



COVER STORY

BANKING ON BRAINS

THE BRAIN IS SAID TO BE AMONG THE MOST COMPLEX KNOWN STRUCTURES IN THE UNIVERSE. SOME 1400 EXAMPLES ARE STORED IN AUSTRALIA BY A NETWORK THAT PROVIDES VITAL SUPPORT FOR RESEARCH INTO DEBILITATING ILLNESSES. TONY JAMES REPORTS.

PHOTOGRAPHER: JAMES ALCOCK

*Therese Gattick, Manager and
Professor Clive Harper, Director,
NSW Tissue Resource Centre.*

Australia has a distinguished record of research into brain disorders ranging from alcohol-related brain damage to dementia, schizophrenia and stroke.

Helping that work is a world-class collaborative network of “brain banks”, which store tissue that can be studied now and for decades to come.

The National Neural Tissue Resource Centre, formerly called the Australian Brain Bank Network, is a collaboration between centres across Australia that aims to optimise the collection, handling and distribution of brain tissue and related samples for research.

Conditions of interest also include bipolar disorder, depression, Huntington’s disease, motor neurone disease, multiple sclerosis, Parkinson’s disease and brain and spinal cord trauma.

The network is supported by the National Health and Medical Research Council and Neurosciences Australia. Initial grants from the NHMRC helped establish the network, and it now provides substantial financial support for this rich resource.

Professor Catriona McLean, director of Anatomical Pathology at Melbourne’s Alfred Hospital, is the national director of the Resources Centre and oversees the management committee with representatives from banks in NSW, Queensland, South Australia, Victoria and Western Australia.

The network of tissue resource centres holds about 1400 brains, carefully categorised by their pathology. Individual centres tend to focus on particular disorders but some apparently normal brains are also included, for comparative purposes.

Researchers from Australia and around the world can apply for access to tissue, and applications are assessed by scientific advisory committees to ensure the precious material is used wisely and productively.



Human brains are fundamentally different to other organs. They are said to be among the most complex structures known in the universe, their anatomy is extraordinarily intricate, their function is often bewildering, and unlike simpler organs, it is not possible to collect truly representative samples during life.

Obtaining a whole brain after death provides a wealth of opportunities for research covering a broad range of normal brain functions as well as disorders and diseases.

Brain banks need donors, who can be people who decide to donate their brains once they die, or deceased individuals whose next of kin consent to donating tissue for research during an autopsy.

Therese Garrick is manager of the NSW Tissue Resource Centre, the Sydney brain bank. While working as a psychiatric nurse she became involved in facilitating brain donation by people with

schizophrenia and other serious mental illnesses. She is now part of a team of about 15 people encompassing doctors, nurses, psychologists and scientists.

With her colleagues, Ms Garrick administers and promotes the Using Our Brains program that recruits people without obvious brain disorders. They will eventually provide normal tissue that can be compared with that from people who have brain disorders recognised during life.

The Gift of Hope program recruits people with schizophrenia and other severe mental illnesses, and is operated in conjunction with the Neuroscience Institute of Schizophrenia and Allied Disorders, a national collaborative research network.

The programs have about 2,300 potential donors registered, allowing a rich set of information to be collected during life and then correlated with findings in the

Professor Harper has a long history as a “brain banker”, having built a stock of brains since he started working in the field in 1974. “The way we can use brain tissue has been revolutionised in the last few decades,” Professor Harper says.

brain after death. Some participants have regular neuropsychological assessments by the team, investigating functions such as memory, language and attention. In a new phase of the study, some also have MRI scans to provide a detailed anatomical image during life.

“Donors have a strong commitment to the program and are very happy to be assessed,” Ms Garrick says. When the inevitable happens, the program handles the mechanics immediately after death and removing the brain does not interfere

with usual funeral arrangements or preclude viewing of the body.

Coroners’ autopsies remain the main source of brains, at least until the donor programs mature. Ms Garrick has been amazed by the altruism of next-of-kin when her team approaches them about releasing tissue for research.

“Our records show that during the last four years more than 60 per cent of families have agreed,” she says. “We review cases being handled by the coroner each morning, and identify those we think might be appropriate. We call the next-of-kin by phone, introduce ourselves, ask whether they would consider consenting, then give them some time to discuss it with other family members.”

Practical issues mean the process has to be concluded within a few hours, so verbal permissions are recorded before the team completes the follow-up paperwork.

The most common reason for not gaining consent is that relatives are unsure of the deceased’s views on donating organs or tissue, or a lack of consensus among relatives. “Often people feel bad that they can’t say ‘yes’,” Ms Garrick says.

Contrary to popular perceptions, relatives are not distressed or offended by being approached about donation. Ms Garrick, with Lisa Azizi and colleagues at the Neuroscience Institute of Schizophrenia and Allied Disorders, reviewed the responses of 48 families approached about donation at the time of autopsy. The team said it was overwhelmed by their generosity in discussing the issue. Most families who gave consent said the decision had been emotionally beneficial: the thought that the deceased could make a contribution to research and the health of others was a considerable comfort at a time of sadness.

Becoming a brain donor

John McNeill was born in 1927. He started work as an office boy when he was 15, then volunteered to join the Royal Australian Navy at the age of 17 near the end of World War II. After the war, he returned to civilian life and rose through the administrative, sales and managerial ranks in manufacturing and airline industries to the level of managing director. An early retirement was less interesting than he thought, so he pursued a new set of careers including real estate.

Mr McNeill contacted the “Using Our Brains” program in 2002, and signed up as a donor. “I had to see a neurologist in the 1980s about possible multiple sclerosis, and I’ve been intrigued since then about how the brain works, and what can go wrong,” he says.

Mr McNeill is also registered as an organ donor for transplantation. “You never know, they might be useful to someone,” he says. “To me, it’s just commonsense. It’s my decision, my family know about it and agree, and my wife, who I lost three years ago, was in favour as well.”

“I’ve been a volunteer all my life. Donating my brain won’t help me, but it can help others. I don’t have any worries about people using my brain – I’ll be dead, and you can guarantee that will happen to all of us one day.”



Donor John McNeill hopes his brain tissue will help someone else.

For information on becoming a brain donor:

- Visit www.braindonors.org
- Email info@braindonors.org
- Call 02 9036 9027 (Dr Antony Harding, national co-ordinator of brain donor programs)

For information about the National Neural Tissue Resource Centre, visit the National Neuroscience Facility – www.nnf.com.au

After a long period in which material was obtained at autopsy and stored for research without the knowledge or consent of relatives, state laws now tightly regulate collection and retention of samples. Coroners' legislation controls the procedures associated with forensic autopsies, researchers are obliged to follow National Health and Medical Research Council policies and guidelines, and health service and university ethics committees also need to approve research.

After death, organs can be donated for transplantation and tissues can be donated for research, but two separate sets of regulations control these two uses and create bureaucratic hurdles. Many members of the public are happy to tick the box on their driver's licence to indicate their willingness to be an "organ donor", but are unaware that separate consent is needed if tissues are retained for research.

Ms Garrick surveyed people registered in the Using Our Brains program and found that about 90 per cent had mistakenly assumed their brains could be collected after death because they had signed the donor section of their licences or had completed donor cards.

They had discussed their views about donation with their families, but thought they should not have to obtain their relatives' "permission" to donate. Professor Clive Harper, professor of neuropathology at the University of Sydney and Sydney South-West Area Health Service, and director of the NSW Tissue Resource Centre, has been campaigning for reform of the donation bureaucracy, advocating a central database administered by Medicare Australia (formerly the Health Insurance Commission) that would allow people to specify unequivocally which organs they were willing to donate and for what purposes: for transplantation, for research and education, or for both.

Professor Harper says such a system would be easy to implement. Cost savings would be enormous, the availability of organs for transplantation and tissues for research would improve and there would be a productive debate in the community about issues associated with death and dying.

Professor Harper has a long history as a "brain banker", having built a stock of



A brain haemorrhage caused by the rupture of a blood vessel due to damage to the vessel by an infection that spread from the heart - a particularly uncommon disease.

brains since he started working in the field in 1974. In the late 1980s he attracted funding from US authorities who recognised the value of the resource, and he continues to receive major research grants from sources including the US National Institute of Alcohol Abuse and Alcoholism.

"The way we can use brain tissue has been revolutionised in the last few decades," Professor Harper says. "When I started researching alcohol and the brain, we simply weighed whole brains and found they were lighter in people with a history of alcohol abuse."

The pathology of alcohol-related brain damage is complicated by issues such as malnutrition, vitamin B deficiency and liver failure, so more information was needed. Routine tests showed the changes were in the white matter rather than the grey matter, and immunohistology provided more sophisticated tools for identifying specific features under the microscope.

"Working with Dr Peter Dodd and his colleagues at the University of Queensland, and using the new tools of genomics and proteomics (the technique of analysing protein expression patterns), we now know that alcohol abuse alters the activity of genes controlling the production of myelin – the main component of white matter," Professor Harper says. "Perhaps most importantly, MRI studies have shown the changes are potentially reversible."

It probably costs \$10,000 - 20,000 to add a brain to the bank, taking account of donor recruitment, consent, and the meticulous processes needed to ensure an accurate diagnostic label is attached to the brain. Advances in technology now mean that tiny, 5 mg samples are sufficient for DNA analyses, and for proteomic studies. For example, well over 100 proteins in the brain that are influenced by alcohol have been identified.

An accurate diagnostic label is essential, as brains are frozen at -80°C and can be used decades into the future. Professor Harper says about one-third of likely candidates are rejected because of diagnostic uncertainty.

Professor McLean is proud of the work of the National Neural Tissue Resource Centre and says its worth is easily measured by research productivity. "In 2004 to 2005, 182 requests for tissue usage in research projects were received from National and International researchers. In the same time span, 87 publications in peer-reviewed journals used research from banked brain tissue and there are currently many exciting research projects underway which use brain tissue as an essential part of the research project." 📌

GPs NOTE: This article is available for patients at <http://pathway.rcpa.edu.au>
