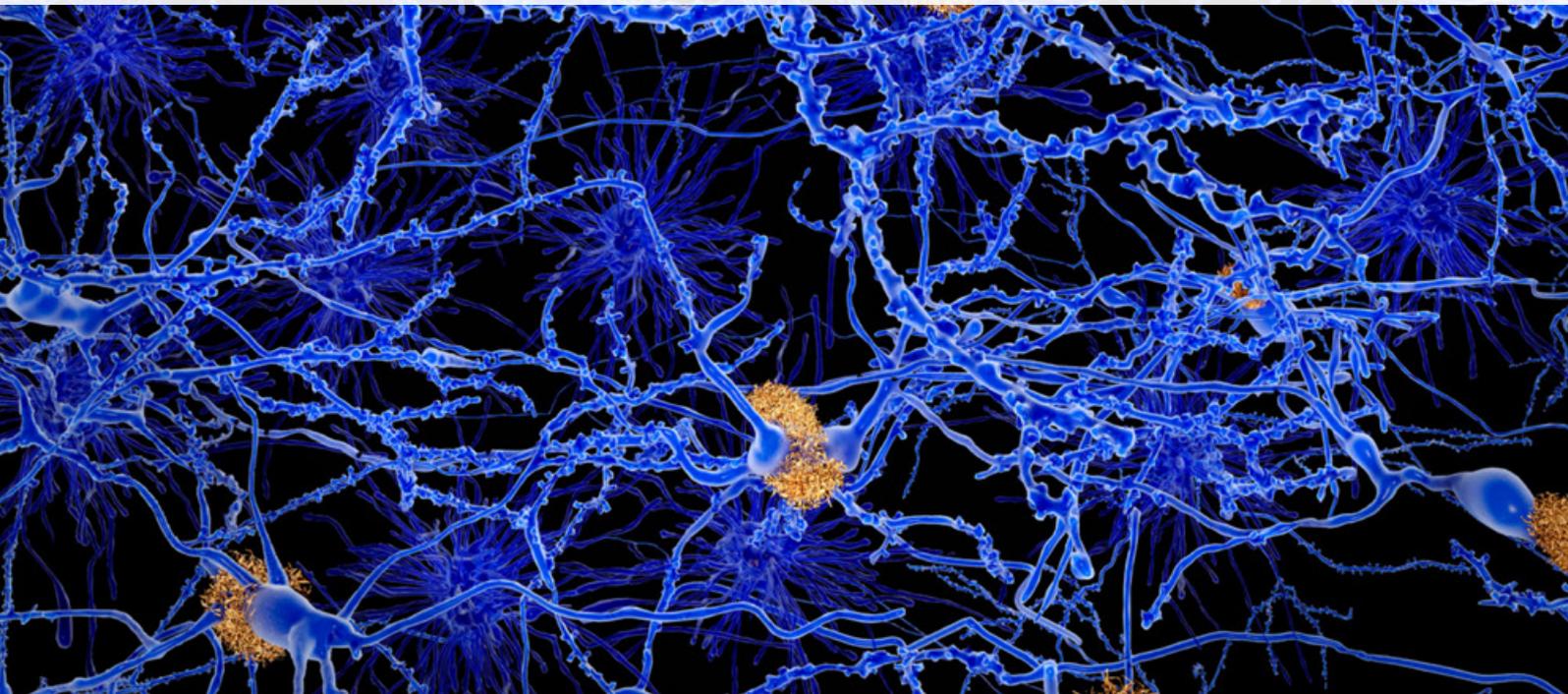


**Dementias
Platform^{UK}**

Translation in a fast-changing world



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Translation in a fast-changing world



Dementia translation is rapidly changing, and so is DPUK as it adapts to new opportunities. From increased Data Portal activity, through enlargement of our trials networks and research registers, to extending our experimental medicine to scalable biomarkers, this year has seen growth in all aspects of DPUK's programme.

To the keen observer, DPUK is about supporting change. Whether this be creating a data standard, generating pre-processing imaging pipelines, or integrating primary and secondary care into our trials registers. Guiding these activities are five principles of achieving change at-scale: collaboration, reducing transaction costs, innovation, trust-by-design, and values-based work programmes.

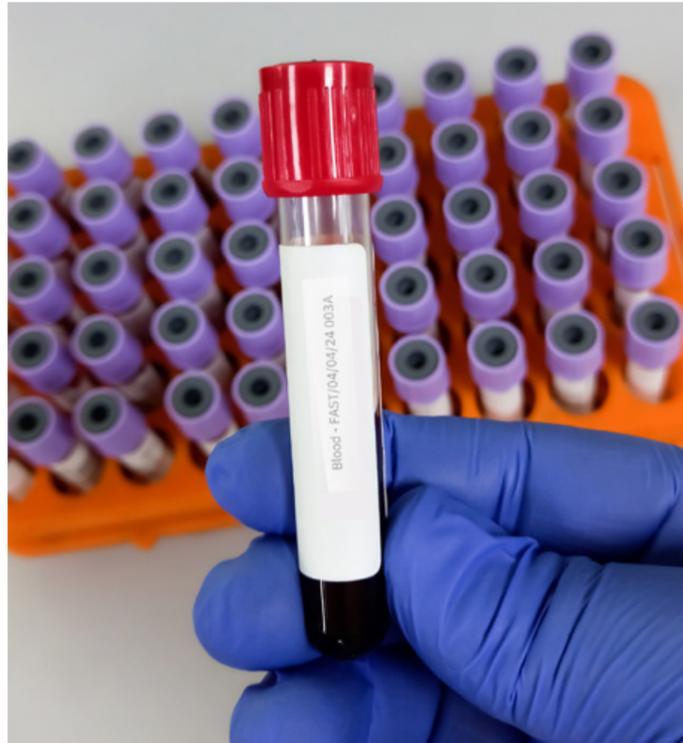
These principles permeate DPUK. The Trials Delivery Framework is working hard to establish a collaborative common dataset for cost-effective recruitment to stratified trials. The Data Portal is developing AI-led trust-by-design solutions for privacy protection. The Experimental Medicine Incubator is supporting the development of innovative simple scalable biomarkers for early detection and diagnosis of dementia. Underpinning all of these activities is our high-trust, pre-competitive ethos. None of these activities are low-risk or bring immediate rewards, but if successful, all will benefit the wider dementia community.

Our international collaborations are increasing. We have projects underway or planned with AD Data Initiative, the International Hundred Thousand Cohorts Collaboration, DZNE, the Korea Dementia Research Centre, The Korea Brain Research Institute, Dementia Platform Australia, and the Global Alzheimer's Platform.

It was a delight to welcome Lord Cameron to see the first-fruits of his 2010 Dementia Challenge. The recent launch of the Dame Barbara Windsor Dementia Mission at 'Number 10' is further evidence of the impact of the Challenge. The Dementia Mission is the backdrop to the development of UK dementia translation. The DPUK programme provides a wealth of data, learnings, and infrastructure that is available to the Mission. We look forward to working closely with the Mission for the benefit of all at risk of dementia.

A handwritten signature in black ink, appearing to be 'JG'.

**Professor John Gallacher,
PhD AFBPsS CPsychol FFPH,
Director of DPUK**



Blood Biomarker Challenge funding can bring accurate and early dementia diagnosis a step nearer

Dementias Platform UK has been awarded £4.5 million from the Blood Biomarker Challenge. Together with the People's Postcode Lottery, the Alzheimer's Society and the NIHR, ARUK is funding the community-based project to assess blood-based biomarkers in real world populations.

Over five years, READ-OUT will conduct an observational study and randomised clinical trial using our UK-wide Trials Delivery Framework of sites. It will assess the utility and cost effectiveness of blood biomarkers for identifying Alzheimer's and other diseases leading to dementia both early and accurately.

Speaking about the READ-OUT funding, Dr Vanessa Raymont said: "This is a hugely exciting opportunity to deliver the data we need for us to start to effectively use blood biomarkers to identify diseases that can lead to dementia more accurately and earlier, in all patients and across the UK. This will allow access to more effective, targeted management and new drugs as they become available."

The aim is to enable faster and more accurate diagnoses, and better prognosis, in real-world memory clinics. It will also provide evidence for health economic models of blood biomarkers and commissioning as well as routes to offer equity of access to improved diagnostic pathways across the UK.

Lord Cameron visit to DPUK

Former Prime Minister David Cameron visited DPUK's team at Oxford in October to hear more about our work. During his visit he took time to speak to each member of our team to better understand what our research teams are doing.

The visit proved to be one of his last engagements before being called back into frontline politics as Foreign Secretary and his entry into the House of Lords.

Lord Cameron has been a committed Patron of Alzheimer's Research UK for several years building up a considerable knowledge about the disease and what needs to be done to make progress in the search for a cure.



DPUK's added value

Dementias Platform UK is providing resources that are widely used in dementia and cognition research. During 2023 projects which leveraged DPUK's facilities and resources totalled over £35 million. Amongst the projects are TBI-Reporter, MND Accelerator, Blood Biomarker Challenge (READ-OUT), and COMMUTE – a Horizon funded project. Director John Gallacher said: "It is an impressive figure demonstrating how our core programmes are leading to valuable research projects."

Since DPUK was established, the additional research leveraged is approaching **£100 million.**

Dementia Mission launch at No.10

Plans are still taking shape for the UK government's £160 million investment in dementia research through the Dame Barbara Windsor Dementia Mission. As part of the wider discussion, Dr Vanessa Raymont, Professor James Rowe and DPUK Director Professor John Gallacher attended an event at No. 10 Downing St, with others from across the dementia community.



Hwan Yeong! A second collaboration with Korea

DPUK has extended its international relationships with an agreement to work collaboratively with the Korea Brain Research Institute from Daegu. Having invested heavily to create the institute, a delegation led by its President Pann-Ghill Suh visited the UK to explore future projects. One of KBRI's research team returned to speak at Translation 2024. DPUK already has strong links to Korea having helped in the foundation of Dementia Platform Korea.



Outreach to south Asian and Afro-Caribbean communities

Dementia can affect us all, but participation in research from some communities falls far short of their representation in the population at large. With this in mind, DPUK has partnered with Karan Jutla at the University of Wolverhampton to assess how best to engage with the south Asian community.

Karan is from a Sikh family and, by using grassroots contacts, an event in Wolverhampton's south Indian population has been staged to help people to learn more about dementia, how it affects all communities and how it is possible to reduce the risk of dementia through lifestyle changes. Participants will hear about the Great Minds register and how they can make a significant contribution to medical research by joining as volunteers.

This event follows a series of art-based activities for the African and Caribbean communities of several cities including Sheffield, Leeds, Oxford and London which also encouraged people to volunteer to help research. DPUK hopes to discover how best to reach under represented groups as part of its expanding register of trials and study volunteers.

Developing guidelines for AI research risk

Artificial intelligence brings new risks and challenges as well as exciting opportunities. DPUK has been funded to investigate risk evaluation in AI models in health research.

With the use of AI with complex health-related datasets, it is important to ensure that trusted research environments are safe. This project will investigate issues facing AI models that render trusted research environments vulnerable to attack and data leakage. There is a need to carefully consider these risks and develop recommendations and guidelines for their mitigation.

The community group funding from DARE UK (Data and Research Analytics Environments UK) is for collaborative community-led initiatives highlighting the importance of working together towards common goals.



Snapshot

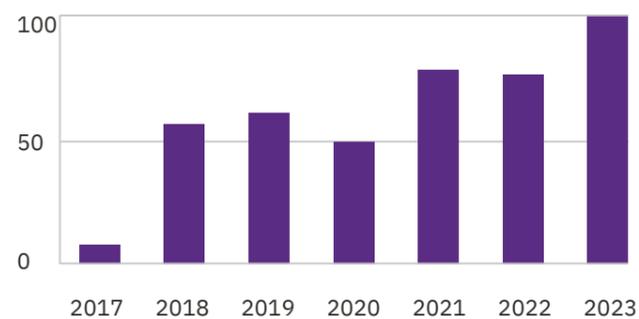
Data Portal



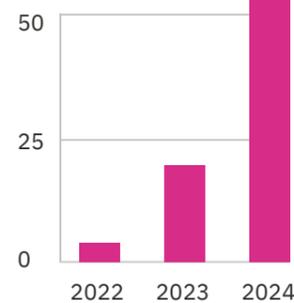
Trials Delivery



Data Portal applications per year



TDF Sites



Experimental Medicine Incubator

Notable outcomes:

- Brain Inflammation is detectable in all of the major dementias
- Blood tests detect increased inflammation in dementias, and indicate rate of progression
- MEG scanning is very sensitive to Alzheimer's disease and its progression
- Good blood pressure treatment goes hand in hand with better brain health

Embracing Complexity



Professor David Bennett of the Rush Alzheimer's Disease Center in Chicago, Illinois believes we need to move ahead confidently despite a myriad of challenges.

Complex diseases are, by definition, well... complex! Loss of memory and other cognitive abilities in old age is among the most common and feared conditions of ageing. It is also among the most complex of complex conditions. More than three decades ago, we launched a series of studies designed to embrace the complexity of age-related cognitive decline. First, we enrolled two groups of older persons in two cohort studies, the Religious Orders Study and the Rush Memory and Aging Project, known as ROSMAP, with many data elements in common.

The only inclusion criteria were the ability to consent to annual detailed clinical evaluation and blood draw, and later neuroimaging and biomedical devices, and sign an Anatomical Gift Act for brain donation. Thus, we studied old people getting older and then examined their brain. Second, we collected multiple streams of clinical data including cognitive and motor function, sleep and circadian rhythms, health and financial literacy and decision making. We measured more than a dozen common brain pathologies, and over the past dozen years, we have generated an unprecedented multi-layer omic dataset from blood and brain. So, as my grandmother would say, have we learned anything?

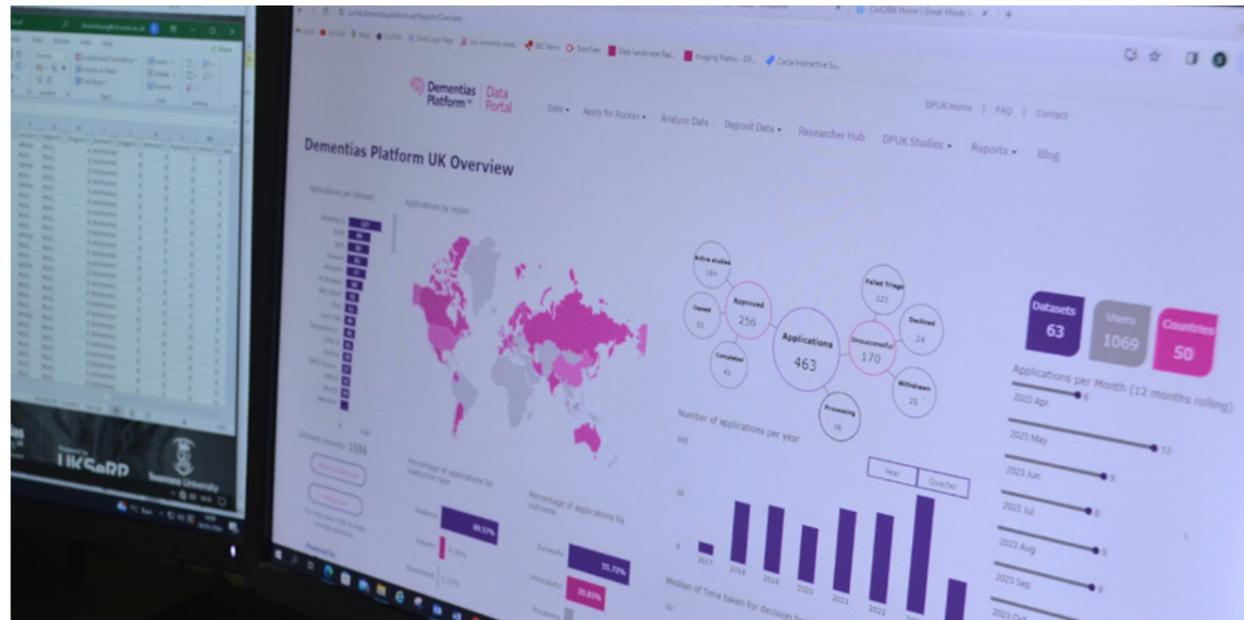
First, age-related loss of cognition is a function of multiple brain pathologies that add up and interact with one another, yet, together, they explain only half of age-related cognitive change and two thirds of dementia. What explains the rest? Great question! Second, your brain does not want to lose cognition and like all physiologic systems it has ways to protect itself. But not in the usual way, e.g., an extra lung or kidney or a liver that can regenerate. The brain is constrained by the skull which is constrained at birth by the size of the

mother's pelvis. The brain is the most plastic organ in the body. It learns. Thus, age-related loss of cognition is also a function of dozens of genes and proteins associated with more or less resilience to brain pathologies. Third, age-related loss of cognition is also a function of additional pathologies and resilience indices that have yet to be discovered – the error term sitting at the end of the equation.

Where do we go from here? Among the things we stored from the blood were cryopreserved lymphocytes. Turns out we can make those into induced pluripotent stem cells (iPSC) which in turn can be coaxed into becoming neurons and glia. We found that a "population" of brain cells, with varying genetic risk, will spontaneously generate amyloid-β and tau proteins, the hallmarks of AD, and that these proteins are associated with brain amyloid-β and tau proteins and with cognition from the same set of humans. Further, they spontaneously generate resilience proteins which when modelled with the clinical and pathologic data from the same set of humans behave just like the proteins measured in the brain. We are now manipulating these cells in a dish hoping to carve out a path to precision medicine for common diseases of the brain and resilience to those diseases.



Data Portal



Responding to rapid change

DPUK's Data Portal is a mature trusted research environment at the cutting edge of rapid and secure data access. Its breadth of research data, multi-modal analysis environment, flexible governance models, and federation capabilities are unrivalled. With users in 51 countries, making over 1500 data access requests, and a median access-request decision time of 22 days, the Data Portal is setting new standards of data discoverability and access for the global scientific community. Big data is a fast-moving ecosystem and the Data Portal is an ongoing programme of development.

Multi-modality

Neurodegeneration is complex. Emerging research questions require data that are increasingly complex. This year we have increased our multi-modal capacity to include 19 imaging data sets and 16 genomic datasets. There is also ongoing development of pre-processing pipelines and access to our HPC cluster. These developments have resulted in over 100 access requests for multi-modal data.

Flexible collaboration

“One size fits all” collaborative models do not take account of the governance needs of different research groups. In response, we have developed a range of cost-effective options, each providing the operational advantage of a trusted research environment at either no cost or a fraction of the cost. Collaborating cohorts are invited to deposit data within the Data Portal at no cost. Collaborative spaces enable large and/or multi-site research projects to overcome local constraints such as storage or high-end computing or increased transparency across collaborating institutions. DPUK supports 3 collaborative spaces including MEMENTO and ON-FIRE. Research Hubs support and fast-track the collection, curation, and access of themed data collections. Each hub has its own identity and governance structures, but uses DPUK security and tooling. DPUK supports 6 hubs including BrainWaves, TBI Reporter, and the MND Accelerator.

“Nowhere else can such a range of high-quality dementia data be made available free at the point of use.”

**EMMA SQUIRES,
SENIOR DATA PORTAL
PROJECT MANAGER**



Federation

An extension of our flexible collaboration programme is federation. As Trusted Research Environments (TREs) proliferate, solutions for efficient data access across differing security requirements are required. In response DPUK has developed two models of data federation. In partnership with AD Data Initiative, DPUK has developed TRFX, a query submission system allowing researchers to submit queries to multiple TREs via any TRE with the TRFX software. Queries are undertaken using metadata ensuring that no researcher has direct access to data. TRFX allows DPUK to access the GA4GH task execution service and provides a standard mechanism for complex analyses across different computing environments. TRFX is being implemented between the Data Portal and AD Data Initiative's WorkBench and will in future be the basis for collaborations with Dementias Platform Australia, Dementia Platform Korea, and the Korean Brain Research Institute.

For situations where access to data is required, TELEPORT has been created in partnership with DARE UK. TELEPORT offers a neutral 'popup' trusted research environment

which incorporates the governance requirements of each participating platform. TELEPORT delivers equivalent security across trusted research environments. With data owners' approval, its use makes access and analysis possible across trusted research environments. Upon project completion, the 'pop-up' trusted research environment and its data contents are deleted. Teams at Swansea and Cardiff universities have recently demonstrated the viability of TELEPORT using data from the SAIL Data Bank and DPUK's Data Portal.

Cutting-edge governance

DPUK is at the cutting edge of how data is shared securely. For federated health data analyses DPUK has developed FEDHD, a six-tiered framework with measurable components for each type of data access. Standardising data governance approaches across trusted research environments enables communication, transparent sharing, and increases the potential of federated analytics.

Although there is heightened complexity, these AI models hold significant promise for integration into clinical healthcare systems, as well as research. In response DPUK has secured funding to establish a

community group to evaluate the risk posed by AI models and to develop guidelines for assessment and release of AI models from Trusted Research Environments.

Privacy and security means that personally identifiable information is not disclosed. The Data Portal team is leading a programme of work into automating methods of detecting personal identifiable information. Automating the detection of personally identifiable information will significantly reduce the time required for approving file-out procedures for trusted research environments.

Looking ahead: improving the user experience

In the coming year we will improve the user experience for data discovery and access. Our landscape tool Data Landscape Report - developed in collaboration with AD Data Initiative and the University of Nevada, will be enhanced to provide metadata for >700 population and clinical cohorts, >180 dementia trials, and >50 dementia research registries to enable researchers world-wide to find the best data, and recruit the best participants for their studies. For accessing data from DPUK collaborating cohorts we will be adopting a 'shopping basket' model for discovery and selection, making it easier to choose the most appropriate data and make request-approval easier.

The Data Portal has a growing number of multimodal datasets. In the last year **more than half the data access requests were for multimodal data.**

Free access to our large number of datasets is particularly valued by Early Career Researchers and appeals to an international community. We now have **users in 51 countries.**

To increase our multi-modal offer, we anticipate developing our genomics collections and **further developing both imaging and genomic pre-processing pipelines.**



Data Curation

A huge task with transformative impact



One of DPUK's most intensive projects is the data curation programme which makes data access significantly quicker and easier.

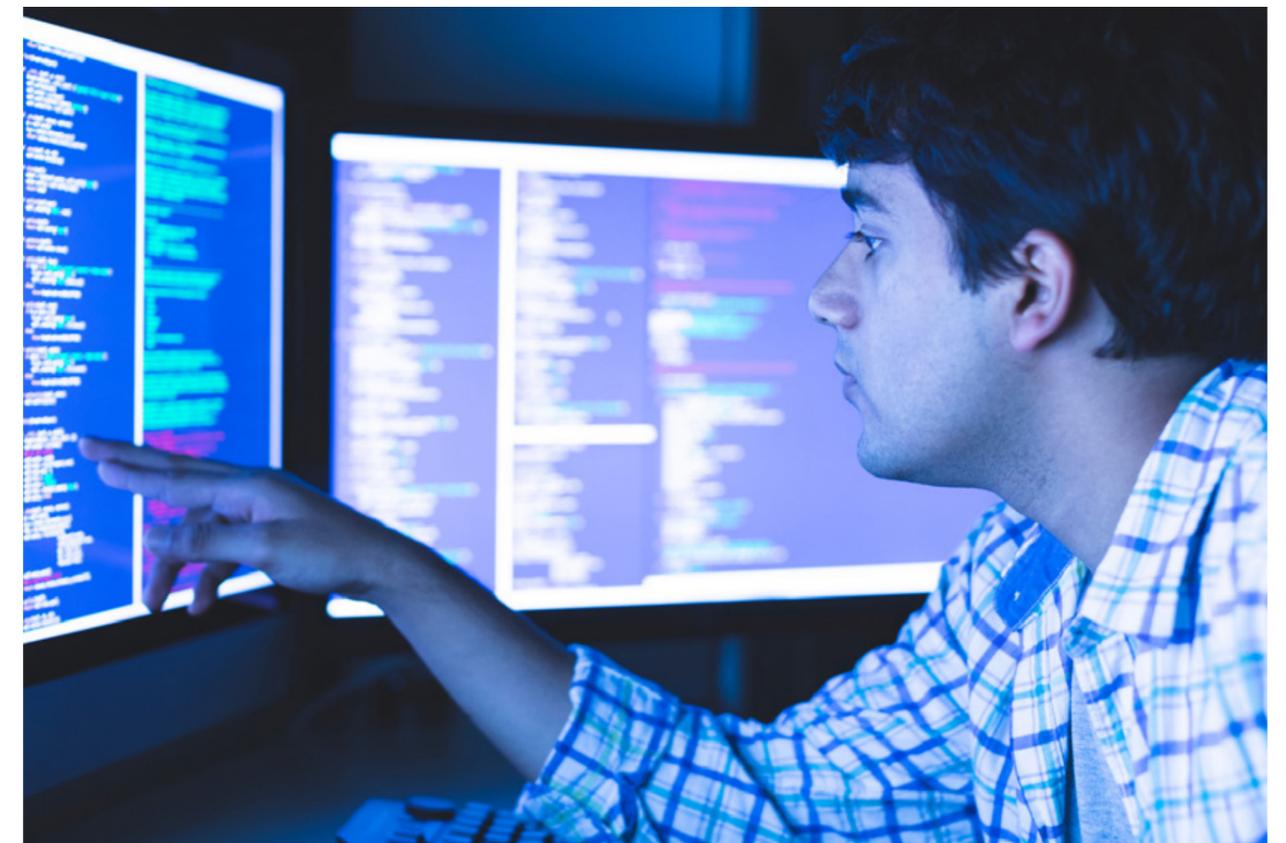
Professor Sarah Bauermeister explains more about our curation work.

Cohort data are highly variable in content and documentation, making discovery and 'cleaning' labour intensive and variable in quality. This leads to delayed and frequently non-reproducible analyses. By curating data to a single research-ready standard, DPUK simplifies data discovery and variable selection, improves rigour, facilitates rapid reproducibility, and reduces research cycle times in general. Our programme of curating DPUK data to the C-Surv model is ongoing with 23 cohorts sufficiently curated for data discovery purposes.

Data curation is labour intensive. To speed-up the process, working in partnership with AD Data Initiative, we are developing automated solutions that will reduce substantially the 'human element' in the process. This work will enable data curation to become accessible globally.

Data curation to a standard model is particularly helpful for federated analyses enabling data in different platforms to have the same structure and variable and value labelling conventions. To explore the potential of using a standard model across platforms, we are working with AD Data Initiative, and Dementias Platform Australia to curate datasets in each platform.

A further benefit of curation across multiple datasets is facilitating exploratory and feasibility analyses. In our data harmonisation programme, also in partnership with AD Data Initiative, we are using the C-Surv model to harmonise data across all cohorts whose data are held on DPUK's Data Portal. This allows preliminary analyses to be undertaken prior to making a formal data access request.



Collaboration

Widening access to vital research data



Dementias Platform UK has been working with the Alzheimer's Disease Data Initiative (AD Data Initiative) on improving ways of collaborating to make data more widely available. Niranjan Bose, Managing Director (Health & Life Science) at Gates Ventures says this federation work is going to significantly widen the availability of datasets to researchers internationally.

Enabling more researchers to find and access valuable study data is key to making breakthroughs in dementia research. The Alzheimer's Disease Data Initiative is a global coalition of leading academic, industry, government and not-for-profit

organisations, including the Medical Research Council, that recognises the need for dementia researchers to discover, access, and share data, tools, and scientific findings. The AD Workbench – a secure, cloud-based environment, is the interoperability layer of the AD Data Initiative's technical suite that supports researchers to make new discoveries by combining and analysing data that may be hosted on different platforms.

AD Data Initiative and DPUK are pursuing ways to overcome some of the biggest barriers to data sharing. Permissioned researchers using the AD Workbench can query data that resides on the DPUK Data Portal, thereby conforming to data governance rules. Expansion of this federated approach can serve to support more ubiquitous data sharing across the dementia research community. The AD Data Initiative also supports DPUK's pioneering work on the C-Surv data model to make dementia data discovery easier on the AD Workbench and DPUK's Data Portal. Ultimately, getting data out of silos is a long-term, wide-ranging effort, but the lessons learned to date help push innovation in data sharing and discoveries in dementia research.

The **Alzheimer's Disease Data Initiative** is a global coalition of leading academic, industry, government and nonprofit organizations that recognizes the need for dementia researchers to find easier ways to discover, access and share unpublished data, analytical tools, and scientific findings. The AD Data Initiative's strategy is based on three pillars: increasing interoperability so that researchers can combine and analyze data hosted on different platforms; unlocking datasets that have never been shared; and empowering researchers to make new discoveries. The coalition and its network of partners are working together to accelerate progress towards new diagnostics, treatments, and cures in Alzheimer's disease and related dementias.



Perspective

Delivering Trials



Treatments are coming. Great. But what next?

Susan Kohlhaas, Executive Director of Research and Partnerships at Alzheimer's Research UK, is one of DPUK's Associate Directors. She's been reflecting on where delivering trials, biomarkers and other new aspects of research are leading us.

We're at a bit of an inflection point in the field at the moment. We've got our first generation of treatments, but at best they have modest effects and some side-effects. However, having

these drugs is going to get people to seek out a diagnosis. This is important because only a third of people with dementia ever get a diagnosis at all.

The next generation of treatments and the arrival of blood biomarkers are both going to drive more people into clinics. That is an opportunity. We need to figure out how to bring these people into studies and start to get much more specific about what we are dealing with and understand the underlying diseases which are causing dementia.

What's really important is getting more triallists into the field. That will be crucial in the next few years. With DPUK's Data Portal, Trials Delivery Framework and Experimental Medicine Incubator, some of the fundamental infrastructure is in place to move ahead confidently.

Of course, we need to think about where the next opportunities lie. Right now, we need to plan on being much more specific about who we are bringing into trials. DPUK's large registers of people who are highly characterised makes a difference. The

more we can match the right people to trials the better. For instance, we know that amyloid is beginning to build up at least 20 years before you get any noticeable symptoms and there are a number of early indications we know to be linked with developing dementia later in life.

There are real challenges with long-term follow-up with trials: retention issues and costs. We have to decide how we collect data and follow people in the long term from an early stage. And we need to think about how we link up this type of data with other datasets.

DPUK makes the use of datasets easier. Now, I think we have to really increase data sharing with a spirit of openness in approach. The worst thing we can do as a research community is split things out and not work openly: it is not in our interests or the interests of people affected by dementia. People affected by dementia want to see their data used to the benefit of developing treatments and finding better ways to diagnose diseases.



"I think we have to really increase data sharing with a spirit of openness in approach."

Delivering Trials

The Trials Delivery Framework:

The right people for the right project in the right place

Overview

DPUK's Trials Delivery Framework (TDF), led by Dr Vanessa Raymont, is in its second year of creating an integrated, UK-wide ecosystem to deliver dementia-focussed clinical trials. Our objective is to provide more representative, real world data for targeted trials; reducing screen failure, mis-diagnosis, and contracting delays.

Trials Network

DPUK now has the biggest characterised dementia trials network in the UK, covering 25% of all NHS Trusts and 25% of UK GP practices.

Trials registers

For trials in patients with early dementia or who are at high dementia risk, we have a network of 52 memory

and brain health clinic sites across England, Wales and Northern Ireland, 14 sites in Scotland, as well as two primary-care networks that cover over 2000 GP practices across the UK. For nine of our network sites we are able to use health records for targeted, risk-stratified, recontact.

For pre-clinical trials, and providing healthy controls, Dr Ivan Koychev leads two public-facing registers. The Great Minds (GM) register comprises >10k volunteers with medical history, genotyping and serial cognition and has a rolling programme of activity assessments. The Clinical Studies Register (CSR) comprises >58k volunteers with medical history and cognition, of which over 20,000 have genotyping. Both GM and CSR allow targeted recruitment to trials through explicit informed consent for risk-stratified recontact. 26 studies have used these registers for recruitment.

Increasing UK capacity

A major limitation for the UK dementia community is the availability of trained staff, standardised procedures and uniform contract processes to conduct trials. To increase UK capacity, we are facilitating mentoring and staff training across our TDF sites. The network is also discussing operational procedures and standardised contracts.

Broad reach

The TDF is closely aligned with DPUK's Experimental Medicine Incubator and industry partners. We are constantly looking for opportunities to expand our network of like-minded organisations to support and deliver dementia research. The TDF is also working with the National Institute for Health and Care Research (NIHR) Join Dementia Research (JDR) initiative and has partnered with 14 sites that are part of NHS Research Scotland to deliver UK-wide recruitment solutions for trials.

We also have agreements with other international networks, such as the Global Alzheimer's Platform (GAP), the Davos Alzheimer's Collaborative and the International Registry for Alzheimer's Disease and other Dementias (InRAD) to provide truly worldwide coverage for the delivery of dementia research.

Biomarker development

We are excited that DPUK's TDF, through the leadership of Vanessa Raymont, Ivan Koychev and James Rowe secured £4.5 million of funding through the Blood Biomarker Challenge. The READ-OUT study, which is a collaboration covering all four home nations and 14 integrated care boards, will conduct an observational study and randomised control trial to assess the utility and cost effectiveness of blood biomarkers for identifying Alzheimer's and other

diseases that lead to dementia with increased precision. The goal of READ-OUT is to identify simple, scalable, multi-modal biomarkers for diagnosis and progression, that will inform trials design. We are also partnering with industry including Lilly, Eisai and Roche Diagnostics to support this project and develop a network of sites able to deliver blood biomarker assays across the UK.

Ecosystem development

Two globally leading industry partners, Lilly and Roche Diagnostics, are working with us to assess the feasibility of increasing cerebrospinal fluid (CSF) biomarker testing in mental health-based memory clinics. So far, four pilot sites at Manchester, Sheffield, Sussex and Oxford are involved in this collaboration and we hope to expand this study to further TDF sites in future. This pilot study aims to assess whether CSF testing improves diagnostic accuracy in real-world memory clinics, and to understand how to implement CSF testing at scale. Together with our health economics team, we will start to assess the benefits of CSF testing for clinicians, patients, and the healthcare system as a whole to develop a compelling case for commissioning this service.

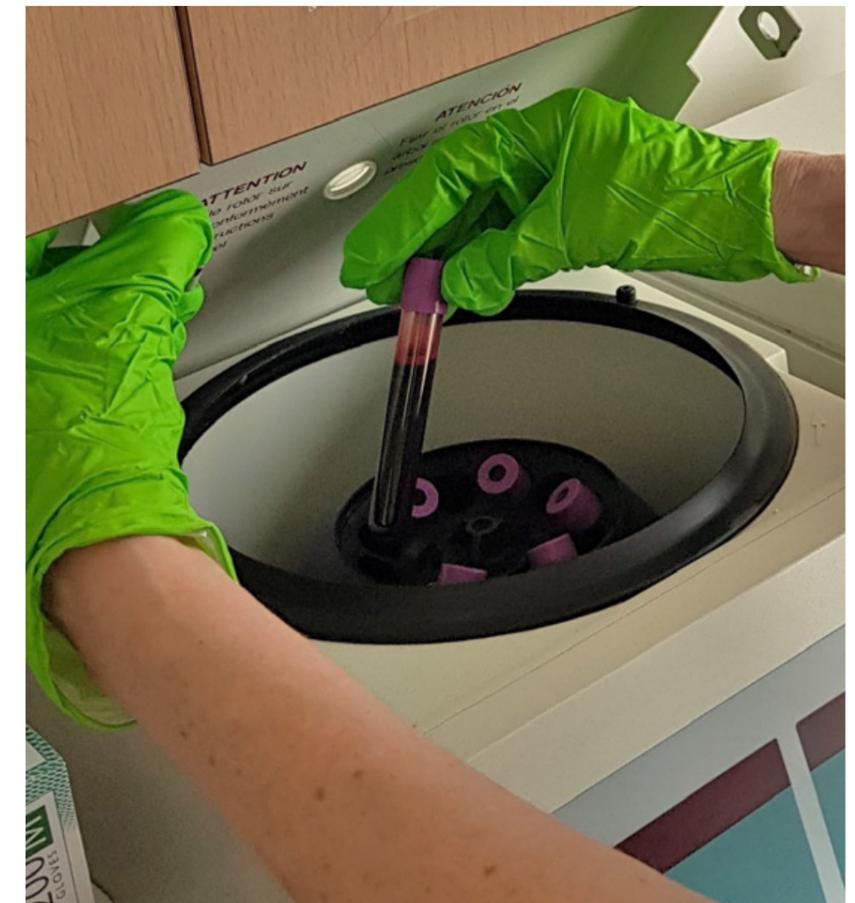
The way ahead

DPUK is committed to collaboration, ensuring clinical trials can be conducted as quickly and effectively as possible. To this end, the TDF looks forward to aligning with the Dame Barbara Windsor Dementia Mission, MRC Dementia Trials Accelerator and the NIHR Dementia Translational Research Collaboration (D-TRC).



Great Minds register surges past 10,000 volunteers

Enrolment into the Great Minds register has continued at a fast rate and in January 2024 passed the milestone 10,000 mark. It is hard to exaggerate the value to researchers of such a large number of people willing to participate in studies. They are highly characterised, enabling faster and more accurate recruitment. It can take time to find suitable volunteers, and assemble the right information about them for a study to begin. Great Minds is making it easier for scientists to overcome these time-consuming obstacles to research.



Perspective

Translation in the dementia landscape



The MRC's new director, Patrick Chinnery says DPUK's translation work is central to the UK's dementia research.

DPUK's translation programmes have never been more relevant or timely. Whether it be informatics, trials recruitment, or human mechanistic

studies, DPUK is at the heart of Government's Barbara Windsor Dementia Mission.

The Mission is grounded in collaboration across the whole dementia landscape, from researchers to regulatory bodies, and of course the NHS. MRC is supporting the Mission with up to £20m being invested through the MRC Dementia Trials Accelerator. This will deliver new measures to boost clinical trials, including rolling out AI technologies to support researchers, and establishing a trial-ready cohort of circa 20,000 at-risk individuals who could be available for community-based trials at short notice.

At the heart of the Mission is involving those directly affected by the condition. This drives and informs the research programme. MRC is delighted

to work with Scott Mitchell, the newly appointed 'People's Champion' to the Mission. Together, and alongside other partners, we will help shape the dementia ecosystem.

Now that the first generation of Alzheimer's treatments is coming through, the UK needs to position itself to support developing the next generation of treatments. This will require fast and flexible mechanistic studies and trials. Delivering these also involves efficient contracting, recruitment and execution. At MRC we will support the innovation necessary at all levels to deliver a fit-for-purpose dementia research ecosystem.

As the Mission unfolds, we at MRC look forward to building on the work of DPUK to position the UK at the cutting-edge of dementias translation.



Experimental Medicine

The Biomarker Revolution



Leading biomarker researcher Professor Charlotte Teunissen describes how we are on the cusp of a biomarker revolution!

The licensing of the first generation of disease modifying therapies for Alzheimer's disease (AD) has generated new interest into the mechanisms underlying neurodegeneration. Key to progressing our understanding are biomarkers. Biomarkers can be used to detect risk of developing disease, diagnosis of existing disease, the likely outcome of a disease process, and the rate of disease progression. For drug development biomarkers can be used for assessing pharmacodynamic response to a new agent, and for safety testing.

However, neurodegeneration is complex with different pathways and multiple pathologies operating simultaneously. If we take AD for example, the genetic risk of APOE status translates into increased amyloid deposition which in turn is related to Tau deposition prior to apoptosis. However, amyloid deposition is also related to inflammatory and vascular changes affecting synaptic function, neurodegeneration generally and

risk of vascular dementia. The value of biomarkers for translation is in their scalability. Blood-based biomarkers are rapidly replacing more expensive and invasive technologies such as molecular brain scans and cerebrospinal fluid. And here lies the revolution.

A new generation of scalable, inexpensive, and mechanism-specific biomarkers have the potential to accelerate drug development. Through targeted recruitment, reduced screen failure, and increased statistical power, biomarkers reduce the risk and cost of trial failure. A new generation of biomarkers also makes feasible population screening and early detection.

Collectively, this makes a virtuous circle where mechanism specific-interventions can be used for early intervention in risk-stratified targeted populations so that whilst we may not be able to eliminate neurodegeneration, we can at least be confident that we needn't die of neurodegeneration.

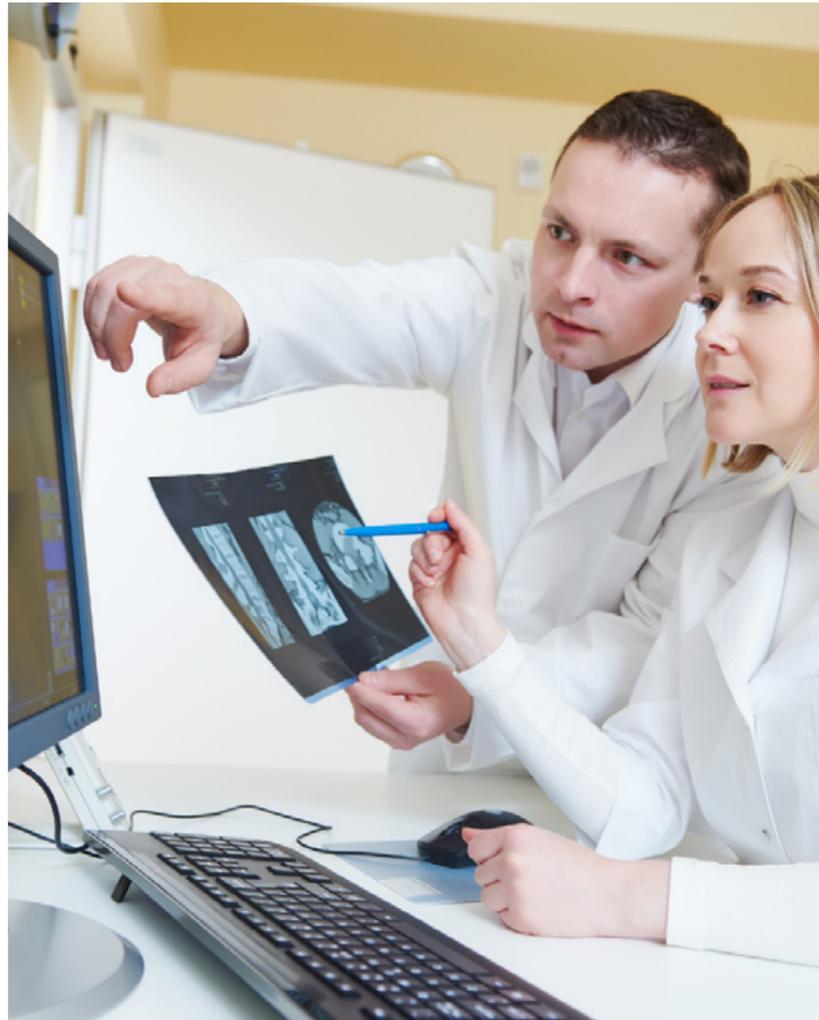
"A new generation of scalable, inexpensive, and mechanism-specific biomarkers have the potential to accelerate drug development."

Experimental Medicine Incubator



Professor James Rowe leads the DPUK Experimental Medicine Incubator. The role of the Incubator is to work with industry and academic partners to develop new methods to improve the success of clinical trials and targeting of therapies.

The Incubator works closely with the DPUK Trials Delivery Framework. For example, the Blood Biomarker Challenge-funded READ-OUT study will evaluate diverse biomarkers for early diagnosis and prognosis. Our experimental medicine ethos underpins the £6m MND Accelerator programme, administered by DPUK on behalf of MRC. The Incubator programme is focussed on three aspects of dementia, synaptic health, neuroimmunology, and vascular health. Our teams comprise academic and industry partners across the UK, working closely with people affected by Alzheimer's disease and other forms of dementia.



Synaptic Health

This theme is working on the determinants of synaptic loss. The Synaptic Health In Neurodegeneration study (SHINE) examines how the loss of synapses (measured by PET, and corroborated in blood), leads to the change in brain physiology (measured by MEG), as the basis for cognitive decline. Synapse numbers are very closely related to cognition in dementias, and they are damaged by multiple “upstream” processes like amyloid- and tau-aggregation, metabolic stress and inflammation. SHINE's longitudinal design will test MEG, PET and blood as suitable tools for synapse-focussed trials.

The New Therapeutics in Alzheimer's disease study (NTAD) tests the ability of MEG to detect and monitor the impact of Alzheimer's disease. MEG was found to be well-tolerated by people with Alzheimer's dementia and mild cognitive impairment, highly reliable, and sufficiently sensitive to change over 12 months to detect a meaningful effect of a drug designed to slow disease progression.

Through the Deep and Frequent Phenotyping study, we are now studying the utility of MEG in pre-symptomatic Alzheimer's disease. In parallel work with synaptic-PET, we have shown that the loss of synapses explains much of the change in MEG. One of the reasons that the brain loses synapses is the direct damage done by the brain's immune system, especially the activated microglia, that are studied by the DPUK Neuroimmunology team.



Neuroimmunology

This theme, led by John O'Brien (Cambridge), is working on blood, brain, CSF and genetic aspects of neuroinflammation. The Immune Profiling in Early Cognitive Disorders study (IMPRINT) is using immunophenotyping to detect the chemical ‘fingerprint’ of immunity in Alzheimer's disease and dementia with Lewy bodies. The team has shown that there is consistent pattern of cytokine increase across all the major degenerative dementias. With 120 participants so far, IMPRINT is already beginning annual follow-up assessments to identify the immunological changes associated with fast and slow disease progression.

The Imaging of the Purigenic P2x7 receptor in Alzheimer's and Lewy Body Cognitive Disorders study (IMPACT) study has undertaken pre-clinical ligand synthesis and autoradiography work of the first of a new generation of PET ligands for inflammation (with Prof. Franklin Aigbirhio and Dr Abhishekh Ashok), and now has ethical approval to scan volunteers with dementia.

Building on the core DPUK collaborative ethos and our Incubator and Data Portal programmes, the new Open Network for Frontotemporal dementia Inflammation Research (ONFIRE), is a national platform with more than 20 UK centres. Cure PSP have funded an extension of this work to PSP and CBD; while ARUK has funded an additional PhD studentship to join ONFIRE.

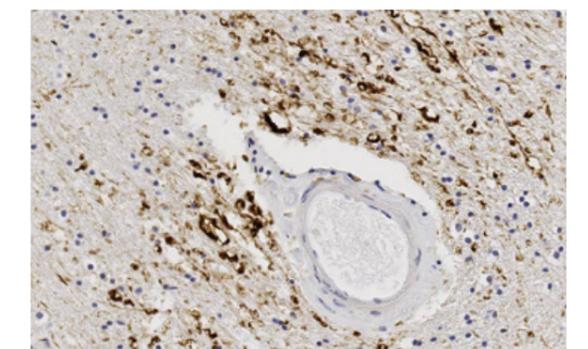
DPUK's Neuroimmunology team works closely with colleagues in the UK Dementia Research Institute, to identify inflammatory genetic biomarkers using largescale human cohort data from the DPUK Data Portal. In collaboration with Professor Valentina Escott-Price, the DPUK Neuroimmunology team is identifying the impact of polygenic inflammatory risk on the onset and progression of cognitive decline. We found a microglia gene-set produces comparable heritability estimates to more complex genetic predictions. The largest GWAS to date found a cluster of variants at the MAPT and APOE loci, and a potential novel locus near RPSA and MOB1 – the latter creating a potential genetic risk in common between frontotemporal dementia to Alzheimer's, motor neuron-disease and PSP.

Vascular Health

This theme, led by Atticus Hainsworth (St George's University of London), uses big data to identify the vascular determinants of brain health and potential therapies. Terry Quinn of Glasgow University is targeting drug repurposing for vascular dementia using UK Biobank. Initial results have identified several drug types as potential therapies. Hugh Markus of Cambridge University is using Mendelian Randomisation to identify risk factors for small vessel disease. Joanna Wardlaw of Edinburgh University continues to refine imaging biomarkers for small vessel disease. This programme is significant in identifying non-amyloid and non-tau related pathways for treating dementia.

The vascular theme is highly collaborative. A focussed workshop, chaired by Stuart Allan and Atticus Hainsworth in partnership with the Medicines Discovery Catapult, brought together representatives from DPUK, pharma industry, Dementia Mission, charitable funders and the UK Dementia Research Institute. Their report, on the priorities for vascular dementia research, is published at <https://md.catapult.org.uk/resources/collaborative-opportunities-in-vascular-dementia>.

A DPUK-DRI workshop, co-chaired by Atticus Hainsworth and Joanna Wardlaw, led to a position statement on preclinical research relevant to vascular dementia (Sri et al., 2023). A second DPUK-DRI workshop, in partnership with the Physiological Society, focused on opportunities for early career researchers. This contributed to the DPUK partnership being awarded a new UK Alzheimer's Society doctoral training programme spanning Manchester, Edinburgh, St Georges, UCL and Imperial, will support 29 PhD studentships, building substantial research capacity in the field of vascular and inflammatory determinants of dementia.



Vascular and degenerative processes in dementia are linked: here one can see swollen axons containing hyper-phosphorylated neurofilaments (brown), around a small artery in the deep white matter of an older person with small vessel disease. From Hainsworth et al. 2024.

Data Portal Hubs

Embracing the unexpected to accelerate the search for treatments for MND



DPUK's resources are helping motor neuron disease research to progress at a quicker pace. Dr Jane Haley, Director of Research at MND Scotland and a member of the MND Accelerator's Executive explains more.

Following a year-long campaign by patients, charities and researchers, in November 2021 the UK Government announced a £50 million investment into motor neuron disease (MND) research. Fast forward two years and much of that money is starting to be made available, and sometimes in unexpected ways.

In Autumn 2023, Dementias Platform UK (DPUK) launched the MND Accelerator – a funding call which

will make available £6 million from the Medical Research Council and National Institute for Health and Care Research. On first inspection, releasing funding for MND research via a dementia platform seems unusual. However, embracing the unexpected is sometime the route which bears most fruit.

MND research has historically suffered from under investment but, more recently, it has grown exponentially, leading to the identification of many new targets, and placing it at the forefront of neurodegeneration research. What remains lacking is access to large, integrated facilities such as those created to support dementia research. With a shared interest in the mechanisms of neurodegeneration and a clear overlap between some types of MND and frontotemporal dementia, there are good reasons to believe that research in one area could inform and illuminate the other.

The MND Accelerator invited researchers interested in MND to create applications that address key mechanistic questions that could lead directly to translation into humans, whilst drawing on DPUK and UK DRI facilities, thus providing a new spectrum of support and expertise.

Equally, by sharing facilities and knowledge with their colleagues in MND, dementia researchers have the opportunity to collaborate and help speed up the search for MND treatments. This is something that I hope will be embraced.

Of course, collaboration and sharing of knowledge and experience isn't only the preserve of researchers and it was very important to the three main UK MND charities (MND Association, MND Scotland and My Name's Doddie Foundation) that the perspectives of people affected by MND were also part of the process. DPUK embraced this and, as well as inviting the charities to participate, every stage of the grant reviewing process involves lay members who either have MND or have been affected by it.

There is strength in working together and I sincerely hope that with dementia and MND researchers converging, together with input from people affected by the disease, we can accelerate the search for meaningful treatments for people with MND, one of the most devastating diseases imaginable.

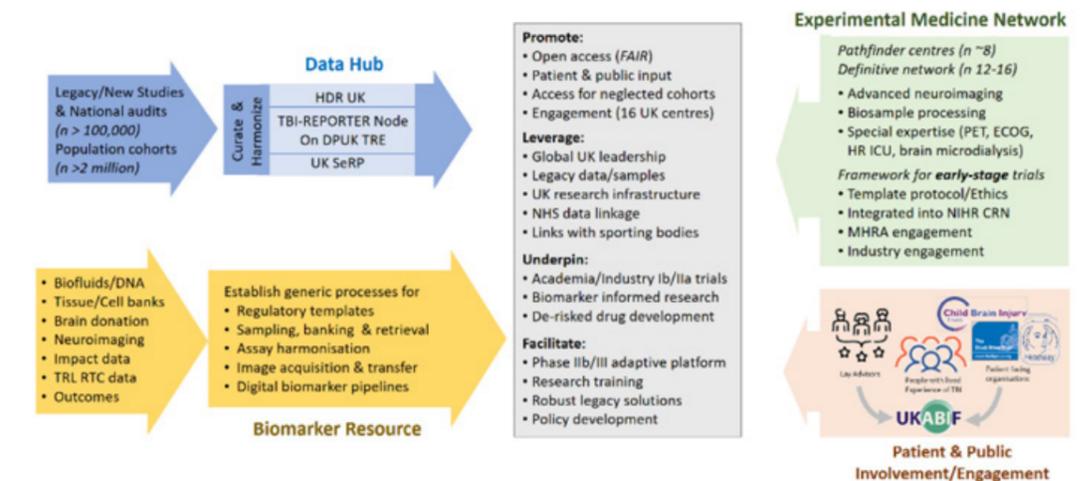
You can find out more about the MND Accelerator at www.mndacc.com



TBI-Reporter hub

UK TBI-Repository and Data Portal Enabling Discovery (TBI-REPORTER)

Traumatic brain injury (TBI) is a leading cause of death and disability, with a cost to the UK economy over £10 billion/year, and the global economy over \$400 billion annually. Further, TBI impacts lifelong health outcomes in survivors, contributing to increased risk of neurodegenerative disease, epilepsy and adverse mental health outcomes and reducing life expectancy. **UK-TBI REpository and data PORTal Enabling discoverY (TBI-REPORTER; <https://tbi-reporter.uk/>)**, is a £10 million project, funded by a consortium of UK research funders led by the Medical Research Council. TBI-REPORTER will facilitate research in TBI across the lifespan, addressing all injury severities and a broad spectrum of exposures (including: military personnel, athletes, prisoners, homeless individuals, and victims of intimate partner violence). TBI-REPORTER comprises a Data Hub, a National Biomarker Resource, and an Experimental Medicine Network, supported by a strong Patient and Public Involvement and Engagement initiative (see figure below). The TBI-REPORTER Data Hub will collate and curate TBI research data at scale, working as a node in the DPUK Data Portal and work with HDRUK to establish linkage with existing UK datasets.



UK Nervous Tissue Network hub

A one-stop-shop for neurological tissue research

Professor Alan Thomas, Director of Brains for Dementia Research, says huge advances have been made in recent years in understanding how our brain and the related nervous system works and DPUK's Data Portal is making a contribution to a network for researchers.

Much of this learning has either come from, or is confirmed by, donated nervous tissue. However, human nervous tissue is not currently widely available, especially that from outside the brain.

The UK Nervous Tissue Network aims to provide high-quality tissue, cells and data to neuroscientists around the world, to enhance our ability to understand the many pathologies underlying neurodegeneration.

Through partnership with DPUK, the UK Nervous Tissue Network (bringing together expertise from Newcastle, Oxford, Swansea, Exeter, King's College London and University College London) will provide a one-stop-shop enabling researchers from academia and industry to identify and apply for use of data and materials. In the DPUK Data Portal, genomic, epigenomic, and ultimately NHS data will be brought together and linked to individuals within a secure, privacy preserving, environment. These data will, in turn, be linked to the biofluids, organoids and spheroids and, finally, the donated nervous tissue. These materials will be stored in Human Tissue Authority approved tissue banks. Using prompt tissue distribution procedures from the Brains for Dementia Research study, tissue will be made accessible to the wider scientific community.

Perspective

Expanding horizons for population datasets can impact the direction of dementia research in future



The UK's largest health research programme, Our Future Health, is gathering data from people across the country. A game-changing opportunity awaits, says its chief executive, Dr Raghbir Ali OBE

What could dementia researchers learn if they had access to millions of peoples' genotypes, health records, and lifestyle information? What translational research could they conduct if they had the ability to identify subsets of these people and re-contact them for follow-up studies? We will soon start to see the answers to these questions – and it could be a

game-changing moment in the field of dementia research.

18 months ago, Our Future Health launched to the public, with the aim of building the largest longitudinal research cohort in the world to enable new discoveries in the prevention, detection, and treatment of common diseases. We're bringing together up to five million people, who share with us their genetic data, their linked health records, and information about their lifestyle. They also consent to a feedback and re-contact mechanism, which means we can go back to them in the future and ask for further participation in research.

Since we launched, on average one adult has signed up every minute of every day. Over one and a quarter million people in the UK have now consented to link their health data – and 600,000 have attended appointments to donate blood samples. We're committed to building a cohort that reflects the UK population and includes groups that have previously been under-represented in this type of research – particularly from ethnic minorities and more deprived backgrounds.

For dementia researchers, Our Future Health's resource should offer rich opportunities for discovery and translational research. We already have data from over 400,000 people in the 60+ age bracket. By studying linked health records and stored blood samples, researchers will be able to see who goes on to develop dementia, and use the results to better identify people at high risk of the disease. From there, we can develop disease risk scores and feed them back to consenting participants. The process will enable dementia researchers to test the clinical utility and cost effectiveness of new risk-stratified screening programmes.

Of course, identifying people at high risk is of no great use when interventions either don't exist or aren't practicable. Here, our re-contact mechanism will help researchers to use a pre-screened cohort who are at higher risk for clinical trials. Those trials should be quicker and cheaper to run as a result. We're working with the Dementia Mission, DPUK, Dementia Research Institute, and HDRUK, as well as researchers from the NHS, academia and industry, to make sure our resource is as useful as possible.



Collaborative advanced data infrastructure can accelerate neurodegenerative research



Professor Andrew Morris, Director of Health Data Research UK sees close collaboration as essential feature of the dementia landscape

Collaborative research fosters validation and reproducibility of findings and accelerates impact. When multiple research teams independently analyse shared datasets and corroborate each other's results, it increases confidence in the reliability and robustness of the findings. The United Kingdom has the opportunity to

assemble an outstanding trustworthy data research ecosystem to power neurodegenerative research. DPUK has led the way in assembling data that is FAIR – findable, accessible, interoperable and reusable. Its Data Portal, led by the outstanding Secure eResearch Platform (SeRP) team at the University of Swansea, is working in partnership with researchers and data controllers of 63 population and clinical research cohorts describing 3.5 million participants. The Data Portal has solved many of the knotty issues of data curation and data management, and the pipelines and tools provide insight to common data management challenges. It has exemplified the power of delivering an advanced data infrastructure as a service to empower innovative research.

Neurodegeneration research generates vast amounts of diverse data including genomic, proteomic, imaging, clinical, laboratory and behavioural data. These data require sophisticated analysis platforms to support advanced computational approaches (e.g.

AI), while maintaining security and privacy. Health Data Research UK (HDR UK) and DPUK have existing strong partnerships with the European Bioinformatics Institute and UK Dementia Research Institute, ensuring a seamless interface to the molecular data resources and expertise available across these organisations, which will be vital to understanding the underpinning determinants of a wide range of neurodegenerative diseases.

It has been a privilege for HDR UK to work in partnership with DPUK in our quest to assemble infrastructure data and services that meet the diverse needs of the research community. We are, however, only in the foothills of where we need to be – the opportunity now is to integrate complex data – at the pace and scale required to enable neurodegenerative research and to support clinical trial delivery to ultimately provide new and much needed treatments and preventive strategies for patients.



Perspective

The dementia research community has a mission to manage complexity at pace and scale



A perspective by Professor Siddharthan Chandran – Director, UK Dementia Research Institute

With disease-modifying therapies on the horizon, the rapid evolution of cutting-edge technologies and the staggering possibilities opened by data science and AI, we are now at a tipping point for dementia research. Now more than ever, it is the time to accelerate our pace, scale up and step up to new

levels – and we must do so together.

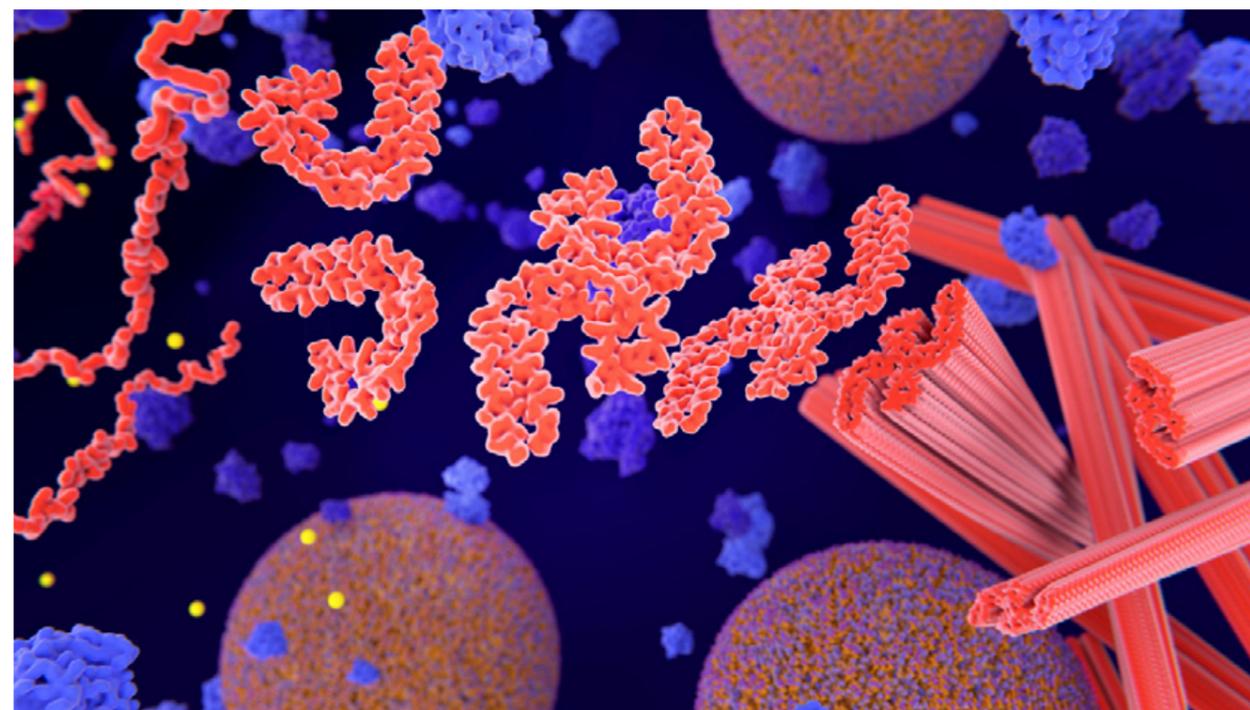
Unravelling the complexity of dementia requires a multidisciplinary approach, where synergistic interplay between in-human and pre-clinical experimental research models becomes pivotal to advance translational medicine.

But more can be achieved if we are able to fully realise the bi-directional opportunities of working with DPUK and taking advantage of its experimental medicine, cohorts and clinical trials programmes to inform our understanding of disease biology through the ‘translational circle’. We need to get better at linking discovery science with highly phenotyped longitudinal cohorts, leading to identification of new biomarkers, disease mechanisms and targets. This will be one of the key objectives for the UK DRI in this second quinquennium, and we will be able to achieve it only in collaboration with partners

including HDR UK and DPUK in a more connected and integrated UK dementia ecosystem.

Central to this, will be working alongside DPUK and HDR UK to efficiently integrate clinical and preclinical insights, leverage large datasets including those produced by the advanced ‘omics revolution. Here too, there is still much room for improvement, starting from the need of reaching consensus in data/metadata standards, to harmonisation in dementia phenotyping measures, and implementation of appropriate strategies and infrastructure, such as those of DPUK, to incentivise data sharing.

It is only by embracing data integration, interdisciplinarity and meaningful public engagement that we will ultimately begin to improve outcomes for people living with or at risk of dementia.



Alzheimer's disease: Tau proteins aggregate to neurofibrillary tangles and neuritic plaques in a neuron axon (Getty Images)

Next steps for the Dame Barbara Windsor Dementia Mission



Hilary Evans, Chief Executive of Alzheimer's Research UK and Co-Chair of the Dame Barbara Windsor Dementia Mission

I'm one year into my tenure as Co-Chair of the Dame Barbara Windsor Dementia Mission, and I find myself invigorated by the ongoing momentum in UK dementia research. The Dame Barbara Windsor Dementia Mission is driven by a clear and ambitious goal - to accelerate the search for effective dementia treatments. And it's been

brilliant to work alongside my fellow Co-Chair, Nadeem Sarwar, and Scott Mitchell, the husband of the late, beloved Dame Barbara Windsor, as well as other experts and organisations in the field, to get this work off the ground.

At the forefront of our work is the establishment of the Neurodegeneration Initiative. Forged in partnership with leading life science companies, the Initiative will develop new biomarkers to improve the way people are matched to clinical trials and help bring us closer to finding new treatments. Central to this programme is Dementias Platform UK. With its big-data infrastructure, trials registers and networks, and experimental medicine programme, DPUK is well placed to make a significant contribution to this initiative. Through DPUK and other partners we want to ensure that the UK is a choice location for industry, to enable people here to take part and benefit from potential new medicines.

This area of work extends beyond the realms of scientific inquiry and is an

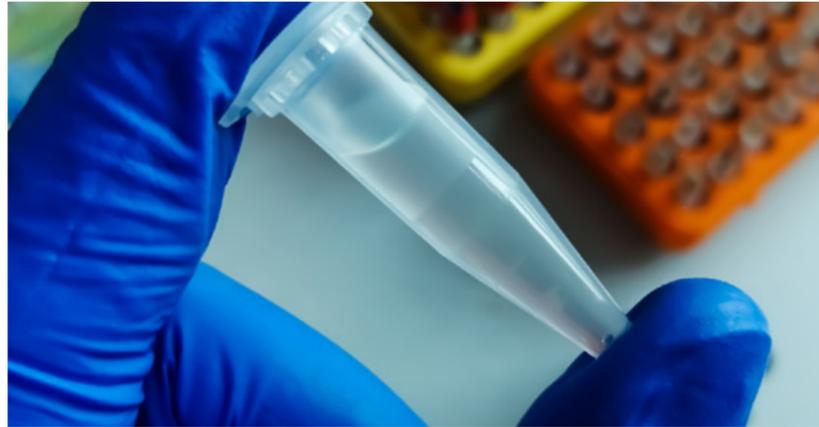
important area where the UK economy is growing. Recent modelling from Alzheimer's Research UK showed that every £1 invested in dementia research generated £2.59 within the UK economy during 2019/2020.

The Mission has also offered a platform for the UK to make progress on preparing the health system for the arrival of first-of-a-kind treatments. The Mission is bringing together key government agencies, such as the Medicines and Healthcare products Regulatory Agency, to explore what more can be done to decrease the time it takes to get new treatments to people who need them.

Putting first the views and experience of people affected by dementia remains at the heart of what we do. And as we stand on the cusp of a new era in dementia research, I hope the Mission will serve as a shining example of what can be achieved when we work together towards a common goal.

Associated studies

Dementias Platform UK's resources and capabilities exist to enable research by providing the infrastructure, services and tools to achieve high quality research. Here are some of the studies and projects which are using DPUK to further their research activities.



CSF project

Clinicians and researchers in Oxford, Manchester, Sheffield and Sussex, together with partners at Lilly and Roche Diagnostics, are working to pilot the at-scale collection and testing of CSF tests in memory clinics.

Analysing cerebrospinal fluid (CSF) is a simple procedure which may help to diagnose diseases of the brain, particularly dementias. Our goal is to improve diagnostic accuracy and to understand the effect of an accurate diagnosis for patients and their families. By the end of this project we will understand how CSF testing can be implemented across the United Kingdom, and will develop a case for commissioning this service in NHS trusts.

Gotcha!

The Gotcha! study is an investigation into whether people with Alzheimer's disease presenting with difficulty naming people they know well would benefit from a digital-neurointervention. The study, which is run by University College, London, will assess whether the intervention is effective at improving naming impairments. Both the Great Minds register and the Trials Delivery Framework sites provided recruits to this study.

CognoSpeak

CognoSpeak is a study which uses a tool to assess cognition by engaging participants in conversation – something that is known to place a high demand on multiple cognitive domains involving memory, language and attention. Led by Dan Blackburn from the University of Sheffield, the study has recruited from DPUK's Great Minds register. The early detection of memory problems is important for patient care and wellbeing, and the tool provides potential improvements in cost, speed and accuracy of the NHS memory assessment pathway.

LACI studies

The Lacunar Intervention Trial-2 (LACI-2) tested two widely available drugs licenced for other vascular diseases on 400 participants after lacunar stroke, using a factorial design. It showed that these drugs could potentially prevent recurrent stroke and improve cognitive outcomes and quality of life, with synergy between the drugs. DPUK are planning to support the testing of these drugs in other clinical presentations of small vessel disease in a trial assessing vascular cognitive impairment and dementia, and a phase 3 trial in 1300 patients with lacunar stroke, to facilitate licence extension for the drugs considered.

FAST study

The Feasibility and Acceptability of Scalable Tests (FAST) brain health study, conducted by the Dementias Platform UK team, has recruited 573 participants across 15 active sites, with more than 10 additional sites in set-up. This research investigates the relationship between changes in memory and cognition, and corresponding changes detectable from blood samples. Serving as a pilot study, FAST will pave the way for a larger nationwide investigation into blood biomarkers for brain health, particularly focusing on dementia and memory disorders. Notably, over 100 participants have completed their six-month visit, and more than 20 have successfully finished their 12-month follow-up, showcasing the commitment and engagement of participants in contributing to the research.

The study spans a one-year commitment, involving three visits: an initial clinic visit, a remote cognitive test at six months, and a final clinic visit at one year. During clinic visits, participants undergo blood sample collection, computer-based cognitive testing, and provide feedback via a short questionnaire. Remote cognitive testing comprises the six-month follow-up. The study aims to gauge participant acceptability and feasibility of the processes involved, laying the foundations for future nationwide research.



Dr. Maura Malpetti is working on the ON-FIRE study

DPUK APOE genotyping

DPUK has recognised the importance of variations in the Apolipoprotein E (APOE) allele and the contribution this makes to the progression of Alzheimer's Disease. We have increased testing and genotyping amongst our various registers, including the Great Minds register.

By analysing whether individuals have specific polymorphisms of APOE we can ascertain the polygenic risk individuals have of developing the Alzheimer's disease. Utilising this data is aiding the development of precision medicines tailored to individuals and to cohorts, whilst, at the same time, indicating new avenues for early treatment.

ON-FIRE

The DPUK Neuroimmunology Team has set up a new national study of frontotemporal dementia. The Open Network for Frontotemporal dementia Inflammation Research (ON-FIRE) works with blood samples from >20 specialist and non-specialist clinics across the UK, including communities and remote areas that are too often under-represented in research. Dr Malpetti who leads the ON-FIRE study has recently discovered that blood tests of the immune system can detect changes associated with brain-inflammation and clinical progression.

The new study will also look at genetic and environmental factors that influence the immune system signatures, and optimise inflammation assays for frontotemporal dementia. Associated with DPUK's Neuroimmunology Theme, ON-FIRE is based on collaboration and sharing, with the goal of accelerating clinical trials and new immunotherapeutic strategies.

BIOFIND

BIOFIND and BIOFIND-FTD, are large EEG data releases for AD/MCI and FTD respectively: the former is already available on the Data Portal and the latter will be released later this year. "BIOFIND provides a large multicentre EEG dataset for researchers to study the effects of Alzheimer's disease on brain function - whether to develop better diagnostics or test advanced models of the human disease. Through the Data Portal, we will shortly release a companion dataset of EEG and MEG data to study the effects of Frontotemporal dementia, which is biologically and clinically distinct from Alzheimer's disease.

SENDER (Synaptic evaluation in neuro degeneration dementia and related conditions)

DPUK's PET imaging network, including Franklin Aigbirhio, John O'Brien and James Rowe (Cambridge), have been leading the study of synaptic health in diverse dementias, including Alzheimer's disease, PSP, CBD, Frontotemporal dementia, and Lewy body dementia. We have shown that synaptic loss is severe, early, progressive, and closely linked to cognition because of its impact on microscopic and macroscopic connectivity.

Supranuclear palsy Inflammation study

As part of the Neuroimmunology Theme, Cambridge's research team has started a new study looking at the inflammation signature in people with progressive supranuclear palsy and corticobasal syndrome.

This complements the already ongoing research within the theme on Alzheimer's, DLB and FTD. They are looking at blood-based biomarkers for inflammation, including cytokines, immune cells and the complement system. Samples will be shared across the 22 participating centres and internationally using the DPUK Data Portal. It will facilitate the safety of the digital storage and data sharing.



Training

Training the dementia and health data analysts of tomorrow is vital to DPUK's work. Our programme is helping to inspire a new generation of cohort analysts and equipping existing researchers with enhanced statistical skills.

DPUK is committed to developing the next generation of researchers to work on datasets. This is particularly important as the complexity of data-based dementia research increases.

The DPUK Training Programme provides researchers with affordable online training and experience of working with cohort data, giving them the skills required to work with complex and multimodal data.

So far, our initiatives have provided over 250 researchers with training opportunities focused on working with longitudinal largescale datasets at our annual Elementary and Advanced Academies and at a Datathon.

To encourage widespread participation, we hold all these events online. This helps us to offer training opportunities to anyone, particularly internationally and supports equality of opportunity globally.

All events run over 5-days in either Spring, Summer or Autumn. Each provides teaching and informative lectures on cohort-data-specific topics.



The Elementary Academy

Aimed at those new to cohort data analysis. Presented in conjunction with the University of Edinburgh, it is a 5-day online course. The teaching is focused on the essential skills for statistical work and analysis for researchers. It is for people new to the field AND those wanting to refresh their core skills.

The Advanced Academy

For more experienced data analysts, this is a 5-day online event featuring expert tutors, group working. Participants get an in-depth insight into cohort analysis techniques including linear/logistic regression, machine learning, survival analysis, and latent growth curve models.

Datathon

This is a flagship event, popular with people already working to some degree with data. Researchers join multidisciplinary teams to generate valuable new findings in dementia research using datasets in the DPUK Data Portal and retain access to the data afterwards to generate valuable findings and even published research.

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

Professor Emrah Düzel
Professor Martin Hofmann-Apitius
Professor Riccardo Marioni
Professor Jonathan Mill

Medical Research Council

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

Scientific project leads

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

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

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

Professor Sarah Bauermeister leads Data Curation programme

Dr Vanessa Raymont leads the Trials Delivery Framework workstream

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

Dr Ivan Koychev leads Work Package 23b: Great Minds

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

Professor James Rowe leads the Experimental Medicine Incubator workstream

Dr Atticus Hainsworth leads the Vascular Health theme

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

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

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

Professor James Rowe leads the Synaptic Health theme

Professor James Rowe leads the Work Package 26a: Synaptic loss and its functional consequences in early Alzheimer's disease, using pre-synaptic markers and magnetoencephalography

Professor James Rowe leads the Work Package 26b: Synaptic loss and its functional consequences in early Alzheimer's disease, using a new post-synaptic TARP $\gamma 8$ AMPAR ligand

Professor John O'Brien leads the Neuroimmunology theme

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

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

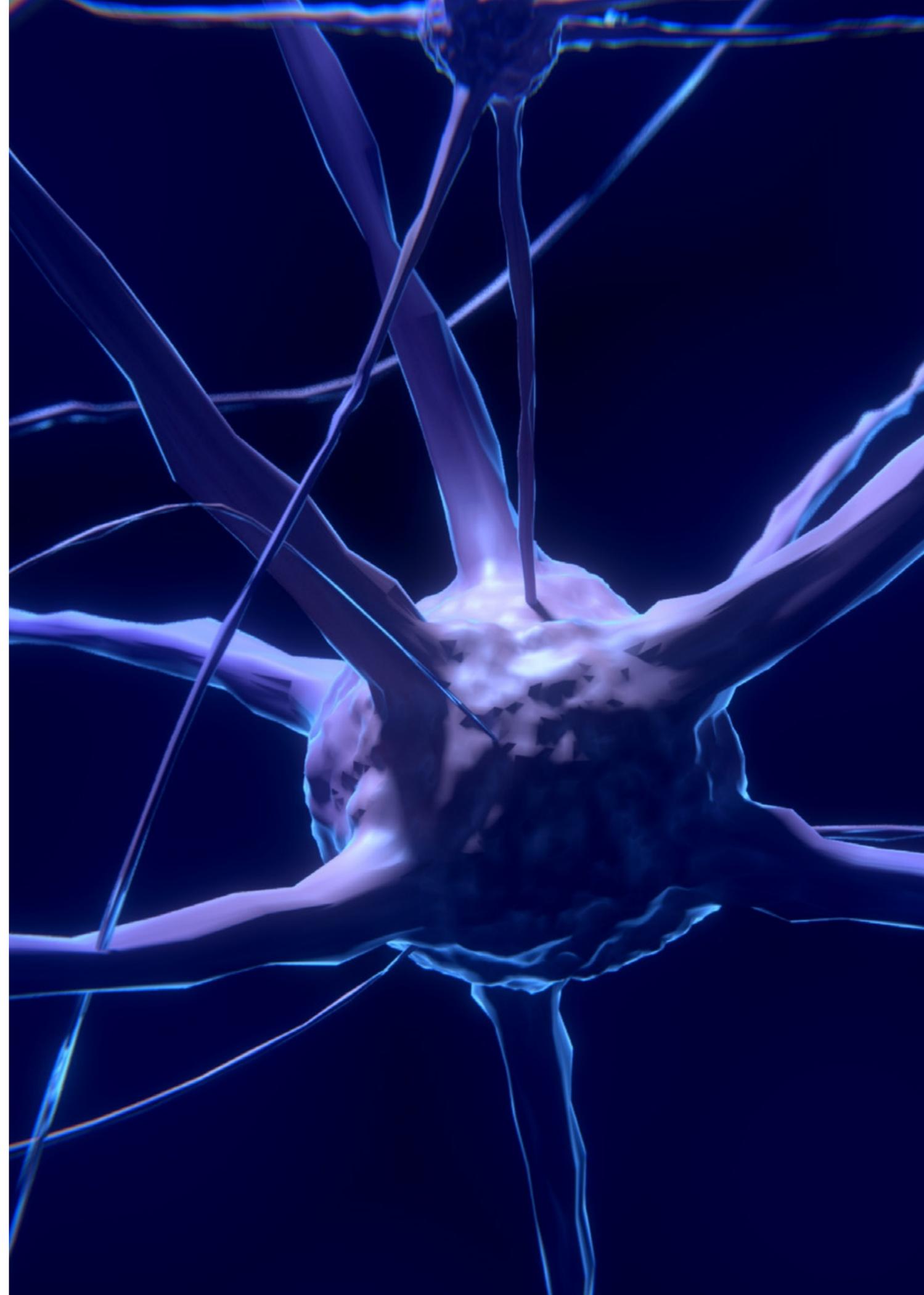
Professor Paresch Malhotra, Professor Paul Matthews, Professor John O'Brien and Dr Alastair Reith lead Work Package 27c: Dynamic PET-MR and brain inflammation

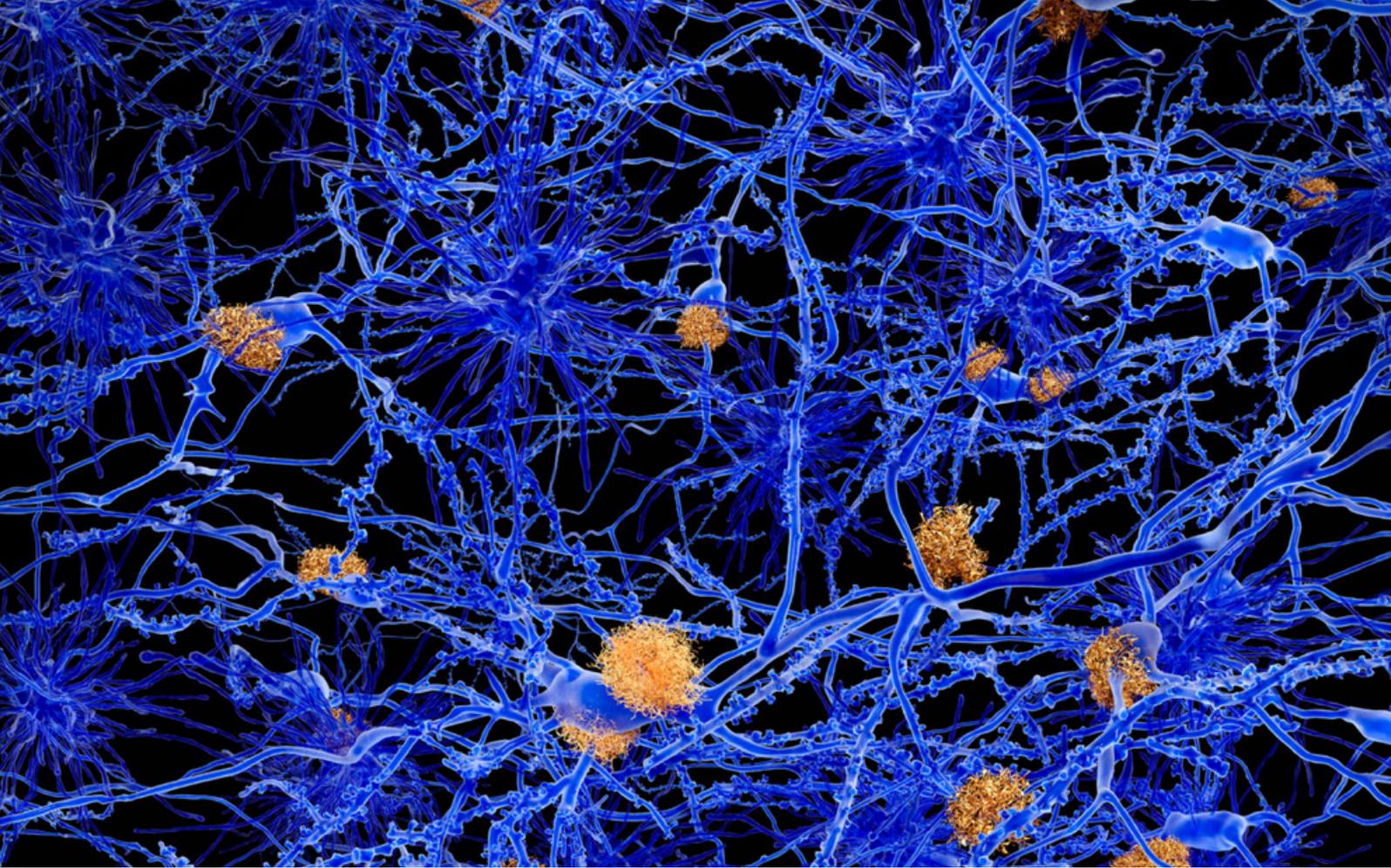
Dr Vanessa Raymont leads the Deep and Frequent Phenotyping study workstream

Professor Richard Wade-Martins leads the Stem Cell Network

Professor Sarah Bauermeister leads the data analyst training programme

You can register your interest in training at dpuk@psych.ox.ac.uk





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