methods.

National Institute of Mental Health
Brain intitiative: technology sharing and propagation (R03)

Closing Date: 06-Jan-16 Award amount: US$100,000

Encourages the transfer of new technologies and new data analysis techniques into a research laboratory. One of the key goals is to develop new technologies to improve our understanding of the brain. This funding opportunity announcement seeks applications from investigators who can identify new technologies which if introduced into their laboratory will enable or promote new research activities that further the aims of the BRAIN initiative.

Paris School of Neuroscience
Graduate programme

Deadline: 10-Jan-16 Award amount: unspecified

This four-year programme is open to international students primarily trained outside France, and leads to a PhD in neuroscience. All applicants are required to hold a diploma that is obtained outside France in any relevant field related to neuroscience.

Department of Health
Invention for innovation (i4i) challenge awards

Deadline: 13-Jan-16 Award amount: unspecified

Aim to comprise the clinical development of laboratory-validated technologies or interventions, requiring minimal preclinical development. Any level of funding will be considered if appropriately justified. Funding will be provided for up to three years.

Department of Health
Health services and delivery research programme – researcher-led workstream

Closing Date: 14-Jan-16 Award amount: unspecified

Supports research into the quality, effectiveness and accessibility of health services, including evaluations of how the NHS might improve delivery of services. The workstream has a continued interest in: dementia; primary care interventions; very rare diseases.

NIHR will fund HEIs at a maximum of 80 per cent of FEC, except for equipment worth over £50,000.

The Academy of Medical Sciences
Daniel Turnberg Travel Fellowships

Closing date: 18-Jan-16 Award amount: £3,500 for 1 month or £9,000 for 3 month fellowships

To encourage researchers to experience an alternative research environment, to learn new techniques and develop ideas for future collaborations. The Fellowships are aimed primarily at early- and mid-career scientists, particularly those just embarking on a career in research. Funds will provide an opportunity for biomedical researchers to visit a research institution of their choice in the Middle East.

NIHR
Fellowship Programme

Closing date: 20-Jan-16 Award amount: unspecified

Open to all professions and offer five levels of fellowship. The awards cover the salary costs, research costs, and training and development costs of the trainee. The following fellowships are available on an annual basis: Doctoral Research Fellowship (PhD); Post-Doctoral Fellowship; Career Development Fellowship; Senior Research Fellowship; Transi-

tional Research Fellowship.

NIHR

Call 15/174 - Cognitive Behavioural Therapy: An overview of systematic reviews and meta-analyses

Closing date: 21-Jan-16 Award amount: unspecified

CBT is recommended in numerous NICE guidelines and is widely used in NHS clinical practice for a variety of mental and physical health problems. A plethora of systematic reviews and meta-analyses have examined the effectiveness of CBT compared to a variety of comparators for a wide range of individual conditions. There is no single definition of CBT and it can be delivered by qualified or relatively unqualified practitioners to a range of ages in a variety of formats. Although these disorder-, age- or format-specific treatment protocols may show considerable differences in some of the treatment techniques, they all share the same core model and general approach to treatment. A comprehensive 'panoramic' overview of all systematic reviews and meta-analyses examining the evidence base for the effectiveness of CBT is needed to aid evidence-based clinical decision making and the direction of future research. The review should build on previous overviews and aim to "take stock" to determine the current position regarding what works for whom. A consideration of the likelihood of the relevance of current CBT effect sizes to as yet unexplored patient sub-groups would be welcomed.

NIHR

15/156 - Interventions to improve eating ability in children with neurodisability

Closing date: 21-Jan-16 Award amount: unspecified

Many children with a neurodisability have difficulties with the skills associated with eating, which can lead to specific morbidities. They also have profound psychosocial impact, quality of life and participation implications for the child, carer and wider family. Interventions to help improve a child's ability to safely and adequately consume food are therefore vital yet the supporting evidence base is extremely weak and current practice in the UK appears varied and mixed. Qualitative work is therefore proposed, as outlined above, to help establish if current interventions are effective and to develop the scope for a potential future trial.

NIHR

15/161 - Non-pharmacological intervention for treatment resistant generalised anxiety disorder in older people

Closing date: 21-Jan-16 Award amount: unspecified

GAD is the most common anxiety disorder in later life. Despite evidence for the effectiveness of treatments for GAD, a significant proportion of patients fail to respond, or respond inadequately, to first line interventions such as selective serotonin reuptake inhibitors and cognitive behavioural therapy. These 'treatment resistant' patients have been shown to

have a very poor quality of life and, in older patients, persisting anxiety disorders may be associated with an increased mortality rate, social isolation and loneliness. At present the management of treatment resistant GAD in older adults is not evidence based. This vulnerable group of patients is often in receipt of multiple drug treatment regimens including prescription benzodiazepines and other psychotropic drugs for their anxiety which may increase the risk of falls and the likelihood of delirium. The proposed feasibility study to develop and pilot a complex non-pharmacological intervention could be a first step towards advancing the standard of care received by this population of older adults.

University of Bristol
International Strategic Fund 2015-16

Closing date: 22-Jan-16 Award amount: unspecified

To invest in new and nascent collaborations between the University of Bristol and some of its key international partners. Funding will cover travel and subsistence costs incurred in the course of initiating or building upon international collaboration. Requests for other support including equipment or seed funding for research projects will be considered on a case by case basis.
Funds are available to support: the institutional partnerships between Bristol and Kyoto University and University of Heidelberg.; activities with any partner country within the Newton Fund scheme which will lead to a collaborative bids for future Newton Fund calls; WUN Universities.

Alzheimer's Research UK
Interdisciplinary research grant

Closing Date: 27-Jan-16 Award amount: £250,000

Encourages researchers from other fields into dementia research who have expertise and ideas which could benefit the field. Lead applicants must be researchers who have not previously received funding for dementia research- one or more co-applicants must be researchers with a track record in the dementia field.

Alzheimer's Research UK
Major project grants

Closing Date: 27-Jan-16 Award amount: £1M
Fund high-quality research projects on Alzheimer’s disease and related dementias.

Sparks
Research grant

Closing date: 27-Jan-16 Award amount: £60,000

For research into the causes and prevention of cerebral palsy and other neurodevelopmental disorders. Grants can cover any combination of salaries, equipment and consumables.

Grants are only made for research projects where the PI has a contract at the host university that extends beyond the life of the proposed project.

Alzheimer's Research UK
Research fellowships

Closing Date: 27-Jan-16 Award amount: £20,000

Support PhD qualified non-clinical investigators pursuing research on Alzheimer's disease and related dementias. Applicants should either be emerging from PhD training or within five years of obtaining a PhD.

Alzheimer's Research UK
Senior research fellowship

Closing Date: 27-Jan-16 Award amount: £420,000

Supports researchers who have the potential to become leading principal investigators within the field of Alzheimer's disease and related dementias, but have not yet attained a tenure or tenure-track position. Applicants must have obtained their terminal degree within the last three to 10 years. Fellows are required to have secured the sponsorship of a senior established investigator in the institution where the fellowship is to be held.

Alzheimer's Research UK
Travelling research fellowship

Closing Date: 27-Jan-16 Award amount: £60,000

Enables researchers to travel abroad to develop collaborations and learn new techniques within the field of Alzheimer's disease and related dementias. Applicants must have obtained their terminal degree within the last 10 years.

Institute for Advanced Studies
Enhances research and intellectual life at the University of Bristol by funding workshops and fellowships in pursuit of new ideas. They offer resources and opportunities to develop novel areas of research through funding for workshops (including virtual seminars) and for visits by experts and colleagues from abroad through the IAS Benjamin Meaker Visiting Professorships scheme.
Application Deadlines:

- Research Workshop: 29-Jan-16
- Benjamin Meaker Visiting Professorships: 31-Mar-16 (May to August 2016), 26-Feb-16 (medium-term)
- University Research Fellowships: 12-Feb-16 (for University Research Fellowships, University Senior Research Fellowships, IAS Research Fellowships and Translational Neuroscience Research Fellowships)

Contact Ralph Pite, Director, or Susie Jim, Research Development Manager, with any questions.

National Institute of Mental Health
BRAIN initiative: development and validation of novel tools to analyse cell-specific and circuit-specific processes in the brain (R01)

Closing Date: 02-Feb-16 Award amount: unspecified

Aims to develop and validate novel tools to facilitate the detailed analysis of complex circuits and provide insights into cellular interactions that underlie brain function. The development of new genetic and non-genetic tools for delivering genes, proteins and chemicals to cells of interest or approaches that are expected to target specific cell types and circuits in the nervous system with greater precision and sensitivity than currently established methods are encouraged. Tools than can be used in a number of species or model organisms rather than those restricted to a single species are highly desired. Applications that provide approaches that break through existing technical barriers to substantially improve current capabilities are sought.

National Institute of Neurological Disorders and Stroke
BRAIN initiative: new technologies and novel approaches for large-scale recording and modulation in the nervous system (U01)

Closing Date: 24-Feb-16 Award amount: unspecified

Aims at understanding the dynamic activity of neural circuits and seeks applications for proof-of-concept testing and development of new technologies and novel approaches for large scale recording and manipulation of neural activity to enable transformative understanding of dynamic signalling in the nervous system. In particular proposals should be creative approaches to address major challenges associated with recording and manipulating neural activity, with cellular resolution, at multiple spatial or temporal scales, in any region and throughout the entire depth of the brain.

British Neuropathological Society
Small grant scheme

Closing Date: 01-Mar-16 Award amount: £5,000

Aims to advance neuropathology by supporting both substantive and pilot projects, and projects related to education and training in the field of neuropathology. Applicants or the principal investigator must be members of the society. Preference will be given to early career applicants, but applicants at later stages in their careers may be considered.

NIHR
Programme Development Grants

Closing date: 8-Mar-16 Award amount: £100,000

Produce independent research findings that will have practical application for the benefit of patients and the NHS in the relatively near future. Programme Development Grants are a complementary scheme to allow investigators to undertake preparatory research that will position them to submit a competitive Programme Grant application.

Scottish Government
Clinical research fellowship in progressive supranuclear palsy

Closing Date: 18 Mar 16 Award amount: £30,000 stipend plus fees and £2,000 research costs

Aims to improve the evidence base on routes to diagnosis and care of people living with progressive supranuclear palsy by undertaking a PhD. Applicants who have already worked or wish to develop their career in neurodegenerative disorders are particular suited to apply. The host institution must be based in Scotland. The fellowship is tenable for up to three years, starting in October 2016.

Medical Research Council
Clinical Scientist Fellowship

Closing date: 06-Apr-16 Award amount: unspecified

Develops talented medically and other clinically qualified professionals who have gained a higher research degree to lead their own research plans and establish their own research team to make the transition to independent investigator.

British Council
BIRAX regenerative medicine initiative

Closing Date: 12-May-16 Award amount: £400,000

Enables scientists in both the UK and Israel to carry out collaborative research which furthers advances in the field of regenerative medicine. The scheme funds research that: explores the use of stem cell technology and tissue engineering in the context of fundamental disease processes; discovers new mechanisms that might be targeted to develop novel therapeutic applications of regenerative medicine; advances understanding of stem cell biology, using lessons learnt from developing tissues and organs, or the mechanisms underlying cell fate and the principles of cellular pluripotency for the development of stem cell-based therapies; advances cell and gene therapies. This third call also prioritises research that is related to Alzheimer's, arthritis, cardiovascular disease, type 1 diabetes, multiple sclerosis and Parkinson's.

NIHR
15/33 - Promising pharmacological therapy for treatment resistant bipolar depression

Closing Date: 19-May-16 Award amount: unspecified

Treatment resistant depression, or depression that has failed to respond adequately to initial interventions, is characteristic of the disorder with reports suggesting that bipolar depression typically is poorly responsive to antidepressants. In addition, the risk of mania with traditional antidepressant treatment is high. This highlights the importance of finding promising interventions for patients with treatment resistant bipolar depression. One potential candidate is augmentative pramipexole, a dopamine agonist approved for the treatment of Parkinson's disease. Systematic reviews have demonstrated its short-term efficacy and tolerability for treatment resistant bipolar depression. However, along with several other drugs that have been evaluated, high quality data are very scarce and not sufficient to allow recommendation. There is a need for an HTA trial of one or more promising pharmacological interventions involving patients with bipolar depression using a clear definition of treatment resistance.

Grünenthal GmbH

Research Grants for Clinical and Human Experimental Pain research

Closing date: 31-Dec-16 Award amount: €40,000

Support early-career scientists to carry out innovative clinical pain research in any member country of the European Pain Federation (EFIC). Grants are intended for clinical and human experimental pain research. Research proposals on animals, computer simulations, cell lines etc. will not be considered.

THIS ISSUE'S SHOWCASED ARTICLE

Activation of Muscarinic M1 Acetylcholine Receptors Induces Long-Term Potentiation in the Hippocampus

SH Dennis, F Pasqui, EM Colvin, H Sanger, AJ Mogg, CC Felder, LM Broad, SM Fitzjohn, JTR Isaac and JR Mellor

Muscarinic M1 acetylcholine receptors (M1Rs) are highly expressed in the hippocampus, and their inhibition or ablation disrupts the encoding of spatial memory. It has been hypothesized that the principal mechanism by which M1Rs influence spatial memory is by the regulation of hippocampal synaptic plasticity. Here, we use a combination of recently developed, well characterized, selective M1R agonists and M1R knock-out mice to define the roles of M1Rs in the regulation of hippocampal neuronal and synaptic function. We confirm that M1R activation increases input resistance and depolarizes hippocampal CA1 pyramidal neurons and show that this profoundly increases excitatory postsynaptic potential-spike coupling. Consistent with a critical role for M1Rs in synaptic plasticity, we now show that M1R activation produces a robust potentiation of glutamatergic synaptic transmission onto CA1 pyramidal neurons that has all the hallmarks of long-term potentiation (LTP): The potentiation requires NMDA receptor activity and bi-directionally occludes with synaptically induced LTP. Thus, we describe synergistic mechanisms by which acetylcholine acting through M1Rs excites CA1 pyramidal neurons and induces LTP, to profoundly increase activation of CA1 pyramidal neurons. These features are predicted to make a major contribution to the pro-cognitive effects of cholinergic transmission in rodents and humans.

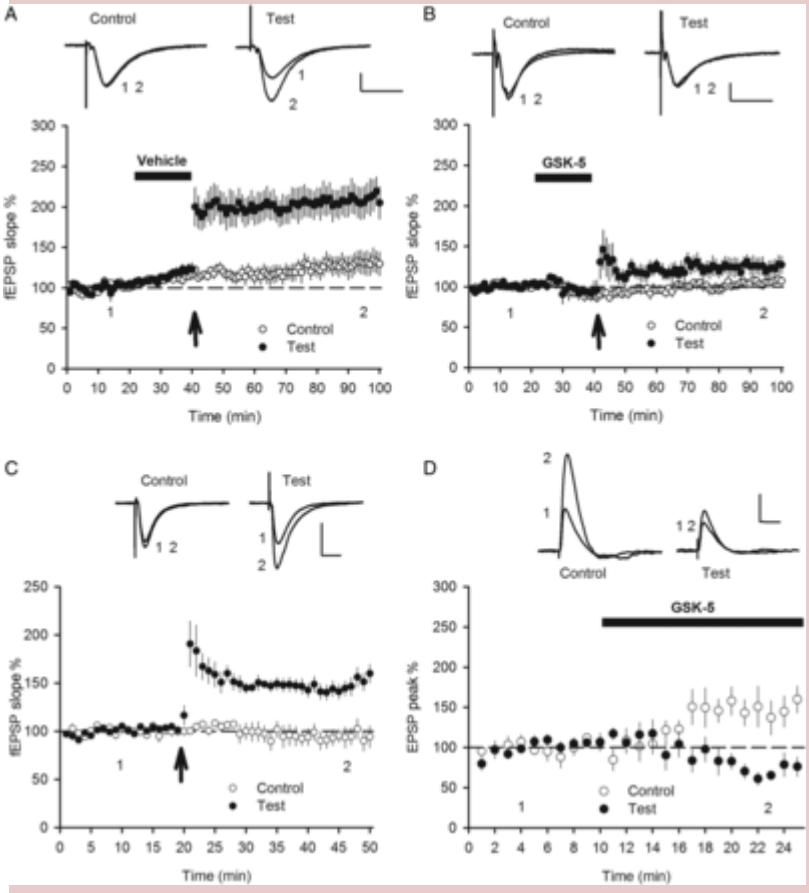


Image caption: M1R-induced EPSP enhancement bi-directionally occludes with LTP. (A) Theta burst stimulation (arrow) induced pathway-specific LTP after a 20-min application of vehicle (DMSO) in extracellular field potential recordings from stratum radiatum. (B) Theta burst stimulation (arrow) failed to induce LTP after a 20 -min application of GSK-5 (500 nM). (C) Extracellular recording demonstrated pathway-specific LTP induction by theta burst stimulation (arrow) in the test pathway. (D) In the same slices as (C), subsequent whole-cell recording from CA1 pyramidal cells showed that GSK-5 (500 nM) caused an increase in EPSP amplitude only in the control synaptic pathway that did not receive theta burst stimulation. Data plotted as mean ± s.e.m. Example field potential and voltage traces in response to synaptic stimulation taken from Points 1 or 2 as indicated. Scale bars: 0.2 mV and 10 ms (A, B), 0.5 mV and 10 ms (C), 2 mV and 50 ms (D).

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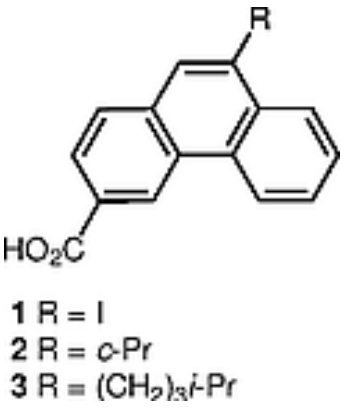

Image caption: NMDA receptor allosteric modulators

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Chen C, Buhl E, Xu M, Croset V, Rees JS, Lilley KS, Benton R, Hodge JJL & Stanewsky R (2015). Drosophila Ionotropic Receptor 25a mediates circadian clock resetting by temperature. *Nature*. 527(7579), pp. 516-20

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Molnar E (2015). Investigation of neurotransmitter receptors in brain slices using cell surface biotinylation. *Neuromethods: Receptor and ion channel detection in the brain.* Lujan R & Ciruela F (eds). Springer, Vol. 110

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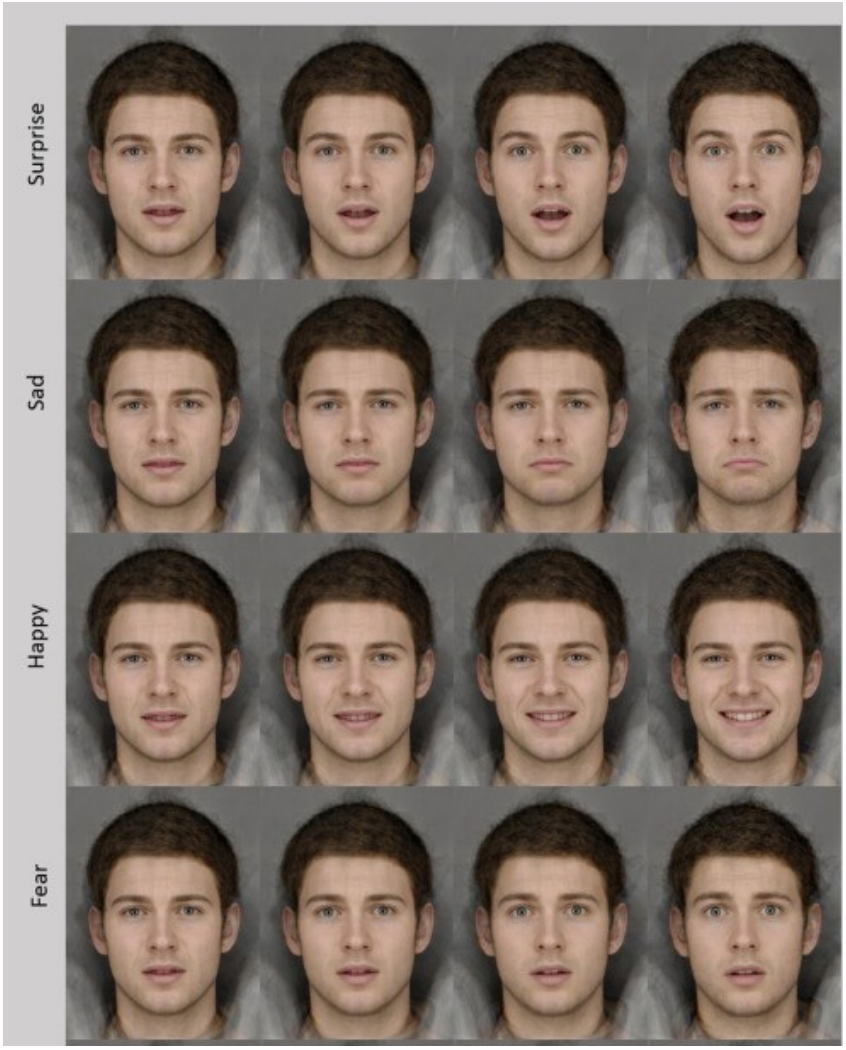

Image caption: Selected pictures from forced choice task.

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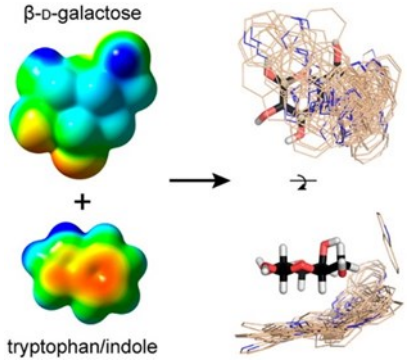

Image caption: Together, our data indicate that electrostatic and electronic complementarity between carbohydrates and aromatic residues play key roles in driving protein–carbohydrate complexation. Moreover, these weak noncovalent interactions influence which saccharide residues bind to proteins, and how they are positioned within carbohydrate-binding sites.

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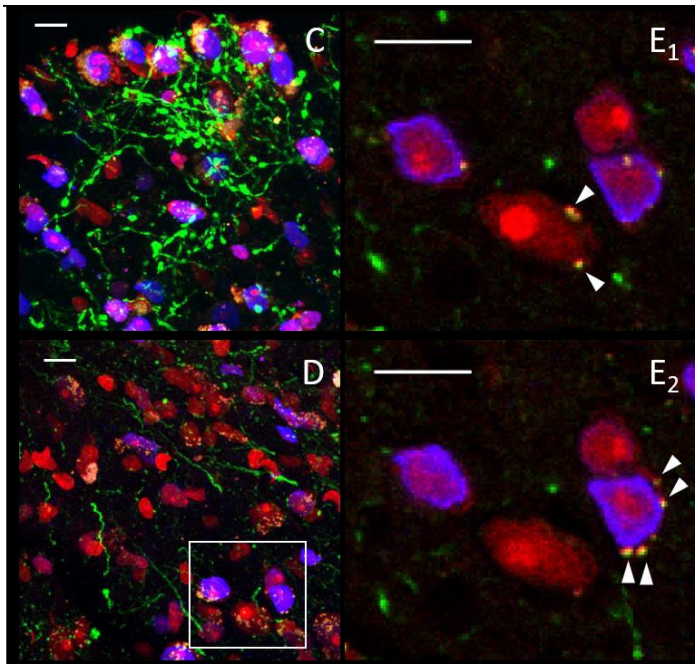

Image caption: GABAergic projections in the Kölliker-Fuse (KF) of Mecp2+/−/GAD67-eGFP compared to the same region in Mecp2+/+/GAD67-eGFP littermate female mice. GABAergic neurones express eGFP under the control of the GAD67 promoter via a knock-in transgene (green); perikarya are labelled in red (Nissl stain); and MECP2 protein immuno-reactive (MECP2ir) nuclei are pseudo-coloured in blue. This GAD67-eGFP knock-in strain identifies only parvalbumin GABA processes. (C) Representative projection of a z-stack across the KF region in a Mecp2+/+/GAD67-eGFP female and (D) in a Mecp2+/−/GAD67-eGFP littermate female. Reduction in MECP2ir is expected in Mecp2+/− mice. Note the marked reduction in GFP-expressing GABAergic projections in MECP2 deficient females. (E1-2) Two sequential images of a single confocal plane of the region of interest outlined in (D) showing eGFP -expressing perisomatic puncta (arrowheads) on IR+ and IR- cells. Scale bars = 10 μm.

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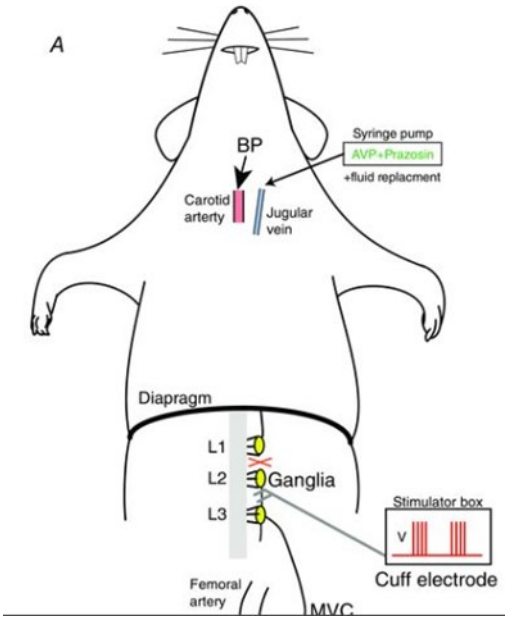

Image caption: Schematic of the in vivo *rat preparation. Recordings of blood pressure (BP) from the carotid artery and blood flow (BF) from the femoral artery were made. The* profunda femoris *was tied, to increase flow past the recording probe. The sympathetic ganglia (L3) was located and the sympathetic chain between L2–L3 connected to a cuff electrode for stimulating with current pulses, increasing muscle vasoconstrictor (MVC) drive to the hindlimb.*

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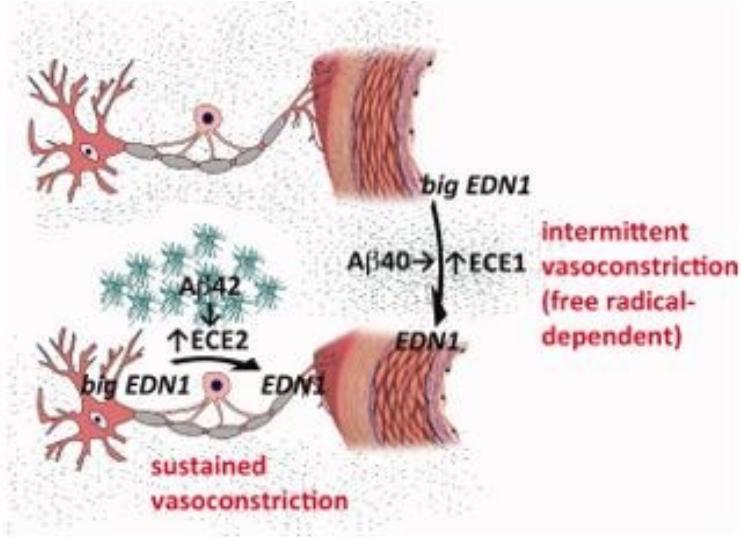

Image caption: *Proposed differences in stimuli and function between ECE2- and ECE1-mediated cerebral vasoconstriction. The present data implicate Aβ42 in the elevated EDN1 level that correlates with a sustained reduction in tissue oxygenation (and therefore of MAG:PLP1) in AD, whereas Aβ40 has been implicated in impairment of transient modulation of arteriolar calibre needed for functional hyperaemia.*

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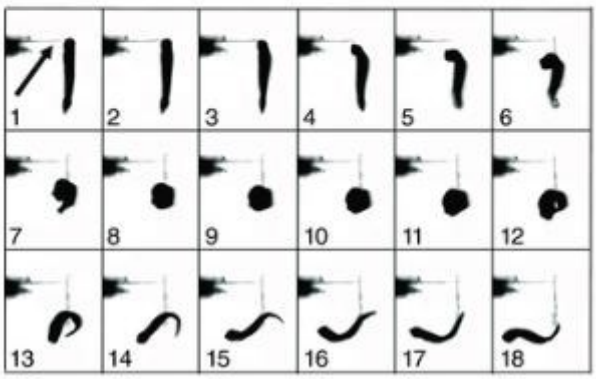

Image caption: *tadpole and video frames (150 frames s^{-1}) showing a tadpole viewed from above responding to touch on the left side of the head with a fine hair (arrow) by flexing to the left (frames 4–10) and then swimming off (frames 14–18).*

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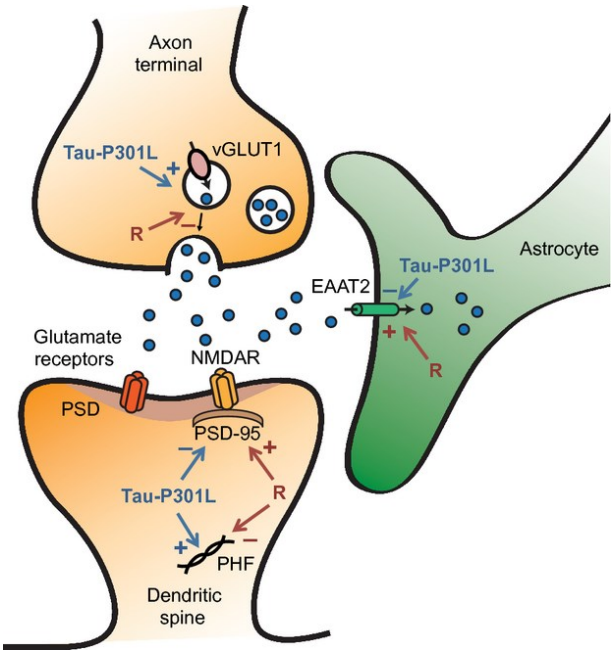

Image caption: Schematic representation of riluzole effects on tau-induced changes at hippocampal glutamatergic synapses. Riluzole (R) counteracts the tau-P301L expression (Tau-P301L)-induced increase in glutamate release, decrease in glutamate uptake and reduction in PSD-95 levels at hippocampal synapses (based on Hunsberger et al. 2015). EAAT2, excitatory amino acid transporter 2; NMDAR, N-methyl-D-aspartate-type ionotropic glutamate receptor; PHF, paired-helical filaments; PSD, postsynaptic density; PSD-95, postsynaptic density protein 95; vGLUT1, vesicular glutamate transporter 1.

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