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Brief report

Tissue banking and EURAGE

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EURAGE is the European organisation coordinating research in aging and dementia. During the EURAGE meeting on 6 May 1987 at the Netherlands Institute for Brain Research in Amsterdam, a subcommittee on Tissue Banking was installed in order to give advice to EURAGE concerning European efforts. One of the central questions the committee had to deal with was whether EURAGE should aim at establishing a "European brain/tissue bank". The opinion of the subcommittee on the organization of European brain banks is as follows:

(1) A number of European countries collaborating in EURAGE have established human brain bank facilities over the last years, i.e., a collection of brain and other tissue samples from clinically and neuropathologically well-documented demented patients and controls. These countries are France (Lyon, Paris (2)), Italy, U.K. (10, only 3 of which are founded in order to provide tissue for other research groups), and the Netherlands (see EURAGE Report 1987). In addition, we have obtained information on collections in Sweden, Austria and West Germany. Those countries which have not established such a facility are urged to do so, since an increasing number of research groups from such countries are currently contacting the existing banks in other countries for tissues that cannot be easily provided. Within the EURAGE organization, brain banks are not only essential for the group on aging of the brain and senile dementia, but also for the subgroup on molecular biology and for EURODERM (epidemiology).

(2) As already mentioned in the EURAGE report of 1987, there is considerable variation in the procedures used in different tissue banks, e.g., in the type of dissection used, the exact site of the brain area selected for freezing or fixation, post-mortem interval, the extent of neuropathological analysis, storage, etc. It is clear that standardization is necessary for the neuropathological diagnosis and that some degree of standardization could even be reached in research, e.g., concerning the exact borders of the brain structures that are dissected and the minimal amount of information needed for a given specimen (age, sex, anatomical borders, agonal state, pre-mortem treatment, post-mortem delay, storage conditions, neuropathological investigations; cf. Swaab and Uylings 1988). On the other hand, it is our feeling that it would be a waste

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of time to strive for one standardized European way of brain dissection and storage. The number of theoretically good procedures is unlimited and the best solution fully depends on the requirements of the scientific projects involved (being, for instance, of a quantitative morphological, immunocytochemical or molecular biological nature). With the rapidly increasing number of sophisticated neurobiological techniques that can be applied on the human brain one can expect even wider variations and more rapidly changing demands from scientists. As soon as the *in situ* hybridization techniques will improve in sensitivity, the demand for specifically prepared tissues will increase and that for freshly frozen tissue – a method generally used in brain banking (Tourtellotte and Berman 1987) – may diminish. At present it is therefore impossible to foresee exactly how samples should be collected for future projects. In our opinion, the most efficient way of using human brain tissue is therefore to collect the tissue on the basis of sound detailed research proposals. There is, of course, one drawback to such a policy: the samples cannot be provided immediately, it will take time to collect the requested samples. This disadvantage can be reduced, however, by an increase of the capacity and number (cf. section 1) of brain banks, and a good system of contacts between banks. Here EURAGE may have a function.

(3) The demand for other tissues than brain tissue will increase in neurosciences as well, e.g., owing to the introduction of molecular biological techniques into neurosciences. The Italian bank (see Rocca et al. 1988) already collects kidney, muscle, heart, cerebrospinal fluid, urine, serum, skin fibroblasts (which may even be cultured from a skin biopsy obtained within 72 h after death and stored frozen, e.g. until Alzheimer's disease has been confirmed by the neurologist) and lymphoblasts. One might extend this list with astrocytes, neurons, etc. Other banks should also anticipate this research development, although ultimately, collection on the basis of detailed research proposals will certainly be advisable for aspects of such a tissue collection as well. Of course, such an extension of brain banking also depends on the interest of the bankers themselves, and one should distinguish "service" from project-oriented banking.

(4) The entire brain will seldom be used on the basis of research proposals, so there will be "left-over" tissue at every brain bank. In addition, tissue from some diseases is hard to obtain. Here lies a clear task for EURAGE in establishing contacts as well. It might be valuable to have one coordinating person per country who is responsible for such contacts with other EURAGE countries and scientists. A few times a year scientists should announce which rare samples they would like to collect, while brain bank coordinators could meet, say, twice a year and announce which samples are available for research. In addition, one should aim at some specialized collections of rare diseases. It should be stated clearly if costs are involved if samples are obtained, and whether the samples are available on the basis of "service" or "collaboration" (i.e., co-authorship). Our opinion is that the mere dissection and freezing of samples does not warrant co-authorship. We know, however, that others think differently about this point. Indeed, the difficulties and efforts put into "brain banking" are often underestimated. Moreover, there are time-consuming procedures, e.g., serial sections and sophisticated staining procedures in order to localize a particular small structure, that might allow co-authorship. On the basis of frequent and extensive information between the banks and their users the various European tissue banks might form a valuable EURAGE network.

It seems appropriate not to restrict such an effort to Alzheimer's disease and controls, but at the same time try to obtain information on, e.g., multiple sclerosis, cerebral tumors, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, Friedreich's disease, psychiatric disorders, etc. Certainly we recognise that some brain banks have concentrated on obtaining tissues from one or more of these diseases.

(5) The usefulness of brain bank material depends full on a rigorous neuropathological diagnosis not only of diseased brains (Khachaturian 1985) but also of controls. Good neuropathology is a *conditio sine qua non* before carrying out elaborate and highly specialized studies on this material.

Ideally, a trained neuropathologist should not only confirm a diagnosis, but also be present during dissection of the brain, since otherwise defects, both in the possibly demented and in the control brains may pass unnoticed. This ideal is unrealistic at present. Even for diagnostic purposes, however, the shortage of

such specialists in most European countries, at the same moment that neurosciences are technically advanced enough to move into the study of the human brain, is of great concern. EURAGE should encourage the different European organizations to address to this problem.

(6) A point of general concern is the way safety measures should be taken in brain banking. Those involved in post mortem handling should be immunized against hepatitis B, and protect themselves during dissection as if the material is contagious and test the material for example for the presence of Creutzfeldt-Jakob disease and AIDS. Safety is also an issue on which EURAGE information exchange might be very valuable for all participants.

(7) Brain banking demands the establishment and the continuous maintenance of time-consuming contacts in order to motivate relatives of demented patients, doctors and nurses in homes, neuropathologists and scientists to collaborate. Intensive personal contacts, therefore, are absolutely essential for a successful brain bank organization. Such contacts can only be maintained in a local setting.

(8) Some investigations demand fresh tissue with extremely short post mortem intervals (e.g., DNA studies on damage in Alzheimer). Such research is only possible if banks are organized on a local level. Therefore, the establishment of one European Brain Bank does not seem to be a good idea. We should rather aim at a European network of local tissue banks, and at efficient exchange of information. In the long run, such a service will undoubtedly stimulate research on the human brain and other tissues with regard to aging and dementia. At the same time, however, the service will put more pressure on the tissue bankers. EURAGE has to realize that such a trend will ultimately result in a request for more tissue bank personnel, a problem for which the local organizations may not have the appropriate financial resources.

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