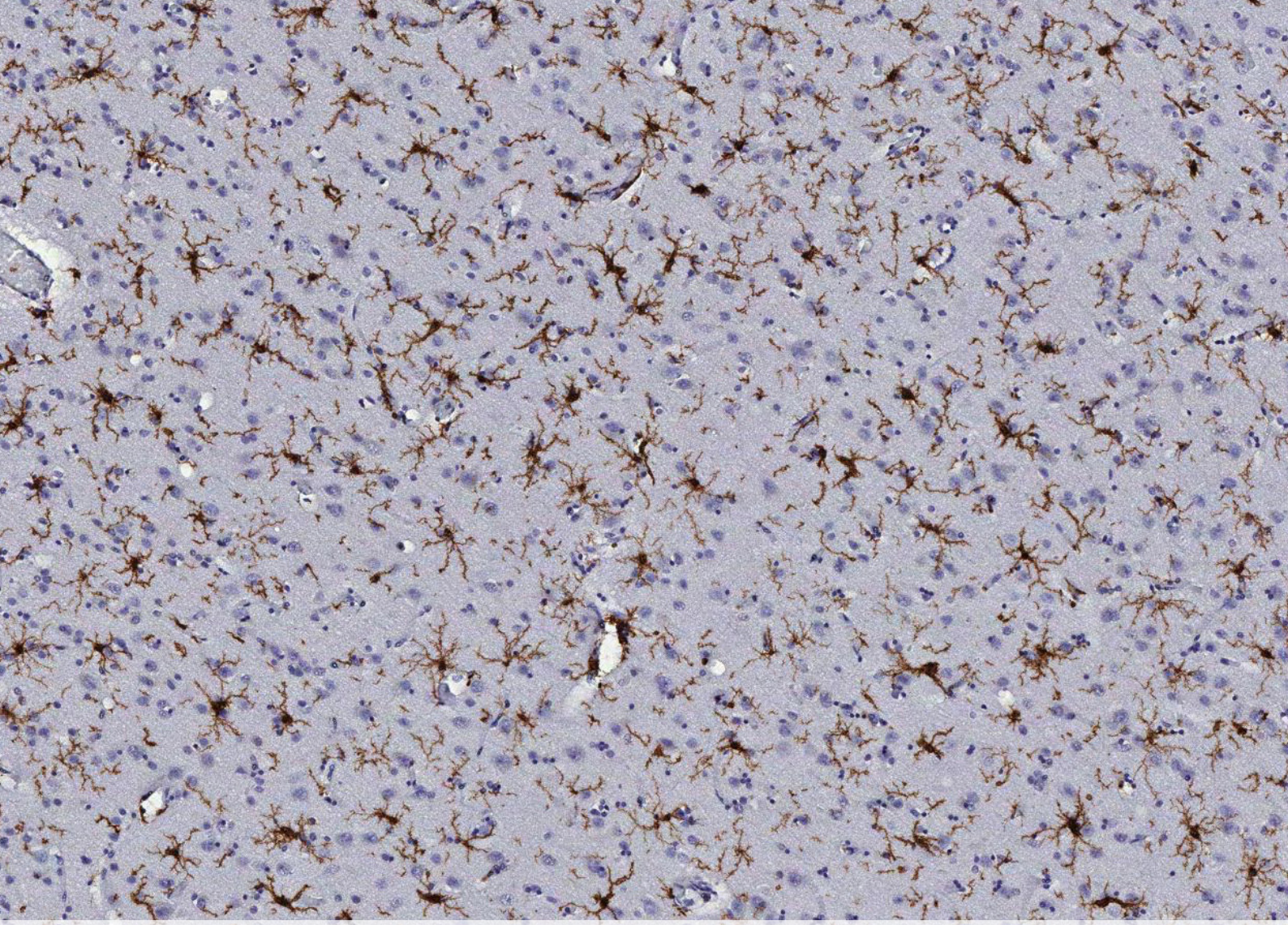
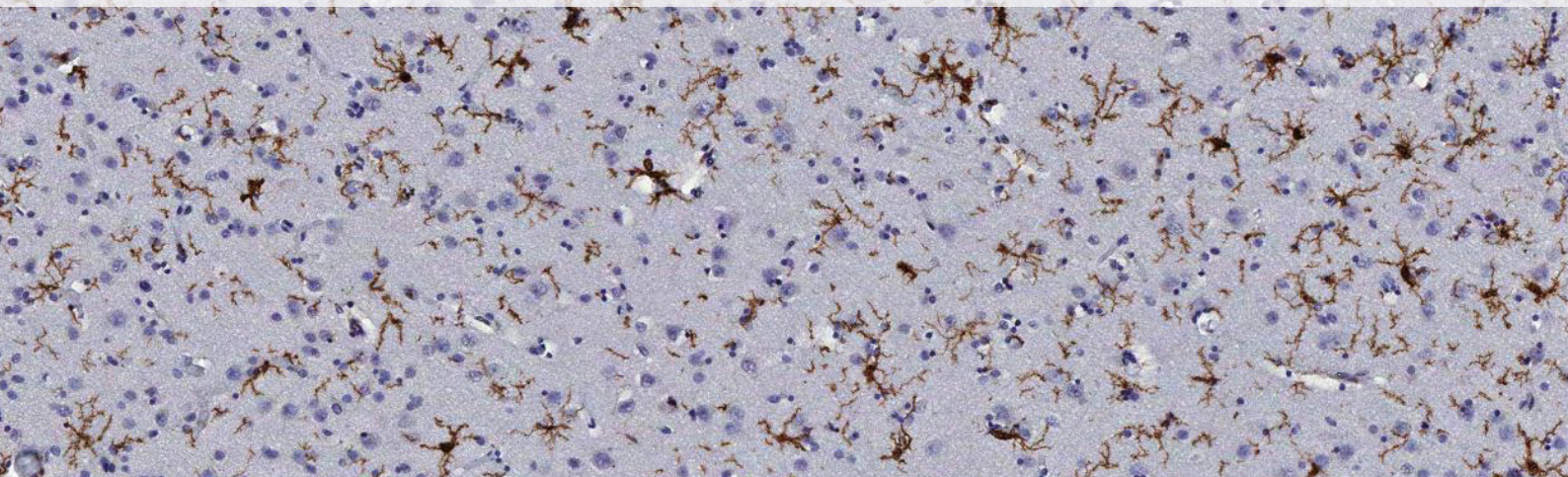


Dementias Platform UK

Accelerating translation for dementia research



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Cover Image: Iba1 immunohistochemistry in the cortex of a PSP brain.

Welcome

Our high quality research environment: making translation easier, better & faster

One of the highlights of being a scientist is belonging to a truly international community that transcends race and creed whilst making sense of the world around us. Key to the effectiveness of this community is creating and sustaining high quality research environments. For dementia, stakeholders from industry, academia, and charities are coming together to share risks and benefits in finding life-changing treatments. Dementias Platform UK (DPUK) is at the heart of this endeavour.

The mission is to address barriers to translating research into treatments. Through our big data theme, we have built a world leading Data Portal; enabling end-to-end data management for cohorts, clinical studies and trials. Our research-ready data enable rapid discovery and access to 60 datasets totalling 3.5 million people (p.14-15). Our Trials Delivery Framework enables precise recruitment to, and delivery of, mechanistically targeted multi-site studies for pre-clinical and early clinical disease (p.16-17). Our Experimental Medicine Incubator is where academic and industry partners co-design studies to address specific mechanistic questions that inform drug development (p.18-19).

Our high-trust pre-competitive ethos has been critical to developing the collaborative relationships that underly these programmes. It has allowed flexible knowledge and technology sharing, and the incremental development of innovative solutions that don't always work first time! This also means DPUK is conducting what is essentially an ongoing natural experiment of strategic change to the research environment.

DPUK is continually looking for new ways to make translation easier, better, and faster. We look forward to working with you in this. We also anticipate aligning closely with the Government's recently announced Dame Barbara Windsor Dementia Mission; making our learnings and technologies available to ensure the Mission 'hits the ground running'.

This report reflects the enthusiasm and hard work of colleagues in the UK and beyond. I sit, sometimes uncomfortably, on the shoulders of creative scientists, innovative technologists, and a dedicated support team. DPUK is their achievement.

Professor John Gallacher, PhD AFBPsS CPsychol FFPH
Director of DPUK

DPUK at a glance

Dementias Platform UK is a collaboration between academic research and the pharmaceutical industry to find new ways of detecting, treating and preventing dementia.

Our data-driven platform gives scientists fast access to findings, technology and volunteers – powering research to stop dementia in its tracks.

- The DPUK Data Portal gives researchers rapid, secure access to millions of health research records.
- Our Trials Delivery Framework matches public volunteers to the right dementia studies.
- Our Experimental Medicine Incubator accelerates and de-risks the development of new treatments.

Dementia Platform UK is continuing to grow with additional data sets, more imaging and greater numbers of researchers using our resources.

Trials Delivery Framework

Participants	TDF Sites	Ongoing Studies	APOE Data
67,003	19	22	1,021

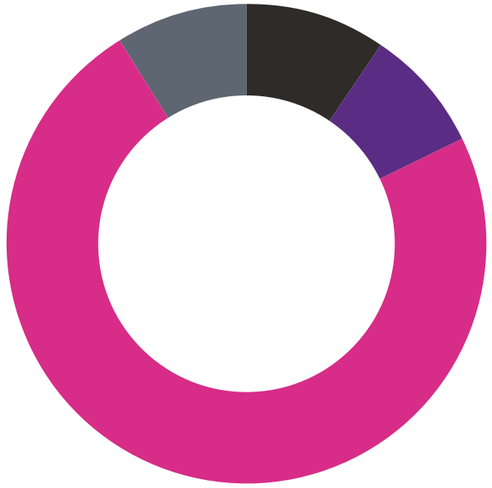
Data Portal

Data Set Requests		Countries	Users
1,197	60 Cohorts (n=3.5m)	40	919

Experimental Medicine

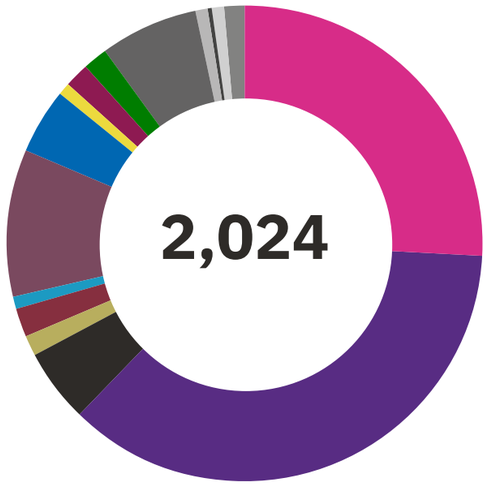
Participants	Locations	Dementia biomarkers studied	Samples collected
961	39	407	16,442

1,039 Milestones



DPUK WORKSTREAMS

- Scientific Programmes – 21
- Experimental Medicine Projects – 18
- Career Development – 160
- Education & Training networks – 19



OUTPUTS

- Publications
- Engagement
- Protocols
- Facilities
- Algorithms
- Awards
- Collaborations
- Influence
- Research Tools
- Other
- Next Destinations
- Funding
- Models
- Medical Products
- Software
- Creative

Source: Researchfish

Translation

The importance of partnership working in translation

Professor Patrick Chinnery, Clinical Director, Medical Research Council believes that the time is right for significant progress in translation from research to new therapies and treatments.

2023 began with the publication of the Lecanemab trial (NEJM 2023; 388:9-21). Lecanemab is a humanised IgG1 monoclonal antibody that binds to Aβ soluble protofibrils. In a randomised controlled trial of 1795 patients with mild cognitive impairment or mild Alzheimer's disease, Lecanemab reduced biomarkers of amyloid and slowed down the cognitive decline measured after 18 months of treatment. Whilst the clinical impact of Lecanemab was modest, the strategic significance of the trial is far reaching. The nihilistic position defining the last two decades is no longer tenable: an effective treatment for neurodegenerative disorders is not unachievable goal. With the prevalence of these continuing to rise globally, the results of the Lecanemab trial put even greater pressure on the research community to deliver advances with greater clinical impact.

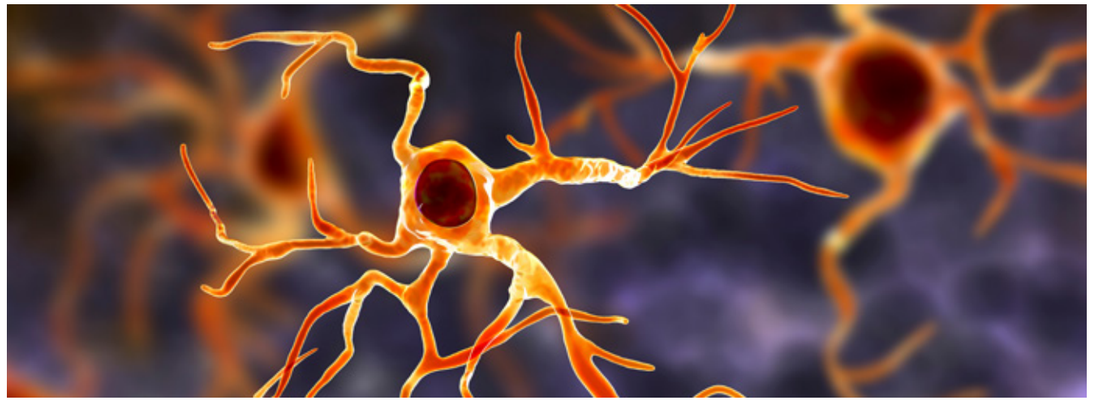
Over a decade of investment from the Medical Research Council (MRC), UK Research and Innovation (UKRI) and the National Institute for Health Research (NIHR) places the UK in a strong position to develop new approaches to minimise the impact of neurodegenerative diseases. Effective partnership is the key to success across the whole sector.

One component will be leveraging mechanistic discoveries emerging from UK universities and industry, including the UK Dementia Research Institute, to drive early clinical translation through experimental medicine and early phase trials. Dementias Platform UK was established to do this, and is already playing a key role in this endeavour, networking our Universities and the NHS in partnership with National Institute for Health Research (NIHR) and the Translational Research Collaboration in Dementia (TRC-D).

Established in 2014, and jointly funded by the MRC/UKRI, NIHR and industry, DPUK brings together the major clinically facing neurodegeneration initiatives across the country. It harnesses existing data resources and builds clinical cohorts for experimental medicine studies that will advance our understanding of the disease mechanisms in vivo, paving the way for new therapeutics. New tools have been assembled, including the national 7-Tesla imaging and positron emission tomography (PET) networks across the UK. We now need to work in closer collaboration across all four UK nations to leverage our world-leading expertise and research infrastructure. This must be done in partnership with patients, the public, and support groups to ensure we remain focussed on what they consider to be important.

Now is the time for translational progress in neurodegeneration that will have impact both on individuals and society as a whole.

"Effective partnership is the key to success across the whole industry."



Collaboration

Taking the UK DRI vision into human studies

Professor Bart De Strooper and Giovanna Lalli of the UK Dementia Research Institute at University College, London reflect on their collaborations with DPUK on thematic areas of interest in synaptic health, vascular health and neuroimmunology.

Dementia is not a disease. It is a symptom appearing only in the very late stages of different devastating neurodegenerative disorders. Compared to other fields like cancer, dementia remains poorly understood, due to historic under-investment in research and the sheer complexity of the human brain. This is why the UK Dementia Research Institute (UK DRI) was set up in September 2017. We are committed to filling the 'knowledge gap', diving deep into early disease mechanisms – a fundamental step to develop new ways to diagnose, monitor, treat and hopefully one day prevent dementia.

This is an exciting time for dementia research, thanks to recent extraordinary technological advances that are allowing us to better study the brain, from single molecule/single cell through to system level. In parallel, new data-driven approaches are allowing us to link research on molecules, cells and tissues to clinical phenotypes and outcomes. These interdisciplinary approaches have already started to identify novel hypotheses and to provide new biological/clinical insights into neurodegeneration. Central to this is data integration: linking mechanistic research, including human-derived samples, with clinical observations and translation is crucial to deepening our understanding.

It is in this spirit that we have been developing a series of joint DPUK-UK DRI events across shared thematic areas of interest: synaptic health and vascular health and Neuroimmunology. These events include interactive workshops and scientific symposia exploring innovative disease models, molecular mechanisms highlighting novel potential targets, and biomarkers. As an example, the joint DPUK-UK DRI workshop on 'Experimental models of vascular disease and cognitive impairment' (Manchester, March 2022) brought together more than 50 pre-clinical and clinical researchers from across the UK, promoting the formation of collaborative research groups and knowledge exchange.

UK DRI and DPUK share a commitment to developing the next generation of dementia researchers in an interdisciplinary environment. Together, we have empowered our early career researchers (ECRs) through a series of joint DPUK-UK DRI virtual and in-person ECR events, including research talks, plenary lectures, methodology sessions and lively scientific debates. We will continue to nurture a scientific community that thrives on mutual learning and builds bridges between basic and clinical research.

Collaborative projects are already underway. DPUK and UK DRI members are working together on aspects that are crucial to tackling dementia. This includes leveraging human genetics and innovative biomarkers for early diagnosis to developing novel diagnostic PET ligands, unravelling causes of disease through human stem cell models based on polygenic extremes (through the IPMAR platform), and testing novel therapeutic approaches. Together, we need to build on this momentum, using discovery science as the foundation of an intensely collaborative ecosystem. By connecting across the disciplines, we will continue to foster a dynamic research environment, attract investment and achieve real progress in defeating dementia.

"We are committed to filling the 'knowledge gap', diving deep into early disease mechanisms."

Study Profiles

Transformative blood tests for Alzheimer's disease

The search is on for a simple blood test to screen for Alzheimer's

By Professor Masud Husain, University of Oxford

Every now and then, you think you get a glimpse of the future. Often it is a fleeting vision, promising much but ultimately fading into obscurity. Very occasionally, though, it is a longer lasting apparition, one that reveals itself sufficiently to consider its true significance. The last few years have witnessed such a revelation. For the first time, we can seriously consider the possibility of a blood test to screen for Alzheimer's disease, and the ramifications are profound.

In recent years, phenotyping of Alzheimer's has seen a major change with the advent of cerebrospinal fluid amyloid and tau biomarkers, amyloid-PET (positron emission tomography) and tau-PET brain imaging. Together with structural MRI and cerebrospinal fluid measures of neurodegeneration – atrophy and neurofilament light chain levels (NFL) respectively – this has led to the ATN (Amyloid, Tau and Neurodegeneration) classification system. Characterization of patients into subgroups according to whether they are amyloid positive or negative (A+ or A-), tau positive or negative (T+ or T-) and have evidence of neurodegeneration or not (N+ or N-), has helped to stratify individuals in observational studies and for recruitment into clinical trials.

This has been a steep change in Alzheimer's research. But what has been equally evident is that such high-level phenotyping is only possible in a few centers around the world. Both the costs and the invasive nature of some tests (which require a lumbar puncture) have prevented their widespread use. Over the last few years research has led to a sharp reconsideration of what might be possible, even in non-research clinical settings. The key development has been the establishment of plasma biomarkers as reliable measures of Alzheimer's disease. These include phosphorylated plasma tau (P-tau), amyloid beta, NFL and glial fibrillary acidic protein (GFAP) in blood.

Plasma P-tau and GFAP have now been shown to be present in significantly higher levels in people who have preclinical Alzheimer's – individuals who are cognitively unimpaired but nevertheless A+. Recent evidence also suggests that the combination of plasma P-tau181 and plasma NFL predicts well, on an individual basis, which patients with mild cognitive impairment (MCI) are likely to progress to dementia.

These findings make it increasingly likely that a combination of plasma biomarkers – p-tau, amyloid beta species, NFL and GFAP – will provide a means to detect Alzheimer's at early stages of the disease. This increases the likelihood of diagnostic blood tests being available in memory clinics on a routine basis, and perhaps even population screening for the condition becoming a reality within the next few years. Of course, a positive screen result would need to be taken into context, followed-up with 'high resolution' cognitive testing. These are likely to be computerized tests that are sensitive, have dynamic range and can track small changes in performance over time.

DPUK is now supporting the FAST (Feasibility and acceptability study of scalable biomarkers of brain health) study led by Ivan Koychev to do just this. Healthy volunteers and patients are being tested using a combination of plasma biomarkers and online cognitive tests developed by the Oxford Cognitive Neurology group. This makes it likely that it will be possible in the future to recruit people with Alzheimer's disease before the onset of dementia into clinical trials, and monitor the effects of new treatments far better than we can now. A serious vision is taking shape.

FAST Brain Health

Great Minds volunteers are helping to shape the future of early dementia by Dr. Ivan Koychev.

In December 2022 the Great Minds team began the Feasibility and Acceptability of Scalable Tests of Brain Health (FAST Brain Health) study. This research is seeking to assess the value to both participants and study sites of regular blood- and digital technology-based monitoring of dementia risk.

In addition, the FAST Brain Health study will allow us to further characterise the Great Minds group of healthy ageing individuals and our Clinical Studies Register of people post-diagnosis. This includes blood-derived plasma biomarkers of dementia and cognition.

The study team invites participants to a session close to their home, where blood samples and cognitive ability digital tests are undertaken. These activities are in collaboration with Professor Masud Hussain's Cognitive Neurology group at the University of Oxford. Following this, people's cognition is remotely assessed after 6 months, before another face-to-face meeting at 12 months for further blood tests and cognition assessments.

So far, the Great Minds team has focused on people from the south of England, but we hope to expand to cover more people and locations will be added over time.

Current FAST locations

1. Newport
2. Swindon
3. Brighton & Sussex
4. Cornwall
5. Devon
6. Somerset
7. KCL
8. Portsmouth

Finding early biomarkers for Alzheimer's from Deep and Frequent Phenotyping study

A single observational study with extensive potential benefits by Dr. Vanessa Raymont.

The DPUK's Deep and Frequent Phenotyping (DFP) study is seeking to identify a set of biomarkers that can be used for early Alzheimer's disease identification. The value of biomarkers in this area of research wide-ranging, crucially in tracking, to allow more efficient early phase drug development.

The study also includes identifying less invasive biomarkers, finding more effective markers of disease progression, and finding remote markers that might substitute for face-to-face assessments.

DFP was conceived to provide solutions to all these challenges in a single observational study in prodromal Alzheimer's disease, using the broadest set of both established and novel markers to date (www.dementiasplatform.uk/research-hub/experimental-medicine-incubator/deep-and-frequent-phenotyping).

Specifically, the study assesses PET imaging and CSF biochemistry for amyloid and tau, functional and structural MRI, electrophysiology for synaptic function including EEG and MEG, measures of gait and use of remote monitoring for ecologically valid assessment of a range of phenotypes, measures of retinal pathology, and a collection of bio-samples unparalleled in potential utility for molecular biomarkers and to establish stem cells for in vitro studies. It is also establishing the single largest cohort of individuals with prodromal AD and sample bank for further research. It has been recruiting since October 2019, and despite delays through the COVID pandemic, is now on track to recruit 250 participants aged over 60 over the next two years across 6 UK sites. We have been able to achieve this recruitment by access to existing cohorts within DPUK and UKBiobank. Naturally, all of the research has only been possible thanks to the amazing dedication of our participants.

Data at scale

UK Biobank provides unique opportunities to identify effective ways of preventing and treating dementia

Most studies of dementia have focused on people who already have the disease. Although this provides information about the later stages of dementia, it gives few clues about its causes and early course. Yet, as Prof. Rory Collins explains, it is understanding the biology of the early period, particularly when people are still feeling well, that offers the greatest opportunities for prevention and treatment.

Given the different forms of dementia and the heterogeneity of risk, such understanding requires large numbers of people to have been assessed many years before the disease develops. UK Biobank is almost uniquely positioned to do this due to its prospective longitudinal design and unprecedented depth of genetic, phenotypic, exposure and clinical data from so many people. Although UK Biobank participants were relatively healthy when they joined the project in 2006-10, about 40,000 of them will have developed dementia by 2027, and this number will rise rapidly as the cohort ages.

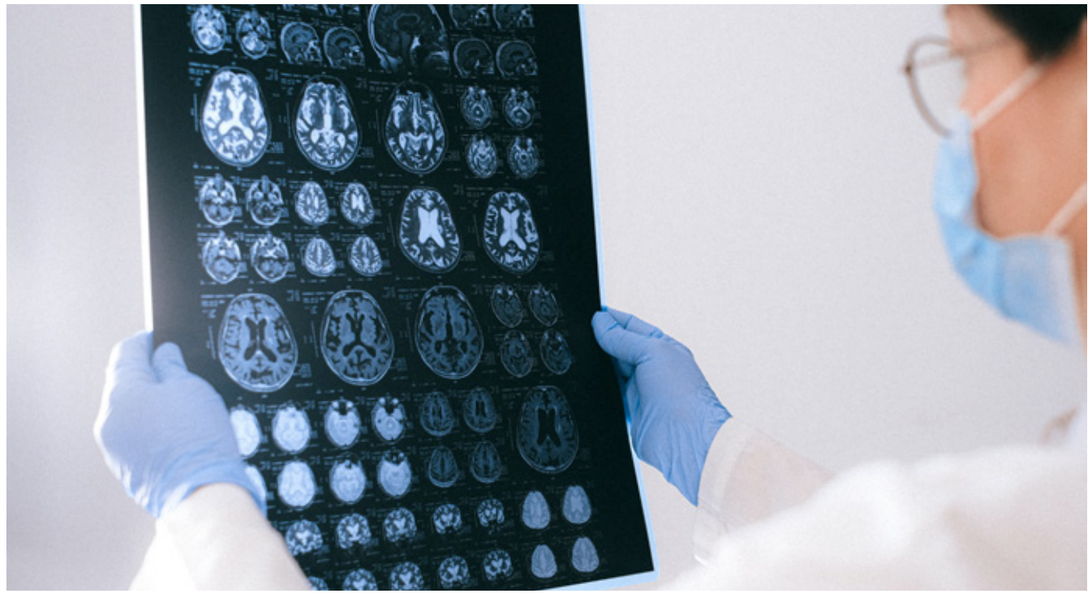
The availability of lifestyle, environmental and healthcare data is enabling the relationships between dementia and modifiable risk factors to be defined with greater confidence than ever before. Considerable work has already been undertaken by scientists in many countries using UK Biobank to understand causal relationships between exposures (e.g., for air pollution, alcohol, smoking and diet) or the impacts of co-morbidities (such as cardiac disease, hypertension, and diabetes) on dementia. The availability of whole exome and genome sequencing has dramatically accelerated understanding of the genetic basis of different major forms of dementia, as well as the effects of targeting them with new therapeutics.

UK Biobank is continuing to be further enhanced for dementia research. An ambitious programme of advanced clinical imaging (MRI, DXA and carotid ultrasound) of the participants' brains, as well as their hearts, bodies and large vessels, has been progressing since 2015. Over 60,000 participants have been imaged to date, with a target of 90-100,000 by 2025. This uniquely large imaging dataset is enabling novel discoveries related to understanding disease risk and its genetic basis (e.g. associations of microscopic iron deposition in the brain with genes that cause premature neurodegeneration). In collaboration with DPUK, repeat imaging of 60,000 of these participants is now underway, yielding information about trajectories of changes in the size and shape of the brain that are even more sensitive indicators than the baseline images of early disease and its antecedents.

Biological samples have been collected not only at enrollment, but also at the subsequent imaging assessments. Likewise, cognitive function profiling has been conducted serially since enrolment. Targeted assays of the plasma proteome in the cohort has already begun, and this is likely to be extended to untargeted -omics assays which promise even greater insights into disease mechanisms. Epigenetic characterization of participants' blood cells may also be of value in defining the genes contributing to dementia that are turned on or off as a result of environmental exposures and aging.

UK Biobank's 'open science' model, which attracts researchers from academia and industry across the globe, has been transformative. Opportunities for expansion of the phenotyping of participants with digital tools (e.g. AI driven voice recognition, autonomic nervous system functions and movement monitoring), low-cost wearable electrophysiological ('brain wave') monitors, and characterization of the microbiome are examples of cutting edge approaches that could fundamentally advance the understanding of dementia when undertaken at the scale of UK Biobank.

"This uniquely large imaging dataset is enabling novel discoveries"



Helping to break through barriers in developing dementia therapeutics. Why DPUK's consortium model is helping the pharmaceutical industry

Dr. Iain Chessell, Head of Neuroscience at AstraZeneca

These are exciting times for dementia translation research. Licensing of the first disease modifying therapies for dementia has focussed industry on how to de-risk and accelerate dementia drug development. From an industry perspective, particular needs include informing 'go - no go' decisions on compounds in development, and how to test the 'go' compounds rigorously and rapidly.

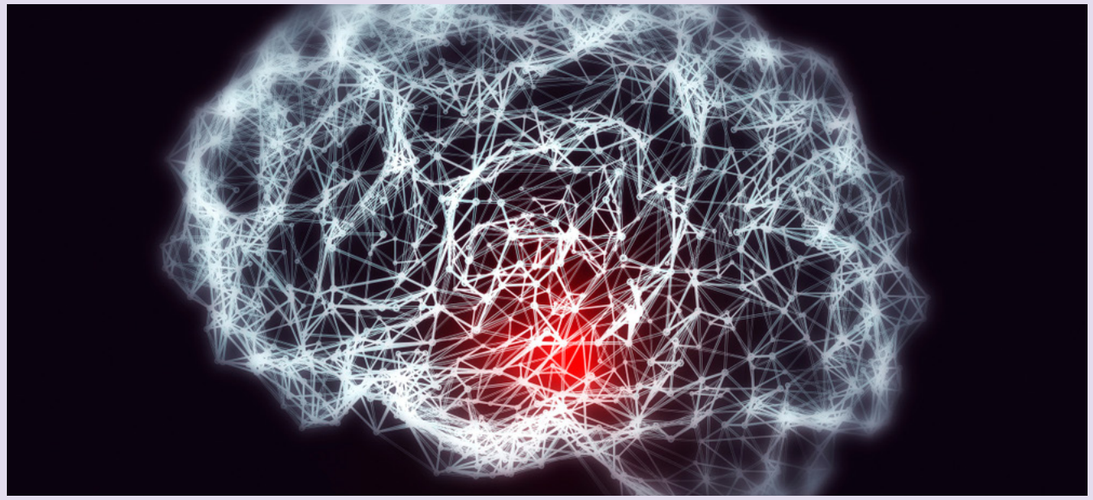
The DPUK consortium model addresses these needs by laying strong foundations for collaboration. This provides the framework for tackling the scientific questions and structural challenges that hold us back. The DPUK precompetitive, high-trust ethos enables industry partners to share technologies and learnings with confidence and to co-design studies with academic partners to focus on specific mechanistic questions. For example, how to develop imaging, digital, and blood-based biomarkers of disease and progression.

What I find encouraging about working with DPUK is the willingness to adapt. DPUK will incrementally and systematically improve its structures to make them relevant to a wider range of stakeholders and research questions. An example of this is expanding the scope of the DPUK research registers from pre-clinical disease to early clinical disease, and developing its networks to include trials delivery sites.

The recently announced Barbara Windsor Mission is recognition by the UK Government of the importance of dementia translation science to the UK dementia ecosystem. This is an opportunity for the UK to become a world leader in experimental medicine and trials. In this I am confident DPUK will play a central role.

"What I find encouraging about working with DPUK is the willingness to adapt."

DPUK in a wider landscape



Dementias Platform UK is a catalyst for a more inclusive, easier and quicker ‘research-scape’

The dementia research environment is changing. Susan Kohlhaas, Director of Research at Alzheimer's Research UK believes the Dementias Platform is playing a significant part in its transformation.

Dementias Platform UK is a one-of-a-kind research programme designed to accelerate developing new treatments for dementia. Since its launch in 2015, DPUK has developed innovative programmes around data science, experimental medicines and trials delivery, that provide a valuable resource to the wider dementia community.

What’s unique about the platform is its interdisciplinary approach, working across industry, academia, charity and government to tackle some of the big questions in translating discoveries into treatments. From a charity perspective, working closely with DPUK helps us stay up-to-date on the latest translational research, and informs the development of our programmes and policies.

Apart from its scientific programmes, DPUK has been quietly developing the dementia ‘research-scape’ to make translation more inclusive, easier, and quicker. From a charity perspective this is welcome, as it means we can obtain better value from the generosity of our donors. We particularly recognise the value of the DPUK career development and training programmes. In supporting the next generation of researchers and analysts, DPUK is investing in the future of dementia research.

There are many reasons to be optimistic about the future for people living with dementia. We’re on the cusp of seeing the first generation of treatments coming through. This gives us something to build upon to make next generation treatments even better. There is much more work to do to ensure that, working with DPUK, we’re able to do high quality translational studies taking our understanding of the mechanisms underlying dementia into clinical studies that help us change practice.

With the government’s launch of the Dame Barbara Windsor Dementia Mission and their renewed commitment to doubling dementia research funding, DPUK is well placed to help us deliver our goal to find life changing treatments for dementia.

"DPUK is investing in the future of dementia research."

Data Sharing Across Borders: The Alzheimer’s Disease Data Initiative and DPUK

By Dr. Tetsuyuki Maruyama, Executive Director, Alzheimer’s Disease Data Initiative

The Alzheimer’s Disease Data Initiative (ADDI) is a non-profit organization founded by a group of leading academic, industry, government, and non-profit partners. As one of our key supporters, DPUK was among the first data platforms to work with ADDI to address interoperability.

Sharing many of DPUK’s goals, ADDI is dedicated to accelerating new discoveries in dementia by sharing the vast amounts of relevant data that could be made available, especially data collected from human research participants. Many researchers, patients, and governments agree that data sharing accelerates science by increasing the utility of data. This allows for new analysis, meta-analysis, and replication, inspiring new ideas and approaches.

There are, however, challenges to data sharing. These include accessible and affordable infrastructure, tools, and resources to support data curation, sharing, and analysis. There also needs to be more incentives – to move away from siloed efforts and towards global collaboration.

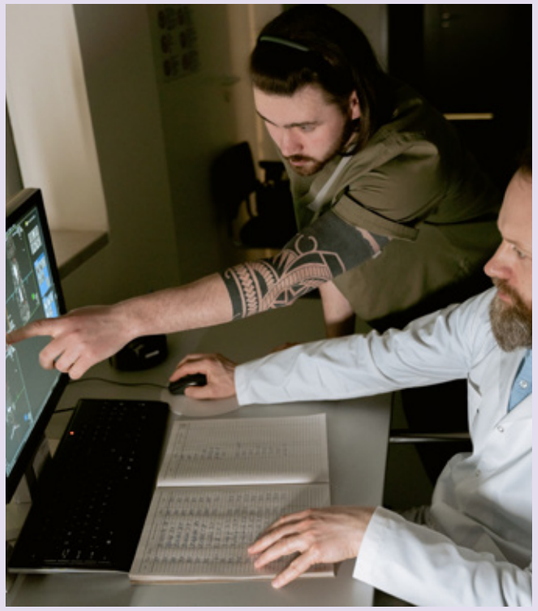
ADDI is advancing solutions through the AD Workbench, which provides the infrastructure to share and discover data within a secure, cloud-based environment. ADDI offers support to data contributors with their data harmonization and curation efforts and provides permissioned access options such as centralized, distributed, or fully federated access on the AD Workbench. For researchers, ADDI can provide compute resources, data analysis tools, and other supports, all at no cost to users.

ADDI’s approach to data sharing and collaboration is global. We strive to partner with data contributors from around the world, including those with datasets from diverse populations. We are also working to increase awareness and engagement among a broad range of researchers – building upon our 3,400 registered users from 94 countries (including 560 users from 47 low- and middle-income countries).

Our partnership with DPUK is an important part of advancing these global solutions. Along with Swansea University, DPUK and ADDI are working on the “Democratising Dementia Data” project, which is addressing rapid access to large multi-modal datasets across jurisdictions. In addition, datasets from the Airwave Health Monitoring Study (Airwave) and the English Longitudinal Study of Ageing (ELSA) are currently discoverable on the AD Workbench. Looking ahead, ADDI and DPUK are working to increase these offerings. This level of interoperability expands the number of researchers who may potentially find novel and insightful ways to use this data in their work.

Another global solution is AD Connect, ADDI’s online community. Members can find AD Workbench resource materials, discussion forums, special events, and more. We know that meaningful advances will not be made by any one person or organization. ADDI looks forward to finding opportunities to work with DPUK to bring researchers from the UK and beyond together, to engage, interact, and inspire each other.

“Our partnership with DPUK has the potential to accelerate dementia research not just in the UK but around the world. By working on data harmonization projects and increasing data interoperability, we can take meaningful steps forward to accelerate new discoveries.”

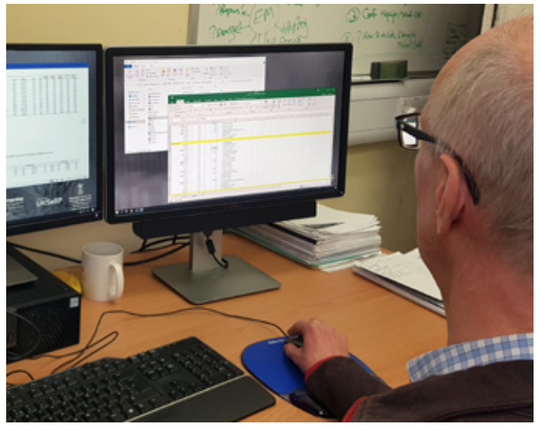


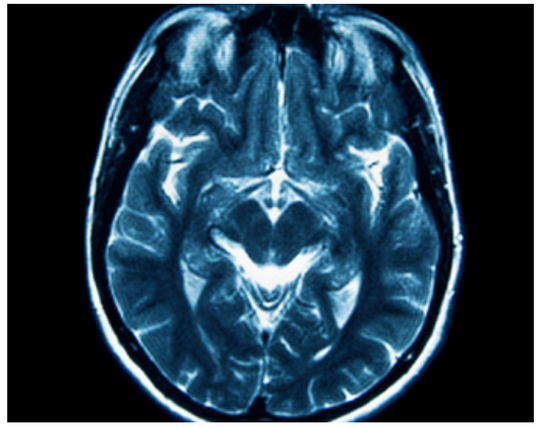
The Data Portal

The DPUK Data Portal, hosted at Swansea University, is opening up new research opportunities and speeding up progress in our understanding of dementia.

The portal is firmly established as a broad and powerful resource offering access to its data both at scale and pace for researchers anywhere in the world. It lies at the heart of our drive to create a ‘data driven economy’ for dementia research. Its ever-growing range of data sets support high-end dementia science globally.

With our world-leading Trusted Research Environment (TRE), researchers can access data on the data portal to find new ways of detecting, treating and preventing dementia.





Data acquisition

The successful acquisition of multimodal data for researcher access has created a rich repository for advanced data analysis, and applications to access this data have increased as a result.

During 2022 there has been a focus on acquiring and provisioning imaging, genomics and proteomics. Combining these with existing epidemiologic data, enables multimodal, multi-cohort analysis to test realistically complex hypotheses. This means the portal now supports computationally heavy analysis of very large and complex datasets

Creating and expanding this resource requires extensive data curation to make it research ready. A team at the University of Oxford is enabling work across data sets to significantly widen research potential. To be effective, the portal itself needed a streamlined access procedure to have free access at the point of use, and host user-led analytic capabilities.

New discovery tools have been developed to allow researchers to explore the data available and our virtual desktop environments are preloaded with more specialised software such as FSL, Freesurfer, Matlab and newly released Jupyter hub. Advanced infrastructure has also been implemented such as High Performance Computing access (HPC) and access to GPU’s.

Supporting specialist hubs

Being a mature trusted research environment (TRE), DPUK wants to establish and support start-up TREs, utilising its already established SeRP UK infrastructure.

This is achieved by providing each hub with its own identity (branding), web-presence, and hub-specific utilities, whilst making available the governance, data processing and data analysis pipelines that have already been developed in DPUK.

The advantages for new projects include

- Lower development risk
- Shorter development time
- Lower cost

An imaging hub has been created and hubs for genomics, the IPMAR Stem cell platform, and the UK Tissue Bank Network (UKTBN) are being developed. New hubs may also be developed for Parkinson's disease, traumatic brain injury, and motor neurone disease.

State of the art imaging pipelines

The DPUK Portal team in Swansea is dimplementing state-of-the-art brain MRI analysis pipelines, and work is already underway to adapt them for inclusion as imaging data within DPUK. These pipelines will automate image quality control and generate image-derived phenotypes.

As part of a collaborative initiative, the Image Processing team in Oxford is adapting state-of-the-art brain MRI analysis pipelines to be part of the imaging data available at DPUK. This involves actively collaborating with the UK Biobank pipeline developers so it can work with other brain imaging data

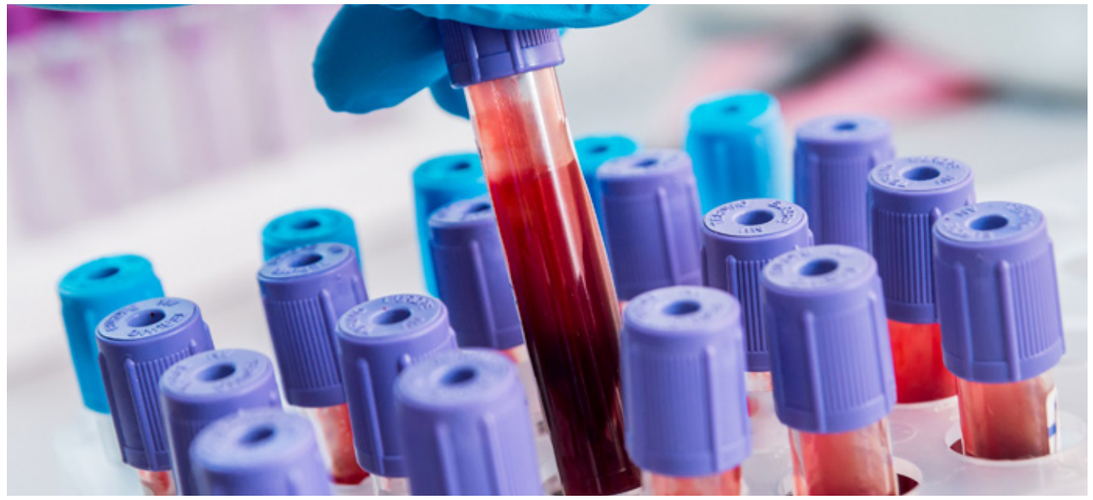
Federation

DPUK has explored approaches which provide federated access to data across global repositories. Working with the US based Alzheimer's Disease Data Initiative (ADDI), data held within DPUK have been configured to allow federated analysis with other global datasets available through ADDI’s workbench. Funding has been secured from ADDI to further develop the platform and to enable more datasets to be available. DPUK are also exploring a Privacy Enabling Technology (PET) platform which will provide a different method of enabling federated analysis across repositories.

Work is underway to create a pop-up TRE between DPUK and Dementias Platform Australia (DPAU) which will provide an intermediate TRE. This will overlap both country TRE's allowing data to be accessed for federated analysis. The Pop-up TRE will be used to run imaging pipelines developed by DPAU across datasets in both organisation’s TREs.

Moving into 2023, the Data Portal team will look to further develop multimodal data and federation capacities and work will begin linking cohort data with NHS digital data to create a more enriched data repository.

Trials Delivery Framework



DPUK's Trials Delivery Framework is establishing an integrated UK-wide network to deliver successful clinical trials. Dr. Vanessa Raymont and Dr. Ivan Koychev explain how they are meeting an important industry need by enabling stratified recruitment from preclinical and clinical populations.

The Trails Delivery Framework brings together high volumes of participants ranging from volunteers with no current memory problems through to patients from research registers set up in existing memory and brain health services across the UK.

Designed to improve the efficiency of dementia trials in the UK, the framework collects detailed information on genetic, cognitive and lifestyle characteristics whilst recruiting participants. This process offers the opportunity to effectively match participants to trials, helping to identify who will benefit from new drugs and interventions that can treat, and ultimately prevent, dementia.

The Trials Delivery Framework is also creating a network of clinical research sites that have pre-agreed processes around the set up of trials, to ensure these happen as quicky and effectively as possible. The Trials Delivery Framework aligns with the newly announced Dame Barbara Windsor Dementia Mission, which is built on the 10 year Life Sciences Vision to use research to innovatively address key health care issues.

UK and global reach

The Trials Delivery Framework is closely aligned with the DPUK's Experimental Medicine Incubator and our industry partners. It is also working with NIHR's Joint Dementia Research initiative, and brain health clinics across the UK and Brain Health Scotland to deliver UK-wide recruitment solutions for trials. We also have agreements with similar international networks, such as Global Alzheimer's Platform (GAP) in the USA and Neuronet in Europe to provide truly worldwide coverage for the delivery of dementia research.

Volunteers

DPUK has registers for members of the public that can be used to recruitment people into studies; Great Minds and the Clinical Studies Register. Great Minds consists of almost 9,000 highly characterised volunteers, primarily recruited from existing DPUK-affiliated cohort studies (8 cohorts to date). We have rapidly expanded the register over the past year, adding 3,204 new participants and 3 more cohorts within 12 months. These volunteers complete six-monthly questionnaires and cognitive tests, and we are expanding genotyping and actigraphy assessments across the cohort. We have supported a total of 22 studies by facilitating recruitment, 10 of those being approved in the past year. Most recently, we have set up a study (FAST Brain Health study) to collect blood biomarker data and online cognitive assessments from 1,000 of the participants. This is now being extended across sites within the clinical arm of the Trials Delivery Framework.

In addition to facilitating clinical studies, the team organises a programme of public engagement through Great Minds. This includes bi-annual hybrid and in-person events, and quarterly newsletters.

Accessible recruitment resource

Our Clinical Studies Register comprises more than 58,000 research participants who have already undergone extensive characterisation and have pre-existing consent for re-contact through their parent DPUK cohort. This makes it possible to provide stratified recruitment, with reduced screen fail rates, based on individual hypotheses in a study.

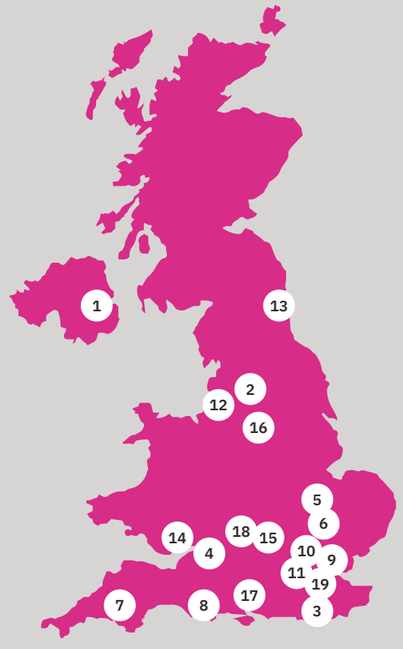
The clinical arm of the Trials Delivery Framework has established 19 sites, at NHS and academic research bodies, as well as brain health clinics across the UK. It is currently agreeing a common data set, which will include cognitive and blood biomarker data, for characterisation that will be gathered across all sites. By developing such an extensive network, our objective is to provide more representative, real world data to trials.

Continuing developments

Further capabilities are being developed through our relationships with commercial organisations. Most significantly, is the capacity to further streamline processes. These include the trial set-up process and other key pieces of infrastructure in the UK dementia research landscape, such as the TRC-D and BRC networks. Data from these clinical sites will be centrally managed within the DPUK Data Portal and over the next year DPUK will be establishing centralised sample processing and a depository along with templates for standardised consenting, costings and contracts.

Trials Delivery Framework Locations

1. Belfast (Belfast Health & Social Care Trust BHC)
2. Bradford (Bradford District Care NHS Foundation Trust)
3. Brighton and Sussex
4. Bristol (Bristol Brain Health Clinic)
5. Cambridge (Addenbrooke Memory Clinic)
6. Cambridge (Cambridgeshire and Peterborough NHS Foundation Trust - CPFT)
7. Cornwall and West
8. Dorset (Dorset Healthcare University Foundation University Trust)
9. East London (East London NHS Foundation Trust)
10. Imperial College London
11. Kings College London (South London & Maudsley NHS Trust Brain Health Clinic)
12. Manchester (Brain Health Manchester)
13. Newcastle (Newcastle Memory Clinic)
14. Newport (Pilot MCI)
15. Oxford (Oxford Brain Health Clinic)
16. Sheffield (Sheffield Memory Clinic)
17. Southampton (Memory Assessment and Research Centre Southampton)
18. Swindon (AWP NHS Trust — Kingshill Research Centre)
19. University College London (National Hospital for Neurology and Neurosurgery)



Experimental Medicine Incubator

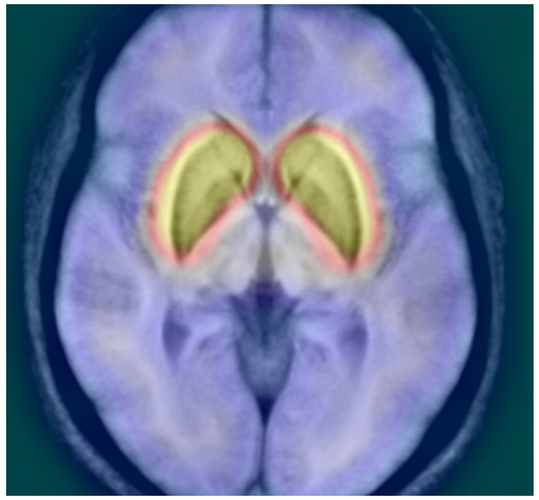
A new approach, reducing costs and risks in pre-competitive collaborations

Professor James Rowe at the University of Cambridge, with Dr. John Isaac, Senior Director of Neuroscience External Innovation at Johnson & Johnson lead the DPUK Experimental Medicine Incubator. It represents a new way of academic industrial partnership.

With over 30 academic, clinical, and industry partners, and patient guidance, DPUK is accelerating the development of new treatments for dementias. We jointly set cross-sector priorities, delivering experimental medicine studies through pre-competitive collaborations that include multiple companies and institutions.

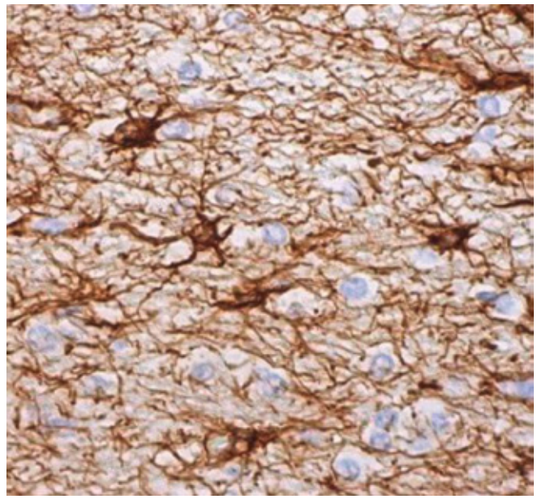
Many candidate therapeutics hit a bottleneck in early phase clinical trials, which increases the costs and risks of drug development. With Phase II studies costing tens of millions, and Phase III studies hundreds of millions of pounds, there is the urgent need to de-risk clinical trials. We also need to minimise the time needed to know which new treatments justify further investment, and which can be set aside.

This is the work of the Experimental Medicine Incubator – building the tools to direct new treatments to the right people, and showing if a treatment is working as it should. The Experimental Medicine Incubator is not restricted to a particular disease, or particular molecule. Instead, we focus on three processes that cause or accelerate multiple dementias.



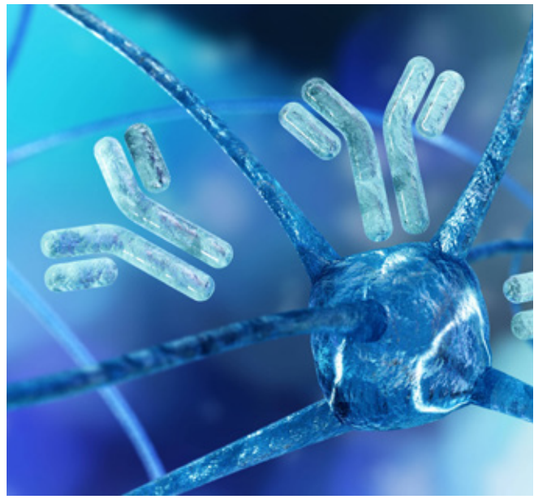
Neuroimmunology

Professor John O'Brien at Cambridge University and Alastair Reith, Senior Scientific Director at GlaxoSmithKline Pharmaceuticals R&D, lead EM activity in neuroimmunology. Many dementia patients have an over-activation of the brain's immune system. Inflammation in the brain is evident from neuropathology, brain imaging studies and examination of cerebrospinal fluid, and immunological signals can often be measured in blood. For treatments to work, we need to separate cause and effect in people, and measure the effect of treatment on brain inflammation. We are looking at the link between inflammation genes and dementia using the Data Portal. With this immune-mediated genetic risk, and immune-based treatments on the way, how best can we measure brain inflammation for clinical trials? We are investigating how changes in the immune system in blood and cerebrospinal fluid may drive disease progression and are investing in new PET scanning technology to detect brain inflammation; and comparing these specialist scans to simpler and cheaper blood tests. Look out for IMPRINT and IMPACT study updates.



Vascular Health

Work in vascular health is led by Dr. Atticus Hainsworth at St George's Hospital, London. Vascular health is essential for brain health. A major cause of cognitive impairment and dementia is vascular disease, including strokes and small vessel disease, amyloid angiopathy, changes in neurovascular coupling and the blood brain barrier. Not surprisingly, drugs acting on the vascular system have the potential to prevent or slow dementias. We are defining the genetic and environmental risks of vascular cognitive impairment, and the genetic basis of the mediation of cognitive impairment by the vascular pathologies evident in brain imaging. The team are also identifying disease-modifying effects of drugs that are already in use, in order to repurpose useful drugs and accelerate new vascular health treatments.



Synaptic health

Synaptic work in the Experimental Medicine Incubator is led by James Rowe. Inflammation, vascular impairment and the accumulation of toxic proteins, like amyloid and tau, act together to damage the important connections between brain cells called synapses. Synapses are how the brain cells communicate and remember information, and their loss causes cognitive decline. Our Synaptic Health team can now measure synapses in people with or at risk of dementia, determining their role in developing dementia. Our new PET scans measure where and when people lose synapses; we can measure the impact of this loss on the way the brain works for memory and perception. New blood and spinal fluid tests complement these brain imaging studies of synapses. We are testing MEG and EEG as a platform for improving early phase trials. They not only give signals of drug efficacy, but combined with advances in brain modelling they reveal mechanisms of disease with unparalleled precision in living people.

The Experimental Medicine Incubator began with studies of mild cognitive impairment, Alzheimer's disease and Dementia with Lewy-bodies. Now the technologies extend to early phase trials of frontotemporal dementia, motor neuron disease, traumatic brain injury and post-stroke dementia, and bring together the work of DPUK's other invaluable resources - the Data Portal and Trials Delivery Framework.

Inside DPUK's Translation Programme

There is an increasing number of Experimental Medicine studies using DPUK resources. Together, they illustrate the range of impacts of Dementia Platform UK on the translational dementia research-scape.

New Therapeutics in Alzheimer's Disease (NTAD): MEG biomarker platform development

PI: James Rowe, Cambridge University

This study aimed to increase knowledge and awareness of synaptic health, developing a multidisciplinary research network from across academia and industry. The network has initiated innovative experimental medicine studies in synaptic health, including the NTAD study – a validation of a human neurophysiology longitudinal biomarker platform to support early-stage interventional studies and early-phase clinical trials; with increased sensitivity and mechanistic insights into human Alzheimer's disease pathogenesis.

The group has identified, and facilitated, broader opportunities for understanding synaptic health in dementia as part of national and international research initiatives. It has proved to be an excellent example of a successful public-private partnership with academics, clinicians and industrial company staff contributing to meet the challenge experimental medicine studies and planning for new treatment studies. This work led directly to a successful application for the NTAD study (MEG-based neurophysiological biomarker platform for AD). The NTAD study has completed all baseline investigations, with longitudinal assessments to be completed by June 2023. The initial results confirm the excellent reliability and sensitivity of MEG to early AD/MCI and its progression, making the approach ideally suited to early phase trials. This project benefits from additional industry investment to support further fluidic and PET biomarkers of synaptic health, connecting brain physiology to cognition.

How do peripheral and central vascular markers relate to cognitive decline?

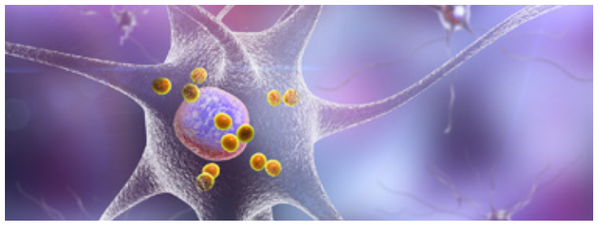
PI: Ian Deary, Edinburgh University

This project aimed to investigate the links between plasma lipids/lipoproteins, cognitive change and neurovascular imaging parameters that explain age-related cognitive decline. DPUK enabled many thousands of metabolites to be measured in the plasma of Lothian Birth Cohort 1936 participants, allowing investigation of their association with cognitive ability and variation in brain health measured by MRI. Penalised regression models identified sets of metabolites that predict variation in brain health, for example the finding that UPLC-MS-POS measured lipids predicted 19% of the variance in total brain volume and 17% of the variance in the volume of grey matter and normal appearing white matter.

Integration of clinical and cellular phenotypes in the DPUK Deep and Frequent Phenotyping cohort

PI: Richard Wade-Martins, University of Oxford

The DPUK Deep and Frequent Phenotyping study has one of the most intensively assessed cohorts of people with very early AD and Mild Cognitive Impairment (MCI). All participants have extensive clinical and biological assessments including detailed cognitive measures and biological measures of pathology including both Amyloid and Tau PET and molecular assays of both in CSF. During follow-up, all participants have multiple re-assessments to discover which research methods could support the shortest and most accurate clinical trials. This experimental medicine project generated iPSC stem-cell lines from participants in the DPUK Deep and Frequent Phenotyping pilot study. Using neurons derived from these iPSC lines, we showed that the impact of beta-amyloid on synapse loss was proportional to the changes in MEG measures of brain function in the individuals from whom the iPSC's were derived. New studies using excitatory glutamatergic neurons derived from the iPSC's are underway. It is a major step forward to confirm that iPSC-derived cortical neurons are suitable for large-scale in vitro analysis of multiple patients' cell lines, and can be used to address hypotheses from clinical work.



Rates, Risks and Routes to Reduce Vascular Dementia (R4VaD)

PI: Joanna Wardlaw, Edinburgh University

Stroke is known to affect cognition but risk factors for post stroke cognitive impairment (PSCI) are not well defined and the mechanisms are not well understood. Currently there are no effective preventions or therapies.

R4VaD is a large, UK-wide, inclusive, observational study in which cognition, functional outcome and neuropsychiatric symptoms are assessed for at least two years after a stroke. It aims to determine the rates of PSCI, understand the reasons for its progression, and to gain better mechanistic understanding and risk-prediction models. It is a comprehensive study employing blood sampling to provide information on genetic and inflammatory markers along with routine and advanced neuroimaging, together with quantification of pre-morbid and pre-stroke cognition, lifestyle and socioeconomic factors, and medical history.

Regulatory approvals for the study were obtained in Spring 2018 in all four UK nations. Staff were appointed, and patient recruitment started in September 2018, expanding to a total of 53 stroke centres in all four nations with 1271 patients enrolled by 23/3/20 when recruitment was interrupted due to COVID-19. The study reopened recruitment in this 'COVID-19 sub study' in April 2020. R4VaD will be the most important national prospective study able to provide objective data on the relationship between COVID-19 and stroke, in addition to its original objectives.

The original DPUK-funding was key to supporting the study while it was established. The success is visible in the large number of centres that have been set up (53), involving all parts of the UK to obtain a representative sample, and recruiting to target despite COVID-19. The COVID-19 interruption has delayed the end date and discussions continue with co-funders to manage the extension.

Multi-modal astroglial imaging

PI: Paul Matthews, Imperial College, London

The imidazoline I2 binding sites (I2-BSs) are widely distributed in the brain but found principally on glial cells, including a functional role in astrocytes. The aim of this study was to evaluate [11C] BU99008 uptake, a novel marker of glial activation, in people who were cognitively impaired by AD (Mild Cognitive Impairment, MCI, or early dementia) compared to age-matched controls. We showed increased [11C] BU99008 uptake in people with AD/MCI, suggestive of astroglial activation. The increased uptake was widely distributed in grey matter, where it was associated with amyloid deposition.

Crosstalk: the impact of cardiac anatomy and function on brain structure and health

PI: Steve Williams, Kings College, London

It is widely recognised that typical cardiovascular risk factors also present greater risk of brain pathology and cognitive impairment. We examined the relationship between cardiovascular risk factors (high blood pressure, abnormal cardiac function) and brain health. The results cofirmed that hypertension is associated with greater volume and severity of white matter hyperintensities. There was also localised cerebral cortical thinning and weaker functional connectivity with regions previously implicated in blood pressure regulation, such as the insula.

MRI-PET tau population risk study

PI: Paul Matthews, Imperial College, London

The aim of the current project is to test a second-generation Tau PET ligand as a DPUK-funded Experimental Medicine sub-study linked to the highly phenotyped PREVENT cohort. Accurate in vivo quantification of tau aggregation, in addition to Amyloid PET data and the comprehensive biomarker profile, will create an unprecedented dataset for modelling of the early stages of Alzheimer's disease pathology and risk of subsequent Dementia.

100 volunteers from the PREVENT cohort are undergoing an intravenous injection of PI-2620 with dynamic imaging for accurate modelling of the tau, its amount and locations in the brain. Study outcome measures will relate Tau deposition in individuals to their Amyloid burden, and their joint relationship to longitudinal cognitive and structural imaging change.

Expanding DPUK genetics and integrating with inflammation/ immunity research

PI: Julie Williams, Cardiff University

The aim of this work was to increase the genetic data available within the DPUK portal by genotyping samples available through the DPUK cohorts. The goal was to show the feasibility of enriching the DPUK portal by inclusion of genotype data and to then make this data available to the wider research community. The generation and inclusion of a polygenic risk score means that the wider community can simply integrate genetics into their research. This is an important step towards cost-effective integration of differing data types across cohorts, that would otherwise be unfeasible. As part of the project genotype data and polygenic risk scores for over 2000 participants already enrolled in DPUK cohorts have been generated. The team conclude that increasing the availability of genotype data within DPUK is feasible and it is possible to provide a simple single variable polygenic risk score to allow the wider research community to integrate genetics into their research.

The development of an Alzheimer's disease clinical trial simulator

PI: Roy Anderson, Imperial College, London

Alzheimer's disease (AD) is a progressive disease, with no effective treatments or cure. Over 98% of clinical trials of AD drug candidates have failed or been discontinued and the failure rate of clinical trials for AD treatments is far higher than that of trials in other therapy areas.

The Clinical Trials Simulator is founded on a stochastic mathematical model that has been developed to describe the movement of individuals through distinct health and disease states (e.g. Cognitively Normal (CN), Mild Cognitively Impaired (MCI) and AD) and predict the development and progression of AD. The Clinical Trials Simulator has incorporated continuous and composite outcomes which are used as primary endpoints in clinical trials. and will help to improve the design of clinical trials by providing insight to the most relevant trial endpoints and the optimal time point to administer treatment. This informs the delivery of novel therapeutic options to a therapy area of high unmet need.

Perform analysis of PVS and vascular lesion burden using UK Biobank and other data sources

PI: Terry Quin, Glasgow University

This study will identify intermediate markers vascular dementia. It will automate the quantification of brain vascular lesion progression via DPUK's Data Portal and test the relationships of vascular and dementia risk factors with change in SVD related lesions, (WMH, lacunes, microbleeds PVS), DTI parameters and composite metrics (brain age, brain health index). The analysis is ongoing.

Synaptic Health in Neurodegeneration (SHINE)

PI: James Rowe, Cambridge University

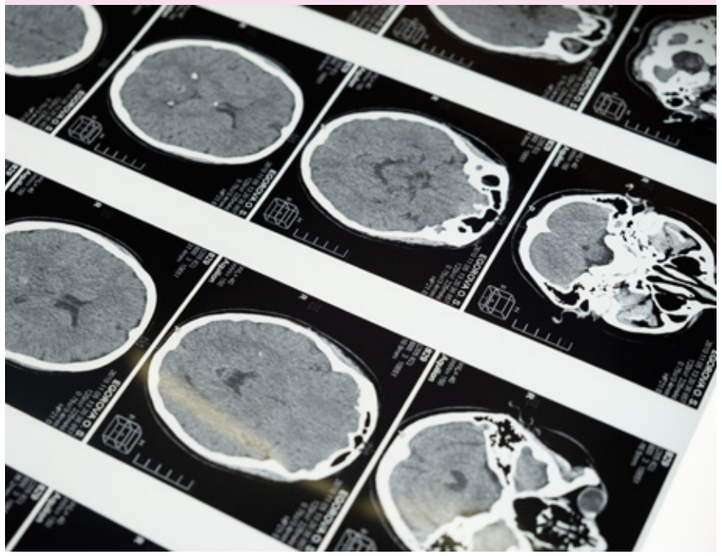
Synapses are the junctions where electric impulses are transmitted between brain cells (called neurons). These synapses carry the messages which enable us to move, see, or think and the cellular foundations of memory. Severe loss of synapses occurs in Alzheimer's Disease (AD) and other forms of dementia. They can be an early indicator of the development of these conditions. The main aim of this project is to understand the relationship between synaptic health and the progression of Alzheimer's disease from its early MCI stage through to dementia (and other neurodegenerative diseases). We use advanced brain imaging tools with magnetoencephalography of brain function (MEG) and positron emission tomography of synaptic density (PET): this will link the number of synapses to how effective they are, and how they change with the development of Alzheimer's disease. We will assess and validate new technologies that could accelerate and de-risk clinical trials of new treatments. The research may also lead to new diagnostic tests and to better design of future clinical trials. Recruitment is underway.

Investigation of the impact of polygenic inflammatory pathway risk score and inflammatory comorbidities on onset and progression of cognitive decline and

PI: Valentina Escott-Price, Cardiff University

This study uses the DPUK Data Portal to investigate the genetic impact of inflammatory pathway(s) by means of polygenic risk scores and inflammatory comorbidities on onset and progression from cognitive impairment to dementia. There is a poor understanding of the timing and impact of innate inflammatory changes along the course of the disease pathway in Alzheimer's disease (AD) and dementia with Lewy bodies (DLB), yet this is of key importance as at the time dementia presents considerable brain damage has already occurred. Biomarker and brain imaging studies in human concur with animal work in finding inflammation an early feature in AD and DLB; for example, in DLB inflammatory biomarkers in blood and brain normalize in mild dementia. A similar pattern is shown for AD. These findings strongly emphasise the need to study the prodromal stages of disease.

By building a cohort of prodromal AD and DLB patients, and undertaking detailed blood and CSF immunoprofiling we will characterise the immune signature at the prodromal stages and, by following subjects over 3 years and repeating measurements at 18 months, we will determine 1) the immunophenotype in blood and CSF characterizing prodromal AD and DLB; 2) how this immune profile changes over time as these diseases progress to dementia, and 3) how immune profiles are predictive of disease progression. Our work will inform the stratification of patients for clinical studies and determine the most effective point(s) of therapeutic intervention. Our study will utilize the DPUK data portal and latest GWAS information to examine polygenic inflammatory risk scores as well as inflammatory conditions as predictors of dementia and its prodromes in DPUK cohorts. Analyses are ongoing.



Assess whether post-synaptic levels of TARP γ8 AMPAR are reduced in early AD and if this correlates with memory impairment

PI: James Rowe, Cambridge University

This workstream focuses on testing the impact of Alzheimer's disease on synaptic health, focused on post-synaptic health in terms of the levels of transmembrane AMPA receptor regulatory protein (TARP γ8 AMPAR). We will test where and when this is reduced in early AD, and how strongly this change is linked to memory impairments. This study will evaluate the first-of-its-kind TARP γ8 AMPAR PET ligand for human use ([18F] JNJ-64511070), developed by DPUK partner Janssen. Preclinical and unpublished human data have been made available to DPUK, in developing the plans for its assessment in people with Alzheimer's disease. The high density of postsynaptic binding to hippocampal glutamatergic synapses is especially useful in the context of AD.

Define drug targets using Mendelian randomisation

PI: Hugh Marcus, Cambridge University

This study wanalyses the effect of candidate genes, using Mendelian randomisation to identify risk factors for small vessel disease using UK Biobank data and other large-scale cohorts. These analyses will be used to identify therapeutic targets for small vessel disease. Mechanisms of interest include the genetic basis of hypertension, diabetes, smoking and body mass index. The large-scale multivariate data are currently being prepared for analysis.

Define drug targets using analysis of cardiovascular disease and drug history

PI: Terry Quinn, Glasgow University

The study analyses the mechanistic pathways for cardiovascular risk factors and vascular dementia using data from a variety of cohorts including UK Biobank, Airwave and R4VAD. Of interest are the moderating effects of known cardiovascular medicines and the opportunity they offer for re-purposing as treatments for the prevention or slowing of Vascular Dementia. The datasets are currently being prepared for analysis.

Peripheral immunoprofiling in people with prodromal and early Alzheimer's disease and Lewy body dementia (IMPRINT)

PI: John O'Brien, Cambridge University

To identify the cellular and chemical signatures of the immune system which characterise early Alzheimer's disease and early Dementia with Lewy bodies.

Abnormalities of inflammatory markers in the blood and the brain have been described in Alzheimer's disease and in dementia with Lewy bodies. Studies to date suggest these changes occur early in the disease process and may be associated with more rapid clinical decline. However, there are inconsistencies between studies which make prevent the sufficiently robust interpretations required to plan immunotherapeutic trials. This is partly because earlier studies have been cross-sectional and have focussed on cytokines and other immune markers. A more detailed and longitudinal characterisation of the immunophenotype is required. IMPRINT will undertake immunophenotyping and exosome analysis of blood and CSF in new patient cohorts of prodromal Alzheimer's and Lewy body disease. Repeat assessments will define the longitudinal changes in immune biomarkers. Analyses are ongoing.

Pilot PET-MR imaging using a novel inflammatory PET ligand impact

PI: John O'Brien, Cambridge University

While blood and CSF measures of the immune system would make it easy to scale up studies, and repeat measurements many times during a trial, new PET imaging methods will allow direct quantification and localisation of inflammation in the human brain. Several studies have suggested microglial activation in Alzheimer's disease and dementia with Lewy bodies, but their use of PET ligands binding the translocator protein are suboptimal as they lack specificity, sensitivity and/or have binding properties influenced by genetic polymorphisms making them unsuitable for a third of people. Recent advances in PET ligands include developments of new targets including the P2X7 and CSF1R receptor. DPUK is undertaking an innovative study of PET imaging in prodromal AD and DLB using a novel ligand, targeting the P2X7 receptor.

Acknowledgements

DPUK is grateful to all our partner and collaborative organisations and many individuals offering their support for our work. We need them all to realise our goal of enabling vital breakthroughs in dementia research. We benefit from the endeavours of experts drawn from many fields working towards this goal. All make significant contributions, here in the UK and globally.

In particular, we want to thank our research project and network leads, and those helping to oversee the governance and scientific direction of DPUK.

Executive team

Professor John Gallacher (Director)
Dr Iain Chessell
Dr Susan Kohlhaas
Professor Ronan Lyons
Dr Vanessa Raymont
Professor James Rowe
Professor Simon Thompson

International scientific advisory board

Professor David Bennett (Chair)
Professor Richard Frackowiak
Professor Agneta Nordberg
Dr Susan Resnick

Scientific steering group

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Professor Uta Griesenbach
Professor Martin Hofmann-Apitius
Dr Riccardo Marioni
Professor Jonathan Mill

Medical Research Council

Dr Robin Buckle (Chief Science Officer)
Dr Joanna Latimer (Head of Neurosciences and Mental Health)
Dr Natasha Jardine (Programme Manager for Neurodegeneration)

Scientific project leads

Professor Ronan Lyons and Professor Simon Thompson lead the DPUK Data Portal workstream

Professor Ronan Lyons and Professor Simon Thompson lead DPUK Work Package 21: Data Portal enhancements

Professor Clare Mackay and Dr Ludovica Griffanti lead DPUK Work Package 22: Image processing pipelines

Dr. Sarah Bauermeister leads DPUK Data Curation programme

Dr Vanessa Raymont leads the Trials Delivery Framework workstream

Dr Ivan Koychev leads DPUK Work Package 23a: Clinical Studies Register

Dr Ivan Koychev leads DPUK Work Package 23b: Great Minds

Dr Vanessa Raymont leads DPUK Work Package 24: Clinical recruitment and research facilities

Professor James Rowe leads the Experimental Medicine Incubator workstream

Dr Atticus Hainsworth leads DPUK's Vascular Health theme

Professor Joanna Wardlaw leads DPUK Work Package 25a: Early vascular lesion MRI biomarkers and dementia risk

Professor Hugh Markus leads DPUK Work Package 25b: Identifying potential drug targets using Mendelian randomization

Dr Terry Quinn leads DPUK Work Package 25c: Identifying the most promising cardiovascular drugs for a cognitive endpoint trial

Professor James Rowe leads DPUK's Synaptic Health theme

Professor James Rowe and Dr John Isaac lead DPUK Work Package 26a: Synaptic loss and its functional consequences in early Alzheimer's disease, using pre-synaptic markers and magnetoencephalography

Professor James Rowe and Dr John Isaac lead DPUK Work Package 26b: Synaptic loss and its functional consequences in early Alzheimer's disease, using a new post-synaptic TARP γ8 AMPAR ligand

Professor John O'Brien leads DPUK's Neuroimmunology theme

Professor Valentina Escott-Price leads DPUK Work Package 27a: Polygenic risk and inflammatory pathways

Dr Paresh Malhotra, Professor Paul Matthews, Professor John O'Brien and Dr Alastair Reith lead DPUK Work Package 27b: Prodromal dementia immunoprofiles

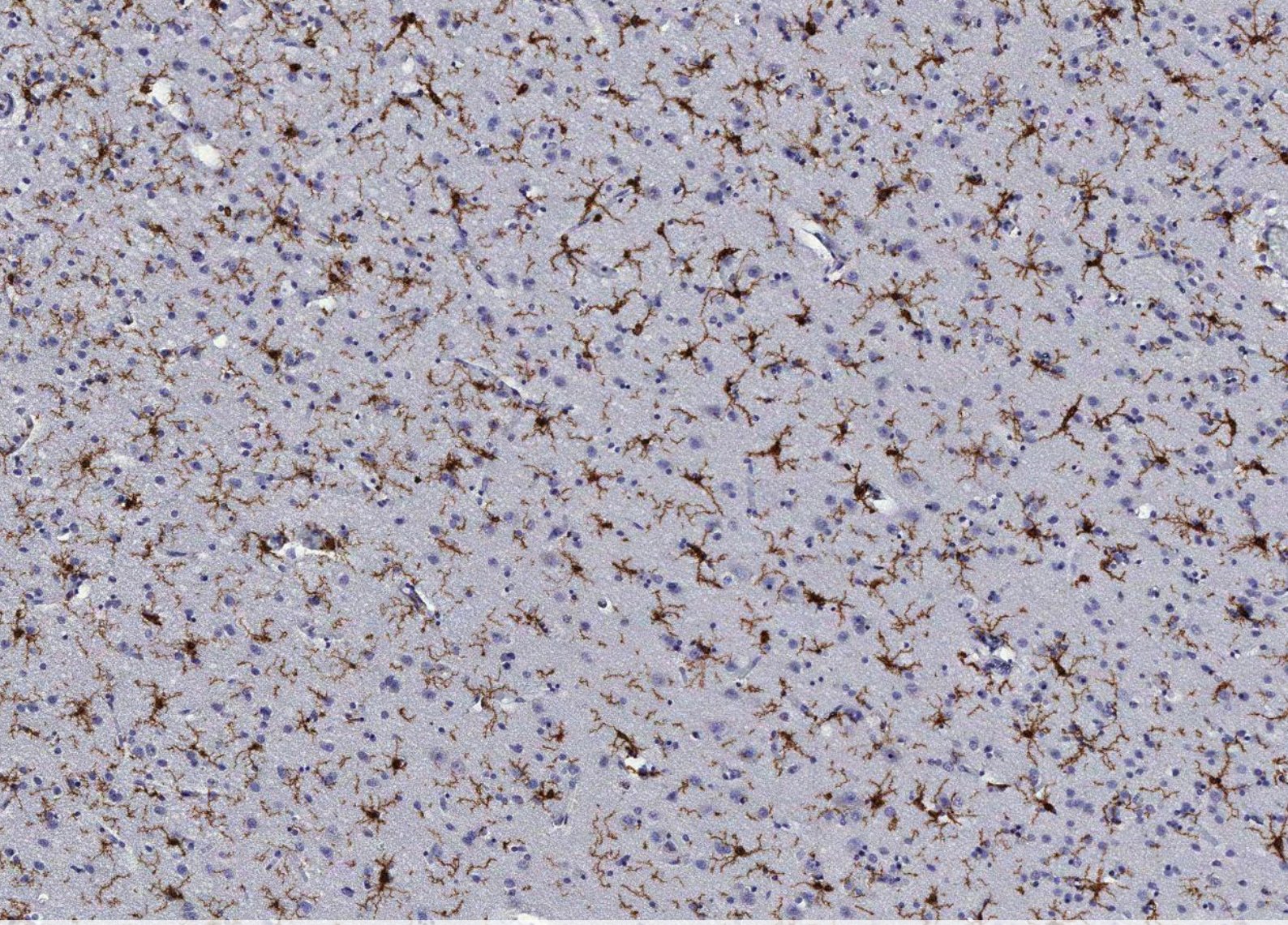
Dr Paresh Malhotra, Professor Paul Matthews, Professor John O'Brien and Dr Alastair Reith lead DPUK Work Package 27c: Dynamic PET-MR and brain inflammation

Dr Vanessa Raymont leads the Deep and Frequent Phenotyping study

Dr. Julian Matthews leads the DPUK Imaging Network

Professor Richard Wade-Martins leads the DPUK Stem Cell Network

Dr Sarah Bauermeister leads DPUK's data analyst training programme



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Dementias Platform UK

www.dementiasplatform.uk