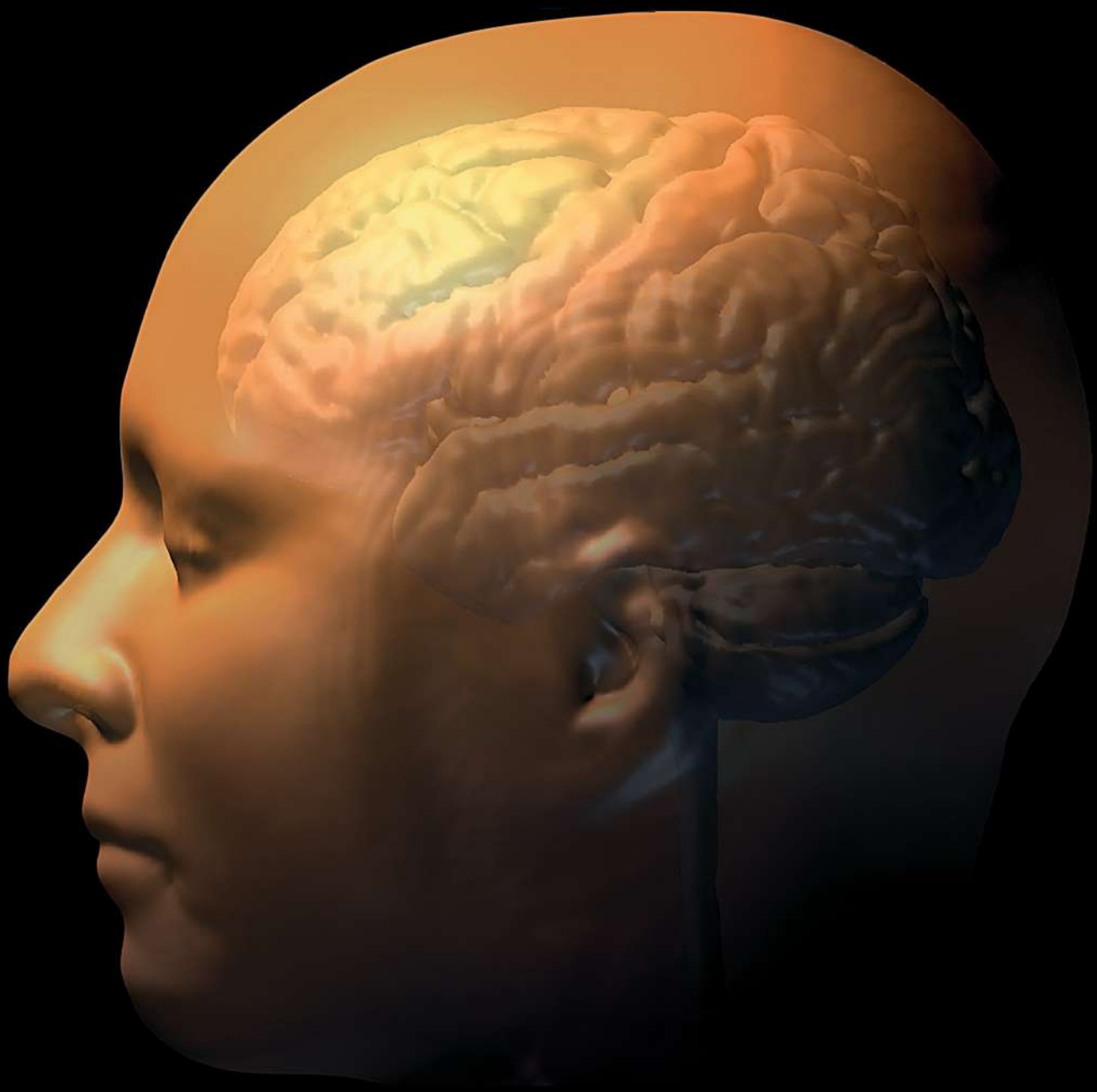
wellcome centre human neuroimaging



UCL

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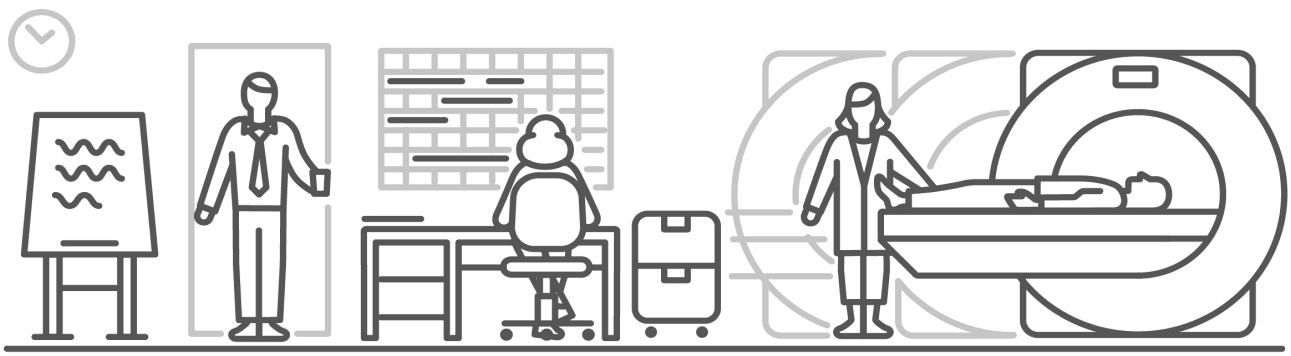
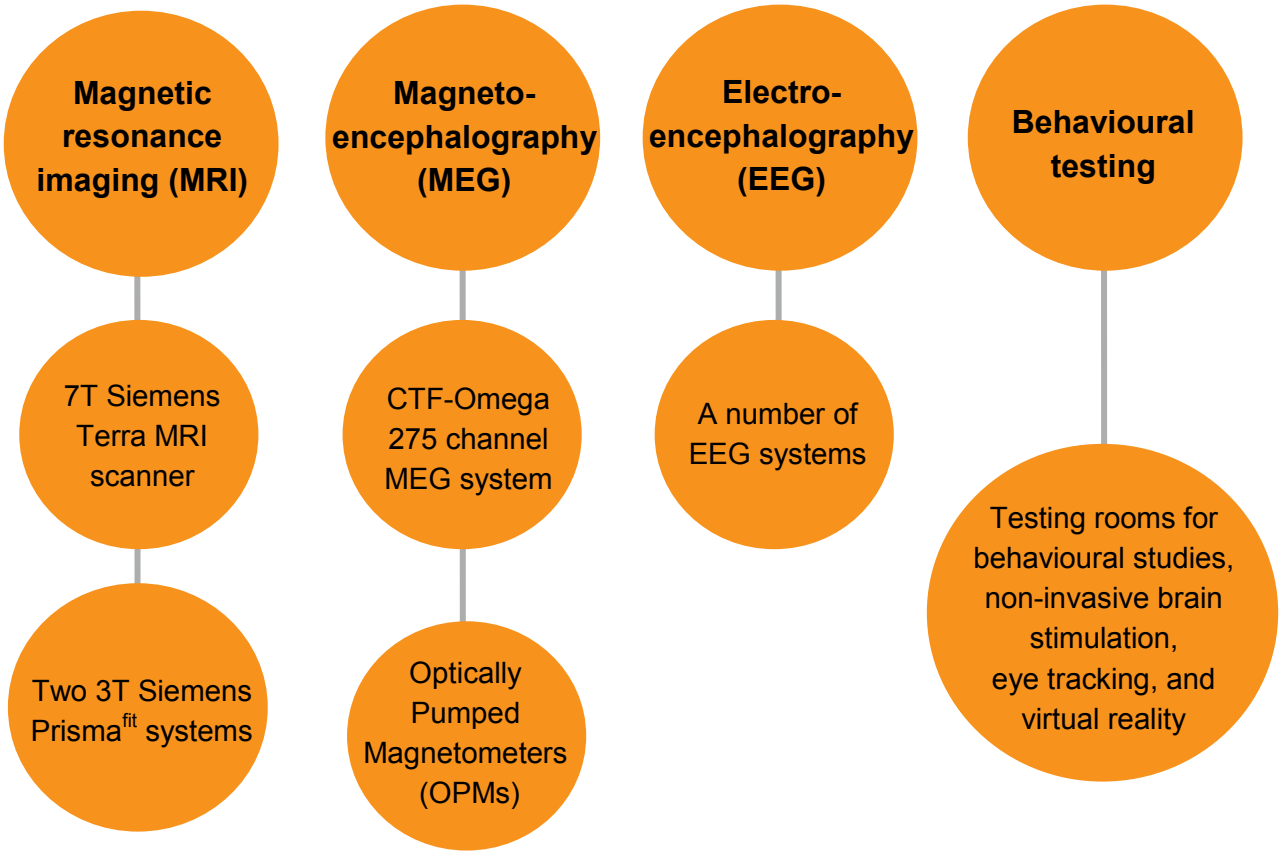


About the Centre

We develop and use non-invasive techniques to investigate how the human brain generates behaviour, thoughts and feelings and how this knowledge can be used to help patients with neurological and psychiatric disorders.

As well as conducting scientific research we offer educational and training opportunities (page 38) to support the development of imaging neuroscience and have an active public engagement agenda (page 39).

Our in-house facilities include:



Home to SPM

The analytical methods we invent, develop, distribute, teach and use for testing hypotheses about functional anatomy from neuroimaging data, are incorporated within our freely available statistical parametric mapping (SPM) software.

Our History

Over 25 years we have pioneered innovation and applications in imaging neuroscience, addressed fundamental biological questions, and played a leading role in transforming cognitive and systems neuroscience.

1994 Founding Director: Richard Frackowiak

The **Functional Imaging Laboratory (FIL)** was founded at 12 Queen Square in 1994, following a major award from the Wellcome Trust. It was incorporated within UCL's Institute of Neurology as the Wellcome Department of Cognitive Neurology. Our early work pioneered and openly shared new neuroimaging techniques and analyses for understanding human cognition.

2002 Director: Ray Dolan

Scientific Director: Karl Friston

In 2006, we were awarded Wellcome Trust Centre status (renewed in 2011), becoming the **Wellcome Trust Centre for Neuroimaging**. A key development was our computational models of behaviour that could be linked to dynamic brain activity. In 2014, we opened the Max Planck UCL Centre for Computational Psychiatry and Ageing Research (page 18), which is located in Russell Square, a short walk away from the FIL.

2015 Director: Cathy Price

Deputy: Eleanor Maguire / Martina Callaghan

Renamed the **Wellcome Centre for Human Neuroimaging** after funding renewal in an open competition in 2016, the focus of our mission is to promote the clinical translation of human neuroimaging (Page 6). Our current activities and progress (2017-2019) are documented in the following pages.

Our Clinical Vision

Our goal is to use neuroimaging and computational analyses to understand and help patients with neurological and psychiatric disorders.

We start by understanding brain structure and function in healthy people, then identify how these change in neurological and psychiatric disorders, thereby offering new insights for clinical solutions.

Learning about disorders

To understand the causes and consequences of neurological and psychiatric disorders, we ask:

How does it go wrong?

We use neuroimaging to study patients with neurological and psychiatric disorders so we can identify abnormalities in their brain structure and function.

Can we reclassify disorders?

We aim to reclassify disorders in terms of the structural and functional brain abnormalities that cause symptoms.

Applications for clinical practice

Neuroimaging discoveries can be used to improve patient diagnosis, prognosis and treatment.

Early Diagnosis

Can we detect hidden abnormalities in brain structure and activity before clinical symptoms?

Prognosis

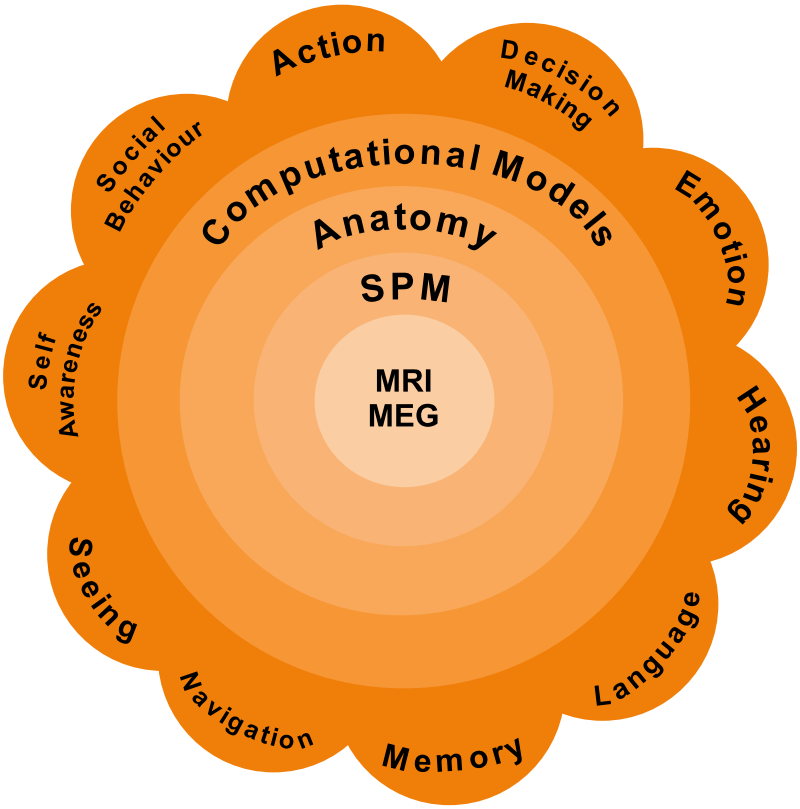
Can we accurately predict how patients' symptoms will change over time?

Treatment

How are prognoses improved by treatment?

Research Strategy

We use neuroimaging techniques (MRI, MEG) and computational models to investigate brain anatomy and the neural systems that support different perceptual, cognitive, emotional and motor functions.



Each brain function is underpinned by complex neural systems with many inter-connecting brain regions. We tackle this complexity with highly specialised research teams that focus on understanding the neural system associated with a particular type of function (e.g. visual perception or emotion) and how this system is affected in neurological, psychiatric or developmental disorders. For example, researchers specialising in motor functions will primarily study patients with neurological conditions that affect movement (e.g. Stroke and Parkinson's disease) whereas those specialising in emotion will primarily study patients with psychiatric conditions (e.g. depression and anxiety).

Other research teams specialise in the early detection and phenotyping of specific clinical disorders (e.g. Parkinson's disease), adaptation to sensory or motor loss (e.g. deafness or amputation), or the methodologies required to investigate these conditions.

Research Teams

The Wellcome Centre for Human Neuroimaging includes all the staff at the Functional Imaging Laboratory (FIL) and the Max Planck UCL Centre for Computational Psychiatry and Ageing Research (MPC). Together, these form the UCL Department of Imaging Neuroscience.

In addition, we support the neuroimaging research programmes of Principal Investigators employed at other UCL departments and institutes.

Key

FIL and MPC	UCL Department of Imaging Neuroscience
ICN	UCL Institute of Cognitive Neuroscience
BRR	UCL Department Brain Repair & Rehabilitation
CMN	UCL Department Clinical & Movement Neuroscience
ND	UCL Department Neurodegenerative Disease
CDB	UCL Department Cell & Developmental Biology

Newcastle University (**NU**), Oxford University (**OxU**) and Virginia Tech (**VT**)

Principal Investigators, their affiliation and research programmes are listed below in the order they are presented on pages 10 - 36

Core technologies

SPM, Anatomical and Dynamic Modelling

Computational Psychiatry

Specific Brain Functions

Other Research Programmes

MRI

The Physics Group focuses on the development and optimisation of novel neuroimaging methods to non-invasively characterize the structure and function of the human brain using MRI.

Martina Callaghan

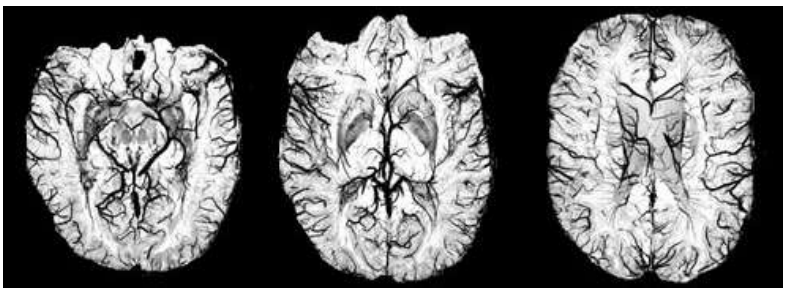
The Physics Group's developments span all aspects of the neuroimaging chain, including pulse sequence design for data acquisition, bespoke image reconstruction schemes, and the development of post-processing and data modelling tools.

In May 2019, we installed an ultra-high field 7T MRI scanner, which offers vast increases in signal and contrast levels over lower field strengths. This increased sensitivity will allow us to characterise the cyto- and myelo-architecture of the brain and to dissociate discrete units of neuronal computation. We will seek to identify very small, subtle changes in the brain's microstructure at early stages of disease, ideally before clinical symptoms are present. Such advances would allow us to develop and assess therapies targeting several different neurodegenerative diseases with our clinical partners across Queen Square.

Arrival of the 7T scanner

Continuing our strong history of methodological development, we aim to address the technical challenges posed by the ultra-high field MR scanner and establish 7T techniques for an array of neuro-physical measures, neurochemical studies, and MRI analysis software. Targeting progress in healthcare, there are also plans to use the 7T to identify more informative ways to use existing hospital scans.

In 7T MRI, the signal-to-noise ratio more than doubles relative to 3T, as does susceptibility-based contrast. This leads to high sensitivity and specificity for both functional and structural neuroimaging and exquisite depiction of small features, such as the vasculature in the images below.



Wearable MEG

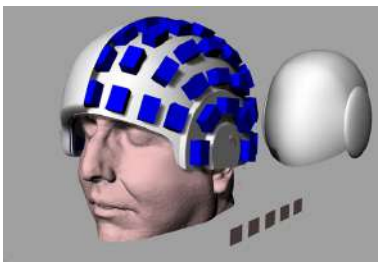
In collaboration with Nottingham University, we are leading the development and application of a new generation of wearable magnetoencephalography (MEG) systems.

Gareth Barnes

The new technology is based around optically pumped sensors (OPMs) which, unlike traditional MEG systems, do not require cryogenic cooling. It is now possible to measure field changes much closer to the scalp, increasing field magnitude significantly and ensuring maximal signal for any head-size. By minimizing the static field around the subject's head, we have shown that it is now possible to produce electrophysiological images of brain function whilst subjects move naturally (Boto et al., 2018).

Besides the neuroscientific avenues this technology opens up (see page 28) it also has significant clinical potential. MEG has long been used for pre-surgical mapping and spike localisation in epilepsy. In children, the earlier epilepsy surgery can take place, the better the prospects for normal development. However, the surgical planning stage is often delayed until the child can remain still.

We have replicated pre-surgical language mapping paradigms at Great Ormond St Hospital using this motion-robust OPM technology (Tierney et al., 2018) and now work towards our first cohort of younger subjects. In adults, where the main benefits are improved spike localization and longer duration recordings, we are working with colleagues at the National Hospital for Neurology and Neurosurgery to validate the technology.



As the size of the sensors decreases, we are moving from individualised helmets (upper) to generic, clinically practical, designs (lower).

Methodologically, the main challenges will be

- To devise new field-nulling methods to allow greater freedom of movement within the room.
- To push the spatial and depth resolution made possible from the increased sensitivity and longer-term recordings.
- To use these absolute magnetic field sensors to measure static fields generated by the human brain.

Equipment

We will shortly have an array of 50 of the latest OPM devices and we have installed a dedicated magnetically shielded OP-MEG suite at our Centre.

We are part of an Innovate UK funded partnership with Magnetic Shields Ltd, The University of Nottingham and Great Ormond St Hospital. This partnership will install a new affordable magnetically shielded room at Young Epilepsy (a residential centre for young people with epilepsy).

SPM Software

Our Statistical Parametric Mapping (SPM) software consists of a suite of tools for analysing brain imaging data, which may be images from different cohorts or time series from the same subject (fMRI, PET, EEG, MEG, etc).

John Ashburner
Image Processing

Guillaume Flandin
Head of SPM

Peter Zeidman
DCM

Open Science

SPM has been freely available to the brain imaging community since its launch in 1991 as an open source, academic software. Much of our efforts go into developing new functionality and offering support to more than 5,000 users in our online community.

As with any software project, ongoing maintenance is essential to ensure that SPM continues to work effectively within an ever-changing computing and research environment. For example, increasingly large datasets have led us to parallelise some of the code, with explorations into GPU support for certain functionality.

MATLAB was the obvious interpreted programming language choice for numerical computing in 1991, but its widespread use within academia is becoming increasingly uncertain. A standalone SPM version is now available, and work has been done to enable GNU Octave compatibility. SPM developers are also investigating how best to integrate future modules, written in Julia or Python, into SPM.

The push towards data sharing and the introduction of the Brain Imaging Data Structure (BIDS) standard has led to ongoing SPM developments to enable easier sharing of data and results.

Diverse image types

We prioritise making SPM applicable to a wide range of brain images. Efforts have gone into extending the software to make it applicable to patient scans acquired within hospitals. This has included developing super-resolution techniques for dealing with thicker sliced scans, as well as extending SPM's segmentation/normalisation approach to better handle patient MR and CT scans. Other work has been on dealing with quantitative MRI, and further modifications are needed for scans acquired at 7T.

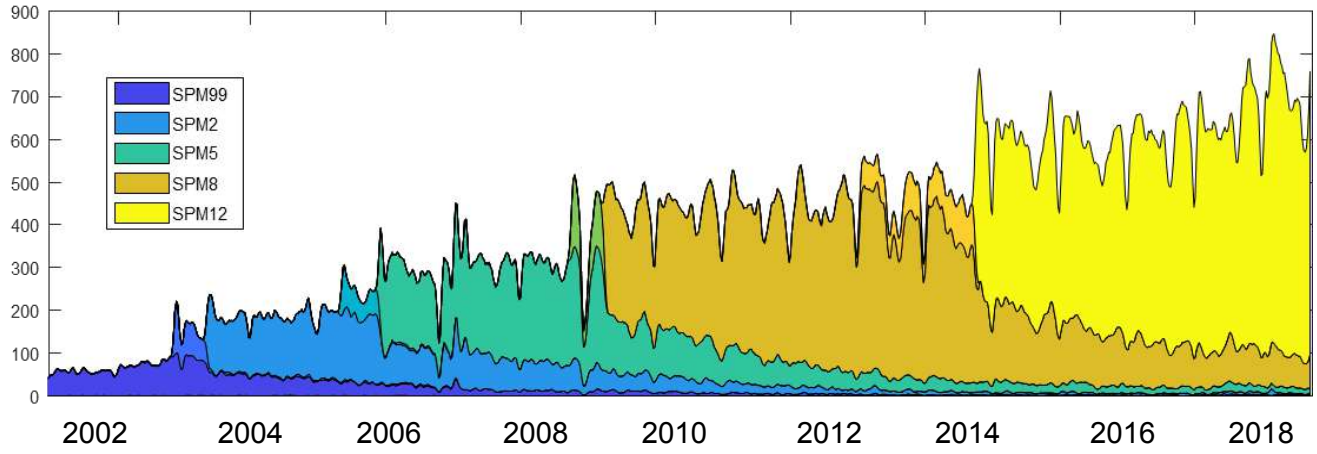
Dynamic Causal Modelling (DCM)

DCM is a framework embedded in the SPM software for investigating the neural circuitry that gives rise to functional MRI, EEG or MEG measurements. It was invented, at the Centre, by Friston, Harrison and Penny (2003). Our recent focus has been to develop DCM in two key areas:

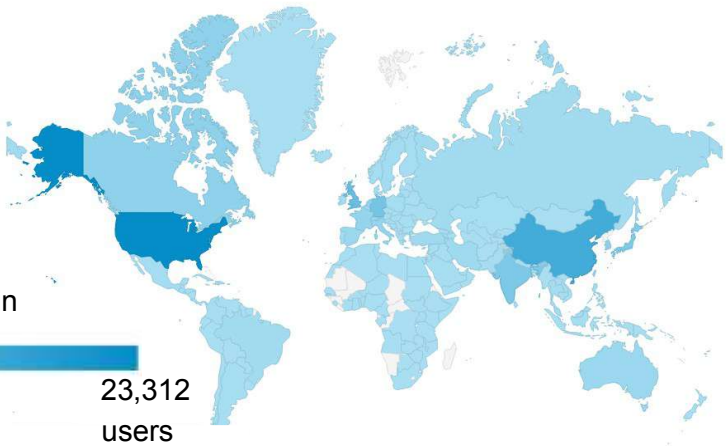
New statistical tools for group analysis, namely the Parametric Empirical Bayes (PEB) framework. This enables people to ask: what is the effect of an experimental manipulation on particular neural connections? How does this differ between patient groups, or vary across people according to particular cognitive or clinical scores? Furthermore, can we predict a person's diagnosis or clinical outcome from their connection strengths? (Friston et al., 2016; Zeidman et al., 2019).

Neurovascular coupling refers to the connections between neural activity and changes in cerebral blood flow (CBF). Alterations to these mechanisms occur due to ageing and a variety of clinical conditions including Alzheimer's disease. We have been developing modelling tools for investigating neurovascular coupling, through multi-modal fusion of MRI and MEG data. This may also help us to better understand the source of the functional MRI signal, which itself depends on neurovascular coupling. (Friston et al., 2017; Jafarian et al., 2019).

Number of downloads of the SPM software from our website (per week)



110,000 visitors to the SPM website (Sept 2018-19)



Geographical origin

1 — 23,312 users

5,436
subscribers to the SPM mailing list

Quantitative Neuroanatomy

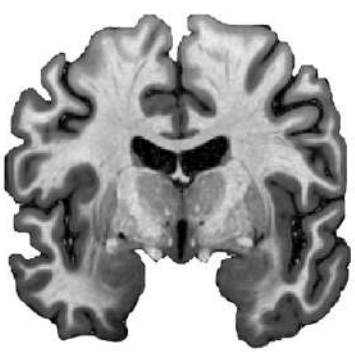
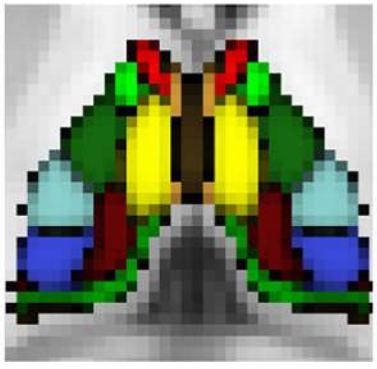
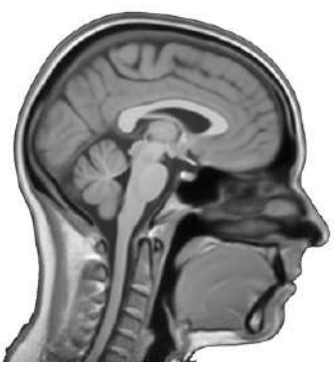
The anatomy group develops advanced neuroimaging methods for the study of human brain structure in health and disease.

The brain is composed of multiple, anatomically distinct, processing units that are uniquely interconnected via white matter pathways. Though these specialised functional regions tend to occur in similar areas of the brain, their precise location and size are highly variable among individuals. Many of these "*cytoarchitectual*" structures cannot be seen using routine MRI sequences. Furthermore, accurate alignment of brain anatomy is a key requisite for many other neuroimaging analysis techniques. The structural properties of these cytoarchitectual regions not only help support their discrete functions (e.g. vision, hearing), but can also help explain some of the observed inter-individual variability, from how people perceive and interact with the world, through to how they are affected by neurological disease.

- **John Ashburner** develops methods for computational anatomy to improve the mapping, quantification and alignment of brain microarchitecture. These techniques provide precise, reproducible, non-invasive measures of brain structure, which is fundamental to understanding the link between anatomy and function in health, disease and longitudinal studies.

- **Martina Callaghan** develops MRI methods for non-invasive *in vivo* quantification of a wide range of brain tissue microstructural properties, including measures sensitive to myelin and iron content, cellular packing density, water density, diffusivity as well as connectivity. These quantitative MRI (qMRI) properties are used to identify structures such as cortical lamina, cyto– or myelo-architectonic boundaries, subcortical nuclei, and to characterise links with function and behaviour. They also provide insight into the underlying biophysical processes that contribute to structural brain changes (e.g. during neurodegeneration).

- **Christian Lambert** develops methods using qMRI to map brain structures that are not normally visible on MRI, such as brainstem and thalamic nuclei, cortical lamina and white-matter architecture. These help provide more accurate measurements of structural brain changes, and have applications in functional neurosurgical procedures such as deep brain stimulation.

Anatomical Phenomics

We study the link between brain structure and inter-individual variability in health and disease.

Christian Lambert

The causes of variability in brain function and disease between individuals are complex, with contributions from genetic, metabolic and environmental factors. We specialise in the relationship between brain anatomy and inter-individual variability. We develop quantitative MRI (qMRI) based techniques to study how histological differences in brain microstructure relate to the genetic and phenotypic variability observed in health and disease.

Improving our understanding of these relationships will allow:

- Earlier, more accurate diagnoses in conditions such as Parkinson's disease (PD)
- Better predictions of future disease progression at an individual subject level
- Insight into the biological foundations of structural-functional variation

Our vision is to develop clinical tools to identify and accurately diagnose neurodegenerative conditions before the obvious signs of disease emerge, help provide more personalised treatments tailored to individual subjects, and create a framework where disease-modifying therapies can be started before brain tissue has been irreversibly lost.

Ongoing work

We have (i) developed techniques to map thalamic nuclei at an individual subject level using probabilistic tractography; (ii) improved pre-processing pipelines for cerebral small vessel disease, (iii) used the patterns of damage to predict future vascular dementia, (iv) demonstrated a spectrum of disease phenotypes based on anatomy and (v) improved the segmentation of brainstem structures *in vivo*.

Quantitative MRI for Anatomical Phenotyping in Parkinson's disease (qMAP-PD)

Parkinson's disease (PD) is the second most common neurodegenerative condition. It is diagnosed based on clinical signs, that become detectable once 50-60% of the substantia nigra dopamine producing neurons have been lost. However, PD is thought to begin between 10 and 20 years before this, with some of the earliest changes found within the brainstem and enteric plexus. When the condition manifests, both the presentation and progression is highly variable between individuals. While groups at high risk of developing PD can be identified, it is not possible to accurately predict who will later develop PD. qMAP-PD is a longitudinal study to examine phenotypic variability in the presentation and progression of early and pre-clinical PD. It is using the latest novel anatomical qMRI imaging methods, combined with detailed clinical phenotyping, high-throughput genotyping and other blood-based biomarkers, and will also leverage other large imaging-genetic datasets from the UK Biobank and International Parkinson's Disease Genomics Consortium.

Theoretical Neurobiology

We develop and apply advanced mathematical techniques that provide testable, theoretical models of dynamic brain function in health and disease.

Karl Friston

We treat the brain as a (Bayesian) statistical organ that predicts current and future events based on beliefs about the state of the world. Perception and action operate under one unified (free energy) principle – and its corollary active inference – whereby we make hypotheses about the most likely cause of our observations and update these hypotheses to minimise uncertainty about the world.

We model brain function (e.g., vision, motor control, learning, decision making, speech recognition) using active inference, by associating neuronal dynamics with a gradient flow on variational free energy, in neurobiologically plausible architectures. Behavioural and neural responses are simulated under different conditions (e.g., prior beliefs, noise and optimization processes) and used to predict behavioural, neuronal or physiological observations (e.g., the P300 and mismatch negativity in EEG signals that can be used to measure Bayesian surprise). The models that best explain the data can then be selected (and validated) using Bayesian model comparison.

Neurobiologically plausible implementations of the models are tested and optimised, using a range of data from non-invasive neuroimaging (fMRI, EEG, MEG) and invasive electrode recordings. Neuronal architectures are inferred from neuroimaging data by model inversion. For example, we used EEG recordings to estimate receptor function in N-methyl-d-aspartate (NMDA) antibody encephalitis (Symmonds et al., 2018).

The software we use to analyse neuronal dynamics, Dynamic Causal Modelling (DCM, see page 13) has been used recently to: (i) distinguish forward and backward neuronal signalling in different layers and levels of the cortex (Preller et al., 2019), (ii) specify the mechanisms of neuronal communication at the synaptic and neurotransmitter level (Rosch et al., 2018) (iii) elucidate the principles of inference in the brain and its role in psychopathology (Hamburg et al., 2019), and (iv) detect abnormalities in neurovascular coupling (Friston et al., 2017b).

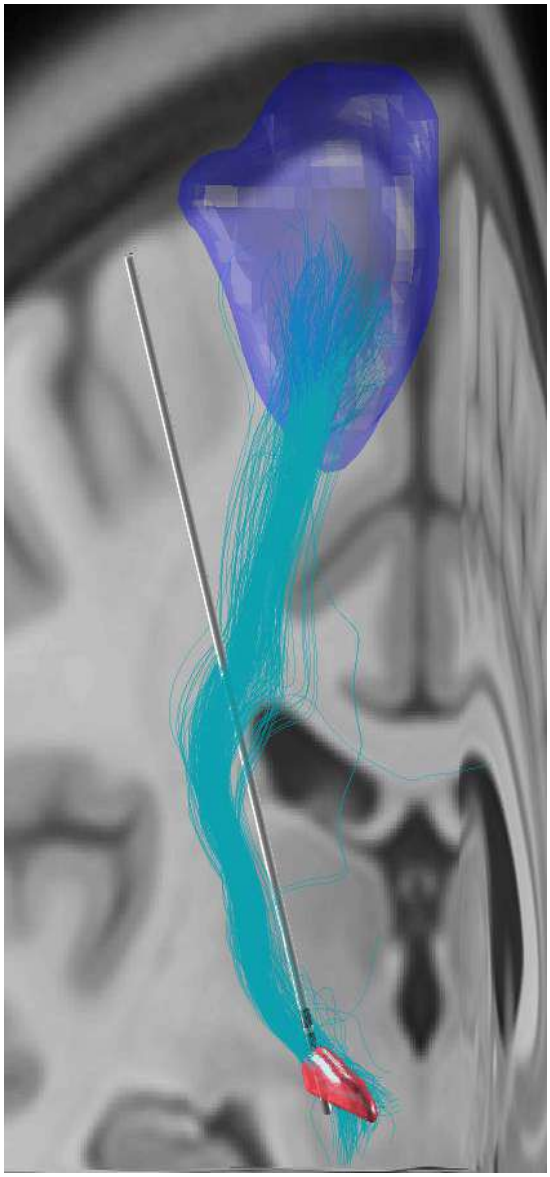
Recent developments to the underlying theoretical formulation include: **deep** (hierarchical) temporal models where the outcomes of one (slower) level generate the hidden states at a lower (faster) level (e.g. reading), **mixed** generative models where continuous sensations inform discrete representation (e.g. speech recognition), and **continuous** space models where continuous sensations inform continuous representations (e.g. motor control).

Clinically, we aim to understand pathophysiology and psychopathology in computational (i.e. functional) terms – in a variety of neurological and psychiatric syndromes.

Translational Neurophysiology

Our goal is to understand the function and dysfunction of oscillatory brain networks and precisely map out their anatomy. To achieve this we use simultaneous MEG and invasive recordings in Deep Brain Stimulation (DBS) and epilepsy patients.

Vladimir Litvak

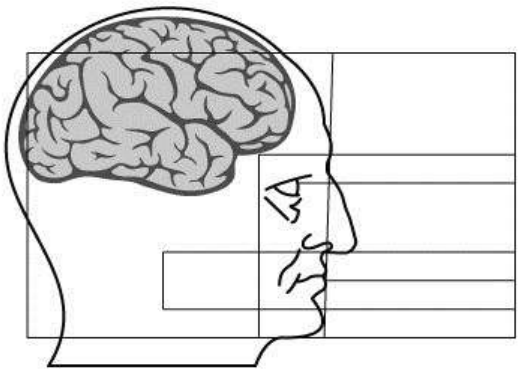


Using atlas connectome to map out the structural connectivity between the STN and a motor cortical area coherent with the STN in the beta band (Oswal et al. in preparation).

Our research will help focus DBS treatment on pathological brain activity and avoid the locations and stimulation patterns that could cause side effects. Simultaneous invasive recordings also help validate MEG analysis methods, particularly analyses of functional and effective connectivity.

Ongoing studies

- Studying the role of the Subthalamic Nucleus (STN) in evidence accumulation and conflict resolution. Using a unique task design in Parkinson's patients undergoing DBS surgery, we examine neural responses to individual cues in a sequence, showing distinct roles of theta and beta oscillations. We are currently examining how cortical inputs could explain the observed STN activity.
- Characterising oscillatory activity and connectivity of the Ventral Tegmental Area (VTA) in patients with chronic pain and associated depressive symptoms, and the role of the VTA in reinforcement learning.
- Analysing simultaneous intracranial EEG and MEG recordings in patients with epilepsy in collaboration with Ruijin Hospital JiaoTong University School of Medicine in Shanghai and the OHBA analysis group in Oxford.
- Combining anatomical and physiological data to map out physiological biomarkers such as power, coherence, and cross-frequency coupling in the subcortex.



MAX PLANCK
UCL CENTRE
for Computational Psychiatry
and Ageing Research

The strategic goal of the Max Planck UCL Centre for Computational Psychiatry and Ageing Research is to identify causes of psychiatric disorders and of individual differences in lifespan cognitive development.

The Max Planck UCL Centre's most important theoretical tools are computational and statistical models of differences, fluctuations, and changes in brain–behaviour relations. The Centre is developing efficient and sensitive methodologies that reveal core cognitive deficits in psychiatric disorders and ageing. Progress towards this goal will enable earlier intervention and more efficient treatment for psychiatric diseases, as well as better maintenance of cognitive functions into old age.

The Centre consists of two directors, one based in London, representing University College London (Ray Dolan), and the other based in Berlin, representing the Max Planck Society (Ulman Lindenberger). Principal investigators at the London site are Quentin Huys, Tobias Hauser, Dominik Bach and Robb Rutledge.

In 2016, the *International Max Planck Research School on Computational Methods in Psychiatry and Ageing Research* (IMPRS COMP2PSYCH) was added to the Centre, providing a joint platform for graduate training in core concepts and methods from computer science and statistics in relation to substantive research questions in psychiatry and lifespan psychology.

Work at the Centre is structured into three interconnected research domains: (i) computational psychiatry; (ii) lifespan development; and (iii) computational and statistical methods.

During the 2019–2024 funding period, we aim to bring about a greater integration between activities at the London and Berlin sites, arising out of a pursuit of common questions that pertain to both psychiatry and ageing. This builds on our past collaborative work which has included fundamental discoveries on how normal ageing is related to changes in risk preference (Rutledge et al., 2016), how the trajectory of brain development in adolescence relates to psychiatric traits (Ziegler et al., 2019), and how structural equation modelling techniques can be used to characterise individual differences in behavioural and neural development (Kievit et al., 2017; 2018).

Going forward we foresee increasing engagement in relation to the development of methodologies that maximise the inferences that can be drawn from longitudinal observations, given that both the Berlin and London groups have rich and unique longitudinal data sets. Our ability to further enhance the degree of overlap and convergence in research aims will be greatly facilitated by new emerging interactions that we are developing in the context of our joint research schools.

Emotion and Cognition

Our vision is to understand the neural codes and computational principles enabling us to build, represent, and update a mental model of the world.

Ray Dolan

This work is informed by theoretical treatments, particularly ideas derived from reinforcement learning. Understanding how such models are constructed and represented in the brain is a fundamental question for neuroscience, and has particular importance for psychiatric research. Our research programme has two major strands:

Decision making and its impairments in psychopathology

Our previous work on this topic has concerned model-based reasoning, in particular its integration with model-free reasoning. This has motivated us to address the question of intermediate points on a spectrum between the two. Here we have shown a greater degree of complexity than implied in previous accounts, particularly in relation to credit assignment (Moran et al., 2019) with striking explanatory implications for psychopathology (Shahar et al., 2019). In social decision making we have described a novel effect on preferences engendered by having to make inter-temporal choices for a partner. This observation inspired us to provide a theoretical treatment of this effect, one that focused on uncertainty regarding one's own values (Moutoussis et al., 2016). In work under review we have shown in our NSPN cohort that this has important implications for the trajectory of social development during adolescence.

An important methodological innovation, opening avenues for us to address more sophisticated questions in relation to decision making, has been our ability to capture the course of model-based planning through decoding of MEG signals. Our initial work here includes revealing the temporal structure of associative retrieval as well as identifying fast, non-spatial, sequence replay using MEG (Kurth-Nelson et al. 2016). Building on this, using a decoding strategy, we have shown forward and reverse replay in an MEG signal (Liu et al., 2019). In related research we examined the neural representation of serial and parallel computation, both of which are involved in model-based planning (Elgar et. al, 2016). Most recently, we have characterised the relative contribution of on-task and off-task replay to model based and model free decision making.

Neuromodulation and psychopathology

Previously in theoretical work we have proposed a mechanistic framework for how affect-learning interactions contribute to mood dynamics (Eldar et al., 2018). Empirically, we showed how unexpected outcomes alter affective state, including providing evidence that a varying reward sensitivity is predictive of subsequent fluctuations in mood (Eldar et al., 2016). Theoretically, this two-way relationship can set in train an escalating positive feedback loop, one wherein good outcomes improve mood which, in turn, improves perception of subsequent outcomes leading to further mood elevation. Building on this idea we have revealed that a positive impact on mood is best accounted for by a boost in subjective reward perception during learning, and this results in a delayed mood response. Importantly, this effect is amplified by SSRI's, in a manner that can explain a delayed impact of these treatments. Thus, instead of influencing affect or reward sensitivity directly, SSRIs amplify a bilateral interaction between mood and reward perception.

Decision and Mood

We build computational models for mood and behaviour that help us understand psychiatric disorders.

Robb Rutledge

What is happiness? We are interested in describing the factors that determine subjective affective states like happiness. We build computational models linking affective states to ongoing experience and quantitatively relating feelings and behaviour. We use neuroimaging, pharmacology, electrophysiology, and smartphone-based data collection to study the relationship between decision making and emotion across the lifespan and in people with psychiatric disorders like depression.

$$\text{Happiness}(t) = w_0 + w_1 \sum_{j=1}^{t} \gamma^{t-j} CR_j + w_2 \sum_{j=1}^{t} \gamma^{t-j} EV_j + w_3 \sum_{j=1}^{t} \gamma^{t-j} RPE_j$$

Ongoing studies

Computational models of affective experience

We find that happiness depends not on how well you are doing, but whether you are doing better than expected. Happiness relates to neural activity in dopamine projection areas and can be manipulated pharmacologically with dopaminergic drugs. We are extending this quantitative understanding of happiness to multiple dimensions relevant to mood disorders including effort, intrinsic reward, future prospects, environmental volatility, confidence, and altruistic behaviour.

Neuromodulatory influences on decision making and mood

We consistently find that dopamine plays a valence-dependent but value-independent role in reward seeking. We are testing how dopaminergic and serotonergic drugs influence mood and behaviour across multiple tasks. Through collaboration at Yale University, we are evaluating how ketamine, a rapid glutamatergic antidepressant, influences mood dynamics during decision tasks. We will test whether mood effects due to serotonergic antidepressants gradually accumulate while ketamine effects are immediate. We will test whether mood dynamics predict later depressive symptoms.

Smartphone-based data collection in mood disorders

We co-developed The Great Brain Experiment, a smartphone app for cognitive science research with over 130,000 users. We remotely tested over 500 individuals with a history of depression, finding that model parameters relate to depression severity. We are building a new app, The Happiness Project, for longitudinal testing. Through collaboration at the National Institute of Mental Health, we are testing 150 adolescents with anxiety and depression to ask how model parameters relate to symptoms over months. We will also test patients with bipolar disorder to test whether a computational parameter for the influence of mood on learning is elevated and can predict future manic and depressive episodes.

Developmental Psychiatry

We investigate why most psychiatric disorders arise before adulthood and how this is related to aberrant neurocognitive development.

Tobias Hauser

Why do most mental health problems emerge before adulthood? With 75% of all psychiatric disorders arising before young adulthood, adolescence is a critical period of vulnerability for developing mental health problems. However, it is unknown why this is the case.

The goal of the Developmental Computational Psychiatry Group is to understand the neural and cognitive mechanisms that underlie the emergence of mental health problems during adolescence, and how we can use this knowledge to prevent adolescents from becoming ill.

Adolescence is also a time of prolonged cognitive development when the brain undergoes fundamental reorganisation. We believe that it is thus critical to understand the developmental trajectories of cognition and brain development and to assess how these processes go awry in youths that are developing mental health problems. To assess this, we conducted a longitudinal study to investigate how brain development is tied to the presence of psychiatric symptoms (Ziegler, Hauser et al., 2019). Using a novel marker for myelin, we showed that widespread myelin development continues well into adulthood. Moreover, we showed that this ongoing brain development was modulated by the presence of psychiatric traits. Subjects with high trait impulsivity or compulsivity scores showed reduced myelination in prefrontal regions, in areas known to be impaired in adults with these disorders. Our findings thus suggest that the emergence of psychiatric disorders is a consequence of aberrant brain developmental trajectories.

A key to understanding how neurocognitive development goes awry and leads to mental health problems, is to identify the cognitive functions that are impaired in psychiatric patients and to trace their normative and aberrant development during childhood and adolescence (Hauser et al., 2018). Only by understanding normative development, we can detect a derailing of specific sub-processes. We thus combine decision neuroscience studies with developmental and patient studies. For example, we have shown that obsessive-compulsive disorder (OCD) patients suffer from excessive indecisiveness characterised by increased information gathering (Hauser et al., 2017). Using computational modelling, we showed this was driven by a delayed emergence of subjective sampling costs (Hauser et al., 2017), and is linked to noradrenaline functioning (Hauser et al, 2018). Using paediatric OCD patients and normative developmental studies, we demonstrated that information gathering matures in early adolescence and that juvenile OCD patients already show the same indecisiveness as adults (Hauser et al., in prep). This means that a neurocognitive derailing takes place early during development and that prevention is necessary before onset of adolescence.

Threat Avoidance

We investigate how the neural system forecasts threat and selects pre-programmed survival actions, with the goal of developing novel psychiatric treatments.

Dominik Bach

Threat to survival comes in many forms: starvation, predation, self-defending animals, accidents, or inter-human conflict. The human brain has access to a large repertoire of defensive actions.

A requirement to act ultra-fast and with high precision poses interesting computational challenges. Emitting defensive actions in the absence of threat is a hallmark of several psychiatric conditions. By combining behavioural assays with neuroimaging and pharmacological intervention, we seek to understand how the neural system predicts threat and selects appropriate action. Novel interventions to rectify inappropriate threat prediction are tested in experimental models of psychiatric disorders.

Ongoing studies

ActionContraThreat: To elicit threat-related action in the laboratory, we use virtual reality computer games with full body motion, and track actions with motion-capture technology. Based on a cognitive-computational framework, we characterise the space of actions under threat, investigate the cognitive mechanisms by which these actions are selected in different scenarios, and describe them with computational algorithms that allow quantitative predictions. To assess their systems-level neural implementation, we use wearable magnetoencephalography (MEG) while people move freely and interact with the virtual environment.

Threat forecasting: Psychotherapy for anxiety disorders is based on learning mechanisms. We seek to optimise psychotherapeutic interventions by better understanding the underlying learning dynamics. We use a computational approach to study how the neural system establishes and adjusts threat predictions. Experimentally, we combine simplified cross-species laboratory models of threat prediction (such as Pavlovian fear conditioning) with various behavioural and physiological assessments. We develop these assessments of implicit learning to achieve optimised signal-to-noise ratio. To verify the neural systems underlying our learning indices we capitalise on patients with rare subcortical lesions. Our novel data analysis methods are freely available to the community (PsPM - psychophysiological modelling).

Novel treatments: In order to facilitate translation into clinical practice, we are testing a range of candidate treatments in laboratory models of psychiatric disorders. Our focus is on interventions that reduce synaptic plasticity to impair the consolidation of threat predictions, or to disrupt established predictions. Our approach encompasses pharmacological interventions with synaptic plasticity-inhibiting drugs, temporary cortex lesions with transcranial magnetic stimulation guided by fMRI, and behavioural interventions.

Metacognition

Our goal is to understand the human brain's capacity for metacognition and self-awareness, and how these processes are altered in disorders of mental health.

Steve Fleming

Metacognition refers to the ability to reflect on, monitor and control other cognitive processes. Metacognitive sensitivity is the extent to which our self-estimates of performance track objective success in a variety of domains including perception, decision-making and memory.

Distortions in metacognitive sensitivity may underpin the lack of insight that is common in a range of neurological and psychiatric disorders. The Metacognition Group combines computational models with behavioural and cognitive neuroscience approaches to deconstruct metacognition into its component parts, such as how we recognise our errors and develop beliefs about our skills and abilities. We have a special interest in the prefrontal cortex and how its functional anatomy supports self-awareness.

Ongoing studies

Revealing the neural foundations of metacognition

We have designed new psychophysical paradigms to distil processes supporting metacognitive confidence from lower-level (e.g. perceptual) uncertainty. In conjunction with fMRI, this has led to us identifying distinct neural contributions to metacognition in prefrontal subregions (Bang & Fleming, 2018; Fleming et al., 2018) and has revealed that such signals generalise across unrelated tasks, indicating a domain-general resource (Morales et al., 2018).

Identifying relationships between metacognition and mental health

We have identified systematic links between metacognition and mental health in large-scale general population samples (Rouault et al., 2018), and developed web-based tools to train and improve domain-general metacognitive sensitivity (Carpenter et al., 2019). These findings have led to ongoing clinical collaborations that are characterising changes in metacognition in depression (Zurich) and dementia (London). To facilitate analysis of datasets from brief clinical assessments, we have developed hierarchical Bayesian models of metacognitive sensitivity (Fleming, 2017).

Testing computational models of self-awareness

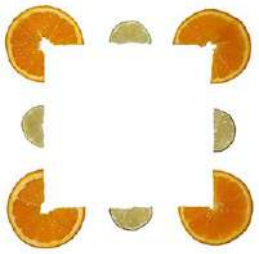
We have developed computational (generative) models of metacognitive judgments that seek to account for lack of insight (Fleming & Daw, 2017) and the relationship between higher-order cognition and conscious awareness (Fleming, 2019). These models provide predictions for neural responses at different levels of a hierarchical model of metacognition that we are testing using functional imaging.

Visual Perception

The goal of our research is to understand how prior knowledge and expectations influence how we perceive the world, and how this is realised by the brain.

Peter Kok

Visual perception is not simply a product of the light that hits our eyes, but is instead strongly influenced by our prior knowledge and expectations. For instance, we have a strong impression of a white square in the image to the right, because our visual system deems a square surface occluding parts of circular orange and lime slices a likely cause of this image. In other words, perception can be seen as a process of inference, trying to arrive at the most likely explanation for our sensory inputs given our knowledge of the world. We use advanced neuroimaging methods to reveal the neural mechanisms whereby prior knowledge influences perception.



Ultimately, these insights may improve our understanding of disorders like psychosis and autism, which are characterised by aberrations in perception.

Ongoing studies

Revealing the fundamental computational architecture of visual cortex.

There is much we don't know about how the visual cortex is organised. Our group uses ground-breaking ultra-high field (7T) functional magnetic resonance (fMRI) techniques to study neural signals in the different layers of human visual cortex (Kok et al., 2016). This allows us to study how neural representations in the different cortical layers are influenced by expectations, thereby revealing the computational architecture of visual cortex.

Establishing how the neural computations underlying perception unfold over time.

There is currently much debate on whether visual processing is biased by expectations from the moment they arrive in the cerebral cortex, or whether expectation only influences later decision-making processes. We are addressing these and other questions using magnetoencephalography (MEG), allowing us to study the unfolding of neural signals with millisecond precision (Kok et al., 2017).

Revealing the neural source of expectations.

In recent work, we revealed that an important memory region, the hippocampus, contains representations of expected visual stimuli (Kok & Turk-Browne, 2018). We are using high-resolution fMRI to study the communication between visual cortex and specific subfields of the hippocampus, to reveal the neural networks by which the brain generates visual expectations from memory.

Auditory Cognition

Auditory cognition (the mind's ear) describes a group of processes by which the brain makes sense of the sound world. We study the normal processes and how these go wrong in brain disorders.

Tim Griffiths

We study the normal perception of complex sound relevant to the analysis of speech, music and environmental sounds, and their associated brain bases. We study the brain bases using behavioural and neurophysiological models, functional imaging with functional MRI, electroencephalography, magnetoencephalography and electrode recordings in neurosurgical patients.

Our work concerns auditory perception and involves the auditory system in the brainstem and auditory cortex—but auditory cognition also involves attention, memory and emotional responses and requires many brain systems that are not conventionally considered parts of the auditory brain. A complete understanding of auditory processes will include both low level perceptual processes and higher level cognition.

We also study the effect of brain disorders on auditory cognition. A number of disorders are associated with deficient auditory cognition, including common developmental disorders like dyslexia, acquired disorders like stroke, and degenerative disorders like dementia. Tinnitus and auditory hallucinations can also be considered as derangements of auditory cognition. Another cognitive phenomenon is misophonia—a disorder of emotional sound analysis. By combining measurements of brain activity with neurophysiological models, we have provided key insights into the functional architecture of these disorders.

Our work is benefited by collaborations between the Wellcome Centre for Human Neuroimaging, Newcastle University Medical School, and the Human Brain Research Laboratory at the University of Iowa. We have members of our group at each of these three centres, and complementary work is carried out at all three locations.

Ongoing studies

Many people experience pronounced difficulty understanding speech when background noise is present. A major focus of our current work is to establish key aspects of auditory cognition that determine the ability to understand speech in noisy places. Problems with speech perception can be associated with hearing loss when the ear does not work properly, but even subjects who have ‘normal hearing’ on traditional clinical measures have widely differing abilities. Our current work seeks to develop measures of auditory working memory and scene analysis that can explain why some people find it difficult to understand speech in noisy places. We hope to establish the brain mechanisms associated with these processes, and apply the measures to patients who have recently undergone cochlear implantation, which offers potential for predicting patient outcomes.

Motor Decisions

Our ambition is to understand the neural and behavioural underpinnings of healthy and pathological movement, and to develop better interventional approaches for the treatment of movement disorders.

Sven Bestmann

Without movement or action, our thoughts would remain silent. We study the behavioural and neurophysiological basis of healthy and pathological movement. We use a multi-disciplinary approach comprising of behavioural studies of motor control, human neurophysiology (MEG), non-invasive brain stimulation, and computational approaches.

Ongoing studies

High-precision neurophysiology of human movement control

One of our long-standing ambitions is to understand the fine-grained neurophysiological processes of movement control, disorders of movement, and the processes underpinning recovery. To achieve this, we develop novel approaches for high-precision magnetoencephalography, together with Prof Gareth Barnes' group.

This now enables laminar-resolved assessment of cortical responses (Bonaiuto et al., 2018), and the trial-wise measurement of motor cortical transient (burst) signals (Little et al., 2019). We now extend these approaches to wearable (OPM) MEG to study the physiological basis of natural movements and patient groups characterized by abnormal movement control.

Computational Neurostimulation

We have introduced computational neurostimulation as a framework to interrogate the behavioural and physiological effects of non-invasive brain stimulation in health and disease. We use biophysically grounded neural network models to predict the behavioural consequences of non-invasive brain stimulation, and utilise simulations of current flow to optimize existing approaches for the delivery of brain stimulation in patient populations (Evans et al., in press).

The neuroscience of upper limb rehabilitation

Stroke is the most common cause of long-term neurological disability worldwide, with a large proportion of patients left with impairments of limb movement. Recovery of movement is of high importance for stroke survivors but the behavioural principles for therapy are not well understood, nor is the physiological basis of recovery.

Bringing together our progress in high-precision neurophysiology during movement with wearable MEG technology, and cutting-edge brain stimulation approaches, we study the basis of recovery after stroke in patients undergoing intensive upper limb therapy. This work leverages the unique clinical service set-up by Prof Nick Ward.

Language

Our goal is to provide a model of the neural basis of language that predicts and explains speech and language difficulties and their recovery after brain damage (stroke or neurosurgery).

Cathy Price

Currently, the clinical tool we are developing inputs a brain scan and other information about the patient and outputs how well other patients matched for lesion site and initial severity of symptoms recovered their speech and language difficulties over time. In addition to providing patients with much needed prognoses, the tool could be used by stroke researchers to provide an *a priori* stratification scheme for testing the efficacy of new therapies, i.e. is recovery faster than predicted when the patient has therapy? And does the effect of therapy depend on the type of therapy, its dose and when it is delivered? This would allow clinicians to select targeted (and personalised) interventions that facilitate the best possible recovery for an individual patient.

Ongoing studies

PLORAS: Predicting language outcome and recovery after stroke

This study is acquiring structural MRI (and CT) scans from thousands of stroke survivors, along with demographic details (age, gender, education, etc), hours and type of speech and language therapy received, and extensive behavioural data that focuses on their speech production, comprehension, reading and writing abilities from the first week after stroke to many years later. As of 2019, we have data from more than 1300 patients, many of whom have been tested on multiple occasions to monitor their recovery over time. The data are being analysed to identify lesion and non-lesion factors that accurately predict outcome. Confidence in the rules depends on finding consistency in lesion-outcome associations in very large cohorts of patients, and validating the findings in longitudinal studies of new patients.

ELORAS: Explaining language outcome and recovery after stroke

This study is acquiring multi-task fMRI from hundreds of individuals with and without brain damage. The data are being used to build a mechanistic model of language function that specifies (i) which brain regions are typically activated for specific language tasks, (ii) how activity is propagated between different regions, (iii) the degree of variability within and between participants and (iv) whether normal inter-subject variability provides the constraints under which recovery can occur after brain damage. The findings guide the discovery of new predictions, refine known predictions and offer new hypotheses for therapeutic interventions.

PLORAN: Predicting language outcome and recovery after neurosurgery

Our newest study is using, and contributing to, the results of the PLORAS and ELORAS studies by acquiring data from patients pre and post surgery for brain tumours and testing how well we can predict outcome and recovery of language skills after surgery.

Memory and Space

Our goal is to understand how autobiographical memories are represented and recollected by the human brain. Our aim is to identify the mechanisms involved and thereby establish a theoretically enriched account of their breakdown in pathology.

Eleanor Maguire

Our past experiences are captured in autobiographical memories that serve to sustain our sense of self, enable independent living and prolong survival. The goal of the Memory and Space Group is to understand how autobiographical memories are built, how they are re-constructed during recollection and how these memory representations change over time. This endeavour is enabled by a multi-modal approach involving neuropsychological studies of memory-impaired patients, technologies such as MRI, SQUID-MEG, OP-MEG, intracranial EEG, and naturalistic paradigms including immersive, interactive virtual reality (VR). We are particularly interested in how interactions between the ventromedial prefrontal cortex (vmPFC) and hippocampus produce the seamless encoding and recollection of our lived experiences.

Ongoing studies

Our recent MEG work allowed us to resolve the neural dynamics of autobiographical memory retrieval, showing that oscillatory activity in vmPFC precedes, and drives, that of the hippocampus. Moreover, we found these effects only for memories that were more than one month old. These and other findings led us to publish a provocative new theory of autobiographical memory retrieval which helps to reconcile findings of hippocampal involvement in perpetuity with the apparent absence of hippocampal memory traces in the longer-term. In other studies of memory consolidation, we examined sleep in amnesic patients with selective bilateral hippocampal damage, observing a highly specific near-absence of both slow wave sleep and dreaming in the patients. These results highlight that vital sleep functions depend upon hippocampal integrity.

Using our new wearable OP-MEG, we have recently shown that activity in vmPFC and hippocampus can be readily detected. We are currently integrating OP-MEG and immersive, interactive VR to study the neural basis of autobiographical memory formation in real time and in naturalistic contexts. In due course, this approach will be used to assess at what point memory processing becomes aberrant in patients with memory impairments. We will conduct related autobiographical memory studies using our newly-installed 7T MRI scanner which will provide a novel window on how these memories are realised at the laminar and hippocampal subfield levels.

Overall, the Memory and Space Group is working towards exposing autobiographical memories as never before, revealing the millisecond temporal dynamics, and the laminar-specific and hippocampal subfield processing that supports their evolution from the point of inception, through initial sleep cycles and then over longer timescales.

Space and Memory

We study the neural mechanisms of spatial and episodic memory and model-based learning in healthy volunteers.

Neil Burgess

Many of our experiments are driven by, and feed into, our development of a comprehensive neural-level model of the different computations across brain regions that support spatial memory and imagery (Bicanski and Burgess, 2018). These address many of the key topics in cognitive neuroscience of memory:

Scanning at 7T

We have extended our previous finding on hippocampal 'pattern completion', (Horner et al., 2015), by using 7T fMRI to show that this is specifically associated with hippocampal region CA3 (Grande et al., 2019; in collaboration with Magdeburg DZNE). Current work characterises the grid firing patterns using 7T fMRI in more detail (in collaboration with Oxford WIN).

Emotion and memory

We extended the above model to show memory is affected by negative emotional content in post -traumatic stress disorder (PTSD; Bisby and Burgess, 2017). We identified the neural systems learning about spatial contextual fear in an ecologically valid setting (Suarez-Jimenez et al., 2017). Current work extends this by investigating the model's prediction that deliberate and intrusive memories in PTSD reflect opposing patterns of (increased or decreased) activity in hippocampus versus amygdala.

Theta rhythmicity, Epilepsy and Schizophrenia

We used intra-cranial recording in patients with Epilepsy to show that increases in hippocampal theta power precede navigational trajectories and predict their length (Bush et al., 2018). With MEG, we found that medial temporal-medial prefrontal theta coupling is associated with spatial navigation (Kaplan et al., 2017). Current work is finding that this coupling is reduced in Schizophrenia (Adams et al., submitted) and that performing hippocampal-dependent tasks promotes the occurrence of inter-ictal 'spikes' in Epilepsy (Vivekananda et al., 2019).

Hippocampal processing, pathology and model-based learning

Our hippocampal-dependent spatial tasks (developed using fMRI) are being used for detection of impairments in Alzheimer's (Howett et al., 2019) and Huntington's (Harris et al., 2019) diseases. We also used one of these tasks to show that 'model-based' learning strategies correlate with hippocampal-dependent spatial processing in healthy volunteers, and are specifically impaired in temporal lobectomy patients (Vikbladh et al., 2019). We have developed MEG-decoding methods to identify the brain encoding of sequences (Korneysheva et al., 2019) which will be used to detect sequential 'replay' during model based planning.

Computational Neurology

As UCL's Pro-Vice-Provost for Artificial Intelligence, I am committed to delivering AI for public benefit. My own research promotes the use of machine learning in a variety of ways to boost diagnoses, prognosis and treatment in neurology.

Geraint Rees

Machine learning can combine the intuitive flexibility of a clinician with the formality of the statistics that drive evidence-based medicine. Models that pull together thousands of different variables can still be rigorous and mathematically sound. Using machine learning we can now capture the complex relationship between brain anatomy, function and outcome with high precision. For example, machine learning can be used to detect anomalies in brain scans, determine how a drug or intervention is working in the brain and reveal new ways that interventions can be targeted.

Translational machine learning

In collaboration with Parashkev Nachev (UCL), Jorge Cardoso and Sebastien Ourselin (King's College, London), we are leading a translational programme in neuroradiology funded by an Innovation Award from the Wellcome Trust . Our goals are to (i) synthesise high-dimensional, multi -modal clinical and neuroimaging data and (ii) develop new machine learning tools to enable high-fidelity, individual-level prediction, inference, and prescription, for operational and clinical decision-making in stroke, neuroradiology, and acute cognitive dysfunction.

We also work with external partners including Google DeepMind to deliver new and innovative approaches to using AI in healthcare for patient benefit.

Neuro-feedback training

Neuro-feedback aims to teach patients how to change their behaviour by focusing attention on the type of processing that is required for the most effective recovery strategies. With neuro-feedback training, we present patients, in real time, with an indication of how much activity there is in brain regions that need to be engaged for good task performance. Patients learn to control this brain activity by changing the way they perform the task. This induces neuroplasticity that supports recovery (Ekanayake et al., 2018).

Autism

Autism is a disorder that affects how people interact with others. My team has shown that differences in the structure and function of local brain areas are linked to higher-order cognitive symptoms in autism (Watanabe et al., 2019). This could lead to earlier diagnosis if these differences also exist in young children and better diagnosis for autistic people who do not present typical behavioural symptoms.

Neurotherapeutics Group

We investigate how best to rehabilitate language and cognitive deficits caused by stroke and dementia.

Alex Leff Jenny Crinion

The principal aim of our group is to provide a brain -network account of the treatment of language and cognitive disorders in patients with brain damage.

Our research is multidisciplinary and integrates neuroimaging, behavioural and treatment studies of patient populations with neurological disorders including aphasia, hemianopic alexia and dementia.

We use neuroimaging (MEG, fMRI and sMRI (including MPM)) to identify in patients the neural models of brain areas involved in language and cognitive functioning. Through new technological innovations, in developing digital interventions (i.e. apps and web-based therapies) and using non-invasive brain stimulation (trancranial direct current stimulation -tDCS and tACS) we then test how these interventions modulate brain plasticity and accelerate recovery. Not only will this advance neuroscientific understanding of language and cognitive functioning following brain damage, it will also reveal the mechanisms of behavioural and non-invasive brain stimulation intervention effects.

By linking data and theoretical models from these complementary questions we seek to deliver an integrated picture of cognitive rehabilitation. This will allow us to target subgroups of patients who are likely to respond to specific non-invasive brain stimulation and behavioural therapies, a means of **tailoring treatment to individual patients**. It will also provide an empirical basis from which to investigate specific interventions in clinical trials that would greatly improve the quality of patients' treatment.

Our vision is that suitable patients will use these computer-based therapies linked with non-invasive brain stimulation to supplement and boost their rehabilitation. This same technique could be used for other hard-to-treat speech, language and cognitive disorders, opening up many new avenues for treatment and prevention.

Therapy apps

We have already conducted randomised controlled trials to test the clinical effectiveness of a range of different practice-based therapy apps.

Read-Right is for patients with reading problems (hemianopic alexia).

Eye-Search is for patients with visual search problems.

i**ReadMore** is for post-stroke patients with reading problems.

Listen-In is for post-stroke patients with speech comprehension impairments.

i**TalkBetter** for patients with speech production problems, and

Gotcha! for patients with dementia and problems naming the people they know well.

Now trialling

Neural Codes for Behaviour

Our work focuses on how neurons in our brains build models of the relationships between objects and events in the world to allow flexible behaviour.

Tim Behrens

This raises interesting computational problems, such as how best to organise knowledge of the world. It requires rich tasks that are most easily developed in humans, but it requires solutions expressed at the level of neuronal representation that is most easily studied in animal models. Through cross-species investigations, we relate large-scale measurements that can be made in humans to cellular measurements and direct interventions that can be made in non-human species.

Ongoing studies

Theoretical understanding of neuronal representations in hippocampus and frontal cortex

One of the few places where we do have a detailed understanding of how neuronal activity produces flexible behaviour is open-field spatial navigation (leading to John O'Keefe from UCL winning the 2014 Nobel prize). We have shown that these same cellular computations also represent relationships outside of spatial reasoning. We are developing new theoretical frameworks that generalize these representations to arbitrary (non-spatial) relational reasoning. They provide a formal bridge between two domains of neuroscience (spatial cognition and reinforcement learning) and therefore, new opportunities to understand neural computations in both domains.

New animal experiments to test these theories

In collaboration with Neil Burgess (page 29) and other researchers at UCL (Barry, Caccucci) and Oxford (Walton, Akam), we have a major new endeavour to build rodent assays to test these theories. They will provide a substantial neuronal dataset from hippocampus and frontal cortex in both spatial and non-spatial tasks. Critically these tasks are extremely rich by comparison to usual rodent assays, yet under precise mathematical control. Therefore, they permit strong tests of representational theories. Simultaneously, with Steve Kennerley, we are developing new macaque behavioural assays where animals can build knowledge structures that contain hundreds of elements.

New tools to index these representations in humans

We are developing tools using fMRI and MEG to index these representations and computations in humans. For example, with Ray Dolan, we have developed new ways of measuring replay with MEG. We have shown that this replay shares many properties with rodent replay, but also that it can perform functions much more sophisticated than have been reported in rodents. It recombines knowledge to represent new potential experiences. It re-orders events to fit with prior knowledge. These rapid subconscious events are likely a key mechanism for flexible cognition.

Personality Disorders

We investigate the neural correlates and computational mechanisms of social processes that are fundamental for understanding and treating personality disorders.

Read Montague

In the framework of computational psychiatry, we are searching for biomarkers or endophenotypes specific to Borderline Personality Disorder (BPD) and Antisocial Personality Disorder (ASPD). Our goal is to offer a radically new route to nosology and understanding, and ultimately to the design and implementation of more effective therapies.

BPD and ASPD represent a common but often extremely debilitating form of severe psychopathology – for both the individual and society. Both groups have a tendency for impulsivity that might explain difficulties in interpersonal relationships with ASPD showing more exploitative and callous behaviour and a pervasive pattern of disregard for, and violation of, the rights of others. ASPD is also termed psychopathy, sociopathy or dyssocial personality and can have a range of presentations. It may be possible to discriminate between an impulsive, high-affect and disinhibited group on the one hand (that might benefit from psychological therapy) and a callous, unemotional group on the other (more overlapping with a psychopathy classification).

Ongoing studies

fMRI

Using a multi-task fMRI paradigm, with hundreds of participants (healthy, BPD, ASPD), we have measured a range of behavioural and brain responses during two person interactions (person-person or person-computer agent) that approximate to the interpersonal difficulties experienced by BPD and ASPD. The tasks are designed to tap the mechanisms underlying second order belief reasoning, strategic deception, trust, and impulsivity. We are using the data to understand i) how several variables relate to one another within one participant and ii) how the vectors vary across healthy populations and those with emerging or manifest personality disorders.

Electrochemistry

The same social exchange tasks are being used to pioneer the development of a new method for electrochemical recordings of the neuromodulators dopamine, serotonin, and norepinephrine – all key players in depression, psychosis, attention-deficit disorder, Parkinson's disease and more. This new development couples modern computational methods to traditional electrochemical procedures, and has already provided the first ever sub-second recordings of dopamine and serotonin in human subjects during active cognition. The methods promise to transform standard electrodes used in neural recordings into sources of ultra-fast neurochemistry crucial for healthy cognition. The findings emerging from its application also promise new insights into diseases that impact the brain's dopamine, serotonin, and norepinephrine systems (Parkinson's disease, schizophrenia, ADHD, anxiety disorder, addiction, psychosis).

Affiliated Programmes

Amputees

Tamar Makin

Our research seeks to define the boundaries of brain plasticity. We study individuals with congenital and acquired hand loss, investigating what happens to the cortical territories of the hand following arm amputation. We want to know why amputees experience vivid, even painful, sensations of their missing hand decades after amputation. We are also interested in how the brain best supports the acquisition of new skills such as prosthetic limb usage. We combine experimental models performed on healthy participants and experimental manipulations. For example, we use robotic motor augmentation as a model for plasticity in body representation, or local anaesthetics as a model for sensory input loss. Our research builds on an array of neuroimaging techniques: functional MRI and multivariate brain decoding, 7T neuroimaging, MR spectroscopy, DTI and more.

Huntington's Disease

Sarah Tabrizi

Huntington's Disease (HD) is a genetic, neurodegenerative disorder that is characterised by motor, cognitive and neuropsychiatric dysfunction. We recently completed the HD-YAS study for which structural, diffusion, functional (resting state and task) and multi-parametric mapping data were acquired in a group of young adults with the HD-gene. The goal is to investigate the point at which brain changes begin to occur in HD gene-carriers; this is particularly important given the ongoing Phase 3 HD 'gene silencing' antisense oligonucleotide therapy trial and our understanding of the optimal time for therapeutic intervention.

Vision in Parkinson's Disease

Rimona Weil

Parkinson's disease is a common, debilitating neurological condition. As well as causing tremor and slowness of movement, dementia is a common symptom, affecting around half of all patients within 10 years of diagnosis. Our work is funded by a Wellcome Career Development Fellowship and aims to identify patients at highest risk of dementia in Parkinson's disease and to understand the brain mechanisms that cause these cognitive changes. In a large cohort of patients with Parkinson's disease we are running a multimodal longitudinal study that uses advanced neuroimaging techniques alongside detailed neuropsychology, retinal imaging, visual measures, plasma markers and genetics to gain insights into markers of cognitive change in Parkinson's disease. For example, we have shown that thinning of specific layers in the retina is related to higher risk of dementia in Parkinson's disease and that levels of brain tissue iron are higher in the hippocampi linked with poorer cognitive function in Parkinson's disease. Ultimately, our aim is to refine these techniques to develop robust markers of cognitive involvement in Parkinson's disease that can be used in clinical trials to slow down the process of dementia in Parkinson's disease.

Affiliated Programmes

Deafness, Cognition and Language

Mairéad MacSweeney

We use deafness as a model system to examine how altered sensory and language experience influences the development of language, cognition and the brain. Research with those born profoundly deaf offers unique insights into the limits of neural plasticity and the cognitive and neurobiological conditions under which language develops. We use both behavioural and neuroimaging approaches tofurther understand how we process visual forms of communication: sign language, reading, visual speech (lip-reading) and gesture. For example, we have shown that the brain engages very similar networks to process signed and spoken language. This suggests that the brain treats language as language, regardless of whether it comes in via the eyes or the ears. We are also interested in plasticity: what is the function of 'auditory' cortices in superior temporal cortices in those born profoundly deaf? We have shown extensive activation in response to visual input in these regions in deaf participants. Current studies are examining the functional relevance of this activation. In addition to informing our basic understanding of brain development and the neurobiology of language, aspects of our research will also ultimately inform educational intervention strategies for those born profoundly deaf.

Mental Health

Jon Roiser

Our work addresses the psychological and brain mechanisms driving symptoms of mental illness, especially depression. Work at the Centre has been funded by a Wellcome Investigator Award and an MRC New Investigator Research Grant. We focus on the brain's reward system, which controls motivated behaviour and is likely to make an important contribution to symptoms such as anhedonia. Over the past 5 years my group has led landmark studies examining the role of a small, little-studied brain structure called the habenula in controlling both aversive and appetitive processing. Due to the habenula's small size, this required important MRI development, performed by the Centre Physics team, to create high-resolution fMRI sequences. Consistent with prior work in experimental animals, we showed that the habenula tracks a key computational quantity, negative associative value (here the negative outcomes were painful electric shocks (Lawson et al., 2014)). In a subsequent study using a similar design we found that, surprisingly, individuals with depression exhibit the opposite pattern of habenula responses (Lawson et al., 2017). More recent work has expanded on this finding by investigating the role of the habenula in controlling action in the face of aversive stimuli, in particular active avoidance. We showed that the habenula activates both during the anticipation of aversive stimuli and when action is required to avoid them, which may help to understand our earlier findings in depression. Finally, an ongoing study is examining the role of dopamine in effort-based decision-making in depression. We are using the drug L-DOPA (usually used to treat Parkinson's Disease) to boost dopamine synthesis in an experimental medicine study in depressed individuals, who perform an effort-based decision-making task while being scanned.

Affiliated Programmes

Decision-making and neuroeconomics

Benedetto de Martino

Our research focuses on understanding the neural basis of decision-making. Every time we are faced with a decision - even a simple one like what to have for lunch - our brains perform a complex set of computations, gathering information from the sensorium and recalling past memories of consuming these foods. It must then integrate all this information with our current homeostatic state ('how hungry am I?') to quickly compute the value of each of these options. In our group, we aim to elucidate precisely how the brain constructs value and uses it to guide decisions. Our approach is highly interdisciplinary, integrating economics and computational models with advanced neuroimaging techniques with the aim of developing a more realistic account of economic behaviour. Our aim is to dispel the myth of economic rationality by showing how the constraints and computational limitations of the human brain shape our choice behaviour. At the same time, we are using these insights to understand why decision-making abilities are impoverished in psychiatric disorders like OCD.

Memory guided behaviour

Emrah Duzel

Our research focuses on the mechanisms through which memories can be formed and retrieved in the service of flexible, adaptive and goal-directed behaviour. We investigate how the medial temporal lobe memory system interacts with prefrontal mechanisms of cognitive control. We also investigate how basal forebrain, striatal and dopaminergic midbrain regions modulate this prefrontal-mediotemporal interaction by prediction errors, anticipation, motivation and reward. This line of research integrates functional imaging, electrophysiology and magnetoencephalography with genetic and structural anatomical information as well as pharmacology. It is relevant for a better understanding of cognitive dysfunction in healthy ageing as well as a number of neurological and neuropsychiatric conditions that we are studying such as amnesia and neurodegenerative diseases.

Beauty and the brain

Semir Zeki

We continue our experiments on the visual brain and its organization. Perhaps the most significant of our findings relates to the demonstration, using magneto-encephalography and functional magnetic resonance imaging, that all visual areas, including ones specialized for objects and faces, receive very fast latency inputs, at about 35-45 ms after stimulus onset. This may necessitate a revision of the interpretation commonly given to how visual signals, especially those related to form and to faces, are processed. In addition, we are pursuing experiments on how visual inputs trigger an affective, aesthetic and emotional experience, concentrating in particular on the experience of beauty, desire and love.

The FIL Building at Work

4th floor
Seminar room
Fellows rooms

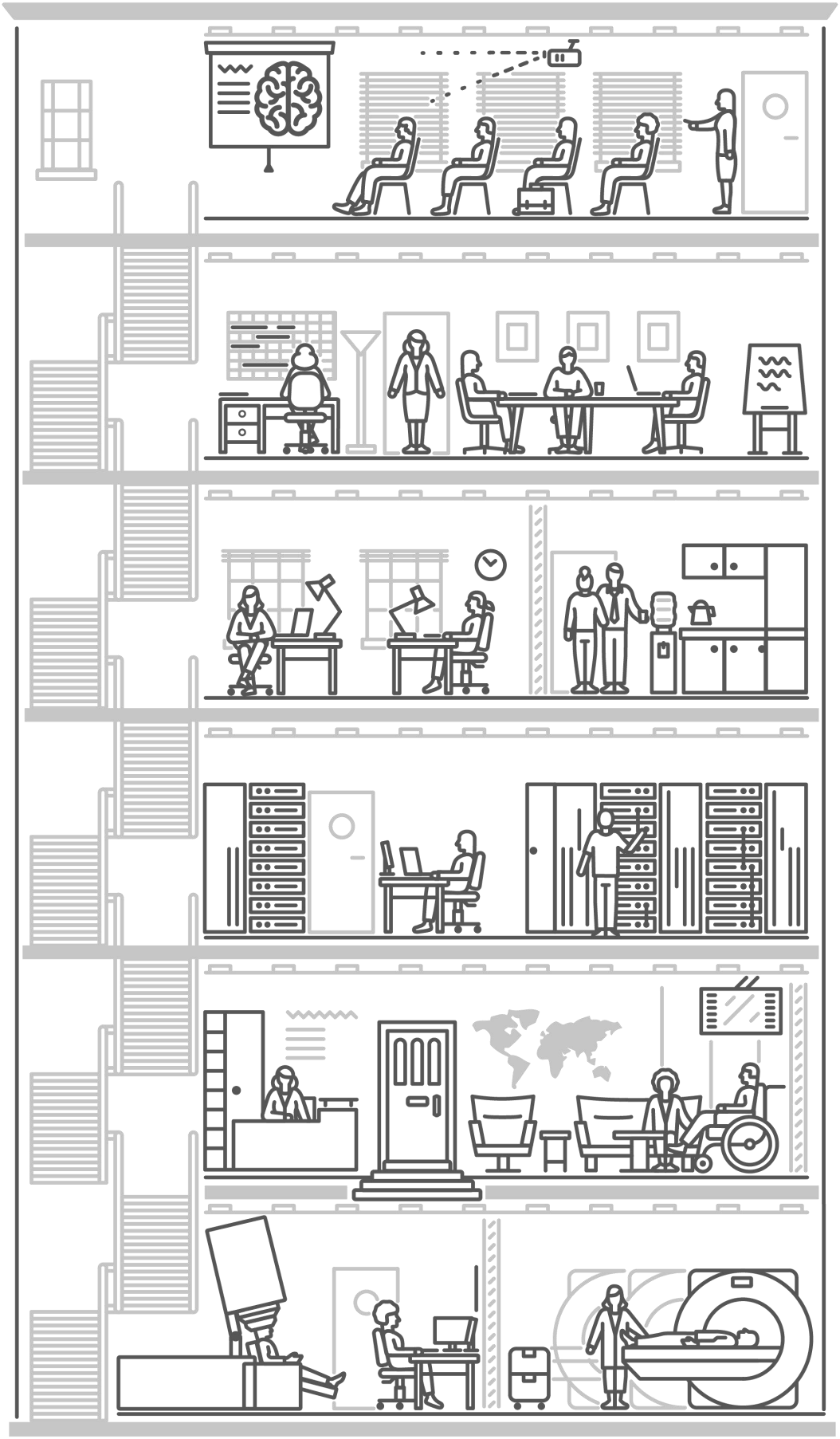
3rd floor
Management

2nd floor
Open plan
fellows rooms

1st floor
Board room
Computing
Fellows rooms

Ground - floor
Reception
Administration
& SPM team

Basement
Scanners
& testing rooms



Education

Our goal is to nurture and promote the careers of the next generation of neuroimaging researchers and clinicians, providing them with interdisciplinary skills in a culture of responsible, open and inclusive science.

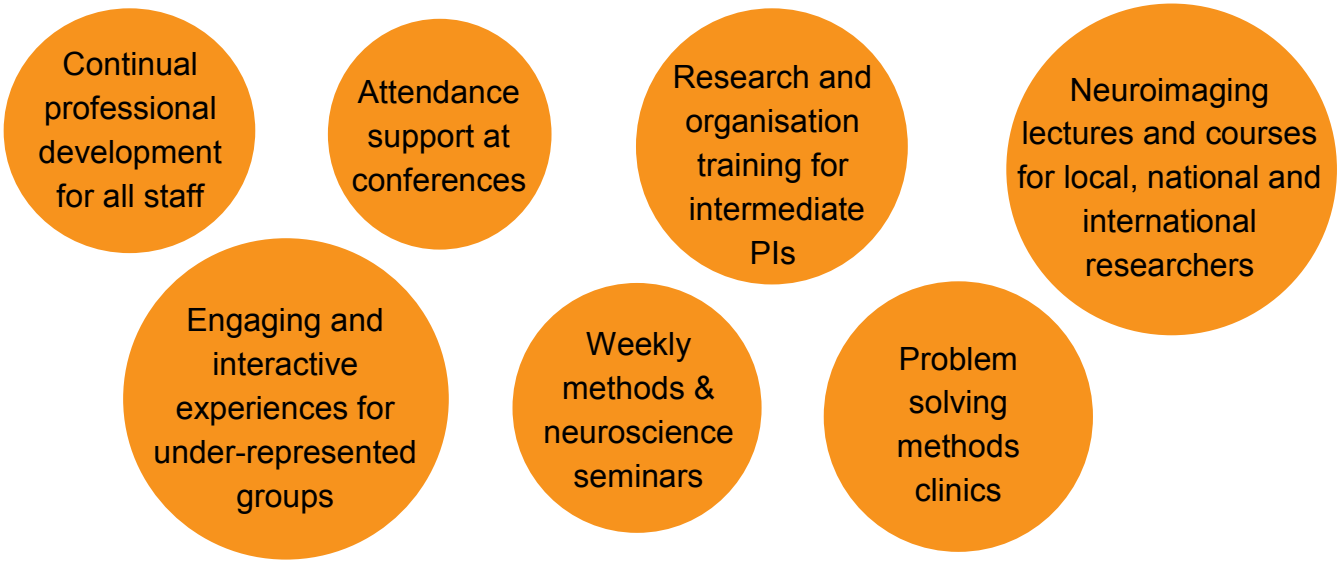
Our trainees range from students (PhD and MSc) to professors and clinicians.

Student training

Our student-centred training promotes future generations of neuroscientists, highly skilled in technical development and neuroscientific methods, and confident in conducting collaborative, cross-disciplinary projects. To support this, we provide:

Wider training

To support our in-house staff and widespread collaborators, we provide:



Public Engagement

Our public engagement programme aims to empower people with neurological and psychiatric conditions to contribute to, and influence, neuroscience research.

We embed our researchers in a culture where they can develop the skills and experience to readily engage public groups in the evolution of neuroscience. To support this, we are creating platforms to build relationships with and engage targeted audiences that are traditionally under-represented in neuroscience.

Our Core Programmes

Working with students from Young Epilepsy, we are co-producing three elements of the new OPM scanning process (see wearable MEG, page 11); (1) the design and implementation of new child-friendly wearable scanners; (2) the process and experience around the scanning procedure; and (3) an engaging room interior.

UCL WORLD STROKE DAY FORUM

Our annual World Stroke Day Forum brings together researchers, clinicians, charities, stroke survivors and their families. We hope to empower stroke survivors to engage with, and contribute to, our work, with the aim to improve prognosis and rehabilitation after stroke.

Our Dear World Project invites people to talk about their perceptions of mental health and explore how this interacts with approaches taken by researchers and clinicians. Through our Dear World Exhibition in 2020 we will explore the use of labels in mental health. Are they helpful? For whom?

Further Initiatives

Public Engagement Awards

The annual Public Engagement Awards recognise and reward the outstanding public engagement work of the staff in our Centre.

In2Science UK

Each year we host six students from disadvantaged backgrounds for a two week internship, providing experience of, and motivation for, a career in research.

Core Teams

Administration

The work of the administration team covers all operational planning and management of the centre including finance, services, reception, and strategic development.

Mark Alderson, Centre Manager | Kamlyn Ramkissoon, Office Manager | Susan Fischer, Research Coordinator at the MPC | Silpa Shah, PA to Centre Director | Toyah Perkins, Executive PA to MPC Director | Maddy Scott, PA/Office Administrator | Shivkumar Jhala, Receptionist | Monica Bumbury, Receptionist

Imaging support

The Imaging Support team perform neuroimaging scans covering MRI, MEG and EEG scanning modalities, and support all aspects of scanning. They ensure day-to-day oversight of health and safety aspects and pastoral care of research participants.

Megan Creasey, Head of Imaging Support | Clive Negus, Head of Imaging Support | Daniel Bates, MEG Technician | Alphonso Reid, Cognitive Interface Engineer | Eric Featherstone, Cognitive Interface Engineer | Curt Strangward, Senior Radiographer

Facilities

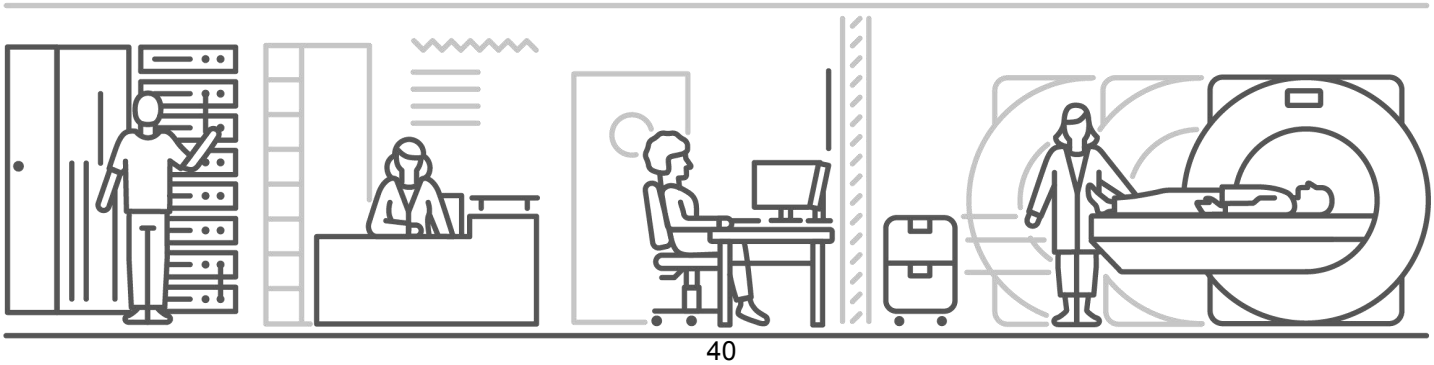
This team manages the laboratory facilities infrastructure (Page 37); they work closely with both UCL Estates and UCL safety services to manage building infrastructure and safety.

David Bradbury, Laboratory Manager | Peter Aston, Head of Facilities

IT

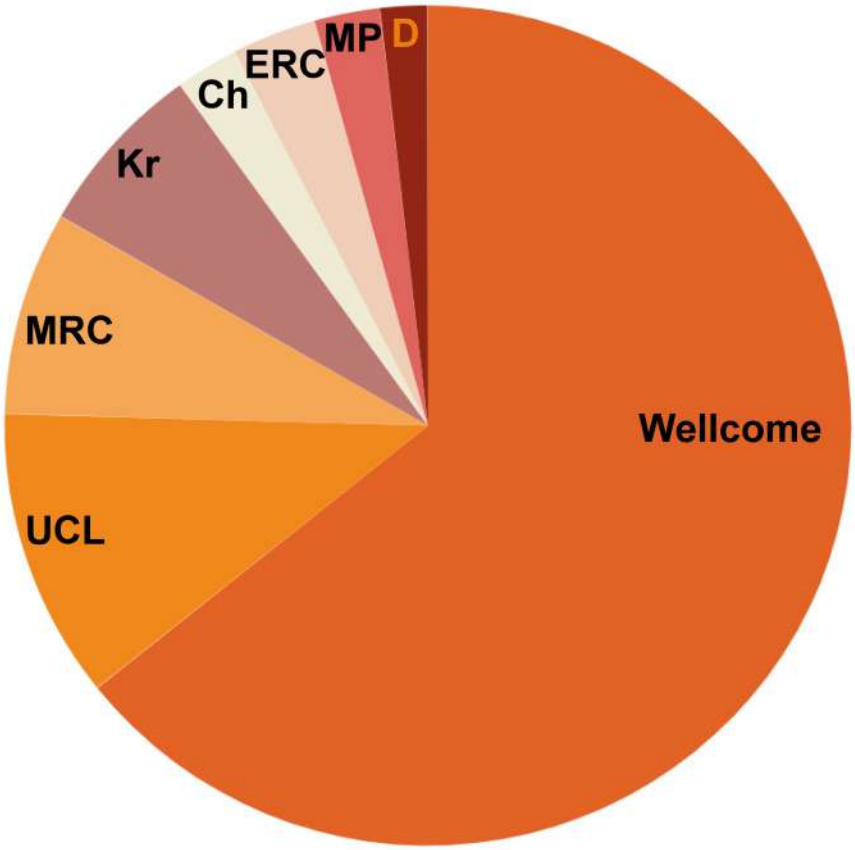
The team delivers comprehensive IT infrastructure support and data handling expertise, which underpins generating and managing the large volume imaging data outputs and the enhanced computing requirements associated with this.

Ric Davis, IT Manager | Chris Freemantle, Data and AV Manager | Liam Reilly, Senior IT Officer | Mohammed Mazid, Senior IT Officer



Staff Funding

A breakdown of the funding source for the 81 staff (Principal Investigators, Research Fellows, and Core Staff) at the FIL and MPC (which together comprise UCL's Department of Imaging Neuroscience).



Key

Wellcome	Wellcome Centre Award (2016-2021) and Wellcome Research Grants
UCL	HEFCE Funding from UCL
MRC	Medical Research Council
Kr	Kinross Endowment to Ray Dolan
Ch	Other Charity Grants (e.g. from the Stroke Association)
ERC	European Research Council
MP	Max Planck Society
D	Discretionary Accounts (e.g. income from scanner use)

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