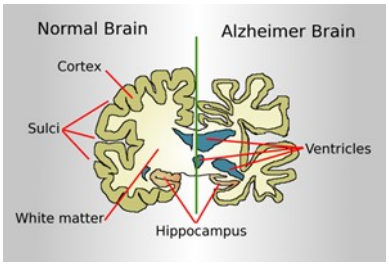
BDR NEWS

Brains for Dementia Research

Brains for Dementia Research Newsletter winter 2023

BDR's contribution to our understanding of Alzheimer's disease

In past newsletters, we have looked at two dementia sub-types, dementia with Lewy bodies and fronto-temporal dementia, but the most common form of dementia is **Alzheimer's disease (AD).**



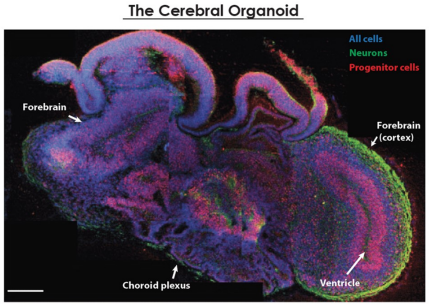
We have had a number of applications to access BDR data to look at the biochemistry and genetics of AD. For example, one study group is using BDR data to look at mitochondrial dysfunction which has been shown to be present in AD. The mitochondria are the powerhouses of the cell, and it is unclear whether problems in the mitochondria causes AD, contributes to the progression of AD or is simply a result of the damage brought about following Alzheimer-type neurodegeneration. The researchers want to investigate this further, because if damaged mitochondrial function is one of the causes of AD, then this may create an opportunity to target future drug therapies.

Other studies have employed a technique known as **machine learning**. We have heard a lot recently about both the threats and benefits of artificial intelligence, commonly referred to as A.I.. Machine learning is one such application of A.I. By using high-powered computers, researchers can look at millions of pieces of information in a relatively short time, and they can programme the computer to look for patterns in the data. A dementia research group is now using anonymised BDR data and applying machine learning, to create "polygenic risk models." These models may help predict whether a person with memory impairment is likely to develop AD, or AD plus another dementia type, or AD plus several dementia types. This is important as it will help target therapies more accurately, thereby leading to individualised medical care, the benefits of which have been demonstrated in the treatment of many cancers.

Although BDR data has great value on its own, when paired with human brain tissue, the potential for learning truly escalates. A study team led by Professor Jonathan Mill, a researcher working in Exeter, looked at BDR tissue taken from two different areas of the brain. The team compared how the genes expressed themselves in the different areas and they found that although the genetic material is the same, the way they affect the brain cells in the areas selected, can be different. This shows the importance of taking samples from more than one brain area but also illustrates the true complexity of dementia and the difficulty in finding effective, targeted treatment. Further information about this study can be found in the journal, Nature Communications, https://www.nature.com/articles/s41467-022-33394-7

Developments in the use of BDR brain tissue to create stem cells and beyond.

In our Winter 2019 Newsletter, we featured Dr Chris Morris from the BDR Centre in Newcastle. Dr Morris has been using samples of BDR brain tissue to create human induced Pluripotent Stem Cells (hiPSC). These cells, commonly referred to simply as "stem cells," have the identical genetic make-up as the donor cells from which they originate. They can be replicated over and over again and can even self-organise in a three-dimensional culture to create "mini organs" known as **organoids.**



An **organoid** is a miniaturised and simplified version of an organ, in this case, the brain, and so they are sometimes called 'mini-brains' (see image, left). They can be produced outside of the human body, and they mimic the biology and some of the key functional and structural characteristics of the brain. A selection of the BDR hiPSC lines have been used to pilot the production of such brain organoids. This disease-specific, living tissue, can be used for a broad range of applications. These include gene and cell therapies, drug discovery, personalized diagnostics, tissue engineering and regenerative medicine and so, present a new age of opportunities to increase our understanding of why people get dementia.

Alzheimer's Society
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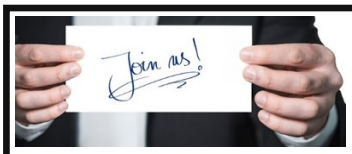
What's happening in your local BDR?

Changes to brain donations for those registered with the BDR Centre in Cardiff

BDR participants registered at our Cardiff Centre are regularly seen for assessment reviews by staff member Rachel Marshall and her colleagues based in Wales.

Although this will continue, we have decided to update the plans for donating tissue. Currently, participants registered with the Cardiff BDR Centre, have given their consent to donate their brains to the London Brain Bank based at King's College, London. This arrangement has worked successfully for many years, but as the costs of donating tissue, and in particular the travel costs, have risen significantly in the last few years, it has become increasingly expensive for the team in London to accept these generous donations. To reduce costs as well as post-mortem delays, it has been agreed that, providing participants give their consent, future brain donations from participants registered with the Cardiff Centre will go to one of the nearby brain banks, either at Manchester or Bristol. Staff will be in touch about this proposal, and we hope to introduce the change early in the new year.



Our next, online BDR Engagement Event is due to take place on **Tuesday 12th March 2024** and will be hosted by the BDR team based in Bristol.

Details of the event and how to join will be emailed to BDR participants and study partners nearer the event date.
If you have not attended any of the previous events but would like to do so, you can register your interest by going to the BDR website: [Online Engagement Events - Brains for Dementia Research (alzheimersresearchuk.org)]

BDR Blood study update

Over several years, many of our BDR participants have generously donated samples of their blood and some are giving blood samples for the first time. But why are these blood samples so important?

In the quest to detect neurodegeneration at its earliest stage, there has been an increasing interest in blood biomarkers. A biomarker, or biological marker, is a measurable indicator of some biological state or condition.

Dementia is a slow, gradual deterioration in mental function but at the early stage, known as the prodromal stage, changes are taking place in the brain without necessarily having any impact on the individual's day-to-day function. Research has shown that this early stage can be detected in samples of blood, as the brain changes are associated with an increase in inflammation and specific biomarkers for diseases, e.g. the amyloid protein in Alzheimer's disease. If we are to make meaningful progress in our ability to offer effective treatments for dementia, it is essential that we have early and accurate diagnoses. The reasons for this are two-fold. Firstly, dementia is such a complex illness. Rarely does someone have a pure dementia type such as Alzheimer's disease or Vascular dementia. More often, several dementia sub-types will co-exist. This means that it is unlikely that a single treatment regime will be effective with all individuals. Knowing exactly which type or types of dementia diseases are appearing, will help target treatments more accurately. The second reason for wanting an early diagnosis is because dementia leads to the destruction of brain cells. The earlier we can intervene; the fewer brain cells will be damaged, and the affected individual can keep a higher level of mental function for longer.

We have had several requests from researchers to use BDR bloods. A recent approved application involved looking at whether blood samples can differentiate between individuals experiencing mild, age-related memory loss, from those who are in the first stages of dementia. As we have associated blood samples and brain tissue, we can work backwards. In other words, we can find exactly which diseases the person has at death, and then compare with the blood biomarkers found in blood samples taken at a much earlier time when the person was alive. This may allow us to create a simple test, showing who is most at risk of developing dementia and thus targeting appropriate treatments as they become available.

Finally, we would like to send Season's Greetings to our participants, study partners, friends, and family members and wish you all the best for 2024!