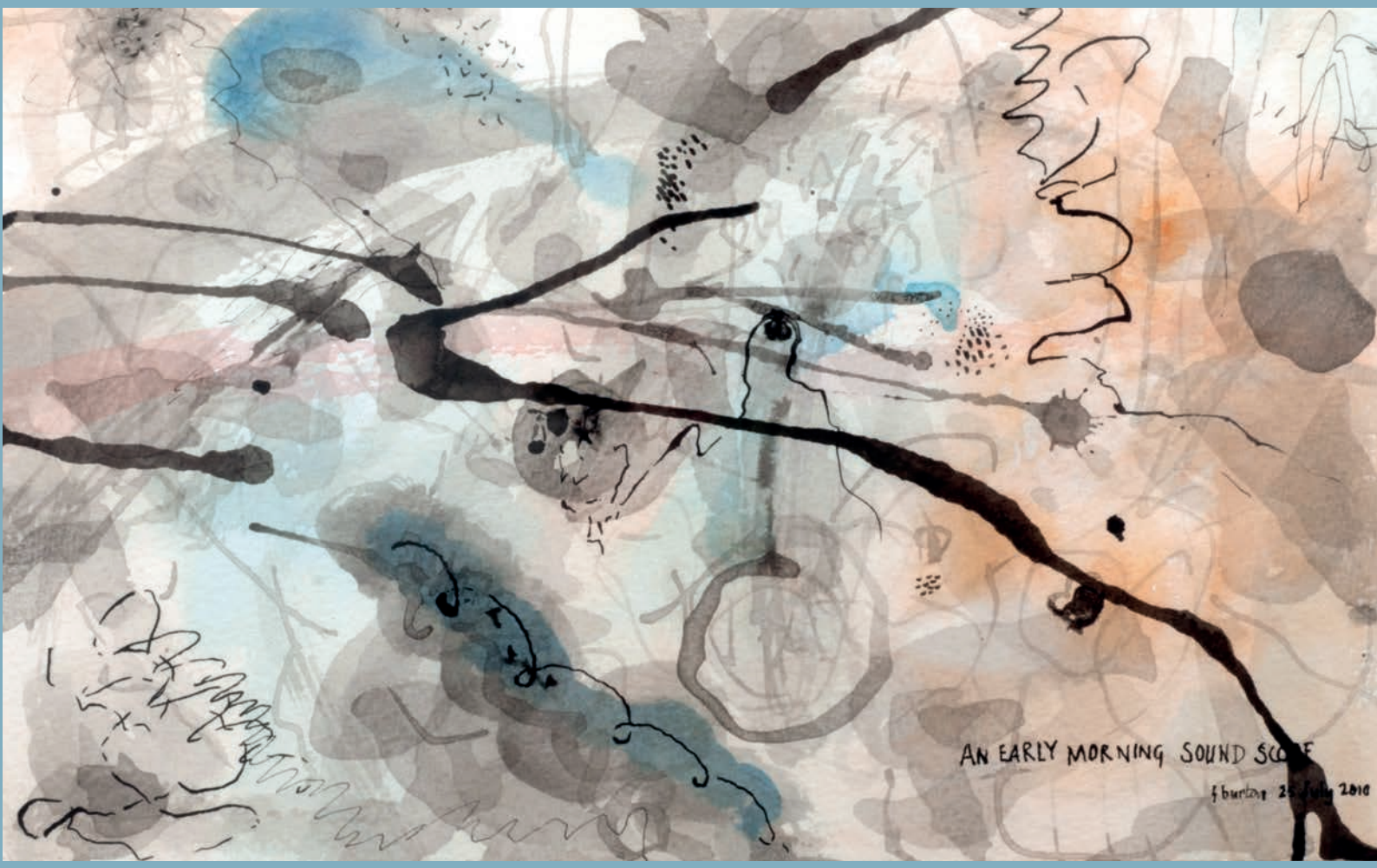
UNIVERSITY OF OXFORD



Department of Psychiatry

Annual Report 2015

Contents

Professor John Geddes
Head of Department
of Psychiatry

Introduction

This Annual Report of the Department of Psychiatry at the University of Oxford provides an overview of our research and educational activities. I will just highlight a few of the many outstanding developments over the last 12 months.

In 2014 we made some major senior recruitments to the Department:

Mike Denis, Senior Research Fellow (and Director of Information Strategy for AHSC and AHSN)
Professor John Gallacher, Professor of Cognitive Health
Professor Willem Kuyken, Professor of Clinical Psychology
Professor Simon Lovestone, Professor of Translational Neuroscience
Professor Kia Nobre, Professor of Translational Cognitive Neuroscience (joint with Experimental Psychology)
Professor Ilina Singh, Professor of Neuroscience and Society

Welcome to them and to all other staff joining the Department.

It has also been a very successful year for funding. This year I would particularly like to highlight, and express our gratitude, to the Wellcome Trust who fund several of our large scale programmes via their Strategic Award scheme. The Department is now either the lead Department or a partner in the following strategic awards:

- ConBRIO Collaborative Network for Bipolar Research to Improve Outcomes
- Wellcome trust Consortium for Neuroimmunology of Mood Disorders and Alzheimer's Disease
- Promoting mental health and building resilience in adolescence: investigating mindfulness and attentional control
- Sleep and Circadian Neuroscience Institute (SCNi) for Mental Health
- Integrated Multimodal Brain Imaging for Neuroscience Research and Clinical Practice
- The Use of the internet to train clinicians to implement psychological treatments

The forthcoming year will see major expansions in research activity in a number of our core areas, accompanied by substantial improvements in our infrastructure and continued productive collaborations across Oxford and beyond. We will focus on developing our partnership with the National Institute for Health Research, building on the sound foundations that we have put in place over the last few years. We already have major programmes within the Oxford Collaboration for Leadership in Applied Health Research and Care, an NIHR supported Clinical Research Facility as well as the existing Programme Grants for Applied Research, clinical trials and smaller grants. Our main strategic focus over the next 12 months will be to develop our translational activity, creating even stronger links with other Oxford Departments and Institutes across Neuroscience and the Medical Sciences Division – and more widely across Oxford Sciences and Humanities. This will make complex mental and cognitive disorders tractable and to develop novel treatments for patients based on deep understanding of basic mechanisms.

As always, thanks to our magnificent academic and support staff, led by Pam Taylor, for their indefatigable support. Finally, thanks to Dr Liz Tunbridge, who has led our Athena Swan process with great energy and creativity. Whatever the future result of our recent Silver application, there can be no doubt of the major benefits to the whole Department of our enthusiastic, Liz-led, engagement with this process.

Finally, the 2014 Research Excellence Framework highlighted Oxford's world leading position in Psychology, Psychiatry and Neuroscience, so thanks and congratulations to all – and especially to Paul Harrison and the REF committee for coordinating so wonderfully well. This is just the start!

Clinical Medicine Undergraduate Course

Dr Jonathan Price

The University Department is responsible for the management and delivery of an eight week course in psychiatry for 160 medical students (reading for BM BCh) each year.

Dr Jonathan Price is the Clinical Tutor in Psychiatry, and is supported by Suzanne Williams, Course Administrator.

The BM courses

There are two streams of students:

a) *The conventional BM course (A100) – six years in duration – the majority of the students, typically entering the Medical School straight after A levels or equivalent; and b) The accelerated BM course (A101) – four years in duration – designed for graduates with a degree in applied or experimental sciences, some of whom will also have had periods of employment.*

The final two years of these courses follow an identical path. Therefore, although the undergraduate course in psychiatry is delivered during year 5 of the six-year conventional course and year 3 of the 4 year accelerated course, the conventional and accelerated students are treated identically in psychiatry, and are mixed within each eight week course.

We also host occasional overseas elective students, both within and without the Oxford Elective Programme.

The psychiatry course

At the beginning of the course, students have little experience of the management of mental disorders, and the course represents their main opportunity within six years of undergraduate medical education to learn about them. Each student is expected to pass the end-of-course assessment in order to pass on to year 6.

The course is managed by the University Department, but delivered jointly with NHS partners. The main partner is the Oxford Health NHS Foundation Trust (OHFT), which provides about 22 placements each eight weeks. Berkshire Healthcare NHS Trust provides three placements each eight weeks, and we have recently started placements in the new liaison psychiatry service at Oxford University Hospitals. These NHS partnerships are key to providing high quality undergraduate education.

The course places strong emphasis on small group tutorials, and on the attachment of only one or, at most, two students to each teaching consultant. This provides the potential for focused support and development of individual students.

Educational and emotional support for students

This is especially important in psychiatry: the subject matter is likely to be unfamiliar to students; they are often attached singly to teams who are geographically spread; and, if it is familiar to them, it may be because of personal or family experiences of mental illness. Our focus here is on providing close mentoring and support by consultants, through one-to-one or two-to-one clinical attachments, and by tutors, through academic and clinical skills 'small group' tutorials. We also use introductory lectures to raise the issue of students' own vulnerability to mental disorder, to encourage appropriate help-seeking, and to propose lifestyle changes to increase resilience.

Small group tutorials represent an important opportunity for local NHS psychiatry trainees to train in and deliver high quality teaching.

Course evaluation

The Oxford BM course is widely considered by students to be the best undergraduate medical course in the UK. Evidence to support this includes comprehensive data from the National Student Survey, for the students leaving from 2010 onwards, and available at http://unistats.direct.gov.uk/ In each of those years, student feedback was better than for any other UK medical school. In 2013 and 2014, 99% of leaving students were satisfied with the course – the highest proportion ever recorded for a UK medical course.

Within the BM course, the psychiatry course is highly regarded by students, who in 2013-14 rated psychiatry as equal first of six major year 5 courses on the generic Course Evaluation Questionnaire. For example, 95% of students agreed or strongly agreed with the statement that 'the course was well organised', and 86% of students either agreed or strongly agreed that 'I received appropriate support as and when I needed it'.

Course outcomes

Subjectively, our external examiner, Professor Danny Smith, reported in 2014 that 'the academic standards and the achievements of students are at least comparable to other medical schools… as a group they probably out-perform students in many other medical schools.' Objectively, in the last year Oxford students obtained the highest marks of any UK medical school in the pilot Prescribing Skills Assessment; and the highest marks of any UK medical school in the Foundation Programme's Situational Judgement Test. This adds to research data indicating that Oxford graduates are more likely than graduates of any other UK medical school to pass postgraduate exams (MRCP, MRCGP, MRCOG, FRCA), and that the school 'adds value' to an already capable cohort (see e.g. McManus I et al, BMC Medicine 2008; 6: 5, and McManus I & Wakeford R, BMJ 2014; 348: g2621).

Collaborations with other University Departments

With the University Department of Experimental Psychology, we deliver and examine a short course on 'Psychology for Medicine', for year 2 (of 6) students. Members of the Department also contribute to the Final Honours School (year 3 of 6) course in Neurosciences, which is the most popular year 3 option.

Development / initiatives

The recruitment of capable undergraduates into psychiatry and, in particular, into academic psychiatry, remains a challenge. Our aim is to deliver a highly respected training course in psychiatry, in which to showcase the specialty, some of the many very capable doctors and other professionals working in it, and some of the very high quality research taking place in the Department.

In each of 2013 and 2014 we have hosted an Oxford Psychiatry Autumn School, each being attended from across the UK by 40 of the brightest medical students and foundation doctors interested in academic psychiatry. Lectures, visits and small group discussion showcased the ground-breaking interdisciplinary research taking place in Oxford, and allowed delegates to develop their career plans, with Oxford very much in mind as a destination. Plans are now underway for a 3rd Autumn School in September 2015.

We continue to encourage students to pursue academic interests alongside their clinical training, and this is starting to bear fruit. For example, final year student Ed Chesney was first author of a meta-review of mortality in mental disorders published in World Psychiatry, and medical students are currently involved in a variety of projects in the Department.

Group members

Dr Jonathan Price is the Clinical Tutor in Psychiatry, and is supported by **Suzanne Williams**, Course Administrator, and **Wayne Davies**, Facilities Manager.

Honorary Senior Clinical Lecturers
2014-2015

The Honorary Senior Clinical Lecturers are Consultant Psychiatrists in the partner NHS Trusts who play a key leadership role in undergraduate education, postgraduate research supervision or research collaboration with Departmental Principal Investigators.

Oxford Health NHS Foundation Trust

Alastair Reid
Alvaro Barrera
Andrew Molodynski
Anne Stewart
Digby Quested
Gerti Stegen
Peter Sargent
Phil Davison
Philip Wilkinson
Rob Chapman
Clive Meux
Rupert McShane
Julie Chalmers
Tony James
Julia Cartwright
Susan Shaw
Rob Bale
Emma Fergusson
Tim Andrews
Nick Hindley

Graduate Studies – Phil Burnet *(Director of Graduate Studies)* and Dr Jennifer Rendell *(Tutor for Graduate Studies)*

Research degrees

Supervision and support for postgraduate students is a core activity within the Department of Psychiatry providing students with a wide range of transferable skills alongside in-depth knowledge and expertise in one of our extensive range of research fields ranging from molecular biology to brain imaging and from behavioural research to epidemiology.

The Department of Psychiatry offers two research degrees, a DPhil and an MSc(Res) with an annual intake of around twelve students and total number at the start of the 14/15 academic of forty four students (39 DPhil and 5 MSc[Res]). The majority of students are psychology, biological science graduates with a small number of psychiatric trainees. Students provide valuable contributions to the current research activity of the department and the training they receive will enable them to become research leaders in the future.

Supervision and support

Supervision is provided by senior Principal Investigators (PIs) in all areas of the research undertaken within the department including neurobiology, psychological treatments, developmental psychiatry and social psychiatry.

In addition to their main supervisor, all students are assigned a co-supervisor or advisor. Where appropriate co-supervisors may be from other departments within the university including Experimental Psychology, Clinical Neuroscience and Pharmacology and/or the Centre for Functional Magnetic Resonance Imaging of the Brain (fMRIB). The role of co-supervisor can also be filled by junior researchers who are able to develop their own supervisory skills whilst providing valuable support to the student.

Alongside the academic supervision, the Graduate Studies Team (Director, Dr Phil Burnet; Graduate Tutor. Dr Jennifer Rendell and Administrator. Tracy Lindsey) follow the progress of each student closely throughout their time in the department, and offer continuous support and advice in order to ensure smooth transition through the various stages of a research degree and to address academic or personal problems. They organise regular opportunities for students to meet together to present their work and discuss their experiences of postgraduate study. A recent outcome from one such discussion time has been the setting up of a facebook page to facilitate networking between students within the department.

In addition to department activities, students are encouraged to take advantage of the comprehensive, flexible training programme offered by the Medical Sciences Graduate School which includes general and specific research skills and more advanced academic courses.

Student representation

The majority of postgraduate students are female and the Department espouses the aims outlined in the Athena Swan charter which include a commitment to advancing women's careers in areas including science and medicine. The Athena Swan working group includes a student representative who organised focus groups earlier in 2014. The results of this and a discussion group held with the Director, Tutor and Administrator has been the provision of a buddy (usually a student just starting year two) for each new student.

There is also a student representative at the Departmental Meeting. This meeting includes regular reviews of departmental policies and funding as they relate to post-graduate research and training.

Funding

One of the biggest challenges for students wanting to undertake postgraduate study is securing funding for fees and living expenses. The Graduate Medical School offers competitive DPhil awards using funding from the MRC and a number of charities and some PIs are able to offer DPhil and MSc(Res) funding from their research grants. In addition to this, the Department offers a number of

full DPhil studentships each year which cover university and college fees and living costs. The department provides support in the form of a reduction in university fees for individuals employed within the department whose research can be developed into a DPhil/MSc project. All students whose funding does not specifically cover research consumables (such as the costs of photocopying and stationary and of conference travel) are eligible for a Research Training Support Grant (which is currently £1,300).

Future careers

Following completion of their research degree, students in recent years have chosen a variety of career paths. These have included further postdoctoral research (domestic and overseas) frequently supported by independent funding awards from the MRC and Wellcome Trust, medical and clinical psychology training, employment in the pharmaceutical industry and university teaching posts. Supervisors and co supervisors support students, making the transition from postgraduate to researcher and the department is developing a mentoring system which will help students plan their future careers in research or other in other fields.

Post-graduate Medical Training

Professor Klaus Ebmeier

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 Oxford Cognitive Health and Neuroscience Clinical Trials Unit, Oxford Mindfulness Centre and the newly opened Oxford Centre for Human Brain Activity. The Oxford Collaboration for Leadership in Applied Health Research and Care (CLAHRC) will fund 4 new academic clinical fellow (ACF) positions in psychiatry this year. We are also delighted to announce a new DPhil (PhD) scheme for clinicians in Oxford, dedicated to mental health, and funded by the Wellcome Trust.

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 Centre for Functional Magnetic Resonance Imaging of the Brain (fMRIB).

We provide the Oxford MRCPsych Course. The course provides a stimulating and thorough grounding in the basic and clinical sciences relevant to psychiatry and prepares candidates for the Paper I & 2 and Paper 3 of 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 Foundation School and arrange a 4 month academic placement with the Department (see projects above).
2. Academic Clinical Fellows 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 post, such as last year, when we appointed ACFs in Old Age and Child and Adolescent Psychiatry. The Oxford Collaboration for Leadership in Applied Health Research and Care (CLAHRC) will fund 4 new academic clinical fellow (ACF) positions in psychiatry this year in addition to other NIHR-funded posts. The Academic Clinical Fellowship Programme offers training to new entrants to psychiatry who can demonstrate that they have outstanding potential for development as a clinical academic in psychiatry. Training is flexible and trainee-centred, as far as possible, with suitable mentoring and supervision to ensure the attainment of both academic and clinical goals. The trainee selected for the Fellowship Programme will be awarded an NTN (a) at the start of the Programme. The purpose of ACF posts is to provide training leading towards an academic career, typically continuing with a Training – (PhD/DPhil) – Fellowship after national and interdisciplinary competition. Such fellowships are primarily offered by the MRC, by certain charities, such as the Wellcome Trust or Alzheimer UK, and also locally in Oxford. We are also delighted to announce a new DPhil (PhD) scheme for clinicians, dedicated to mental health, and funded by the Wellcome Trust. Applications require submission of a project under the supervision of an academic researcher of international standing, with high quality scientific input from one of the basic science departments within Oxford University Medical Sciences Division, as well as usually an interview before a multidisciplinary panel. The ACF training is designed to prepare the candidate for these rigours, as well as continuing clinical training in Psychiatry. Research time is available at 25% of the total training time and will preferably be taken as a block or blocks of 3-9 months, as required by the research. An academic mentor will be assigned who will meet the trainee on at least a six monthly basis to ensure that mutually agreed academic milestones are being achieved, and a plan put in place to address any deficiencies identified.
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, incl. the Master of Science (MSc) by Research, require a background in medicine, psychology or a biological science. To start with, we suggest that you identify a potential supervisor in your area of interest and then contacting them direct. A list of potential projects can be found on our website (http://www.psych.ox.ac.uk/study/graduate-studies). We are happy to discuss your research ideas and indicate whether we are likely to be taking on graduate students next year, as well as what, if any, funds are available to support you.
4. Academic Clinical Lecturers require 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, each. Competition is typically against other neuro-disciplines, although from time to time, NIHR advertises for specific specialty post, such as this coming year for a Clinical Academic Lecturer in Old Age Psychiatry.

RESEARCH REPORTS FROM DEPARTMENTAL PRINCIPAL INVESTIGATORS

Dr Matthew Broome

Early Detection and Neuroscience of Psychopathology

My research has focused on the prodrome and first episode of psychosis, and the formation of delusions, utilizing both cognitive neuropsychology and neuroimaging, to understand the pathophysiology of schizophrenia and other psychotic disorders. More recently, I've worked on mood instability across diagnoses and in expanding the early intervention paradigm to non-schizophreniform disorders

Current research

Ongoing work involves collaborations with colleagues in longitudinal neuroimaging studies in those who may be developing a psychotic illness. The first of these studies is with the Department of Psychosis Studies at the Institute of Psychiatry, Psychology and Neuroscience (IoPPN) and uses multi-modal imaging techniques to examine those at risk of developing psychosis, and is funded by the EU and the Wellcome Trust. The second is with Stephen Wood in Birmingham, and is an MRC-funded study looking at structural brain changes in those at risk for psychosis serially over time.

Together with colleagues in Oxford, Warwick, and UCL, I've been involved in epidemiological work on mood instability transdiagnostically, and the relationship between adverse life events across development and the onset of psychotic disorder and its symptoms. Currently I am working with the Mental Health Foundation and the University's Faculty of Philosophy to examinine communication in clinical settings (funded by the Wellcome Trust and John Fell).

Members of the wider group have related interests in the early detection and development of psychiatric illness (body perception in those at risk of eating disorders, predictors of recurrence of self-harm, clinicians' ability to detect subtle psychosis) and the aetiology of psychopathology (bullying and psychosis, Bayesian accounts of delusion formation)

Planned research

In 2015 I aim to apply for funding for two different projects related to early psychotic illness. First, Fellowship applications to examine plasticity, GABA and the functional dynamics in the brains of those with psychosis (in collaboration with Behrens, Browning, Goodwin, Harrison, Lennox, Vogels). Secondly, to develop a collaboration with colleagues at Oxford and at the IoPPN to study in vivo neurochemistry (via PET, MRS) and treatment response in those with a first episode of psychosis (in collaboration with Cowen, Harrison, Howes, Lennox, MacKay, Stagg).

Group members

Dr Helen Bould (Wellcome Clinical Doctoral Training Fellow), Dr Stefan Brugger (Academic Foundation Doctor), Dr Angharad de Cates (Academic Clinical Fellow), Dr Gennaro Catone (Visiting Psychiatrist, University of Naples), Dr Juliana Lindau Fortes (Visiting Psychiatrist, Sapienza University, Rome)

We are delighted that Emma Cernis, Nicole Evans, and Rachel Lister have all gained places on clinical psychology training courses.

Collaborators

- **Oxford Psychiatry:** *Dr Mike Browning, Prof Phil Cowen, Prof Dan Freeman, Prof Guy Goodwin, Prof Catherine Harmer, Prof Paul Harrison, Dr Belinda Lennox, Dr Clare MacKay, Dr Mark Woolrich.*
- **Oxford University:** *Prof Tim Behrens (NDCN), Dr Edward Harcourt (Philosophy), Prof Julian Savulescu (Uehiro Centre), Dr Charlotte Stagg (NDCN), Dr Tim Vogels (DPAG).*
- **External**: *Prof Paul Bebbington (UCL), Dr Oliver Howes (KCL), Dr Lisa Jones (Birmingham), Prof Elizabeth Kuipers (KCL), Dr Steven Marwaha (Warwick), Prof Philip McGuire (KCL), Dr Rachel Upthegrove (Birmingham), Prof Stephen Wood (Birmingham).*

Recent publications

1. Gibbs, Melanie, Catherine Winsper, Steven Marwaha, Eleanor Gilbert, **Matthew Broome,** and Swaran P Singh. 2015. "Cannabis Use and Mania Symptoms: a Systematic Review and Meta-Analysis." Journal of Affective Disorders 171 (January): 39–47. doi:10.1016/j.jad.2014.09.016.

2. Marwaha, Steven, **M R Broome,** Paul Bebbington, Elizabeth Kuipers, and Daniel Freeman. 2014. "Mood Instability and Psychosis: Analyses of British National Survey Data.." Schizophrenia Bulletin 40 (2). Oxford University Press: 269–77. doi:10.1093/schbul/sbt149.
3. Modinos, G, P Allen, M Frascarelli, S Tognin, L Valmaggia, L Xenaki, P Keedwell, **M. Broome,** I. Valli, J. Woolley, J.M Stone, A. Mechelli, M.L. Philips, P. Mcguire, P. Fusar-Poli 2014. "Are We Really Mapping Psychosis Risk? Neuroanatomical Signature of Affective Disorders in Subjects at Ultra High Risk.." Psychological Medicine 44 (16): 3491–3501. doi:10.1017/S0033291714000865.
4. Stanghellini, Giovanni, and **M R Broome. 2014.** "Psychopathology as the Basic Science of Psychiatry.." The British Journal of Psychiatry : the Journal of Mental Science 205 (3): 169–70. doi:10.1192/bjp.bp.113.138974.
5. Stein, Kate, and **M R Broome. 2014.** "Neuroprogression in Schizophrenia: Pathways and Underpinning Clinical Staging and Therapeutic Corollaries.." The Australian and New Zealand Journal of Psychiatry, October. doi:10.1177/0004867414556321.

Dr Phil Burnet

Neurobiology and Experimental Therapeutics

My research explores ways to preserve or improve brain function. In aging and psychiatric disorders, there is an impairment of memory and positive mood, but the currently available medication is not always effective. My work will ultimately offer either supplements or alternatives to contemporary treatments of psychiatric and age-related illness.

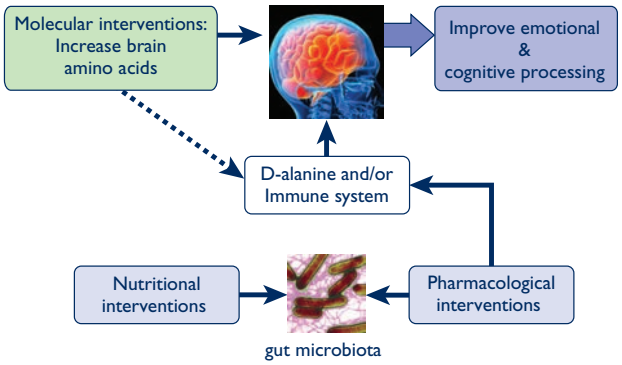
Current research

I head the Neurobiology and Experimental Therapeutics (NET) group which tests the therapeutic potential of molecular, pharmacological and nutritional interventions in healthy individuals and in established models of impaired emotion and cognitive function. For instance, we have used a gene therapy tool called RNA-interference, to reduce the production of a schizophrenia risk gene, D-amino acid oxidase (DAO), which is overactive in psychotic illness and decreases the levels of an important brain amino acid, D-serine. This D-amino acid is a potent activator of the glutamic acid N-methyl-D-aspartate (NMDA) receptor (NMDAR), a key player in healthy cognitive function. We have shown that reducing DAO increases brain D-serine, and that the direct ingestion of this compound has pro-cognitive effects. Studies exploring the psychopharmacology of D-serine and other D-amino acids are on-going.

We are also investigating how gut bacteria influences mood and cognition, and examining whether substances which encourage their growth can augment the action of psychotropic agents. Our research has revealed that prebiotics (nutritional substances that grow indigenous, beneficial gut microbes) affect emotional processing in healthy volunteers, and reduce the levels of the stress hormone, cortisol. The work is now being extended to test if prebiotics have anxiolytic actions in younger populations and improve cognitive performance in elderly subjects with mild cognitive impairments.

In parallel, we are examining the key mediators that link gut bacteria with brain function. Of particular interest is the immune system, which is significantly modulated by intestinal microbiota and influences the function of NMDARs. We have recently found that prebiotics reduce the inflammatory response in the brain, attenuate inflammation related anxiety, and increase central NMDAR activity. Furthermore, nurturing gut bacteria increases the levels of circulating D-amino acids which may also contribute to the psychotropic effects of prebiotics via the NMDAR. A summary of our interactive, multidisciplinary research strategies is shown below *(Fig 1)*.

FIGURE 1: Current strategies used by the NET group to improve brain function



Planned research

In 2015 we will apply to the BBSRC for a three-year Industrial Partnership Award to study the long-term effects of manipulating gut bacteria in early-life. The study will focus on the role of the intestinal immune system on brain development and maturation. This investigation will incorporate novel technology, such as 'metabolomics' which is an expertise at the University of Reading. We hope this work will also involve the participation of an NIH-OXCAM graduate student, and a specialist laboratory at the NIH, USA. In separate studies, we will be investigating the effects of dietary prebiotics on anxiety and cognition in school children, and cognitive health in an elderly population. These latter investigations will be supported by our industrial partners.

Group members

Dr Liliana Capitao (Clinical Psychologist), Miss Shi Yu Chan (DPhil Student), Miss Mia Thomaidou (Placement student, Westminster University, London), Mrs Li Chen (Technician)

Collaborations

We collaborate extensively with several departments in Oxford including: Experimental Psychology, Pharmacology, and Physiology, Anatomy and Genetics, and Social Policy and Intervention, as well as groups within the department of Psychiatry. These collaborations provide the necessary expertise to ensure that our research is both multidisciplinary (from molecule to behaviour) and translational. For similar reasons, we have links and on-going collaborations with other Universities including, University College London, Reading University (School of Food Biosciences) and DeMontfort University (School of Pharmacy). We also have links with Industry, particularly Clasado Ltd, which is supporting our work on nutritional interventions and brain health. International links include those with the National Institutes of Health, USA (Dr Yasmine Belkaid) and University of Barcelona, Spain (Dr Belen Ramos). Our group also plays an active role in the practical teaching of undergraduate and graduate students of Oxford University and international academic institutions.

News and impacts

Our work is disseminated in scientific journals specialising in neuroscience and psychiatry-related disciplines (see examples below), but we also ensure that our publications are accessible to the general public, which has been facilitated through press releases. In addition, I participate in public engagement in science schemes. For instance, in 2014 I participated in the Cheltenham Science Festival in a forum about how food can affect the brain.

Recent publications

1. Schmidt K, Cowen PJ, Harmer CJ, Tzortzis G, Errington S, **Burnet PWJ (2014).** Prebiotic intake reduces the waking cortisol response and alters emotion bias in healthy volunteers. Psychopharmacology (in press).
2. Tao R, Cousijn H, Jaffe AE, **Burnet PW,** et al (2014). Expression of ZNF804A in Human Brain and Alterations in Schizophrenia, Bipolar Disorder, and Major Depressive Disorder: A Novel Transcript Fetally Regulated by the Psychosis Risk Variant rs1344706. JAMA Psychiatry.71:1112-20.
3. **Burnet PWJ** and Cowen PJ (2013) Psychobiotics highlight the pathways to happiness. Biological Psychiatry 74: 708-9.
4. Savignac HM, Corona G, Chen L, Mills H, Spencer JPE, Tzortzis G, and **Burnet PWJ (2013).** Prebiotic feeding elevates central BDNF, NMDAR subunits and D-serine. Neurochemistry International 63: 756-64.
5. **Burnet PWJ (2012).** Gut bacteria and brain function: the challenges of a growing field. Proc Natl Acad Sci U S A.109:E175.

Emeritus Professor Tom Burns

Social Psychiatry Group

The Social Psychiatry Group is a multi-disciplinary research unit focusing on outcomes of community mental health services. The group was established in 2003 and developed rapidly, attracting grants from our first year. We conduct rigorous clinical evaluations and pragmatic trials of complex interventions in the community.

Current research

Our interest is on how services are provided for and experienced by those with severe mental illnesses. As a group we have focused as much as possible on improving the rigour in community mental health services research studies. Most of our work consists of experimental studies (RCTs) although we also conduct rigorous cohort and qualitative studies. These illuminate the mechanism of action in our intervention trials. We completed a major body of work on coercion, both that imposed via the mental health act and also the more pervasive informal pressures patients are exposed to. Our RCT of legal compulsion in the community continues to generate controversy as the results (that there are no significant benefits) have been unwelcome to many clinicians.

We have now completed a follow-up of this RCT and it appears that there are no long-term benefits either. Three DPhils are currently being completed based on this work. We have focused on the questions that clinicians consider they need answers for and we pride ourselves on pursuing these questions with the maximum possible rigour. This takes longer and is labour intensive. Avoiding the compromises so common in this complex area means that the answers we provide have greater certainty and generalisability. They also have the potential to influence policy (and generate controversy).

With retirement in Sept 2014, I am continuing in an emeritus capacity in 2015 to supervise the completion of the papers from the OCTET follow-up and the DPhils associated with it.

Group members

Ksenija Yeeles – Research Fellow in the Social Psychiatry Group and a third year DPhil student at the Department of Psychiatry. She has been managing the ULTIMA study, IPS-LITE and FIAT RCTs, Feasibility RCT REFLECT and most recently the OCTET follow-up study.

Stephen Puntis – Research Assistant on the OCTET RCT and the OCTET follow-up study in the Social Psychiatry Group. He is also a DPhil candidate in Psychiatry. His thesis investigates the association between continuity of care and patient outcomes. From 2015 he will be a post-doctoral research student with Professor Michael Sharpe.

Francis Vergunst – Research Assistant on the OCTET RCT and the OCTET follow-up study in the Social Psychiatry Group. He is also a DPhil student and his thesis explores the association between community compulsion and long-term social outcomes.

Collaborations

Dr Jorun Rugkåsa – Senior Researcher at the Health Service Research Unit at Akershus University Hospital, Oslo, Norway. She is also Senior Research Fellow in the Social Psychiatry Group currently working on the OCTET RCT and the OCTET follow-up study.

News and impacts

The recent parliamentary reviews of the MHA have recommended a careful reconsideration of the extent of CTO use "in the light of the OCTET results". In addition, the RCPsych is establishing a review to decide whether it ought to issue guidance on restrictions in their use.

Recent publications

1. Hwang S, **Burns T (2014).** Health interventions for people who are homeless. The Lancet, 384: 1541 - 47.
2. **Burns T (2014).** Community psychiatry's achievements. Epidemiology and Psychiatric Sciences, DOI: 10.1017/S2045796014000560 October 2014.
3. Rugkåsa J, Dawson J, **Burns T (2014).** CTOs: what is the state of the evidence? Social Psychiatry and Psychiatric Epidemiology, DOI: 10.1007/s00127-014-0839-7.
4. **Burns T,** Yeeles K, Langford O, Vazquez Montes M, Burgess J, Anderson C (2014). A Randomised Controlled Trial of time limited Individual Placement and Support: the IPS-LITE trial. BJP, in press.
5. Puntis S, Rugkåsa J, Forrest A, Mitchell A, **Burns T (2014).** Is continuity of care associated with patient outcomes in mental health?: A systematic review. Psychiatric Services, in press.

Professor Andrea Cipriani

Systematic Review and Meta-Analysis Group

My research focuses on the evaluation of treatments in psychiatry, mainly major depression, bipolar disorder and schizophrenia. My main interest in psychiatry is to promote evidence-based mental health, as a tool to select and use the best available scientific literature to answer real-world clinical questions and materially improve practice.

Current research

I am currently working on some systematic reviews and pair-wise meta-analyses about very promising compounds in psychiatry (like calcium channel antagonists in bipolar disorder and ketamine or other glutamate receptor antagonists in mood disorders) and on two important network meta-analyses: one about pharmacological treatment of post-traumatic stress disorder (in collaboration with colleagues from South Africa) and the second about psychological treatments for bipolar disorder (in collaboration with David Miklowitz from University of California, Los Angeles). I am also involved in the design and conduct of a placebo controlled study that will start in Oxford in 2015 about lithium and mood instability in bipolar disorder.

My interest in the methodology of evidence synthesis has now a specific focus on network meta-analysis and individual patient data meta-analysis, trying to assess the validity, breadth, structure and interpretation of these statistical approaches to better inform the mental healthcare decision-making process.

Until 2016 I am the Editor in Chief of Evidence-Based Mental Health.

Planned research

During the next year, I'd like to focus on two new big research projects. The first one is the update of the network meta-analysis on antidepressants for major depression we published in the Lancet in 2009. In this new analysis we will include not only all the most recently marketed drugs, but also two tricyclics (amitriptyline and clomipramine) and placebo. We will be able to compare efficacy and tolerability of new versus old antidepressants and address the crucial issue of placebo effect in major depression using a database of more than 100,000 participants.

The second project will focus on implementation of research evidence. Clinical decision making cannot rely on evidence alone. Although significant advances have occurred in the development of high quality evidence, similar efforts must be made to develop and evaluate tools that can be used routinely to individualise treatment decisions and facilitate the incorporation of our patients' unique preferences and circumstances into the decision-making process. In particular, in this research project we will focus on developing decision support tools that express the risks and benefits of treatments in concise, intelligible formats, feasible for use on busy clinical psychiatric services and tailoring treatments to patients' clinical characteristics and values.

Group members

I've joined the Department in September 2013 after 8 years as Lecturer in Psychiatry at the University of Verona. In the past 12 months I've started coordinating a group of people interested in evidence synthesis. Jennifer Rendell, Sarah Stockton, John Geddes and I have regular meetings every month to present and discuss ongoing research projects. This year some new members have joined our systematic review group: from the Department (Mary-Jane Attenburrow and Rebecca McKnight), from around the UK (James Stefaniak and Edward Chesney) and also from other countries in Europe (Juliana Fortes Lindau from Italy and Ben Amit from Israel).

Collaborations

In the past few years I have been working closely with world class academic institutions (University of Bristol and Centre for Reviews and Dissemination, University of York in the UK; Universities of Ulm and Munich in Germany; University of Verona in Italy; University of Ioannina in Greece; Universities of Nagoya and Kyoto in Japan; University of Cape Town in South Africa) and important organisations, such as the National Institute for Health and Clinical Excellence in the UK, the Istituto Superiore di Sanità in Italy and the World Health Organization in Geneva. New collaborations on research projects and

funding opportunities will start soon with colleagues working at the Johns Hopkins Bloomberg School of Public Health, the Department of Health and Social Care at the London School of Economics and the Department of Health Economics, Centre for Public Health at the University of Vienna.

Recent publications

1. Furukawa TA, Levine SZ, Tanaka S, Goldberg Y, Samara M, Davis JM, **Cipriani A,** Leucht S. (2014) Initial Severity of Schizophrenia and Efficacy of Antipsychotics: Participant-Level Meta-analysis of 6 Placebo-Controlled Studies. JAMA Psychiatry (in press).
2. **Cipriani A,** Geddes JR. (2014) Placebo for depression: we need to improve the quality of scientific information but also reject too simplistic approaches or ideological nihilism. BMC Medicine 12, 105.
3. Geddes JR, **Cipriani A,** Horne R. (2014) Communicating the harmful effects of medicines. BMJ 348, g4047.
4. Barbui C, Girlanda F, Ay E, **Cipriani A,** Becker T, Koesters M. (2014) Implementation of treatment guidelines for specialist mental health care. Schizophrenia Bulletin. 40, 737-9.
5. **Cipriani A,** Barbui C, Rendell J, Geddes JR. (2014) Clinical and regulatory implications of active run-in phases in long-term studies for bipolar disorder. Acta Psychiatrica Scandinavica 129, 328-42.
6. Barbui C, Conti V, **Cipriani A.** (2014) Antipsychotic drug exposure and risk of venous thromboembolism: a systematic review and meta-analysis of observational studies. Drug Safety 37, 79-90.
7. Efthimiou O, Mavridis D, **Cipriani A,** Leucht S, Bagos P, Salanti G. (2014) An approach for modelling multiple correlated outcomes in a network of interventions using odds ratios. Statistics in Medicine 33, 2275-87.

Professor Phil Cowen

Psychopharmacology Research Group

The Psychopharmacology group aims to understand the mechanism of psychotropic drug action at a neurobiological and neuropsychological level. We also aim to identify new targets for drug treatment using in vivo investigations in healthy volunteers and patient groupsnovel treatments.

Current research

The funding of the group comes from a Programme Grant Award from the Medical Research Council ('The Clinical Psychopharmacology of Depression'). Our current research makes use of the 7T MRI camera at the Oxford Centre for functional imaging of the brain which has unrivalled sensitivity for spectroscopic identification of brain neurochemicals.

Our current work uses MRS to identify the neurochemical correlates of inflammation and depression in patients undergoing interferon treatment for hepatitis C infection. This work is carried out in collaboration with Professor Ellie Barnes (Nuffield Dept of Medicine). We have shown that interferon treatment increases brain levels of the glutamate precursor, glutamine. This is a novel finding which links brain inflammation with changes in a neurotransmitter known to be involved in mood regulation. A parallel investigation is studying patients with major depression stratified for the presence of inflammatory markers which are raised in about a third of patients with major depression. Also, in collaboration with Professor Catherine Harmer, we are using challenge with typhoid vaccine in healthy participants as a means of establishing the effects of inflammation on emotional processing and other neuropsychological parameters linked to mood and cognition.

Another important strand of work consists of the repurposing of established drugs for psychiatric indications. We are engaged in a collaboration with the Department of Pharmacology where Grant Churchill and colleagues have identified an antioxidant drug called Ebselen as a possible lithium-mimetic through its ability to inhibit inositol monophosphatase. In a recent study funded by the BBSRC we were able to show that Ebselen lowers brain inositol levels and produces changes in emotional processing consistent with the effects of a mood stabiliser.

In a further collaboration with Professor Catherine Harmer's group we have established that changes in emotional processing as measured by fMRI in the first few days of antidepressant treatment is a significant predictor of those patients who will show a subsequent therapeutic response. This work confirms the importance of early changes in emotional processing in antidepressant action and suggests that it may be possible to predict antidepressant responders early in treatment- a finding of great potential utility to clinicians

Planned research

Future research will continue to identify the neural substrates of inflammation with the aim of developing new treatments for depressed patients unresponsive to conventional antidepressant agents. We also plan to carry out a clinical trial of Ebselen in bipolar patients to pursue the notion that Ebselen might prove to be a better tolerated and safer treatment than lithium. We will also collaborate with Prof David Nutt at Imperial College with whom we will use PET imaging to identify ways of measuring 5-HT release in the human brain in vivo. This would have important application to the study of the role of 5-HT neurones in a wide range of mental health problems.

Group members

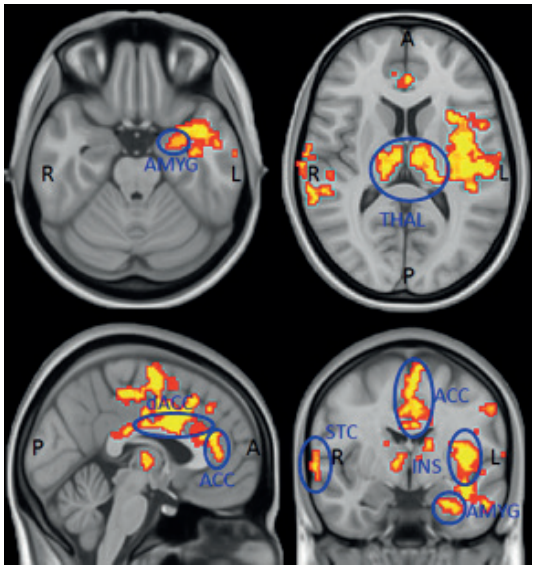
Dr Beata Godlewska – Clinical Scientist and Consultant Psychiatrist
Dr Charles Masaki – DPhil student
Ms Charlotte Cooper – DPhil student
Dr Uzay Emir – postdoctoral physicist
Dr Ann Sharpley – Research manager and Sleep Scientist
Ms Clare Williams – Research Nurse

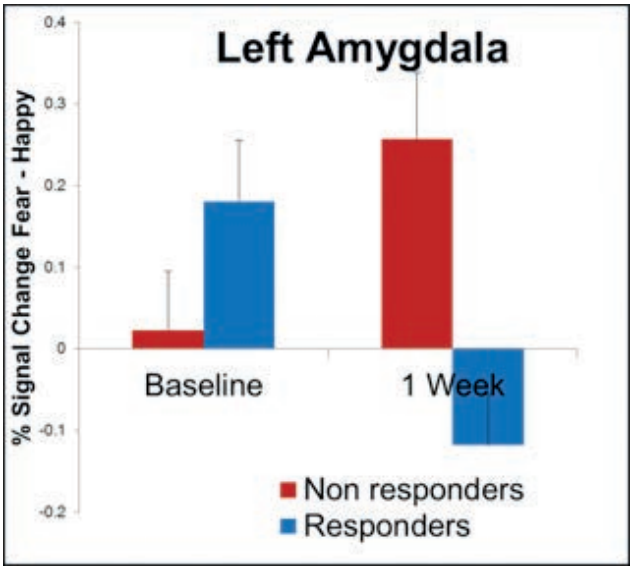
Collaborations

Professor Ellie Barnes (Nuffield Dept Medicine)
Dr Grant Churchill (Pharmacology)
Professor Catherine Harmer (Psychiatry)
Professor Peter Jezzard (FMRIB)
Professor David Nutt (Imperial College)
Professor Trevor Sharp (Pharmacology)

Recent publications

1. Taylor, M. J., Godlewska, B., Near, J., Christmas, D., Potokar, J., Collier, J., & Cowen, P. J. (2014). Effect of interferon -αon cortical glutamate in patients with hepatitis C: a proton magnetic resonance spectroscopy study. Psychological Medicine, 44, 789-795.
2. Godlewsk, B.R., Near, J. & Cowen, P.J. (2014) Neurochemistry of major depression: A study using magnetic resonance spectroscopy. Psychopharmacology (in press).
3. Mannie, Z.N., Filipinni, N., Williams, C., Mackay, C.E. & Cowen, P.J. (2014) Structural and functional imaging of the hippocampus in young people at familial risk of depression. Psychological Medicine (in press).
4. Diamond, P. R., Farmery, A. D., Atkinson, S., Haldar, J., Williams, N., Cowen, P. J., & McShane, R. (2014). Ketamine infusions for treatment resistant depression: a series of 28 patients treated weekly or twice weekly in an ECT clinic. Journal of Psychopharmacology, 0269881114527361.
5. Harmer, C. J., & Cowen, P. J. (2013) 'It's the way that you look at it'—a cognitive neuropsychological account of SSRI action in depression. Philosophical Transactions of the Royal Society B: Biological Sciences, 368(1615), 20120407.





The decrease in the amygdala response to fearful faces after one week of escitalopram administration in depressed patients predicts therapeutic response six weeks' later

Professor Klaus Ebmeier

Neurobiology of Ageing

Why do some people suffer from depression and memory loss as they age, while others are well throughout their lives? We examine the effect of genes and life history on ageing using neuropsychology and neuro-imaging and as part of large scale cohort and experimental studies. Our group is funded by MRC, NIHR, ARUK and Parkinson's UK.

Current research

- We test if the quality of white matter integrity measured by diffusion tensor imaging is associated with resilience of participants against localised brain damage, such as hippocampal atrophy in patients with amnestic cognitive impairment or indeed depression.
- We test if such good white matter integrity is associated with good quality (compensatory) functional resting networks, using resting fMRI.
- We examine mid-life risk and protective factors associated with white matter integrity. These will cover vascular risk factors, genetic risk, inflammatory markers, as well as psychosocial stress and life style experienced during working lives.

Planned research

- Cellular immune responses and endobiome compared with other indicators of (mental- and brain-) health in collaboration with Harri Alenius and Mika Kivimäki, Helsinki & Tunbridge/Harrison.
- Exercise and cognitive/emotional activation programmes in older volunteers and patients with MCI, part Oxford BRC Cognitive Health theme in collaboration with Johansen-Berg & Nobre.
- Quantifying participants' gait in collaboration with Helen Dawes, Elizabeth Casson Trust Chair, and Patrick Esser, of the Movement Science Group, Oxford Brookes University.
- DNA methylation as a risk marker for developing age-related cognitive decline in the Whitehall Imaging Cohort, with Chouliaras, Academic Clinical Fellow funded by the Oxfordshire Health Services Research Committee (OHSRC).

Group members

Charlotte Allan, Academic Clinical Lecturer in Old Age Psychiatry (NIHR); Sophie Behrman, CT3 in Psychiatry; Leonidas Chouliaras, Academic Clinical Fellow (NIHR); Nicola Filippini, Post-Doctoral Research Fellow (Wills Trust); Jane Fossey, Consultant Clinical Psychologist; Panagiotis Giannopoulos, Honorary Clinical Research Fellow (ST4); Rita Haapakoski-Helldan, Post-doctoral Research Fellow (ESCR); Verena Heise, DPhil Student (Alzheimer Research UK); Abda Mahmood Research Assistant (Wills Trust); Rupert McShane, Clinical Leader Thames Valley DeNDRoN; Ricarda A. L. Menke, Post-Doctoral Research Fellow (Parkinson's UK); Amanda Pipkin, PA Prof Klaus Ebmeier; Claire Sexton, Postdoctoral Research Assistant (NIHR); Sana Suri, DPhil Student (Clarendon Trust); Anya Topiwala, Clinical Lecturer (MRC), Ruth and Nevill Mott Scholar at Linacre College; Vyara Valkanova, Honorary Clinical Research Fellow (ST4); Philip Wilkinson, Honorary Senior Clinical Lecturer; EnikαZsoldos, Research Assistant, DPhil Student (MRC)

News and Impacts

- Talk to 6th-formers to stimulate interest in psychiatry: 'Didn't know psychiatry was so scientific'!
- Member of international Jury to decide on the establishment and funding of tripartite networks
- (University-Hospital-INSERM) for translational research in Lille (Centre covering a population of 5m in Northern France)
- Fortnight's Summer School Seminars: Depression: Life, science, or business interest? – Greifswald, German National Scholarship Foundation (largest and oldest German Foundation for academically gifted students to promoting future excellence)
- International Brain Banking Workshop, Royal Society of Edinburgh.

Recent publications

1. Filippini, N., E. Zsoldos, R. Haapakoski, C. E. Sexton, A. Mahmood, C. L. Allan, A. Topiwala, V. Valkanova, E. J. S. M. Smith, J. R. Geddes, A. Singh-Manoux, C. E. Mackay, M. Kivimaki, and K. P. Ebmeier. 2014. "Study protocol: The Whitehall II imaging sub-study." BMC Psychiatry 14:159. doi: 10.1186/1471-244X-14-159.
2. Heise, V., N. Filippini, A. J. Trachtenberg, S. Suri, K. P. Ebmeier, and C. E. Mackay. 2014. "Apolipoprotein E genotype, gender and age modulate connectivity of the hippocampus in healthy adults." Neuroimage 98:23-30. doi: 10.1016/j.neuroimage.2014.04.081.
3. Pievani, M., N. Filippini, M. P. van den Heuvel, S. F. Cappa, and G. B. Frisoni. 2014. "Brain connectivity in neurodegenerative diseases-from phenotype to proteinopathy." Nat Rev Neurol 10 (11):620-633. doi: 10.1038/nrneurol.2014.178.
4. Suri, S., A. Topiwala, C. E. Mackay, K. P. Ebmeier, and N. Filippini. 2014. "Using structural and diffusion magnetic resonance imaging to differentiate the dementias." Curr Neurol Neurosci Rep 14 (9):475. doi: 10.1007/s11910-014-0475-3.
5. Suri, S., C. E. Mackay, M. E. Kelly, M. Germuska, E. M. Tunbridge, G. B. Frisoni, P. M. Matthews, K. P. Ebmeier, D. P. Bulte, and N. Filippini. 2014. "Reduced cerebrovascular reactivity in young adults carrying the APOE epsilon4 allele." Alzheimers Dement. doi: 10.1016/j.jalz.2014.05.1755.

Professor Chris Fairburn and Professor Zafra Cooper

Centre for Research on Eating Disorders at Oxford (CREDO-1)
Centre for Research on Dissemination at Oxford (CREDO-2)

The mission of CREDO-1 is to further the understanding of the nature and treatment of eating disorders. The mission of CREDO-2 is to develop and evaluate methods to facilitate the global dissemination of effective psychological interventions.

Funding

Wellcome Principal Research Fellowship (Professor Fairburn)
Wellcome Strategic Award

Current research

CREDO is funded by a Strategic Award from the Wellcome Trust. It is engaged in two inter-related lines of research. The first is concerned with furthering the understanding and treatment of eating disorders, and the second is focused on the development of methods to facilitate the global dissemination of effective psychological interventions.

The research on eating disorders has established that CREDO's new transdiagnostic approach to treatment, "enhanced CBT" (CBT-E) is the most effective treatment for eating disorders in adults and that it can be used across all eating disorder diagnoses and in all treatment settings. There is great interest in the treatment worldwide. CBT-E is therefore being used as one of the exemplar psychological treatments in CREDO's dissemination research programme.

The dissemination research has two strands to it. The first is concerned with the development and evaluation of a scalable method for training therapists ("web-centred training"). The second line of is on delivering psychological interventions direct to sufferers using the internet ("web-centred treatment").

The work on web-centred training has necessitated the development of a sophisticated multi-modal training website. This includes a nine-hour training course and the development of a library of training material (including multiple recorded clinical demonstrations, learning exercises, handouts, etc.). Two such website have been constructed, one on CBT-E and the other on behavioural activation (BA).

This year we conducted a proof of concept study of web-centred training in CBT-E. This took place across all of Ireland. All eligible eating disorder therapists in Ireland took part. Each received guided web-centred training using our new CBT-E training website, the guidance being provided remotely from Oxford. Levels of compliance and satisfaction were high. The effects on therapist competence are being analysed.

This work has necessitated a major adjacent line of research on the measurement of therapist competence. This work is being led by Professor Cooper. It has resulted in the development and validation of both an emeasure and a role-play based measure.

The work of CREDO is described in more detail at **credo-oxford.com**.

Planned research

CREDO will be engaging in two lines of work, one on web-centred training and the other on web-centred treatment. The former will involve two studies:

1. North America Study – This study has just started. It involves two complementary RCTs, one on web-centred training in CBT-E and the other on web-centred training in behavioural activation (BA). Both RCTs involve eligible therapists (recruited from across North America) being randomised either to unguided training or guided training.

2. Global Study – This cohort study is designed to identify predictors of response to unguided web-centred training. Recruitment will be worldwide.

The work on web-centred treatment is in the developmental phase. We are creating an online version of CBT-E designed for direct access by sufferers. It will retain all the core strategies and procedures of CBT-E including the personalisation. It will undergo extensive preliminary testing before being formally evaluated as an unguided direct-to-user intervention

Core staff

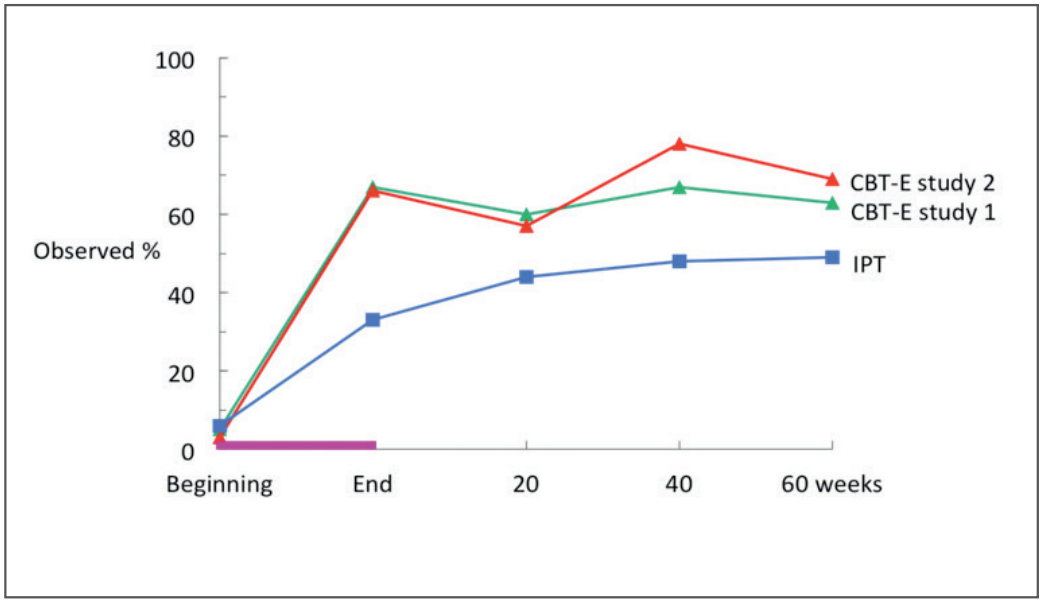
Kristin Bohn – Senior Research Clinician
Caroline Caddy – Research Assistant
Zafra Cooper – Principal Research Fellow, Deputy Director of CREDO
Christopher Fairburn – Wellcome Principal Research Fellow, Director of CREDO
Layla Hamadi – Research Assistant
Rebecca Murphy – Senior Research Clinician
Marianne O'Connor – Senior Research Coordinator
Katy Sivyer – Senior Research Assistant and doctoral student
Susanne Straebler – Senior Research Clinician

Key Collaborators

CREDO is collaborating with other research groups on complementary lines of work. The main collaborations are with the following inveatigators:
Riccardo Dalle Grave (Verona)
Helen Doll (UEA)
Stephen Hollon (Vanderbilt)
James Lock (Stanford)
Christopher Martell (Wisconsin-Milwaukee)
Marion Olmsted (Toronto)
Vikram Patel (LSHTM and Delhi)
Ray Rosen (NERI)
Joseph Ruzek (US VA)
G Terence Wilson (Rutgers)

Recent publications

1. Dalle Grave R, Calugi S, El Ghoch M, Conti M, Fairburn CG. Inpatient cognitive behavior therapy for adolescents with anorexia nervosa: Immediate and longer-term effects. Frontiers in Psychiatry 2014; 5: 1-7.
2. Fairburn CG, Patel V. The global dissemination of psychological treatments: a roadmap for research and practice. American Journal of Psychiatry 2014; 171: 495-498.
3. Patel V, Weobong B, Nadkarni A, Weiss HA, Anand A, Naik S, Bhat B, Pereira J, Araya R, Dimidjian S, Hollon SD, King M, McCambridge J, McDaid D, Murthy P, Velleman R, Fairburn CG, Kirkwood B. The effectiveness and cost-effectiveness of lay counsellor-delivered psychological treatments for harmful and dependent drinking and moderate to severe depression in primary care in India: PREMIUM study protocol for randomised controlled trials. Trials. 2014;15:101. doi: 10.1186/1745-6215-15-101.
4. Loucas CE, Fairburn CG, Whittington C, Pennant ME, Stockton S, Kendall T. E-therapy in the treatment and prevention of eating disorders: A systematic review and meta-analysis. Behaviour Research and Therapy 2014; 63: 122-131.
5. Poulsen S, Lunn S, Daniel SIF, Folke S, Mathiesen BB, Katznelson H, Fairburn CG. A randomized controlled trial of psychoanalytic psychotherapy versus cognitive behavior therapy for bulimia nervosa. American Journal of Psychiatry 2014: 171: 109-116.



Proportion of eating disorder patients in remission at each time point.

Professor Seena Fazel

Risk Factors for Mental Illness and Violent Crime

Current Activity

I am a Wellcome Trust Senior Research Fellow in Clinical Science and Honorary Forensic Psychiatrist. I apply novel methods and large population-based datasets to examine risk factors for violent crime and repeat offending, and develop clinical prediction rules for adverse outcomes in patients and mentally disordered offenders.

Current research

Over the last year, with colleagues at the Karolinska Institute, we have examined adverse outcomes in individuals with schizophrenia, including trends over time, risk factors, and a pharmaco-epidemiological study that found potentially important associations with antipsychotics and mood stabilizers. We have also completed reviews on mortality in psychiatric disorders (with Guy Goodwin), gun violence and suicide in individuals with mental illness, and an overview of health problems in homeless persons (with John Geddes). In addition, taking advantage of population-based datasets, we have reported links between psychiatric disorders and premature mortality in people who have suffered head injuries:

Planned research

Next year, we are completing a series of projects on risk factors for repeat offending and mortality in released prisoners, including psychiatric determinants and associations with treatment. We are also investigating clinical prediction rules for violent crime in patients with psychosis and mentally disordered offenders:

Group members

Zheng Chang, Achim Wolf, Omar Aziz, Isabel Yoon, Elizabeth Naomi Smith, Zuzanna Flimska, Jelle Lamsma, Adrian Hayes (ACF), Mark Toynbee (ACF). ZC has been awarded a prestigious post-doc at the University of Chicago and Karolinska Institute from 2015.

Collaborations

Outside Oxford: Medical Epidemiology and Biostatistics Unit, Karolinska Institute (Paul Lichtenstein, Henrik Larsson, Amir Sariaslan, Johan Zetterqvist, Yasmina Molero Samuelson, Niklas Långström), Jenny Shaw (Manchester). Within Oxford: Dept Primary Care Health Sciences (Susan Malett, Tom Fanshawe).

News and impacts

A number of our papers attracted considerable media attention including on the BBC, Guardian, Forbes, Telegraph, London Times, Wall Street Journal, Spiegel – our paper on head injury has attracted the 4th highest Altmetric score in JAMA Psychiatry's history, the mortality review on mortality the highest ever Altmetric score in World Psychiatry, and a review on mental illness and gun violence in Annals of Epidemiology, the 2nd highest. I have been interviewed for podcasts twice for the Lancet, and once for the Lancet Psychiatry 2014.

Recent publications

1. **Fazel S,** Zetterqvist J, Larsson H, Långström N, Lichtenstein P. (2014) Antipsychotics, mood stabilisers, and risk of violent crime. Lancet 384(9949):1206-14.
2. **Fazel S,** Wolf A, Palm C, Lichtenstein P. (2014) Violent crime, suicide, and premature mortality in patients with schizophrenia and related disorders: a 38-year total population study in Sweden. Lancet Psychiatry 1(1):44-54.
3. **Fazel S,** Pillas D, Wolf A, Lichtenstein P, Långström N. (2014) Suicide, fatal accidents, and other causes of premature mortality in traumatic brain injury: A 40-year Swedish population study. JAMA Psychiatry 71:326-333.
4. **Fazel S,** Geddes JR, Kushel M. (2014) The health of homeless people in high-income countries: descriptive epidemiology, health consequences, and clinical and policy recommendations. Lancet 384: 1529-1540.
5. Chesney E, Goodwin GM, **Fazel S.** (2014) Risks of all-cause and suicide mortality in mental disorders: a meta-review. World Psychiatry 13(2):153-60.

Professor Daniel Freeman

Oxford Cognitive Approaches to Psychosis (O-CAP)

Our research has shown that delusions and hallucinations are far more common than previously believed. Indeed many people in the general population will have experienced them in a relatively mild form. For others, however, these experiences can cause real distress. We work to understand why they happen and how they can be much more successfully treated.

Current research

Alongside a number of experimental studies developing the psychological understanding of psychosis, we have three main translational clinical trials taking place:

Better Sleep Trial (BEST) – Our latest theoretical research indicates the importance of insomnia in the occurrence and persistence of psychotic experiences. We are evaluating a CBT intervention for insomnia for individuals with delusions and/or hallucinations within the context of a diagnosis of psychosis. The trial is funded by the National Institute for Health Research (NIHR).

Virtual reality (VR) treatment – Many patients have difficulties going into situations with other people present. We are examining whether immersive virtual reality can help individuals with persecutory delusions feel safer. We will use virtual reality environments to help patients practice being with others.

Virtual reality (VR) treatment – Many patients have difficulties going into situations with other people present. We are examining whether immersive virtual reality can help individuals with persecutory delusions feel safer. We will use virtual reality environments to help patients practice being with others.

The Feeling Safer Programme (FSP) – We have been carefully developing a theoretically-driven and precisely targeted psychological treatment for persecutory delusions. Each of the components has now been successfully evaluated. In a case series we are currently evaluating a full treatment that combines all the evaluated modules. The aim is for recovery in persistent persecutory delusions in 50% of patients who receive the treatment. The trial is funded by the Medical Research Council.

Group members

Daniel Freeman, Jonathan Bradley, Bryony Sheaves, Felicity Waite, Angus Antley, Emilie Bourke, Natalie DeWeever, Josie McInerney, Georgina Geddes, Sarah Reeve.

We are delighted that Emma ernis, Nicole Evans, and Rachel Lister have all gained places on clinical psychology training courses.

In the news

This year our research has featured on BBC Radio 4's Today Programme, ITV Daybreak, 5 Live Breakfast, BBC World, and in many broadsheet and tabloid newspapers. Daniel Freeman has been writing a monthly article for The Guardian (see http://www.theguardian.com/profile/daniel-freeman)

Recent publications

1. **Freeman, D.,** Dunn, G., Murray, R., Evans, N., Lister, R., Antley, A., Slater, M., Godlewska, B., Cornish, R., Williams, J., Di Simplicio, M., Igoumenou, A., Brenneisen, R., Tunbridge, E., Harrison, P., Harmer, C., Cowen, P., Morrison, P. (2014). How cannabis causes paranoia: Using the intravenous administration of Δ9-tetrahydrocannabinol (THC) to identify key cognitive mechanisms leading to paranoia. Schizophrenia Bulletin. Jul 15. pii: sbu098.
2. **Freeman, D**. Pugh, K., Dunn, G., Evans, N., Sheaves, B., Waite, F., Cernis, E., Lister, R. & Fowler, D. (2014). An early Phase II randomised controlled trial testing the effect on persecutory delusions of using CBT to reduce negative cognitions about the self: the potential benefits of enhancing self confidence . Schizophrenia Research.
3. **Freeman, D**. Evans, N., Lister, R., Antley, A., Dunn, G., & Slater, M. (2014). Height, social comparison, and paranoia: an immersive virtual reality experimental study. Psychiatry Research, 30, 348-352.
4. Zavos, H.M.S., **Freeman, D.,** Haworth, C.M.A., McGuire, P., Plomin, R., Cardno, A.G., Ronald, A. (2014). Consistent etiology of severe, frequent psychotic experiences and milder, less frequent manifestations: A twin study of specific psychotic experiences in adolescence. JAMA Psychiatry, 71, 1049-1057.
5. **Freeman, D**. Startup, H., Dunn, G., Wingham, G., Cernis, E., Evans, N., Lister, R., Pugh, K., Cordwell, J., & Kingdon, D. (2014). Persecutory delusions and psychological well-being. Social Psychiatry and Psychiatric Epidemiology, 49, 1045-1050.

Grants

Medical Research Council Senior Clinical Fellowship. Nov. 2010-2015. Award: £1.4 million. 'Understanding and treating persecutory delusions: an interventionist-causal model approach.' Grantholder: Daniel Freeman

NIHR Research for Patient Benefit. 2012-2015. Award: £250,000. 'Treating insomnia in patients with delusions and hallucinations. Grantholders: Daniel Freeman (PI), H.Startup, E.Myers, J.Geddes, A.Harvey, L-M.Yu.

MRC/NIHR Efficacy and Mechanism Evaluation Programme. 2011-2014. Award: £670,000. 'The effects of reducing worry in patients with persecutory delusions: an explanatory randomised controlled trial.' Grantholders: Daniel Freeman (PI), David Kingdon, Helen Startup, Graham Dunn.

Wellcome Trust Strategic Award. 2012-2017. Award: £4.1 million. 'Sleep and Circadian Neurosciences Institute'. Grantholders: Foster (PI), Bannerman, Clifford, Davies, Freeman, Goodwin, Harrison, Holmes, Peirson, Wulff.

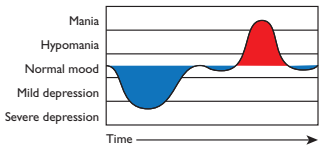
Maudsley Charity. 2012-2015. Award: £199,089. Improving cognitive therapy for persistent distressing delusions. Grantholders: Garety, P., Freeman, D., Jolley, S.

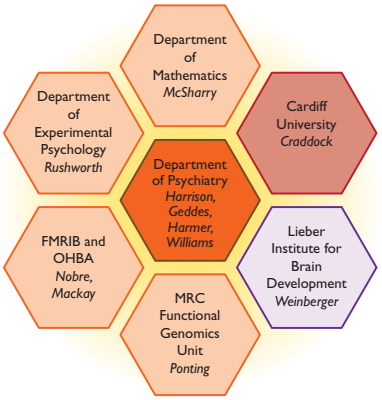
Professor John Geddes

Experimental Epidemiology and Bipolar Disorder

Our aim is to develop new treatments for people with mood disorders based on deep understanding of the underlying neurobiological mechanisms. Our research programmes include designs ranging from cell biology to clinical trials and large scale observational studies. In 2014, we produced our first stem cells derived from people with bipolar disorder (StemBANCC), analysed the CEQUEL trial and started work on Wellcome Trust funded CONBRIO programme.

CONBRIO





Current research

The Collaborative Oxford Network for Bipolar Research to Improve Outcomes (CONBRIO), our Wellcome Trust Strategic Award, started in earnest in 2014. CONBRIO is investigating the genetic and neural mechanisms underlying mood instability with the aim of developing successful intermediate outcomes to use in experimental medicine studies. JG leads Theme 1 of CONBRIO which aims to characterize and mathematically model the mood instability underlying bipolar disorder and other psychiatric conditions. Theme 1 will upscale our existing True Colours mood monitoring across the large Bipolar Disorder Research Network (collaboration with Nick Craddock, Lisa Jones et al) and augment self-reported mood monitoring with objective measures of activity, sleep, physiology and executive cognitive function, currently being developed in the AMoSS study. An exciting cross-theme development in CONBRIO has been the design of the OXLITH trial which will deeply characterise the short term effects of lithium on mood instability, behaviour, cognitive function and physiology. We also continue to collaborate widely across the Department and more broadly across Oxford on large scale projects such as StemBANCC (Cader), the Oxford Dementia Drug Discovery Institute (Lovestone/ Bountra) and OxDARE (Nobre/Mackay). Within the Oxford Collaboration for Leadership and Applied Health Research (CLAHRC), I lead Theme 1, which aims to evaluate innovative service developments and the bipolar self-management project within Theme 4:

Planned research

2015 will start with the final CEQUEL Investigator's Meeting see a further upscaling of CONBRIO activity across all themes. We are also developing plans and protocols for clinical trials in mood disorders across several stages.

Group members

Dr Mary-Jane Attenburrow, Dr Amy Bilderbeck
Dr Jennifer Rendell, Dr Chris Hinds, Hannah McMahon, Dr Kate Saunders, Zoe Reed, Dan Brett, Mike DiSanto, Ash Wadekar, Simon Bond, Bindi Chen, Matthew South, Maxim Osipov, Dr Katharine Smith.

Collaborations (within the Department)

Prof Andrea Cipriani (MTM, OxLith)
Prof Guy Goodwin (OXTEXT, CONBRIO, CEQUEL)
Prof Paul Harrison (CONBRIO, CEQUEL)
Prof Kia Nobre (CONBRIO, OxDARE)
Prof Clare Mackay (CONBRIO, OxDARE)
Prof Cath Harmer (CONBRIO)
Prof Simon Lovestone (CRIS, O3DI)
Prof David Miklowitz (CONBRIO)

Recent publications

1. Fazel S, **Geddes JR,** Kushel M The Health of Homeless Persons in High-Income Countries: Descriptive Epidemiology, Adverse Outcomes, and Public Health and Policy Recommendations Lancet 384, 9953, 1529 – 1540,doi:10.1016/S0140-6736(14)61132-6.
2. Miura et al Comparative Efficacy and Tolerability of Pharmacological Treatments in the Maintenance Treatment of Bipolar Disorder: A Network Meta-Analysis Lancet Psychiatry DOI: 10.1016/S2215-0366(14)70314-1.
3. Shine B, McKnight RF, Leaver L, **Geddes JR** The long-term effects of lithium on renal, thyroid and parathyroid function Lancet (in press).
4. Moore PJ, Little MA, McSharry PE, Goodwin GM, **Geddes JR** Correlates of depression in bipolar disorder Proc Biol Sci 281(1776):20132320 07 Feb 2014 doi: 10.1098/rspb.2013.2320 .
5. Sharpley, A.L., Hockney, R., McPeake, L., **Geddes, J.R.,** Cowen, P.J. Folic acid supplementation for prevention of mood disorders in young people at familial risk: A randomised, double blind, placebo controlled trial Journal of Affective Disorders 2014 167 306-311 DOI: 10.1016/j.jad.2014.06.011.

Professor Guy Goodwin

Experimental Medicine and Neurobiology of Mood Disorders

The future of psychiatry lies in the application of science and particularly neuroscience to its core problems. Bipolar disorder defines the challenge for understanding aetiology, co-morbidity and treatment. It is the paradigm functional disorder of the brain. My work is directed by these axioms.

Current and planned research

OXTEXT is a programme of research that looks at how self monitoring may be able to benefit people with bipolar disorder. It is organised around a simple to use web-based self monitoring system known as True Colours. The idea is that True Colours helps a person with bipolar disorder to live their life by helping them monitor their mood. Someone using True Colours will regularly record their mood states. Any major events or features of lifestyle are logged as well. By carefully tracking changes of mood, patterns begin to emerge. Relating even quite subtle shifts to external factors enables people to learn more about their condition. In this way, self monitoring gives people more control over their lives. It is a way of turning better self knowledge into better self management.

We have now extended this approach to automatic measures of movement and physiology using devices linked to a mobile phone app which acts as an extension of the mood monitoring system TrueColours.
This approach forms the basis for work in the Wellcome Trust **CONBRIO** Strategic award.

The Oxford Sleep and Circadian Neuroscience Institute, supported by a strategic award from the Wellcome Trust has been established. This virtual institute exemplifies the principle that cutting edge neuroscience can be applied to clinical problems.

Supported by:
Development and evaluation of a multidisciplinary service for people with bipolar disorder NIHR Programme Grants for Applied Research: RPPG-0108-10087 (with John Geddes)

A Sleep and Circadian neuroscience institute Wellcome Trust Strategic award (With Foster, Davies).

Group members

Jonathan Price
Amy Bilderbeck
Kate Saunders
Hannah MacMahon
Daniel Freeman
Bryony Shreeves
Kate Porcheret

Collaborations

Russell Foster
Kay Davies
Emily Holmes
ECNP bipolar network
P1vital

News and impacts

NIHR Senior Investigator (renewal)
President, ECNP Highly Cited Researcher 2014 (Thomson Reuters)

Recent publications

1. Yip, S. W., Worhunsky, P. D., Rogers, R. D., & **Goodwin, G. M.** (2014). Hypoactivation of the Ventral and Dorsal Striatum During Reward and Loss Anticipation in Antipsychotic and Mood Stabilizer-Naive Bipolar Disorder. Neuropsychopharmacology (in Press).
2. Ivins, A., Di Simplicio, M., Close, H., **Goodwin, G. M.,** & Holmes, E. (2014). Mental imagery in bipolar affective disorder versus unipolar depression: Investigating cognitions at times of 'positive'mood. Journal of Affective Disorders, 166, 234-242.
3. Bilderbeck, A. C., Saunders, K. E., Price, J., & **Goodwin, G. M.** (2014). Psychiatric assessment of mood instability: qualitative study of patient experience. The British Journal of Psychiatry, 204(3), 234-239
4. Rosa, A. R., Singh, N., Whitaker, E., de Brito, M., Lewis, A. M., Vieta, E., & **Goodwin, G. M.** (2014). Altered plasma glutathione levels in bipolar disorder indicates higher oxidative stress; a possible risk factor for illness onset despite normal brain-derived neurotrophic factor (BDNF) levels. Psychological medicine, 1-10
5. Clark, I. A., Mackay, C. E., & **Goodwin, G. M.** (2014). Pituitary gland volumes in bipolar disorder. Journal of affective disorders, 169, 197-202.

Professor Catherine Harmer

The Psychopharmacology of Emotion Research Laboratory

The Psychopharmacology of Emotion Research Lab (PERL) focuses on the mechanisms of treatment action in mood and anxiety disorders using a neurocognitive perspective. We have shown early psychological and neural effects of drug and psychological treatments which predict treatment efficacy in patient groupsneurocognitive perspective.

Current research

Wellcome Trust 'CONBRIO: Collaborative Network for Bipolar Research to Improve Outcomes.' £1.5M. Together with Paul Harrison, John Geddes and Kia Nobre.

UCB-Oxford Alliance funding: Early markers of cognitive enhancement: Developing and validating implicit measures of cognitive performance. **£350K**

Janssen Research & Development, investigator led grant: Stratification of treatment in depression using an experimental medicine model. **$915K**

Planned research

Our current research focuses on early markers of lithium treatment on mood instability in bipolar disorder, as part of the Wellcome Trust strategic grant **CONBRIO**.
We are also developing a research programme exploring mechanisms of treatment action in adolescents with depression in collaboration with local and international experts. A major challenge for improving treatment in psychiatry is the optimal combination of pharmacological and psychological treatments and part of our research focuses on understanding and facilitating the mechanisms for combined treatment approaches.

Group members

Research Assistant: Claire Shuttleworth
DPhil students: Maria Ironside, Kristin Schmidt, Jacqueline Scholl, Charlotte Cooper, Annabel Walsh, Matthew Warren, Helen Bould
Post-doctoral researchers: Corinna Klinge, Liliana Capitao, Deepa Pal
Clinician scientists: Michael Browning, Nathan Huneke, Andrea Reinecke
Research Fellow: Abbie Pringle

Collaborations

Our Collaborations within the Wellcome Trust strategic **CONBRIO** project include Daniel Weinberger (USA), Nick Craddock (Cardiff), Hugo Critchley (Brighton). See http://conbrio.psych.ox.ac.uk/who-we-are for full details. Professor Staffrod Lightman (Bristol): Pulsed glucocorticoid replacement therapy for patients with adrenocortical insufficiency secondary to Addison's disease and congenital adrenal hyperplasia. MRC project grant.

Professor Glyn Lewis: (London) What are the indications for prescribing antidepressants that will lead to clinical benefit (PANDA)?

Dr Kyle Pattison (Oxford): Effect of d-cycloserine on brain processing of breathlessness in patients with COPD undergoing pulmonary rehabilitation, Dunhill Medical Trust Award.

Dr Rebecca Park (Oxford) Hungry for reward – a translational study of brain processes underpinning Anorexia Nervosa" CIC, MRC award

News and impacts

Andrea Reinecke has been awarded a MQ fellowship on pharmaco-psychological approaches to the treatment of anxiety: understanding and improving underlying mechanisms of action.

Recent Publications

1. Reinecke A, Thilo K, Filippini N, Croft A, **Harmer CJ.**(2014) Predicting rapid response to cognitive-behavioural treatment for panic disorder: The role of hippocampus, insula, and dorsolateral prefrontal cortex. Behav Res Ther. E-pub.
2. Groenewold NA, Roest AM, Renken RJ, Opmeer EM, Veltman DJ, van der Wee NJ, de Jonge P, Aleman A, **Harmer CJ** (2014). Cognitive vulnerability and implicit emotional processing: imbalance in frontolimbic brain areas? Cogn Affect Behav Neurosci. E-pub.
3. Di Simplicio M, Doallo S, Costoloni G, Rohenkohl G, Nobre AC, **Harmer CJ** (2014) 'Can you look me in the face?' Short-term SSRI Administration Reverts Avoidant Ocular Face Exploration in Subjects at Risk for Psychopathology. Neuropsychopharmacology. 39(13):3059-66.
4. Miskowiak KW, Vinberg M, Christensen EM, Bukh JD, **Harmer CJ,** Ehrenreich H, Kessing LV (2014) Recombinant human erythropoietin for treating treatment-resistant depression: a double-blind, randomized, placebo-controlled phase 2 trial..Neuropsychopharmacology. 39(6):1399-408.
5. Scholl J, Günthner J, Kolling N, Favaron E, Rushworth MF, **Harmer CJ,** Reinecke A (2014). A Role Beyond Learning for NMDA Receptors in Reward-Based Decision-Making-a Pharmacological Study Using d-Cycloserine. Neuropsychopharmacology;39(12):2900-9

Professor Paul Harrison

Translational Neurobiology of Psychosis

The group focuses on neurobiological mechanisms which underlie bipolar disorder and schizophrenia, particularly those which have therapeutic potential. The research uses a wide range of approaches and methods, and involves many collaborations within the Department and beyondpublications.

Current research

Funded by a Wellcome Trust Strategic Award, **CONBRIO** (the Collaborative Oxford Network for Bipolar Research to Improve Outcomes), which I lead with John Geddes, is now in full swing. We have appointed to 10 posts. Projects include novel technologies for remote monitoring, molecular work, neuroimaging, and neuropsychology. An experimental medicine trial of lithium (OxLith), with several unique features, has been designed and should start early next year.

Liz Tunbridge and I continue to run the MRC-funded study of the dopamine-metabolising enzyme COMT, which is investigating how genotype, stress, and a COMT inhibitor drug interact to affect behaviour and brain activity. The first few subjects have completed the study, and recruitment will continue over the next year.

I also contribute to work on several other projects, including: anti-NMDA receptor antibodies in schizophrenia (led by Belinda Lennox); human and molecular studies within the Sleep and Circadian Neuroscience Institute Wellcome strategic award; and the bipolar disorder component of the EU IMI StemBANCC project.

Planned research

There are plans to extend CONBRIO, and a second research assistant will be appointed to the COMT study. In addition, I am involved a proposed European consortium on inflammation in psychiatric disorders, and a strategic initiative on autoimmune mechanisms in psychosis.

Group members

Tracy Lane (senior research assistant)
Jessica Laidlaw (research assistant)
Aintzane Garcia Bea (research fellow)
Esther Coutinho (DPhil student, with Angela Vincent)
Thomas Boerner (DPhil CASE student, with David Bannerman)
Katharina Stumpenhorst (DPhil student, with Liz Tunbridge)
Mary Walker (lab manager)
Li Chen (technician)
Sarah Atkinson (PA)

Collaborations

- **CONBRIO:** *John Geddes, Cath Harmer, Kia Nobre, Mark Williams, Clare Mackay, Matthew Rushworth (FMRIB), Chris Ponting (MRC FGU), Daniel Weinberger (Lieber Institute for Brain Development), Nick Craddock (Cardiff).*
- **COMET study:** *Liz Tunbridge, Clare Mackay, Cath Harmer, Rob Rogers (Bangor)*
- **StemBANCC**: *John Geddes, Guy Goodwin, Zam Cader (NDCN), Caleb Webber (MRC FGU).*
- **Sleep and Circadian Neuroscience Institute:** *Russell Foster (NDCN), Guy Goodwin, Daniel Freeman, David Bannerman (Experimental Psychology)*
- **Anti-NMDA receptor antibodies in schizophrenia:** *Belinda Lennox, Angela Vincent (NDCN).*

News and impacts

Tracy Lane (re)joined the group to work on the **CONBRIO** project.
Aintzane Garcia Bea joins us from Spain, having been awarded a Martin Escudero Fellowship.

I co-direct the new Wellcome Trust Oxford Mental Health Clinical Doctoral Programme, which funds psychiatrists in training to carry out a DPhil.

Recent Publications

1. Tao R, Cousijn H, Jaffe AE, Burnet PWJ, Edwards F, Eastwood SL, Shin JH, Lane TA, Walker MA, Maher BJ, Weinberger DR, **Harrison PJ,** Hyde TM, Kleinman JE (2014) Expression of ZNF804A in human brain and alterations in schizophrenia, bipolar disorder and major depression. A novel transcript fetally regulated by the psychosis risk variant rs1344706. JAMA Psychiatry 71 1112-1120.

2. Cousijn H, Haegens S, Wallis G, Near J, Stokes M, **Harrison PJ,** Nobre AC. Resting GABA and glutamate concentrations do not predict visual gamma frequency or amplitude. Proceedings of the National Academy of Sciences USA 111 9301-9306.

3. Betts JF, Schweimer JV, Burnham KE, Burnet PWJ, Sharp T, **Harrison PJ** (2014) D-amino acid oxidase is expressed in the ventral tegmental area and modulates cortical dopamine. Frontiers in Synaptic Neuroscience 6 11.

4. Schweimer JV, Coullon GSJ, Betts JF, Burnet PWJ, Engle SJ, Brandon N, **Harrison PJ*,** Sharp T* (2014) Increased burst firing of ventral tegmental area dopamine neurons in D-amino acid oxidase (DAO, DAAO) knockout mice in vivo. European Journal of Neuroscience 40 2999-3009. *Joint senior authors.

5. Barkus C, Sanderson DJ, Rawlins JNP, Walton ME, **Harrison PJ,** Bannerman DM (2015). What causes aberrant salience in schizophrenia? A role for impaired short-term habituation and the GRIA1 (GluA1) AMPA receptor subunit. Molecular Psychiatry 19 1060-1070. PMID: 25224260.

Professor Keith Hawton

Centre for Suicide Research

The aim of our research research is to investigate the causes of self-harm and suicide in order to contribute to better treatment and prevention of suicidal behaviour. Our research has resulted in initiatives which have prevented many deaths and influenced policy in other countries.

Current research

Multicentre Study of Self-harm in England
The CSR is the lead centre in the three-centre (Oxford, Manchester, Derby) six-hospital Department of Health-funded collaboration whereby specially collected data on patients presenting to the hospitals because of self-harm (intentional self-poisoning or self-injury) are combined to allow large-scale studies of trends in self-harm, clinical management, evaluation of national prevention initiatives, and outcomes (including suicide and other causes of death). The Oxford data are collected through the 39-year database of all self-harm episodes presenting to the John Radcliffe Hospital, which is the longest-standing monitoring system of its kind in Europe.

A multi-centre programme of clinical and public health research to guide health service priorities for preventing suicide in England
In collaboration with colleagues at the universities of Bristol and Manchester , the CSR is involved in a second National Institute for Health Research Programme Grant on a series of studies to contribute to health service initiatives relating to self-harm and suicide.

The Oxford-end work resulted in the recent launch of a module for the Healthtalk.org website (http://www.healthtalk.org/peoples-experiences/mental-health/self-harm-parents-experiences/topics) exploring parents' and carers' experiences of young peoples' self-harm, in collaboration with colleagues at the University of Oxford Health Experiences Research Group. The resource is based on detailed interviews with parents whose children have self-harmed. The module should provide support for families who are going through a similar experience and the site will serve as a teaching and clinical resource. From this work we have produced a pamphlet for parents and carers of young people who self-harm which we plan to make available to the public. We will also produce a guide for clinicians on this topic.

We are also studying the relative toxicity of a range of drugs commonly used for self-poisoning. The information will be used to inform prescribing practices.

Oxford-McGill Workshop Awarded
With colleagues at McGill University we won an Oxford-McGill Award which was used to host a workshop to explore the possibility of future collaborations with Professor Gustavo Turecki and his group on suicide research.

Cochrane Reviews
Three Cochrane systematic reviews are near completion on the effectiveness of psychosocial interventions following self-harm in adults, pharmacological interventions following self-harm in adults, and interventions following self-harm in children and adolescents.

Evaluation of safe storage of pesticides
This is a Wellcome Trust funded large-scale (162 villages) cluster-randomized trial of provision of lockable pesticide storage boxes to try to reduce suicide by pesticide ingestion in Sri Lanka. A separate study funded by the American Foundation for Suicide Prevention is examining the role of vendors in selling pesticides to individuals who use them for self-poisoning.

ALSPAC:
Professor Hawton is part of a group researching self-harm in adolescents using the Avon Longitudinal Study of Parents and Children (ALSPAC) cohort.

Internet research:
We have recently undertaken a study with Dr. Anne Stewart of the types of internet sites visited by young people who may be at risk of suicide.

Planned research

The Mindlock Project:
This is a collaboration with Drs Bergljot Gjelsvik and Catherine Crane at the Oxford Mindfulness Centre, in which cognitive mechanisms underlying persistent suicide risk, and their treatment, are being investigated.

Group members

Liz Bale, Deborah Casey, Dr Anne Ferrey, Dr Galit Geulayov, Professor Camilla Haw, Dr Kate Saunders, Dr Kat Witt.
Barnes Unit Research Nurse: Fiona Brand
Suicide Prevention Lead (Oxford Health NHS FT) Karen Lascelles.

Collaborations

Collaboration with Scandinavian researchers Professor Hawton is involved in a study with Margda Waern in Gothenberg to assess the long-term outcomes of women who were suicidal in middle age. He is also involved in an evaluation of reduced pack sizes of paracetamol in Denmark with Professor Merete Nordentoft and Dr Annette Erlangsen in Copenhagen.

Other Collaborations

Dr Seena Fazel; Dr. Louise Locock; Dr Anne Stewart; Dr Bergljot Gjelsvik; Professor Rory O'Connor (Glasgow University); Professor David Gunnell and Dr Becky Mars and Dr Chris Metcalfe (Bristol University); Professor Nav Kapur, Dr. Jayne Cooper (Manchester University); Keith Waters (Derbyshire NHS Foundation Trust); Dr. Ellen Townsend (Nottingham University), Dr Ella Arensman (Cork University), Professor Margda Waern (Gothenburg University); Professor Preben Mortenson (Aarhus University); Professor Merete Nordentoft, Dr. Annette Erlangsen and Professor Flemming Konradsen (Copenhagen University); Dr. Michael Eddleston (Edinburgh University); Professor Andrew Dawson and Professor Jane Pirkis (Melbourne University); Dr. Greg Carter (Newcastle University, Australia).

News and impacts

Professor Hawton was presented with the Medal of the Finnish Psychiatric Association at its Annual Meeting in Helsinki in October 2014.

We organise the annual British Isles Research Workshop on Suicide and Self-harm. This year the workshop included a second Lancet Symposium on Suicide in collaboration with The Lancet Psychiatry.

In February, Professors Hawton and Fazel (with Dr. Lisa Marzano) presented their work on self-harm in prisons to the All-Party Parliamentary Group on Prevention of Suicide and Self-harm.

We have been commissioned by Public Health England to develop a guide for preventing and responding to suicide clusters.

Recent publications

1. **Hawton, K**., O'Connor, R. C. Suicide (2013). Routledge. (A four-volume collection of classic papers)
.
2. Bergen, H., **Hawton, K.,** Webb, R., Cooper, J., Steeq, S., Haigh, M., Ness, J., Bergen, H., Hawton, K., Webb, R., Cooper, J., Steeq, S., Haigh, M., Ness, J., Waters, K., & Kapur, N. (2014). Alcohol-related mortality following self-harm: A multicentre cohort study. JRSM Open, 5, doi: 10.1177/2054270414533326.
3. **Hawton, K**., Linsell, L., Adeniji, T., Sariaslan, A. & Fazel, S. (2014). Self-harm in prisons in England and Wales: An epidemiological study of prevalence, risk factors, clustering, and subsequent suicide. The Lancet, 383, 1147-54. doi:10.1016/S0140-6736(13)62118-2.
4. Mars, B., Heron, J., Crane, C., **Hawton, K.,** Kidger, J., Lewis, G., Macleod, J., Tilling, K. & Gunnell, D. (2014) Clinical and social outcomes of adolescent self-harm: population based birth cohort study. BMJ, 349:g5954 doi: 10.1136/bmj.g5954.
5. O'Connor, R. C., Rasmussen, S. & **Hawton, K.** (2014). Adolescent self-harm: A school-based study in Northern Ireland. Journal of Affective Disorders, 159, 46-52.

Professor Emily Holmes

Experimental Psychopathology and Cognitive Therapies (EPaCT)

The Experimental Psychopathology and Cognitive Therapies (EPaCT) Team aims to use experimental techniques to increase our understanding of the mechanisms underlying psychiatric disorders and improve treatment. We are particularly curious about the role of mental imagery and emotion. Our research takes an interdisciplinary approach including psychology (basic and clinical), psychiatry, and cognitive (neuro) science.

Emily Holmes: Emily Holmes is a Visiting Professor in Clinical Psychology, Department of Psychiatry, University of Oxford, and Programme Leader at the MRC Cognition and Brain Sciences Unit, Cambridge.

Current research

Bipolar disorder, mental imagery, mood instability and cognitive therapy.

Group Members

- Susie Hales, Kerry Young, Martina Di Simplicio, Lalitha Iyadurai, Craig Steel, Rachel Manser and Emily Holmes (PI).

Oxford Collaborators

- Fairburn, Geddes, Goodwin, Attenburrow, Bonsall and the OxTEXT team.

Grant support

- The Wellcome Trust, NIHR
  We apply a cognitive approach to bipolar disorder. Our theory concerning mental imagery's role in mood instability (Holmes, Geddes, Colom & Goodwin, 2008) fuels the research and treatment development. Our clinic OxMAPP (Oxford Mood Action Psychology Programme) has been embedded in the Professorial Mood Disorders Clinic. We have now offered MAPP (Mood Action Psychology Programme) in a case series study of brief imagery-focused cognitive therapy (imCT) for Bipolar Disorder also with Psychological Services in Oxford Health NHS Foundation Trust.

Psychological trauma and involuntary mental images

Group Members

- Lalitha Iyadurai and Emily Holmes (PI).

Oxford Collaborators

- Mackay, Geddes, Nobre, Tunbridge, Harrison, Porcheret, Goodwin, Wulff, Foster.

Grant support

- NIHR, The Wellcome Trust, MRC
  We seek to better understand intrusive memories of trauma and develop an early preventative intervention after a traumatic event. We are doing the groundwork for translation to a clinical setting – the Emergency Department at the John Radcliffe Hospital, alongside experimental studies including sleep.

Depression, mental imagery and ageing

Group Members

- Simon Blackwell, Stephanie Burnett Heyes and Emily Holmes (PI).

Oxford Collaborators

- Nobre, Johansen-Berg, Murphy, Geddes, Browning.

Grant support

- NIHR, Lupina Foundation
  We are interested in cognitive biases in depression and the potential to modify them via computerised training programs known as Cognitive Bias Modification (CBM). We have recently completed a clinical trial for depression via the Internet (**OxIGen:** Oxford Imagery Generation). We have piloted this approach for resilience in ageing as part of our NIHR funding with **Nobre** (OHBA) and **Johansen-Berg** (FMRIB).

Recent Publications

1. Holmes, E. A., M. G. Craske, and A. M. Graybiel. "A Call for Mental-Health Science. Clinicians and Neuroscientists Must Work Together to Understand and Improve Psychological Treatments [Comment]." Nature 511, no. 7509 (2014): 287-89.
2. Blackwell, S. E., M. Browning, A. Mathews, A. Pictet, J. Welch, J. Davies, P. Watson, J. R. Geddes, and E. A. Holmes. "Positive Imagery-Based Cognitive Bias Modification as a Web-Based Treatment Tool for Depressed Adults: A Randomized Controlled Trial." Clinical Psychological Science (in press).
3. Malik, A., G. M. Goodwin, L. Hoppitt, and E. A. Holmes. "Hypomanic Experience in Young Adults Confers Vulnerability to Intrusive Imagery after Experimental Trauma: Relevance for Bipolar Disorder." Clinical Psychological Science (2014): 1-10.
4. Ivins, A., M. Di Simplicio, H. Close, G. M. Goodwin, and E. A. Holmes. "Mental Imagery in Bipolar Affective Disorder Versus Unipolar Depression: Investigating Cognitions at Times of 'Positive' Mood." Journal of Affective Disorders 166 (2014): 234–42.
5. Clark, I. A., C. E. Mackay, and E. A. Holmes. "Low Emotional Response to Traumatic Footage Is Associated with an Absence of Analogue Flashbacks: An Individual Participant Data Meta-Analysis of 16 Trauma Film Paradigm Experiments." Cognition and Emotion (2014).

Group members and news

Emily Holmes: Received the American Psychological Association (APA) Distinguished Scientific Award for Early Career Contribution to Psychology in the area of Psychopathology (2014). Advisor to the charity "MQ: transforming mental health" for their Fellows Programme, and Associate Editor *"Clinical Psychological Science"*. Goodbyes go to **Ian Clark** who has moved from an MRC postdoctoral position in Oxford to a new postdoctoral research associate position at University College London, and **Arnaud Pictet**, who has finished his DPhil in Oxford and now holds a postdoctoral research position at the University of Geneva. Goodbye to **Ella James** who has finished her DPhil in Oxford and now holds a postdoctoral researcher position at the MRC-CBU. Congratulations to Stephanie Burnett Heyes who will be taking up a lectureship in Birmingham in 2015. Congratulations to **Susie Hales** currently on maternity leave. **Simon Blackwell** continues as an Investigator Scientist at the MRC Cognition and Brain Sciences Unit (MRC-CBU) in Cambridge. – continues as a Career Development Fellow at the MRC-CBU.

It's a way of keeping the blue away

She feels like a big red blob as a result of feeling so exited

It has been a week and the blue circle is remaining small and out of the way

Josephine McInerney – Artist in Residence Warneford Hospital 2010-2011, reproduced in Di Simplicio, M., McInerney, J. E., Goodwin, G. M., Attenburrow, M., & Holmes, E. A. (2012). Revealing the mind's eye: Bringing (mental) images into psychiatry. American Journal of Psychiatry, 169(12), 1245-1246. doi: 10.1176/appi.ajp.2012.12040499)

Professor Belinda Lennox

Enhancing Outcomes for Early Psychosis

My research is on the causes and treatment of psychotic illnesses. I am exploring both the neuro-immunological basis of psychosis, and the translation of evidence based care into practice for those experiencing a first episode of psychosis.

Current research

We are undertaking a screening study for pathogenic antibodies in first episode psychosis across England, funded by MRC. We are also undertaken antigen discovery. We are also undertaking a feasibility study for the treatment of patients with psychosis and antibodies with immunotherapy, funded by MRC Confidence in concept. This will assess the feasibility of large scale screening of patients with psychosis from across England.

We are undertaking the implementation and evaluation of early intervention in psychosis services across the Thames Valley, funded by NIHR CLAHRC Oxford and Oxford AHSN. This is in collaboration with networks of clinicians and patients from across the region

Planned research

We are planning a phase IIa RCT of immunotherapy in patients with psychosis and antibodies. We are planning a large programme of work to understand the mechanism of action of these antibodies in collaboration with colleagues from across Oxford.

Group members

Emma Palmer, postdoc researcher
Jane Hainsworth, administrator

Collaborations

- Paul Harrison, Dan Freeman, Matthew Broome, John Geddes Department Psychiatry, Oxford
- Angela Vincent, Camilla Buckley, Sarosh Irani, Isabel Leite Department Clinical Neurosciences Oxford
- Alasdair Coles, Mike Zandi Department Clinical Neurosciences Cambridge
- Peter Jones, Julia Deakin, Department Psychiatry Cambridge
- Sarah Amani, Oxford AHSN
- Alex Gardiner, Angela Aristidou, Richard Hobbs Oxford CLAHRC

News and impacts

I run a joint psychiatry-neuroimmunology service at OUH NHS Trust with Dr Camilla Buckley, linked with Prof Angela Vincent's neuroimmunology laboratory service, with national and international referrals.

I have been appointed Clinical Director for the NIHR Clinical Research Network for Thames Valley and South Midlands April 2014.

Recent Publications

1. Plaistow J, Masson K, Koch D, Wilson J, Stark R, Jones PB, Lennox BR 2014 Young People's views of UK mental health services Early Intervention In Psychiatry 8(1):12-23.
2. Deakin J, Lennox BR, Zandi MS 2014 Antibodies to the NMDA receptors and other synaptic proteins in psychosis. Biological Psychiatry 75(4):284-291.
3. Rickards H, Jacob S, Lennox BR, Nicholson T 2014 Auto-immune encephalitis: A potentially treatable cause of mental disorder. Advances in Psychiatric Treatment 20: 92-10.
4. Zandi MS, Paterson RW, Ellul MA, Jacobsen L, Al-Diwani A, Jones J, Cox A, Lennox B, Stamelou M, Bhatia KP, Schott J, Coles AJ, Kullman D, Vincent A.2014 Clinical relevance of serum antibodies to extracellular N-methyl-d-aspartate receptor epitopes. Journal Neurology Neurosurgery Psychiatry epub 22nd Sept 10.1136/jnnp-2014-308736.
5. Khandaker GM, Cousins L, Deakin J, Lennox BR, Yolken R, Jones PB 2014 Inflammation and immunity in schizophrenia: implications for pathophysiology and treatment Lancet Psychiatry in press.

Professor Simon Lovestone

Translational Neuroscience and Dementia Research Group

We have three main areas of activity; all aiming towards secondary prevention of dementia. By understanding disease mechanisms we seek potential therapeutics; through discovery of biomarkers we hope to enable preventative trials and with informatics we utilise large biological and clinical datasets in the support of translational neuroscience.

Current research

From mechanisms to drug development

Alzheimer's disease has two main pathological lesions – the plaque and the tangle – although many other pathological processes are involved in the brain, including inflammation and vascular damage. Some twenty years ago I worked in the group of Brian Anderton at KCL to try and find the enzymes responsible for phoshorylating tau protein, a process thought to underlie the formation of tangles. This work led me, and others, to Glycogen Synthase Kinase-3 (GSK-3) and from there to the regulation of this kinase by insulin and the wnt signalling pathways. My group has over the years demonstrated that GSK3 is one of the predominant tau-kinases and that inhibition of GSK-3 prevents tau phosphorylation in model systems and that inhibition of GSK-3 activity is necessary for long term potentiation, a mechanism of brain plasticity that perhaps is at least in part responsible for some of the cellular processes necessary in forming memories. We have led trials of GSK-3 inhibitors as potential disease modification agents and are now further refining our understanding of the disease process and developing alternative targets for drug development for disease modification.

Blood based biomarkers to enable clinical trials

Alzheimer's disease has a long prodromal period – a time when the pathological process is active in the brain but not yet causing substantial, if any, symptoms. If we could identify people in this pre-clinical phase then there might be a 'window of opportunity' whereby drugs would be more likely to be effective than later when the disease was more fully established and neurons were being lost. In this window of opportunity a disease modification that was effective would be in effect a preventative therapy. However, in order to identify people in this phase of disease for clinical trials and one day for intervention, then biomarkers are needed. We have chosen to focus our attention on searching for blood based biomarkers to complement the work of many other groups that has been so successful in identifying spinal fluid markers and using imaging, including PET imaging, as markers of disease. A blood based marker would be less invasive and more readily available than CSF or PET imaging. Using a range of approaches we and our collaborators have looked for such a biomarker in the proteome, the transcriptome, the epigenome and the metabolome. We have used a range of approaches in all of these studies in discovery and then replication and validation phase. Perhaps the most important contribution we have made is not just in the actual findings, many of which have been replicated by others, but also in the design of studies as we have moved away from a case-control and more towards an 'endophenotype' approach whereby we search for a biomarker in comparison to a continuous and quantitative indication of disease status. Using these technologies and this design we have got close to a set of markers to be used as a biomarker, most likely in combination with other specific markers of pathology.

The power of numbers – informatics in translational research

In both our mechanisms and biomarkers work we are analysing relatively large datasets using a range of statistical approaches including machine learning. As a consequence of this informaticians and statisticians have come to play an increasingly important role in the group. Building on this expertise, we are now turning attention to datasets beyond genomic and proteomic to clinical and imaging data. Through initiatives such as the Case Records Interactive Search process, generated first at the Maudsley and now rolling out across the UK, to the European Medical Information Framework our group has access to very large datasets from cohort and other research studies and from routine care and are using these data to advance experimental medicine seeking preventative strategies for dementia.

Planned research

Over the next year my group and I will seek to accelerate work towards disease modification of dementia including:

- The Deep and Frequent Phenotyping study; a very detailed multimodal biomarker study to identify markers of progression in preclinical dementia
- Further drug development programmes building on successful compound identification in primary and secondary screens
- Validation and then qualification of blood based biomarkers of dementia and preclinical disease
- Identification and replication of blood based biomarkers for Parkinson's disease
- Working to establish the Dementias Platform UK, especially the informatics components, establishing the European Prevention of Alzheimer's Disease public private consortium and building on the European Medical Information Framework, a data aggregation and access programme
- Using medical informatics from electronic medical records to understand the role of inflammation in dementia aetiology.

Group members

Elena Ribe Garrido – senior post doctoral researcher in mechanisms and drug discovery
Alison Baird – senior post doctoral researcher in biomarkers
Alejo Holgado Nevado – senior post doctoral bioinformatician
Laura Thei – post doctoral researcher in mechanisms
Sarah Westwood – post doctoral researcher in biomarkers
Jessica Ash – post doctoral research worker; data analysis and project management
Jennifer Lawson – clinical trials co-ordinator
Benjamine Liu – student working on bioinformatics and Parkinson's disease
Corinne Prescott – research administrator

Collaborations

- The European Medical information Framework (www.emif.eu) – a public private consortium with more than 50 partners in Europe
- The Wellcome Trust Strategic Award in neuroinflammation including three companies and more than five universities
- The MRC COEN award in wnt signalling between Cuadrado (Madrid), Lovestone (Oxford) and Woodgett (Toronto)
- The Dementias Platform UK bringing together groups across the UK
- The IMI European Prevention Of Alzheimer's Disease grant bringing together more than 50 partners to establish cohorts and clinical trials for AD prevention

Recent Publications

1. Hye, A., J. Riddoch-Contreras, A. L. Baird, N. J. Ashton, C. Bazenet, R. Leung, E. Westman, A. Simmons, R. Dobson, M. Sattlecker, M. Lupton, K. Lunnon, A. Keohane, M. Ward, I. Pike, H. D. Zucht, D. Pepin, W. Zheng, A. Tunnicliffe, J. Richardson, S. Gauthier, H. Soininen, I. Kloszewska, P. Mecocci, M. Tsolaki, B. Vellas, and **S. Lovestone. 2014.** "Plasma proteins predict conversion to dementia from prodromal disease." Alzheimers Dement. doi: 10.1016/j.jalz.2014.05.1749.
2. Killick, R., E. M. Ribe, R. Al-Shawi, B. Malik, C. Hooper, C. Fernandes, R. Dobson, P. M. Nolan, A. Lourdusamy, S. Furney, K. Lin, G. Breen, R. Wroe, A. W. To, K. Leroy, M. Causevic, A. Usardi, M. Robinson, W. Noble, R. Williamson, K. Lunnon, S. Kellie, C. H. Reynolds, C. Bazenet, A. Hodges, J. P. Brion, J. Stephenson, J. P. Simons, and **S. Lovestone. 2014.** "Clusterin regulates beta-amyloid toxicity via Dickkopf-1-driven induction of the wnt-PCP-JNK pathway." Mol Psychiatry 19 (1):88-98. doi: 10.1038/mp.2012.163.
3. Leung, R., P. Proitsi, A. Simmons, K. Lunnon, A. Guntert, D. Kronenberg, M. Pritchard, M. Tsolaki, P. Mecocci, I. Kloszewska, B. Vellas, H. Soininen, L. O. Wahlund, and **S. Lovestone. 2013.** "Inflammatory proteins in plasma are associated with severity of Alzheimer's disease." PLoS One 8 (6):e64971. doi: 10.1371/journal.pone.0064971.

Professor Clare Mackay

Translational Neuroimaging Group

Neuroimaging provides a window into the living brain, and is an increasingly vital experimental medicine tool for neuro-psychiatric disease. With a particular focus on early and pre-clinical disease, the Translational Neuroimaging Group explore how the brain changes before symptoms take hold.

Current Research:

The main focus of our work is to use neuroimaging to investigate and ultimately predict risk for neurodegenerative disease. Our current portfolio includes:

- **Genetic risk for Alzheimer's disease** (Alzheimer's Research UK and the HDH Wills 1965 Charitable Trust)
- **Oxford Parkinson's Disease Centre opdc.ox.ac.uk;** Parkinson's UK and the Monument Trust
- **Deep & Frequent Phenotyping** feasibility study (NIHR/MRC)
- **Whitehall II imaging study** (MRC, more details on Prof Klaus Ebmeier's page)
- **Cognitive Health in Ageing** (NIHR programme),
- **Collaborative Oxford Network for Bipolar Research to Improve Outcomes (CONBRIO, Wellcome Strategic Award)**

Planned research

The core **OPDC** grant was recently renewed for a further 5 years. As well as forward translating our imaging methods to the clinic, we will be back-translating to incorporate imaging for OPDC animal models.

As imaging becomes more mainstream within experimental medicine and clinical practice, new informatics strategies are required. Clare Mackay is leading **imaging informatics** for the MRC Dementia Platform UK, which will take shape in the coming year.

Plans will continue to be developed for **clinical translation** of state-of-the-art neuroimaging for memory clinic patients at the newly expanded OHBA (see separate page).

Group members

Postdoctoral Researchers: Dr Nicola Filippini, Dr Ludavica Griffanti. DPhil Students: Michal Rolinski, Sana Suri, Eniko Zsoldos, Clare O'Donaghue, Anya Topiwala. OxDARE Assistants: Sophie Hockley, Aimie Gornall.

Collaborations

Collaboration is at the heart of what we do, as exemplified by the creation of **OxDARE** (see separate page). In addition we are active contributors to local **(OPDC, ARUK local network, CONBRIO)** and national **(MRC Dementia Platform UK, NIHR Translational Research Collaboration for Dementia, TRC-D)** collaborative initiatives.

News and impacts

Our functional imaging marker of early PD received international media attention this year **(http://goo.gl/eVJ5Cy).** Clare Mackay also participated in radio and newspaper/magazine articles to promote dementia research in Oxford.

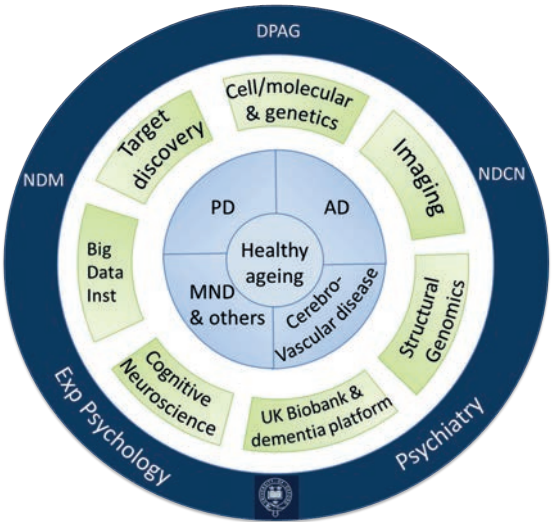
Recent publications:

1. Szewczyk-Krolikowski K, Menke RA, Hu M, Filippini N, Talbot K, & **Mackay CE.** Functional connectivity in the Basal Ganglia network differentiates PD patients from Controls. Neurology, 2014; 83;3;208-14.
2. Suri S, **Mackay CE,** Kelly ME, Germuska M, Tunbridge EM, Frisoni GB, Matthews PM, Ebmeier KP, Bulte DP, Filippini N. Reduced cerebrovascular reactivity in young adults carrying the APOE 4 allele. Alzheimer's and Dementia, 2014 (in press).
3. Heise V, Filippini N, Trachtenberg AJ, Suri S, Ebmeier KP, **Mackay CE.** Apolipoproten E genotype, gender and age modulate connectivity of the hippocampus in healthy adults. NeuroImage, 2014; 98; 23 – 30.
4. Filippini N, Zsoldos E, Haapakoski R, Sexton CE, Mahmood A, Allan CL, Topiwala A, Valkanova V, Brunner EJ, Shipley MJ, Auerbach E, Moeller S, Ugurbil K, Xu J, Yacoub E, Andersson J, Bijsterbosch J, Clare S, Griffanti L, Hess AT, Jenkinson M, Miller KL, Salimi-Khorshidi G, Sotiropoulos SN, Voets NL, Smith SM, Geddes JR, Singh-Manoux A, **Mackay CE,** Kivimai M, Ebmeier KP. Study protocol: The Whitehall II Imaging Sub-study. BMS Psychiatry, 2014, 30; 14; 159.

5. Suri S, Heise V, Trachtenberg AJ & **Mackay CE.** The forgotten APOE allele: a review of the evidence and suggested mechanisms for the protective effect of APOE 2. Neuroscience and Biobehavioral Reviews, 2013; 37:2878-86.

Oxford Dementia and Ageing Research (OxDARE) (www.oxdare.ox.ac.uk)
(Clare Mackay & Kia Nobre) was established in 2012 by the NIHR Oxford Biomedical Research Centre to 1) define the vision and set strategic priorities to establish Oxford as a world-leading centre for translational research promoting Cognitive Health, and 2) to create and maintain the infrastructure, to achieve the vision.

OxDARE's first objective was to map out the landscape of dementia research in Oxford, and began the process of identifying and attracting major new appointments. We are now in a period of major infrastructure expansion. In 2014 alone, OxDARE's leaders attracted >£100M of new funding, and are major contributors to the NIHR Translational Research Collaboration for Dementia (TRC-D) and the MRC Dementia Platform UK



Preserving health in old age is our core objective, and this can be best achieved by gaining a deep understanding of the diseases and disorders that threaten cognitive health, using the full range of world-leading expertise and technologies that are spread across several University departments, embedded within the NHS trusts and rich network of public-private partnerships.

Within Oxford, internationally leading programs of integrated basic and patient-based research, centred on target discovery, analysis of 'big data', imaging and cognitive neuroscience across the major dementia disease areas: Alzheimer's disease (Prof Simon Lovestone), Parkinson's disease (Drs Richard Wade Martins, Michele Hu), vascular dementia (Prof Peter Rothwell), amyotrophic lateral sclerosis (Prof Kevin Talbot & Dr Martin Turner) and frontotemporal dementia (Dr Chris Butler) are now aligned around a vision to become an international leader in understanding, treating and preventing dementia across a range of neurodegenerative diseases.

Professor Kia Nobre

Oxford Centre for Human Brain Activity

I am a cognitive neuroscientist interested in the principles of organisation of neural systems supporting cognition. In 2014 I became the inaugural incumbent of the Chair in Translational Cognitive Neuroscience at Oxford, through which I hope to integrate fundamental cognitive neuroscience research with clinical and applied research to promote cognitive health.

Leadership positions

I head the Brain & Cognition Lab, direct the Oxford Centre for Human Brain Activity (OHBA), and lead the Cognitive Health Working Group and Research Programme of the Oxford Biomedical Research Centre (BRC). Other positions of responsibility I currently hold include being: psychology and neuroscience delegate for Oxford University Press, reviewing editor for the Journal of Neuroscience, associate editor for the Journal of Cognitive Neuroscience, advisor to the Understanding Human Cognition Program of the James S McDonnell Foundation, and member Society for Neuroscience Young Investigator Award and International Research Award Selection Committees.

Research

My research is aimed at revealing how the human brain proactively, dynamically, and flexibly shapes the construction of our percepts and memories. I use a cognitive-neuroscience approach to reveal the mechanisms of adaptive cognition, as well as to understand cognitive deficits in neuropsychiatric and neurodegenerative conditions. Through my Wellome Trust Senior Investigator Award, I am investigating how memories and current goals influence perception of events in dynamic environments. Through the Wellcome Trust **CONBRIO** strategic award, we are investigating whether volatility in neural networks involved in the regulation of cognitive and emotional functions contributes to mood instability in bipolar disorder in order to develop an experimental model of the disorder to support treatment development (in collaboration with Matthew Rushworth, Catherine Harmer, John Geddes, and Paul Harrison). Through an EU Initial Training Network, my group joins collaborators in Oxford (Glyn Humphreys and Masud Husain) an in Europe to investigate deficits in attention and means for their rehabilitation. Through the NIHR Cognitive Health in Ageing (CHA) programme, we are exploring the ability of neural and cognitive plasticity to mitigate cognitive decline during ageing (in collaboration with Emily Holmes and Heidi Johansen-Berg). A collaborative activity award from the James McDonnell Foundation enables my research group to explore the nature of neural oscillations and their putative causal contributions to cognition with other groups around the world. A Partnership Grant from the MRC links OHBA to other MEG centres in the UK to build capacity, develop common procedures, and train future MEG researchers. Several members of my research group also hold their own competitive sources of funding through individual fellowships and studentships (Wellcome Trust, Royal Society, NIHR, ESRC, and Rhodes).

Group members

The Brain & Cognition Lab is a large and vibrant research group straddling the Departments of Psychiatry and Experimental Psychology. Postdoctoral fellows include: Susie Murphy, Céline Gilebert, Zita Patai, Nahid Zokaei, Natalie Nelissen, Adam Baker, and Andrew Quinn. Graduate students include: Nick Myers, Joshua Chauvin, Robert Mok, Theresa Wildegger, Lali Iyadurai, Paul Greig, Juliian de Freitas, Simone Heideman, Malcolm Proudfoot, Sophie Raeder, and Nora Rouast. Visitors and research assistants include: Priyanka Panchal, Gerardo Salvato, Jasper Hajonides van der Meulen, and Tayla McCloud. Undergraduate project students are: James Baker, Jessica Bone, and Sammi Chekroud.

Collaborations

My research group collaborates widely in Oxford and further afield. Our collaborators in Oxford include: Chris Butler (NDCN), John Geddes, Catherine Harmer, Paul Harrison, Helen Higham (NDCN), Glyn Humphreys (EP), Heidi Johansen-Berg (FMRIB), Clare Mackay, Matthew Rushworth (EP), Gaia Scerif (EP), Mark Stokes,

Liz Tunbridge, Martin Turner (NDCN), Mark Woolrich. We also have many outside collaborators: Duncan Astle (CBU Cambridge), André Cravo (São Paulo), Jenny Coull (Marseille), Sonia Doallo (Santiago de Compostella), John Duncan (CBU Cambridge), Karl Friston (UCL), Adam Gazzaley (UCSF), Emily Holmes (CBU Cambridge), Sabine Kastner (Princeton), Robert Knight (Berkeley), Marsel Mesulam (Notherwestern), Gustavo Rohenkohl (Frankfurt), and Kimron Shapiro (Birmingham).

News

My main achievement this year was to become the first Chair in Translational Cognitive Neuroscience at Oxford, a position held jointly between the Departments of Psychiatry and of Experimental Psychology. I was also fortunate to receive major funding from the Wellcome Trust in the form of a Senior Investigator Award and as part of the Strategic Award on Bipolar Research to Improve Outcomes (PI Harrison & Geddes). This year, our substantial tome, the Handbook of Attention (AC Nobre and S Kastner, Eds) was published by OUP. I gave several invited seminars and international keynote lectures, including at the Federation of European Neurosciences Societies (FENS) Forum (Milan, Italy) and the European Society for Cognitive and Affective Neuroscience (ESCAN) Conference (Dortmund, Germany). I continued engaging with public dissemination of science by contributing to the production of a documentary by BBC4, Everyday Miracles, and by joining amazing colleagues at the World Science Festival in New York, in the programmes: The Deceptive Watchman: **Mind, Brain, and Time and Are We There Yet? Brain Science And The Mystery Of Time.**

Recent Publications

1. Kuo BC, Murray AM, Stokes MG, **Nobre AC (2014)** Attention Biases Visual Activity in Visual Short-term Memory. J Cogn Neurosci 26(7):1377-89.
2. Cousijn H, Haegens S, Wallis G, Near J, Stokes MG, Harrison PJ, **Nobre AC (2014)** Resting GABA and glutamate concentrations do not predict visual gamma frequency or amplitude. Proc Natl Acad Sci USA 111(25):9301-9306.
3. Myers NE, Stokes MG, Walther L, **Nobre AC (2014)** Oscillatory brain state predicts variability in working memory. J Neurosci 34(23):7735-43.
4. Rohenkohl G, Gould IC, Pessoa J, **Nobre AC (2014)** Combining spatial and temporal expectations to improve visual perception. J Vis. 14(4).
5. **Nobre AC,** Kastner S (Eds) (2014) Handbook of Attention. Oxford: Oxford University Press .ncbi.nlm.nih.gov/

Follow me on Twitter: @kianobre

Dr Rebecca Park

Oxford Brain and Body Research in Eating Disorders (OxBREaD)

We focus on defining the psychological, and neural processes underpinning anorexia nervosa, and translating this deeper understanding into the development of novel treatments.

My research group **OxBread** has developed transdisciplinary collaborations with clinical, behavioural and neuroscientists,. We primarily investigate the most severe form of eating disorder, Anorexia Nervosa which has the highest mortality of any psychiatric disorder and leads to chronic morbidity, yet there is a paucity of evidence based treatments. It is thus essential to develop novel, more effective treatments based on an understanding of key processes maintaining the illness.

Extensive clinical experience is central to guiding our translational research: I am Consultant Psychiatrist to the Oxfordshire NHS specialist eating disorders service and we particularly value the experience of individuals affected by eating disorders in guiding our studies. Additionally, I lead teaching on eating disorders within the University of Oxford to undergraduates, clinical medical students, and postdoctoral students.

Current research

We investigate the neural basis of Anorexia Nervosa and from our findings are deriving and developing novel forms of treatment targeting these processes. We have recently completed data collection on a multimodal neuroimaging study of AN incorporating parallel resting state and task based fMRI and MEG. With the help of an MRC Confidence in Concept Award we are in the final stages of two complimentary studies;

1. **A multimodal imaging study** of neural processing and reward in individuals with current and past Anorexia Nervosa, in collaboration with the groups of Catherine Harmer (Neurosciences) and Kia Nobre (OHBA).
2. **A pilot intervention study of Deep Brain Stimulation** for severe enduring Anorexia Nervosa, targeted at neural reward centres in collaboration with Professor Tipu Aziz, (Oxford Neurosurgery) with an ethical substudy in collaboration with Dr Jacinta Tan (Swansea)

These sister studies contribute to our knowledge of the ethics and practice of neuromodulation, and in tandem to deeper understanding of neural circuits and processes underpinning Anorexia Nervosa. Together they inform the development novel treatment strategies. Further funding for our DBS study has recently been awarded by a grant from the Charles Wolfson Charitable Trust.

Current Funding:

- **HEFCE Clinical Senior Lecturer award**
- **MRC PhD studentship**
- **MRC Confidence in concept award**
- **Charles Wolfson Charitable Trust grant**

Planned research

Over the coming year we will continue to investigate in tandem the neural processes underpinning AN using multimodal imaging and investigate DBS incorporating multimodal imaging to track the effects of intervention.

Group members

- Rebecca Park – Clinical Senior Lecturer, Head
- Lauren Godier – DPhil Student , MRC studentship
- Helen Bould – Wellcome Clinical DPhil studentship
- Jessica Scaife – Postdoctoral Research assistant

Key Collaborators:

- Professors Tipu Aziz, Catherine Harmer, Kia Nobre: *Oxford UK*
- Dr Jacinta Tan; *Swansea UK*
- Dr Claire Gillan; *NYU, New York*
- Dr Sanne De Wit; *Amsterdam University, Netherlands.*

News

We have ongoing the first registered pilot trial of DBS for severe Anorexia Nervosa in the UK and 2nd only in Europe.

Recent publications

1. Cowdrey, F. A., Finlayson, G., & **Park, R. J.** (2013). Liking compared with wanting for high- and low-calorie foods in anorexia nervosa: aberrant food reward even after weight restoration.. Am J Clin Nutr, 97(3), 463-470. doi:10.3945/ajcn.112.046011.
2. Rawal, A., Harmer, C. J., **Park, R. J.,** O'Sullivan, U. D., & Williams, J. M. (2014). A sense of embodiment is reflected in people's signature size. PLoS One, 9(2), e88438. doi:10.1371/journal.pone.0088438.
3. Godier, L. R., & **Park, R. J. (2014).** Compulsivity in anorexia nervosa: a transdiagnostic concept.. Frontiers in psychology, 5, 778. doi: 10.3389/fpsyg.2014.00778.
4. **Park, R. J.,** Godier, L. R., & Cowdrey, F. A. (2014). Hungry for reward: How can neuroscience inform the development of treatment for Anorexia Nervosa? Behaviour Research and Therapy. doi:10.1016/j.brat.2014.07.007.

Dr Andrea Reinecke

Improving Treatments for Emotional Disorders (OXITED)

Our research aims to identify the cognitive and neural mechanisms underlying emotional disorders and their successful treatment, using behavioural and MRI approaches. We then use this knowledge to develop novel, ultra-brief psychological-pharmacological combination treatments, logically based on these key effects.

Current research

Traditional cognitive-behaviour therapy (CBT) approaches for anxiety disorders are long and time-consuming, expensive, and difficult to access. We have recently shown that a well-designed single session of CBT already leads to drastic improvements in anxiety, with 1/3 of patients being symptom free. Most importantly, this work has identified a neuropsychological mechanism that determines how well patients recover after CBT, with those patients improving particularly well who show a stronger attenuation in attention bias for threat stimuli immediately after CBT. Such findings have wide implications for the development of novel treatments. They suggest that optimal treatment doses might be much lower than previously thought, and that identifying add-on treatments boosting early bias reduction has the potential to develop minimal CBT designs into stand-alone treatments. Our recent work has explored the basic effects of drugs known to augment standard CBT courses, such as the antibiotic cycloserine, on basic learning and attention bias in healthy volunteer models. We are also currently running clinical studies exploring the potential of cycloserine in augmenting bias reduction and clinical outcome of single-session CBT for panic disorder and specific phobia. This work has been funded by small grants from the Oxfordshire Health Services Research Committee and the Oxford University John Fell OUP Research Fund (PI), and by a major research grant from the Medical Research Council (Co-PI).

Planned research

Translational research in animals has shown that the safe antihypertensive drug losartan targets brain areas relevant for threat bias, and that it improves fear extinction, which is the equivalent to CBT for anxiety. Over the next few years, we will investigate the potential of losartan in enhancing the clinical outcome of single-session CBT, and whether the effect underlying this augmentation is an improved impact on the mechanistic parameter driving recovery. The findings will have crucial implications for the development of a new and cost-economic treatment with the potential for low-threshold access for a higher number of patients with anxiety disorders. This work is funded by an MQ: Transforming Mental Health fellowship.

Group members

Dipl. Psych. Heike Rohrbacher, External PhD Student; **Dr Susann Steudte,** Visiting Postdoctoral Researcher and Clinical Psychologist Trainee; **Mareike Suesse,** Clinical Psychologist Trainee

Collaborations

Dr Sonia Bishop, University of Oxford, **Prof Michelle Craske,** University of California, Los Angeles, **Prof Heidi Johansen-Berg,** University of Oxford, **Prof Juergen Margaf,** Ruhr University Bochum, **Prof Kyle Pattinson,** University of Oxford, **Prof Kerry Ressler,** Emory University, **Dr Marcella Woud,** Ruhr University Bochum

News and impacts

Dr Reinecke has recently been awarded a prestigious fellowship from the MQ: Transforming Mental Health charity. Our recent work has been covered in The Times, Mail Online, and Oxford Mail, and on Irish National Radio and Radio 2UE Sydney.

Recent publications

1. **Reinecke A,** Harmer C. A cognitive-neuropsychological account of treatment action in anxiety: Can we improve clinical efficacy? Psychopathology Review. 2014. [Epub ahead of print].
2. **Reinecke A,** Thilo K, Fillipini M, Croft A, Harmer C. Predicting rapid response to cognitive-behaviour therapy for panic disorder: The role of hippocampus, insula, and dorsolateral prefrontal cortex. Behav Res Ther. 2014. [Epub ahead of print].
3. Scholl J, Guenthner J, Kolling N, Favaron E, Rushworth MFS, Harmer C, **Reinecke A.** A role beyond learning for NMDA receptors in reward-based decision-making – a pharmacological study using d-cycloserine. Neuropsychopharmacology. 2014. [Epub ahead of print].
4. Rohrbacher H, Blackwell S, Holmes E, **Reinecke A.** Optimizing the ingredients for imagery-based interpretation bias modification for depressed mood: is self-generation more effective than imagination alone? Journal of Affective Disorders. 2014;152;212-218.
5. **Reinecke A,** Waldenmaier L, Cooper M, Harmer C. Changes in automatic threat processing precede and predict clinical changes with cognitive-behaviour therapy for panic disorder. Biological Psychiatry. 2013;73;1064-1070.

Professor Michael Sharpe

Oxford Psychological Medicine Research Group

PMR studies clinical problems at the interface between psychiatry and the rest of medicine. Our current focus is on developing interventions for psychiatric illness in the medically ill (medical-psychiatric comorbidity) and evaluating these in rigorous clinical trials.

Current Research

The group leads the medical-psychiatric comorbidity themes in both the Oxford NIHR Collaboration for Leadership in Applied Health Research and Care (CLAHRC) and the Oxford Academic Health Sciences Network (AHSN). This work is also part of the Oxford Academic Health Science Centre (AHSC) chronic illness theme.

Current projects include:

- Management of psychiatric comorbidity in patients who require palliative care.
- Systematic reviews to determine the prevalence of medical-psychiatric comorbidity and the evidence for its treatment.
- Understanding the obstacles to compassionate psychological care of patients in general hospitals.
- Implementation of our system of depression management in cancer centres.

Our main funders are the Oxford NIHR CLAHRC and Sir Michael Sobell House Charity.

Group members

- **Dr Jane Walker,** Senior Clinical Researcher and Consultant Psychiatrist. **Ms Marta Wanat,** Postdoctoral Research Assistant. **Dr Becks Fisher,** Academic Clinical Fellow. **Dr Josie Fielding,** Clinical Researcher. **Dr Katy Burke,** Clinical Researcher. **Mr Stephen Puntis,** Postdoctoral Research Assistant. **Ms Ariane Petit,** Administrative Assistant. **Ms Christine Hedges,** Research Administrator. **Dr Matt Appleby,** Academic Foundation Doctor. **Dr Tom Grew,** Academic Foundation Doctor.
- **Dr Bart Sheehan, Dr Zehanah Izmeth, Dr Michael Yousif, Dr Iain Jordan and Dr David Okai** are NHS Consultant Psychiatrists who provide Psychological Medicine clinical services and also participate in teaching and research.
- **Ms Michelle Acum, Ms Michelle Degli Esposti and Mr Sam Rogers** are AHSN Research and Implementation Assistants who contribute to our work.

Links and collaborations

We have collaborations with:

- Oxford University Departments of Primary Care, Experimental Psychology and Clinical Neurosciences.
- Clinical teams in both Oxford University Hospitals NHS Trust and Oxford Health NHS Foundation Trust.
- International links via the Research Committee of the American Academy of Psychosomatic Medicine (www.apm.org) which Michael Sharpe chairs.

News and impacts

- We published a trio of three papers on depression in cancer patients and its treatment in Lancet Journals in August 2014 (see below). These publications attracted substantial media coverage including appearances by Michael Sharpe on BBC Television News and the BBC Radio 4 Today programme and articles in the Guardian, Times, Telegraph and other national newspapers.
- Michael Sharpe was shortlisted by the UK Royal College of Psychiatrists for the award of 'Psychiatrist of the year'.
- The Oxford University Hospitals NHS Trust Psychological Medicine service, which is the clinical arm of PMR, was also shortlisted by the UK Royal College of Psychiatrists for the award of 'Psychiatric team of the year'.

Selected publications

- **Walker J,** Holm Hansen C, Martin P, Symeonides S, Ramessur R, Murray G and **Sharpe M.** 2014. Prevalence, associations, and adequacy of treatment of major depression in patients with cancer: a cross-sectional analysis of routinely collected clinical data. Lancet Psychiatry: 1, 343-50
- **Sharpe M, Walker J,** Holm Hansen C, Martin P, Symeonides S, Gourley C, Wall L, Weller D and Murray G. 2014. Integrated collaborative care for comorbid major depression in patients with cancer (SMaRT Oncology-2): a multicentre randomised controlled effectiveness trial. The Lancet: 384, 1099-108.
- **Walker J,** Holm Hansen C, Martin P, Symeonides S, Gourley C, Wall L, Weller D, Murray G and Sharpe M. 2014. Integrated collaborative care for major depression comorbid with a poor prognosis cancer (SMaRT Oncology-3): a multicentre randomised controlled trial in patients with lung cancer. Lancet Oncology: 15, 1168-76.
- Carson A, Stone J, Holm Hansen C, Duncan R, Cavanagh J, Matthews K, Murray G, **Sharpe M.** 2014. Somatic symptom count scores do not identify patients with symptoms unexplained by disease: a prospective cohort study of neurology outpatients. Journal of Neurology, Neurosurgery and Psychiatry; doi:10.1136/jnnp-2014-308234.
- **Sharpe M.** 2014. Psychological medicine and the future of psychiatry. The British Journal of Psychiatry; 204: 91-2.

Professor Ilina Singh

Neuroscience Ethics and Society

Our Research focuses on the social and ethical implications of innovations in neuroscience and psychiatry. In the therapeutic realm, we are particularly interested in impacts for children and families; a key focus is on bringing the first person experiences of young people into clinical decision-making and policy-making. We also work on brain health and environmental neuroethics in healthy people.

Current Research

Becoming Good: Early intervention and moral development in child psychiatry Wellcome Trust Senior Investigator Award £1million.

This project investigates the scientific, social and ethical challenges involved in prediction and early intervention of psychiatric disorders associated with antisocial and aggressive outcomes. A primary goal is to develop ethical guidelines for the use of predictive testing and early intervention strategies in child psychiatry. Empirical components of the project focus on the acceptability of biomarker-based predictive testing and related intervention strategies among young people with diagnoses of ADHD and conduct disorder, and those with anti-social behaviour orders (ASBOs). We are also conducting a longitudinal study of attachment experiences and maternal-infant care practices among 'high risk' mothers participating in a pre-natal early intervention programme.

NERRI: Neuroenhancement, Responsible Research and Innovation, EU 7th Framework Programme: €3.5 million.

NERRI's remit is to facilitate an EU-wide public dialogue on the development of neuro-enhancing technologies and their translation into society. Scholars from 15 EU member states and several professional groups are collaboratively creating a range of events for diverse publics, scientists, professionals and policy-makers to exchange information and perspectives. The primary goal is to develop an empirically informed ethical framework for neuroenhancement that supports EC goals of responsible research and innovation in the brain and mind sciences.

Urban Brain Project ESRC, £250,000

This project is funded under the ESRC programme "Transforming Social Science." It investigates 'urbanicity' – the connections between the social and the neurological lives of urban citizens, with particular attention to mental health. Following several workshops of a core multi-disciplinary group, we will produce a major research proposal in this area.

Planned research

We are working with colleagues in the UK and the US in an effort to include interviews with a group of young people at risk of psychosis as part of the Wellcome Trust senior investigator project. We are also planning a collaboration with colleagues at Birkbeck's BabyLab to interview mothers about their experiences of an early intervention programme for infants at risk of autism. The work on neuroenhancement will continue, with planned research on the military context.

Group members

These will be established in 2015-16.

Collaborations

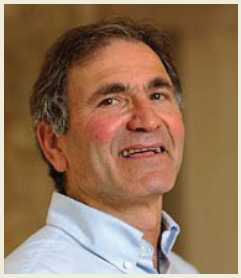
Wellcome Trust Senior Investigator Award: Dr Richard Tremblay (UCD) and Dr Orla Doyle (UCD) will work with us on the epigenetics and maternal interventions dimension of this project.

ESRC Urban Brain Project: Professor Nikolas Rose (KCL) and Dr Des Fitzgerald (KCL) are co-investigators on this project.**NERRI:** There are 15 European partners on this project. We work particularly closely with the other UK NERRI members: Professor George Gaskell at LSE and Genetic Alliance UK

Publications

- **Singh I,** Bard I, Jackson J (2014). Robust Resilience and Substantial Interest: A Survey of Pharmacological Cognitive Enhancement among University Students in the UK and Ireland. PLoS ONE 9(10): e105969. doi:10.1371/journal.pone.0105969.
- Fitzgerald, D, Rose, N & **Singh, I.** Revitalising Sociology: Urban Life and Mental Illness between History and the Present. British Journal of Sociology. Forthcoming.
- **Singh, I.,** Sinnott-Armstrong, W., & Savulescu, J. (Eds). (2013). BioPrediction, Biomarkers and Bad Behavior: Scientific, Legal and Ethical Challenges. Oxford University Press.
- **Singh, I.,** Filipe, A.M., Bard, I., Bergey, M., & Baker, L. (2013). Globalization and Cognitive Enhancement: Emerging Social and Ethical Challenges for ADHD Clinicians. Current Psychiatry Reports, 15(385). Accessed 10 November 2014 doi: 10.1007/s11920-013-0385-0.
- **Singh, I.** (2013). Brain Talk: Power and negotiation in children's discourse about self, brain and behavior. Sociology of Health and Illness 35(6): 813-827.

Child and Adolescent Psychiatry



Professor Alan Stein

(Developmental Psychiatry)

Young Children in the Face of Adversity

We aim to promote the healthy development, both psychological and physical, of children in adversity. Our work focuses on elucidating the mechanisms underlying disturbed development and in creating appropriate interventions to help these children and their families. Much of our research focus is on the early years of life, a critical time for child development. We are interested in the effects of both parental psychiatric disorders including depression, anxiety and eating disorders; and parental physical illness including HIV, malaria and cancer. Furthermore, we are interested in the underlying brain mechanisms of development, including the neural basis of parenting. We have programmes of work both in the UK and in Low and Middle Income Countries (LMIC).

Current Research

We are currently conducting two clinical treatment trials in the UK:

The Oxford Postnatal Treatment (OPT) Study

The Oxford Postnatal Treatment (OPT) Study, is funded by the Wellcome Trust and is designed to test treatments aimed at helping postnatally depressed mothers and their children. Postnatal depression (PND) is a major public health issue: it affects around 13% of mothers, and compared to children of non-depressed mothers, the children of mothers with PND are at increased risk of cognitive, behavioural and attachment problems. We are testing a combination of treatments in order to help with the mother's depression and improve child development.

Furthermore, since treatment can be targeted at critical aspects of functioning, a treatment trial provides an opportunity to examine potential causal factors in determining child outcome. This study has been proceeding very well and all participants have now completed their therapy sessions. We are still gathering final outcome data.

SPOCCL

Supporting Parents Of Children with Cleft Lip (SPOCCL) is funded by the Barclay Foundation. This study is being conducted in collaboration with Tim Goodacre in Plastic Surgery at the John Radcliffe Hospital, Oxford Cleft lip and/or palate is the most common congenital disorder, affecting 1 in 700 infants.

SPOCCL is testing whether, compared to a control treatment, a psychological intervention, Video Feedback Treatment (VFT), improves maternal sensitivity and infant cognitive development when given to mothers of babies with cleft lip prior to surgical correction. Both interventions are in collaboration with and Lynne Murray and Peter Cooper at the University of Reading.

Low and Middle Income Countries (LMICS)

We have a large programme of work in Low and Middle Income Countries (LMICS). In collaboration with the Africa Centre for Health and Population Studies, we are carrying out two large studies in KwaZulu-Natal, South Africa (with Tamsen Rochat and Ruth Bland). In the first we are following up the development, especially the cognitive functioning, of school-aged children who were exclusively breastfed in order to reduce the risk of HIV transmission. This is funded by the Canadian Grand Challenges, Saving Brains initiative. The second, funded by NICHD, USA, is a treatment trial testing an intervention to help parents disclose their HIV status to their children and enhance family communication.

We work closely with Linda Richter and Shane Norris on range of studies including the Birth-to-20 longitudinal study and early intervention studies.

We have developed a substantial collaboration with a large demographic surveillance unit on the South Africa / Mozambique border (led by Kathy Kahn and Stephen Tollman). There are two aspects to this work. In the first we are studying the mental health of children in schools in a very socio-economically disadvantaged area. In the second we are collaborating on a longitudinal 15 year analysis of family mortality and morbidity data. In particular we have been examining the relationship between children's survival and death in relation to a mother's illness and mortality, which has major policy implications.

Planned research

We are working towards submitting a grant in collaboration with a number of other departments in Oxford and overseas. This will build on our previous work of elucidating mechanisms underlying disturbed development and creating appropriate interventions to help affected children and their families. Critically the model we propose for the future will apply to both high income countries (HIC) and low and middle income countries (LMIC).

We are also collaborating on two new studies: one lead by Paul Ramchandani at Imperial, comprising an early intervention to prevent behavioural problems in children at high risk: and the second with Nicola Fear at the Institute of Psychiatry studying adolescents of fathers in the military

Group members

Sarah Atkinson, Ezra Aydin, Helen Bould, Bev Davies, Hannah De Jong, Andreas Giannakakis, Julia Goodwin, Denise Jennings, Symon Kariuki, Barbora Krausova, Pete Lawrence, Olivia Moran, Liz Murray, Elena Netsi, Rebecca Pearson, Elizabeth Rapa, Ruth Reed, Eloise Stark, Anne Stewart, Nienke Verkuijl, Valerie West.

Collaborations

We have close collaborations with Michelle Craske (UCLA), Gaia Scerif, Elaine Fox, Anke Ehlers and Glyn Humphreys (Experimental Psychology, Oxford), Stephen Kennedy, Jose Villar and Michelle Fernandes (Obstetrics & Gynaecology, Oxford), Tim Goodacre and Louise Dalton (Cleft Spires Unit, Oxford University Hospitals), Tamsen Rochat & Ruth Bland (Africa Centre, University of Witwatersrand), Linda Richter (Centre of Excellence for Human Development, South Africa), Stephen Tollman and Kathy Kahn (Agincourt, University of Witwatersrand), Amina Abubakar (Kilifi) and Lisa Berkman (Harvard University).

News and impacts

The Lancet Perinatal Mental Health Series, Comment author and podcast.
Howard, L.M., Piot, P. & Stein A. (2014) No health without perinatal mental health. The Lancet, 384;9956:1723-4.
Carnegie Visiting Fellowship, University of Witwatersrand, South Africa (2014)
Member of the MRC/Wellcome/DfID Global Health Trials panel and a member of the MRC Global Health Advisory Group.
New Journal Appointments: Lancet HIV International Advisory Board.

Recent publications

1. **Stein A,** Pearson, R.M., Goodman, S.H., Rapa, E., Rahman, A., McCallum, M. Howard, L.M. & Pariante, C.M. (2014) Perinatal mental health 3: The Impact of Perinatal Mental Disorders on the Fetus and Child. The Lancet, 384;9956:1800-19.
2. Howard, L. M., Molyneaux, E., Dennis, C., Rochat, T., **Stein, A,** & Migrom, J. (2014) Non-psychotic mental disorders in the perinatal period. The Lancet, 384;9956:1775-88.
3. Rotheram-Borus, M.J., Richter, L.M., van Heerden, A., van Rooyen, H. Tomlinson, M., Harwood, J.M., Comulada, W.S. and **Stein, A.** (2014) A Cluster Randomized Controlled Trial Evaluating the Efficacy of Peer Mentors to Support South African Women Living with HIV and Their Infants. PLoS One, 22;9(1):e84867.
4. **Stein A,** Desmond C, Garbarino J, Van IJzendoorn MH, Barbarin O, Black MM, Stein AD, Hillis SD, Kalichman SC, Mercy JA, Bakermans-Kranenburg MJ, Rapa E, Saul JR, Dobrova-Krol NA, Richter LM. (2014) Predicting long-term outcomes for children affected by HIV and AIDS: perspectives from the scientific study of children's development. AIDS, Suppl 3:S261-8.
5. Rochat TJ, Arteche AX, **Stein A,** Mkwanazi N, Bland RM. (2014) Maternal HIV disclosure to young HIV-uninfected children: an evaluation of a family-centred intervention in South Africa. AIDS, Suppl 3:S331-41.

Professor Morten Kringelbach

(Developmental Psychiatry)

Hedonia: Trygfonden Research Group

Our research goal is to understand pleasure in the human brain since it may offer us novel and more effective ways to treat anhedonia, the lack of pleasure, which is a major component of affective disorders.

Background

My transnational research group, Hedonia: TrygFonden Research Group, is based at Oxford and Aarhus University in Denmark. We use a range of behavioural, neuroimaging, neurosurgical and computational methods to investigate the many facets of pleasure in health and disease. Our funding comes from the ERC, TrygFonden Charitable Foundation, Braveheart/Lloyd's Royal British Legion. The main research into the fundamental human brain networks involved in pleasure and reward can roughly be divided into three strands: 1) investigating fundamental pleasure networks with neuroimaging and computational modelling, 2) elucidating the development of parent-infant relationship, and 3) alleviating anhedonia in clinical populations using deep brain stimulation (DBS) and less invasive methods.

Current group members

Dr Christine Parsons, Dr Tim Van Hartevelt, Dr Joana Cabral, Dr Maria Witek, Dr Katie Young, Henrique Fernandes, Angus Stevner, Eloise Stark, Louis-David Lord, Kira Vibe Jespersen and Alexander Fjældstad.

Current research

I am interested in the fundamental pleasures afforded by food, sex and social interactions, which are central to survival, but I am also interested in higher order pleasures such as music and art which have strong links to eudaimonia, the meaningful and engaging life.

Supported by a five-year ERC grant, infants are a focus of my research and especially how their sounds, looks and smells strongly influence the parental brain. Understanding this special relationship is not only exciting but may also help to shape the way we can intervene when things go awry, e.g. in post-natal depression. Another main focus is understanding and modelling how pleasure systems are fundamental in the dynamic allocation of brain resources. The study of human brain networks with in vivo neuroimaging has given rise to the field of connectomics, furthered by advances in network science and graph theory informing our understanding of the topology and function of the healthy brain. We have pioneered the use of whole-brain computational modelling of connectomic data to find novel biomarkers and treatments for neuropsychiatric disorders As we have come to understand more of the delicate balance and transitions between different brain states, we can now directly rebalance and recalibrate brain networks through deep brain stimulation. When pleasure systems become unbalanced, it can be very difficult to rebalance the brain. One of my main interests is to help advance our understanding of the effects of war and disaster for which we have setup the Scars of War Foundation at The Queen's College. One current five-year project is investigating the brain changes related to post-traumatic stress-disorder in war veterans. Future planned projects include focused family-based interventions supporting serving soldiers and veterans.

Overall, the time is now ripe for modern neuroscience to study the many faces of pleasure, opening up for new treatments and perhaps even better lives – especially if coupled with early interventions

Collaborations with other departments and institutions

Oxford collaborators include: Prof. Alan Stein, Dr Tony James, Prof Mark Woolrich, Prof. Tipu Aziz, Mr. Alex Green, Mr James FitzGerald & Mr Tim Goodacre. International collaborators include: Prof. Gustavo Deco (Pompeu Fabra University, Barcelona); Prof. Kent Berridge (Univ. Michigan, USA); Prof Eus Van Someren (Amsterdam, Holland); Prof. Peter Vuust (Aarhus Univ., UK); Dr. Arne Møller (Aarhus Univ., UK); Prof. Therese Ovesen (Aarhus Univ., UK); Prof. Marinus van Ijzendoorn (Univ Leiden, Holland); Prof. Peter Whybrow (UCLA, USA); Prof. Hugo Lagercrantz (Karolinska Institute, Stockholm); Prof Raymond Chan (Chinese Academy of Sciences).

Key publications

Books

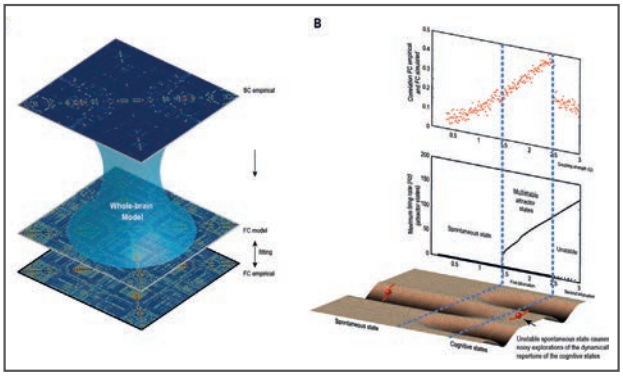
1. **Kringelbach M.L.** & Phillips, H. (2014) Emotion: pleasure and pain in the brain. Oxford: Oxford University Press.
2. Preston S., **Kringelbach M.L.** & Knutson, B., eds. (2014) The Interdisciplinary Science of Consumption. Cambridge, Mass.: MIT Press.

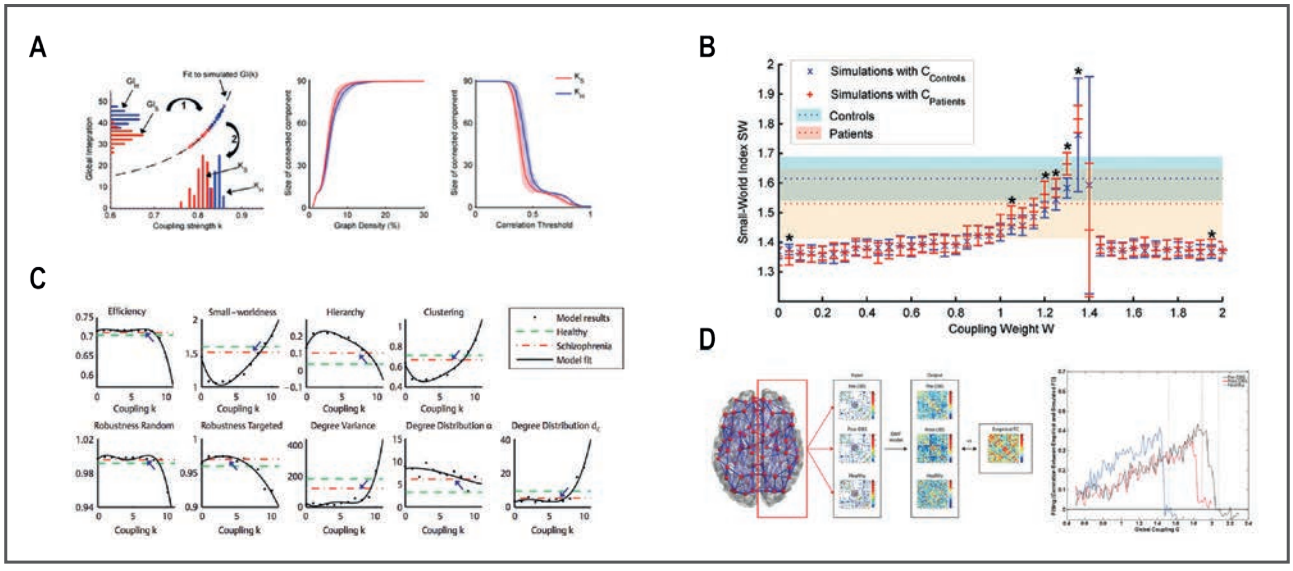
Papers

1. Deco G. & **Kringelbach M.L. (2014)** Great expectations: using whole-brain computational connectomics for understanding neuropsychiatric disorders. Neuron, in press.
2. Van Hartevelt, T.J., Cabral J., Deco G., Møller A., Green A.L., Aziz T.Z. & **Kringelbach M.L.** (2014) Neural plasticity in human brain connectivity: the effects of long term deep brain stimulation of the subthalamic nucleus in Parkinson's Disease. PLoS ONE, 9(1): e86496.
3. Parsons C.E., Young K.S., Mohseni H., Woolrich M.W., Rømer Thomsen K., Joensson M., Murray L., Goodacre T., Stein A., **Kringelbach M.L.** (2013) Minor structural abnormalities in the infant face disrupt neural processing: a unique window into early caregiving responses. Social Neuroscience, 8(4):268-74.
4. Parsons C.E, Young K.S., Craske M.G., Stein A. & **Kringelbach M.L.** (2014) Introducing the Oxford Vocal (OxVoc) Sounds Database: A validated set of non-acted affective sounds from human infants, adults and domestic animals. Frontiers in Psychology, 5:562.

Figure 1. Overview of whole-brain computational models

A) Linking between the structural and functional dynamics can be explored using whole-brain computational modelling of empirical neuroimaging data. Structural connectivity data can be obtained using DTI and tractography between a parcellation of the human brain that can provide a structural connectivity matrix. A whole-brain model can be constructed using a set of stochastic differential equations coupled according to the connectivity matrix, where the model can be validated by comparing model and empirical spatiotemporal neuroimaging data. B) The whole-brain model is able to best fit the empirical resting functional magnetic resonance imaging data when the brain network is critical (i.e., at the border of a dynamical bifurcation point), so that, at that operating point, the system defines a meaningful dynamic repertoire that is inherent to the neuroanatomical connectivity (Deco and Kringelbach, 2014).





Professor Charles Newton

(Developmental Psychiatry)

Autism and Developmental Disorders

Autism

Charles Newton is leading a programme of work related to Autism in Oxford.

A pilot study to compare Magnetoencephalography and Magnetic Resonance Imaging in collaboration with Steven Chance and Sven Brautigam is in progress. In addition we have created a web site for Autism Research in Oxford, and held a meeting about Autism which brought together people involved in basic science, clinical assessment and those providing services for Autism. We have Clinical Symposia (for health care workers), Journal Club (run by Hannah Buxton) and Scientic Seminars (run by Steve Chance).

Global Burden of Disease

The group has been involved in the estimating the global burden of disease for epilepsy, neonatal insults and other neurodevelopmental conditions such as autism.

Low and Middle Income Countries (LAMICS)

We have a large programme of work in Low and Middle Income Countries (LAMICS).

Work in Africa

Charles Newton's programme of work includes autism (Africa and Oxford), epilepsy (Africa), neurodevelopment disorders (Kenya), psychiatric conditions (Africa) and sickle cell disease (Tanzania). The epilepsy studies included epidemiological surveys in five sites in Africa to study the prevalence, risk factors and mortality associated with epilepsy. In addition we are examining the magnitude and risk factors of the treatment gap and tested an intervention to reduce the treatment gap.

The work on Autism in Africa, continues in Kilifi, Kenya and Dar-es-Salaam, Tanzania with the adaption of tools to screen for Autism in epidemiological studies and assessments to help confirm the diagnosis e.g. ADOS. We organized the first meeting of Autrism in Ghana during April 2014. The focus of the work on neurodevelopmental disorders occurs in Kilifi, where we are examining the outcome of infectious diseases (malaria, HIV) and neonatal insults (birth asphyxia, jaundice and sepsis). The work on sickle cell disease has focused on silent infarcts as detected by magnetic resonance imaging and psycho-social well-being.

Selected Publications:

1. Alcock KJ, Rimba K, Holding P, Kitsao-Wekulo P, Abubakar A, **Newton CR.** Developmental inventories using illiterate parents as informants: Communicative Development Inventory (CDI) adaptation for two Kenyan languages. J Child Lang. 2014 Aug 27:1-23. [Epub ahead of print] PubMed PMID: 25158859. Available on CJO2014. doi:10.1017/S0305000914000403.
2. Ibinda F, Wagner RG, Bertram MY, Ngugi AK, Bauni E, Vos T, Sander JW, **Newton CR.** Burden of epilepsy in rural Kenya measured in disability-adjusted life years. Epilepsia. 2014 Jul 31. doi: 10.1111/epi.12741. [Epub ahead of print] PubMed PMID: 25131901.
3. Ibinda F, Mbuba CK, Kariuki SM, Chengo E, Ngugi AK, Odhiambo R, Lowe B, Fegan G, Carter JA, **Newton CR.** Evaluation of Kilifi Epilepsy Education Programme: A randomized controlled trial. Epilepsia. 2014 Jan 21. doi: 10.1111/epi.12498.
4. Abubakar A, Van Baar A, Fischer R, Bomu G, Gona JK, **Newton CR.** Socio-cultural Determinants of Health-Seeking Behaviour on the Kenyan Coast: A Qualitative Study. PLoS ONE 8(11): e71998. doi:10.1371/journal.pone.0071998.
5. Kariuki SM, Gitau E, Gwer S, Karanja HK, Chengo E, Kazungu M, Urban B, **Newton CR.** The value of Plasmodium falciparum HRP2 and malaria retinopathy in distinguishing cerebral malaria from other acute encephalopathies in Kenyan children. J Infect Dis. 2013 Sep 16. [Epub ahead of print] PubMed PMID: 24041795.
6. Ba-Diop A, Marin B, Druet-Cabanac M, Ngoungou EB, **Newton CR,** Preux PM. Epidemiology, causes, and treatment of epilepsy in sub-Saharan Africa. Lancet Neurology 2014; 13: 1029–44.
7. Thwaites CL, Beeching NJ, **Newton CR.** Maternal and neonatal tetanus. Lancet. 2014 Aug 19. pii: S0140-6736(14)60236-1. doi: 10.1016/S0140-6736(14)60236-1.

News and Public Engagement

Members of the team were involved in radio programmes BBC Oxford and Voice of America.

Dr Mina Fazel
(Developmental Psychiatry)

Mental Health of Refugees and Asylum Seekers

The main aim of this research programme is to develop an understanding of the role that school-based mental health services can play in improving young people's access to mental health care and how this might impact on a range of important developmental outcomes.

Current research

During the school years, children and young people not only develop their cognitive and analytic skills but they learn to regulate their emotions, build social relationships and establish a blueprint and trajectory for their future lifecourse. It is during these years that a significant proportion of psychiatric problems emerge yet young people have poor access to mental health services, which is worse in those from more vulnerable populations. Schools could potentially help in addressing some of the problems encountered when accessing mental health services as the majority of young people are attending school. Working in an integrated manner within schools provides an opportunity to democratise access to mental health care, yet little is known about how to integrate the best models of school-based treatments.

My current research covers two areas:
1. Developing psychotherapeutic interventions for school staff to use with refugee children: This NIHR funded post-doctoral fellowship is developing cognitive-behavioural tools for school staff to use. Refugee and asylum-seeking children find accessing traditional mental health services difficult for reasons that can include cultural, linguistic and service-related barriers. Providing psychological support within the school can potentially help the young people in a sustainable and acceptable manner. I have created a psychotherapeutic 'toolbox' for school staff to use- that is for professionals who have no formal mental health training but spend a considerable amount of their time supporting the emotional and behavioural difficulties of children. By training in these skills, it is hoped that the time they are already sending with the young people will be used in applying some evidence-based mental health interventions.

2. Developing evidence-based school mental health services in Oxfordshire: This area of research is focusing on what methods and approaches can best support the mental health of young people within the school context. It draws from the experience of services developed in North America where over 2000 school based mental health services exist and have demonstrated how such services substantially improve the accessibility of mental health services for young people. How to translate these experiences into the UK context and implement different models of school-based mental health interventions are the key quesitions that are being addressed, which has received some support from the NIHR CLAHRC. Working together with Oxford Health NHS Foundation Trust, school-based mental health services are being systematically introduced across Oxfordshire state-funded secondary schools and how this impacts on a number of psychological and educational variables is being evaluated.

Planned research

1. Embedding mental health interventions in schools: developing a future programme of research to address this question for the UK context.
2. Exploration of the ALSPAC database to address key questions regarding the relationship between psychological difficulties that emerge in childhood and adolescence with educational and social outcomes.
3. Follow-up of Kulani cohort: this is a sample of children from a rural, socio-economically deprived part of South Africa and we are planning to evaluate their social and educational outcomes 7 years after their baseline mental health measures were taken.

Selected publications:

1. **Fazel M,** Hoagwood K, Stephan S, Ford T. Mental health interventions in schools in high-income countries. Lancet Psychiatry 2014; 1: 377–87
2. **Fazel M,** Patel V, Thomas S, Tol W. Mental health interventions in schools in low-income and middle-income countries. Lancet Psychiatry 2014; 1: 388–98.
3. **M Fazel,** U Karunakara, E Newnham. Detention, denial and death: migration hazards for refugee children Lancet Global Health 2014; 2(6), e313-e314.
4. R Tyrer, **M Fazel.** School and community-based interventions for refugee and asylum seeking children: A Systematic Review PLoS ONE 2014; 9(2):e89359.
5. **IN PRESS: M. Fazel A Moment of Change:** facilitating refugee children's mental health in UK schools International Journal of Educational Development (Schools in Extreme Settings Special Issue).

Dr Mark Stokes

Attention Group, Oxford Centre for Human Brain Activity

We study the brain processes that bias perception and memory in the service of adaptive behaviour, and the consequences when these systems go wrong.

Current Research

Our everyday view of the world is necessarily biased: we focus our attention on information that is most relevant to our current goals, and ignore behaviourally irrelevant distractions. Without such bias, we would be lost in a world of information-overload, unable to accomplish even the simplest tasks.

Research in the Attention Group uses a diverse range of complementary brain measurement techniques to explore how perceptual biases are coordinated for goal-directed behaviour. We tackle this over-arching theme by addressing two fundamental questions: 1) how working memory pre-configures the brain for processing task-relevant events, and 2) how expectations suppress distractions in the environment that compete for our attention. Within the broader framework, we also explore the relationship between attention and individual differences in working memory capacity, fluid intelligence and personality traits associated with increased risk of mood disorders.

Our research is supported by the Medical Research Council (MRC), Biotechnology and Biological Sciences Research Council (BBSRC), James S. McDonnell Foundation, St John's College, Wellcome Trust and NIHR.

Planned research

We are currently working to integrate diverse experimental methods to leverage complementary advantages in measurement precision unique to each approach. In particular, our latest work involves combining insights from non-invasive neuroimaging with more direct brain recordings performed by our neurosurgical collaborators. We are also working to bridge the gap between neuroscientific research in human and non-human model systems.

The results of our research will provide a richer understanding of the fundamental neural mechanisms of attention, and how they influence perception and decision-making. A clearer understanding of how individuals differ in controlling attention will provide a foundation for further research into how cognitive factors could play a role in neuropsychiatric models of depression and anxiety

Group members

Dr MaryAnn Noonan (Postdoctoral Researcher)
Dr Ben Crittenden (Postdoctoral Researcher)
Nicholas Myers (DPhil Student)
Lev Tankelevitch (DPhil Student)
Michael Wolff (visiting student)
Janina Jochim (lab manager)

Collaborations

We work closely with other research groups in Oxford, and further afield. Here is a list of our currently most active collaborations:

- Prof Nobre; Brain and Cognition Laboratory (Dept. Experimental Psychology, Oxford)
- Prof Rushworth; Decision and Action Laboratory (Dept. Experimental Psychology, Oxford)
- Dr Summerfield; Summerfield Lab (Dept. Experimental Psychology, Oxford)
- Drs Voets/Green/Sen; Oxford epilepsy research group (Nuffield Department of Clinical Neurosciences, Oxford)
- Prof Duncan; Attention & Cognitive Control Group (MRC Cognition and Brain Sciences Unit, Cambridge)
- Prof Axmacher; Clinic of Epileptology (Bonn University)
- Prof Buschman (Princeton University)
- Prof Miller (MIT)

News and Impacts

- "Temporary connective architectures in mind and brain: role of functional connectivity in working memory" BBSRC project grant (principal investigator: Stokes; approx. £400k, 2015-2018)
- "Stability of mind in a dynamic brain: neural principles of working memory for flexible human cognition" James S. McDonnell Foundation Scholar Award (principal investigator: Stokes; $600K (USD), 2014-2020)

- "Big Data in Neuroscience" St John's Research Centre Grant (principal investigator: Stokes; £40K, 2014-2015)
- Dr Noonan was appointed to St John's College Supernumerary Teaching Fellowship
- Mr Myers was appointed to Research Associate of St John's College
- Mr Wallis was a awarded a DPhil in Experimental Psychology
- "Neuroskepticism: What do insights into Neuroscience tell us about the Brain and Behaviour" Workshop at King's College London Neuroscience Symposium (by Stokes)
- Talk at the Pint of Science Festival: "Beyond blobs on brains" (by Stokes)

Recent publications

1. Myers, **Stokes,** Walther & Nobre (2014) Oscillatory Brain State Predicts Variability in Working Memory. Journal of Neuroscience 34, 7735-7743
2. Morin, Hadj-Bouziane, **Stokes,** Ungerleider & Bell (2014) Hierarchical Encoding of Social Cues in Primate Inferior Temporal Cortex. Cerebral Cortex [Epub ahead of print]
3. Poliakov, **Stokes,** Woolrich, Mantini, & Astle (2014) Modulation of alpha power at encoding and retrieval tracks the precision of visual short-term memory. Journal of Neurophysiology.
4. Stokes, **Myers,** Turnbull & Nobre (2014). Preferential encoding of behaviourally relevant predictions revealed by EEG. Frontiers in Human Neuroscience, 8:687.
5. Voets, Zamboni, **Stokes,** Carpenter, Stacey & Adcock (2014) Aberrant functional connectivity in dissociable hippocampal networks is associated with deficits in memory. Journal of Neuroscience 34, 4920-4928.

Dr Elizabeth Tunbridge

Neural Correlates of Gene Function

Our research uses a multi-disciplinary approach to clarify how human genetic variation impacts on the dopamine systems, given their key role in cognition and reward processing, and their dysfunction in psychiatric disorders.

Current research

Our research has two strands.
1) We use mouse models to study the impact of genetic factors and drugs on dopamine function, and related behaviours, e.g., we have recently shown interactive effects of genetic variation in the COMT gene and THC (the main psychoactive compound in cannabis) on dopamine levels, providing a possible mechanism for COMT genotype-dependent effects of cannabis observed in humans.
2) We study the separate and interactive effects of genetic factors and drugs that alter dopamine on human behaviour and brain activity, e.g. we are investigating COMT genotype-dependent effects of a COMT inhibitor on brain activity, using magnetoencephalography.
Liz is funded by a Royal Society Research Fellowship and our research is funded by Wellcome Trust studentships (to KS and CK), and project grants from the MRC.

Planned research

We are now investigating how COMT-dependent changes in mouse behaviour relate to differences in dopamine release at the sub-second scale (with Dr Mark Walton). We are also studying the separate and interactive effects of COMT genotype and COMT inhibition on emotional processing and reward function (with Profs Paul Harrison and Catherine Harmer).

Current group members:

Anna Huber (Final year DPhil student)
Clio Korn (Second year DPhil student)
Jessica Laidlaw (Research Assistant)
Katharina Stumpenhorst (Final year DPhil student)

Collaborations

Prof David Bannerman and Dr Mark Walton (Experimental Psychology)
Profs Daniel Freeman, Catherine Harmer, Paul Harrison, Kia Nobre and Mark Woolrich (Psychiatry)
Dr Trevor Sharp (Pharmacology)
Dr Daniel Weinberger (Lieber Institute for Brain Development, US).

News and impacts

- Liz presented the group's research in "The Next Big Thing" session at the Hay Festival
- Liz was elected Treasurer of the British Association of Psychopharmacology by the Society's membership
- Katharina was selected to represent the University at the Global Young Scientists Summit in Singapore
- Clio was awarded an internship at the Academy of Medical Sciences, supported by the Wellcome Trust

Recent publications

1. Laatikainen, L. M., T. Sharp, P. J. Harrison, and **E. M. Tunbridge.** "Sexually Dimorphic Effects of Catechol-O-Methyltransferase (Comt) Inhibition on Dopamine Metabolism in Multiple Brain Regions." [In eng]. PLoS ONE 8, no. 4 (2013): e61839.
2. **Tunbridge, E. M.,** S. M. Farrell, P. J. Harrison, and C. E. Mackay. "Catechol-O-Methyltransferase (Comt) Influences the Connectivity of the Prefrontal Cortex at Rest." [In eng]. Neuroimage 68 (Mar 2013): 49-54.

Professor Mark Woolrich

Analysis Group, Oxford Centre for Human Brain Activity

The OHBA Analysis group develops novel computational methods for analyzing neuroimaging data. This incorporates data from a range of imaging modalities – including functional MRI, diffusion MRI and MEG/EEG. We use an array of techniques from computational neuroscience, machine learning and image/signal processing, in order to ask novel questions about the function and dysfunction of the human brain.

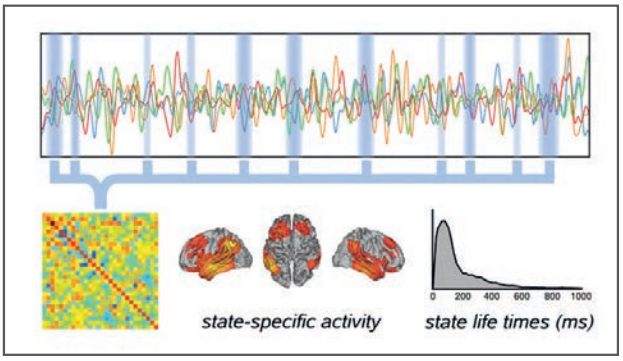
Current research

In the last few years we have worked on advancing our understanding of spontaneous, or resting, brain activity. This is of central importance as all cognition arises as a perturbation in background activity. Spontaneous brain activity may also play a central role in maintaining the health of brain networks recruited in tasks.

We are developing approaches that can use the rich temporal information available from M/EEG, in order to capture fast dynamics changes in spontaneous brain activity. Using MEG, and with our collaborators at Nottingham, we have been able to identify resting state networks independently in MEG for the first time.

Most recently, we used hidden Markov models (HMMs) to show that resting state networks fluctuate at very fast time scales (~100ms). This is at time scales hundreds of times faster than had been shown previously.

Taken together, these methods are being used to gain new insights not only in basic neuroscience, but also in clinical research into psychiatric disorders. In particular, we are now applying these new methods to data collected as part of the Collaborative Oxford Network for Bipolar Research to Improve Outcomes **(CONBRIO),** and the Human Connectome Project.



Resting state networks in spontaneous human brain activity revealed to be fluctuating on sub-second time-scales [Baker et al. Elife (2014)].

Current funding

- Wellcome Trust Grant. (co-I, PI: Kia Nobre) Oxford Centre for Human Brain Activity Infrastructure Grant.
- NIHR (co-I, PI: Heidi Johansen-berg) – The effects of physical activity on brain plasticity and cognitive wellbeing.
- NIHR (co-I, PI: Kia Nobre) – The effects of cognitive stimulation on brain structure and function .
- Wellcome Trust Strategic Award. (co-I, PI: Steve Smith) – Integrated multimodal brain imaging for neuroscience research and clinical practice.
- MRC/EPSRC UK MEG Partnership award (co-I).

Planned research

Much of the research on large-scale networks has been largely descriptive in nature. Our plan now is to complement this with explanations of how these networks arise through the use of biophysical network models. These biophysical network models combine knowledge of the anatomical (white matter) connectivity from diffusion MRI, with models that capture the synaptic dynamics of populations of neurons within local brain areas. These will be used to predict the spatio-temporal dynamics of real functional neuroimaging data, and also the manner in which these dynamics may become dysfunctional in psychiatric disease.

Current members

Post-docs

Diego Vidaurre, Adam Baker, Andrew Quinn.

DPhil students

Giles Colclough, Faysal Ahmad, Sam Harrison, Kareem Ayoub, Angus Stevner, Jonathan Hadida.

Collaborations

We have a number of collaborations within OHBA and the Department of Psychiatry. Elsewhere, we collaborate extensively with the FMRIB Analysis Group, including Stephen Smith and Tim Behrens. We also collaborate with Steve Roberts in Engineering Science, with David Dupret in the Anatomical Neuropharmacology Unit on the analysis of invasive local field potential recordings, and with Tim Vogels in the Dept. of Physiology, Anatomy and Genetics on the development of biophysical network models. Externally, we collaborate with Gustavo Deco in Barcelona on the computational modeling of brain networks. Finally, and as part of a MEG UK collaboration grant, we have strong links with Gareth Barnes at UCL and Matt Brookes at the University of Nottingham.

Recent publications

1. Cabral J, Luckhoo H, **Woolrich M,** Joensson M, Mohseni H, Baker A, Kringelbach ML, Deco G (2014). Exploring mechanisms of spontaneous functional connectivity in MEG: How delayed network interactions lead to structured amplitude envelopes of band-pass filtered oscillations. Neuroimage.
2. Baker AP, Brookes MJ, Rezek IA, Smith SM, Behrens T, Probert Smith PJ, **Woolrich M (2014).** Fast transient networks in spontaneous human brain activity. Elife.
3. Nakagawa TT, **Woolrich M,** Luckhoo H, Joensson M, Mohseni H, Kringelbach ML, Jirsa V, Deco G (2014). How delays matter in an oscillatory whole-brain spiking-neuron network model for MEG alpha-rhythms at rest. Neuroimage.
4. Luckhoo HT, Brookes MJ, **Woolrich M (2014).** Multi-session statistics on beamformed MEG data. Neuroimage.
5. **Woolrich MW1,** Stephan KE (2013). Biophysical network models and the human connectome. Neuroimage.

Professor Willem Kuyken

Oxford Mindfulness Centre

Our research focuses on depression and evidence-based psychological approaches to preventing depression. The emphasis is on mindfulness-based approaches and the role of compassion. We use the translational framework from basic through to implementation science.

Current research

Wellcome Trust Strategic Award (2015-2018). "Has mindfulness training (MT) in adolescence the potential to shift the secondary school-age population away from psychopathology and toward improved mental health by addressing key processes of mental regulation and executive control that operate across the spectrum of risk/resilience?"

NIHR HTA PREVENT trial (2010-1014). "Is MBCT with support to taper/discontinue antidepressant medication (MBCT-TS) superior to m-ADM in terms of a primary outcome of preventing depressive relapse/recurrence over 24 months?" This trial has recently completed and suggests that MBCT provides an alternative to maintenance antidepressants for long-term recovery; the paper is in press at The Lancet.

NIHR HSRD Accessibility and implementation in UK services of an effective depression relapse prevention programme: Mindfulness-Based Cognitive Therapy (ASPIRE) (2013-2016). The study, co-led with Professor Jo Rycroft-Malone in Bangor, aims to "describe the current state of MBCT accessibility and implementation across the UK, develop an explanatory framework of what is hindering and facilitating its progress in different areas, and develop an Implementation Plan and related resources to promote better and more equitable availability and use of MBCT within the UK National Health Service."

NIHR PenCLAHRC Heart and Living Mindfully (HeLM) project (2012-2015), co-led with Professors Chris Dickens and Barney Dunn in Exeter. This study aims to establish the "feasibility and acceptability of Mindfulness-Based Cognitive Therapy in people with co-morbid mood and vascular disorders."

Additional programmes of work within the group include: mechanisms underlying suicidal vulnerability (Bergljot Gjelsvik), mindfulness to prevent post-partum depression and support for new parents (Maret Dymond) and mechanisms in depression and mindfulness-based interventions (Catherine Crane).

Group members

Chris Cullen, Maret Dymond, Bergjlot Gjeslvik, Marie Johansson, Adele Krusche, John Peacock, Esther Riggs, Christina Surawy, Mark Williams.

Collaborations

Research collaborators include Sarah Byford (KCL), Rebecca Crane (Bangor), Tim Dalgleish (Cambridge), Adele Hayes (Delaware, USA), Felicia Huppert (Cambridge), Christine Padesky (California, USA), Jo Rycroft-Malone (Bangor), Anne Speckens (Nijmegen), and Nancy Bardacke and Larissa Duncan (California, USA).

Willem Kuyken also holds an Honorary Chair with Exeter where he has ongoing collaborations with John Campbell, Chris Dickens, Barney Dunn, Alison Evans, Christina Feldman, Tamsin Ford, Andy Gibson, Anke Karl, Obi Ukoumunne, Dave Richards, Rod Taylor & Katherine Weare.

News and impacts

Clinical work

Since April 2012 we have a service level agreement with Oxford Health NHS Foundation Trust and with IAPT in Oxfordshire and Buckinghamshire to train MBCT teachers and deliver MBCT classes for depression, physical long term conditions (LTC), and Chronic Fatigue Syndrome (CFS). We continue to explore the acceptability of Mindfulness-Based Childbirth and Parenting (MBCP) within the UK, in collaboration with Oxford University Hospitals NHS Trust (OUHT), and supported by an 'Innovating for Life' award from the British Journal of Midwifery (Dr Maret Dymond and Dr Sian Warriner). We also offer MBCT classes to the public.

Policy Input

In the past year OMC associate teacher Chris Cullen has delivered a rolling programme of eight- week mindfulness courses to MPs and Peers in Parliament. The OMC is supporting the Mindfulness Initiative and All Party Parliamentary Group on Mindfulness, which is exploring the place of mindfulness in health, education, criminal justice, and the workplace. The report will be launched in the spring of 2015.

Over the past year the Oxford Mindfulness Centre has delivered training in MBCT in several countries including Singapore, Hong Kong, Ukraine, and Hungary, and is currently in the last phase of supporting colleagues in setting up MBCT Training Centres in Singapore and Hong Kong. The Master of Studies programme in MBCT continues to flourish and we have also established a new 'Foundations in teaching MBCT and MBCP' course, which has graduated its first cohort.

From 2015 the OMC will be running a 5-day Summer School each August, led by Mark Williams and Chris Cullen. This will offer participants the chance to deepen their practice of mindfulness, and broaden their reflection on its place in the world as a source of wisdom and healing.

The centre also continues to deliver Mindfulness courses to the general public and oxford university students.

Recent publications

1. **Kuyken, W.,** Hayes, R., Barrett, B., Byng, R., Dalgleish, T., Kessler, D., Lewis, G., Watkins, E.R., Brejcha, C., Cardy, J., Causley, A., Cowderoy, S., Evans, A., Gradinger, F., Kaur, S., Lanham, P., Morant, N., Richards, J., Shah, P., Sutton, H., Vicary, R., Weaver, A.E., Wilks, J., Williams, M.J., Taylor, R.S., & Byford, S. (2014). Effectiveness and cost-effectiveness of mindfulness-based cognitive therapy compared with maintenance anti-depressant treatment in the prevention of depressive relapse/recurrence: results of the PREVENT randomised controlled trial. Lancet, Manuscript in press.
2. Williams, M. J., Dalgleish, T., Karl, A., & **Kuyken, W. (2014).** Examining the factor structures of the Five Facet Mindfulness Questionnaire and the Self-Compassion Scale. Psychological Assessment. doi: 10.1037/a0035566.
3. Hollinghurst, S., Carroll, F. E., Abel, A., Campbell, J., Garland, A., Jerrom, B., Kessler, D., **Kuyken, W.,** .... Wiles, N. (2014). Cost-effectiveness of cognitive behavioural therapy as an adjunct to pharmacotherapy for treatment-resistant depression in primary care: economic evaluation of the CoBalT Trial. British Journal of Psychiatry, 204(1), 69-76. doi: Doi 10.1192/Bjp.Bp.112.125286.
4. LAbbott RA, Whear R, Rodgers LR, Bethel A, Thompson-Coon J, **Kuyken W,** Stein K, Dickens C. (2014). Effectiveness of mindfulness-based stress reduction and mindfulness based cognitive therapy in vascular disease: A systematic review and meta-analysis of randomised controlled trials. Journal of Psychosomatic Reseach. DOI http://dx.doi.org/10.1016/j.jpsychores.2014.02.012.
5. Rycroft-Malone, J., Anderson, R., Crane, R., Gibson, A., Gradinger, F., Owen-Griffiths, H., Mercer, S., & **Kuyken, W. (2014).** Accessibility and implementation in UK services of an effective depression relapse prevention programme – Mindfulness-Based Cognitive Therapy (MBCT): ASPIRE study protocol. Implementation Science, 9, 62. DOI: 10.1186/1748-5908-9-62.
6. **Kuyken W,** Weare K, Okoumunne O, Lewis R, Motton N, Burnett R, Cullen, C., Hennelly, S., & Huppert, F. (2013). Effectiveness of the mindfulness in schools program: A non-randomized controlled feasibility study. British Journal of Psychiatry, 203, 126-131. doi: 10.1192/bjp.bp.113.126649.
7. Wiles, N., Thomas, L., Abel, A., Ridgway, N., Turner, N., Campbell, J., Garland, A, Hollinghurst, S., Jerrom, B., Kessler, D., **Kuyken, W.,** Morrison, J., Turner, K., Williams, C., Peters, T., & Lewis, G. (2012). Cognitive behavioural therapy as an adjunct to pharmacotherapy for primary care based patients with treatment resistant depression: results of the CoBalT randomised controlled trial. Lancet.
8. **Kuyken, W.** Crane, R. & Dalgleish, T. (2012). Does mindfulness-based cognitive therapy prevent depressive relapse? British Medical Journal, 345:e7194. doi: 10.1136/bmj.e7194. Published online 9th November 2012.
9. Crane, R. & **Kuyken, W.** The implementation of mindfulness-based cognitive therapy in the UK Health Service. Mindfulness. DOI 10.1007/s12671-012-0121-6. Published online 22nd June 2012.
10. Williams, J.M.G. & **Kuyken, W. (2012).** Mindfulness-based cognitive therapy: A promising new approach to preventing depressive relapse. British Journal of Psychiatry, 200, 359-360. doi: 10.1192/bjp.bp.111.104745.

Oxford Centre for Human Brain Activity

The Oxford Centre for Human Brain Activity (OHBA) is a state-of-the-art cognitive neuroscience research centre based in the Department of Psychiatry with the aim of supporting translational research into the neural mechanisms of human cognition and its disruption in neuropsychiatric and neurological disorders.

Methods

In alliance with FMRIB, OHBA provides resources and support for the best-quality science from the broad community of Oxford neuroscientists interested in addressing mental illness and cognitive capacity. OHBA houses an advanced magnetoencephalography (MEG) scanner, as well as other methods with which to measure and stimulate human brain activity with high temporal resolution. These methods enable investigation into the dynamics of neural activity within networks of brain areas supporting cognitive functions.

Exciting plans are under way to extend OHBA in 2015. A top-end research-purpose 3T magnetic resonance imaging (MRI) scanner will be installed to increase Oxford's capacity for translational and clinical research on ageing, dementia, and psychiatric conditions. The upgraded multi-modal facility will link-up world-class discovery science and clinical care, by making state-of-the-art multi-modal brain imaging technology available for experimental medicine studies, clinical trials and innovative clinical care. The University of Oxford has committed significant capital investment to support the developments.

Leadership and Groups

Kia Nobre is the scientific director of OHBA and Mark Woolrich is Head of Analysis. Next year Clare Mackay will join OHBA to lead the translational MRI work. In addition to their research groups, three other research groups constitute the core members of OHBA: Attention Group, lead by Mark Stokes; Neurophysiology Group, lead by Charlie Stagg, and the Ageing Group, lead by Susie Murphy. Sven Braeutigam supports the Centre as the MEG Physicist, and Judith Ponsford as administrator.

Research

OHBA hosts research by its core groups as well as by other groups across several departments at Oxford and collaborating institutions. Current translational projects include investigations into: cognition and plasticity in ageing; genetic factors in Alzheimers' disease and in schizophrenia; cognitive deficits in Parkinson's disease; motor and cognitive disruption in motor neurone disease; the role of inhibitory plasticity in motor plasticity after stroke; memory functions and seizure focus in epilepsy; neural excitability in autism; analysis of resting-state functional networks with basic and clinical applications; methods for assessing mechanisms of deep brain stimulation; and cross-modal integration of neuroimaging data for clinical applications. OHBA works in close collaboration with FMRIB, and is part of UK-wide collaboration of MEG centres.

News

Since its inception, OHBA has gained increased prominence as a leading international centre for the study of dynamics in the human brain. Its leaders have been recognized through various awards and promotions this year: Nobre became the first holder of the Chair in Translational Neuroscience and received a Wellcome-Trust Senior Investigator Award, Woolrich received the OHBM Young Investigator Award; Stokes received a McDonnell Foundation Scholar Award; Stagg received a Royal Society and Wellcome Trust Henry Dale Fellowship. Prestigious individual fellowships and scholarships have also been secured by OHBA's postdoctoral fellows and students.

NIHR Oxford cognitive health Clinical Research Facility (NIHR Oxford CRF)

The NIHR Oxford cognitive health Clinical Research Facility (NIHR Oxford CRF) is at the heart of Oxford Cognitive Health, a local research partnership dedicated to generating a step change in the delivery of major benefits for patients with cognitive, neuropsychiatric and neurodegenerative disorders.

The NIHR Oxford CRF consists of four integrated sites

- Warneford site Clinical Research Facility providing eight staffed research rooms
- Experimental Psychology site – The Oxford Centre for Anxiety Disorders and Trauma (OXCADAT)
- Experimental Psychology site – The Oxford Cognitive Neuropsychology Centre
- West Wing John Radcliffe Hospital site – Charles Wolfson Neuroscience Clinical Research Facility

Supporting Technical Facilities

- The Oxford Centre for Human Brain Activity (OHBA)
- Centre for Functional MRI of the Brain (FMRIB)

Funding

The NIHR Oxford CRF is funded by the National Institute for Health Research (NIHR). Other funders include Oxford University Hospitals NHS Trust, Oxford Health NHS Foundation Trust and the University of Oxford.

The development of specialist facilities at the Warneford site is the focus of the majority of the NIHR award and includes; eight equipped research rooms, including two circadian controlled sleep rooms, a sample processing laboratory, and a pharmacy. MEG imaging is on site at OHBA. The range of research activity includes complex high intensity clinical trials from mid phase 1 to phase 3 with an emphasis on experimental medicine, novel psychological treatment studies, observational research into cognitive health and ageing. Disease areas include, dementia, bipolar disorder, schizophrenia and depression. The CRF is utilised by PIs from across Oxford University and Oxford Health NHS Foundation Trust for studies that are both commercially and non commercially sponsored. The facility is integral to the R&D department of Oxford Health NHS Foundation Trust enabling ready access to research governance, financial and contracts requirements and has close links with the NIHR Clinical Research Network.

There has been significant staff development over the past year, under the leadership of Cindy Whitbread, Matron. Workforce development together with the appointment of further specialist research nurses has increased the capacity and scope of research undertaken at the CRF. The appointment of a research nurse to support the Charles Wolfson centre at the West Wing is a further development. This new Research Nurse will work across sites which will encourage further collaboration and improve efficiency.

The Bipolar Research Clinic led by Professor John Geddes has been relocated to the Warneford CRF. The clinic brings together clinical specialists and researchers increasing research participation opportunities for patients.

Staff Lists at each site

Warneford site
John Geddes, Emma Stratful, Bill Wells, Mary Jane Attenburrow, Cindy Whitbread, Helen Jones Kevin Meek, Jithen Benjamin, Elwira Lubos, Akintayo Oladejo, Sarsha Wilson, Valerie Paulley, Maria Turri Katy Smith, Andrea Cipriani.

Experimental Psychology OXCADAT
David Clark, Anke Ehlers, Jennifer Wild, Emma Warnock-Parkes, Miriam Lommen, Elizabeth Woodward Petrina Cox, Lauren Canvin, Sophie Carruthers Emma Shepherd (PA), Tasnim Shabbir (PA).

The Oxford Cognitive Neuropsychology Centre
Glyn Humphries, Jane Riddoch, Jie Sui, Nele Demeyere, Valerie Bonnelle, Magdalena Chechlacz, Celine Gillebert Dante Mantini, Mihaela Duta, Theresa Wildegger, Zahra Moradi, Sally Thomas, Joshua Chauvin, Laura Monroy (Lab Receptionist).

Charles Wolfson Neuroscience Clinical Research Facility
Peter Brown, Alexandre Mathy, John-Stuart Brittain, Huiling Tan, Petra Fischer (Phd student), Hayriye Cagnan Alek Pogosyan, Helena Gardner, Ned Jenkinson, Muriel Panouilleres, Sarah Voets, Jeff Martin (Phd student).

Email: nihrcrf@oxfordhealth.nhs.uk
http://oxford.crf.nihr.ac.uk/about-us/

OCHNCTU — Oxford Cognitive Health and Neuroscience Clinical Trials Unit – Director Professor John Geddes

UKCRC registered Clinical Trials Unit

OCHNCTU, based in the department of psychiatry, is one of the 45 UKCRC fully registered Clinical Trials Unit (CTU). Registration is awarded by an international committee of expert trialists to CTUs with a track record and experience of coordinating multi-centre randomised controlled trials (phase II-IV) and other well-designed studies. Under its former name, OCTUMI, OCHNCTU was first registered in 2007 when it was the only CTU focussing exclusively on mental health trials.

Background to OCHNCTU

The first application for registration was made following the completion of BALANCE, an international trial of maintenance treatment for bipolar disorder and the development and conduct of CTIMPs (Clinical Trials of Investigational Medicinal Products) continues to be a major part of the CTU's activity. Recent trials include the CEQUEL trial of treatment for bipolar depression and a protocol is being developed for a trial exploring the mechanism of action of lithium for mood instability.

OCHNCTU support for trials

OCHNCTU conducts a small number of trials through the complete lifecycle from development of the trial question through to data lock down. In addition to this, PIs from within the departments of psychiatry, experimental psychology and clinical neuroscience can apply for OCHNCTU services which can be funded through their trial grants. These services include advice and support in trial management and quality assurance.

OCHNCTU can expand and contract in response to direct grant-funded activity and will consider requests for advice and support from external PIs. We would, however, encourage PIs to work with RDS who are core funded to provide specific input relevant to the development of protocols and writing of grant applications.

Development of new outcome measures

Key to the robustness and clinical utility of any trial is the inclusion of outcome measures that provide accurate and sensitive indicators of change and can be reliably collected. The True Colours (TC) online self-management system was developed alongside the trials programme both as a clinical tool and as an outcome measure for research. In the CEQUEL trial, the primary outcome was based on patient self-reports using a validated depression questionnaire and collected through TC. A number of other potential outcome measures based on cognitive performance tests, brain imaging, activity monitors and measurement of hormone levels and gene expression are currently being evaluated with the context of proposed new trial.

Systematic Reviews

Trials are designed to provide robust answers to clinical uncertainties. Conducting a systematic review of existing evidence is an important step in the identification of the nature and extent of uncertainty and the formulation of trial questions. The department has a Systematic Review Group that meets monthly and gives researchers conducting systematic reviews the opportunity share expertise. In 2014 an invitation was given to early career research assistants to join the group to gain experience of the review process.

Networking

Within Oxford: OCHNCTU is linked to the Oxford NIHR Biomedical Research Centre via the Cognitive Health Programme. Professor Geddes is a member of the BRC Steering Committee and Chair of the BRC Working Group on Clinical Trials.

For proposed clinical trials, close links with the Oxford Health NHS Foundation Trust and the NIHR Oxford cognitive health Clinical Research Facility facilitate assessment of the feasibility of protocols in terms of the availability of the support required from clinicians and the development of recruitment strategies.

With psychiatrists in the UK: OCHNCTU maintains a list of investigators who have participated in recent trials and who can be contacted to give feedback on proposed trials and to participate in new trials.

With the UKCRC: The UKCRC hold regular meetings for CTU Directors which provide the opportunity for networking and discussions of changes to legislation and guidelines that apply to clinical Trials. The UKCRC has established a number of subgroups addressing topics such as quality assurance, information systems, trial conduct and development of links with industry which provide useful feedback to CTUs

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With our sincere thanks to Frances Burton for her kindness in allowing us to use one of her paintings for our Report's front cover