Report of a Workshop on Issues in Brain Tissue Acquisition

by Althea M.I. Wagman

Abstract

In the recent past the National Institute of Mental Health (NIMH) has been interested in developing a research initiative to stimulate human brain research on the biological characteristics of schizophrenic brain tissue. The Schizophrenia Research Branch of the Division of Clinical Research of NIMH sponsored a workshop to study the issues of impediments to research on human brain tissue and develop recommendations for solving some of these problems. This article is the first implementation of one of these recommendations, that is, to provide information to the scientific community that brain tissue donations are important and that appropriate means must be taken in order for a donation to proceed.

Introduction to the Problem

Investigators studying the molecular and cellular bases of mental dysfunctions such as schizophrenia, unipolar and bipolar depressive disorder, alcoholism, and Huntington's and Alzheimer's diseases have historically faced the same problem: there were too few scientifically acceptable brains for structural and functional research protocols. Investigators of some disorders, in which the genetic relationship is clear (such as Huntington's and Alzheimer's), have developed their own centers to acquire donors and donations and to facilitate autopsy. Families, clearly disturbed by the potential for genetic transmission of the disorders, have become integral parts of these brain acquisition efforts. Not until recently have the major mental disorders had the benefit of this kind of constituency, but brain tissue donations are still few and far between.

As early as 1968 the need for tissue donation was recognized and the Uniform Anatomical Gift Act was approved by all 50 States. By 1985, when tissue donation became important for transplantation purposes and it was clear that the 1968 act required reworking, the National Conference of Commissioners on Uniform State Laws initiated a committee to draft new language to clarify and facilitate the ethical, procedural, and legal issues about tissue donation. It should be noted that although tissue for transplantation purposes was a primary goal of the redraft of this act, tissues for research purposes were equally covered and that brain acquisition was in no way excluded by the act.

In 1985 the Hastings Center Report (Caplan and Bayer 1985) assessed the contemporary significance of the act in preparation for the Uniform Anatomical Gift Act of 1987. The Hastings Center Report determined that the nine key problems that hinder organ donation of any kind are as follows:

1. Failure of persons to sign written directives.

Citations:

Copies of the Uniform Anatomical Gift Act of 1987 may be obtained from National Conference of Commissioners on Uniform State Laws, 676 North St. Clair St., Suite 1700, Chicago, IL 60611.

This article represents the proceedings of a workshop held at the Stouffer Courcourse Hotel, Arlington, VA, on January 19, 1990, sponsored by the Schizophrenia Research Branch, Division of Clinical Research, National Institute of Mental Health.

Reprint requests should be sent to Dr. A.M.I. Wagman, Schizophrenia Research Branch, NIMH, Rm. 10C-06, 5600 Fishers Ln., Rockville, MD 20857.
2. Failure of police and emergency personnel to locate written directives at the accident site.

3. Uncertainty on the part of the public about circumstances and timing of organ recovery.

4. Failure on the part of medical personnel to recover organs on the basis of written directives.

5. Failure to systematically approach family members concerning donation.

6. Inefficiency on the part of some organ procurement agencies in obtaining referrals of donors.

7. High wastage rates on the part of some organ procurement agencies in failing to place donated organs.

8. Failure to communicate the pronouncement of death to next of kin.

9. Failure to obtain adequate informed consent from family members.

These problems accrue regardless of the tissue type or purpose of tissue acquisition. Impediments to brain tissue acquisition are particularly obstructive for studies of the biology of major mental disorders which must attend to issues such as diagnosis and subtypes of the disorder, cause of death, and psychiatric medication history. Tissue donations most often come from individuals who die in hospital; about 27,000 hospital deaths permit organ recovery each year (Center for Disease Control). Only about 1 percent of these deaths could be expected to be among persons with schizophrenia (270). In addition, method of autopsy, diagnosis, postmortem interval, and comorbidity would further limit the potential availability of this tissue.

The November 1987 hearing held by the National Biomaterial Resource Committee of the National Institutes of Health specifically addressed the need for and management of tissues for research purposes. Represented were many procurement systems that harvest tissue for transplantation purposes, but few of them have a research focus. Few of these services have had any experience with acquiring brain tissue. The one NIMH brain bank that was represented stressed the need for more tissue and the importance of a donor registry and a donor hot line to facilitate the donation process.

The need for tissue was also addressed in the 1989 National Plan for Schizophrenia Research. Of the many recommendations that were made, the need for postmortem brain tissue was mentioned by three of the panels representing five substantive areas: clinical phenomenology (Andreasen et al. 1988), neuroimaging and neuropathology (Wagner et al. 1988), and neurochemistry and neuropharmacology (Friedhoff et al. 1988). Facilitation of brain tissue acquisition is one of the few National Plan recommendations for which NIMH has not yet fully formulated a strategy.

Later, the Schizophrenia Research Branch of the Division of Clinical Research undertook an in-depth evaluation of the problem by inviting a representative sample of brain tissue users, directors of brain tissue banks, and brain scientists who had developed personal tissue acquisition programs to a Brain Resource Acquisition and Information Network (BRAIN) workshop, the agenda of which was to form consensus on the issues and develop recommendations for solving the problems. This working group, listed in an appendix at the end of this report, met on January 19, 1990, to discuss issues of sample identification, sample acquisition, tissue donation, and tissue dispersal.

In the morning session each consultant presented independent assessments of the more pressing issues for brain tissue acquisition. Priority topics included advantages and disadvantages of retrospective and prospective samples, diagnostic groups appropriate for comparison purposes, and diagnostic validity. Registries and networking were discussed in the context of sample acquisition and tissue dispersal. The most important problems surrounding tissue donation appeared to center on the logistics of donation, obtaining an autopsy, and the actual autopsy methods.

General Areas of Consensus

Consensus was reached on some central methodological issues associated with brain tissue acquisition for research. Both retrospective and prospective approaches to brain acquisition should be encouraged, recognizing that prospective studies may have a low but well-characterized yield, while retrospective projects will have higher tissue yield but less precision of diagnosis, knowledge of medication status, and so on. Facilitation of the donation process is also necessary so that the donors' custodians or next of kin can initiate the donation process with ease.

Eight problems were articulated, which generated 18 recommendations.

Problem 1. The need for brain donation from patients with major mental disorders and controls is not well known by health professionals or the public.

Recommendation 1. Make the public aware of the need for brain tissue. Develop articles for targeted populations such as the National Alliance for the Mentally Ill, and the
Mental Health Association to stimulate donor registration and to facilitate prospectively the steps in the donation process. Develop similar material for the necessary comparison populations.

Recommendation 2. Prepare editorials for journals such as Archives of General Psychiatry, Hospital and Community Psychiatry, American Journal of Psychiatry, and Biological Psychiatry to inform scientists, clinicians, and administrators about the donation process, its importance, and their role in facilitating donation.

Recommendation 3. Advertise the importance of registration of clinical, comparison, and "normal" donor groups.

Problem 2. Donations at the time of autopsy need to be facilitated. As a rule, the custodian of the body (i.e., next of kin or hospital director) does not have sufficient investment in the donation process. The legal issues, ethical responsibilities, and need for postmortem material are rarely clarified before the opportunity for donation arises. The need for swift action to obtain fresh tissue is not a high priority for the custodian at the time of death.

Recommendation 4. Explore with the general counsel of the Alcohol, Drug Abuse, and Mental Health Administration and others the current status of laws regarding brain donation.

Recommendation 5. Investigate the use of the Uniform Anatomical Gift Act of 1987 in various States. Determine whether there are common difficulties with implementing it and whether these difficulties stem from legal, social, or ethical reasons.

Recommendation 6. Determine whether supplementary or model legislation is required to facilitate brain donation.

Recommendation 7. Provide funds for a 24-hour, 800 telephone number to provide custodians of donations with the telephone number of the nearest autopsy center. The autopsy center's on-call person should respond with a plan for facilitating donation.

Problem 3. There is a dearth of dedicated mental health personnel interested in brain tissue acquisition at most autopsy sites, and pathologists are not attuned to facilitating brain donation.

Recommendation 8. Obtain pilot data on enhancing tissue acquisition from a large catchment area by placing a dedicated neuropathologist and support staff in an appropriate facility to determine the number and quality of research brains that can be obtained in 1 year.

Problem 4. Donations need to be facilitated from appropriately diagnosed patients.

Recommendation 9. Because many potentially appropriate donors are residents of Veterans Affairs (VA) centers, explore with the VA Research Director mechanisms for cooperation between NIMH and VA. Access to the World War II twin registry may be an important VA resource. Prospective studies might be particularly facilitated by using the VA population.

Recommendation 10. Because longitudinal studies of well-characterized patients by mental health clinical research centers (MHCRCs) are another resource, encourage acquisition of brain material from subjects of these long-term studies. Or encourage these projects to apply for supplementary funding for this purpose.

Recommendation 11. Stimulate donor registration programs. Autopsy planning, donation logistics, and funeral arrangements should be developed well ahead of the donation. Funds may be needed to support autopsy and funeral arrangements.

Recommendation 12. Encourage further development and use of standardized diagnostic instruments to be used in conjunction with postmortem tissue acquisition.

Problem 5. Existing private and public service brain banks do not have sufficient brain material from either normal or comparison donors or those with major mental disorders.

Recommendation 13. Encourage MHCRCs, large longitudinal grantees, centers of neuroscience of mental disorder, and other grantees currently involved in clinical brain research to apply for supplementary funding of existing projects for tissue acquisition.

Recommendation 14. Encourage public service tissue banks to apply for extra funding through contract or supplementary mechanisms. Encourage dissemination of tissue availability.

Recommendation 15. Explore methods to obtain legislative support for brain tissue acquisition efforts.

Problem 6. Tissue useful for postmortem analysis must be accompanied by details of the death-event (e.g., diagnosis, medications, cause of death, life supports).

Recommendation 16. Develop or encourage the adoption of a uniform instrument for characterizing the death-event.
Problem 7. Minimum standards need to be developed for autopsy of brain tissue for research use.

Recommendation 17. Survey brain tissue users for specific as well as general requirements. Determine the amount and anatomical locations of tissues needed for postmortem study. Determine minimum standards for selecting and handling the required autopsy material for different types of research studies.

Problem 8. There are too few psychiatric neuropathologists. The introduction of brain science into the field of mental illness has progressed more rapidly than neuroscience training of psychiatric researchers.

Recommendation 18. Facilitate brain research by training psychiatrists in neuropathology or neuropathologists in psychopathology research. Institutional and individual programs should be stimulated.

References

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Announcement

The University of Limburg at Maastricht, The Netherlands, has been given the opportunity of awarding a scientific award, the Peter Debye-prize, once every 2 or 3 years. The Peter Debye-prize 1992 on “Aging of the Brain” has been awarded to Dr. John Hardy from the Department of Biochemistry, St. Mary’s Hospital Medical School, London, United Kingdom, in recognition of his achievements in uncovering a cause for Alzheimer’s disease.

The prize was presented on January 10, 1992, at the Academic Ceremony of the 16th Dies Natalis of the University.