

What the McLean brain bank malfunction means for autism research

Losing a tissue collection because of freezer failure is a serious setback to neuroscience – and distressing to donors' families



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The sensitivities of organ donation mean that brain banks' tissue collections take years of patient effort to acquire.
Photograph: Graeme Robertson for the Guardian

This week, the freezer at the Harvard-affiliated McLean Hospital broke down, with the loss of about 150 brain samples from people who had died and who had had conditions such as autism, Parkinson's disease, Alzheimer's disease, or schizophrenia. This is bad news for at least five different communities.

First, there are the families of the bereaved individuals who had to make the very difficult decision about whether to donate their loved one's brain for research, hoping that such a donation would result in scientific advance in our understanding of the causes of a condition like autism. For some relatives, such a decision will have meant wrestling with their own religious beliefs, or with their own strongly-held emotions and wishes about how their relative should be treated. For many of these relatives, the decision has to be made in the traumatic context of unexpected bereavement, when the last thing they may want to think about is the role of medical research – yet when the decision has to be made very fast if the brain is to be preserved.

Second, there are those with the diagnosis themselves, who had the "mental capacity" to consent for their brain to be removed in the event of their death, and who also had to face the hugely difficult decision as to whether to do this. Facing death is hard for any of us, but signing a piece of paper authorizing the removal of such a key organ as your brain must feel like an

enormous step. For both the relatives, or for those with the diagnosis itself, if the tissue donation was unable to help science because of a freezer failure, this outcome may feel as if their remarkable generosity was not matched by results, even though this was no one's fault.

Third, there are, of course, the scientists whose research depends on such brain tissue to make progress. Such tissue is hugely precious, and some hypotheses simply cannot be tested in the living brain, for both technical and ethical reasons. For example, if you want to measure if a particular protein, coded for by a particular gene, is expressed in a particular part of the brain, postmortem tissue is the only non-invasive way to answer this. The breakdown of this freezer will mean there is even less of the key "material" with which to test such questions. The scientists will feel frustration that research will progress much more slowly.

Fourth, there are the charity workers, the hospital nurses and the doctors who have devoted their careers to creating such brain banks, painstakingly and sensitively discussing with donors or the next of kin the complex legal, ethical, scientific and practical issues surrounding a brain donation. For them to grow the collection, only to see part of it turn from being one of major value into one with no value in a matter of days must be equally heartbreaking.

And finally, there is the wider public, which has supported the scientific effort to create a brain bank by making financial donations to a charity, or by paying tax to enable a government-funded brain bank. They, too, are keen to have the mysteries of neurological conditions unlocked by careful neuropathological studies, and may be feeling that their financial donation has not ended up delivering the hoped-for results.

The breakdown of the freezer was reported as "setting back research (into autism) by years". This may be true. As an autism researcher myself, I have seen the benefits of elegant studies looking directly at the autistic brain. An example is the work of Manuel Casanova, a professor at the University of Louisville. He studies the "minicolumn", a vertical structure of 80 to 100 neurons (or brain cells). Writing in the journal Neurology in 2002, Casanova and his colleagues studied the brains of nine people with autism and four "controls". They reported that in "area 9" of the frontal lobe, and in "areas 21 and 22" of the temporal lobe, minicolumn width was on average *narrower* in the autistic brains. Casanova and colleagues speculate this may reflect reduced "lateral inhibition" from interconnecting neurons that release the neurotransmitter GABA. Casanova's novel observation opened up important new questions that would not have been possible without an autism brain bank.

However, there are clear limitations of postmortem studies of this kind. First, Casanova's study was obviously on a very small sample. Second, the sample of people with autism in his study ranged from five to 28 years of age, and we know the brain develops enormously across these ages. Third, the cause of death was obviously different every case (two of the nine had drowned, for example), which could affect results. Fourth, seven out of eight cases of autism also had "mental retardation" (MR) (or what, in the UK, we call "general learning difficulties"). This makes it hard to know if these brain changes are specific to autism, or if they reflect the general

learning difficulties. (In the ninth case, there was no record of whether MR was present.) Finally, five of the eight cases of autism also had epilepsy (again, in the ninth case, the presence of epilepsy was unknown), raising similar questions about whether the observed brain changes simply reflect the epilepsy, rather than the autism.

These are not criticisms, however: Casanova's study was small, and the cases were quite diverse, precisely because such brain bank collections are "opportunistic". Despite these limitations, such research has tremendous value, especially if independent researchers confirm the same pattern and are able to tease apart whether these different factors are involved.

As MRI scanning improves, we may be able to image the living brain in finer and finer detail, thereby circumventing many of the ethical and emotional issues surrounding postmortem studies, but there will still be a need for brain banks to help us understand complex neurological conditions. I hope families, people with the diagnosis, the devoted charity workers and medics, and those who fund such collections, will continue to support the scientific effort to advance our basic understanding of conditions such as autism.

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