The MRC London Neurodegenerative Diseases Brain Bank: a resource for neurodegeneration research

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ABSTRACT: Clinically and neuropathologically well-characterised human brain tissue is one of the most important resources for neuroscience research and is essential in the battle to develop new strategies and treatments for neurodegeneration. There has been significant research progress in recent decades and post-mortem tissue has played a major role in enabling advances in diagnosis, characterisation of pathological features, molecular genetics and bioinformatics.

The MRC London Neurodegenerative Diseases Brain Bank (LNDDB) is one of the largest brain banks in the UK. Since its establishment in 1989 it has collected over 2,000 brain cases (formalin fixed and frozen samples). We focus on banking on neurodegenerative diseases, including Alzheimer’s disease, Dementia with Lewy Bodies, Motor Neurone Disease and Frontotemporal lobe dementia and age-associated controls but also house smaller collections, such as psychiatric and parasitic disorders, in order to enhance research in these areas. The LNDDB operates a transparent and open-door policy for provision of central nervous system tissue to researchers. So far we have completed over 2,375 requests and provided over 10,000 samples to national and international institutions. We are part of the MRC UK Brain Banks and Brains for Dementia Research networks which aim to encourage and facilitate both tissue donation and accessibility and use by researchers.

The brain bank also carries out studies into the best methods of preservation of tissue and the research potential of different fixed tissue. We are constantly updating our procedures to ensure tissue is of the best quality for use in current research techniques.

1. Recruitment of cases
a) ‘Diseased’ brains
Brain donations are accepted in the Brain Bank via two routes:
1. Donor programme: The majority of donations from Alzheimer’s, MND and movement disorder patients are registered through cohort studies. These donations are ideal and provide not only well-characterised brain tissue but a fully documented clinical profile, sometimes with neuro-imaging and neuropsychological information. Such donations are very useful in many molecular and genetic studies where knowledge of clinical and pathological heterogeneity is important.

b) Ad-hoc donation: This has noticeably increased in the last few years and is a very useful source of various types of dementias, other neurological conditions and “normal” control tissue.

2. Post mortem and tissue collection
a) Post mortem delays
Ideally, we seek to minimise the post mortem delay (time between death and obtaining tissue for formalin fixation) to less than 48 hours, wherever possible. Generally we accept donations with post mortem delay of up to 72 hours to accommodate deaths that occur over the weekend or Bank holidays.

b) Brain tissue collection and diagnosis
Sets of standard protocols are use for tissue sampling of fresh and formalin fixed material. The brain is divided along the midline in the sagittal plane (left or right hemisphere), the others is freshly sliced. 50 blocks (1 cm x 1 cm) are sampled from the slices from predefined regions, snap frozen and stored at -80°C. The formalin fixed half of the brain is processed by the team of senior neuropathologists to provide diagnosis to a comprehensive protocol which not only reaches a definitive diagnosis, but also includes details of the load and staging of pathology and other information important for researchers.

3. Tissue dissemination
a) The Brain Bank has a transparent and open-door policy for providing services and brain tissue to requestors from any institution without prejudice, on the condition that ethical requirements are satisfied and that a scientifically sound case underlies the application. The researchers are asked to complete a request application form providing an abstract of the project, source of funding and other aspects which is assessed by an approval committee.

b) We have a wide range of national and international collaborations and are considered to be a major resource of brain tissue. We have responded to over 2,200 requests for tissue since our establishment in 1989 with 2,008 completed requests between 2006 and 2010.

4. Data storage
We have a comprehensive database of information on registered donors and on donated brain tissue, detailing clinical and pathological diagnosis, post mortem details of fixed and frozen tissue, CSF etc and non-clinical data such as age, sex and source of donation. Recent donations are also being added to the MRC and BDNF network searchable databases.

5. Environment and links

The MRC Centre for Neurodegeneration

The MRC Centre for Neurodegeneration Research at the Institute of Psychiatry aims to understand the mechanism of neurodegeneration and to translate this into new treatments by carrying out translational research and facilitating new collaborations. The Brain Bank occupies a key role in this and is a critical resource for the execution of the centre’s research.

The National Institute for Dementia Research (NIDR)

The Brain Bank is a member of the Banks for Dementia Research Network which is funded jointly by the Alzheimer’s Research Trust and the Alzheimer’s Society. King’s College London acts as the coordinating centre and the Institute of Psychiatry is one of 6 component Brain Banks. BDIF aims to create and maintain a web-based database for all accessible samples in the component brain banks, host training in organ retention, ethics and governance issues and introduce dedicated Brain Bank research workers who will be responsible for liaising with the donor and their families at the time of consent, the time of donation and afterwards.

MRC UK Brain Banks Network

The Brain Bank is also a member of the new MRC UK Brain Banks Network. This is an independent and coordinated national network of existing brain tissue resources. The network will seek to provide operational efficiency for the benefit of donors, researchers and future patients.

6. Public Engagement

The MRC London Brain Bank is committed to openness and transparency in its regulatory procedures and the research it supports. It regularly submits articles to patient support networks and newsletters and participates in public engagement exercises such as Research Open Days. Lay members and charity reps sit on the steering committee.

7. Tissue Quality Research

Brain banks have large collections of fixed human post-mortem tissue stored as FFPE blocks and as wet tissue in formalin solution. Recent advances have enabled genetic material to be extracted from this tissue, however it is important to establish the quality of this DNA/RNA and its suitability for use in the most current research techniques. The effect of storage in liquid fixative on the RNA and DNA quality is also important to investigate. We have therefore recently been studying the research potential of this archival tissue.

DNA extraction was carried out from a range of fixed tissues, of various disease classes, stored for a range of time (between 8 and 20 years) as blocks or in formalin (in total of 37 cases). The quantity and quality of DNA extracted from original FFPE blocks (taken at time of autopsy), tissue stored in liquid fixative, and new blocks processed from the wet tissue was examined. The effect of long-term storage in formalin on the reactivity of tissue to a number of diagnostic and research-relevant antibodies was investigated by comparing staining intensity in original and newly processed blocks from the same cases, using tissue microarray technology.

Overall, original blocks produced a higher quantity and better quality of DNA than either wet tissue or newly processed blocks. There was no direct correlation between time of storage in formalin and quality of DNA. Extracted DNA was of high enough quality to carry out PCR reactions but showed poor results in a gel electrophoresis run. Newly processed blocks showed a decreased level of reactivity with several currently used antibodies, including HLA-DR and GFAP.

Contact Details: The MRC London Brain Bank Download an open policy towards all peer reviewed research application requests, however proof of ethical research approval for the research project may be required. Tissue request application forms can be requested from Dr Claire Troakes, PD, Institute of Psychiatry, King’s College London, De Crespigny Park, London SE5 9SA Claire.Troakes@kcl.ac.uk. All applications are treated confidentially.

Acknowledgements: We thank the Medical Research Council UK for supporting the Brain Bank. We thank the staff of the Clinical Neuropathology Department, including Dr Ioana Bodi, Dr Andrew King and Dr Thib Horthaguy, for advice and technical support. We also thank Yasminia Spadone and Richard Markham for technical and administrative help.

The study shows that DNA can be extracted from FFPE blocks and wet formalin-stored tissue and that this DNA is of a suitable quality to be used in a number of current research techniques. However the best quality DNA is obtained from the original blocks, suggesting as many as possible should be taken at autopsy. The effect of storage in formalin on immuno-reactivity indicates that this sample should be routinely recorded and included in analysis.

Supplementary material available online.