Over 20,000 people join UK search for new dementia treatments

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More than 20,000 volunteers have been recruited to a resource aimed at

speeding up the development of much-needed dementia drugs. The cohort will enable scientists in universities and industry to involve healthy individuals who may be at increased risk of dementia in clinical trials to test whether new drugs can slow the decline in various brain functions including memory and delay the onset of dementia.

Using the resource, scientists have already been able to show for the first time that two important bodily mechanisms—inflammation and metabolism—play a role in the decline in brain function as we age.

By 2050, approximately 139 million people are expected to be living with dementia worldwide. In the UK, in 2022, the UK Prime Minister launched the Dame Barbara Windsor Dementia Mission, part of the government's commitment to double increase research funding for dementia.

Although there has been recent progress developing drugs that slow down progression of the disease, the two leading treatments only have a small effect, and the vast majority of new approaches that work in animal studies fail when it comes to patient clinical trials.

One explanation for these failures is that the drugs are tested in people who already have memory loss—and by this point, it may be too late to stop or reverse the disease. Hence, there is an urgent need to understand what is going on before people develop symptoms at the very early stages of disease, and to test new treatments before people come to their doctor with cognitive problems. This approach requires a large cohort of participants willing to be recalled for clinical and experimental studies of cognitive decline.

Writing in the journal *Nature Medicine*, scientists led by the University of Cambridge in partnership with the Alzheimer's Society report how they have recruited 21,000 people aged 17–85 to the Genes and

Cognition Cohort within the National Institute for Health and Care Research (NIHR) BioResource.

The NIHR BioResource was established in 2007 to recruit volunteers keen to engage in experimental medicine and clinical trials across the whole of medicine. Approximately half of its participants are recruited to disease specific cohorts, but the other half are from the general public, and detailed information about their genetics and their physical makeup has been collected. They have all given their consent to be contacted about future research studies.

For the Genes and Cognition Cohort, researchers used a combination of cognitive tests and genetic data, combined with other health data and demographic information, to enable the first at-scale study of cognitive changes. This will allow the team to recruit participants for studies of cognitive decline and new treatments for this.

For example, a pharmaceutical company with a promising new drug candidate to slow the cognitive decline could recruit people through the BioResource based on their profile and invite them to join in the clinical trial. Having a baseline measurement for their cognitive performance will allow scientists to observe whether the drug slows their expected cognitive decline.

Professor Patrick Chinnery from the Department of Clinical Neurosciences at the University of Cambridge and co-Chair of the NIHR BioResource, who led the project, said, "We've created a resource that is unmatched anywhere else in the world, recruiting people who are not showing any signs of dementia rather than people already having symptoms. It will allow us to match individuals to particular studies and speed up the development of much-needed new drugs to treat dementia.

"We know that over time our cognitive function decreases, so we've

plotted out the expected trajectory of various different cognitive functions over our volunteers' life course according to their genetic risk. We've also asked the question, 'What are the genetic mechanisms that predispose you to slow or fast cognitive decline as you age?'"

Using the research, the team has identified two mechanisms that appear to affect cognition as we age and could serve as potential targets to slow down cognitive decline and thereby delay the onset of dementia. The first of these is inflammation, with immune cells specific to the brain and central nervous system—known as microglia—causing gradual deterioration of the brain and hence its ability to perform key cognitive functions. The second mechanism relates to metabolism—in particular, how carbohydrates are broken down in the brain to release energy.

Professor Chinnery added, "Cognitive decline is a natural process, but when it drops below a particular threshold, that's when there's a problem—that is when we would diagnose dementia. Anything that slows that decline will delay when we drop below that threshold. If you could put off the onset of dementia from 65 to 75 or even 85, it would make a huge difference at an individual and at a population level."

Dr. Richard Oakley, Associate Director of Research and Innovation at Alzheimer's Society, said, "This exciting study... is an important step in helping us to better understand how the diseases that cause dementia begin, and will aid in the development of new treatments that target the early stages of these diseases. The data, from over 20,000 volunteers, helps us to better understand the connection between participants' genes and cognitive decline and allows for further ground-breaking analysis in future.

"One in three people born in the UK today will go on to develop dementia in their lifetime but research will beat dementia. We need to make it a reality sooner through more funding, partnership working and

people taking part in dementia research."

More information: Rahman, MS et al. Dynamics of cognitive variability with age and its genetic underpinning in NIHR BioResource Genes and Cognition Cohort participants, *Nature Medicine* (2024). DOI: 10.1038/s41591-024-02960-5

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