

- A CONSORTIUM OF EUROPEAN BRAIN BANKS

<http://www.brainnet-europe.org/>

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Map of Europe with Centres Identified



BRAINNET EUROPE is a consortium of brain banks in mainland Europe and UK which commenced activities in 2001, expanding to the present grouping in 2004.

Purpose of BNE

- To promote brain banking as a research resource for European neuroscience through the provision of a range of brain tissue samples.
- To optimise and harmonise methodology, leading to best practice guidelines for brain banking.
- To develop new research methodology applicable to human brain tissue.
- To provide training in brain banking and related methodology.
- To reach out to neuroscience centres worldwide and promote future expertise in Central Nervous System (CNS) research.

HISTORY OF BRAIN BANKING IN EUROPE

In the late 1400s, Leonardo Da Vinci was amongst the first scientists to explore the anatomy of the human brain and eventually he was banned by the Pope from conducting autopsies for several years, following accusations of necromancy. Despite Leonardo's partially successful efforts to preserve brain tissue, morphological understanding of diseases of the brain was still in its infancy 100 years ago. Charcot studied the brain pathology of Parkinson's disease in 1869 and Lewy described the inclusion bodies named after him in 1912. At about the same time, Alzheimer reported the typical pathology of the dementia which bears his name. Neuropathology Departments developed in Europe as laboratory extensions of psychiatric hospitals and collections of post mortem brains came into existence, known as brain banks. The benefits of study of these collections has become clear over the years. For example the identification of dopamine deficits in the brain stem in patients with Parkinson's disease lead directly to the introduction of levodopa as a successful treatment and the detection of neurofibrillary tangles in the brains of boxers gave rise to new legislation designed to protect participants more effectively. Investigation of individuals

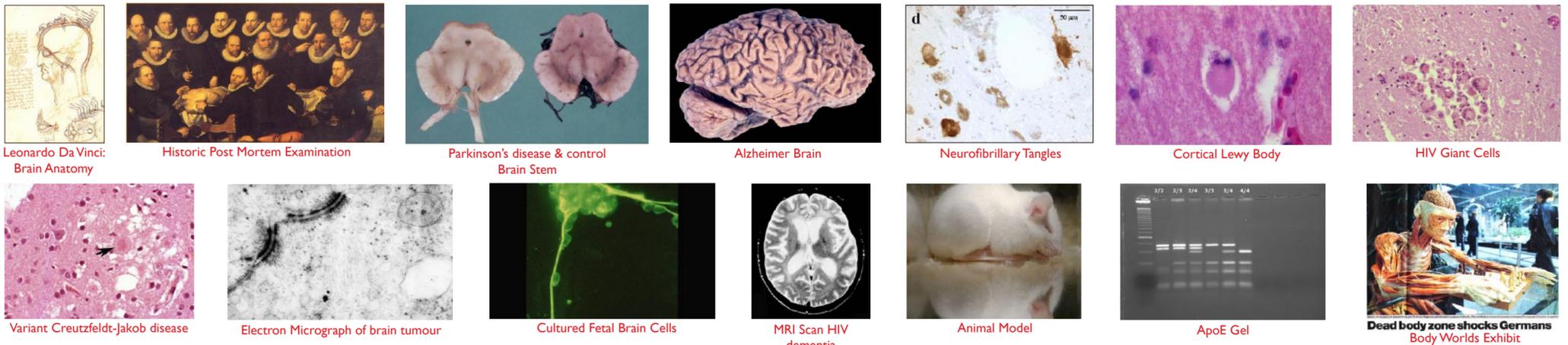
with a history of dementia has identified a variety of causes other than Alzheimer's disease, including Dementia with Lewy bodies, frontotemporal dementias and vascular dementias each with different pathogenesis and likely therapeutic implications. Study of the brains of people with HIV/AIDS revealed the specific HIV-related changes in the brain which underlie AIDS dementia. The availability of large and historic collections of brains provided the evidence (from look-back studies) that new diseases such as variant Creutzfeldt-Jakob disease have emerged only recently. Distinguishing these different disorders one from another facilitates research in the causation of disease as well as the design of more appropriate therapy.

The introduction over the years of new methodology and technological advances such as electron microscopy, tissue culture and neuroimaging have lead to improvements in knowledge and in diagnosis of disease. Animal models have proved useful for the investigation of certain brain disorders and this approach has accelerated markedly since the advent of transgenics. The influence of host genetics on brain pathology has been the focus of

considerable study in recent years. Apolipoprotein E is one example of a polymorphic gene which exerts allele-related effects on a number of brain disorders. Ironically, despite the origins of brain banking, the neuropathology of the major psychoses remains poorly understood.

The study of the anatomy of the brain, and the use of brain banks to facilitate investigation of pathology of the brain, has moved back into the public arena with the advent of internet facilities. It is clear that the general public retains a strong interest in how the human body is put together, as evidenced by the crowds flocking to see the European exhibitions of "Body Worlds". Whatever the views of neuropathologists regarding such events, they create an opportunity to explain to the public the value of brain banking, the benefits which are generated and the possibilities for brain donation.

"BRAIN BANKS LIE BEHIND MOST MAJOR ADVANCES IN CLINICAL NEUROSCIENCES"



The generalised decline in post mortem examination in most countries has lead to a decline in brain donations to organ banks. There are always difficulties in obtaining brains from people with rare diseases in sufficient numbers for meaningful studies. Another significant problem for most brain banks lies in collecting normal control brains from all age groups. One reason for brain banks to form networks is that they can then share knowledge and access to samples. Many brain banks have a long tradition of making tissue samples freely available to bona fide researchers. By spreading expertise across the brain banks of Europe, BrainNet Europe will ensure that brain tissue samples are stored optimally and are readily accessible to researchers.

Individual brain banks within the BNE consortium focus on different CNS disorders. Overall, samples are stored from neurodegenerative and prion diseases, Parkinson's disease, HIV/AIDS, psychoses, movement disorders and motor neuron disease, multiple sclerosis, perinatal brains and from controls. The member banks possess a very wide range of methodological competences including the full range of staining techniques, confocal and electron microscopy, image analysis, morphometry and stereology, neurochemistry, molecular biology and Western blots. Some but not all banks are expert in DNA and RNA extraction and analysis, 2D gel electrophoresis, PET blots, tissue microarray and proteomics.

The work of BrainNet Europe is organised in a number of packages for which individual BNE members take prime responsibility.

- Standardised clinical criteria
- Donor programme
- Tissue sampling and microdissection
- Standardised histochemical staining protocols
- Standardised neuropathological diagnosis
- Morphometry
- DNA analysis
- RNA analysis
- Protein analysis
- Neurochemical analysis
- Mystery cases
- Ethical and legal issues
- Health and safety
- Logistics
- Training
- Information technology

Some or all of the BNE partners participate in each of the work packages. Ring trials of immunohistochemical staining and assessment, morphometry and DNA extraction are in progress. While these methods are standard for most brain banks, newer methods such as proteomics and single cell analysis are not yet routine. BNE provides a forum for rapid spread of expertise relating to brain banking techniques, both in the consortium and to the wider neuroscience community. While the legal framework for brain banking varies between individual European countries, BNE is making efforts to harmonise the major ethical issues, including consent for different aspects of research. Work package updates will be made available through the BNE website. Requests to BrainNet Europe for brain tissue samples are invited provided that potential users have ethical approval for the studies which they wish to pursue. Information is available on the website.