



Department of Psychiatry

Annual Report 2014

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Professor John Geddes
Head of Department
of Psychiatry

Introduction

This is the second Annual Report of the Department of Psychiatry and provides an overview of our research and educational activities. 2013 has been a very busy year for us with major successes in winning external research funding and in making key senior appointments. Particularly notable this year has been the extent of our collaboration with other University Departments and with our NHS partners. The scientific collaborations have increased the scale of our ambitions and, I think, been critical for the success of our applications for research funding. Our extensive clinical collaborations with Oxford Health NHS Foundation Trust and Oxford University Hospitals NHS Trust have ensured that mental and cognitive health are firmly at the heart of both the *Oxford Academic Health Science Network* (www.oxfordahsn.org) and the new *Oxford Academic Health Science Centre*.

All of this success, of course, is thanks to our magnificent academic and support staff. This report contains reviews of each Principal Investigator's research and our educational activities. I would also like to thank our Departmental Administrator, Pam Taylor, and her team for their peerless and much appreciated support.

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 24 placements each eight weeks. Berkshire Healthcare NHS Trust provides three placements each eight weeks, and we have recently piloted 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.

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 in 2010, 2011, 2012 and 2013, 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, 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 2012-13 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 87% of students either agreed or strongly agreed that 'I received appropriate support as and when I needed it'.

Course outcomes

Subjectively, our external examiner reported in 2013 that 'standards and student achievement [in psychiatry] are at least as high, or higher, than in other medical schools, and are more than adequate to prepare students to enter NHS practice.' 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, and that the school 'adds value' to an already capable cohort (see e.g. McManus et al, BMC Medicine 2008; 6: 5).

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.

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.

During 2013, we hosted the first Oxford Psychiatry Autumn School, which was 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 already underway for a 2nd Autumn School in September 2014.

Honorary Senior Clinical Lecturers

2013-2014

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
Gautam Gulati
Gerti Stegen
Josephine Richards
Peter Sargent
Phil Davison
Philip Wilkinson
Rob Chapman
Clive Meux
Rupert McShane
David Elwell
Denis O'Leary
Julie Chalmers
Tony James
John Baruch
Julia Cartwright
Susan Shaw
Rob Bale
Emma Fergusson
Tim Andrews
Rosie Shepperd
Nick Hindley
Hugh Series

Southern Health NHS Foundation Trust

Dr Val Murphy

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



Supervision and support for postgraduate students is a core activity within the Department of Psychiatry which currently has steadily grown since the last RAE to reach 35 postgraduate students undertaking research degrees (DPhil and MSc [research]). 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.

One of the biggest challenges for students wanting to undertake postgraduate study is the lack of available funding. This is provided by a mixture of MRC studentships, competitive awards made by the newly-instituted Graduate Medical School and other charity-based funding secured by individual PIs. This year, the Department is offering full-studentships (covering university and college fees and living costs) for the 2014 intake. In addition, 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).

Supervision is provided by senior Principal Investigators 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 who will often be a more junior researcher providing valuable support to the student whilst developing their own supervisory skills.

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 transitions/ stages of a research degree and to address academic or personal problems.

In addition to activities directly related to their particular areas of research, students are encouraged to develop their presentation and critiquing skills and to learn about the research being carried out by students working in other research groups. Once or twice a term, two students give short 20-minute presentations of their research to date to the other students (no supervisors are present) and, where appropriate, a 2nd or 3rd year student can be offered the opportunity to present or co-present work at a Professorial Unit seminar.

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 as does the Departmental Meeting which regularly reviews departmental policies and funding as they relate to post-graduate research and training.

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 student 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.

Clinical Academic 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 four 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 1 & 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. 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. They 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, including 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 supervisors 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 (Psychiatric Neuroscience)



Current Research:

My research has focused on prodromal and first episode psychosis, and the formation of delusions, utilizing both cognitive neuropsychology

and neuroimaging, to understand the pathophysiology of schizophrenia and other psychotic disorders.

Ongoing work involves collaborations with colleagues in the Department of Psychosis Studies at the Institute of Psychiatry using multi-modal imaging techniques to examine those at risk of developing psychosis, funded by the EU and the Wellcome Trust, and, with Stephen Wood in Birmingham, a MRC-funded study looking at structural brain changes in those at risk for psychosis serially over time. With Nick Dale at Warwick, I am working on developing a bedside technique of examining D- and L-Serine, a marker of the NMDA receptor function, dysfunction of which has been implicated in schizophrenia.

Currently, I am particularly interested in mood instability transdiagnostically and as a potential marker of future psychopathology and, based upon epidemiological work, planning to look at the neural mechanisms that may connect mood instability with paranoia, and the formation of delusions, with colleagues in OHBA and fMRIB. Together with Steven Marwaha at Warwick, we are beginning to pilot measures of mood instability in clinical populations with different diagnoses to try and determine whether the experience is the same in different disorders.

More generally, I work clinically in the adolescent inpatient unit at the Warneford and am interested in how major mental illnesses develop in adolescents and young adults. Together with Dr Lennox and Professor Freeman we are working on applied clinical research into developing youth mental health services that will help young people who may fall between Child and Adolescent and Adult Services, are experiencing distressing symptoms that impair function and wellbeing, yet may not meet clear diagnostic thresholds for services

Recent publications

1. Guo S, Kendrick KM, Zhang J, **Broome M**, Yu R, Liu Z, Feng J. Brain-wide functional inter-hemispheric disconnection is a potential biomarker for schizophrenia and distinguishes it from depression. *Neuroimage (Clinical)*. 2013 Jun 23;2:818-26.
2. Marwaha S, **Broome MR**, Bebbington PE, Kuipers E, Freeman D. Mood Instability and Psychosis: Analyses of British National Survey Data. *Schizophrenia Bulletin*. 2013 Oct25. [Epub ahead of print]
3. The prevalence and clinical associations of mood instability in adults living in England: results from the Adult Psychiatric Morbidity Survey 2007. Marwaha S, Parsons N, Flanagan S, **Broome M**. *Psychiatry Research*. 205(3):262-8, 2013 Feb 28.
4. Transition to psychosis associated with prefrontal and subcortical dysfunction in ultra high-risk individuals. Allen P, Luigies J, Howes OD, Egerton A, Hirao K, Valli I, Kambeitz J, Fusar-Poli P, **Broome M**, McGuire P. *Schizophrenia Bulletin*. 38(6):1268-76, 2012 Nov.
5. Delusional ideation, manic symptomatology and working memory in a cohort at clinical high-risk for psychosis: a longitudinal study. **Broome MR**, Day F, Valli I, Valmaggia L, Johns LC, Howes O, Garety P, McGuire PK. *European Psychiatry: the Journal of the Association of European Psychiatrists*. 27(4):258-63, 2012 May.

Dr Phil Burnet

Neurobiology and Experimental Therapeutics (Psychiatric Neuroscience)



Research:

My research explores ways of modulating brain chemistry so that complex functions, such as memory and emotion, can be preserved or improved.

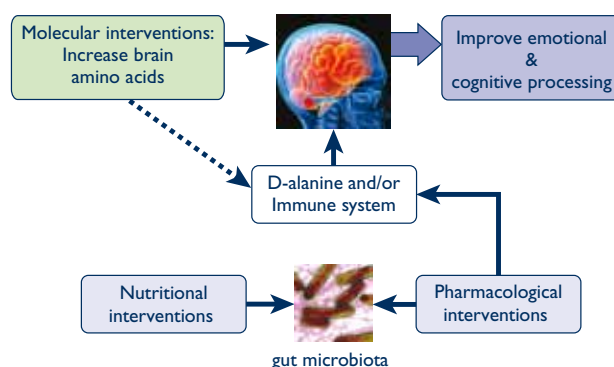
In aging and psychiatric disorders, there is an impairment of memory and positive mood, and only some patients get well with the currently available medication. My work will ultimately offer either supplements or alternatives to contemporary treatments of psychiatric illness.

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 chemical, D-serine. We have shown that reducing DAO increases brain D-serine which, as we have also demonstrated, improves cognitive performance. We are now collaborating with other groups to test drugs which block DAO.

We are also investigating how gut bacteria influences mood and memory, and examining whether substances which encourage their growth can augment the action of psychotropic agents. Studies have shown that ingesting live cultures of 'good' bacteria (probiotics) reduces anxiety, in addition to their overall benefits on metabolism. Our research has revealed that prebiotics (nutritional substances for good bacteria already residing in the gut) also affect emotional processing in healthy volunteers, and reduce the levels of the stress hormone, cortisol, and thus activity of the hypothalamic-pituitary-adrenal (HPA) axis. The work is now being extended to test if prebiotics improve cognitive performance, especially in elderly subjects with mild cognitive impairments.

In parallel, we are searching for the identity of the molecules linking the gut bacteria with the brain. One of these chemicals we are studying is D-alanine, which is rich in bacteria, and stimulates the glutamic acid N-methyl-D-aspartate (NMDA) receptor, a key player in healthy memory function. We have recently found that this D-amino acid not only improves cognition, but also reduces the activity of the HPA axis. The actions of D-alanine on emotional processing are now being explored. Finally, we are exploring whether gut bacteria influences the brain through the immune system. A lot of people feel 'low' or anxious after an infection, and so we are testing if prebiotics can prevent both infection and mood changes. 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



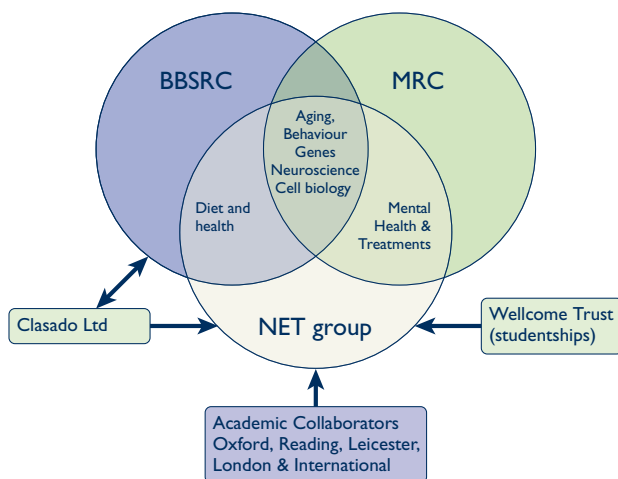
Collaborations and impact

We collaborate extensively with several departments in Oxford including: Experimental Psychology, Pharmacology, and Physiology, Anatomy and Genetics, 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 Esther Sternberg) 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.

Our work is disseminated in scientific journals specializing in neuroscience and psychiatry-related disciplines (see examples below), but we also ensure that our publications are accessible to the general public. In addition, I participate in public engagement in science schemes through 'ScienceOxford UK'

We have attracted funding primarily from the Biotechnology and Biological Sciences Research Council (BBSRC), and also from the Medical Research Council (MRC), the Wellcome Trust and Industry. The strategic priorities of these funding bodies and their overlap with our research, and those of our collaborators are briefly summarised in Fig 2.

FIGURE 2: Research priorities of the NET group, funding organisations, and collaborators



Future Plans

In 2013 I will apply to the BBSRC for a three-year Industrial Partnership Award to study the cognitive and immunological effects of prebiotics in aging. Clasado Ltd are willing to support this application with a financial contribution towards the cost of the study.

My co-applicants will be experts in psychology and old age psychiatry. My postdoctoral research assistant will perform electrophysiological experiments in Leicester to test the direct influence of D-alanine on brain cells. A pre-graduate student from our collaborators in Spain will visit and work in our laboratory for our mutual benefit. Recently acquired data are currently being prepared for publication.

Recent publications

1. **Burnet PWJ** and Cowen PJ (2013) Psychobiotics highlight the pathways to happiness. *Biological Psychiatry* 74: 708-9
2. 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
3. **Burnet PWJ** (2012). Gut bacteria and brain function: the challenges of a growing field. *Proc Natl Acad Sci USA*.109:E175
4. **Burnet PWJ**, Anderson PN, Chen L, Nikiforova N, Harrison PJ, Wood MJ (2011) D-amino acid oxidase knockdown in the mouse cerebellum reduces NR2A mRNA. *Mol Cell Neurosci*. 46:167-75

Professor Tom Burns

Social Psychiatry (Epidemiological and Social Psychiatry)



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.

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 are just completing a major body of work on coercion, both that imposed via the mental health act but also the more pervasive informal pressures patients are exposed to. Our RCT of legal compulsion in the community has generated a number of ethical and legal articles. Similar ethical issues have been raised by our collaboration with Queen Mary's London in a study to pay psychotic patients to take their medicines. Our work arises directly from the questions that clinicians consider they need answers to but we pride ourselves on pursuing these questions with the maximum possible rigour. This may take longer and be more labour intensive but avoiding the compromises so common in this complex area means that the answers we provide have greater generalisability and the potential to influence policy.

Current Trials

- IPS Lite – an RCT of a slimmed down evidence based vocational rehabilitation
- FIAT – A multi-site cluster RCT of paying psychosis patients to take medicine (*with QMUL & Liverpool*)

Current Research Projects

- OCTET Qualitative arm. Explore the way in which CTOs are used and experienced
- OCTET phase II – a follow up to test impact of coercion on disengagement and social functioning
- ULTIMA – Use of Leverage Tools (informal coercion) to Improve Mental health care Adherence
- AMEND – Identifying factors associated with compulsory admission (*with Warwick and Imperial College*)

Funding

All our direct funding has been from the National Institute for Health Research or the HTA.

Recent Publications

1. Burns T, Rugkåsa J, Molodynski A, Dawson J, Yeeles K, Vazquez-Montes M, Voysey M, Sinclair J, Priebe S (2013). Community treatment orders for patients with psychosis (OCTET): a randomised controlled trial. *Lancet*, 381: 1627-33.
2. Singh P, Burns T, Tyrer P, Islam H, Parsons M, Crawford M (2013). Ethnicity as a predictor of detention under the Mental Health Act. *Psychol Med*, DOI: 10.1017/S003329171300086X. [Epub ahead of print].
3. Knapp M, Patel A, Curran C, Latimar E, Catty J, Becker T, Drake R, Fioritti A, Kilian R, Lauber C, Rossler W, Tomov T, van Busschbach J, Comas-Herrera S, White S, Wiersma D, Burns T (2013). Supported employment: cost-effectiveness across six European sites. *World Psychiatry*, 12: 60-8.
4. Canvin K, Rugkåsa J, Sinclair J, Burns T (2013). Leverage and other informal pressures in community psychiatry in England. *Int J Law Psychiatry*, 36: 100-6.
5. Landolt K., Roessler W, Burns T, Ajdacic-Gross V, Galderisi S, Libiger J, Naber D, Kahn RS, Fleischhacker WW & Derks EM (2012). Unmet needs in first episode schizophrenia: a longitudinal perspective. *Psychol Med*, 42, 1461-1473.

Professor Phil Cowen

Psychopharmacology Research Group (Psychiatric Neuroscience)



The focus of the Psychopharmacology group in the last year has been on the development of biomarkers to help identify young people at risk of depression and

investigating the role of inflammation in the causation of depression and as a target for novel treatments.

Dr Zola Mannie and Ms Clare Williams collaborated with Dr Clare MacKay and Dr Nicola Fillipini in a brain imaging study designed to examine the structure and function of the hippocampus in young people at increased risk of depression by virtue of having a parent with a recurrent depressive disorder. They found that the structure of the hippocampus appeared unchanged in people at risk of depression but the functional activation of a hippocampal related memory network was abnormal (Figure), suggesting that risk of depression is associated with the need to recruit a wider neural network to maintain memory performance. We also found that people at risk of depression had increased levels of a measure of the neurotransmitter, glutamate, in the hippocampus. This confirms a previous observation made by Dr Mannie¹ and suggests that increased glutamate might be linked to the abnormal activation seen in the memory networks.

We also carried out some further neuropsychological and medical investigations in young people at risk of depression. We previously found that 'at risk' individuals have increased cardiovascular risk markers in terms of increased blood pressure and insulin resistance² but the mechanism involved was unclear. In a collaboration with Dr Michael Franklin (Oxford Brookes University) we found that, compared to controls, young 'at-risk' people had elevated levels in saliva of a hormone called aldosterone. This is of interest because aldosterone has been linked to cardiovascular disease and diabetes in adults. Also, in animal models aldosterone can cause depressive behaviours. This suggests the possibility of an intriguing link between the mechanisms involved in the medical conditions associated with depression and the experience of depression itself.

There is also interest in whether vulnerability to depression might be associated with abnormal forms of decision-making in situations of uncertainty. This can be modelled using a variety of computerised tasks. We found, using a computerized gambling task, that people at risk of depression employed a conservative strategy to risk- that is not taking chances even when the odds favoured it. A similar strategy has been reported in depressed patients. This might be related to risk of depression because failure to pursue rewarding experiences even when environment factors suggest that a positive outcome is likely could be associated with more disappointments and consequently lowered mood. Abnormal performance in this kind of learning paradigm is also of interest because performance on such tasks can be modified by suitable training which might give an innovative psychological approach to preventing depression in people at risk.

We have continued to collaborate with Dr Ciara McCabe in the use of her fMRI/chocolate model to investigate the neural basis of reward and the effect of novel psychotropic agents. We previously found that cannabinoid drugs produce striking changes in neural responses to reward and punishment³. Most recently, in collaboration with the Pharmaceutical Company, GW Pharma, we tested the effects of a novel plant-derived cannabinoid receptor antagonist, THCv, which in animal studies produces intriguing effects in models of psychosis and appetite disturbance and in our work significantly modified the neural processing of aversive stimuli. Because THCv is a cannabis receptor antagonist it does not produce any psychotomimetic effects and therefore has great potential as a novel treatment for a number of psychiatric and metabolic disorders. Congratulations to Dr McCabe for obtaining a lecturer position at Reading University (though she remains a honorary member of the Department of Psychiatry).

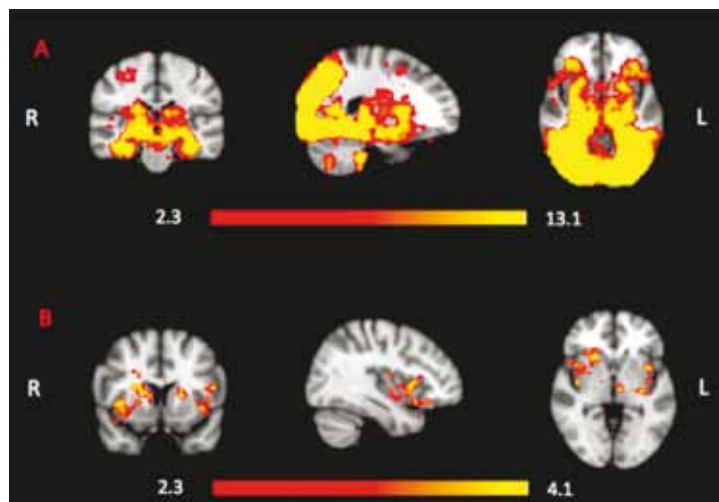
In collaboration with Dr Uzay Emir (FMRIB), Dr Beata Godlewska has begun a study on the neurochemical effects of the cytokine, interferon, which is used to treat hepatitis C but also is associated with a high risk of depression presumably through central inflammation. The study will focus on the use of magnetic resonance spectroscopy at 7T which provides the ability to measure the neurochemical consequences of inflammation with unrivalled specificity and sensitivity.

The effects of interferon could provide an extremely useful model of the effects of inflammation on the brain and a suitable test-bed to examine the effects of drugs with the potential to alleviate depression through anti-inflammatory mechanisms.

Finally we are collaborating with Dr Grant Churchill and colleagues in the Department of Pharmacology in an exciting translational project, designed to repurpose the antioxidant drug, Ebselen, as a potential lithium mimetic agent⁴. This work is being carried out by Dr Nisha Singh and Dr Ann Sharpley who are currently studying Ebselen in a variety of human models in which lithium shows pharmacological activity. Positive results in these models will allow the selection of a dose of Ebselen for subsequent clinical trials in patients with bipolar disorder.

REFERENCES

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3. Horder, J., Harmer, C.J., Cowen, P.J., McCabe, C., 2010. Reduced neural response to reward following 7 days treatment with the cannabinoid CBI. *International Journal of Neuropsychopharmacology* 13, 1103-1113.
4. Singh, N., Halliday, A.C., Thomas, J.M., Kuznetsova, O., Baldwin, R., Woon, E.C.Y., Aley, P.K., Antoniadou, I., Sharp, T., Vasudevan, S.R., Churchill, G.C., 2013. A safe lithium mimetic for bipolar disorder. *Nature Communications* 4, 2320.



fMRI results for the 'novel vs familiar' contrast in the encoding task. (A) Mean activation for the novel vs familiar contrast for all 121 subjects (62 'at-risk' of depression and 59 controls). Activation was found bilaterally in primary and secondary visual cortices as well as regions involved in memory processes: hippocampus, temporal fusiform cortex, parahippocampal gyrus. (B) regions of significantly increased BOLD for FH positive relative to FH negative. Activation in a cluster of brain regions encompassing the insular and putamen regions bilaterally and the

posterior portion of the anterior cingulate cortex was greater in the FH positive relative to FH negative ($p < 0.05$, corrected for multiple comparisons). Red-to-yellow colours define increases in brain activation. R and L define respectively the Right and the Left Hemisphere.

Professor Klaus Ebmeier

Neurobiology of Ageing (Psychiatric Neuroscience)



Why do some people

suffer from depression and memory loss as they age, whereas others stay well for the whole of their lives?

Since 2007 we have

examined the effect of genes and life history on ageing using neuropsychology and neuro-imaging techniques as part of large scale epidemiological and experimental medicine studies. Our group has published over 400 papers, we have now scanned over 350 participants of the Whitehall study and we are funded by MRC, NIHR, ARUK and Parkinson's UK.

Current research

If mental health fails in older age, a large number of factors may be responsible: we aim to isolate these using a variety of large and small-scale studies that use all possible methods of enquiry, from clinical interviews and medical examination to neuropsychology and brain imaging. We have teamed up with the Whitehall Study at UCL and the Oxford Centre for Functional MRI of the Brain (FMRIB) to examine 800 of their volunteers, who have been followed up two-yearly for the last 25 years. We are also part of the Oxford Parkinson's Disease Centre and the Alzheimer's Research UK local network with close links to OPTIMA and Thames Valley DeNDRoN. Under the leadership of Clare Mackay and Klaus Ebmeier, our focus of interest is on the interaction of genetic, environmental, social and psychological factors that confer risk and resilience on people as they age. We are also interested in enhancing brain plasticity and resilience by means of exercise, transcranial stimulation and pharmacology. Our imaging, cognitive and psychiatric research aims to investigate emerging evidence of the brain architecture that enables individuals to compensate cognitively and emotionally, particularly with advancing age.

We are extending these results in the following ways:

1. We will 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 amnesic cognitive impairment or indeed depression.
2. We will test if such good white matter integrity is associated with good quality (compensatory) functional resting networks, using resting fMRI.
3. We will 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.

We are expanding these lines of enquiry in a variety of directions:

1. We will further examine cellular immune responses and endobiome samples to compare with other indicators of (mental- and brain-) health in collaboration with Profs Harri Alenius and Mika Kivimäki, Helsinki, as well as Tunbridge & Harrison in this department.
2. We are currently exploring the effects of exercise and cognitive/emotional activation programmes on healthy older volunteers, and soon patients with MCI, as part of one of the Oxford BRC themes in collaboration with Johansen-Berg & Nobre.
3. We are about to start quantifying participants' gait in collaboration with Prof Helen Dawes, Elizabeth Casson Trust Chair, and Dr Patrick Esser, of the Movement Science Group, Oxford Brookes University, using a movement sensor and remote recording system.
4. We will examine "DNA methylation as a risk marker for developing age-related cognitive decline" in the Whitehall Imaging Cohort with Dr Leonidas Chouliaras, who has joined our group as Academic Clinical Fellow and who was awarded a grant for this project by the Oxfordshire Health Services Research Committee (OHSRC).

Our team

Charlotte Allan, Academic Clinical Lecturer in Old Age Psychiatry (NIHR); **Sophie Behrman**, CT3 in Psychiatry; **Leonidas Chouliaras**, Academic Clinical Fellow (NIHR); **Rocio Eguia Rodriguez**, Specialist in Psychiatry and Psychotherapy, Visiting Fellow (University of Monterrey, Mexico); **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); **Robin Jacoby**, Emeritus Professor of Old Age Psychiatry; **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; **Hugh Series**, Honorary Senior Clinical Lecturer; **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); **David Welchew**, Honorary Clinical Research Fellow (NIHR) (ST5); **Philip Wilkinson**, Honorary Senior Clinical Lecturer; **Enikő Zsoldos**, Research Assistant, DPhil Student (MRC)

News and Impacts 2013

- **Dr Anya Topiwala** had a new daughter, Emeline. Congratulations!
- **Dr Charlotte Allan** was awarded an NIHR Academic Clinical Lectureship in Old Age Psychiatry and the Educator-Development-Group Educator-Innovator-Award 2014 given by the Association for the Study of Medical Education (ASME)
- **Dr Verena Heise** successfully defended her thesis and has taken up a post-doc position at the elite "Helmholtz Centre Bonn" – German Centre for Neurodegenerative Diseases
- **Dr Vyara Valkanova** was appointed to an ST4 training post in psychiatry in the Oxford Deanery
- **Dr Leonidas Chouliaras** joined us as NIHR Academic Clinical Fellow and has already been awarded a research grant by the Oxfordshire Health Services Research Committee (OHSRC)

Selected Publications 2012-2013

1. Cochrane CJ, **Ebmeier KP**. Diffusion tensor imaging in parkinsonian syndromes: a systematic review and meta-analysis. *Neurology*. 2013 Feb 26;80(9):857-64
2. Head J, Stansfeld SA, **Ebmeier KP**, Geddes JR, Allan CL, Lewis G, Kivimäki M. Use of self-administered instruments to assess psychiatric disorders in older people: validity of the General Health Questionnaire, the Center for Epidemiologic Studies Depression Scale and the self-completion version of the revised Clinical Interview Schedule. *Psychol Med*. 2013 Mar 14:1-8
3. Kivimäki M, Shipley MJ, Batty GD, Hamer M, Akbaraly TN, Kumari M, Jokela M, Virtanen M, Lowe GD, **Ebmeier KP**, Brunner EJ, Singh-Manoux A. Long-term inflammation increases risk of common mental disorder: a cohort study. *Mol Psychiatry*. 2013 Apr 9
4. Valkanova V, **Ebmeier KP**, Allan CL. CRP, IL-6 and depression: A systematic review and meta-analysis of longitudinal studies. *J Affect Disord*. 2013 Sep 25;150(3):736-44
5. Valkanova V, **Ebmeier KP**. Vascular risk factors and depression in later life: a systematic review and meta-analysis. *Biol Psychiatry*. 2013 Mar 1;73(5):406-13

Professor Chris Fairburn and Professor Zafra Cooper

Centre for Research on Dissemination at Oxford (CREDO) (Psychological Medicine)



Key Collaborators

Gerhard Andersson (Linköping); **David M Clark** (Oxford); **Riccardo Dalle Grave** (Verona); **Sona Dimidjian** (Colorado); **Helen Doll** (UEA); **Ruth Herman** (Seattle); **Steven Hollon** (Vanderbilt); **Christopher Martell** (Wisconsin-Milwaukee); **Vikram Patel** (Goa, India); **Stig Poulsen** (Copenhagen); **Ray Rosen** (NERI); **Joseph Ruzek** (US VA); **Kenneth Weingardt** (US VA); **G Terence Wilson** (Rutgers).

While effective psychological treatments have been developed for a range of mental health problems, there is good evidence that few people receive them. It is for this reason that research on the dissemination and implementation of psychological treatments is one of NIMH's top priorities. It is for the same reason Oxford received a Strategic Award from the Wellcome Trust to establish the Centre for Research on Dissemination at Oxford (CREDO). The mission of CREDO is to conduct and foster research designed to improve the dissemination and implementation of evidence-based psychological treatments. CREDO is engaged in two main programmes of research:

- i) The development and testing of scalable and cost-effective methods for training therapists in evidence-based psychological treatments, together with new ways of assessing therapist competence
- ii) The development of a novel eTreatment for people with eating problems.

In addition, CREDO is collaborating with certain other research groups on complementary lines of work. The work of CREDO is described in more detail in its website credo-oxford.com.

Core Staff

Kristin Bohn, Senior Research Clinician; **Erin Charlton**, Research Assistant; **Emma Clifton**, Masters student; **Zafra Cooper**, Principal Research Fellow, Deputy Director of CREDO; **Camilla Lindvall Dahlgren**, Research Clinician; **Beth Edwards**, Research Assistant; **Christopher Fairburn**, Wellcome Principal Research Fellow, Director of CREDO; **Fjola Helgadóttir**, Senior Research Clinician; **Rebecca Murphy**, Senior Research Clinician; **Marianne O'Connor**, Senior Research Coordinator; **Katy Sivyler**, Senior Research Assistant and doctoral student; **Susanne Straebler**, Senior Research Clinician

Progress on the three Research Programmes

Programme One – The Development of New Methods for Training Therapists

Under the leadership of Professor Cooper together with Suzanne Straebler and Marianne O'Connor and the support of the rest of the team, CREDO is in the process of developing two clinically-rich therapist training websites, one for CBT-E and the other for behavioural activation for depression (BA). Each website will include an extensive "library" of acted illustrations of the treatment, something that is impossible to provide in conventional workshops. Good progress has been made in developing the CBT-E website. This has involved designing the structure of the website and developing its various components. A large number of acted clinical demonstrations have been recorded in two studios in the Wellcome Building. The first version of the website is being tested in a pilot study involving all eligible therapists across a country in Europe. Simultaneously, we are developing entirely new measures of therapist competence in CBT-E. One is an e-measure of applied knowledge, and the other is a role-play based measure of therapist skill. We are completing tests of their psychometric properties.

Programme Two – The Development of an eTreatment for Eating Problems

This line of work is due to begin in 2014. In preparation for the work, a self-help version of enhanced CBT for eating problems was created and published in 2013. Professor Fairburn is leading this work in collaboration with Professor Gerhard Andersson.

Collaboration with other Research Groups

CREDO has close links with two research groups.

i) **The PREMIUM Research Programme**

This research programme is based Goa (India) and is led by Professor Vikram Patel, Professor of Global Mental Health at the London School of Hygiene and Tropical Medicine. It is funded by a Wellcome Senior Fellowship co-sponsored by Professor Fairburn. The goal of this research is to develop context-sensitive psychological interventions for use in resource-poor settings. The focus is on the development of treatments for those with depression or alcohol misuse. An important additional goal is to formulate a method for developing other interventions for use in similar settings.

ii) **The Development and Testing of a CBT Training Programme for PTSD Therapists**

This research programme is based at the Dissemination and Training Division of the VA National Center for Posttraumatic Stress Disorder in Menlo Park, California. It is led by Professors Josef Ruzek, Director of Dissemination and Training, National Center for PTSD, US Department of Veterans Affairs, together with Dr Raymond Rosen of the New England Research Institute. Professor Fairburn is a Co-Principal Investigator. The goal is to develop and test a web-based training programme in CBT skills for use by those treating US veterans suffering from PTSD.

CREDO also has research links with the following colleagues abroad:

- **Susan Byrne** (UWA, Perth) – CBT-E for adults with anorexia nervosa
- **Riccardo Dalle Grave** (Verona) – CBT-E across all eating disorders and ages
- **Julie Lesser** (Sick Children's Hospital, Minneapolis) – CBT-E for adolescents with anorexia nervosa
- **Hans Hoek** and **Martie de Jong** (The Hague) – CBT-E for adults with eating disorders

CREDO in 2014

Research Programme One

1. The CBT-E website will undergo a major revision early in 2014 based on extensive feedback from users.
2. The major pilot study will be completed by July 2014.

3. The papers reporting the tests of the psychometric properties of CREDO's two competence measures will be completed by spring 2014.
4. The behavioural activation website will be completed by spring 2014.
5. The measures of therapist competence in BA will be tested in summer 2014.

Research Programme Two

The *eTreatment* website will be developed in 2014.

Other Work in 2014

- **Professor Fairburn** will continue to be a governor of a newly formed mental health research charity, MQ.
- **Professor Fairburn** will continue to be a governor of the Oxford Mindfulness Foundation.
- **Professor Fairburn** will continue to be a member of the Council of Beat, the UK's leading eating disorder advocacy organisation.
- **Professor Fairburn** will continue to be a member of the NICE advisory committee on eTherapy.
- **Professor Fairburn** will be on the planning committee of the Wellcome Trust's initiative in digital medicine.

RECENT PUBLICATIONS

1. **Fairburn CG**. Overcoming Binge Eating (Second Edition). New York: Guilford Press, 2013.
2. **Fairburn CG, Cooper Z, Doll HA, O'Connor ME, Palmer RL, Dalle Grave R**. Enhanced cognitive behaviour therapy for adults with anorexia nervosa: A UK-Italy study. *Behaviour Research and Therapy* 2013; 51: 2-8.
3. **Dalle Grave R, Callugi S, Doll HA, Fairburn CG**. Enhanced cognitive behaviour therapy for adolescents with anorexia nervosa: An alternative to family therapy? *Behaviour Research and Therapy* 2013; 51: 9-12.
4. **Crow SJ, Agras WS, Halmi KA, Fairburn CG, Mitchell JE, Nyman JA**. A cost effectiveness analysis of stepped care treatment for bulimia nervosa. *International Journal of Eating Disorders* 2013; 46: 302-307.
5. **Fairburn CG, Wilson GT**. The dissemination and implementation of psychological treatments: Problems and solutions. *International Journal of Eating Disorders* 2013, 46: 516-521.
6. **Serpell L, Stobie B, Fairburn CG, van Schaick R**. Empirically-supported and non-empirically supported therapies for bulimia nervosa: retrospective patient ratings. *Journal of Eating Disorders* 2013;1:41.
7. **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* (in press).
8. **Helgadottir FD, Fairburn CG**. Web-centred training in psychological treatments: a study of therapist preferences. *Behaviour Research and Therapy* (in press).
9. **Fairburn CG, Cooper Z**. Eating disorders: A transdiagnostic protocol. In: Barlow DH (ed). *Clinical Handbook of Psychological Disorders* (4th edition). New York: Guilford Press, in press.

Dr Seena Fazel

Risk Factors for Mental Illness and Violent Crime (Epidemiological and Social Psychiatry)



Current Activity

I am a Wellcome Trust Senior Research Fellow in Clinical Science. This research programme, which started in 2012, is utilising Sweden

population registers to examine relationship between mental illness and violent crime, and develop clinical prediction rules for predicting violent outcomes in patient groups.

Over last year, I have continued to collaborate closely with Medical Epidemiology and Biostatistics Unit at the Karolinska Institute in Sweden, and with colleagues in the department (Keith Hawton to examine suicide risk in prisoners; Charles Newton to investigate mortality in epilepsy and role of psychiatric illness; John Geddes to study adverse outcomes in bipolar disorder).

Main publications – our study on premature mortality in epilepsy was published in the *Lancet* and investigated associations with psychiatric morbidity. It received widespread media interest with reports in Daily Telegraph, US News and Report, The Times of India, among others. It also attracted radio coverage in BBC local and national radio, Swedish national radio, and was the topic of one of the *Lancet's* weekly podcast. Commentaries in the *Lancet*, *Neurology Today*, and *Future Neurology* discussed its implications.

A large study of all self-harm in English and Welsh prisons over six years will be published in the *Lancet* in December 2013.

In terms of systematic reviews, we published a mega-review of genetic associations with violence with colleagues at the Institute of Psychiatry. In addition, Kat Witt, who is soon to finish her DPhil in the department, completed a large review of risk factors for violence in psychosis. We also published a review on authorship bias in violence risk assessment research that generated some debate in the field.

Zheng Chang, post-doc, is joining the team in 2014, and Naomi Smith for an MSc.

Future plans – next year, we will complete a series of pharmaco-epidemiological studies specifically looking at the effects of psychotropic medications and crime outcomes. With Keith Hawton, we are reviewing suicide risk assessment tools. In addition, in a new collaboration with the department of Primary Care Health Sciences, we will start work on developing clinical prediction rules for crime in patient groups. Dr Chang will start work on investigating the determinants of repeat offending in mentally disordered offenders.

Key papers

1. **Fazel S**, Wolf A, Långström N, Newton CR, Lichtenstein P (2013) Premature mortality in epilepsy and the role of psychiatric comorbidity: a total population study. *Lancet*, 382:1646-54.
2. Hawton K, Linsell L, Adeniji T, Sanasarian A, **Fazel S** (2013) Self-harm in prisons in England and Wales: an epidemiological study of prevalence, risk factors, clustering, and subsequent suicide. *Lancet*, 382 (epub 19 December)
3. Vassos E, Collier D, **Fazel S** (2013) Systematic meta-analyses and field synopsis of genetic association studies of violence and aggression. *Molecular Psychiatry* (epub 2 April 2013; doi: 10.1038/mp.2013.31)
4. Witt K, van Dorn R, **Fazel S** (2013) Risk Factors for Violence in Psychosis: Systematic Review and Meta-Regression Analysis of 110 Studies. *PLoS ONE* 8(2): e55942. doi:10.1371/journal.pone.0055942
5. Singh JP, Grann M, **Fazel S** (2013) Authorship Bias in Violence Risk Assessment? A Systematic Review and Meta-Analysis. *PLoS ONE* 8(9): e72484. doi:10.1371/journal.pone.0072484

Professor Daniel Freeman

Cognitive Approaches to Psychosis



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 successfully treated.

Team Members: Daniel Freeman, Katherine Pugh, Bryony Sheaves, Felicity Waite, Emma ernis, Nicole Evans, Rachel Lister, Angus Antley, Helen Startup.

Alongside a number of theoretical studies, we have four clinical trials taking place:

■ **Worry Intervention Trial (WIT)**

Worry brings implausible ideas to mind, keeps them there, and makes the experience more distressing. We are evaluating a new Cognitive Behavioural Therapy (CBT) intervention for worry for individuals with persecutory delusions within the context of a diagnosis of psychosis. The trial is funded by the Medical Research Council and the National Institute for Health Research.

■ **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.

■ **Self Confidence Study**

Our theoretical model predicts that paranoia builds on common negative thoughts about the self. Therefore we are evaluating a new cognitive therapy intervention for low self-esteem for individuals with persecutory delusions within the context of a diagnosis of psychosis. The trial is funded by the Medical Research Council.

■ **Virtual Reality Study**

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 trial is funded by the Medical Research Council.

Key publications in the past year include:

1. **Freeman, D.**, Thompson, C., Vorontsova, N., Dunn, G., Carter, L-A., Garety, P., Kuipers, E., Slater, M., Antley, A., Glucksman, E., & Ehlers, A. (2013). Paranoia and post-traumatic stress disorder in the months after a physical assault: a longitudinal study examining shared and differential predictors. *Psychological Medicine*, 43, 2673-2684.
2. **Freeman, D.**, Startup, H., Dunn, G., Cernis, E., Wingham, G., Pugh, K., Cordwell, J., & Kingdon, D. (2013). The interaction of affective with psychotic processes: a test of the effects of worrying on working memory, jumping to conclusions, and anomalies of experience in patients with persecutory delusions. *Journal of Psychiatric Research*, 47, 1837-1842.
3. **Freeman, D.**, Dunn, G., Fowler, D., Bebbington, P., Kuipers, E., Emsley, R., Jolley, S., & Garety, P. (2013). Current paranoid thinking in patients with delusions. *Schizophrenia Bulletin*, 39, 1291-1297.
4. Garety, P. & **Freeman, D.** (2013). The past and future of delusions research: from the inexplicable to the treatable. *British Journal of Psychiatry*, 203, 327-333.
5. Ronald, A., Sieradzka, D., Cardno, A., Haworth, C., McGuire, P. & **Freeman, D.** (2013). Characterization of psychotic experiences in adolescence using the Specific Psychotic Experiences Questionnaire (SPEQ): Findings from a study of 5000 16 year old twins. *Schizophrenia Bulletin*. 10.1093/schbul/sbt106

Alongside the development of the understanding and treatment of psychosis, we are committed to making our research – and especially therapeutic techniques – available to the widest possible audience, with several books for the general reader published. In 2013 we published *The Stressed Sex: Uncovering the Truth about Men, Women, and Mental Health* (Oxford University Press) and *How to Keep Calm and Carry On* (Pearson). Professor Freeman's recent work has been covered in the national and international media, including BBC Breakfast, BBC Radio 4's Woman's Hour, BBC Radio Five Live, Time, The Guardian, The Daily Telegraph, The South China Morning Post, The Daily Mail, The Daily Beast/Newsweek, The Huffington Post, Forbes, and Grazia.

Professor John Geddes

Experimental Epidemiology and Bipolar Disorder (Epidemiological and Social Psychiatry)



We focus on developing new treatments for people with bipolar disorder based on better understanding of the mechanisms underlying the disorder. We then

formally evaluate the effects of treatments and services for people with bipolar disorders in randomized trials. In 2013, we completed the CEQUEL trial and secured funding from the Wellcome Trust for the *Collaborative Oxford Network for Bipolar Research to Improve Outcomes* (CONBRIO).

The development of the *NIHR Oxford Cognitive Health Clinical Research Facility* continues thanks to the leadership of Dr Mary-Jane Attenburrow and Emma Stratful. We are delighted to have recruited our longstanding collaborator Dr Andrea Cipriani and our new Matron, Mrs Cindy Whitbread.

Our NIHR-funded **OxTEXT** programme (with Guy Goodwin) has now recruited almost 350 people with bipolar disorder into the cohort via the OXTEXT 1 protocol which involved regular remote mood monitoring using True Colours. **True Colours** was implemented across Oxford Health NHS Foundation Trust in 2013 via OXTEXT 7, a step wedge cluster randomized trial. Active recruitment will shortly commence from the OXTEXT cohort into StembANCC – a project which will investigate the role of stem cells in drug discovery in psychiatric disorder

A major event at the end of 2013 was our successful application to the Wellcome Trust for a Strategic Award for the Collaborative Oxford Network for Bipolar Research to Improve Outcomes (CONBRIO). CONBRIO will explore the genetic and neural mechanisms underlying mood instability with the aim of developing successful intermediate outcomes to use in experimental medicine studies. There are four themes, led by John Geddes, Cath Harmer, Paul Harrison, Kia Nobre and involves a wide range of investigators in Oxford, Cardiff, Baltimore, London and Edinburgh. The first step for our theme will be to augment the Oxtext cohort with the Bipolar Disorders Research Network (PI: Prof Nick Craddock) and to demonstrate the validity of the large-scale, big data approaches and mathematical modelling of mood and physiological data (with Dr Patrick McSharry and Prof Terry Lyons).

Research synthesis continues to be a key component of our research programme. Dr Andrea Cipriani joined the Department this year (and published a new analysis of the antisuicidal effects of lithium in the *British Medical Journal*) and we were delighted also to welcome Professor Stefan Leucht and Dr Claudia Leucht to spend a year with us in the Department. Stefan led the major new analysis of antipsychotics recently published in the *Lancet*. In 2014 we plan to make the most of the critical mass of meta-analytic expertise currently available to us in the Department!

Key 2013 Publications

1. **Geddes JR**, Miklowitz DJ. *The Lancet* 381(9878):1672-1682
11 May 2013
2. Leucht S, Örey D, Richter F, Samara M, Kissling W, Stapf MP, Lässig B, Cipriani A, Barbui C, Spineli L, Mavridis D, Salanti G, Engel RR, **Geddes JR**. Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: A multiple-treatments meta-analysis, Davis JM. *The Lancet* 382(9896):951-962 2013
3. Cipriani A, Higgins JP, **Geddes JR**, Salanti G, *Ann Intern Med* 159(2):130-137 16 Jul 2013
4. Cipriani A, Hawton K, Stockton S, **Geddes JR**. Lithium in the prevention of suicide in mood disorders: updated systematic review and meta-analysis. *BMJ* 346:f3646 2013
5. Bourne C, Aydemir O, Balanzá-Martínez V, Bora E, Brissos S, Cavanagh JT, Clark L, Cubukcuoglu Z, Dias VV, Dittmann S, Ferrier IN, Fleck DE, Frangou S, Gallagher P, Jones L, Kieseppä T, Martínez-Aran A, Melle I, Moore PB, Mur M, Pfennig A, Raust A, Senturk V, Simonsen C, Smith DJ, Bio DS, Soeiro-de-Souza MG, Stoddart SD, Sundet K, Szöke A, Thompson JM, Torrent C, Zalla T, Craddock N, Andreassen OA, Leboyer M, Vieta E, Bauer M, Worhunsky PD, Tzagarakis C, Rogers RD, **Geddes JR**, Goodwin GM. Neuropsychological testing of cognitive impairment in euthymic bipolar disorder: an individual patient data meta-analysis. *Acta Psychiatr Scand* 26 Apr 2013
6. Fazel S, Wolf A, **Geddes JR**. *Bipolar Disord* 15(5):491-495 Aug 2013
7. Head J, Kivimäki M, Stansfeld SA, Ebmeier KP, **Geddes JR**, Allan CL, Lewis G. *Psychological Medicine* 43(12):2649-2656 Dec 2013

Professor Guy Goodwin

Experimental Medicine and Neurobiology of Mood Disorders (Psychiatric Neuroscience)



The future of psychiatry will depend upon the successful application of neuroscience to diagnosis and treatment. Developments in the cognitive neuropsychology

of emotion have provided a fruitful starting point for defining the phenotype in mood disorder more precisely and without the constraints of provisional diagnostic systems like DSM5.

An improved theoretical framework could move us beyond the simple phenomenology that still dominates approaches to aetiology. Relevant neurocognitive mechanisms and their supporting brain networks can inform the dimensional approach that the problem clearly merits. In addition, it offers the potential for a subsequent dissection on the basis of brain connectivity, neurotransmitter function and gene expression. It may also offer much needed assays for the actions of new medicines or for psychological treatments: 'experimental medicine' has been identified as the key mission for academic medicine in this country and I have long been strongly committed to it.

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.

I am now developing the *Oxford Sleep and Circadian Neuroscience Institute* with Russell Foster and Kay Davies, supported by a strategic award from the Wellcome Trust.

This virtual institute exemplifies the principle that cutting edge neuroscience can be applied to clinical problems. The challenge for academic psychiatry is to engage the best brains in basic science on our problems.

Current grants

- Development and evaluation of a multidisciplinary service for people with bipolar disorder NIHR Programme Grants for Applied Research: RPPG-0108-10087 (with John Geddes)
- Oxford Centre for Human Brain Activity Wellcome Trust Infrastructure grant (with Nobre, Woolrich, Behrens and others)
- Bipolar affective disorder or borderline personality

Recent publications

1. Bourne, C., Aydemir, Ö., Balanzá-Martínez, V., Bora, E., Brissos, S., Cavanagh, J. T. O., Clark, L., Cubukcuoglu, Z., Dias, V. V., Dittmann, S., Ferrier, I. N., Fleck, D. E., Frangou, S., Gallagher, P., Jones, L., Kieseppä, T., Martínez-Aran, A., Melle, I., Moore, P. B., Mur, M., Pfennig, A., Raust, A., Senturk, V. Simonsen, C., Smith, D. J., Bio, D. S., Soeiro-de-Souza, M. G., Stoddart, S. D. R., Sundet, K., Szöke, A., Thompson, J. M., Torrent, C., Zalla, T., Craddock, N., Andreassen, O. A., Leboyer, M., Vieta, E., Bauer, M., Worhunsky, P. D., Tzagarakis, C., Rogers, R. D., Geddes, J. R., **Goodwin, G. M.** (2013) Neuropsychological testing of cognitive impairment in euthymic bipolar disorder: an individual patient data meta-analysis. *Acta Scand Psychiatrica* 128, 149-162
2. Di Simplicio, M., McInerney, J.E., **Goodwin, G.M.**, Attenburrow, M.-J., Holmes, E.A. (2012) Revealing the mind's eye: bringing (mental) images into psychiatry. *American Journal of Psychiatry* 169:1245-1246
3. Price, J., Cole, V., Doll, H., **Goodwin, G. M.** (2012) The Oxford Questionnaire on the Emotional Side-effects of Antidepressants (OQuESA): Development, validity, reliability and sensitivity to change. *Journal of Affective Disorders* 140, 66-74
4. Moore, P.J., Little, M.A., McSharry, P.E., Geddes, J.R., **Goodwin, G. M.** (2012) Forecasting depression in bipolar disorder. *IEEE Trans Biomed Eng* 59(10):2801-2807
5. Millan MJ, Agid Y, Brune M, Bullmore ET, Carter CS, Clayton NS, Connor R., Davis, S., Deakin, B., Derubeis, R.J., Dubois, B., Geyer, M.A., **Goodwin, G. M.**, Gorwood, P., Jay, T.M., Joels, M., Mansuy, I.M., Meyer-Lindenberg, A., Murphy, D., Rolls, E., Saletu, B., Spedding, M., Sweeney, J., Whittington, M., Young, L.J. (2012) Cognitive dysfunction in psychiatric disorders: characteristics, causes and the quest for improved therapy. *Nat Rev Drug Discov* 11(2):141-68. PMID:22293568

Professor Catherine Harmer

The Psychopharmacology of Emotion Research Lab (PERL)



We focus on the mechanisms underpinning drug and psychological interventions in mental health using a neurocognitive perspective.

Traditional accounts of antidepressant drug action have illuminated the neurochemical, cellular and molecular effects of drug treatment, but these accounts fail to explain how these underlying neurophysiological changes became translated into the efficacy of these drugs in the clinic. The work of PERL has shown that antidepressant drugs reverse key psychological maintaining factors in depression (the negative bias in processing of emotional information) before mood changes are evident. Such early effects of antidepressant drug treatments have been demonstrated in healthy people and depressed patients using both behavioural and neural outcome measures. These early changes in emotional processing may be an important mechanism by which antidepressant drugs affect symptoms seen in depression over time and experience of everyday events and stressors. Our recent work has also started to consider the effects of psychological interventions using this neurocognitive perspective as well as the effects of novel or candidate treatments for depression and the neuropsychology of treatment action in depressed adolescents. We have also received grant funding to explore the cognitive mechanisms of treatment action on mood instability in bipolar disorder (Wellcome Trust), the role of implicit changes in cognition in the effects of cognition enhancing drug treatments (UCB) and the predictive effects of early changes with bupropion treatment on reward and emotional processing in the treatment of depression (Janssen Research & Development).

Group Members

- **Research Assistant:** Claire Shuttleworth
- **DPhil students:** Maria Ironside, Kristin Schmidt, Jacqueline Scholl, Charlotte Cooper, Annabel Walsh, Liliana Capitao, Matthew Warren
- **Post-doctoral researchers:** Corinna Klinge, Jessica Smith
- **Clinician scientists:** Daniel Whiting, Michael Browning, Nathan Huneke, Andrea Reinecke

- **Honorary members:** Abbie Pringle
- **Visitors:** Magdalena Soukupova, Patrick Pflanz, Davide Folloni, Jan Guenther

Public Engagement and Awards

- A BBC documentary entitled *The truth about depression* profiled the work of the group and was aired in February 2013. An article discussing the implications of the cognitive neuropsychological account of antidepressant drug action is just about to be published in *Scientific American Mind* (to appear in January 2014).

PERL members received the following awards in 2013:

- AE Bennett award, Society of Biological Psychiatry to Catherine Harmer;
- Journal of Psychopharmacology, most cited paper in 2013 to Martina DiSimplicio and colleagues
- The Keble Association Award to Liliana Capitao
- An Erasmus Scholarship to Patrick Pflanz

Grants Awarded

- **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

Recent Publications

1. **Pringle, A. et al.,** (2013) Early markers of cognitive enhancement: developing an implicit measure of cognitive performance. *Psychopharmacology* (Berl). 2013 Jul 3 (**Provided evidence that implicit measures of cognition may be more sensitive to cognitive enhancing drugs than explicit or strategic measures. This has implications for the optimal methods for screening and understanding new drug treatments for cognition*).
2. **Reinecke, A. et al.,** (2013) Changes in automatic threat processing precede and predict clinical changes with exposure-based cognitive-behavior therapy for panic disorder. *Biol Psychiatry*. 2013 Jun 1;73(11):1064-70. (**Provided evidence that early change in attentional bias to threat occurs after a single session of CBT in panic disorder and before changes in symptoms. These early changes in cognitive processing are predictive of later clinical improvement, consistent with the cognitive neuropsychological perspective*).
3. **Browning, et al.,** (2012). Using attentional bias modification as a cognitive vaccine against depression. *Biol Psychiatry*. 2012 Oct 1;72(7):572-9. (**Provided evidence that attentional bias modification (training to attend to positive over negative stimuli) can have protective effects on markers of vulnerability in patients recovered from depression*).

Professor Paul Harrison

Translational Neurobiology of Psychosis (Psychiatric Neuroscience)



In 2013 the Translational Neurobiology of Psychosis group has continued to work across a range of projects from genetics to experimental medicine, with colleagues and collaborators both locally and elsewhere. The breadth of work is reflected in our recent (and forthcoming) publications.

We have continued to study the biology of several genes which may be involved in both the cause, and the treatment, of schizophrenia: group II metabotropic glutamate receptors (GRM2 and GRM3), D-amino acid oxidase, and GRIA1. Working with David Bannerman (Department of Experimental Psychology), Trevor Sharp (Department of Pharmacology), and others, our recent data show that these genes all affect dopamine function, providing a direct link to (and possible explanation for) their roles in schizophrenia. Additional work on the function of these genes is underway as part of the Wellcome Trust Sleep and Circadian Neuroscience Institute, led by Russell Foster and Stuart Peirson (Nuffield Department of Clinical Neurosciences).



PICTURED (LEFT TO RIGHT): Tom Hyde (*Lieber Institute for Brain Development, Johns Hopkins Medical School, Baltimore*), Liz Tunbridge, Paul Harrison, Daniel Weinberger (*Lieber Institute*).

Led by Liz Tunbridge, we have investigated further the dopamine-regulating gene catechol-o-methyltransferase (COMT) using a range of experimental approaches. These are showing that it has wider and different effects on behavior and brain activity than had been assumed. We are exploring these effects, and their mechanisms, in particular through a new MRC grant to investigate how genetically- and pharmacologically-mediated changes in COMT activity impact upon emotional processing and reward behavior in healthy volunteers. This work is set against a backdrop of increasing interest in the use of COMT inhibitors as drugs to treat a range of psychiatric disorders.

Finally, with Kia Nobre and our collaborators at the Lieber Institute of Brain Development in Baltimore (see photo), we have completed a multimodal study of the leading psychosis risk gene ZNF804A. We have found that the genetic risk likely operates largely during fetal life, doing so through a previously unknown variant (isoform) of the gene, and with persistent effects on brain function as measured by functional MRI and magnetoencephalography.

In November 2013 we received a Strategic Award from the Wellcome Trust on bipolar disorder: CONBRIO: Collaborative Oxford Network for Bipolar Research to Improve Outcomes. With John Geddes, Kia Nobre, Catherine Harmer, and other colleagues in Oxford, Cardiff, and Baltimore, this will explore four key areas related to mood instability: capturing and predicting symptoms; genetic mechanisms; cognitive and neural correlates; and developing an experimental medicine model. The work will be complemented by work on induced pluripotent stem cells from patients, collection of which has commenced under the IMI StemBANCC program.

We said goodbye in 2013 to Tracy Lane and Helena Cousijn, and welcomed Sarah Atkinson and Jessica Laidlaw.

Publications

1. Lane TA, Boerner T, Bannerman DM, Kew JNC, Tunbridge EM, Sharp T, **Harrison PJ** (2013) Decreased striatal dopamine in group II metabotropic glutamate receptor (mGlu2/mGlu3) double knockout mice. *BMC Neuroscience* 14 102. doi:10.1186/1471-2202-14-102.
2. Laatikainen LM, Sharp TS, **Harrison PJ**, Tunbridge EM (2013) Sexually dimorphic effects of catechol-O-methyltransferase (COMT) inhibition on dopamine metabolism in multiple brain regions. *PLoS One* 8 e61839.
3. Tunbridge EM, Farrell SM, **Harrison PJ**, Mackay CE (2013) Catechol-O-methyltransferase influences the connectivity of the prefrontal cortex at rest. *Neuroimage* 68 49-54
4. **Harrison PJ** (2013) The current and potential impact of genetics and genomics on neuropsychopharmacology. *European Neuropsychopharmacology* dx.doi.org/10.1016/j.euroneuro.2013.02.005.
5. Coutinho E, Harrison PJ, Vincent A. Do neuronal antibodies cause psychosis? A neuroimmunological perspective. *Biological Psychiatry* <http://dx.doi.org/10.1016/j.biopsych.2013.07.040>

Professor Keith Hawton

Centre for Suicide Research (Epidemiological and Social Psychiatry)



The aim of our 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.

Group members

- Liz Bale, Dr. Helen Bergen, Deborah Casey, Louise Harriss, Professor Camilla Haw, Dorothy Rutherford, Dr. Kate Saunders, Sue Simkin, Kat Witt.
- **Barnes Unit Research Nurse:** Fiona Brand
- **Suicide Prevention Lead (Oxford Health NHS FT):** Karen Lascelles

Current research

Multicentre Study of Self-harm in England

CSR is the lead centre in the three centre (Oxford, Manchester, Derby) six hospital 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 38-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 in support of the National Suicide Prevention Strategy for England

The CSR is involved in a second National Institute for Health Research Programme Grant in collaboration with colleagues at the universities of Bristol and Manchester for a series of studies to contribute to health service initiatives relating to self-harm and suicide.

Part of the Oxford component is to produce resources for parents and carers of young people who have self-harmed and the clinicians involved in their care. We are working with colleagues at the University of Oxford Health Experiences Research Group to conduct a UK-wide study to increase understanding of this experience and to provide information and support for parents and carers. We have interviewed 40 parents and carers of young people up to the age of 25 who have self-harmed, and from analysis of these interviews we will develop a module for the Healthtalkonline website (<http://www.healthtalkonline.org>) to support and inform other families going through similar experiences. We will also produce a guide for parents similar to the booklet Help is at Hand developed for people bereaved by suicide, and guidelines for self-harm services.

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.

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.

Cochrane Reviews

We are updating our Cochrane Review of interventions for people who have self-harmed and starting a new review on treatment with ketamine.

Collaboration with Scandinavian researchers

Professor Hawton is involved in a study with Margda Waern in Gothenberg to assess long-term outcome of women who were suicidal in middle age. He is collaborating on an investigation of family transmission of suicidal behaviour with Professor Preben Mortensen and colleagues in Aarhus using the Danish Adoption Case Register. 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.

Internet research

We have recently undertaken studies on the influence of the internet on suicidal behaviour and the types of sites visited by young people who may be at risk of suicide.

Collaborators

Dr Seena Fazel; Louise Linsell; Dr. Louise Locock; Professor Paul Montgomery; Kate Daine; Dr Anne Stewart; Dr Vinod Singaravelu; Dr Jo Adams; Dr Nick Meyer; Bergljot Gjelsvik; Professor Rory O'Connor (Glasgow University); Professor David Gunnell (Bristol University); Professor Nav Kapur, Dr. Jayne Cooper (Manchester University); Keith Waters (Derbyshire NHS Foundation Trust); Professor Margda Waern (Gothenburg University); Professor Preben Mortenson (Aarhus University); Professor Merete Nordentoft and Dr. Annette Erlangsen (Copenhagen University); Dr. Michael Eddleston (Edinburgh University); Professor Andrew Dawson (Melbourne University); Dr. Greg Carter (Newcastle University, Australia).

Other Activities

Professor Hawton was presented with the Morselli Award of the International Academy for Suicide Research at the World Congress on Suicide in Montreal. He was also elected a Fellow of the Academy of Medical Sciences.

■ 20th anniversary

We organise the annual British Isles Research Workshop on Suicide and Self-harm. In September 2013 we held the 20th workshop, and celebrated this with a dinner at Green Templeton College and a Lancet Symposium on Suicide to mark the launch of *Lancet Psychiatry*.

■ Suicide prevention in America

Professor Hawton has been a member of the *Overview Expert Panel of the National Action Alliance for Suicide Prevention's Research Task Force of the US National Institute for Mental Health* which is developing the research agenda for the US national suicide prevention strategy.

- **ALSPAC:** Professor Hawton is part of a group awarded a grant from the Avon Longitudinal Study of Parents and Children (ALSPAC) cohort to research self-harm with and without suicidal intent in adolescence.

Future plans

We hope to conduct an interview study of internet and other media influences on young people who have self-harmed.

Publications from the group in 2013 include:

1. **Hawton, K.**, Bergen, H., Simkin, S., Dodd, S., Pocock, P., Bernal, W., Gunnell, D. & Kapur, N. (2013). Long term effect of reduced pack sizes of paracetamol on poisoning deaths and liver transplant activity in England and Wales: interrupted time series analyses. *BMJ*, 346, f403. doi:10.1136/bmj.f403
2. **Hawton, K.**, Casanas i Comabella, C., Haw, C. & Saunders, K. E. A. (2013). Risk factors for suicide in individuals with depression: A systematic review. *Journal of Affective Disorders*, 147, 17-28. doi:10.1016/j.jad.2013.01.004
3. Gunnell, D., **Hawton, K.**, Bennewith, O., Cooper, J., Simkin, S., Donovan, J., Evans, J., Longson, D., O'Connor, S. & Kapur, N. (2013). A multicentre programme of clinical and public health research in support of the National Suicide Prevention Strategy for England. Programme Grants for Applied Research, 1. doi:10.3310/pgfar01010
4. Cipriani, A., **Hawton, K.**, Stockton, S. & Geddes, J.R. (2013). Lithium in the prevention of suicide in mood disorders: an updated systematic review and meta-analysis. *BMJ*, 346, f3646. doi:10.1136/bmj.f3646
5. Daine, K., **Hawton, K.**, Singaravelu, V., Stewart, A., Simkin, S. & Montgomery, P. (2013). The power of the web: a systematic review of studies of the influence of the internet on self-harm and suicide in young people. *PLOS ONE*, 8, e77555. doi:10.1371/journal.pone.0077555

Professor Emily Holmes

Experimental Psychopathology and Cognitive Therapies (EPaCT) (Psychological Medicine)



The Experimental Psychopathology and Cognitive Therapies Team aims to use experimental psychology 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.

1. Bipolar disorder, mental imagery and cognitive therapy

Researchers: Susie Hales, Kerry Young, Martina Di Simplicio, Lalitha Iyadurai, Craig Steel 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 now offer MAPP (Mood Action Psychology Programme) in a case series study of brief imagery-focused cognitive therapy (imCT) for Bipolar Disorder also in collaboration with Psychological Services in Oxford Health NHS Foundation Trust.

2. Depression, mental imagery and ageing

Researchers: Simon Blackwell, Arnaud Pictet, Emily Holmes (PI)

Oxford Collaborators: Geddes, Browning, Nobre, Johansen-Berg, Murphy

Grant support: Lupina Foundation, NIHR, The Wellcome Trust

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 are currently in the process of finishing a clinical trial for depression via the Internet (OxIGen: Oxford Imagery Generation). We are also adapting this approach for resilience in ageing as part of our NIHR grant with Nobre (OHBA) and Johansen-Berg (FMRIB).

3. Psychological trauma and involuntary mental images

Researchers: Ian Clark, Ella James, Lalitha Iyadurai, Emily Holmes (PI)

Oxford Collaborators: Mackay, Geddes, Nobre, Tunbridge, Harrison

Grant support: NIHR, MRC, The Colt Foundation, The Wellcome Trust

We seek to better understand flashbacks 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 and fMRI studies.

2013 Findings Include:

1. Bourne, C., Mackay, C. E., & Holmes, E. A. (2013). The neural basis of flashback formation: the impact of viewing trauma. *Psychological Medicine*, 43(17), 1521-1533. doi: 10.1017/S0033291712002358. http://journals.cambridge.org/repo_l89eVMtv
2. Williams, A. D., Blackwell, S. E., Mackenzie, A., Holmes, E. A., & Andrews, G. (2013). Combining imagination and reason in the treatment of depression: A randomized controlled trial of internet-based cognitive bias modification and internet-CBT for depression. *Journal of Consulting and Clinical Psychology*. Advance online publication. doi: 10.1037/a0033247
3. Blackwell, S. E., Rius-Ottenheim, N., Schulte-van Maaren, Y. W. M., Carlier, I. V. E., Middelkoop, V. D., Zitman, F. G., Spinhoven, P., Holmes, E. A., & Giltay, E. J. (2013). Optimism and mental imagery: A possible cognitive marker to promote wellbeing? *Psychiatry Research*, 206(1), 56-61. doi: 10.1016/j.psychres.2012.09.047

4. Clark, I. A., Mackay, C. E., & Holmes, E. A. (2013). Positive involuntary autobiographical memories: You first have to live them. *Consciousness and Cognition*, 22(2), 402-406. doi: 10.1016/j.concog.2013.01
5. Burnett Hayes, S., Lau, J. Y., & Holmes, E. A. (2013). Mental imagery, emotion and psychopathology across child and adolescent development. *Developmental Cognitive Neuroscience*, 5, 119-133. doi: http://dx.doi.org/10.1016/j.dcn.2013.02.004

Funding

2012-2017 (£2,500,000)

National Institute for Health Research UK (NIHR) Cognitive Health Programme of Biomedical Research Centre, Oxford). 'Enhancing brain plasticity and increasing resilience against dementia with exercise and cognitive stimulation'. Programme leader **Nobre** (OHBA), co-leaders **Holmes** and **Johansenberg**

2012-2017 (£4,138,475)

Wellcome Trust Strategic Award. 'Sleep and Circadian Neuroscience Institute (SCNi) for Mental Health.' Principal applicants: Bannerman, Clifford, Davies, **Goodwin**, Griber, Harrison, **Holmes**, Peirson, Wulff, **Freeman**, and Foster [PI]

2013-2015 (£449,661)

Medical Research Council 'The impact of COMT on behaviour and neural activity, and its modulation by genotype and acute stress. **Harrison**, **Harmer**, **Tunbridge**, **Rogers**, **Holmes Mackay**

2013-2014 (£29,249)

Medical Research Council (MRC) Centenary Early Career Award; 'Mindreading via neuroimaging: The aetiology of flashbacks after trauma' 1-year post doc Clark

2012-2015 (£186,987)

ESRC Future Leaders Fellowship Scheme for Rathbone [post doc]

2012-2014 (£255,096)

Medical Research Council: 'Facing up to Faces: Changing biases in face perception to improve emotional processing in mental health'. **Harmer**, **Holmes**, **Penton-Voak** [CIs] & **Munafo** [PI]

2011-2014 (£312,092)

National Institute for Health Research UK (NIHR) Doctorate Research Fellowship. 3 year funding for clinician **Iyadurai**

2011-2014 (£344,671)

British Academy Postdoctoral Fellowship Scheme for **Burnett-Heyes** with **Lau**

People in the Group – Awards and Moves in 2013

Emily Holmes: Winner of the Humboldt Foundation Friedrich Wilhelm Bessel Research Award (2013). Advisor to the charity *MQ: transforming mental health* for their Fellows Programme; Associate Editor *Clinical Psychological Science*; Fellow of the Association of Psychological Science. **Simon Blackwell** is now Investigator Scientist at the MRC Cognition and Brain Sciences Unit in Cambridge. **Martina Di Simplicio** is a Career Development Fellow at the MRC-CBU. **Ian Clark** has completed his DPhil and is currently undertaking a MRC Centenary Early Career Award with Emily Holmes and Clare Mackay. Ian was also successful in gaining a Santander academic travel award and a Guarantors of Brain travel award. **Arnaud Pictet** has submitted his DPhil thesis and has gained a post doc in Switzerland. **Ella James** has submitted her DPhil thesis and relocated to Cambridge. Goodbyes go out to **Dhruvi Shah** and **Angela Rylands** (now PIvital).

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



It's a way of keeping the blue away

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

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.jp.2012.12040499)

Dr Belinda Lennox

Enhancing Outcomes for Early Psychosis (Psychiatric Neuroscience)



The main aims of this research programme are to explore the neurobiological basis of psychotic illness and to directly translate research findings into clinical practice. This

is achieved through the integration of the research with the clinical service for young people with a first episode of psychosis.

Particular activity this year:

- **PPiP – Prevalence Pathogenic Antibodies in Psychosis.** We have described pathogenic antibodies in cases of first episode psychosis, and treated patients successfully with immunotherapy. In the last year we have been leading an MRC funded nationwide prevalence study of these antibodies.
- **Service redesign and CLAHRC** – Collaboration in Leadership in Applied Health Research and Care. A new clinical-academic youth service model for treating young people with early psychosis will be implemented across Oxford Health NHS FT in 2014 and will be evaluated through the CLAHRC service design theme.
- **AHSN** – Early Intervention for Psychosis network is an early clinical network adopted by the Oxford AHSN, with the aim of reducing variation in outcome and improving quality of clinical services for young people with across the region, alongside increasing research activity

Collaborators

- **Professor Dan Freeman, Dr Matthew Broome, Professor Paul Harrison**, Department Psychiatry, University of Oxford
- **Professor Angela Vincent, Dr Camilla Buckley, Dr Leslie Jacobsen**, Nuffield Department Clinical Neurosciences, University of Oxford
- **Dr Alasdair Coles**, Department Clinical Neurosciences, University of Cambridge
- **Professor Peter Jones**, Department of Psychiatry, University of Cambridge

Funding support:

- HEFCE Clinical Senior Lecturer Award 2011-2016
- MRC Project grant 2012-2014 “Identifying the prevalence of antibodies to neuronal membrane targets in first episode psychosis”
- NIHR CLAHRC Oxford 2014-2018

Key Publications 2012-13:

1. Zandi, MS, Irani, S, Langan, B, Coles, AJ, McKenna PJ, Jones PB, Vincent A, **Lennox BR** 2010 Autoantibodies detected in first episode psychosis *Journal of Neurology* 258(4):686-8
2. Chen CH, Suckling JS, **Lennox BR**, Ooi C, Bullmore ET 2011 A quantitative meta-analysis of fMRI studies in bipolar disorder *Bipolar Disorder* 13: 1-15
3. **Lennox BR**, Cole AJ, Vincent A 2012 Antibody mediated encephalitis as a treatable cause of schizophrenia *British Journal Psychiatry* 200(2):92-4
4. Nicholson TRJ, Ferdinando S, Krishnaiah R, Anhoury S, **Lennox B**, Mataix-Cols D, Cleare A, Veale D, Drummond L, Fineberg N, Church A, Giovannoni G, Heyman I 2012 Increased prevalence of antibasal ganglia antibodies in adult obsessive compulsive disorder, a cross-sectional study *British Journal Psychiatry* 200:381-6
5. Dean, AM, Goodby, E, Ooi, C, Nathan, PJ, **Lennox, BR**, Scoriels, L, Shabbir, S, Suckling, J, Jones, PB, Bullmore, ET, Barnes A 2012 Speed of facial affect intensity recognition as an endophenotype of first episode psychosis and associated limbic-cortical grey matter systems *Psychological Medicine* 18:1-12.

Dr Clare Mackay

Neurobiology of Ageing (Psychiatric Neuroscience)



Neuroimaging provides a window into the living brain. Working between the Dept of Psychiatry and the Centre for Functional Magnetic Resonance Imaging of the Brain

(FMRIB), Clare Mackay's team use the latest neuroimaging techniques to investigate the structure and function of the brain in health and disease.

Team

Dr Nicola Filippini, Dr Ricarda Menke, DPhil Students: Verena Heise (3rd yr), Konrad Krolikowski (3rd yr), Ian Clark (3rd yr), Sana Suri (1st yr), Michal Rolinski (1st yr), Eniko Zsoldos (1st yr) **Research Assistants:** Claire Burley, Miranda Swagemakers

Introduction

The Neurobiology of Ageing group is co-led by Prof Klaus Ebmeier (clinical lead) and Dr Clare Mackay (Scientific lead). Dr Mackay maintains dual bases in the Department of Psychiatry and the Centre for Functional Magnetic Resonance Imaging of the Brain (FMRIB) and is thus positioned to bring the latest innovations in imaging science to study brain ageing in health and disease.

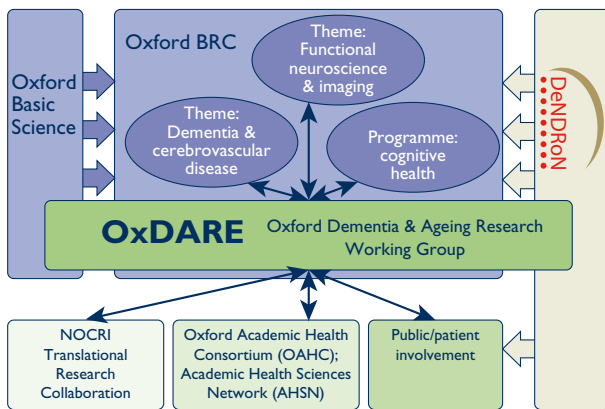
Current Research:

Understanding risk for age-related cognitive decline

The main focus of our work is to use neuroimaging to investigate and ultimately predict risk for neurodegenerative disease. eCarrying an APOE e4 allele confers an increased risk of developing Alzheimer's Disease (AD). Over the past 7 years we have investigated the effect of carrying **genetic risk for Alzheimer's disease** on the brain in healthy adults (funded by Alzheimer's Research UK and the HDH Wills 1965 Charitable Trust). We found clear differences brain function in individuals who are at increased risk, even in young people who are decades from any onset of cognitive or clinical decline. Using similar techniques we are investigating the utility of neuroimaging measures as early markers of disease in the **Oxford Parkinson's Disease Centre (opdc.ox.ac.uk)**; funded by Parkinson's UK and the Monument Trust). In early PD any differences in brain structure are subtle, but there are clear differences in brain function that normalise when patients take levodopa medication. We are now investigating this functional imaging marker in groups of people at increased risk of PD. Ultimately we hope that neuroimaging will contribute to stratifying individuals into groups who are likely to benefit from neuroprotective therapy for diseases such as AD and PD, for which large prospective cohorts will be needed. Using the MRC-funded Whitehall II imaging study (more details on Prof Klaus Ebmeier's page) we will examine brain health in 800 individuals aged 60-80 who will continue to be followed up as some of them will start to suffer from cognitive decline. Finally, as part of the NIHR funded Cognitive Health in Ageing programme, we will investigate how risk for neurodegeneration interacts with individuals' ability to benefit from cognitive and/or physical training.

Neuroimaging in Psychiatry

The neuroimaging techniques we apply to study neurodegeneration are of wide interest to researchers of other psychiatric disorders. In 2013 we discovered that COMT genotype affects resting activity within the frontal lobes (Tunbridge et al), bipolar disorder affects connectivity of the temporo-insular cortex (Yip et al), and both encoding and retrieval of flashbacks are associated with increased activity in the left inferior frontal lobe (Clark et al).



Oxford Dementia and Ageing Research (OxDARE) (www.oxdare.ox.ac.uk)

Since the prime minister's challenge on dementia in early 2012, dementia research has been an area of major strategic focus. Working closely with Kia Nobre and funded by the NIHR Oxford Biomedical Research Centre, Clare Mackay has established OxDARE to coordinate dementia-related biomedical research around the university and set strategic priorities. OxDARE represents Oxford within the Translational Research Collaboration, which was set up by the NIHR's Office for Clinical Research Infrastructure (NOCRI) to foster collaborative dementia research in the UK and attract links with industry. One of the major initiatives planned for 2014 is the expansion of OHBA to include a new translational MRI facility for cognitive health.

Selected 2013 publications:

1. 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 ϵ 2. *Neuroscience and Biobehavioral Reviews*, (in press)
2. Menke RA, Szewczyk-Krolikowski K, Jbabdi S, Jenkinson M, **Mackay CE**, and Hu M, *Comprehensive Morphometry of Sub-cortical Grey Matter Structures in Early-stage Parkinson's Disease*. *Human Brain Mapping* 2013 [Epub ahead of print]
3. SW Yip, **CE Mackay**, GM Goodwin. Increased temporo-insular engagement in unmedicated bipolar II disorder: An exploratory resting state study using independent component analysis. *Bipolar Disorders* (in press)
4. Zamboni G, Wilcock GK, Douaud G, Drazich E, McCulloch E, Filippini N, Tracey I, Brooks JCW, Smith SM, Jenkinson M, & **Mackay CE**. Resting functional connectivity reveals residual functional activity in Alzheimer's disease. *Biological Psychiatry*, 2013 Sep 1;74(5):375-83
5. Tunbridge EM, Farrell SM, Harrison PJ, **Mackay CE**. Catechol-O-methyltransferase (COMT) influences the connectivity of the prefrontal cortex at rest. *Neuroimage*. 2013 Mar;68:49-54

Professor Kia Nobre (Psychiatric Neuroscience)

Oxford Centre for Human Brain Activity



Kia directs the Oxford Centre for Human Brain Activity (OHBA) and leads the BRC Programme and Strategic Working Group in Cognitive Health. She also heads the Brain & Cognition Lab.

I am interested in understanding the principles of organisation of large-scale neural systems that support and regulate cognitive functions in the human brain. Over the last several years, my research has been aimed at explaining the dynamic regulation of perception and cognition according to expectations, task goals, memories, motivation, and emotions. New lines of research are beginning to reveal how these rich regulatory mechanisms are disrupted during ageing and in disorders of mental health.

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*, member of the Wellcome Trust Expert Review Group in Cognitive Neuroscience & Mental Health, advisor to the Understanding Human Cognition Program of the James S McDonnell Foundation, and member of Neuroscience Young Investigator Award Selection Committee and Peter and Patricia Gruber International Research Award Selection Committee.

Brain & Cognition Lab

The Brain & Cognition Lab is an active cognitive neuroscience research group based in the Department of Experimental Psychology. We use a multipronged methodological approach to investigate the nature of perception, decision-making, working memory, long-term memory, as well as their interactions and top-down modulation.

We combine careful measures of behavioural performance with a variety of state-of-the-art methods to measure and stimulate brain activity in human volunteers. In addition to EEG available at the B&C lab; we use MEG, structural and functional MRI, TMS available through OHBA and FMRI.

Current lab members include: Gustavo Rohenkohl, Céline Gillebert, Kathryn Atherton, Helena Cousijn, George Wallis, Nicholas Myers, Joshua Chauvin, Robert Mok, Theresa Wildegger, Lalitha Iyadurai, Paul Greig, Simone Heideman, Malcolm Proudfoot, Julian de Freitas, Nick Morley, and Stefania Pezzoli.

Our collaborators in Oxford include: Chris Butler, John Geddes, Catherine Harmer, Paul Harrison, Miles Hewstone, Glyn Humphreys, Heidi Johansen-Berg, Clare Mackay, Matthew Rushworth, Gaia Scerif, Mark Stokes, Liz Tunbridge. We also have many outside collaborators: Duncan Astle (CBU Cambridge), André Cravo (São Paulo), Jenny Coull (Marseille), Sonia Doallo (Santiago de Compostella), Adam Gazzaley (UCSF), Emily Holmes (CBU Cambridge), Marsel Mesulam (Notherwestern), and Kimron Shapiro (Birmingham).

OHBA

The Oxford Centre for Human Brain Activity is a state-of-the-art research centre based in the Department of Psychiatry with the aim of supporting translational research on human cognition and its disruption during neuropsychiatric and neurological disorders. In alliance with FMRI, 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.

OHBA currently houses four research groups. Group leaders include Mark Woolrich (Analysis Group), Mark Stokes (Attention Group), Susie Murphy (Ageing Group), and me. Support for the centre is provided by Sven Braeutigam (Physics), Jenni Swettenham (research facilitator), and Judith Ponsford (administrator).

OHBA also hosts research 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; 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.

Exciting plans are under way to expand OHBA into a translational cognitive neuroscience hub. We plan to add a 3T MRI scanner, as well as to expand the facilities to include additional testing areas and host new research groups. 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. Clare Mackay will join OHBA to lead the translational MRI work.

Cognitive Health Working Group and Research Programme

The Cognitive Health Working Group was set up by the Oxford BRC to enhance, support, integrate, and coordinate resources and research activities directed at understanding the psychological and neural mechanisms associated with disorders of cognition in order to improve diagnosis and treatment. The initial focus of the working group has been on dementia and ageing. The working group established OxDARE (Oxford Dementia and Ageing Research), coordinated by Clare Mackay. OxDARE has been extremely active over the last year, achieving important landmarks in: recruiting leaders in dementia research to Oxford, supporting young researchers, promoting teaching and training skills, integrating research and clinical activities, and securing research funds. OxDARE also acts as the vehicle for representing Oxford in the in the national Translational Research Collaboration on Dementia (TRC-D) established by the NIHR Office for Clinical Research Infrastructure (NOCRI).

One of the main research initiatives associated with OxDARE is a programme of research funded by the NIHR on Cognitive Health in Ageing. The aim is to evaluate and develop lifestyle-based interventions, based on exercise and cognitive stimulation, to promote healthy ageing and maximise the brain's resilience to cognitive decline. The programme is led by Kia Nobre, Heidi Johansen-Berg (FMRIB), and Emily Holmes (CBU in Cambridge); and draws on expertise of a large number of researchers and clinicians across different University departments and collaborating institutions.

Major Ongoing grants

- **Wellcome Trust Strategic Award (2014-16):** Collaborative Network for Bipolar Research to Improve Outcomes (PI Paul Harrison / John Geddes)
- **EC 7th Framework Programme for Research, EU Initial training Network (2013-18):** Individualised diagnostics and rehabilitation of attention (PI Glyn Humphreys)
- **James S McDonnell Foundation, Collaborative activity grant (2013-15):** Brain Rhythms in Cognition – Instrumental or Epiphenomenal?
- **MRC Partnership grant (2013-18):** Building multi-site clinical research capacity in Magnetoencephalography (PI Krish Singh, Cardiff)
- **National Institute for Health Research (NIHR) Cognitive Health Programme (2012-17):** Improving lifelong cognitive health through cognitive stimulation and physical exercise.
- **Wellcome Trust Equipment Grant (2011-2014):** "Oxford Centre for Human Brain Activity" to support establishment of a multimethodological centre for investigating the human brain with real-time resolution
- **Wellcome Trust Project Grant (2010-2014):** Timing Expectations in the Human Brain

Publications 2012-2013

1. Cravo AM, Rohenkohl G, Wyart V, Nobre AC (2013) Temporal expectation enhances contrast sensitivity by phase entrainment of low-frequency oscillations in visual cortex, <http://www.jneurosci.org/content/33/9/4002.long>. *J Neurosci* 33(9):4002-10. PMID: 23447609
2. Gazzaley A, Nobre AC (2012) Top-down modulation: bridging selective attention and working memory. <http://www.ncbi.nlm.nih.gov/pubmed/22209601>. *Trends Cogn Sci* 16(2):129-35. PMID: 22209601 (Review)
3. Gould IC, Nobre AC, Wyart V, Rushworth MFS (2012) Effects of decision variables and intraparietal stimulation on sensorimotor oscillatory activity in the human brain <http://www.ncbi.nlm.nih.gov/pubmed/23035092>. *J Neurosci* 32(40):13805-18. PMID: 23035092
4. Rohenkohl G, Cravo AM, Wyart V, Nobre AC (2012) Temporal expectation improves the quality of sensory information. <http://www.ncbi.nlm.nih.gov/pubmed/22699922>. *J Neurosci* 32(24):8424-8. PMID: 22699922
5. Stokes MG, Atherton K, Patai EZ, Nobre AC (2012) Long-term memory prepares neural activity for perception. <http://www.ncbi.nlm.nih.gov/pubmed/22109554>. *Proc Natl Acad Sci USA* 109(6):E360-7. PMID: 22109554

Dr Rebecca Park (Psychiatric Neuroscience)

Oxford Brain and Body Research in Eating Disorders (OxBREaD)



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

My research group **OxBread** has developed transdisciplinary collaborations with clinical, behavioral and neuroscientists. We primarily investigate the most severe form of eating disorder, Anorexia Nervosa. This 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 my translational research: I am Consultant Psychiatrist to the Oxfordshire NHS specialist eating disorders service, based at Cotswold House, Warneford Hospital. We particularly value the experience of individuals affected by eating disorders in guiding our research questions. Additionally, I lead teaching on eating disorders within the University of Oxford to undergraduates, clinical medical students, postdoctoral students.

OxBread Group:

Rebecca Park *Clinical Senior Lecturer, group leader.*
Lauren Godier *DPhil Student, MRC studentship*
Felicity Cowdrey *Jessica Scaife Postdoctoral Research assistant, MRC CIC award*

Funding:

- Clinical Senior Lecturer award, HEFCE : 2007- 2014
- Sir Jules Thorn Charitable Trust PhD studentship: 2009-12
- MRC PhD studentship 2012- 2015
- MRC Confidence in concept award 2013- 2014

Current Activity:

Most recently we have been investigating the neural basis of aberrant reward processes in severe eating disorders and from this we are developing new forms of treatment targeting these processes. We have made important advances in understanding the neurobiology of Anorexia Nervosa using fMRI and have developed an international reputation in the field. We have been awarded an MRC 'Confidence in Concept' Award (PI Rebecca Park), in collaboration with Professor Tipu Aziz, Department of Neurosurgery and Professor Catherine Harmer in Neurosciences which funds two complimentary studies; Firstly a multimodal imaging study of neural processing and reward in individuals with current and past Anorexia Nervosa, and secondly a pilot intervention study of Deep Brain Stimulation for severe enduring Anorexia Nervosa, targeted at neural reward centres. This work aims to contribute to develop knowledge of neural processes underpinning Anorexia Nervosa and in tandem develop novel treatment strategies.

Study 1: A neural basis for Anorexia Nervosa?

A multimodal imaging study of neural networks and reward processing in individuals currently ill and recovered from Anorexia Nervosa. Our previous research using fMRI and computer tasks has shown that AN is associated with brain networks involved in ruminative thinking about the self, and abnormal reward processing. In addition to functional magnetic resonance imaging (fMRI) we will use Magnetoencephalography (MEG) together with computer based tasks to investigate the role of food reward and compulsive habit formation in AN. This multimodal imaging study uses fMRI and MEG to map neural networks and reward processing and will inform treatment target development.

Study 2: Can Deep Brain Stimulation help severe enduring Anorexia Nervosa?

In a complimentary study we are piloting Deep Brain Stimulation (DBS) as a novel experimental treatment for severe enduring AN. This study includes investigation of the underlying neural processes and a sub-study of the important ethical issues involved. This study aims to explore the acceptability and feasibility of DBS to treat AN and will also map the neural mechanisms underpinning reward as a basis for further developing novel treatments.

Key Collaborators:

- Professors Tipu Aziz, Catherine Harmer, Kia Nobre: Oxford UK
- Dr Jacinta Tan; Swansea UK
- Dr Claire Gillan; University of Cambridge UK / NYU
- Dr Sanne De Wit; Netherlands.

Key Publications 2012-13:

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. Cowdrey, F. A., Filippini, N., **Park, R. J.**, Smith, S. M., & McCabe, C. (2012). Increased resting state functional connectivity in the default mode network in recovered anorexia nervosa. *Hum Brain Mapp*. doi:10.1002/hbm.22202
3. Cowdrey, F. A., **Park, R. J.**, Harmer, C. J., & McCabe, C. (2012). Neural responses to emotional faces in women recovered from anorexia nervosa. *Psychiatry Research: Neuroimaging*.
4. Cowdrey, F. A., **Park, R. J.**, Harmer, C. J., & McCabe, C. (2011). Increased neural processing of rewarding and aversive food stimuli in recovered anorexia nervosa. *Biol Psychiatry*, 70(8), 736-743. doi:10.1016/j.biopsych.2011.05.028
5. **Park, R. J.**, Dunn, B. D., & Barnard, P. J. (2012). Schematic Models and Modes of Mind in Anorexia Nervosa II: Implications for Treatment and Course. *International Journal of Cognitive Therapy*, 5(1), 86-98

Professor Michael Sharpe

Oxford Psychological Medicine Research Group (Psychological Medicine)



Psychological Medicine refers to work at the interface between psychiatry and psychology and the rest of medicine. The subspecialty of psychiatry involved in this work is called *liaison* psychiatry.

The aim of the Oxford Psychological Medicine Research group (PMR – Oxford) is to improve our understanding and treatment of psychiatric disorders and psychological problems in patients with medical conditions. This problem, called comorbidity, is a major challenge to health services that have been traditionally separated into 'physical' and 'mental' parts. Providing integrated medical-psychiatric treatments can improve patient outcomes, the patient's experience of care and also reduce health care costs. However, the design, evaluation and implementation of successful integrated care poses major challenges. Addressing these challenges is the focus of our work.

We have a particular methodological interest in designing complex interventions and testing them in clinical trials.

The research group

Professor Michael Sharpe moved back to Oxford from the University of Edinburgh in September 2011 with the aim of developing research, teaching and clinical services in Psychological Medicine.

He was previously Clinical Tutor in psychiatry in Oxford until 1997. During his 15 years in Edinburgh he led a number of major studies including: trials of multicomponent treatments for major depression in cancer patients (SMaRT oncology 1, 2 and 3) funded by Cancer Research UK, rehabilitative treatments for chronic fatigue syndrome (PACE) funded by the Medical Research Council and self-help for neurology patients with medically unexplained symptoms (SMaRT neurology) also funded by the Medical Research Council.

Group members

- Dr Jane Walker, Consultant Liaison Psychiatrist and Senior Clinical Researcher combines clinical work as a member of the Palliative Medicine teams of Sir Michael Sobell House with clinical research.
- Mr Michael Loynd, Senior Research Nurse works between Psychiatry and Primary Care on developing an intervention for patients with depression and complications of diabetes.
- Dr Bartley 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.
- Additional NHS Consultant Liaison Psychiatrists are soon to be appointed and will bring the total of new consultant posts since 2011 to ten.
- Our group administrator is Ms Christine Hedges (christine.hedges@psych.ox.ac.uk)



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) Application.

Current projects include:

- Management of psychiatric comorbidity in palliative care patients. Management of depression in patients with diabetes.
- Understanding obstacles to compassionate psychological care of patients in general hospitals.

Links and collaborations

The group has collaborations with the Oxford University departments of Primary Care, Experimental Psychology and Clinical Neurosciences. Our research is done in collaboration with clinical teams in both Oxford University Hospitals NHS Trust and Oxford Health NHS Foundation Trust. The group has strong international links via the Research Committee of the American Academy of Psychosomatic Medicine (APM) which Michael Sharpe chairs.

Selected Publications

1. Walker J, Sawhney A, Hansen CH, Ahmed S, Martin P, Symeonides S, *et al.* Treatment of depression in adults with cancer: a systematic review of randomized controlled trials. *Psychological Medicine*. 2013;1-11.
2. Walker S, Walker J, Richardson G, Palmer S, Wu Q, Gilbody S, *et al.* Cost-effectiveness of combining systematic identification and treatment of co-morbid major depression for people with chronic diseases: the example of cancer. *Psychological Medicine*. 2013;1-10.
3. Underwood M, Lamb SE, Eldridge S, Sheehan B, Slowther AM, Spencer A, *et al.* Exercise for depression in elderly residents of care homes: a cluster-randomised controlled trial. *The Lancet*. 2013;382(9886):41-9.
4. Sharpe M, Burton C, Sawhney A, McGorm K, Weller D. Is co-morbid depression adequately treated in patients repeatedly referred to specialist medical services with symptoms of a medical condition? *Journal of Psychosomatic Research* 2012;72(6):419-21.
5. White P, Goldsmith K, Johnson A, Potts L, Walwyn R, Decesare J, Baber H, Burgess M, Clark L, Cox D, Bavinton J, Angus B, Murphy G, Murphy M, O'Dowd H, Wilks D, McCrone P, Chalder T, & Sharpe M. 2011. Comparison of adaptive pacing therapy, cognitive behaviour therapy, graded exercise therapy, and specialist medical care for chronic fatigue syndrome (PACE): a randomised trial. *The Lancet* 377; 823-836.

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).

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 as we have now completed recruitment and over half of the participants have completed the study to date.

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 and Lynne Murray and Peter Cooper at the University of Reading. 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.

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 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.

We have also been collaborating with a large group in KwaZulu Natal testing an intervention using peer mentors (mothers living with HIV) to support women newly diagnosed with HIV during pregnancy (with Linda Richter and Mary Jane Rotheram-Borus).

The aim is to enhance the mother's social and emotional development and to promote their infants physical and psychological development.

We are collaborating with Stephen Kennedy and Jose Villar (Nuffield Dept. of Obstetrics & Gynaecology, Oxford) on a large longitudinal study investigating the relationship between growth in-utero and cognitive development.

Alan Stein is a member of the MRC/Wellcome/DfID Global Health Trials panel and a member of the MRC Global Health Advisory Group.

The Team

Sarah Atkinson, Jessica Cardy, Julia Cordey, Louise Dalton, Beverley Davies, Henrique Fernandes, Michelle Fernandes, Julia Goodwin, Charlotte Granger, Tim van Hartevelt, Denise Jennings, Claire Kempton, Simon Kariuki, Barbora Krausova, Pete Lawrence, Elizabeth Murray, Elena Netsi, Elizabeth Newnham, Christine Parsons, Rebecca Pearson, Elizabeth Rapa, Natasha Rowbotham, Eloise Stark, Angus Stevner, Anne Stewart, Valerie West, Katie Young.

Key publications 2013

1. Pearson R.M., Evans J., Kounali D., Lewis G., Heron J., Ramchandani P.G., O'Connor T.G. & Stein A. (2013) Maternal Depression During Pregnancy and the Postnatal Period: Risks and Possible Mechanisms for Offspring Depression at Age 18 Years. *JAMA Psychiatry*, Epub doi: 10.1001/jamapsychiatry.2013.2163.
2. Clark S.J., Kahn K., Houle B., Arteché A., Collinson M.A., Tollman S.M. & Stein A. (2013) Young Children's Probability of Dying Before and After Their Mother's Death: A Rural South African Population-Based Surveillance Study. *PLoS Medicine*, 10 (3): e1001409.
3. Stein A., Malmberg L-E, Leach P., Barnes J., Sylva K. and the FCCC Team. (2013) The influence of different forms of early childcare on children's emotional and behavioural development at school entry. *Child: Care, Health and Development*, 39 (5): 676-687.
4. Pearson R.M., Fernyhough C., Bental R., Evans J., Heron J., Joinson C., Stein A.L. & Lewis, G. (2013) Association Between Maternal Depressogenic Cognitive Style During Pregnancy and Offspring Cognitive Style 18 Years Later. *Am J Psychiatry*, 170 (4): 434-441.
5. Prenoveau J., Craske M., Counsell N., West V., Davies B., Cooper P., Rapa E. & Stein A. (2013) Postpartum GAD is a risk factor for postpartum MDD: The course and longitudinal relationships of postpartum GAD and MDD. *Depression and Anxiety*, 30 (6): 506-514.
6. Parsons C.E., Stark E.A., Young K.S., Stein A. & Kringelbach M.L. (2013) Understanding the human parental brain: A critical role of the orbitofrontal cortex. *Social Neuroscience*, 8 (6): 525-543.
7. Cortina M.A., Fazel M., Hlungwani, T.M., Kahn K., Tollman S., Cortina-Borja M. & Stein A. (2013) Childhood Psychological Problems in School Settings in Rural Southern Africa. *PLoS ONE*, 8 (6): e65041.
8. Parsons C.E., Young K.S., Mohseni H., Woolrich M.W., Thomsen K.R., 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): 268-274.
9. Rochat T. J., Tomlinson M., Newell M-L. & Stein A. (2013) Detection of antenatal depression in rural HIV-affected populations with short and ultrashort versions of the Edinburgh Postnatal Depression Scale (EPDS). *Archives of Women's Mental Health*, 16 (5): 401-410.



**Dr Morten
Kringelbach**
(Developmental Psychiatry)
**Hedonia: Trygfonden
Research Group**

My research goal is to understand pleasure in the human brain. Apart from being a lot of fun, this is important 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.

In my research group, Hedonia: TrygFonden Research Group, we use a range of behavioural, neuroimaging, neurosurgical and computational methods to investigate the many facets of pleasure in health and disease. 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.

Infants are a focus of my research and especially how their sounds, looks and smells strongly influence the adult 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. 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. We are also building computational models that allows us further probe and understand the human brain in health and disease.

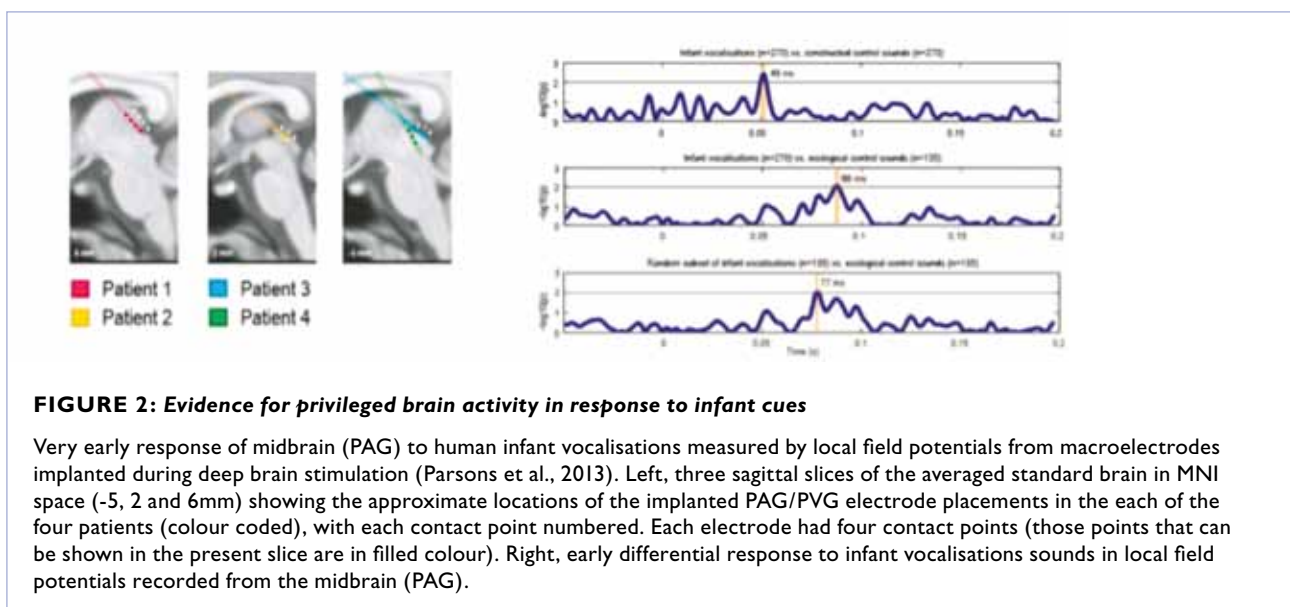
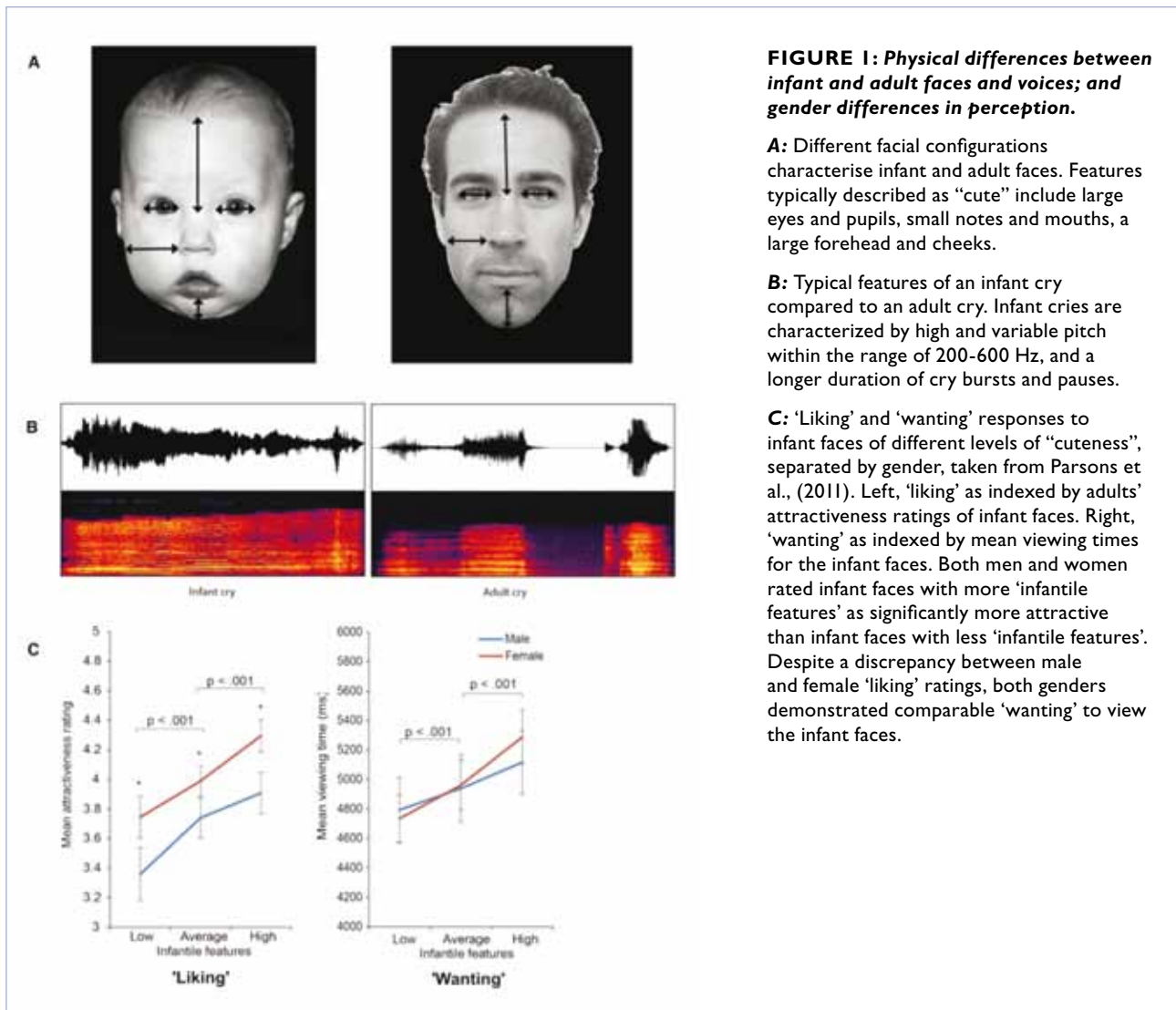
When pleasure systems become unbalanced, it can be very difficult to rebalance the brain. One of my main interests is to help advance our understanding of the effects of war and disaster for which we have setup *Scars of War Foundation* at The Queen's College.

One current project is investigating the brain changes related to post-traumatic stress-disorder in war 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.

Recent publications

1. Parsons C.E., Young K.S., Joensson M., Brattico E., Hyam J.A., Stein A., Green A.L., Aziz, T.Z., **Kringelbach M.L.** (2013) Ready for action: A role for the brainstem in responding to infant vocalizations. *Social Cognitive and Affective Neuroscience*, in press.
2. Rømer Thomsen K., Joensson M., Lou H. C. Møller A., Gross J., **Kringelbach M.L.** & Changeux J.P. (2013) Altered paralimbic interaction in behavioral addiction. *PNAS*, 110(12):4744-9. doi: 10.1073/pnas.1302374110.
3. Parsons C.E, Stark E.A., Young K.S., Stein A. & **Kringelbach M.L.** (2013) Understanding the human parental brain: a critical role of the orbitofrontal cortex. *Social Neuroscience*, 8(6): 525-43
4. Berridge K.C. & **Kringelbach M.L.** (2013) Neuroscience of affect: Brain mechanisms of pleasure and displeasure. *Current Opinion in Neurobiology*, 23(3):294-303. doi:10.1016/j.conb.2013.01.017.
5. Kringelbach M.L. & Berridge K.C. (2012) The joyful mind. *Scientific American*, 307(2):40-45.
6. Hyam J.A., **Kringelbach M.L.**, Silburn P., Aziz T.Z. & Green A.L. (2012) The autonomic effects of deep brain stimulation-a therapeutic opportunity. *Nature Reviews Neurology*, 8(7):391-400.





**Professor
Charles Newton**
(Developmental Psychiatry)

**Newton Autism
and Developmental
Disorders**

Autism

Charles Newton is leading a programme of work related to Autism in Oxfordshire and the surrounding regions.

We have created the Oxford Autism Research Centre which brings together scientists, charities and service providers across the region, including the creation of a website (Elizabeth Rapa). In addition we have regular Clinical Symposia (for health care workers), Journal Club (run by Hannah Hobson) and Scientific Seminars (run by Steven Chance). A Junior Research Fellow (Anna Remington) is studying perceptual load in high functioning autism, and is carrying out a pilot study to compare Magnetoencephalography and Magnetic Resonance Imaging in collaboration with Steven Chance. We have also held a meeting about Autism which brought together people involved in basic science, clinical assessment and those providing services for Autism.

Global Burden of Disease

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

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 include 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 this treatment gap.

The work on Autism in Africa, has started 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. The focus of the work on neurodevelopmental disorders occurs in Kilifi, where we are examining the outcome of infectious diseases (malaria, HIV, meningitis, tetanus) 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. 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.
2. Kariuki SM, Gitau E, Gwer S, Karanja HK, Chengo E, Kazungu M, Urban B, Newton Bunning K, Gona JK, Odera-Mung'ala V, **Newton CR**, Geere JA, Hong CS, Hartley S. Survey of rehabilitation support for children 0-15 years in a rural part of Kenya. *Disabil Rehabil.* 2013 Sep 2. [Epub ahead of print] PubMed PMID: 23991677.
3. Abubakar A, Holding P, Van Baar A, **Newton C**, Van de Vijver F, Espy KA. The Performance of Children Prenatally Exposed to HIV on the A-Not-B Task in Kilifi, Kenya: A Preliminary Study. *Int. J. Environ. Res. Public Health* 2013, 10(9), 4132-4142;
4. Fazel S, Wolf A, Långström N, **Newton CR**, Lichtenstein P. Premature mortality in epilepsy and the role of psychiatric comorbidity: a total population study. *Lancet.* 2013 Jul 19. doi:pii: S0140-6736(13)60899-5. 10.1016/S0140-6736(13)60899-5. [Epub ahead of print] PubMed PMID: 23883699.
5. Ngugi AK, Bottomley C, Scott JA, Mung'ala-Odera V, Bauni E, Sander JW, Kleinschmidt I, **Newton CR**. Incidence of convulsive epilepsy in a rural area in Kenya. *Epilepsia.* 2013 Jun 10. doi: 10.1111/epi.12236. [Epub ahead of print] PubMed PMID: 23750825.
6. Kariuki SM, Rockett K, Clark TG, Reyburn H, Agbenyega T, Taylor TE, Birbeck GL, Williams TN, **Newton CR**. The genetic risk of acute seizures in African children with falciparum malaria. *Epilepsia* 2013 Jun;54(6):990-1001. doi:10.1111/epi.12173. Epub 2013 Apr 24. PubMed PMID: 23614351.
7. Gona JK, **Newton CR**, Hartley S, Bunning K. A home-based intervention using augmentative and alternative communication (AAC) techniques in rural Kenya: what are the caregivers' experiences? *Child Care Health Dev.* 2013 Mar 3. doi:10.1111/cch.12031. [Epub ahead of print] PubMed PMID: 23452318.



Dr Mina Fazel
(Developmental Psychiatry)

Developing school-based mental health interventions

The main aim of this research programme is to determine the potential role that mental health services within schools can play in improving young people's access to services.

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. As the majority of young people are attending school, the school provides an opportunity for providing mental health care, yet little is known about the best models of treatments in this context.

My current research covers two areas:

1. Developing psychotherapeutic interventions for school staff to use with refugee children: My 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.
2. Developing evidence-based school mental health services in general: 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 develop different models of school-based mental health delivery that can be evaluated is the focus of this area of work.

Selected publications:

1. **M. Fazel**, R. Reed, C. Panter-Brick, A. Stein. Mental health of displaced and refugee children resettled in high-income countries: risk and protective factors. *The Lancet* 2011 379(9812):266-282
2. R. Reed, **M. Fazel**, L. Jones, C. Panter-Brick, A. Stein. Mental health of displaced and refugee children resettled in low and middle-income countries: risk and protective factors. *The Lancet* 2011 379(9812):250-265
3. M Cortina, A Sodha, **M. Fazel**, P Ramchandani. Prevalence of child mental health problems in sub-Saharan Africa: A Systematic Review. *Archives of Pediatrics and Adolescent Medicine* 2012;166(3);276-281
4. M Cortina, **M. Fazel**, T Hunglawi, M Cortina Borja, S Tollman, K Kahn, A Stein. Childhood psychological problems in school settings in rural Southern Africa. *PLOS One* 2013; 8(6): e65041. doi:10.1371/journal.pone.0065041
5. R Tyrer, **M. Fazel**. School and community-based interventions for refugee and asylum seeking children: A Systematic Review IN PRESS

Dr Mark Stokes

Attention Group, Oxford Centre for Human Brain Activity (Psychiatric Neuroscience)



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

Background

The Attention Group was established in 2012 to study the brain mechanisms that help people focus on the most important information, whilst ignoring distractions. With support the Medical Research Council, British Academy and Wellcome Trust, we have now launched an extensive research programme to explore the brain mechanisms that direct and maintain the focus of attention, and to discover how things go wrong.

Current group members

Dr MaryAnn Noonan (*Postdoctoral Researcher*),
Dr Ben Crittenden (*Postdoctoral Researcher*),
George Wallis (*DPhil Student*), Nicholas Myers (*DPhil Student*), Alex von Lutz (*MSc Student*)

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 configures brain states for processing task-relevant events, and 2) how expectations suppress competing distractions. Within this 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.

In our experiments, we measure and disrupt human brain activity with high temporal and spatial resolution using magnetoencephalography (MEG), functional magnetic resonance imaging (fMRI) and transcranial magnetic stimulation (TMS). Working with our collaborators in Oxford and further afield, we also explore brain activity recorded directly with intracranial electrodes. By exploiting convergent methodologies, we are better able to overcome specific limitations inherent to any single approach.

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.

Links with other departments and institutions

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

- Prof Nobre/Brain and Cognition Laboratory (Dept Experimental Psychology, Oxford)
- Dr Voets/Oxford Epilepsy Surgery Programme (Nuffield Department of Clinical Neurosciences, Oxford)
- Prof Duncan/Attention & Cognitive Control Group (MRC Cognition and Brain Sciences Unit, Cambridge)
- Dr Axmacher/Clinic of Epileptology (Bonn University)
- Buschman (Princeton University)

News and Impacts: 2012-2013

- **Dr Stokes** was conferred the title of University Research Lecturer and was elected to a Science Research Fellowship, St John's College
- **Dr Crittenden** was awarded a Junior Research Fellowship, Linacre College
- **Dr Stokes** delivered a keynote address: 'Evidence-Based Policy vs. Policy-Based Evidence', Cambridge University Science and Policy Exchange (CUSPE) Committee
- In collaboration with **Dr Voytek** (UCSD), **Dr Stokes** launched Brain Metrics, Neuroscience for students, hosted by Nature Education
- **Dr Stokes** published an article at Nature Blogs: *Crime and punishment: From the neuroscience of freewill to legal reform* and featured by the SpotOn NYC event on Communication and the Brain
- **The Guardian:** *There's a lot more to neuroscience than media 'neuromania'* (by Stokes)
- **The Guardian:** *The folly of science on a shoe-string budget* (by Stokes)
- **The Journal of the Parliamentary and Scientific Committee,** *Science in Parliament: Helium – why recent helium shortages have forced us to temporarily shut down our brain research centre* (by Stokes)
- **The Independent:** *Our research is on ice due to helium shortage* (by Stokes)

Selected Publications from 2013

1. Nelissen, **Stokes**, Nobre & Rushworth (2013). Frontal and parietal cortical interactions with distributed visual representations during selective attention and action selection. *Journal of Neuroscience*, 33(42): 16443-16458
2. Kadohisa, Petrov, **Stokes**, Sigala, Buckley, Gaffan, Kusunoki & Duncan (2013). Rapid emergence of a coherent attentional state in a prefrontal cell population. *Neuron*, 80(1): 235–246
3. de Gardelle, **Stokes**, Johnen, Wyart & Summerfield (2013) Overlapping multivoxel patterns for two levels of visual expectation. *Frontiers in Human Neuroscience*, 7:158
4. **Stokes**, Kusunoki, Sigala, Nili, Gaffan & Duncan (2013). Dynamic coding for cognitive control in prefrontal cortex. *Neuron*, 78(2), 364-375
5. Murray, Nobre, Clark, Cravo & **Stokes** (2013) Attention restores discrete items to visual short-term memory. *Psychological Science*, 24 (4), 550-556

Dr Elizabeth Tunbridge

Neural Correlates of Gene Function (Psychiatric Neuroscience)



We are particularly interested in the genetic modulation of the dopamine system, given its key role in cognition and reward processing in the healthy brain, and its dysfunction in several psychiatric disorders.

Background

The NCGF group was formed in 2009, supported by a Royal Society University Research Fellowship awarded to Liz Tunbridge, and currently receives additional funding from the Royal Society, the Wellcome Trust and the MRC. Our research aims to understand how individual genes, acting both alone and in combination with other genetic and environmental factors, impact on behaviour. We are particularly interested in the genetic modulation of the dopamine system, given its key role in cognition and reward processing in the healthy brain, and its dysfunction in several psychiatric disorders. We use a multidisciplinary approach: our experiments span molecular biology, neurochemical and behavioural analyses, and neuroimaging. We have established strong collaborations with other researchers in Oxford and further afield in order to achieve this.

Current group members:

Dr Chris Barkus (Postdoctoral Researcher), Katharina Stumpfenhorst (DPhil Student), Anna Huber (DPhil Student) and Clio Korn (DPhil Student), Jessica Laidlaw (Research Assistant)

Current Research

We aim to translate findings from rodent models into human studies, and vice versa, in order to understand the mechanisms underlying links between genes and behaviour. Our research centres on the catechol-O-methyltransferase (COMT) gene, which we have shown is important for regulating dopamine levels in the prefrontal cortex (PFC) and is implicated in cognitive function. The human COMT gene contains a genetic variant that alters its enzyme activity. As well as studying the impact of genetic and pharmacological variation in COMT's activity in healthy human volunteers we are also able to conduct similar studies in COMT transgenic mice that mimic the human variant in order to explore the underlying mechanisms.

Healthy volunteer studies

We recently demonstrated that COMT inhibition (using tolcapone) can be either beneficial or detrimental for cognitive function, depending on the variant in the COMT gene that an individual carries. These findings are consistent with the proposed inverted-U relationship between dopamine levels and PFC function, whereby cognitive task performance is optimal at intermediate levels of dopamine and is impaired by both excessive and insufficient levels. We are extending these findings in two ways:

1. We are investigating their neural correlates, since volunteers performed the tasks in the MEG scanner (in collaboration with Kia Nobre, Mark Woolrich and Sven Braeutigam, OHBA)
2. We are investigating the separate and combined effects of tolcapone and the COMT variant on emotional processing and reward function, as well as seeing how this relationship is altered by stress, in healthy human volunteers (in collaboration with Prof Paul Harrison, Prof Catherine Harmer, Dr Clare Mackay, Prof Emily Holmes and Prof Robert Rogers).



COMT genotype modulates the functional connectivity of the left insula/ventrolateral prefrontal cortex (shown in red) with the rest of the executive control network (from Tunbridge, Farrell, Harrison and Mackay, 2013).

Preclinical Studies

Using transgenic mice that mimic the human variant we are investigating the mechanisms underlying links between COMT and brain function:

1. We are measuring dopamine release in real time, to clarify its role in mediating COMT's links with reward processing (in collaboration with Dr Mark Walton [Experimental Psychology])
2. We are investigating the mechanistic basis of a reported gene x environment interaction between COMT and cannabis use in precipitating psychosis and cognitive dysfunction (in collaboration with David Bannerman and Trevor Sharp). We have recently demonstrated that genetic variation in COMT alters the impact of THC (the primary psychoactive ingredient in cannabis)
3. The relative and combined contributions of COMT and the dopamine transporter to striatal dopamine function and associated behaviours (in collaboration with Mark Walton)

Links with Other Departments and Institutions

We have active collaborations with the following researchers in Oxford and elsewhere:

- Prof Daniel Freeman, Prof Catherine Harmer, Prof Paul Harrison, Prof Emily Holmes and Dr Clare Mackay (*Department of Psychiatry*)
- Prof Kia Nobre, Dr Mark Woolrich and Dr Sven Braeutigam (*OHBA*)
- Prof David Bannerman and Dr Mark Walton (*Department of Experimental Psychology*)
- Prof Trevor Sharp (*Department of Pharmacology*)
- Prof Robert Rogers (*University of Bangor*)
- Drs Daniel Weinberger and Thomas Hyde, Lieber (*Institute for Brain Development, US*)
- Dr Jingshan Chen (*National Institute of Mental Health, US*)

News and Impacts: 2012-2013

- We received an MRC Project Grant to investigate the impact of COMT on reward and emotional processing (in collaboration with Prof Paul Harrison, Prof Catherine Harmer, Dr Clare Mackay, Prof Emily Holmes and Prof Robert Rogers)
- Liz Tunbridge presented the group's research findings at the Cheltenham Science Festival

Publications: 2012-2013

1. Decreased striatal dopamine in group II metabotropic glutamate receptor (mGlu2/mGlu3) double knockout mice. Lane TA, Boerner T, Bannerman DM, Kew JN, **Tunbridge EM**, Sharp T, Harrison PJ. *BMC Neurosci*. 2013 Sep 22;14(1):102. [Epub ahead of print]
2. Sexually dimorphic effects of catechol-O-methyltransferase (COMT) inhibition on dopamine metabolism in multiple brain regions. Laatikainen LM, Sharp T, Harrison PJ, **Tunbridge EM**. *PLoS One*. 2013 Apr 16;8(4):e61839. doi: 10.1371/journal.pone.0061839. Print 2013.
3. Catechol-O-methyltransferase (COMT) influences the connectivity of the prefrontal cortex at rest. **Tunbridge EM**, Farrell SM, Harrison PJ, Mackay CE. *Neuroimage*. 2013 Mar;68:49-54.
4. Modulation of hippocampal dopamine metabolism and hippocampal-dependent cognitive function by catechol-O-methyltransferase inhibition. Laatikainen LM, Sharp T, Bannerman DM, Harrison PJ, **Tunbridge EM**. *J Psychopharmacol*. 2012 Dec;26(12):1561-8.
5. The role of catechol-O-methyltransferase in reward processing and addiction. **Tunbridge EM**, Huber A, Farrell SM, Stumpfenhorst K, Harrison PJ, Walton ME. *CNS Neurol Disord Drug Targets*. 2012 May;11(3):306-23.
6. **Tunbridge EM**, Eastwood SL, Harrison PJ. (2011). Changed Relative to What? Housekeeping Genes and Normalization Strategies in Human Brain Gene Expression Studies. *Biological Psychiatry*. 69:173-179.

Professor Mark Williams (Psychological Medicine)

Psychological Models and Treatment of Depression and Associated Emotional Disorders



Overview:

Mindfulness-based Cognitive Therapy (MBCT) and the prevention of major depression (Wellcome Trust).

Staying Well After Depression Trial

Our research focuses on the fact that depression is a chronic, relapsing condition with recurrence rates of 50-80% and a modal age of onset in adolescence, between 13-15 years. We have recently completed a large multicentre trial (Oxford, Bangor N = 274) funded by the Wellcome Trust to compare MBCT, shown in previous trials to reduce relapse to depression by 40-50%, to both a closely matched active psychological control treatment (Cognitive Psychological Education, CPE) and treatment as usual. Our results showed that there were significant beneficial effects of MBCT relative to both CPE and treatment as usual, with MBCT reducing relapse to depression for those with most vulnerability (*greater exposure to trauma during childhood*; see Figure 1).

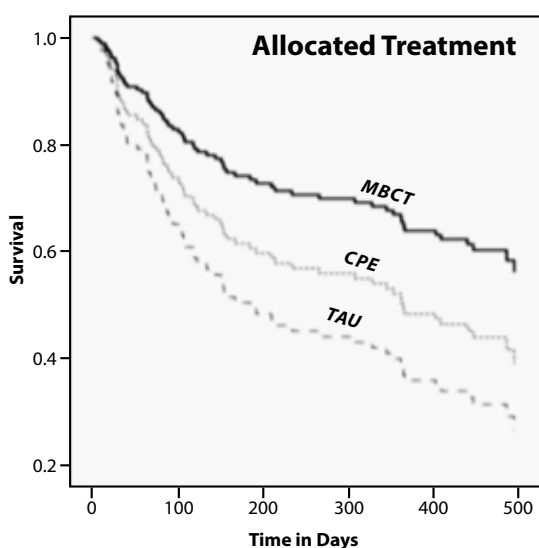


FIGURE 1: Relapse to Major Depression over one year follow-up following treatment with MBCT, Psychological Education or Treatment-as-Usual, for individuals with higher exposure to childhood trauma.

Impacts

Clinical work

Since April 2012 we have worked, within our Service Level Agreement (SLA) with Oxford Health NHS Foundation Trust, with IAPT in Oxfordshire and Buckinghamshire. We have in the past year delivered two courses of MBCT for people with mild/moderate depression, two courses for people with physical long term conditions (LTC) and two courses for people with Chronic Fatigue Syndrome (CFS). We have trained six IAPT practitioners to become MBCT Teachers (all of whom will have completed their training by April 2014), have continued to supervise five already trained MBCT Teachers in the Trust, and supervised the delivery of two course of MBCT for patients with recurrent depression in Psychological Services (step 4).

Mindfulness-Based Childbirth and Parenting

In 2012-2013 we conducted a pilot project to look at 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. Two MBCP groups were delivered by Dr Maret Dymond and Dr Sian Warriner, to a total of 21 women and partners at the John Radcliffe Hospital and a local children's centre, with very positive participant feedback. Dr Maret Dymond also delivered an eight-week mindfulness course to staff at the Women's Centre of OUHT and a second of these to be delivered in January 2014, will be evaluated, both in terms of impact upon staff wellbeing and the experience of participants' patients. In 2014 we will also offer our first MBCP course to the general public. The MBCP team have just been shortlisted for an 'Evidence in Practice Award' from the Royal College of Midwives.

Policy Input

In the past year Professor Mark Williams and OMC associate teacher Chris Cullen have delivered three eight-week mindfulness courses to MPs and Peers in Parliament and have also met with policy advisors at 10 Downing Street to discuss the potential application of mindfulness training in healthcare and education. In early 2013 Mark Williams also attended the *World Economic Forum* in Davos where he gave a series of well-received workshops on Mindfulness, in collaboration with Janice Marturano of the Institute for Mindful Leadership (New York).

UK and International Teaching and Training

Over the past year the Oxford Mindfulness Centre has delivered training in MBCT in several countries including Singapore, Hong Kong and Norway, and are currently in the last phase of supporting colleagues in setting up MBCT Training Centres in Singapore and in Hong Kong. The Master of Studies programme in MBCT continues to flourish and we have also established a new 'Foundations in teaching MBCT and MBCT' course which had its first intake of 20 in September 2013

New Arrivals

We are delighted to welcome a number of academic visitors this year including Dr Tesuji Iezgu, a Professor from Nagoya University, Japan, and Dr Ausias Cebolla, assistant professor at University Jaume I Castelló de la Plana, Spain. Dr Gaetan Cousin also joined us from Switzerland in the spring on a two year postdoctoral fellowship from the Swiss National Science Foundation, to study the effects of personality on reactions to MBCT. Finally congratulations to Dr Bergjot Gjeslvik, who has been awarded a four year fellowship from University of Oslo to conduct a programme of research in Oxford examining aspects of suicidal cognition and their treatment with MBCT. This fellowship will form the basis of a broader on going collaboration between the OMC and wider department and the University of Oslo.

Key Publications this Year

Books

1. **Williams, J.M.G** & Kabat-Zinn, J., (2013) (Eds) *Mindfulness: Diverse Perspectives on its Meanings, Origins and Applications*. Routledge, London
2. Segal, Z.V., **Williams, J.M.G.**, & Teasdale, J.D. (2012) *Mindfulness-based Cognitive Therapy for Depression: Second Edition*. Guilford Publications, New York.

Papers

1. Crane, C., Barnhofer, T., Duggan, D., Shah, D., Eames, C., & **Williams, J.M.G.** (in press). Comfort from suicidal cognition in recurrently depressed patients. *Journal of Affective Disorders*.
2. Warriner, S., Dymond, M., & **Williams, J.M.G.** (2013). *Mindfulness in maternity British Journal of Midwifery*, 21 (7), 520-522
3. **Williams, J.M.G.**, Crane, C., Barnhofer, T., Brennan, K., Crane, R., Duggan, D., ... & Russell, I.T. (in press). Mindfulness-Based Cognitive Therapy for Preventing Relapse in Recurrent Depression: A Dismantling Trial. *Journal of Consulting and Clinical Psychology*.

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