Brain donation at the Netherlands Brain Bank

What you should know

We thank you for your interest in the work of the Netherlands Brain Bank and appreciate your willingness to consider a post-mortem donation of brain tissue for scientific research. This brochure has been comprised in order to provide you with detailed information about registration at the Netherlands Brain Bank (NBB) and the procedure of autopsy.

The objective of the NBB: to collect brain tissue and provide this to researchers in the Netherlands and abroad for research into general brain functioning and brain diseases.

What does it mean to be an NBB-donor?

By registering as a donor at the NBB, a person grants permission to carry out a post-mortem examination (autopsy), in accordance with the law. During this autopsy the brain and optionally the spinal cord, the eyes and the cervical lymph nodes are removed. These organs are dissected and stored at the NBB, in order to be distributed to scientific researchers. Without explicit consent of the donor, the NBB may not carry out an autopsy and remove tissue.

In order to conduct scientific research effectively, researchers need clinical background information concerning the donor of the brain material. For this reason the NBB asks the donor’s permission to access his or her medical records. These records are processed into an anonymized extraction of the clinical data, which can be provided to the scientists who conduct research with the brain material.

Who can register as a brain donor?

In order to optimally carry out post-mortem brain research, the NBB has adapted its donor registration procedure to the demand of the research community . This means that a (temporary) registration stop can be issued for certain diseases.

Currently donors with the following diagnoses can be accepted as NBB donors:

- Multiple Sclerosis
- Parkinson's Disease
- Psychiatric disorders (schizophrenia , depression, bipolar disorder , obsessive-compulsive disorder, ADHD, autism (ASD), posttraumatic stress disorder)
- Frontotemporal dementia
- Alzheimer's disease (registration only through the VUmc Alzheimer Centre)
- Huntington's Disease
- Amyotrophic lateral sclerosis (ALS)
- Narcolepsy
- Transsexualism
- Control donors (no neurological or psychiatric illness)

This means that people with a different disease cannot register (temporarily). www.hersenbank.nl provides current information about this.

NBB-Psy: program for psychiatric diseases

The available brain tissue of donors with psychiatric diseases is currently not sufficient to meet the demand from the research community. In order to change this, in 2012 the NBB along with five Dutch university medical centers (UMC Utrecht, VU University Medical Center Amsterdam, AMC Amsterdam, Radboud UMC Nijmegen and Erasmus MC Rotterdam) received a grant of 3.45 million Euros from the Netherlands Organisation for Scientific Research (NWO). With this contribution, the NBB will set up a national infrastructure to collect brain tissue of well-diagnosed patients with psychiatric diseases for research purposes. Direct access to brain tissue can lead to a breakthrough in research, which is important because there are still many questions about psychiatric diseases that can currently not be answered satisfactorily (see Figure 4).

How can you register as a brain donor?

Every competent adult person can register as a donor at the NBB. If the prospective donor is legally incompetent, the legal representative can handle the registration. The registration takes place by filling in and signing the attached informed consent forms. Once the NBB has received the forms, it is assessed whether registration is possible. If this is the case, the person is registered in the donor database. A registered donor receives a codicil card (figure below) which contains the donor information as well as information on how the NBB should be contacted after the donor's death. The objective of the NBB is to collect brain tissue and to distribute this for scientific research purposes.

NEDERLANDSE
HERSENBANK

Codicilnummer:
Naam donor:
Geboortedatum:

Ik ben donor bij de Nederlandse Hersenbank en stel mijn hersenen na het overlijden beschikbaar voor wetenschappelijk onderzoek.

Figure 1: NBB codicil card

If this is not possible, for example due to the presence of metastases in the brain, or if there is already enough brain tissue available for that particular disease to satisfy researchers' demand, the NBB reserves the right to refuse the registration. It will always be explained in writing why registration is not possible. See also page 1 under "Who can apply as a brain donor?"
For the good conduct of post-mortem brain donation, it is necessary that the family of the donor assents to the procedure. We strongly advise persons who consider brain donation to discuss this decision with the family and to let this information leaflet be read by close relatives. It is essential that the decision made by the donor comes about in consideration of the family's opinion. For this reason, the registration forms require a co-signature of a close relative. This is generally the spouse, a registered partner or other life companion. If such a person is not available, an adult child or other relative up to the third degree can sign. If this is also not possible, the forms can be co-signed by the heir, a confidant (e.g. the general practitioner) or the person designated by the donor to make the funeral arrangements. Of course this could also be a close friend. Although such co-singing is not legally required, the NBB does not carry out autopsies without written consent of the donor also signed by a close relative.

Medical questionnaire and MINI +

Along with the registration form, we ask you to fill in a general medical questionnaire that provides the NBB with information about your health. If you are registered as a control donor, we will request you to update this information after five years by means of a short questionnaire. Donors with a psychiatric disease get this request every year. In the context of NBB-Psy, we also ask the control donors and donors with a psychiatric disease for permission to administer a psychiatric diagnostic interview called MINI +. This interview only needs to be done once. You will be approached by one of our research assistants. More information can be found on www.NBB-psy.nl. If a control donor develops a neurological disorder after registration, the NBB reserves the right not to perform the brain autopsy. It is also possible that the NBB willl not perform an autopsy if the brain tissue supply for that particular disease is amply sufficient to meet the current demand from the research community. This is consistent with the NBB's registration policy.

Is registration binding?

The person registered as a donor can withdraw the registration at any time, without giving a reason. This can be done in writing. The person will be immediately removed from the donor database. All data collected up to that point will be destroyed. Naturally, the person withdrawing the registration will receive a written notice.

Brain donorship and other forms of donation

It is not always possible to combine a brain codicil of the NBB with other forms of body or organ donation:

There are different forms of donation. It is possible to donate organs and tissues for transplantation purposes. Secondly, one can donate the brain (and spinal cord) for scientific research purposes. Finally, the whole body can be made available for the training of medical students. Although the last donation form is referred to as “making the body available to science”, fundamental research is not conducted in this case. After the first two types of donation the body is returned to the relatives for burial or cremation, after the third type this does not happen.

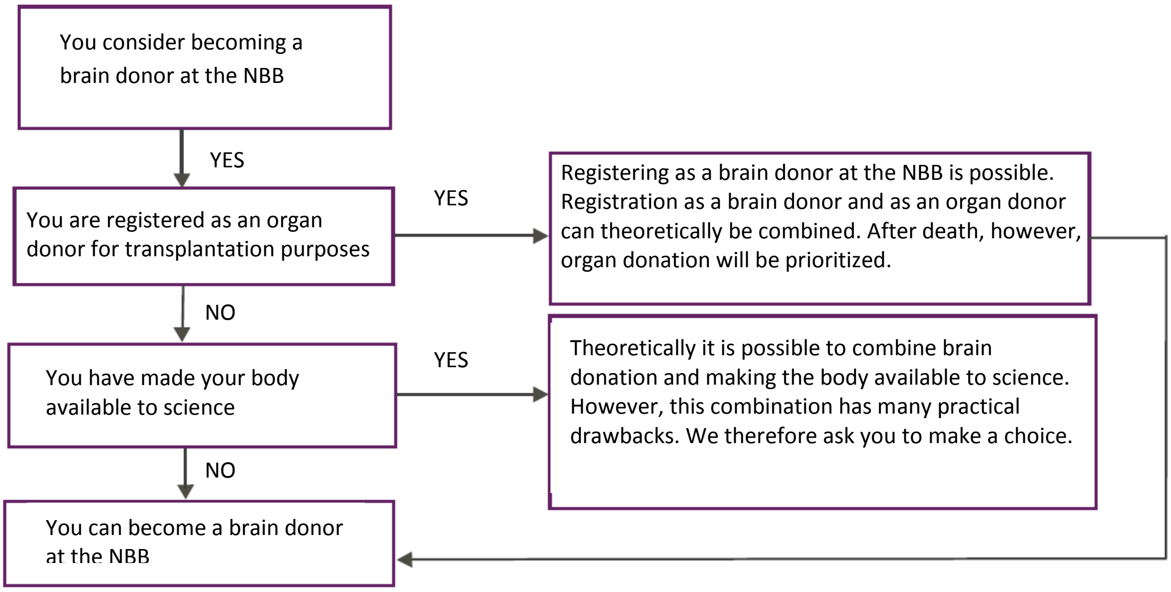

Figure 2: possible combinations with other donation types

The different donation possibilities are arranged by different organizations. This means that, for example, you are not automatically a brain donor if you are a registered organ donor. However, both forms of registration can be combined. In that case, the treating physician will assess after death whether the organs are suitable for organ transplantation, considering the age of death and the diagnosis at the time of death. If this is not the case the brain autopsy can take place. In Figure 2 we have summarized the potential combinations of tissue donation.

Figure 3: The neuropathologist examines very thin brain sections (8/1000 mm) under the microscope. The NBB lab technicians stain the sections in order to be able to distinguish separate brain structures.

Additional donation possibilities

At every autopsy a blood sample is taken (max. 50 ml). In addition to the brain donation there are three possibilities for which you can give explicit permission:

Like the brain, the spinal cord is part of the central nervous system. In case of a brain disease the spinal cord may also show abnormalities. Therefore we ask you to consider donating your spinal cord as well.

The cervical lymph nodes, which are located in the neck, regulate the brain immune system. In order to research immune system reactions in certain diseases, such as multiple sclerosis, cervical lymph nodes are necessary. Therefore the NBB registration form includes the possibility to donate the cervical lymph nodes.

The NBB is a department of the Netherlands Institute for Neuroscience (NIN), which carries out much ophthalmic research. Brain research and ophthalmic research have much in common. Therefore the NBB asks you to consider eye donation in addition to brain donation. For more information on eye research, please refer to the ophthalmogenetic department of the NIN, phone number +31205664592 / +31205665391.

Procedure after the donor's demise

First of all the deceased person must be pronounced dead by the attending medical doctor. When the attending doctor determines natural cause of death (death as a result of old age or a natural course of the disease) a death certificate is issued (form A). In case of euthanasia, which is considered an unnatural cause of death and therefore requires a different procedure, it is very important for the NBB to be informed of plans of euthanasia in advance. *NB. Under Dutch law euthanasia can be performed, provided that certain strict conditions are fulfilled (e.g. terminal illness and explicit written request from the patient).*

The staff of the NBB is available 24 hours a day, to receive notification of a donor's death. As far as the circumstances allow this, the NBB should be informed as soon as possible. It is very important that the time period elapsed from the moment of donor's death and autopsy remains as short as possible (preferably a few hours). Naturally, the wishes of the surviving family of the donor will always be taken into consideration when the transportation and autopsy are arranged by the NBB. In some cases the NBB can decide not to perform the autopsy. Naturally, in that case it will be explained why the autopsy cannot take place.

The body of the deceased donor will be brought to the VU medical center (VUmc) in Amsterdam. The NBB has arrangements with an undertaker for the purpose of the transportation of the deceased donors to the medical center. All personal belongings and/or clothing of the deceased that are taken along by the undertaker will be returned to the appointed funeral director after the autopsy.

The attending doctor of the deceased is asked to hand over the file containing medical records of the donor. Having clinical background information is very important, both for the good conduct of the autopsy as well as for future scientific research with the removed brain material.

At the premises of the VUmc, an autopsy it is performed in accordance with consent given by the donor. It is important to realize that, despite the donor's wishes, the autopsy will not be carried out if the family objects to it. Once more we would like to emphasize the importance of discussing decisions concerning brain donation with the family.

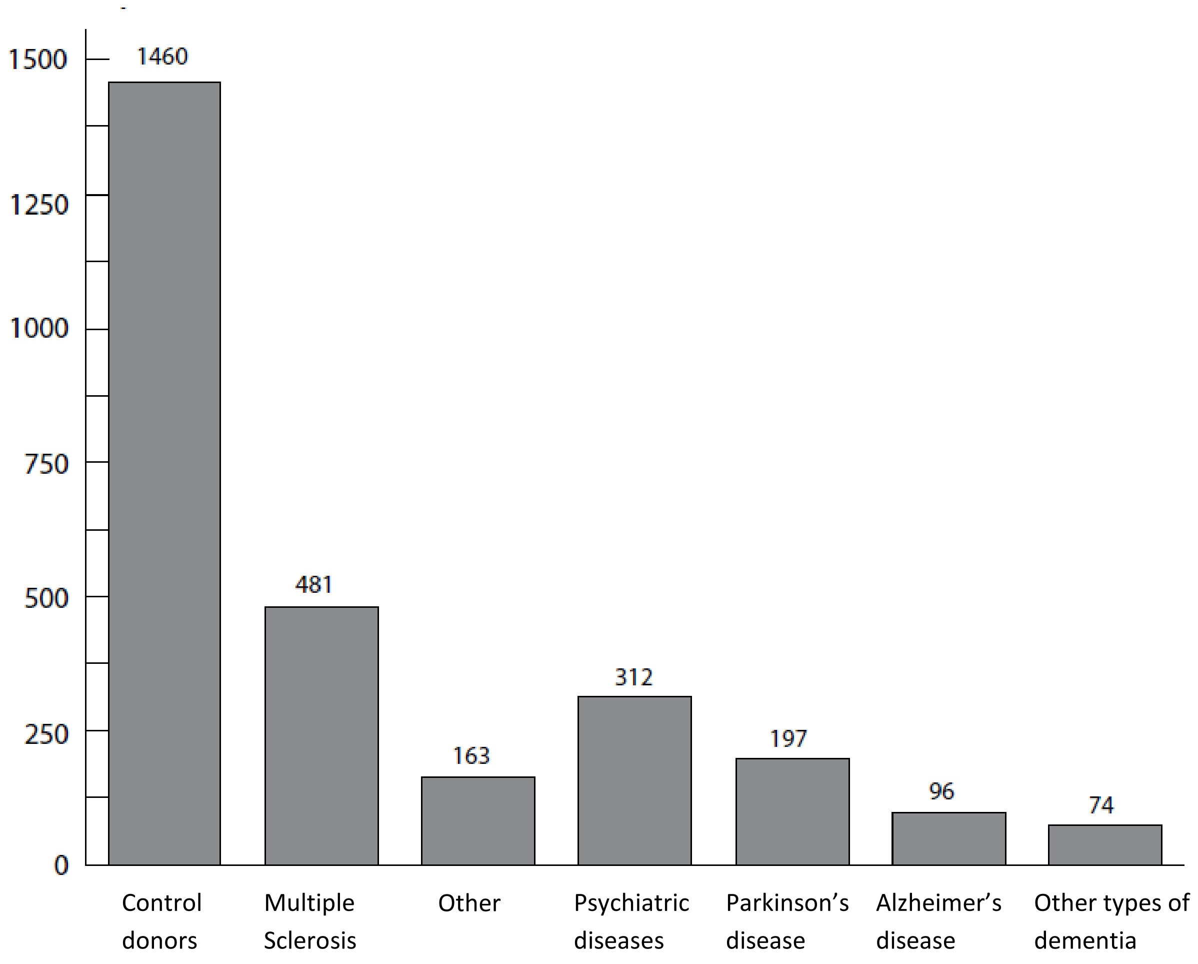

Figure 4: Number of registered donors on September 1, 2012

An autopsy, also known as necropsy or post-mortem is carried out by a specialized doctor (neuropathologist) assisted by an employee of the mortuary and staff members of the NBB. Autopsy can be compared with surgery: by an incision on the back of the head, the cranium of the deceased is opened, so that the brain can be removed. If the donor's consent explicitly allows it, extra material such as the spinal cord is also removed. The procedure is performed with great care by experienced and knowledgeable individuals. The signs of autopsy (sutures) are only visible at the inspection of the back of the head, and in case of spinal cord removal, the back. Therefore autopsy does not prevent an open casket funeral and viewing of the deceased.

After the autopsy the body of the deceased is transported to the place designated by the family (< 24 hours, depending on the distance and time of death).

Further burial or cremation arrangements will be carried out by the designated funeral director.

Naturally all costs of autopsy and transportation are taken care of by the NBB. All costs pertaining to funeral arrangements, burial or cremation, remain for own account.

What happens with the removed material?

After the brain and optionally extra materials have been removed, approximately seventy brain areas are dissected and preserved for future scientific research. In addition, depending on the clinical diagnosis of the donor, at least sixteen brain areas are dissected for diagnostic purposes. These brain areas are examined under the microscope by the neuropathologist (see figure 3).

On the basis of the medical file and the microscopic findings, the neuropathologist issues a diagnostic report in English. After autopsy this takes approximately one to two years. The report focuses on neurological abnormalities that are visible under the microscope. It depends on the disease whether the abnormalities are visible at this level. In psychiatric diseases, for example, this is often not the case.

The primary objective of the NBB is collecting brain tissue in order to distribute the well-diagnosed tissue for scientific research purposes. Therefore the neuropathological report is mainly written for the researcher who will use the brain tissue. To express our gratitude for the co-operation of the relatives of the deceased, a copy of the neuropathology report is sent to the physicians of the deceased donor. The physician is requested to discuss the report with the relatives of the deceased. If the donor has any objection to this, he or she can stipulate this on the registration form.

Displaying brain tissue for educational purposes

One of the objectives of the NBB is to emphasize the importance of research with human brain tissue. Therefore, the NBB sometimes shows brain tissue for educational purposes. This is always done in such a way that the identity of the donor cannot be deduced. Situations where brain tissue is displayed include tours for researchers, grant suppliers or students. Brain tissue can also be shown in communication materials aimed at donor recruitment or supplying general information about the NBB.

How is the NBB material distributed to scientific researchers?

After autopsy the brain tissue is frozen at -196°C and stored at -80°C or it is chemically treated, in order to preserve it for future scientific research. A unique code is assigned to every sample of tissue, so that the person handling the samples cannot trace the identity of the donor. In this way the NBB guarantees the privacy of the donor and his or her family.

Due to the donor program in which people can register during their life, the quick and well-coordinated autopsies and the specialized diagnostic procedures, the NBB provides brain tissue that is of excellent quality for researchers.

We are very well aware what a valuable possession human brain material is. For this reason the material is exclusively sent out to researchers who comply with a number of strict rules. In order to receive brain tissue the researcher must submit a detailed application, in which the research project and the proposed use of the brain tissue are described. Because pharmaceutical companies also perform highly valuable research aimed at finding targets for the development of new drugs and therapies, they can also apply for tissue at the NBB.

The NBB's scientific committee assesses, among other things, the feasibility and quality of the research proposals of all applications from researchers. Only after a research application is approved and a material transfer agreement has been signed shall the researcher receive the brain material. The material transfer agreement stipulates, among other things, that the received tissue can only be used for the approved research project. The agreement prohibits supplying material to third parties or using it in an irresponsible manner.

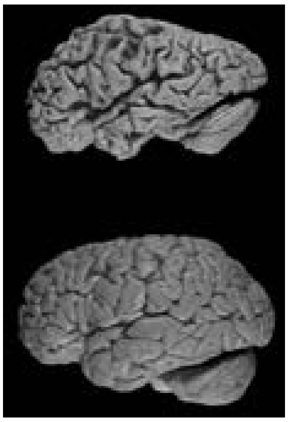

Figure 5: healthy brain (below) vs. brain of a donor with Alzheimer's disease. Note the atrophy that has occurred in Alzheimer's disease and that has caused the brain to decrease in size.

Why are the medical records requested?

The availability of medical background information concerning the donor is essential for good conduct of the scientific investigation. For this reason, the NBB asks donors to complete medical questionnaires and requests all medical records at the treating doctors' offices. A designated assistant of the NBB extracts relevant clinical information from the medical records, such as disease symptoms and use of medication. This summary is composed in such a manner that it does not contain any identifiable data of the donor. The researcher receives exclusively the above -mentioned summary, thus never having full access to the medical records of the donor. Given the sensitive information contained in the medical records, the storage and processing of the data occur entirely in conformity with the rules of medical confidentiality.

What kind of research is performed with the brain tissue?

The NBB distributes donor material to many researchers worldwide. It concerns various types of research in which different histological, cellular and molecular techniques are applied. However, the aim of this research is always the same: to gain more insight in the normal functioning of the human brain and the pathological processes that underlie different neurological and psychiatric diseases.

Sometimes the thin sections of brain tissue (less than 1/10 millimeter) are used to culture brain cells. In addition, skin cells will be cultured for the benefit of the NBB-Psy program. For this purpose a small skin sample (0.2 by 0.2 cm) will be taken from 50 donors. The samples are taken from the back of the head, adjacent to the cut that is made in order to take out the brain. Cultured cells or tissue sections survive only for a limited time (a few weeks). These cells shall never be implanted in humans.

Publication of research results

The results of scientific investigations conducted with donor material are published in several international scientific periodicals. In most cases the results are published years after the actual donation has taken place. Annually the NBB requests researchers to supply a list of publications that have resulted from research projects performed with NBB donor material. These lists are published on the website and in the biennial reports of the NBB. This makes it possible to keep everyone informed of all scientific research made possible by the valuable contribution of NBB donors.
The NBB brain tissue has already made more than 600 research projects possible (see www.hersenbank.nl). The outcome of scientific research projects is not communicated personally to the families of the donors. In very exceptional cases, if information that emerged during the course of research is of obvious clinical importance to the surviving relatives, the NBB can deviate from this rule.

Sciences needs time

At times scientific breakthroughs occur. In most cases, however, it concerns gradual steps towards a better understanding of the functioning of human brain and the different pathological processes which underlie the diseases. Generally, outcomes of scientific research will not be immediately applicable in the clinical practice. These results need to be reviewed in the scientific community in order to prove the importance for the individual patient.
Science needs time. However, gaining insight in the process of the disease in order to develop new effective therapies is impossible without human brain tissue. The solution for brain diseases can be found in the brain!

Contact

We hope that you were able to find all information necessary to make a well-considered decision regarding brain donation. If you believe to be informed sufficiently and wish to become a donor, please fill in the informed consent forms and return them to the address below.

It might be that some of your questions have remained unanswered. In that case you can get in touch with one of our assistants during office hours. You can also visit our website or send us an e-mail.

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