

Brain donation at the



**NEDERLANDSE
HERSENBANK**

What you should know

We thank you for your interest in the work of the Netherlands Brain Bank (NBB) and appreciate your willingness to consider a post-mortem donation of brain tissue for scientific research. This brochure has been comprised in order to inform you and your close surroundings about the NBB.

Brain donation via the NBB contributes to the development of better treatment methods in the future, and thus to a better quality of life for people with brain diseases and their next-of-kins.

The NBB collects brain tissue and distributes this to researchers. The objective of this research is gaining more insight in the normal functioning of the brain and the pathological processes that underlie different neurological and psychiatric diseases. Hereby, better treatment methods can be developed eventually. This is not possible without research with human brain tissue.

By registering as a brain donor, you allow the NBB to perform autopsy after death (also called dissection).

At every autopsy, the brain, cerebrospinal fluid, and maximally 50 mL of blood, and incidentally a saliva sample are taken. In case of multiple sclerosis, and incidentally in other cases, an MRI-scan of the brain will be made.

In addition, there are three extra possibilities for which you can explicitly grant permission:

- In case of a brain disease, there could also be abnormalities present in the **spinal cord** (for example in the case of multiple sclerosis). Also for studying the normal functioning of the brain (of which the spinal cord is a part of), donation of the spinal cord is desirable.
- With **cervical lymph nodes**, immune system reactions in certain brain diseases can be studied.
- Brain research and eye research show a close relationship. Therefore, several researchers in the field of neurological functions and neurological diseases are also interested in **eyes**.

The spinal cord, the cervical lymph nodes, and the eyes are not always dissected, even though the donor had given consent for dissection of these. These are only dissected when at the moment of the autopsy there is a demand for this from researchers.

If you want to register as a new donor at the NBB, you can request a registration form via www.hersenbank.nl. After receiving your registration, the NBB judges whether registration is possible.

Registration at the NBB is possible from the age of 18 years. The NBB is always looking for control donors, meaning persons without neurological or psychiatric illness. In addition, the following diagnoses (diagnosed by a medical specialist) are currently the main focus of the NBB:

- Multiple Sclerosis
- Parkinson's Disease
- Frontotemporal dementia
- Other types of dementia, such as Alzheimer's disease or vascular dementia
 - Registration is possible if the donor lives in Noord-Holland, Zuid-Holland, Utrecht or Flevoland. Otherwise, registration is only possible via the Alzheimer Center Amsterdam VUmc, or the PreDiva-cohort of the AMC.
 - If you are unsure about the registration because the specific type of dementia is not mentioned, you can contact us.
- The following psychiatric diagnoses: schizophrenia and/or psychoses, major depression, bipolar disorder, autism spectrum disorders, obsessive-compulsive disorder, AD(H)D, and posttraumatic stress disorder.
- The following (hereditary) neuro-developmental disorders: triple-X-syndrome, Klinefelter's syndrome (XXY), 22Q11-deletion/-duplicationsyndrome, fragile-X-syndrome, FXTAS, Neurofibromatosis type 1, Tuberous Sclerosis Complex, Angelman syndrome, Rett syndrome, Prader-Willi syndrome, Williams syndrome, Fetal alcohol syndrome, Costello syndrome, Phelan McDermid syndrome, Cardio-Facio-Cutaneous syndrome, Cornelia de Lange syndrome, Velocardiofacial syndrome and Rubinstein-Taybi syndrome.

In addition, donors with the following diagnoses can be accepted as NBB donors:

- Multipele system atrophy (MSA)
- Progressive supranuclear palsy (PSP)
- Corticobasal degeneration (CBD)
- Lewy body dementia
- Huntington's Disease
- Amyotrophic lateral sclerosis (ALS)
- Narcolepsy
- Transsexualism
- Celiac disease

- Ataxia
- Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS)

The NBB adapted her donor registration policy according to the demand from researchers. This means that for some diagnoses, a (temporarily) registration stop can be set. On www.hersensbank.nl you can find the up-to-date information on this.

After registration, you will always receive a message, also when registration is not possible. Are you in doubt whether you are eligible for registration? Please contact us.

The registration as a brain donor requires a co-signature of a close relative.

The NBB finds it essential that the decision made by the donor comes about in consideration of the family's opinion. Therefore, without a co-signature, the NBB will not perform the autopsy. You can choose yourself which (adult) person you want to designate for this. This is generally the spouse, a registered partner or other life companion. Other possibilities are for example an adult child or other relative, a close friend, your general practitioner or the person designated by the donor to make the funeral arrangements. In case we want to contact you but cannot reach you, we will contact the co-signer to ask whether your contact details are still correct.

A medical questionnaire is part of your registration. If you have a psychiatric diagnosis, we also request your DSM-classification at your General Practitioner after registration.

Filling out the medical questionnaire along with the registration is required, and will be used to judge whether you are eligible for registration as a brain donor. To update the medical questionnaire, control donors and donors with a psychiatric diagnosis get a request to update this information every five years.

An incapacitated person can be registered by a designated representative (mentor or written authorized person) or a close family member (spouse, partner, parent, child, brother or sister).

The mental incapacity needs to be permanent and choices should be made in line with the wishes of the mentally incapacitated person.

In some cases, the NBB can perform an autopsy while the deceased is not yet registered at the NBB at the point of death.

In this case, after the deceased person is pronounced dead by the attending medical doctor, the NBB should be contacted. The NBB determines if the brain autopsy can take place and the close family fills out a form 'Consent form Netherlands Brain Bank for Next of Kin'.

If you are registered as an organ donor, you are not automatically also a brain donor. For this, a separate registration at the NBB is required. Both forms of registration can be combined.

You can donate organs and tissues for transplantation via the Donor Register. In addition, you can donate your brain for scientific research via the Netherlands Brain Bank. Finally, the whole body can be made available for the training of medical students ("making the body available to science"), via a university medical center. 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.

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 the case, the physician needs to contact the Dutch Transplant Foundation (www.transplantatiestichting.nl). Here you can also find more information about organ and tissue donation.

Aside from brain donation via the NBB, it is also possible to donate your heart via the Heart Bank (www.hartenbank.nl).

In case you are interested in this, you need to register separately at the Heart Bank. It is possible to be both brain donor at the NBB as well as heart donor at the Heart Bank. The NBB and Heart Bank are separate organisations, however they work closely together. Autopsy of the brain and the heart will take place at the same time in the Amsterdam UMC, location VUmc.

In case you change your mind, you can withdraw the registration as a brain donor at any time.

This can be done in writing and without giving a reason. The person will be immediately removed from the donor database. All data collected up to that point will be destroyed. Even though it is not required, we would like to be informed about the reason of withdrawal, as we could possibly change our way of education and information provision towards our donors.

After death, the NBB needs to be contacted as soon as possible (24 hours a day reachable). The autopsy of the brain can take place maximally 12 hours after death. In case of euthanasia, it is important to notify the NBB beforehand.

It is possible to say goodbye even before the transport to Amsterdam. In order to keep the clothes in which the person arrives at the Amsterdam UMC, location VUmc tidy, the deceased is shrouded. All clothing of the deceased that are taken along by the undertaker will be returned to the appointed funeral director after the autopsy.

It is possible that the NBB can decide to not perform the autopsy of a brain donor.

A possible reason for this is that the NBB holds a maximum number of 150 donations per year. Thereby, the NBB will focus on diagnoses for which there is a high demand from

the scientific community for research, and donations from persons that are enrolled in a specific study, a so-called cohort study. The NBB expects that donations will rarely be declined because of this reason.

In addition, brain donation can never take place in case there are tumors in the brain, or if the donor suffered from a brain haemorrhage which caused permanent complaints. The reason for this is that the NBB distributes the brain tissue for scientific research purposes, and this research is made more difficult by possible tumors or haemorrhages. In addition, the brain donation cannot take place if there is a (suspected) corona-virus infection. Finally, the brain donation cannot take place if the donor is infected with Hepatitis B, Hepatitis C or HIV.

All costs of autopsy and transportation (through funeral transport) are taken care of by the NBB. The deceased is brought back at most one day after death. All costs pertaining to funeral arrangements, burial or cremation, remain for own account. If after death the family objects to the autopsy, the autopsy will not take place.

The autopsy takes place by an incision on the back of the head. What is still visible, is a scar, at the lower part of the back of the head, from ear to ear. Because it concerns a drastic surgery, it is necessary that the deceased stays at least 8 hours at the mortuary after the autopsy. The final care and dressing of the deceased will take place after the autopsy via the funeral director. The funeral can take place as planned and autopsy does not prevent an open casket funeral and viewing of the deceased.

A neuropathologist together with a few assistants performs the autopsy at the Amsterdam UMC, location VU medical center. Based on the medical file and the microscopic findings, the neuropathologist writes a report with the findings.

Dependent on the clinical diagnosis, the neuropathologist examines the relevant brain areas under the microscope. It depends on the disease whether the abnormalities are visible at this level. In psychiatric diseases this is often not the case. The neuropathological conclusion is often a combination of the medical details and the presence of visible abnormalities under the microscope.

Based on the medical file and the microscopic findings, the neuropathologist writes an English report, written for researchers. In some cases, the neuropathological diagnosis turns out to be different than the diagnosis that was set during life. The treating physician receives the in Dutch translated neuropathological conclusion. In case the donor gave permission for this, the treating physician can discuss the report with the relatives of the deceased.

The conclusion of the neuropathological report written by the neuropathologist, is ready after circa 1,5 to 2 years. We realise this is a long period of time. The NBB uses up-to-date techniques to be



Figure 1: The neuropathologist examines very thin brain sections (8/1000 mm) under the microscope. The slides are in reality twice as big as in the photo. The sections are stained in order to be able to distinguish separate brain structures.

able to determine the conclusion more accurately, and unfortunately this takes more time. In addition, the annual number of autopsies has increased in recent years. To accelerate the administrative process, in most cases the NBB chooses to send the conclusion directly to the co-signee of the donor. Only if the conclusion differs from the clinical diagnosis or if there might be a genetic factor, will the NBB send the conclusion to the donor's physician and request them to communicate this with the co-signee. In that case, the co-signee will receive a notification that the conclusion has been sent to the physician with a request to discuss it with them.

The NBB requests all medical records at the treating physicians.

The medical file is important for the execution of the autopsy as well as for the scientists that perform research on the brain tissue. From the medical records an employee of the NBB composes a summary with the relevant clinical information, such as disease symptoms and the 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.

Researchers from all over the world receive brain tissue and anonymized information, for various types of research.

Many researchers are affiliated to universities and other non-profit research institutes, but pharmaceutical companies can also request tissue, as they also perform highly valuable research aimed at finding targets for the development of new drugs and therapies.

The tissue is available for various types of research (among which is genetic research), in which different histological, cellular and molecular techniques are applied. Sometimes, the thin sections of brain tissue are used to culture brain cells and generate cell lines. These cultured cells shall never be implanted in humans. In addition, for some research projects, skin cells are cultured. For this

purpose, from a few donors, a small skin sample will be taken, invisibly, from the back of the head adjacent to the incision for the autopsy.

The NBB sometimes shows brain tissue for educational purposes, such as 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. This is always done in such a way that the identity of the donor cannot be deduced.

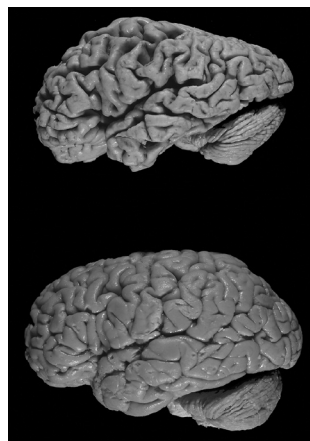


Figure 2: Healthy brain (below) vs. brain of a donor with Alzheimer's disease. Note the atrophy that has occurred in Alzheimer's disease, and that has caused the brain to decrease in size.

In order to receive brain tissue, researchers must submit a detailed application. After approval they sign an agreement that stipulates how the researchers must handle the tissue.

In the application the research project and the proposed use of the brain tissue are described. 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 tissue. The material transfer agreement stipulates, among other things, that the received tissue can only be used for the approved research project. The tissue remains property of the NBB. The agreement prohibits supplying material to third parties or using it in an irresponsible manner.

Scientific results are published in international scientific journals, mostly years after the brain donation took place.

At times, scientific breakthroughs occur. In most cases, however, it concerns gradual steps towards a better understanding of the functioning of the human brain and the different pathological processes which underlie the diseases. Generally, outcomes of the scientific research will not be immediately applicable in the clinical practice. The researchers inform the NBB about publications that came about with the use of NBB-tissue. The publication lists are placed on the website and in the year reports of the NBB.

All procedures of the NBB are in line with the national and European law^{1,2} and are adapted to the declaration of human rights (self-determination, dignity and integrity).

The ethical principles to which the NBB adheres and the legal embedding of the procedures of the NBB are summarized in our ethical and legal declaration (www.hersen-bank.nl/hersendonatie/werkwijze-voor-hersendonatie/).

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.

Netherlands Institute for Neuroscience
Attn: The Netherlands Brain Bank
Antwoordnummer 20010
1100 VV Amsterdam Zuidoost

www.hersenbank.nl

e-mailaddress: info@hersenbank.nl

Report a death?

During office hours: 020-5665499

Outside of office hours: 020-4444330 (control room VUmc)

Questions?

Business days from 9.30 - 11.30: 020-5665499

Fax number: 020-6918466

1 General Data Protection Regulation (GDPR)

2 Art. 72 lid 1 of the Wet op de Lijkbezorging