See what happens to brain tissue at the Harvard Brain Bank.
As these maps show, over a 5 year period, the Brain Bank took in 1,474 brains from around the country (green map) and sent 14,018 tissue samples to researchers (yellow map).
The first step in the process. Our administrative staff takes calls from bereaved families, obtains their written consent, arranges for a pathologist to remove their family member’s brain, and coordinates with the airlines and ground couriers the transport of the tissue to the Brain Bank.
The brain tissue arrives at Logan Airport by plane and then taken from the airport to the Brain Bank via courier. We also have local ground couriers delivering brain tissue in the New England area.
The Brain Bank’s dissection room, where the brain tissue is received, weighed, examined, imaged, dissected and frozen for storage.
A whole fresh brain, sitting upside-down, awaits dissection. An average human brain weighs about 1400 grams, although brains can normally weigh anywhere from 900 to over 2000 grams. Diseases such as Alzheimer’s and Huntington’s significantly reduce the size and weight of a brain.
Bisecting a whole brain

Holding the brain by the brainstem, our dissectionist uses a knife to cut the brain in half.
The Two Halves Of the Brain

The two halves of the brain. One half will be sliced and frozen. The other half will be preserved in formaldehyde (fixed) for our neuropathologist to examine.
Digital images are made of both halves of the fresh brain. The half to be frozen will be sliced from front to back, and these slices will also be imaged.
Slicing the cerebral hemisphere

After the brainstem has been removed from the half brain, the cerebral hemisphere is sliced from front to back.
Coronal slices of the cerebral hemisphere

The coronal slices from the cerebral hemisphere are arranged on the corkboard, from front to back.
Shown on top are the lateral and medial surfaces of the left half of the brain. Below are slices of a half brain after the brainstem has been removed. A half brain with its brainstem removed is called a cerebral hemisphere.
Freezing The Brain

The brain slices are then put in between two teflon-coated aluminum plates. The plates are in turn sandwiched in between two layers of dry ice that fills the styrofoam containers. Then liquid nitrogen is poured over the plates to speed up the freezing process.
Frozen brain slices

When the aluminum plates are opened, the slices of brain tissue have been completely frozen, and are now ready for storage.
Storing frozen brain tissue

The brain slices are sealed in a plastic bag, labeled with a case number, and stored in a freezer that keeps the tissue at –80 degrees centigrade.
Freezer Room

One of the Brain Bank’s two freezer rooms. All the freezers have liquid CO2 tanks as a back-up and all are connected to multiple alarm systems that are monitored 24/7 and tested weekly.
Meanwhile, the other half of the brain is immersed in formaldehyde for 3 weeks. The formaldehyde changes the color of the brain tissue from pink to brown. It is this half of the brain that is used by our neuropathologist to screen the tissue.
Our neuropathologist first examines the exterior of the half brain (left), and then slices the half brain from front to back so that he can examine the interior of the brain tissue (right).
The neuropathologist then removes 15 different brain areas to be studied microscopically and puts them into processing cassettes. Here he is putting one of the areas into a cassette.
Tissue cassettes from fifteen cases are now ready to be processed in the neuropathology laboratory. Each cassette is labeled with a case and block number.
The tissue cassettes are then put into a tissue processor where they will be infiltrated with paraffin. The wax will harden the tissue so that it can be sliced into extremely thin sections.
Embedding the Tissue

A piece of brainstem is put into a metal mold and surrounded by more wax. The labeled cassette bottom is then put on top, and the mold transferred to a freezing plate where the wax hardens around the tissue into a solid block.
This picture shows the pieces of brain tissue being embedded in wax. To the left is the freezing plate where the blocks are hardening.
Thin sections are cut from the wax blocks on a microtome. These sections will be stained with various dyes that will show the microscopic structure of the brain tissue and the damage done to the brain by various diseases.
Set of Embedded Brain Samples and Stained Sections

On the top is shown a complete set of wax blocks taken from a single brain; on the bottom is the set of stained sections taken from the blocks. The thin sections are embedded in a resin and then sandwiched in between two pieces of glass.
Our Fixed Tissue Room

The remainder of the fixed tissue is stored in plastic containers in our fixed tissue room. This tissue is also available for researchers.
Our neuropathologist examines the stained sections with a microscope. He will produce a neuropathology report that either confirms, corrects, or expands upon the clinical diagnosis.
Our staff psychiatrist reviews the clinical records and family questionnaires to confirm or correct the psychiatric diagnosis that accompanies cases such as schizophrenia or bipolar disorder. He also assigns a final or “distributive” diagnosis that accompanies all tissue that we send to researchers.
Now that the tissue has been screened, our staff can remove the frozen slabs of tissue from the freezer bags and dissect out the areas that a researcher requests.
Our dissectionist lays out the slices on the freezing dissecting table that keeps the tissue at −20°C while the tissue is being dissected. He will dissect out pieces of tissue for researchers with a scalpel.
Tissue ready for researchers

Pieces of formaldehyde-fixed tissue sit ready to be put in shipping boxes and send to a researcher.
Once the neuropathology report and psychiatric screening are complete, a set of microscopic images is taken on each case, showing the damage a particular disease does to brain tissue. These are combined with the macroscopic images and made available to researchers on our website.
The slides that follow show some examples of the macroscopic and microscopic images that are obtained for each brain processed at the HBTRC. The appearance of the brain and its cellular and molecular composition varies greatly in different disease states.
On the left is an Alzheimer’s case. On the right is a normal brain. Notice the smaller size and wrinkled (atrophic) surface of the Alzheimer’s brain. As the nerve cells (neurons) die, the convolutions that make up the cortical surface shrink (atrophy) and thus give the surface of the Alzheimer’s brain a more wrinkled appearance.
On the left is a normal brain. On the right is an Alzheimer’s case. Notice how much smaller the Alzheimer’s brain is. Notice in particular the size difference between the temporal lobes. The temporal lobes contains critical areas for emotion and memory and are some of the first areas affected by Alzheimer’s.
Senile Plaques in Alzheimer’s Disease Brain

This is a slice through a convolution (gyrus) of the cerebral cortex, stained with silver nitrate, from an advanced case of Alzheimer’s. All of the brown spots you see are called senile plaques, one of the two hallmarks of Alzheimer’s Disease. A normal brain has few or none of these plaques.
Senile Plaques

An up-close view of two senile plaques from visual cortex, stained with silver nitrate. The orange core and periphery of the plaques is composed of the abnormal protein called beta-amyloid.
The other hallmark of Alzheimer’s disease are called neurofibrillary tangles, seen here as the brown streaks filling the dying nerve cells of the hippocampus, the brain structure responsible for constructing memories. The tangles are composed of a distorted enzyme called Tau.
The beta amyloid protein found in senile plaques is also frequently found in the blood vessels of Alzheimer’s patients. This vessel, cut length-wise, and stained with a dye called Congo Red, shows large amounts of beta amyloid in its walls.
Normal and Huntington’s Disease Brain

On the left is a normal half brain. On the right is one from a Huntington’s patient. The arrows point to the striatum, a deep brain region that choreographs context-relevant movement, thoughts and habits. Notice that the normal brain fills up the lateral ventricle. However, in the Huntington’s brain, the lateral ventricle is much larger because the striatum (the brown crescent within the ventricle) has all but melted away.
Huntington’s Disease

Two slices through the brain’s striatum. The normal slice is on the right; the Huntington’s slice is on the left. The Huntington’s striatum has severe atrophy, and because the cerebral cortex is connected to the striatum, Huntington’s Disease patients not only suffer from movement disorders but eventually become demented as well.
In this microscopic image of Huntington’s Disease brain tissue, the nerve cells (neurons) in the striatum have totally disappeared. The astrocytes, a type of support cell, stained in red, are reacting to the damage caused by the disease.
The brain is composed of neurons that generate electrical activity that is transmitted from one neuron to another. These so-called neural circuits give rise to what we perceive as behavior affecting virtually every aspect of our daily activities, including those involving thought, movement and emotion. The photomicrograph above shows a row of Perkinje neurons in a part of the brain called the cerebellum. These neurons are part of the motor systems and their firing coordinates motor skills and even learning. The second neuron from the right shows a cluster of fibers from other neurons interacting with the body of its cell. Although there are many different subtypes of neurons, certain ones are preferentially affected in different disease states affecting the human brain. A graphic example of this is found in Huntington’s disease and Parkinson’s disease. These two disorders are discussed in the next series of slides.
This image compares Parkinson Disease brain slices (left) and normal brain slices (right). The two small slices in the middle of the picture are from the uppermost part of the brainstem. Notice the black streak in the normal midbrain on the right, called the Substantia Nigra. These neurons produce dopamine, a chemical necessary for normal movement. The black streak is absent in the Parkinson’s midbrain, because the dopamine-producing neurons have been destroyed by the disease.
Normal and Parkinson’s Disease
Substantia Nigra

Two microscopic images from a normal (left) and Parkinson’s (right) Substantia Nigra. In the normal Nigra (left), we see a large number of dopamine-producing neurons (DPN: reddish-brown dots). On the right, however, the Nigra in Parkinson’s Disease shows only a very small number of these neurons.
Neuron Affected by Parkinson’s Disease

An up-close look at a dying dopamine-producing neuron in the Substantia Nigra of a Parkinson’s patient. The abnormal round, red spheres within the dying cell are called Lewy Bodies, the hallmark of Parkinson’s Disease.
Unexpected Findings from Neuropathological Assessment of Brains

In the course of performing a very detailed neuropathological assessment of the cases we receive, there are occasionally unexpected pathological changes that are unrelated to the person’s diagnosis. In the above photo, lung cancer was found and appeared to have spread to the brain. Arriving via blood vessels, the cancerous cells multiply and radiate out from their point of entry, destroying normal brain tissue in the process. When changes of this type are found, the brain may not be suitable for neuroscience studies.
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