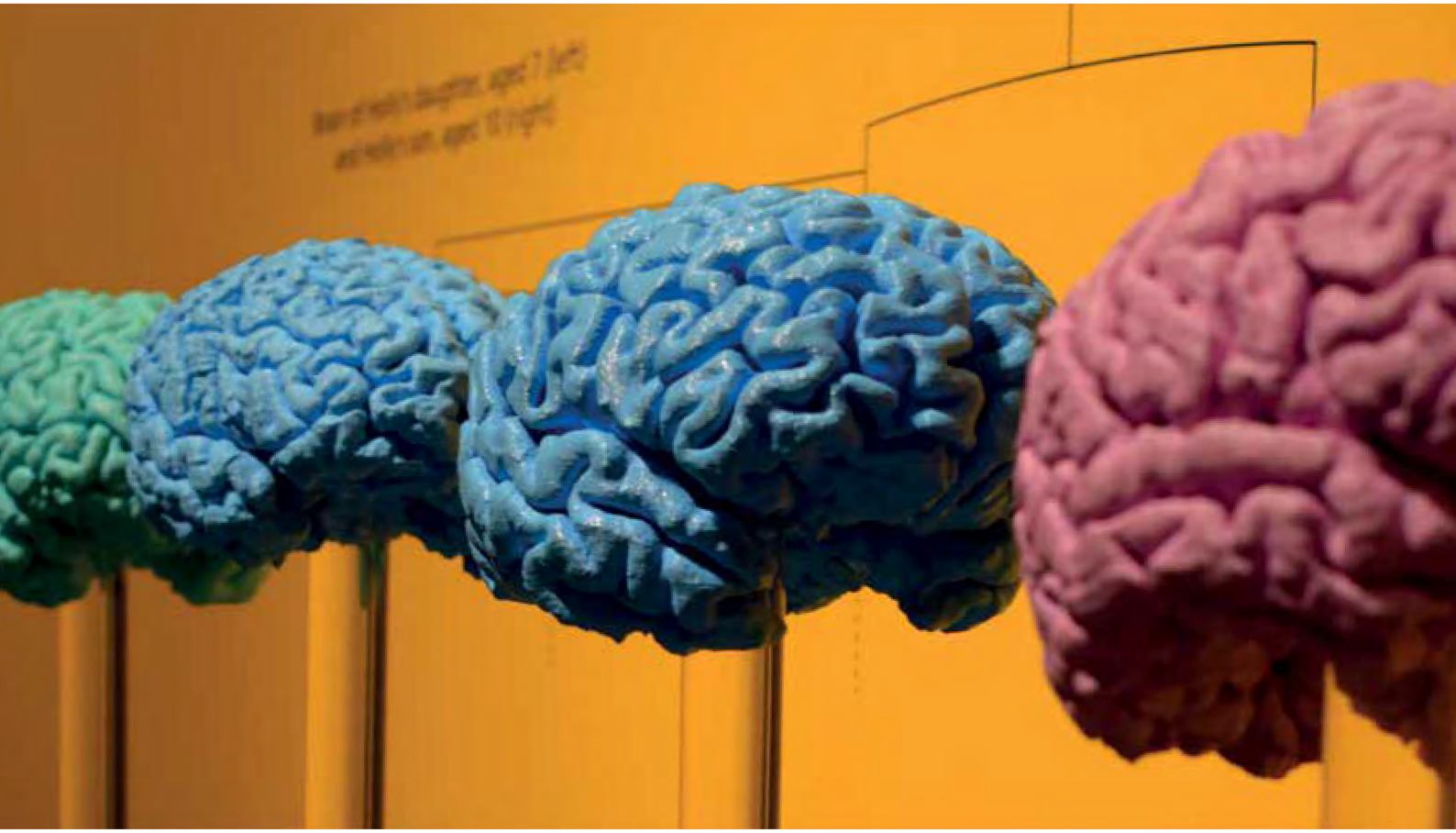
UNIVERSITY OF OXFORD

Department of Psychiatry



Annual Report 2018

Contents

Introduction

Now fully infrastructured with the Wellcome Centre for Integrative Neuroimaging, the NIHR Oxford Health Biomedical Research Centre and renewed NIHR Oxford cognitive health Clinical Research Facility, the next big challenge for the Department is to maximise research power by using Oxford's position as a global beacon of academic excellence. This provides us with an excellent opportunity to create productive collaborations with other centres of excellence – whether they be in UK, Europe or globally. Simon Lovestone, who was knighted in The Queen's Birthday Honours list 2017 for services to neuroscience research, provides an inspiring example of leadership for us.

The second key objective for the next few years is to increase our development of clinical and translational academics. Like many UK departments of academic psychiatry we have struggled with recruitment of clinical academics over the past few years although recruitment of non-clinical academics has remained strong. But the signs are that our success and growth are beginning to attract increasing numbers of young scientists - both clinical and non-clinical. Again, there is the obvious attraction of the unique and unequivocally world class scientific and broader academic Oxford environment. We need to ensure that we nurture the talent that comes to us, teaching and modelling the very highest scientific standards, and sharing our experience and wisdom on how to select the most productive and rewarding career trajectories. Developing the next generation of academics is essential for the sustainability of what we have achieved so far - and what we will achieve together in the next few years. Sustainability is one of the hardest challenges and this will need to be a core component of all our strategic planning.

Our training and development leads will play a central role in ensuring our sustainability. Jonathan Price will be leaving after many years of amazing leadership of our undergraduate programme (our thanks and see page 2) to be replaced by Kate Saunders who will also lead the postgraduate clinical programme. Susie Murphy leads our Athena Swan programme which is now preparing for the renewal application for our Silver Award in 2018. Phil Burnet and Jennifer Rendell lead our postgraduate programme and the development of the exciting new MSc in Clinical and Therapeutic Neurosciences and Liz Tunbridge is the training lead for the BRC. With such a stellar cast working together, I'm sure that we can expect great things and I know that all members of the Department will give them their full support.

Professor John Geddes
Head of Department

Clinical Medicine Undergraduate Course

It is with mixed feelings that I write this year's update for the Annual Report. After a full two decades in the Department, and almost 17 years as Clinical Tutor, I have decided to move on to 'new challenges'. This brings sadness, tinged with a little anxiety.

But it also brings excitement and anticipation, for two reasons. First, I am delighted that Dr Kate Saunders, an Oxford medical student (2000-2003), will be taking on the role of Director of Medical Studies. I am sure that she will bring talent, vigour and fresh new ideas to an undergraduate course that is already very strong and held in high regard not only in Oxford but across the UK.

Which brings me to the second reason. This Autumn, I was delighted to see the Royal College of Psychiatrists carefully collating data from the UK Foundation Programme Office, to determine a 'league table' of recruitment to specialty training in psychiatry, across English medical schools. Delighted because I knew the answer before they had even thought of the question, having been quietly collating these statistics for several years. And delighted to see Oxford confirmed as the (equal) top recruiter of the 24 English medical schools, and indeed clearly beating the 6 medical schools from Wales, Scotland and Northern Ireland.

So what's going on? Is this some flash in the pan? Surely we can't be crafting almost three times as many psychiatrists as Cambridge? Well, the data show considerable consistency over several years, and there is anecdotal evidence that, if anything, recruitment to psychiatry from among Oxford graduates is accelerating. There's something special going on around here, and I know that Kate is eager to curate and augment it, with the ongoing help of energetic colleagues in the University Department and of course, vitally, the local NHS.

So here are my tips for ongoing success, along with my thanks and best wishes to the many of you who have helped this Department's educational mission over the last two decades.

1 Psychiatry is where it's at. We are psychiatrists because psychiatry is important and really, really interesting. And challenging. If a student wants an interesting, important and challenging job, they should train to be a psychiatrist. The best way to deliver this message is implicitly, not explicitly.

2 Don't try to push a paperweight with a piece of string. Place students with enthusiasts for psychiatry who want to infect others with that enthusiasm.

3 Make teaching and learning exciting, at least some of the time. Don't just tell the students the boring but important stuff – they can (and will) learn that in their own time. Challenge and excite them.

4 Psychiatry is part of medicine. We are doctors. We do medical stuff. We do it well. Look, see?

5 Psychiatry is at the centre of the scientific revolution that is 21st century brain science. Look again.

6 Watch out for the low fliers, and make time to find out what's going wrong. You might be the only person who notices and takes the time to help. This can change lives.

7 And watch out for the high fliers. Set them free, for at least part of the week, to do something exciting, preferably in this Department. They are you in twenty years' time!

Jonathan Price

Graduate Studies

The Department currently has around 50 full-time research degree students including graduates in psychological and biological science and psychiatric trainees. The majority are DPhil students but each year we admit a smaller number of MSc[Res] students. We offer the opportunity to work in areas as diverse as molecular biology, behavioural research, epidemiology and ethics. Students have access to well-equipped laboratories, neuroimaging scanners, large existing datasets and clinical facilities and are able to collaborate with researchers in other departments such as Experimental Psychology, Neurosciences and Population Health.

Students are funded through competitive DPhil Studentships which are available from the Department and the Medical Sciences Division Graduate School every year. In addition to these, a number of PIs have new funding awards this year which allow them to advertise a studentship and, for the first time, we have joined with a college to offer a studentship.

Throughout their time in the Department students take full advantage of the opportunities for training and skills development offered by the Psychiatry Graduate Studies Committee (PGSC) and by the University. Each student is assigned a primary supervisor and a co-supervisor. Together with the PGSC, the supervisors provide both academic and personal support to help students transition through the stages of their research degree towards successful graduation and a future career. Feedback from students is crucial and highly valued by the PGSC which is continually looking to improve provision and quality of the students' graduate career.

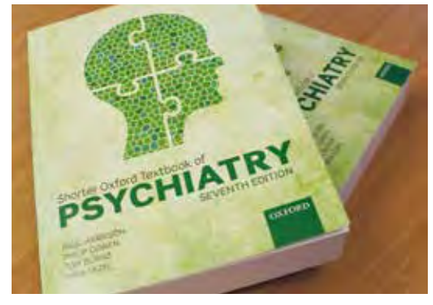
From October 2018 we have approval to admit students to part-time research degrees. Part of the motivation for requesting approval arose from concerns from students with caring responsibilities, clinical commitments and/or the need to work part-time. We believe that this will facilitate the admission of highly able students who are unable to commit to full-time study.

Jennifer Rendell

Maintaining Tradition of High-Quality Textbooks

The seventh edition of the popular Shorter Oxford Textbook of Psychiatry (formerly called the Oxford Textbook of Psychiatry) was published in October 2017 by Oxford University Press. As with all previous editions, it is written by senior members of the Department, on this occasion, Paul Harrison, Phil Cowen, Tom Burns, and Mina Fazel. Paul comments:

"I remember reading the first edition in 1983 when I was a medical student and being struck by its clarity, common-sense, and the focus on evidence. We have tried to retain these qualities in the latest edition, as well as introducing new features, including a new chapter on global mental health, and of course cover DSM-5 and the advances in the understanding and treatment of psychiatric disorders since the previous edition in 2012."



The New Oxford Textbook of Psychiatry, 3rd Edition, edited by John Geddes, Nancy Andreasen, and Guy Goodwin will be published in January 2019.

Paul Harrison

Post-Graduate Medical Training

The Department of Psychiatry offers opportunities for research training in its core areas of neurobiology, psychological treatments, developmental psychiatry and social psychiatry. We host the NIHR Oxford Health Biomedical Research Centre, Oxford Mindfulness Centre and the newly expanded Oxford Centre for Human Brain Activity. We are also delighted to have the Wellcome DPhil (PhD) scheme for clinicians in Oxford, dedicated to mental health.

Our research is an important component of the University's strategy for neuroscience and the themes of the neurobiology and psychological treatments programmes have an important translational component. We also encourage applications involving joint supervision with the University's Departments of Experimental Psychology, Clinical Neuroscience and Pharmacology, as well as the Wellcome Centre for Integrative Neuroimaging (WIN).

We provide the Oxford Postgraduate Psychiatry Course. The course provides a stimulating and thorough grounding in the basic and clinical sciences relevant to psychiatry and prepares candidates for the MRCPsych examinations.

Training in Academic Psychiatry

Projects for Academic Psychiatrists in Training are advertised on our website "Clinical DPhils, Clinical Training and Continuing Professional Development" (**www.psych.ox.ac.uk/study**). There are four levels of involvement:

1. Academic Foundation doctors will apply to the Academic Foundation Programme and arrange a four month academic placement with the Department.
2. Academic Clinical Fellows (ACF) are appointed by the Deanery/Oxford University Clinical Academic Graduate School, who organise transferable skills courses and the Master in Clinical Research Course. Competition is typically against other medical disciplines, although from time to time, NIHR advertises for specific specialty posts. The Academic Clinical Fellowship Programme offers training to new entrants to psychiatry who have outstanding potential for development as a clinical academic in psychiatry. We currently have seven ACF post (ST1-3) filled by trainees. Training is flexible, with suitable mentoring and supervision to ensure the attainment of both academic and clinical goals. The ACF posts provide the training necessary for an academic career, typically continuing with a Training - (PhD/DPhil) – Fellowship after national and interdisciplinary competition. Locally we host a DPhil (PhD) scheme for clinicians, dedicated to mental health, and funded by Wellcome.
3. DPhil and MSc by Research at Oxford are not taught courses, but start from the outset with expecting a high degree of independence from its graduate students. Research degrees, including the Master of Science (MSc) by Research, require a background in medicine, psychology or a biological science.
4. Academic Clinical Lecturers are required to have completed their core training and have submitted their doctoral thesis at the time of applying for this type of post. The posts are interviewed by the Oxford University Clinical Academic Graduate School and typically half-funded by the deanery and NIHR. Competition is typically against other neuro-disciplines, although from time to time, NIHR advertises for specific specialty post, and we have appointed two such Clinical Academic Lecturers in Old Age Psychiatry.

Kate Saunders

New Short Course

NIHR Oxford Health BRC Training Plans

The NIHR Oxford Health Biomedical Research Centre (BRC) Training Theme aims to equip researchers with the multidisciplinary skills and collaborations they will need to translate basic science findings into clinical benefit. We are developing a new short course – the Oxford Certificate in Experimental Medicine for Mental Health – that will provide researchers from different backgrounds with the basic information and skills needed to conduct experimental medicine studies in human volunteers.

This course, and the new Taught MSc in Clinical and Therapeutic Neuroscience, will be embedded in the Experimental Medicine Network, which will host seminars and informal networking events. The aim of this network is to bring together researchers from diverse backgrounds to allow them to learn from one another and share expertise. It will also provide opportunities for those new to the field to get involved in research. In addition to these core plans, we aim to work with those within the NIHR Oxford Health BRC to identify key training needs and will work to address these as we become established.

Liz Tunbridge

New MSc Course

Future: Taught MSc in Clinical and Therapeutic Neuroscience

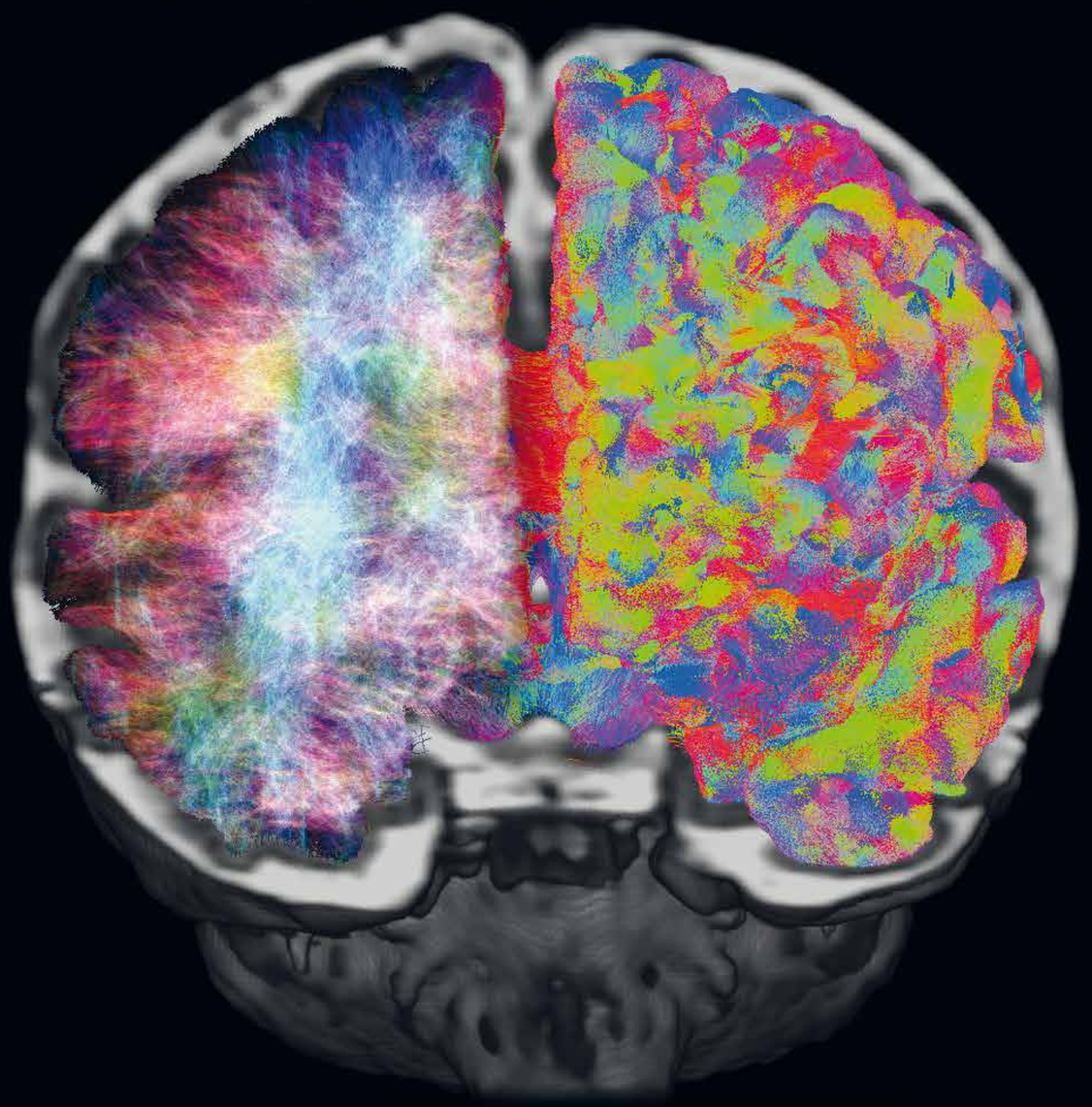
In recent years, Oxford has developed a unique constellation of expertise in target discovery and translational neuroscience, which makes it uniquely placed to address the need for new treatments for neuropsychiatric and neurological disorders.

Following approval from the University of Oxford, and on behalf of the Department of Psychiatry and colleagues within the Medical Sciences Division, we are developing a 1 year, postgraduate taught MSc in Clinical and Therapeutic Neuroscience, starting October 2019. The aim of the course is to provide graduate students with the knowledge and skills of advanced technologies, to conceptualise and run research projects that develop and test novel psychotropic and neurological agents. In their subsequent post-graduate careers, therefore, students will be suitably trained to engage in and expedite treatment discovery for brain disorders.

The course will bring together research groups within the Oxford Neuroscience community and beyond, that are engaged in drug development, in vitro modelling (e.g. stem cell technology), brain imaging, and psychiatric and neurological research. It will provide lectures, tutorials and research projects on the neurobiology/pathology of mental and neurological disorders, diagnostic and therapeutic strategies, state-of-the-art approaches to design/screen, develop and initially test new agents, clinical trials and digital health.

Phil Burnet

THE DEVELOPING BRAIN



'Diffusion Imaging of the neonatal brain' – The Developing Human Connectome Project. The image show an anatomical scan of a baby born at term overlaid with directionally resolved properties of the brain tissue and a visualisation of anatomical connections which were both derived from multi-shell high angular resolution diffusion data.

The MYRIAD Project

The Mindfulness and Resilience in Adolescence (MYRIAD) project is a Wellcome Strategic Award. It is based on the knowledge that adolescence is a vulnerable time for the onset of mental illness.

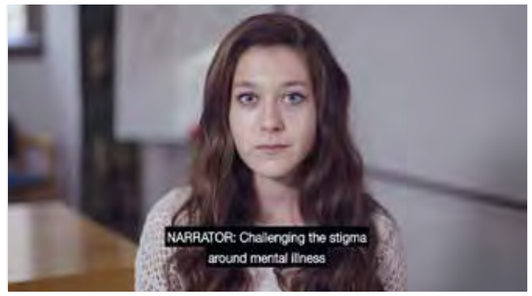
We are using the .b mindfulness in schools programme developed by the Mindfulness in Schools Project as a Mindfulness Training (MT) intervention. The .b programme is based on the 8-week MBCT course which is known to be effective in preventing depression and promoting mental health in adults, adapted to appeal to teenagers and work in a mainstream classroom setting.

University of Oxford Research Lead Dr Catherine Crane says, "The aim of the trial, which will produce preliminary results in 2021, is to provide robust evidence on whether or not the introduction of a mindfulness programme to schools produces measurable improvements in pupil mental health and wellbeing".

This evidence will be useful to schools considering whether or not to implement a mindfulness programme and wishing to make an evidence-based decision.

Willem Kuyken

BeGOOD



What constitutes 'good practice' in early intervention for mental health conditions such as autism and psychosis? What are the societal and ethical implications of early screening and predictive genetic testing for these mental health conditions and for dementia? What constitutes 'flourishing' from a young person's perspective, and how can mental health risk prediction and screening policies take these values into account?

Funded by Wellcome, NEUROSEC's project, Becoming Good: Early Intervention and Moral Development in Child Psychiatry (BeGOOD), critically examines early intervention as a political, scientific, and psychiatric means of shaping the moral development of children and young people, for the benefit of the individual, the family, and society more widely.

Involving young people as both participants and collaborators (see page 28), BeGOOD aims to achieve a systematic understanding of young people's moral experiences, attitudes, and challenges. Our goals include a set of innovative and scalable tools that will enable better ethics research into early intervention and treatments for young people facing mental health challenges.

Ilina Singh

Interventions for Refugee Children

We have worked with medical students to provide a health support service for newly arriving refugee families and have completed a large review of the literature on preventive mental health interventions for refugee children in high-income settings. In this review, we present preventive interventions as those that support parents and families as well as cultural supports including linguistic, school and community structures.

Conceptualising how young people perceive and access services has led to our researchers working closely with clinical colleagues to change services so that they are more accessible to young people. In particular, mental health workers are now providing a weekly InReach service to all local secondary schools and we are evaluating what impact this has on improving access to services and also how best to work to support school staff manage the emotional and behavioural difficulties presenting in the classroom.

Mina Fazel

The Amagugu Trial

Intervention for HIV positive mothers to communicate with their children about diagnosis

The Amagugu trial, funded by the NICHD/NIH, was a randomised controlled trial, with over 450 families, in which we tested a lay-counsellor guided intervention to help HIV positive mothers talk to their children about their diagnosis using a family approach. We found the intervention significantly increased maternal HIV disclosure to children aged six to 10 years, leading to important benefits including increased health engagement and health promotion with children, custody planning and improvements in the parent-child relationship.

Amagugu takes a skills building training approach to empowering parents and caregivers to deal with HIV through more direct communication about HIV in the family and with children. Lay counsellors provide mothers with six structured home-based counselling sessions which include training on child friendly activities using age appropriate language about health and HIV. Tools include games and storybooks and the counsellors help mothers to prepare for difficult questions children might ask. The intervention was flexible enough for mothers to adjust content to suit their personal circumstances, level of readiness and family needs. A key principle of Amagugu is that counsellors do not intervene directly with children; instead, following training mothers lead activities with their children. Amagugu has been developed in a 'train the trainer' model, with training materials, supervision schedules and videos already developed to ensure it can be delivered at a larger scale by community healthcare workers.

The principles derived from this trial, provide pointers to the way in which serious illness in families can be communicated successfully to children and enhance parent-child relationships. The principles are transferrable to a range of contexts, including in the UK, where families face serious illnesses which are difficult to talk about and where stigma is an issue. Thus the tools and games are adaptable to a range of community contexts including for families where a parent has a serious psychiatric illness.

Alan Stein

Neurodevelopmental Disorders

Mental health in Sub-Saharan Africa

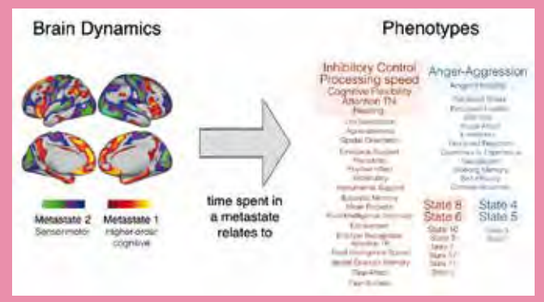
We are working on mental health, neurological and substance abuse (MNS) disorders in sub-Saharan Africa, particularly Kenya. We are particularly interested in supporting vulnerable populations, identifying MNS in different cultural contexts and developing early interventions that can be used in low-resource areas.

Our focus is on the following areas: the burden of MNS on the Kenyan health system, long-term outcome of neonatal insults and the burden of behavioural and emotional problems in young children. We have conducted epidemiological studies of neurodevelopmental disorders, in particular autism. We are piloting interventions such as the World Health Organisation (WHO) parent skills training programme to support families of children with neurodevelopmental disorders in the informal settlements of Nairobi. We are studying the effect of HIV on mental and physical health in adolescents, particularly examining the effect of executive function in making life decisions and its influence on risky behaviour.

The work on MNS and neurodevelopmental disorders is providing the basis of multi-site genetic studies of autism, psychosis and epilepsy in sub-Saharan Africa. We are also interested in cultural perceptions of neurodevelopmental disorders, in particular autism, and we are examining the tools used for the diagnosis in these areas.

Charles Newton

Nature vs Nurture



Co-ordinating brain activity across different regions

The brain needs to activate multiple brain networks in a temporally coordinated manner in order to perform cognitive tasks. We used imaging of the brain's spontaneous activity in twins to show that genetics plays a bigger role than environmental factors on the form of these brain networks, demonstrating the greater importance of nature over nurture in terms of how the brain coordinates its activity across different brain regions.

We then investigated the temporal dynamics of these brain networks to see how different networks switch on and off over time. We established that the switching is not random, with certain transitions being much more frequent than others. Intriguingly, we found that there was a tendency for the brain to either switch between networks associated with sensorimotor processing, or to switch between networks associated with more complex cognition, with only occasional switches between the two types.

As with the form of the brain networks, the pattern of dynamic switching was also found to be a heritable trait. However, we also found that the patterns of dynamic switching relate to the individual's psychology; with subjects that spend more time spontaneously activating cognitive networks exhibiting more positive psychological traits. We are now following up this work with investigations to see if this pattern of switching of dynamic brain networks can be used as a potential biomarker in psychiatric disorders including depression, bipolar disorder and Alzheimer's disease. There is also the possibility in the future for interventions to be designed, for example in the young developing brain, to encourage networks dynamics that are linked to more favourable psychological traits.

The right part of the figure shows that the average time spent in each metastate holds a relationship with many psychological phenotypes of the subjects. Also, they are inheritable and represent a strongly subject-specific fingerprint.

Mark Woolrich

Memory Guides Perception

Long-term Memory Guides Perception from First Stages

The fundamental role that our long-term memories play in guiding perception is increasingly recognised, but the functional and neural mechanisms are just beginning to be explored. Though experimental approaches are being developed to investigate the influence of long-term memories on perception, these remain mostly static and neglect their temporal and dynamic nature.

We have shown that our long-term memories can guide attention proactively and dynamically based on learned temporal associations. Across two experiments we found that detection and discrimination of targets appearing within previously learned contexts are enhanced when the timing of target appearance matches the learned temporal contingency.

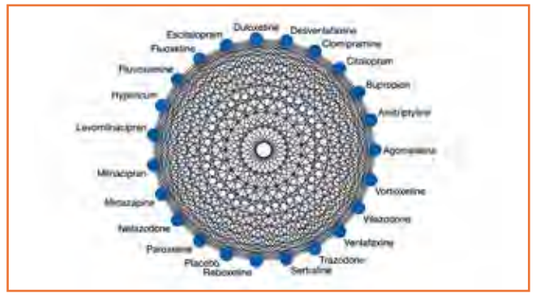
Neural markers of temporal preparation revealed that the learned temporal associations trigger specific temporal predictions. Our findings emphasize the ecological role that memories play in predicting and preparing perception of anticipated events, calling for revision of the usual conceptualisation of contextual associative memory as a reflective and retroactive function.

The findings open new lines of investigation into the mechanisms through which mnemonic temporal associations guide perception. A fuller understanding of human perception will require understanding of dynamic regulation by both top-down signals from long-term memories and short-term biases related to current goals and expectations.

Kia Nobre

MOOD DISORDERS

Optimising Evidence



While antidepressants are used worldwide to treat major depressive disorder, there is still a debate among scientific literature regarding their effectiveness and potential differences. Clinicians, patients and carers are confronted with a range of drug choices, and require sound evidence to make the best decisions for treatment.

To better inform practice and mental health policies, we conducted - with colleagues from UK, Europe, Switzerland, Japan and the US - the largest network meta-analysis ever carried out in medicine, using trial data from 1979 and 2016. These findings were published in The Lancet. The analysis involved 21 commonly-used antidepressants, examined in 522 double-blind randomised controlled trials. The final results represented data from 116,477 participants.

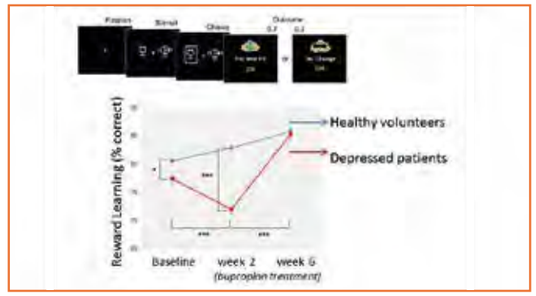
We found that of the 21 commonly used antidepressants for major depression among adults, all were found to be more efficacious than the placebo. However, there were small but important differences among them in terms of efficacy and acceptability. While certain drugs showed comparatively favourable balance in terms of overall response and dropout rate, others were less so.

Interestingly, the data from adults differed in children and adolescents where only fluoxetine was found to be significantly more effective than placebo. However the large uncertainty around this effect raises the question whether this estimate is robust enough to inform clinical practice. This contrast in efficacy across age groups may reflect the heterogeneous mechanisms and causes of depression.

We hope that this extensive study will improve overall mental healthcare for patients suffering from major depression, both in developed and low and middle income countries. Even though differences between common antidepressants are small, they are not negligible, and they are clinically significant and important enough that patients and physicians need to be informed in order to make the best choices in their treatments.

Andrea Cipriani

Industrial Collaboration



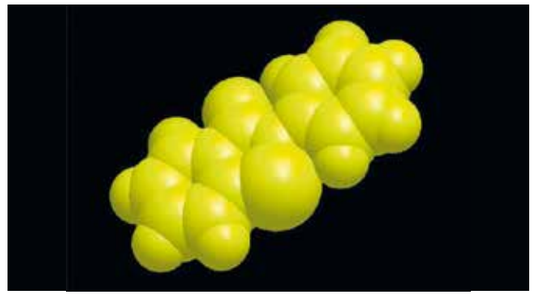
2017 marks the completion of a three year programme of work in partnership with Johnson and Johnson to validate experimental medicine models of reward in depression and antidepressant drug treatment. The overall aim was to develop better models which could be used for precision medicine approaches and preclinical screening of novel agents with a focus on anhedonia or loss of pleasure.

We tested the hypothesis that changes in reward processing would be important for therapeutic response to the dopamine and noradrenaline reuptake inhibitor bupropion and that these changes would be dissociable from the well characterised effects of antidepressants on negative affective bias. In line with this hypothesis, bupropion was found to reduce negative biases in emotional processing, specifically by reducing the likelihood that patients would misclassify an emotional facial expression as sad and the recall of negative affective memories. These effects were seen by 2 weeks and maintained after 6 weeks of treatment. By contrast, bupropion actually initially decreased reward learning at 2 weeks before its beneficial effect on reward learning at 6 weeks. The initial dip in reward processing predicted later non-response to bupropion.

The results from this collaborative study suggest that effects of treatment on negative bias and reward processing occur across different timescales. These effects could help to explain why anhedonia is so difficult to effectively treat and why it often resolves later than the other symptoms of depression. This approach could be used to screen novel treatments to target more effectively deficits in reward processing seen in depression as well as for the early prediction of patients unlikely to respond to current treatment.

Catherine Harmer

Drug Discovery: Ebselen



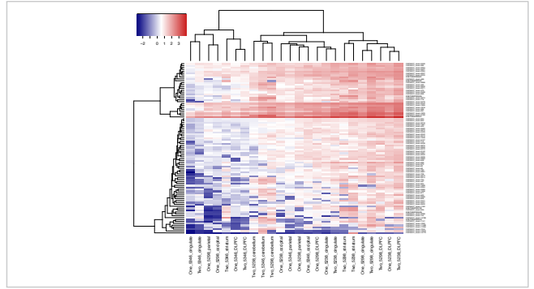
Lithium was discovered to be helpful in the treatment of bipolar disorder about 70 years ago, and is still the most effective mood stabilising drug available. Lithium is also useful in the treatment of severe depression and is the only psychotropic drug clearly demonstrated to decrease suicide rates - an important consideration in patients with mood disorders where suicide rates are much higher than in the general population. Unfortunately, despite these advantages lithium is not always well tolerated and can also have toxic effects on the kidney. A better tolerated alternative to lithium is therefore badly needed.

In collaboration with scientists in the Department of Pharmacology we have been developing an antioxidant drug called ebselen as a lithium replacement. Ebselen inhibits an enzyme called IMPase, which is thought to be a key target for the action of lithium. In addition, Dr Charles Masaki, a DPhil student in the Department, used magnetic resonance spectroscopy to show that ebselen lowers levels of a neurochemical called glutamate in the human brain. Glutamate is an important neurotransmitter implicated in the causation of depression and in experimental human models of mood disorder, Dr Masaki found that ebselen produced neuropsychological changes that predict antidepressant and mood stabilising actions.

Ebselen therefore has a unique pharmacological profile with effects that resemble lithium together with an additional action on glutamate. These exciting findings have prompted us to plan clinical trials of ebselen in patients with mood disorders. Currently, with the support of the Stanley Medical Research Institute and Sound Pharmaceuticals, we are conducting the first trial of ebselen in bipolar patients suffering from mania, where we aim to recruit sixty patients for a three-week, placebo-controlled trial.

Phil Cowen

Novel Therapeutic Targets



Recent advances in psychiatric genomics have the potential to revolutionise our understanding of the causes of mental illness, as well as to identify new treatment targets. The challenge is now to move from genomic loci to pathophysiological insights. The voltage-gated calcium channels (VGCCs) are arguably the most tractable targets to have emerged from these studies. However, surprisingly little is known about the function of VGCCs in human brain. Researchers in the Department are addressing some of these unknowns using convergent approaches.

Funded by a recently-awarded MRC grant, we are characterising the profile of VGCC isoforms present in the human brain, and are identifying those of greatest relevance for psychiatric illnesses. They have already discovered the existence of a vast number of novel VGCC isoforms in human brain, and are in the early stages of understanding the functional implications of this diversity.

Paul Harrison and his collaborators are approaching this question from a different angle, by investigating the effect of an existing VGCC blocker on brain function in the OxCaMs study. This study is looking at the impact of the VGCC blocker nicardipine on a range of measures relevant to psychiatry, including mood, neuroimaging parameters and peripheral markers of calcium signalling.

The hope is that these research streams will ultimately converge, with the molecular data providing information about the VGCC isoforms most relevant to psychiatry, and the OxCaMs study demonstrating the likely brain impact of targeting such channels. As well as advancing the therapeutic potential of VGCCs in psychiatry, these studies also provide an example of the experimental approaches required to move from genomic region to pathophysiological insights and novel treatments for psychiatric illness.

Liz Tunbridge

DEMENTIA AND COGNITIVE HEALTH

Neuronal differentiation from human induced Pluripotent Stem Cells (iPSCs). The whole cell population is shown in blue (nuclear staining), whereas neuronal progenitor cell subpopulation is characterised by yellow speckles in the nuclei or yellow nuclei (Ki67 staining, a marker of cellular proliferation), and the cellular body of non-proliferative, differentiated neurons can be seen in red (MAP2 staining, a marker of neuronal cytoskeleton). Adrià Dangla Valls / Noel Buckley.

Dementias Platform UK

We bring together rich data from diverse cohort studies in a secure, free-to-access resource for researchers – the DPUK Data Portal

DPUK – a public-private partnership project led from the Department of Psychiatry, Oxford – is designed to make doing good science easier. We are setting up core infrastructure which facilitates dementia-focused experimental medicine (EM) in a number of ways: rapid access to longitudinal data via our data portal, recruitment from the portal to highly-targeted studies through a clinical studies register, and the ability to conduct multicentre studies using our Imaging, Stem Cells and Informatics networks. Over this year we have populated the Data Portal with data for over 560,000 individuals and look forward to adding a further 1.5m individuals during the next 12 months.

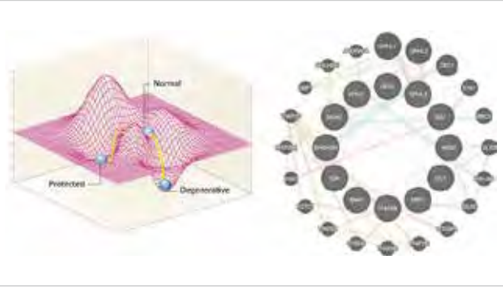
DPUK is an enabling infrastructure. The potential of DPUK will be realised through researchers exploiting our infrastructure to prepare competitive grant proposals and in developing our relationships with industry. Over the last year six awards totalling £12m have been won by DPUK research teams.

The security, convenience and cost-effectiveness of a central repository for cohort data is attractive to many research groups, particularly as the size and complexity of their datasets grows. The DPUK model of 'bringing researchers to data' is proving increasingly popular, with cohorts from the Republic of Ireland, France, South Korea and China joining the collaboration.

For the remainder of the project we look forward to conducting our first multicentre studies, further supporting the development of science communities, and further expanding the envelope of dementia funding for distributed research.

John Gallacher

Neuroprotective Targets



Discovering Neuroprotective Targets

Attempts to identify therapeutic targets to combat neurodegenerative diseases such as Alzheimer's Disease have largely and unsuccessfully- focussed on unravelling the underlying neurodegenerative process and then to subsequently identify targets that can halt or slow the degeneration.

We have discovered an alternative strategy founded on shifting neurons to an alternate neuroprotective state that is refractory to neurodegenerative insults. This strategy is based on our observations that deletion of the Alzheimer's Disease (AD) risk gene, clusterin, confers resistance to ß-amyloid toxicity, most recently with Simon Lovestone's demonstration that CRISPR/CAS9 silencing of CLU in human iPSC neurons confers neuroprotection.

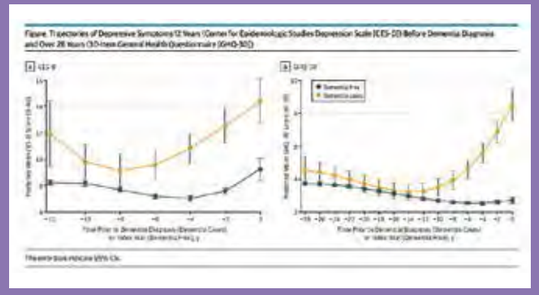
This transition of CLU-/- neurons to an alternate neuroprotective state is accompanied by the activation of >12 key transcription factors (TF) nearly all of which are associated with one of the most fundamental biological transitions in metazoa epithelial to mesenchymal transition (EMT). EMT is a reversible cell state transition prevalent in development, regeneration and pathological stress that is frequently accompanied by elevated resistance to apoptosis.

We are now using gene editing to (i) identify which TFs are sufficient to confer neuroprotection (ii) engineer those TFs to develop screens to identify novel therapeutic compounds that can drive the transition to a neuroprotective state and confer resistance to neurodegeneration.

We believe that this provides a novel therapeutic discovery pipeline and one that we are in a position to exploit using our partnerships with Oxford ODDI, TDI and OxStem.

Noel Buckley

Pre-Dementia Depression



Trajectories of Depressive Symptoms before Diagnosis of Dementia - A 28-Year Follow-up Study

Depression has been listed amongst the risk factors for dementia in later life. There are even animal models and observations in humans that suggest chronic stress in depression is associated with hippocampal atrophy, i.e. shrinkage of the brain structure primarily associated with memory impairment in Alzheimer's dementia. Such a connection would predict a dose effect: the longer lasting the depression, the greater the risk of dementia.

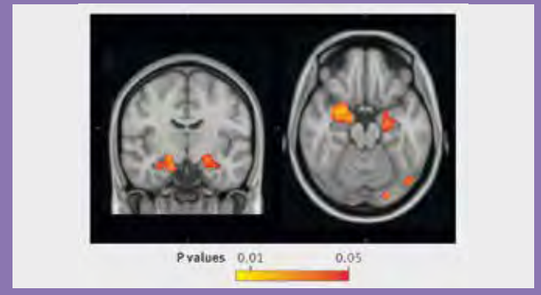
The 30-year old Whitehall II study that started with over 10,000 participants in 1985, and involves regular follow-up with assessment every 5 years, provides an opportunity to test this hypothesis.

By splitting the sample into participants with dementia and those without, depressive symptoms over the previous 28 years can be compared (Figure ©JAMA Psychiatry). The two graphs start separating at 11 years ($p = 0.02$) before dementia diagnosis and depressive symptoms become more than 9 times greater in the year of diagnosis ($p < 0.001$). This fits better with the assumption that depression before dementia is a precursor or early symptom of the dementing process, and that midlife depression is of no particular relevance to future dementia. It also fits the observation from many smaller case-control studies that show greater and wide-spread brain abnormalities and cognitive impairment in late-onset, as compared with early-onset depression, despite much longer illness duration in the latter.

The division of depression into early onset with maybe hippocampal atrophy and late-onset depression with wide-spread grey and white matter changes may also explain the greater risk of relapse in the latter, if treatment is withdrawn: the underlying brain vulnerability persists or may even get greater and increases the risk of relapse.

Klaus Ebmeier

Moderate Alcohol Harms



Moderate alcohol consumption and harmful associations with brain structure and function

The Whitehall II cohort, with its rich longitudinal data is a perfect group to investigate whether moderate alcohol consumption is protective or harmful to brain health and cognition. In a paper published in BMJ in June 2017 we examined whether self-reported alcohol consumption over a 30-year period was associated with brain imaging and memory decline in a group of 550 individuals.

We found no evidence for a protective effect of light-moderate drinking over abstinence on brain health and cognition. On the contrary, we found evidence of harmful associations. Specifically:

- People who drank more over the 30 years had smaller hippocampi (a part of the brain important for memory, and one of the first affected regions in Alzheimer's disease) compared to those who did not drink. Individuals who drank more had poorer quality white matter tracts ('cabled wiring' in the brain).
- People drinking more than 7 units of alcohol per week (approximately 3 glasses of wine) experienced a faster decline in language fluency over the study compared to those not drinking.

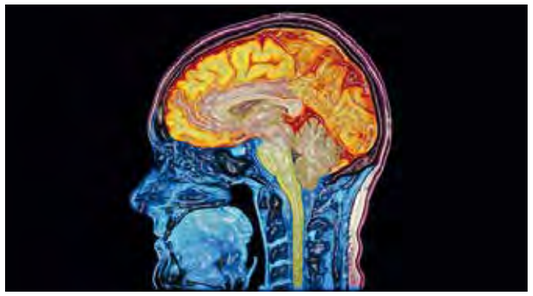
Although these results are striking, it is important to remember they are from one study on a specific group and will need replication. Robust evidence of a link between moderate drinking and adverse brain outcomes would have serious public health implications, and raise a question mark over the safety of current alcohol guidelines internationally.

Anya Topiwala

IMMUNOTHERAPY

Images p16-18: Wellcome images, kindly sourced by Biodep

The Immune System



For many years it was thought that the brain was impervious to immune influences. There is now a large body of evidence demonstrating reciprocal interactions in both health and disease via multiple mechanisms. This has potentially important therapeutic implications for psychiatry.

Immunotherapy includes: long-established and fairly non-specific treatments such as corticosteroids and non-steroidal anti-inflammatories, those more focused on humoral mechanisms such as plasma exchange or intravenous immunoglobulin, and newer monoclonal antibodies specifically targeted against cell-surface or secreted immune molecules.

Monoclonal antibodies in particular have transformed many areas of medicine. Notable examples include: anti-TNF and other cytokine-directed therapies markedly modifying rheumatologic disease, and immune checkpoint inhibitors to upregulate T-cell directed immunity improving outcomes in cancers like melanoma.

Application of immunotherapy in these fields has grown from an understanding of basic disease mechanisms. This is clearly more complicated in heterogenous psychiatric syndromes, but not impossible. The most striking example of translation to clinical neuroscience comes from autoimmune encephalitis. These are brain disorders caused by antibodies against neuronal-surface signalling molecules such as NMDA, GABA, and AMPA receptors. As predicted by knowledge of these targets' physiology and pharmacology these diseases cause striking psychiatric morbidity as a presenting, and occasionally sole feature. Just as striking is their potential reversibility with antibody-modifying, or increasingly antibody-secreting cell-directed therapies.

Inspired by this, Belinda Lennox and colleagues were the first to describe similar antibodies in peripheral blood of some patients with first episode psychosis. She is now carefully assessing the role of immunotherapy in this sub-group with the SINAPPS2 randomised controlled trial. Indeed, balance between benefit and risk must be borne in mind, and stratification starting with plausible and validated disease mechanisms should anchor translational interest. With this in mind Oxford is also participating in the BIODEP study, a multicentre approach to characterise the immune phenotype in depression.

The brain and the immune system remain two vastly complex systems and understanding their interaction in the most complex human illnesses will be challenging. Nonetheless, this field is inspiring young doctors and scientists to enter psychiatry. Perhaps Oxford psychiatry's best asset lies in contextualising and integrating vast local and international experience in basic immunology and neuroscience to guide the 'who, when, and why' of neuropsychiatric immunotherapeutics. From molecule to mind – maybe.

Adam Al-Diwani

BIOdep

The Wellcome Consortium for Neuroimmunology of Mood Disorders and Alzheimer's Disease (NIMA) led by Cambridge (CI Professor Ed Bullmore) brings together seven leading UK academic centres and four multinational pharma companies (Janssen, Lundbeck, GSK, Pfizer) to work collaboratively and pre-competitively on the neuro-immunology of mood disorders and Alzheimer's disease - **www.neuroimmunology.org.uk**.

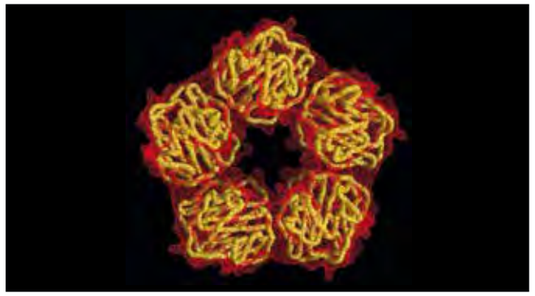
Oxford is a site for the clinical major depressive disorder study, BIOdep, 'A clinical biomarker study of immunological phenotypes associated with monoaminergic anti-depressant response, and the brain and cognitive phenotypes associated with variation in peripheral C-reactive protein (CRP) levels, in patients with major depressive disorder (MDD)' is designed to identify peripheral and central markers of neuroinflammation in depression. NIMA is a fully translational programme with Part 1 concerning preclinical animal models for proof of concept and the identification of a large clinical cohort both of which will inform Part 2, an experimental medicine study using a neuroinflammation agent from one of the commercial partners.

The University of Oxford with NHS partner, the NIHR cognitive health Clinical Research Facility, has successfully recruited to the clinical cohort (ongoing) which is in two stages. Across the sites, the first stage was recruited (N=252, per protocol) to target. All participants completed clinical assessments and provided venous blood for analysis of cytokines and C-reactive protein, transcriptional expression of candidate genes and whole genome, cytometry, and cell functional assays in vitro. Analysis of these primary cohort data is ongoing. In the second stage of BIODEP (recruitment ongoing), about 50% of the planned secondary cohort (N=135) has been recruited , which will comprise MDD patients with CRP < 3 mg/L MDD patients with CRP > 3 mg/L, and healthy controls. All participants in the secondary cohort will complete MRI assessments of brain structure and function and provide a venous blood sample for immuno-phenotyping. Participants providing additional consent will also be assessed using [11C]-PK11195 PET and lumbar puncture for CSF sampling.

Preliminary analysis of data from Part 1 has generated new evidence for the prior hypothesis that treatment resistant depression is associated with peripheral inflammation and has identified candidate peripheral biomarkers which will inform the choice of immune markers and imaging endpoints for the proposed phase 2 study in NIMA Part2.

Mary Jane Attenburrow

Antibodies in Psychosis



New treatment hope for people experiencing psychosis

The study – 'Prevalence and clinical characteristics of serum neuronal cell surface antibodies in first episode psychosis' - published in The Lancet Psychiatry, reveals that certain kinds of antibodies appear in the blood of a significant percentage of people presenting with a first episode of psychosis. These antibodies, including those against the 'NMDA receptor', have previously been shown to cause encephalitis, a life threatening inflammation of the brain. This study now shows for the first time, that these same antibodies are also found in people with early presentations of schizophrenia. We have shown that 8.8% of 228 people with a first episode of psychosis have an antibody in their blood that may be responsible for their illness. The only way to detect these antibodies is through doing a blood test, as patients with antibodies do not have different symptoms from other people with psychosis.

The discovery offers fresh hope in terms of new treatment possibilities for people experiencing psychosis. This is because the rapid identification and removal of the same antibodies associated with encephalitis leads to a dramatic improvement, and often complete a cure from the illness. Professor Lennox and her team have successfully treated a number of patients experiencing psychosis, who have these antibodies, using this same form of immunotherapy, with patients often making a dramatic improvement from their psychosis. Our thinking is that what initially appears to be a psychiatric illness is caused by an immune malfunction requiring a completely different kind of treatment. This discovery therefore has the potential to lead to a seismic shift in our understanding of mental illness and open up a new field of medical investigation.

We are now undertaking a randomised clinical trial of immune treatments in patients with psychosis and antibodies. The SINAPPS2 study is recruiting 80 patients across England and giving infusions of intravenous immunoglobulins and rituximab or placebo to patients over a month, alongside their routine psychiatric treatments. The primary outcome measure is remission of psychosis. The trial is therefore bold in its design – we are not aiming to improve symptoms, as in all previous treatment trials in psychosis, we are instead aiming to treat the cause of the disorder and provide a cure.

If successful, the implications for the care of people with psychosis are profound. The investigations and treatments required would be the same as those required for other brain disorders, in neurological treatment centres, rather than community based mental health services.

Belinda Lennox

IMAGING AND COMPUTATIONAL PSYCHIATRY

Images p19 & 20: John Cairns

Oxford Neuroimaging – the stars align

2017 was a big year for neuroimaging in Oxford as we became the new Wellcome Centre for Integrative Neuroimaging (WIN; **www.win.ox.ac.uk**). WIN is directed by Heidi Johansen Berg, and brings together the Centre for Functional MRI of the Brain (FMRIB), the Oxford Centre for Human Brain Activity (OHBA) and preclinical imaging facilities in the Department of Experimental Psychology.

WIN provides core infrastructure to support research across 5 themes:

Cross-species neuroimaging: By recording comparable signals associated with comparable behaviours across species we aim to address causal and mechanistic questions in animal models and translate these findings directly to humans.

Cross-scale neuroimaging: To better understand the brain and tackle brain diseases requires us to integrate between different scales of investigation. Researchers in the Centre will be developing detailed biophysical models to relate imaging data to cellular and synaptic computations.

Population data mining: In this theme, we will exploit population data mining techniques to identify patterns in large neuroimaging datasets and identify brain phenotypes that are relevant for human health.

Clinical Translation: Combining our experience across a range of neurological and neuropsychiatric disorders, with our integrative imaging approaches, will transform our ability to define relevant clinical markers through both forward and backward translation.

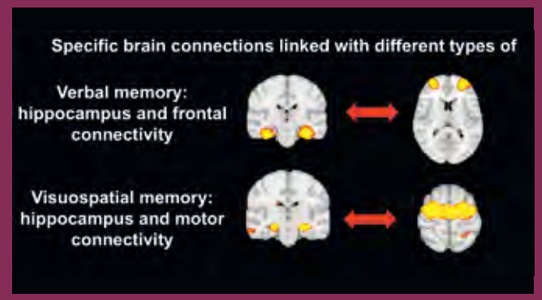
Open Neuroimaging: Open science improves scientific robustness, facilitates discovery and accelerates the translation of methods and results to the clinic. All members of the WIN management board are committed to sharing their data, tools, tasks and protocols openly by the end of the 5 year project, and all Centre members are encouraged to do so.

The Department of Psychiatry houses OHBA and four of the WIN 'Group Leaders' (Paul Harrison, Mark Woolrich, Kia Nobre and Clare Mackay), and is thus a major partner of WIN. As well as being WIN group leaders, Clare, Paul and Kia are also Theme Leaders in the NIHR Oxford Health Biomedical Research Centre. This cements the close relationship between the Department, the BRC and the WIN. In particular, theme 4 of the WIN (Clinical Translation) and the BRC Neuroimaging and Cognitive Neuroscience BRC theme (led by Kia Nobre) share the ambition to translate WIN-developed neuroimaging methodology into clinically useful tools, including the development of a standardised 'brain health assessment'.

The WIN was launched with an amazing week (30th Oct-3rd Nov) that included scientific discussion with the external advisory board, a symposium of early career researcher talks, an evening of fun and games at the Museum of Natural History, and a public engagement extravaganza (also at the Museum). A highlight was '21st Century Phrenology'; a play that was written, performed and directed by WIN members (see page 31).

Clare Mackay

Resting State Connectome



Distinct resting-state functional connections associated with episodic and visuospatial memory in older adults

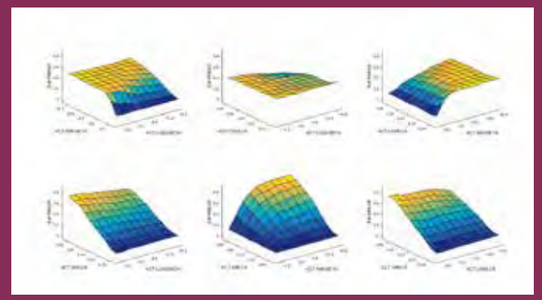
Episodic and spatial memory are commonly impaired in ageing and Alzheimer's disease. Brain imaging studies have shown that the resting brain is organised into large networks, made up of several interacting regions that are functionally connected. Here we used advanced network modeling methods to study how the individual connections of these larger brain networks were related to memory in 497 older adults (60-85 years old) from the Whitehall II Imaging sub-study.

First, we split the brain into 58 key regions and mapped all their connections to each other, creating a macroscopic 'functional connectome' of the resting brain. This connectome was organised into five large networks reflecting auditory, somatosensory, motor and visual activity, as well as higher cognitive processes like memory, introspection and executive function.

We then identified the unique connections within this connectome that were associated with performance on tests of verbal episodic memory and visuospatial ability. We found that both types of memory had a shared dependence on a structure called the hippocampus, which is one of the first brain regions to be compromised in Alzheimer's disease. Interestingly, while verbal memory was associated with interactions between the hippocampus and frontal brain areas, visuospatial memory engaged connections between the hippocampus and motor regions. Visuospatial memory was also linked with motor-parietal interactions. These findings provide new insights into brain-behaviour relationships and suggest that while the hippocampus may be central to both types of memory, the functional connections of the hippocampus with other brain structures vary depending on the memory demand. Studying how the strength of these specific connections change as we get older may help us understand the neural underpinnings of episodic and spatial memory decline.

Sana Suri

Computational Psychiatry



Depression is a common mental health disorder and an important public health concern. Established theories of depression suggest that negative bias, a tendency to be more influenced by negative events in our thinking and decision making, can cause people to develop symptoms of the illness. This suggests that if we find a way to take out negative biases from the equation, depressed mood should improve.

The work of the computational psychiatry laboratory is focussed on understanding why some people develop negative biases, by understanding what kind of situations would actually warrant developing the negative biases in the first place. To do so, we develop novel experimental tasks in which people need to learn when positive and negative events (winning and losing money) will occur.

We then design a "computer model" (a simple program) which is able to play the same task and modify the parameters of this model (the parameters are like control knobs which change how the model makes decisions) until its choices closely matches the decisions made by a participant. When we get the model behaving like a particular participant we can look inside the model to work out what calculations are happening in the participant's mind when they make decisions. It is very difficult to understand these calculations if you don't use some sort of model.

Using this method we can compare the parameters used by individuals with depression with those from people who are not depressed to understand the "computational" processes underlying why people might develop the negative biases which lead to depression. We can also use this approach to better understand the role of the brain networks and neurotransmitters which are involved in developing biases. Understanding these processes is essential in the development of new psychological and pharmacological treatments for depression. For example, in an ongoing study we are testing whether a new online intervention, based on these computational models, will help to reduce symptoms in depressed patients.

Michael Browning

DIGITAL INNOVATION

Still from nowican VR treatment programme

Treating Psychosis with VR

Our group – Oxford Cognitive Approaches to Psychosis (O-CAP) have been pioneering the development of state-of-the-art immersive virtual reality (VR) for patients with psychosis. VR treatment is especially suited to this patient group. Patients with severe fears are willing to try simulations of the situations they find very difficult, and the learning transfers to the real world. Importantly, our new treatment work includes a virtual coach to teach patients to deal with their fears. A trained therapist is not needed. The result is a treatment that is potent, low cost, and offers immense potential for scalability. VR could help transform NHS services for patients with severe mental health problems. In the past year, we have reported on our first treatment outcome study that showed large benefits for patients with severe paranoia and started a new Medical Research Council (MRC) grant to take the work forward. We have also launched Nowican (www.nowican.com), a University of Oxford startup, which aims to become the world-leading company in the development of VR treatments for mental health.

Daniel Freeman

Scalable and Valid tool to Assess Violence Risk

Current approaches to stratify psychiatric patients on the basis of violence risk are limited by inconsistency, variable accuracy, and unscalability. To address the need for a scalable and valid tool to assess violence risk in patients with schizophrenia spectrum or bipolar disorder, we developed a prediction score based on routinely collected factors, and tested its external validation in over 16,000 patients. The model showed good measures of discrimination (c-index 0·89) and calibration. It was particularly accurate at screening out low risk individuals. We used the model to generate a simple web-based risk calculator (Oxford Mental Illness and Violence tool [OxMIV]). Such a tool can be used as an adjunct to decision making in clinical practice by identifying those who are at low risk of violent offending. In those identified at high risk, further clinical assessment is required to establish who might benefit from additional risk management.

Seena Fazel

Digital Revolution in Phenotyping and Managing Mental Health Disorders

The World Health Organisation (WHO) stated that mobile technologies have "potential to transform the face of health service delivery across the globe". Mobile technologies and wearable devices provide access to high frequency, prospective data about mental health disorders. This method of data capture combined with the expansion in machine learning technologies present the possibility of not only minimising the inherent bias of retrospective descriptions of pathology, but the chance to identify proxy markers for emergent crises, run efficient treatment trials, and deliver individualised healthcare in a more responsive way.

True Colours is an online platform for the collection of prospective mood data which was developed in the department 10 years ago. It has been a powerful component of clinical trials for example the MRC/NIHR-funded CEQUEL trial of lamotrigdine. This prospective mood data has been augmented by behavioural (e.g., activity,) and environmental (e.g., daily stress, contextual threat) data collected remotely using sensors and data from smartphones, including accelerometers, specific 'apps', and behavioural data (e.g. keystroke errors, time an app is used). This approach of deep and frequent digital phenotyping has become central to a range of studies conducted in the department. We have already demonstrated that geolocation parameters correlate well with mood states in people with bipolar disorder and can be used to predict future mood. In individuals with borderline personality disorder we have uncovered a specific misalignment in the regularity of sleep, activity and heart rate which represents a new objective treatment target in this disorder. Digital approaches are also allowing us to better characterise how drugs like lithium or nicardipine work enabling a more efficient approach to new drug development.

Most importantly the use of technology in mental healthcare empowers patients to become more actively involved in the management of their condition by enhancing insight and enabling a more individualised approach to the treatment of mental disorders.

Kate Saunders

Online CBT for insomnia

Treating insomnia with online CBT was found to reduce anxiety, depression, and paranoia, according to a large randomised controlled trial published in The Lancet Psychiatry.

Researchers at this department and the Sleep and Circadian Neuroscience Institute, University of Oxford, aimed to improve sleep in young adults (university students) with an average age of 25, in order to determine the effect on mental health problems such as paranoia (excessive mistrust), anxiety, and depression. 3,755 university students across the UK were randomised into two groups. One group received online cognitive behaviour therapy (CBT) for insomnia; the other group did not but had access to standard treatments.

It is thought to be the largest ever randomised controlled trial of a psychological treatment for mental health and the first study large enough to determine the effects of treating insomnia on psychotic experiences.

The cognitive-behavioural therapy was delivered through an online programme and provided in six sessions, lasting an average of 20 minutes each, presented by an animated sleep expert. The sessions included behavioural, cognitive and educational components, such as learning to associate bed with sleep, encouraging people to put time aside to reflect on their day before going to bed, and facilitating a pro-sleep environment. The programme was interactive, with participants' daily sleep diaries used to tailor the advice.

Individuals who received the CBT sleep treatment showed large reductions in insomnia, as well as small, sustained reductions in paranoia and hallucinatory experiences. The treatment also led to improvements in depression, anxiety, nightmares, psychological well-being, and daytime work and home functioning.

Bryony Sheaves

Oxehealth

Digital innovation of inpatient mental health care

Being admitted to a mental health hospital can be a daunting experience, but it does not need be. In fact, there is an urgent need to transform the way inpatient mental health care is delivered and digital technology can help to bring about that change.

Our department, in partnership with Oxford Health NHS Foundation Trust and Oxehealth, a spin out from the University of Oxford's Institute of Biomedical Engineering, are introducing a novel digital monitoring system aimed at changing the way in which therapeutic nursing observations are carried out. This is being piloted on Vaughan Thomas Ward, Warneford Hospital. The digital system uses information obtained by cameras to produce anonymised information about patients' behaviour on their bedrooms as well as breathing rate and pulse.

The novel digital technology has the potential to improve the quality of patients' sleep, hastening recovery, and shortening length of admission whilst releasing time for staff to focus on therapeutic engagement, all without compromising patients' safety.

Alvaro Barrera

Biodesign Project

Digital health technologies offer the potential to transform healthcare by making it more convenient for patients to access, cost-effective and efficient for providers to deliver. Yet there are significant barriers to the adoption of such technologies, including a lack of evidence of their impact on cost and outcomes, and a lack of collaboration between clinicians and technologists in product development.

As part of the Oxford Biodesign Healthcare Innovations program, we approach problem-finding in a systematic and deliberate way prior to developing engineering based solutions. We are currently observing clinical teams in the Warneford hospital, looking at unmet clinical needs. The aim is to produce a medical technology innovation to improve mental health care or services. Our team includes two PhD engineer/physicist from Oxford University and a clinician.

Maarten De Vos

CLINICAL IMPACT

Early Intervention in Psychosis services

Early Intervention in Psychosis services (EIPS) are community services that have been introduced across England over the last 15 years, and are now the subject of the first ever Access and Waiting time target for mental health. EIPS are youth focused community mental health teams that focus on recovery and hope, working around the individual and their family. EIPS are multidisciplinary and flexible and respond to people and provide extra help quickly, when needed. Previously, young people with psychosis went from CAMHS services that didn't understand psychosis, to adult services that didn't understand young people There is evidence that EIPS engage young people in treatment early, keep them out of hospital, get them back to work or college, help people recover and prevent premature death. Over half of patients are helped back into work or education. Most people are discharged back to primary care, either because they are better, or because they are empowered to manage any ongoing difficulties themselves. EIP save the NHS an estimated £63 million every year.

In Oxfordshire the EIPS has grown over the last few years, and now provides a high quality service to over 240 people experiencing a first episode of psychosis. Belinda Lennox is academic lead with a responsibility to embed research in the service. Over the last year the Oxford EIPS has supported 15 different research studies, ranging from stem cell research through to psychological treatment trials, and 211 patients have participated.

Oxford Early Intervention in Psychosis service

Oxford Health NHS Foundation Trust: Global Digital Exemplar

Oxford Health's digital innovations in patient care have been recognised by the trust being named a global digital exemplar in 2017. This means that the trust will be spearheading the development of digital technology in mental healthcare nationally, with £5m in NHS funding.

The trust was just one of seven NHS trusts delivering mental healthcare to be named a global digital exemplar, and will be sharing its learning and practice locally, nationally and internationally.

The trust's innovations include its consultant psychiatrists using video conferencing to support patients at the Horton Hospital in Banbury, with 90% of the patients giving positive feedback. Clinicians can also access the trust's electronic health records system from anywhere, using one of more than 3,000 iPads.

Future planned developments include:

- Patients, and families being able to remotely access personal health records to review their care plans, progress and research preferences.
- Up to date electronic patient notes being available to clinicians across the NHS trust and partner organisations.
- More people receiving physical and virtual treatments in their own home with virtual treatments online.
- Together with Oxford University, developing a platform for online therapeutic interventions, accessible anywhere.

Oxford Health NHS Foundation Trust

Depression and Cancer Care

Depression Care for People with Cancer

Depressive illness is a common and serious problem affecting 10% of people receiving cancer treatment. Depression can limit the person's ability to participate in cancer treatment and has a negative effect on their quality of life. Unfortunately, it often goes untreated.

We have designed a system of care for depression which is integrated with patients' cancer care. Systematic assessment of patients identifies those suffering from depression and these people are offered treatment called "Depression Care for People with Cancer" (DCPC).

DCPC is delivered by a team of cancer nurses and specialist psychiatrists working with the patient's oncology team and GP. It includes both talking therapy and antidepressant medication.

Our previous research has found DCPC to be highly effective and cost effective in improving depression and quality of life 1. As a result DCPC is recommended by the 2015 NHS Cancer Taskforce report.

We are currently researching the implementation of DCPC in the Oxford Cancer Centre. The aim of this translational research is to learn about barriers and facilitators, in order to inform national implementation. The Oxford DCPC service became operational in a number of cancer clinics in late 2017.

This work is jointly funded by the Oxford NIHR CLAHRC, Macmillan Cancer Relief and Oxford University Hospital NHS Foundation Trust.

Michael Sharpe

Schools Mental Health Support

Mental Health Support to Young People Via Schools and Social Media

We have been working closely with Oxford Health NHS Foundation Trust to ensure that local clinical services are informed of the best available evidence. This has led us to be at the forefront of innovations in children's clinical services as a result of this collaborative working. Over the last few years we have developed an 'InReach' service that has now been commissioned and is being delivered to all state-funded secondary schools in Oxfordshire. These schools now have a member of children's mental health services visiting them for half a day each week. They can use this time to find ways to improve how young people access mental health services and to work more closely with education colleagues and support the environment where young people spend such a significant proportion of their time.

The 'Coping with your low mood' poster (pictured) was developed to enable young people to have access to as much information as possible about the most common mental health problem of their generation: depression. We created a poster that, through the use of images, could educate young people about what causes depression, how depression can make them feel and then what they can do to help themselves if they are feeling like this.

We hoped to make the most evidence-based interventions readily available so that they are in a position to do what they can to help themselves: this is especially because many young people still experience stigma and fear around mental health problems. We also had the input of a young person's advisory group to help us make sure it was as relevant as possible to young people. A charity made the poster for us and so were able to make it freely available to download. It was promoted using social media, and has been re-tweeted over 600 times with a number of other charities planning to make it more widely available to schools.

Mina Fazel

Centre for Suicide Research

Some activities at the Centre for Suicide Research focus on interventions for people who self-harm, especially those who present to general hospitals. These include systematic collection of data on presentations to five large general hospitals (in Oxford, Manchester and Derby) as part of the Multicentre Study of Self-harm in England. This provides information about both hospital and psychiatric care, together with subsequent repetition of self-harm and deaths, which allows identification of impacts of clinical management on key outcomes.

With health economists in the Nuffield Department of Population Health and London School of Economics we are also investigating the economic costs of general hospital medical and psychiatric management of self-harm. This has provided estimates of overall costs to the NHS and will be used to identify impacts of clinical interventions on healthcare costs.

Through Cochrane Collaboration reviews we have identified the most effective psychosocial interventions for people who self-harm, which are now included in national clinical guidelines. We are also investigating the toxicity of psychotropic and analgesic drugs commonly used for fatal and non-fatal self-poisoning, which will assist clinicians in making prescribing decisions, especially for people who may be at risk of self-harm. Further work involves development of resources regarding self-harm for parents, young people and schools.

Keith Hawton

CBT-E for Eating Disorders

Over the past 15 to 20 years The Centre for Research on Eating Disorders at Oxford (CREDO) has developed and evaluated a new form of cognitive behaviour therapy termed CBT-E ("enhanced CBT"). It is designed to be suitable for all forms of eating disorder seen in adults and it pioneered the term "transdiagnostic".

In May 2017 NICE published new clinical guidelines on eating disorders. CBT-E is recommended as the leading treatment for all eating disorders in adults bar anorexia nervosa where it is one of three recommended treatments. In addition, it is the leading second-line treatment for adolescents.

The demand for training in CBT-E is extreme and worldwide. Accordingly Professor Fairburn and his team have developed a scalable web-based training method. It has now been evaluated in a countrywide test across Ireland and in a RCT across North America. These studies have shown that web-based training in CBT-E is both popular and effective.

Christopher Fairburn

Evidence-based medicine in practice

The scope of how we "do" evidence-based mental health here in Oxford is to introduce and promote the practice of evidence-based medicine in real-world clinical settings. Scientific literature is continuously made available (sometimes too much and too often misleading) with websites and other sources regularly updating, almost in real time, with the latest content.

Our mission is rather different. We want to help interested clinicians and students learn how to select and use the best available evidence to answer their questions and materially improve their own clinical practice. Taking an evidence-based approach is not a one-size-fits-all solution and it is can be harder in mental health because psychiatry and clinical psychology have specific features that are unique from the rest of medicine. Bearing this in mind, however, we need to answer clinical questions for mental health problems adopting a rational and scientific approach, as our colleagues do in the other fields of medicine. Evidence-based medicine is not like following a recipe: it is not a warranty of clinical success and it is challenging because it requires medical knowledge, critical appraisal and clinical skills. We are constantly striving to refine and improve our tools to offer the best-possible evidence-based guidance to clinicians by collaborating together in research projects and scientific publications, through hands-on tutorials/course, dedicated websites and via social media.

Andrea Cipriani

PATIENT AND PUBLIC INVOLVEMENT

– AT THE CORE OF RESEARCH

In collaboration with colleagues, NEUROSEC is leading the work on Patient and Public Involvement (PPI), in the newly awarded NIHR Oxford Health Biomedical Research Centre (BRC) dedicated to mental disorders and dementia.

NEUROSEC's Principal Investigator and PPI Theme Lead at the Oxford Health BRC, Prof. Ilina Singh, has a longstanding commitment to bringing the first-person experiences of children and young people into ethical evaluation, clinical decision-making and policy-making. It is at the core of the group's research.

In 2016, NEUROSEC formed their Young People's Advisory Groups (YPAG) to give adolescents the opportunity to get involved in decision-making about research and policy in mental health that may affect their lives. YPAG members are between 14-18 years old, meet every two months, and are given the chance to learn about mental health, ethics, and the research process, interacting closely with researchers undertaking cutting-edge work in their field.

YPAG members advise and collaborate with researchers, acting as co-participants in the design and implementation of research studies; including participant recruitment, the testing and developing of interview questions, online surveys and face-to-face interviews. The group is also involved in developing educational materials and innovative, digital methodologies for research with teenagers, including apps and games. This year, the NEUROSEC YPAGs have consulted on several Department of Psychiatry research grants; have presented at the BeGOOD team's research day; and have participated in a BBC-Wellcome programme.

In Oct 2017, Prof. Singh and NEUROSEC YPAG members were filmed by the BBC for an episode of Tomorrow's World, concerning the use of artificial intelligence in mental health treatment. The group were asked to consider the pros and cons of mental health therapy apps, or 'chatbots', reflecting on questions such as: Would you trust a chatbot therapist? Can a chatbot provide a replacement for face-to-face mental health therapy? If you told a chatbot about your problems, how would it provide a solution?

Images show a range of activities undertaken by the YPAG group over 2017, including experiencing therapeutic VR, discussing the design of research studies and trying out a mental health therapy app for a BBC-Wellcome film: 'Would you trust a chatbot therapist?

By engaging with young people and incorporating their voices throughout the research process, the NEUROSEC YPAG will help develop research projects and research tools that make research questions, processes, outputs and interventions more ethical, relevant and impactful for young people.

In addition to their Young People's Advisory Group (YPAG), Prof. Ilina Singh's NEUROSEC team run an annual Work Experience Programme for 15-18 year olds, and a 3 week Undergraduate Summer Placement Scheme on the Citizens: Early Intervention Ethics study, which forms part of the project, Becoming Good: Early Intervention and Moral Development in Child Psychiatry (BeGOOD), funded by the Wellcome Trust.

In 2017, Work Experience students were given the task of developing a digital game, or app, designed to explore young people's moral attitudes in relation to advances in biomedicine, psychiatry and neuroscience. 2017 Summer Placement students worked on the implementation of a research study looking at young people's moral experiences in everyday life using a digital diary methodology, and developed a computer game that is being pitched to Oxford Sparks, Wellcome Trust and other potential partners.

Plans are underway for NEUROSEC to run sustainable mentorship schemes for under-18 year olds, and undergraduate students in the future.

Ilina Singh / NEUROSEC

PUBLIC ENGAGEMENT

2017 was a year of firsts for Public Engagement with Research (PER) at Oxford and the Department. Three major events lit up the city with energy and innovation: Brain Diaries, Curiosity Carnival and the launch of the Wellcome Centre for Integrative Neuroimaging (WIN). The Department of Psychiatry contributed creativity, passion and imagination to all.

Dr Clare Sexton, from the Department of Psychiatry, scooped the Early Career Researcher award in the Vice-Chancellor's Public Engagement with Research Awards 2017 for her work promoting healthy ageing in the brain.

The Department launched its inaugural Public Engagement with Research Prize to celebrate the success of its public engagement activity. Results will be announced in January 2018.

Clare Sexton

Clare Sexton was recognised at this year's Vice-Chancellor's Public Engagement with Research Awards for her work engaging the public through delivering Dementia Friends information sessions and public talks about her research, film screenings of the documentary "The Age of Champions", and through her work as Founding Chair of Dementia Friendly Chipping Norton. Since January 2015, Dr Sexton has delivered Dementia Friends Information Sessions to over 900 people, from different ages and backgrounds with the aim of increasing awareness about dementia and how healthy. brain ageing can be encouraged through non-pharmacological means.brain ageing can be encouraged through non-pharmacological means.

Brain Diaries

In March 2017, 'Brain Diaries: Modern Neuroscience in Action' opened at the Museum of Natural History in Oxford. The University of Oxford's neuroscience community collaborated with the museum to stage an interactive exhibition and a programme of events aimed at a diverse range of audiences that was extended to 1 January 2018. Here, Liz Tunbridge touches a 3D printed brain created from MRI scans at the University of Oxford.

Curiosity Carnival

Curiosity Carnival was held on 29 September 2017 as part of European Researchers' Night. It was the largest single public engagement event ever staged in Oxford and took over venues and streets across the city. The Department took part in numerous events including Phil Burnet hosting part of 'Boost Your Brain' neuroscience activity and Andrea Reinecke talking about phobias in the lift at the Ashmolean Museum.

Fairground of the Brain

Sana Suri, named "Rising Star in Dementia Research" by the Alzheimer's Society this year, helped to host the Fairground of the Brain on Broad Street, as part of Curiosity Carnival. A range of fairground attractions illuminated the magic of our brains to visitors and passers-by in central Oxford.

Mixing Neurococktails

Rounding off Curiosity Carnival with a Neurococktail bar, Liz Tunbridge's ever-popular event explored the effects of alcohol on the brain and how our genetic make-up influences the ways our brains respond to drugs of abuse.

WIN launch: 21st Century Phrenology

On 1 November 2017 the Wellcome Centre for Integrative Neuroimaging (WIN) launched – and with it a host of public events, based at the Museum of Natural History, including '21st Century Phrenology' - a play that was written, performed and directed by WIN members, including the Department's Clare Mackay as Franz Joseph Gall (pictured left).

This way: meet the researcher

A chance to sit down and chat to researchers in an informal setting at the WIN launch.

Department in Numbers

In this year's annual report we have presented a selected highlights of the Department of Psychiatry in 2017, showcasing the diverse range of the work undertaken at the Department. For full and comprehensive details of our research groups and academics please visit: **www.psych.ox.ac.uk/research**. Below is a snapshot of how the Department looks in numbers:

University of Oxford
Department of Psychiatry

www.psych.ox.ac.uk

Contact: information@psych.ox.ac.uk

follow us @OxPsychiatry 

Photo credit for cover image: Catharina Zich / Brain Diaries