Bright Brains Newsletter

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Welcome to the spring edition of our 'Bright Brains' Newsletter! We are pleased to present you with an impressive variety of thought-provoking articles that have been composed and edited by BNA students, postdocs and early-career researchers from a diverse array of neuroscientific disciplines throughout the UK.

During the course of your life you have probably wondered and asked yourself: 'Why am I here?', 'What am I doing here?', 'What is the purpose of my life?' We often rely on the people around us to make life meaningful. We learn from others how to emotionally connect to others, how to see the bigger picture, how to grow and become better people each and every day. Yet we simply know that there must be more to life than what life just throws at us, or what is simply visible to us.

The French poet Remy de Gourmont once said, life is a series of sensations connected to different states of consciousness. As scientists we study the brain and the mind, trying to answer questions such as how the brain produces conscious thought or what connects our conscious experience of different emotions to our brain activity. Thus, as scientists we can feel highly privileged to have turned our philosophical musings into a profession in which we have the luxury to scientifically pursue questions that tap into the connection between consciousness and neuroscience, exploring questions such as what happens if our usual conscious experience is deposed, defaced or discontinued. To help you expand your consciousness, and expose you to different ideas around the nature of consciousness, 'Bright Brains' has provided you with a list of the latest and classic books that will help you understand your conscious journey from a scientific, philosophical and creative perspective.

Also, 'Bright Brains' has many more exciting features in store for you in this edition. Our 'Nuntia' section reviews the inspiring annual NeuroConference held by the University of Glasgow, and provides an insightful student report on the 2017 Brain Prize Lectures. Our 'Socialia' section offers you a brilliant student perspective on what it means to do research overseas, and delivers an excellent evaluation of the 2017 Cajal Summer School. 'Varietas' shines light on a recently identified form of cell death called ferroptosis in Parkinson's patients, and presents to you a unique understanding of the functional architecture of the auditory cortex. 'Numquid sciebat...?' highlights the urgent need for invigorating the dialogue between the arts and sciences to foster multidisciplinary thinking, while 'Quid novi?' invites you to take a closer look into research that reveals which neurons are involved in helping us face an originally fearsome experience once more without trauma. Last but not least, we are challenging you to the first BNA 'Bright Brains' puzzle!

Finally, we sincerely hope that you will have as much joy in reading our eighth 'Bright Brains' newsletter as we had in producing it. On that note, we would like to encourage you to get involved in science communication by joining our newsletter team. Please direct enquiries to jayanthinykangatharan@gmail.com

Jayanthiny Kangatharan, 'Bright Brains' newsletter coordinator

Books on consciousness
Into the Grey Zone: A Neuroscientist explores the border between life and death by Adrian Owen (2017)
From Bacteria to Bach and Back by Daniel Dennett (2017)
Other Minds: The Octopus, the Sea, and the Deep Origins of Consciousness by Peter Godfrey-Smith (2016)
Tense bees and Shell-Shocked Crabs by Michael Tye (2016)
Consciousness and the Brain by Stanislas Dehaene (2014)
Making up the Mind: How the Brain creates our Mental World by Chris Frith (2007)
Conversations on Consciousness by Susan Blackmore (2005)
Phantoms in the Brain by Vilayanur S Ramachandran (1998)
The Conscious Mind by David Chalmers (1996)
The Origin of Consciousness in the Breakdown of the Bicameral Mind by Julian Jaynes (1976)

Adela Beloucif
Undergraduate student in Neuroscience, University of Glasgow

University of Glasgow NeuroSociety Conference 2017

On Saturday 11 November 2017, the University of Glasgow NeuroSociety hosted its sixth annual NeuroConference. The Royal College of Physicians and Surgeons of Glasgow welcomed 108 delegates, including junior doctors, students and future scientists. The conference's main goal is to showcase the various ways CNS disorders can be treated and researched, and for the first time, the theme expanded beyond neurosurgery to include a range of neuroscience topics. Growing on this strength of interdisciplinary communication, the society hopes to reach an even broader audience in 2018. Watch out engineering and computer science students!

Five guest speakers shared their insights on a wide range of topics. Foo Liew (Glasgow) presented his research on the role of interleukin-33 in Alzheimer's disease, and how after promising results in several animal studies, it is now entering a phase I clinical trial as an Alzheimer's treatment.

Next to speak was Rudolf Fahlbusch (Hannover, Germany) who shared progress made in computer-assisted surgery, thanks to a variety of novel imaging techniques. Tipu Aziz (Oxford) presented his work on how surgical stimulation of the pedunculopontine nucleus can reduce the symptoms of Parkinson's disease. Alastair Compston (Cambridge) spoke on the history of multiple sclerosis and the mechanisms underlying various drug treatments, including alemtuzumab, a drug he helped to develop and is now the first-line treatment in most of the world.

Lastly, Andrew Schwartz (Pittsburgh, USA) gave an overview of 30 years of working on high-performance neural prosthetics, sharing some videos of paralysed patients controlling robotic arms via electrodes implanted in their motor cortex.

The conference closed with a panel discussion, gravitating around the challenges of combining clinical and research skills, cultural differences between scientists and engineers, and shifting priorities in funding bodies. In addition, the panel members answered questions from the audience and offered their parting wisdom to students. Professor Liew said: "Be bright, driven and organised"; Professor Schwartz warned that "There will be ups and downs; when you're down, have the confidence to keep going"; and consultant neurosurgeon Jennifer Brown advised: "Do what you love and do it well". I left the conference excited and inspired, and with the impression that most delegates felt the same.

Matthew Buchan
PhD student in Neuroscience, University of Oxford

The 2017 Brain Prize Lectures

The Brain Prize is awarded annually by the Lundbeck Foundation (1) to scientists who have made an outstanding contribution to neuroscience research. The 2017 Brain Prize was awarded to three UK-based researchers, Peter Dayan, Ray Dolan and Wolfram Schultz, for their investigations of the dopaminergic system in reward-based learning. Their work has implications not only for the understanding of psychiatric disorders, such as addictive behaviour, whereby this system is hijacked, but also for reinforcement-based machine learning. Thanks to the BNA, on 25 October 2017 I was able to attend the annual Brain Prize Lectures at the Royal Society in London. Somewhat inevitably, Brexit hung heavily over the proceedings, with all speakers citing it as a significant challenge for science over the coming years.

The first speaker, Professor Schultz, talked us through the elegance by which economic theories of utility can predict choice behaviours. Stressing that the theories he mentioned can be found in any economics textbook, one cannot help but wonder how much there is yet to be 'married up' between behavioural neuroscience and classical economics. Secondly, Professor Dayan described how computational approaches can aid our understanding of the role of dopamine in reward prediction error, allowing insight into the optimisation of decision-making behaviour.

Lastly, Professor Dolan outlined the origins of his research career, from medical training in Ireland, to how his early experiences working within the psychiatric care system in London led him to become interested in the relationship between self-image and cognition. It was refreshing to hear accounts of how our knowledge of reward systems in the brain, applied together with economic theory, can inform difficult problems, from the constraint of financial industries, to the treatment of drug addiction and the real-world implications of new technological insights, such as Google DeepMind's AlphaGo (2).

The closing remarks on behalf of the Lundbeck Foundation were provided by Kim Krogsgaard, Managing Director of the Brain Prize. Stressing the importance of international collaboration, he announced increased funding for brain research from the Lundbeck Foundation, and reaffirmed the agenda of the Brain Prize as being 'completely international'. Opportunities afforded by increasing convergence across a number of fields, including neuroscience and economics, together with the creative potential of collaborative, interdisciplinary research, will have important implications for understanding human decision-making behaviour and its malfunctions. I hope that the Brain Prize will continue over the coming years as a tool by which such a collaborative atmosphere is encouraged.

1. **The Brain Prize Lecture.** Available at www.thebrainprize.org/ [Accessed 11 January 2018]
2. **Silver D *et al.*** (2016) Mastering the game of Go with deep neural networks and tree search. *Nature* 529: 484–489.

Ash Chetri
Research Software Engineer,
UCL

Reflecting on my UK–Taiwan research experience

During my year as an MSc student in Edinburgh, I was fortunate to be surrounded by a diverse and stimulating academic community in the Department of Neuroscience. It was not until I met Jane Haley that I was given the opportunity to volunteer for an outreach event in Roslin, Edinburgh. As well as meeting Dr Haley at the event, I also met Szu-Han Wang (PI of the Wang Lab at the Centre for Clinical Brain Sciences).

The conversation I had with Dr Wang about my undergraduate research project on implicit memory truly cemented my decision to work under her supervision towards my MSc thesis. So naturally when Dr Wang advertised a placement for an MSc project, I applied immediately. To my relief, Dr Wang kindly accepted.

From my perspective, the best part of the project was the opportunity to participate in collaborative research in Taiwan. As expected, magnetic resonance imaging (MRI) research requires a wide knowledge of varied subject areas. Furthermore, it tends to involve researchers from a range of backgrounds. For example, animal research is particularly important as it bridges the understanding between cognition and behaviour (psychologists/cognitive neuroscientists) with the physics and physiology of MRI (radiologists, engineers). Hence, collaboration between various fields is absolutely key in MRI research.

Before setting off for Taiwan, for months I focused on the technical gaps in my knowledge by iterative trouble-shooting and rote-learning through best practices. The sheer novelty of doing awake-rodent fMRI research became growingly apparent through the limited number of specific tools and research papers available (compared to human fMRI research). Thankfully, my collaborator Sun-Lin Han (a PhD student at Chang-Gung University) guided me through the technicalities of independent component analysis and dynamic causal modelling.

Not only was I working in a beautiful country, but also I made many friends in the lab, connections I am grateful for. Taiwanese people are friendly; I never once felt daunted, alone, or even hungry (the canteen was filled with delicious Taiwanese food). I would recommend anyone to visit or consider working in Taiwan or in any international institution when given the opportunity. The learning experience was rich, something that perhaps cannot be rivalled with any of my peers at the University of Edinburgh. This would be something I would do again without a moment's hesitation.

Cristiana Vagnoni
PhD student in Neuroscience,
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Interacting with Neural Circuits Summer School

The Cajal summer school 'Interacting with Neural Circuits' was held on 2–22 July 2017 at the Champalimaud Centre for the Unknown (Lisbon, Portugal), a state-of-the-art research facility named in 2012 the best place worldwide, outside the USA, to do postdoctoral work (1). This course is part of the Cajal Advanced Neuroscience Training Programme, a partnership between five leading neuroscience institutions (FENS, IBRO, the Gatsby Charitable Foundation, University of Bordeaux and the Champalimaud Foundation) to establish a core neuroscience training facility in Europe (2).

The course combined lectures with hands-on training in the latest techniques for investigating neural circuits, from viral tracing to all-optical circuit interrogation. Students were provided with enough practical experience to understand the advantages and disadvantages of each technique, to interpret experimental data correctly, and to apply their learning in their home laboratories. The first two weeks of the course were structured with morning lectures given by international leading experts of the field, including Winfried Denk, Mark Schnitzer, Kenneth Harris and Michael Häusser. Topics ranged from neuronal subtype identification and connectomics to *in vivo* circuit dissection and behavioural modelling. One lecture, by Rui Costa, focused on animal experimentation, with reflections about scientists' responsibility in conducting animal research and in communicating its utility to the general public.

Afternoons and evenings were dedicated to intensive hands-on training on viral neuronal tracing, *in vitro* and *in vivo* patch-clamp recording, high density *in vivo* extracellular recordings, fibre-optic fluorescence microendoscopy, *in vivo* calcium imaging, and all-optical circuit interrogation (3).

During the last week, students were divided into groups and worked on a mini-project to gain independent experience with these techniques. My project focused on the predictive features of the visual cortex, comparing juvenile and adult mice, using *in vivo* calcium imaging and extracellular recordings with Neuropixels probes.

Besides highlighting cutting-edge science, the course provided ample time to interact with course mates, teaching assistants, speakers and course organisers through many social events, including two poster sessions, a football match, a surfing trip and daily shared meals.

Whether you are a first-year PhD student or an experienced post-doc, I can definitely recommend 'Interacting with Neural Circuits' as an incredible opportunity for scientific growth and for establishing an international network of highly specialised researchers.

1. The Champalimaud Foundation History, available at w**ww.fchampalimaud.org/en/the-foundation/history/**
2. About the CAJAL Advanced Neuroscience Training Programme, available at **www.fens.org/Training/CAJAL-programme/About-the-CAJAL-programme/**
3. Interacting with Neural Circuits Website, available at **https://sites.google.com/site/interactingneuralcircuits/**

Hayley Earle
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Iron in the Parkinson's brain

Iron is essential for many metabolic processes such as DNA synthesis. While variations in iron concentration exist throughout development, a general increase occurs with age. This is particularly marked in the substantia nigra (SN) brain region, which is involved in Parkinson's disease (PD).

This age-dependent increase may be caused by an upregulation of the divalent metal transporter 1 (DMT1), a protein that transports ferrous ions (Fe^{2+}) into cells. Research by Saadat and colleagues suggested a link between a polymorphism of the *SLC11A2* gene (which encodes DMT1) and PD. Additionally, Song and colleagues determined that silencing of the iron transporter ferroportin 1 caused an elevation in intracellular iron levels, demonstrating its potential role.

Dopamine (DA) metabolism occurs via the monoamine oxidases (MAO-A and -B). In both aged and PD individuals, MAO-B is upregulated. Metabolism of DA through this enzyme leads to hydrogen peroxide (H_2O_2) production, which in turn can produce reactive oxygen species (ROS) through reversible Fenton and Haber-Weiss reactions. ROS are normally produced during aerobic respiration. Excessive production causes damage to proteins, lipids, DNA and RNA, and consequently induces cell death.

Ferroptosis is a novel iron-dependent form of regulated cell death that can be induced by depletion of glutathione. This can occur through the inhibition of a glutathione-dependent enzyme, GPX4, which under normal physiological circumstances limits the rate of iron-dependent lipid peroxidation in cells. Ferroptosis can be prevented using ferrostatin and iron chelators. However, applying such conclusions to PD requires caution – most of the research into ferroptosis has been conducted in cancer cells.

There is currently very little research into PD-associated ferroptosis. Do Van determined that erastin, a ferroptosis inducer, can provoke cell death characteristic of ferroptosis, and confirmed Dixon's findings that ferroptotic death is preventable by ferrostatin-1. In contrast to previous research, Do Van also reported GPX4 to be upregulated in PD, possibly due to the co-localisation of GPX4 with neuromelanin, an iron chelator found in high concentrations within the SN. The SN is rich in dopaminergic neurons and iron, which may render it particularly vulnerable to the degeneration observed in PD.

While evidence remains limited, the implication of ferroptosis as the mode of cell death in PD presents a novel research direction, through which we may discover novel preventative or curative measures against this debilitating disease.

A fully referenced version of this article can be found at **www.bna.org.uk/publications/bright-brains/bb-online/**

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Finding the cracks in the maps

An explorer attempting to map the masses of forest on our planet starts her quest through reconnaissance flights. From the air, she sees the dark colours of the European pine forests, the bright greens of the dense tropical forests, and the snowy boreal forests of the north. She might conclude that the forests are extremely uniform, perhaps made of one type of tree transitioning smoothly from one to another as a function of geographic location. In order to fully appreciate the diversity of the canopy underneath, she would have to descend into the forests below.

Like our explorer, neuroscientists have for decades investigated the topographic representations of the sensory world on the surface of the brain, and they have called these 'cortical maps'. Such maps include representations of sensory organs such as the skin, retina and cochlea, which render our conscious perception of the somatic, visual and auditory world, respectively. In auditory maps, the representation of sound frequencies is known to occur in an orderly or tonotopic fashion, from low to high frequencies. This gradient was previously thought to exhibit a precise and consistent shift in frequency representation along the cortical surface. Our mapping of the functional architecture of the auditory cortex recently challenged such a view by revealing a considerable degree of functional diversity at the micro-scale (1).

We investigated the functional organisation of the projections delivering sensory information to the auditory cortex through the characterisation of their anatomical distribution and the sensory information they carry. Up-close examination of small cortical patches revealed representations of almost all the sound frequencies that the brain can perceive. Returning to the explorer analogy, we must imagine the auditory cortical map as the span of global forests, from the tundra to the tropics. Our finding is therefore akin to discovering, within any patch of forest, pines growing next to palm trees growing next to cacti.

By revealing what information cortical neurons have access to, our work provides some clues about the function of cortical micro-circuits. Moreover, it demonstrates how much is still to be explored within the most mysterious of forests: the mammalian brain.

1. **Vásquez-López SA *et al.*** (2017) Thalamic input to auditory cortex is locally heterogeneous but globally tonotopic. *Elife*, 6: pii: e25141.

VARIETAS NUMQUID SCIEBAS...?

Tamsin Nicholson
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Bridging the Gap: Finding a place for neuroscience in the arts

The gap between the sciences and the arts has been expanding exponentially since the Renaissance. But why do we separate them? And what happens if we bring them together?

As specialising in one field became more and more respected, being multidisciplinary gradually lost its respect. Now people are often encouraged to choose between the sciences and arts at a very early age, even if they demonstrate equal ability in both. This system is inherently limiting, and has led to an emergence of people who defiantly identify as 'multipotentialites' (having multiple interests or specialisms). Unfortunately, society often required us to curtail our interests when choosing a career path, restricting people into more narrow fields. But this is a great loss to interdisciplinary individuals. There is limited dialogue between arts and sciences and at times we may even find an 'us-and-them' attitude. This leads to a lack of cross-disciplinary communication and an intellectual 'no-man's land' between the arts and sciences, where many great concepts and ideas lose momentum as they near the boundaries of their fields.

Our nervous system allows us to experience and engage with our environment, and from history to music, the arts are also interested in how we experience, engage and interpret with the world around us. Given the innate relevance of neuroscience to humanity, perhaps it could be a great place to start bridging the gap between the fields.

Imagine an architect designing a hospice: would it not be helpful for them to understand what may happen to the mind and the nervous system of the building's inhabitants? A deeper knowledge of neuroscience may enable greater sensitivity to the delicate needs of the patients, allowing the architect to create the optimum environment. Or what about an art historian, who wants to understand the real effect of propaganda? A better understanding of cognitive neuroscience could help them improve their ability to interpret and relay our social responses to art. Could knowledge of placebo effects – and their influences on cognition – help out a packaging designer responsible for over-the-counter pharmaceuticals? Perhaps it could give them an edge, or even improve results for patients?

The intersection between the arts and sciences is an area calling out for exploration. A revival of the importance of multidisciplinary thinking will provide us with an opportunity to improve our knowledge and ultimately our lives. Unfortunately, these areas are often neglected as we find ourselves pushed towards one or the other. It is time to explore these areas more, to bridge the gap and find a place for neuroscience in the arts.

VARIETAS QUID NOVI?

Adela Beloucif
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New Findings on Neurons and Brainwaves Associated with Fear Suppression After Extinction Learning

Fear and learning seem counterintuitive, but learning about danger or a threat is essential to the purpose of fear. Most human fear is learned through classical conditioning, whereby animals associate a cue with something inherently dangerous or unpleasant. They can learn something is not dangerous through repeated experience of that cue without trauma. This is termed extinction learning.

A recent study (1) investigated the potential neurons responsible for suppression of fear memories after extinction learning. The researchers used transgenic TetTag mice expressing inhibitory DREADD (designer receptors exclusively activated by designer drugs) receptor hM4Di, to allow control of basolateral amygdala (BLA) parvalbumin-expressing (PV) interneurons, through inhibition of cell activity by injection of DREADD ligand clozapine-N-oxide (CNO).

Mice were taught to fear a cage by receiving an electric shock, after which fear was extinguished by removal of the shock. Mice were then injected with CNO. Their fear response was measured as time spent frozen and immobile. Neuronal activity was measured through expression of ZIF protein and GFP. Freezing behaviour and activity of fear-associated neurons in the BLA increased after CNO injection.

The authors predicted PV interneuron control to be due to greater levels of innervation between PV interneurons and BLA fear-associated neurons, compared with extinction behaviour-associated neurons. However, the results of perisomatic analysis through use of the mCherry virus did not support this.

To determine which other processes may potentially be influenced by PV interneurons, more hM4Di-expressing mice were tested, and local field potentials (LFPs) measured using surgically implanted electrodes. LFP oscillations between 3 and 6 Hz were consistently linked with fear and freezing behaviour. As fear neurons were reactivated after CNO injection, the BLA LFP exhibited a shift from 6–12 Hz towards 3–6 Hz.

This research could inform the development of treatments for anxiety disorders such as post-traumatic stress disorder (PTSD). Greater understanding of how LFP oscillations compete and interact could allow a more targeted approach using neurofeedback training (2).

1. **Davis P *et al***. (2017) Cellular and oscillatory substrates of fear extinction learning. *Nat Neurosci* 20(11):1624–1633.
2. **Shalev A *et al***. (2017) Post-traumatic stress disorder. *NEJM* 376 (25):2459–2469.

PUZZLE

BNA Bright Brains Puzzle

How much conscious effort does your brain require to solve a puzzle? Find out by putting together the parts of the first BNA Bright Brains puzzle! This puzzle has a hidden message, which will be displayed once the puzzle is solved. The message will be revealed in the next edition. Answers to last edition's crossword are provided at the bottom of the page.

Enter this edition's competition by sending the message of the puzzle to **jayanthinykangatharan@gmail.com**. Entries received before 1 June 2018 will be entered into a prize draw to win a unique contribution towards the 'Bright Brains' summer edition!

Answers to the crossword from Issue 7 – Autumn 2017
Horizontal 3: Viola; 4: stapes; 8: haiku; 10: absolute pitch; 14: cochlea; 15: free verse.
Vertical 1: Holst; 2: timbre; 5: amygdala; 6: pitch; 7: parietal; 9: Beethoven; 11: Schubert; 12: USA: 13: colour; 16: eight.