A GOLDEN STANDARD PROTOCOL FOR THE BRAIN BANKING SOCIETY?
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The network of European brain banks forms the necessary bridge between clinicians, neuropathologists and neuroscientists investigating the various mental and neurological disorders. It aims at improving our understanding of the aethiological, epidemiological and pathological basis of psychiatric and neurological disorders and at the same time increasing the technical knowledge related to this field. Post-mortem tissue of patients who died from brain disorders is quite difficult to obtain and the same holds for control patients to be matched with. The search for controls for neurodegenerative diseases, who did not suffer from any neurological or psychiatric disorders is still more difficult.

One of the goals of the European collaboration is to reach consensus and standardization of brain bank protocols (1) which include the following steps:

a. improve and standardize clinical diagnosis,
b. standardize the criteria for neuropathological diagnosis of the various diseases by developing new approaches, e.g. by searching for new biological markers such as the use of monoclonal antibodies and in-situ hybridization on post-mortem material,
c. introduce standard protocols for collecting material which will include:
   — *Sampling*: selection criteria for patients, e.g. by making a distinction between sporadic or familial cases.
   — *Dissection protocols*: comparing the various protocols for the use of fresh, snap frozen or formaline fixed tissue (2). The method which is most currently used in brain banking, i.e. fixing one hemisphere and freezing the other limits the number of modern techniques which can be applied on this tissue and ignores possible lateralization of brain systems and compounds.
   — *Matching* for various factors. Antemortem factors will include age, sex, agonal state, seasonal variation, circadian variation, medication and lateralization. Postmortem factors will include the post-mortem delay, freezing procedure, fixation duration, storage time. The pH of the cerebrospinal fluid (CSF) has recently proven to be a good parameter for agonal state and correlates strongly with m-RNA levels. Measuring the pH of the tissue or CSF is thus a good measure to control for the quality of the specimens and therefore vital for brain banks supplying those specimens (3, 4, 5, 6, 7).

d. *Quantitative vs. qualitative* diagnosis by comparing the classical histopathological diagnosis with quantitative measurement of biochemical markers in brain tissue and CSF. This can be achieved by making use of specific monoclonal antibodies to validate and try to quantify the histopathological changes in the brain or antigenic determinants in the CSF(8, 9).

This paper outlines the global operations of The Netherlands Brain Bank, based on protocols developed and used by the authors in the past 10 years. The way this brain bank has been run from the very beginning related mainly to the never-ending changes in scientific emphasis on research protocols. Each researcher requires a subset of tissues which differ in age, sex, anatomical site, post-mortem delay, medical history and the clinical and neuropathological diagnoses. The drawback of our rapid autopsy system and the fresh dissection procedure, is however that it requires highly qualified staff around the clock. Computerized storage of this information in a database enables the brain bank personnel to identify and select the appropriate cases. A common need of all users is getting tissues from normal controls or other neurological diseases matched as closely as possible by all the factors reviewed earlier in this paper. We very often request scientists to perform pilot animal experiments to standardize and optimize their methods and techniques before applying them on the precious human tissues.

The Netherlands Brain bank has developed in the past 10 years an efficient rapid autopsy programme and uses a fresh dissection procedure which is advantageous in increasing the range of conventional as well as modern neurobiological techniques to be applied on human post-mortem specimens. So far we have supplied tissue and CSF from 1100 patients to a total of 205 scientific research projects in the Netherlands, other European countries, the USA, Canada and Japan. We have been involved from the very beginning in the development of a European Brain Bank network and we hope to expand our experience and scientific expertise on European level and later on also on intercontinental level by collaboration with American Brain Banks (10). This will hopefully lead to a scientific output which will exceed the summed end results of the local brain banks and will make it possible to have a large amount of tissue for research, many patient data, reliable statistical analysis of the obtained re-
sults and the possibility to apply sophisticated molecular biological techniques. It will also make it possible to efficiently use the specific skills of the local banks and in this way certainly help to improve the state of the art and fill up some information gaps and exchange of knowledge and controls and rare cases.

A European collaboration can match the objectives mentioned earlier by allowing the necessary infrastructure which will liaise the various European Brain Banks in a single on-line network, simultaneously meeting the very particular needs of the researchers. This collaboration is also necessary for the pooling of knowledge and expertises of modern neurobiological techniques as well as resources and material which are certainly not evenly distributed at the present time between the various European countries.

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References