

Matter of mind

Professor Kia Nobre, the Director of the Oxford Centre for Human Brain Activity at Oxford University, describes the 'buzz' surrounding learning and dissemination that the centre fosters

Could you begin by providing an overview of the aims of the Oxford Centre for Human Brain Activity (OHBA)?

Its strategic aims are to develop methods to investigate the networks in the human brain involved in supporting cognition. We want to be leaders in the analysis and integration of brain-imaging data, and are building a first-class, mutually supportive hub for fundamental and clinical human neuroscience.

Our priority area is the crossroads where methods development, basic cognitive neuroscience, and clinical neuropsychiatric and neurological research meet. We aim to underpin research activities with advanced but accessible approaches in data analysis, providing users with the methodological and analytical tools they need and offering excellence in training and support.

How is the OHBA collaborative research project funded?

OHBA received a Wellcome Trust Equipment Grant (2010-13) which has provided infrastructure funding during the pivotal initial transitional phase so that OHBA can attain long-term sustainability. OHBA members and colleagues have recently secured a substantial grant from the National Institute for Health Research to set up a Cognitive Health Programme for improving lifelong cognitive health through cognitive stimulation and physical exercise (2012-17). Funding for other specific research projects comes from a large number of sources.

What factors come into play when deliberating research priorities at OHBA?

Foremost, the quality of the science. Any hypothesis must be well articulated, and the method and experimental design must address the hypothesis in question. The second vital factor is the 'clinical translational promise'. This is the requirement that the research has the potential to inform clinical research and, ultimately, clinical practice. A third consideration is the scientific impact of the work. We acknowledge the importance of fundamental research and support studies that address important questions in new ways, with the aim of facilitating intellectual

breakthroughs. We believe that useful clinical research must rest on the broad and strong shoulders of basic and fundamental research.

How important is public dissemination to OHBA?

As our source of inspiration and our ultimate judge, the public is of utmost importance to us. We want to understand the public – the developing child, the adolescent, the university student or the grandparent; and the individual with depression, schizophrenia, Alzheimer's disease or Parkinson's disease.

We want to engage the public and we do this by participating in open days and media events. I have recently been on UK BBC popular science programmes such as Bang Goes the Theory and Horizon. We recognise the importance of an updated presence on the web. We are also forming focus groups with individuals from the public to discuss and develop research ideas together. For example, in our major new ageing project, members of an elderly focus group will tell us their concerns and ideas about cognitive health.

Researchers at OHBA recently attended the Oxford Biomedical Research Centre Open Day to meet members of the public and discuss research activities. We also hold open days for schoolchildren and other members of the public, to visit our centre, discuss how we perform research on brain function and talk about specific projects they are interested in.

On a personal note, what inspired you to follow a career in neuroscience, and what excites you most about your role as Director of OHBA?

I grew up marvelling at the puzzle of 'thought'; how it could possibly come about from a brain. The most exciting element of my role is firstly the learning. I interact closely with and learn a lot from colleagues interested in all different aspects of the human brain at the University and collaborating institutions.

Another benefit to my role is the opportunity to promote young scientists of high promise. The best feature of OHBA is the buzz and exchange of original and critical ideas by its young members. It is a privilege to work

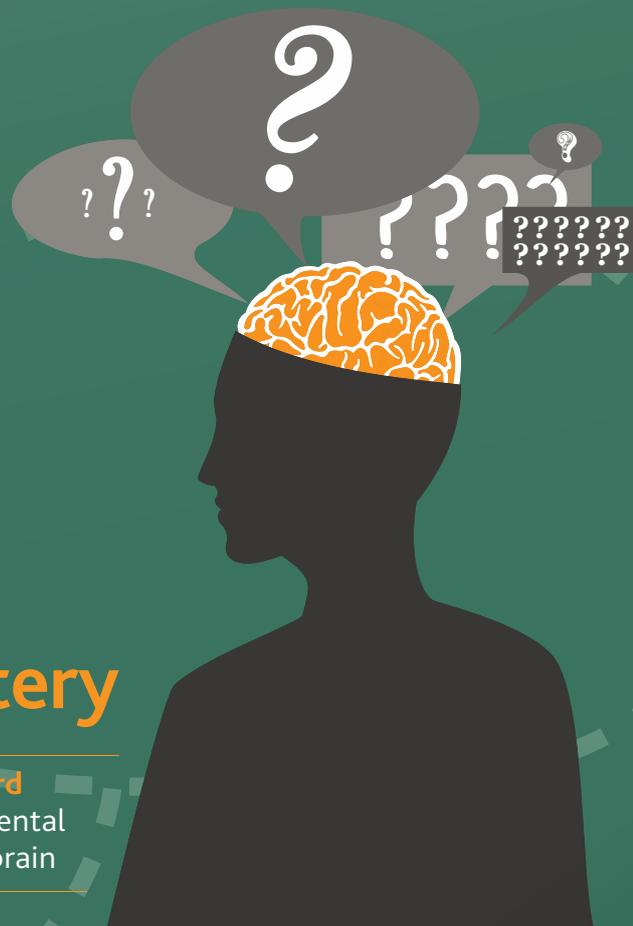
alongside such gifted people, and it is gratifying to help provide the right context for them to achieve their potential.

In the future, how would you like to see the role of OHBA develop? In your opinion, which areas of neuroscience research need to be prioritised today?

We want to see OHBA continue to develop into a self-sustaining and thriving research centre, well integrated into the Oxford research community and the international community of premier brain-imaging centres in the world.

Our immediate future aims are: to develop powerful and accessible methods to analyse magnetoencephalography (MEG) data and to integrate the analysis of MEG data with the analysis of signals from other, complementary brain-imaging methods and with measures of behavioural performance; to create an energetic and rigorous scientific environment for intellectual exchange between basic and clinical neuroscience research; and to spark excellent translational research.





The brains **behind the mystery**

By combining old and new techniques, researchers at the **Oxford Centre for Human Brain Activity** are trying to answer fundamental questions related to cognitive and emotional responses of the brain

THE OXFORD CENTRE for Human Brain Activity (OHBA), established in 2010 and directed by Professor Kia Nobre, is a state-of-the-art experimental centre situated in the grounds of Oxford's psychiatric Warneford Hospital, adjacent to the University Department of Psychiatry; both literally and metaphorically at the centre of neuropsychiatric research at Oxford. Work at OHBA is committed to answering a range of questions – from why children with autism have deficits in communication and social functions, to risk factors in developing Alzheimer's disease – straddling the border between basic neuroscience and neuropsychiatric research.

Clinical neuropsychiatric and basic cognitive neuroscience researchers collaborate at the Centre in their exploration of how cognitive, motivational and emotional biases influence perception, decision making, action and memory formation in the normal brain and in psychiatric conditions. Researchers examine genetic, pharmacological and anatomical factors, and how they influence neural dynamics at the level of functional networks. Analysis is also a key part of this effort: "We aim to underpin research activities with advanced but accessible approaches in data analysis," notes Nobre. "We want to provide users with the methodological and analytical tools they need and offer excellence in training and support." The group effort benefits all fields, as it allows strands of basic and applied research to become mutually informative.

COLLABORATION IS KEY

Collaboration is crucial to success and advancement when understanding the brain. Various laboratories combine at OHBA, holding discussions and training, and using shared knowledge and equipment to develop methods for the analysis of brain function.

OHBA partners the nearby Oxford Centre for Functional MRI of the Brain (FMRIB) closely. The two centres use different neuroimaging technologies and approaches which complement one another to study neuroscience topics. At OHBA, the four main technologies used are high temporal resolution magnetoencephalography (MEG), electroencephalography (EEG), transcranial magnetic stimulation (TMS) and eyetracking. Whereas at FMRIB, researchers focus their efforts mainly on magnetic resonance imaging. OHBA and FMRIB analysis teams were recently awarded a prestigious Strategic Award from the Wellcome Trust. This will allow them to develop and disseminate user-friendly methods for analysing different types of brain-imaging data that can be translated into clinical practice.

In addition, OHBA members collaborate closely with a number of labs within Oxford and beyond, and host research from around 20 groups across multiple Oxford Departments including Psychiatry, Experimental Psychology, Clinical Neurosciences, Physiology, Anatomy and Genetics, Engineering, Biomedical Engineering and Oncology. The exciting atmosphere of sharing and learning from

each other extends far beyond Oxford to include leading institutions in London, Cambridge, Cardiff, Nottingham, York, Aston, Glasgow, and further afield in San Francisco, Chicago, Washington, New York, Paris, Marseille, Leipzig, Nijmegen, Barcelona, Granada and São Paulo.

MAGNETOENCEPHALOGRAPHY

OHBA has an exceptional machine which underpins many of the methods used in their cognitive investigations. The MEG scanner measures the magnetic fields associated with the changes in voltage resulting from neuronal communication in the brain, and has the best available combined temporal and spatial resolution. MEG signals track brain activity much more quickly and directly than functional MRI (fMRI) and related imaging methods, which rely on indirect changes in blood flow resulting from the coupling of neuronal activity to metabolic demands.

The Centre also has a high-density EEG system, which measures voltage potentials. EEG technology has been around for more than a century, but high-resolution MEG is a far more recent addition to the scientist's toolbox. By simultaneously taking EEG measurements with MEG, better estimations of the source of neural activity in real time can be made. This is a crucial breakthrough, because magnetic fields are not significantly distorted by the skull and the scalp, so the patterns of neural activity recorded are much sharper and closer to what would be measured directly from the surface of the brain.

OHBA also has methods for stimulating the human brain, which complement the magneto/ electrophysiological and haemodynamic brain-imaging methods.

TECHNOLOGICAL CHALLENGES

MEG datasets still pose significant challenges for analysis as they are voluminous and complex. Understanding these patterns over time and over the many sensors covering the head is difficult. Activity is measured across around 300 sensors at millisecond resolution. Scientists are able to look at the brain activity triggered by an event of interest to see how it affects the ongoing activity in the brain.

For instance, MEG allows investigations into whether people with mood disorders perceive emotional stimuli differently at early, perceptual or late deliberative stages of the process. Similarly, scientists can identify the stage at which information processing is affected by therapeutic or pharmacological interventions. It is also a powerful tool for characterising dysfunctions that play an important role in many types of psychiatric and neurological disorders such as schizophrenia and Parkinson's disease.

TRIUMPHS AND SUCCESSES

The researchers have already made vital progress in the quest to map thought in the brain, and this work can be broadly broken down into three interrelated categories:

- Development of analysis methods – Dr Mark Woolrich and his team are introducing new, powerful and user-friendly methods to analyse MEG data. The lab is now able to pinpoint the sources of brain activity measured during cognitive functions, and to identify networks of brain areas with correlated activity
- Advances in basic cognitive neuroscience – the Brain & Cognition Laboratory (B & C Lab), also led by Nobre, is one of several groups that use the OHBA facilities to conduct their studies. Research at the B & C Lab is fundamentally focused on understanding how the brain dynamically transduces and transforms stimulus energy from the world into thoughts that occupy our minds; and how our goals, our memories and our motivations shape what we perceive. Members of Nobre's B & C Lab have used MEG to identify the patterns and networks of brain areas involved in forming memories about locations of events, and to investigate how these memories subsequently change excitability in perceptual areas. This line of research shows how our memories serve a forward-looking, proactive function to enhance our perception of anticipated events

- Clinical neuropsychiatry – using MEG, members of the Molecular Psychiatry Group headed by Professor Paul Harrison have observed a striking interaction between a genetic factor and drug delivery in mediating cognitive functions; revealing the relation to working memory and decision making. These striking results were observed for behavioural performance and also for brain activity linked to these cognitive functions

CURRENT RESEARCH

One of many fundamental and clinical neuroscience research projects that have stemmed from the collaboration of the various laboratories and data from the MEG method and interrelated methods is 'Modulation of emotional processing by antidepressants'.

While antidepressant treatments are often assumed to reverse depression effects over time, it is unknown how these actions arise. Dr Catherine Harmer and colleagues from OHBA have hypothesised that early changes in how emotional information is processed may be important in the later changes in mood and anxiety symptoms.

Antidepressants often need to be administered for weeks or months before changes in mood are seen, but increased positive bias is seen almost immediately after antidepressant administration in healthy volunteers and in depressed patients. For example, short-term administration of antidepressants to healthy people leads to decreased recognition and response to fearful facial expressions and increased bias to positive facial expressions of happiness.

The high temporal resolution of MEG means scientists can now observe which stage or stages of neural processing the antidepressants' affect. A better understanding of the timing of antidepressant functionality will help illuminate the neuropsychology of drug action, and the translation of this basic collaborative approach into clinical studies with depressed patients will allow this research group to validate and explore the role of changes in emotional processing to recovery from depression. This project clearly illustrates how basic findings from neuroscience can be translated into experimental medicine models and ultimately into clinical studies with implications for clinical treatment and practice.

Nobre has been instrumental in embarking upon this journey of scientific cooperation, fundamental good scientific practice and cutting-edge technology. By continuing along this path, she and her collaborators should unlock some of the greatest mysteries of the mind.

Collaboration is crucial to success and advancement when understanding the brain

INTELLIGENCE

OXFORD CENTRE FOR HUMAN BRAIN ACTIVITY

OBJECTIVES

The Oxford Centre for Human Brain Activity (OHBA) is a state-of-the-art experimental laboratory for investigating neural dynamics in the human brain. The research focus lies at the critical interface between basic and clinical human neuroscience research.

KEY COLLABORATORS

Oxford Centre for Functional MRI of the Brain (fMRIB)

Magnetoencephalography centres across the UK: **Aston Brain Centre**, Aston University; **Cardiff University Brain Research Imaging Centre**; **MRC Cognition & Brain Sciences Unit**, University of Cambridge; **Sir Peter Mansfield Magnetic Resonance Centre**, Nottingham University; **Wellcome Trust Centre for Neuroimaging**, University College London; **Centre for Cognitive Neuroimaging**, Glasgow University and University of York Neuroimaging Centre

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CONTACT

Professor Kia Nobre
Director

Oxford Centre for Human Brain Activity
University of Oxford
Department of Psychiatry
Warneford Hospital
Headington
Oxford OX3 7JX
UK

T +44 1865 283800
E judith.ponsford@psych.ox.ac.uk
E kia.nobre@psy.ox.ac.uk

PROFESSOR KIA NOBRE completed her higher degrees in the US, obtaining her PhD from Yale University (1992), before moving to the University of Oxford in 1994. She is currently a Professor of Cognitive Neuroscience and a Tutorial Fellow in Psychology at New College, directs the Oxford Centre for Human Brain Activity and heads the Brain & Cognition Laboratory.

