



## The NSW brain tissue resource centre: Banking for alcohol and major neuropsychiatric disorders research



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### ABSTRACT

The New South Wales Brain Tissue Resource Centre (NSWBTRC) at the University of Sydney (Australia) is an established human brain bank providing tissue to the neuroscience research community for investigations on alcohol-related brain damage and major psychiatric illnesses such as schizophrenia. The NSWBTRC relies on wide community engagement to encourage those with and without neuropsychiatric illness to consent to donation through its allied research programs. The subsequent provision of high-quality samples relies on standardized operational protocols, associated clinical data, quality control measures, integrated information systems, robust infrastructure, and governance. These processes are continually augmented to complement the changes in internal and external governance as well as the complexity and diversity of advanced investigation techniques. This report provides an overview of the dynamic process of brain banking and discusses the challenges of meeting the future needs of researchers, including synchronicity with other disease-focus collections.

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### Introduction

Over the past three decades our understanding of the factors that contribute to and the consequences of schizophrenia and alcohol-related brain damage (ARBD) has been advanced through studies of neuroimaging, neuropsychology, genetics, and neuropathology of the human brain. In particular, the field of neuropathology has been transformed by the molecular techniques of the so-called genomic age (Sutherland, Sheedy, & Kril, 2014). For the past decade many of these studies have been facilitated by the New South Wales Brain Tissue Resource Centre (NSWBTRC), a specialized research resource, supported by the National Institutes of Alcohol Abuse and Alcoholism and Schizophrenia Research Institute (Australia), and established to provide clinically and pathologically characterized post-mortem brain tissue to researchers.

The NSWBTRC at The University of Sydney, Sydney, Australia has engaged with the neuroscience community for over 20 years. The NSWBTRC collection is primarily focused on cases with histories of alcohol-use disorder, major neuropsychiatric disorders, and healthy

controls. The associated brain donor program, Using our Brains, has engaged the wider community to participate in brain donation and research since being launched in 2002.

Over these years the NSWBTRC has encountered challenges in terms of funding sustainability, researcher expectations, incorporation of technical advances, maintaining quality, and data-sharing management. New management and operational strategies introduced to strengthen the growth of the NSWBTRC are described herein along with contributions made to this research community.

Recently the NSWBTRC has undergone changes to its organizational structure in an effort to safeguard the continuation of the resource. These changes are primarily related to institutional governance, new infrastructural opportunities, and tissue access.

#### Governance

The NSWBTRC is housed at The University of Sydney and is under the Sydney Local Health Network (Protocol No X15-0199) and University of Sydney Biobank Committee jurisdiction.

In an effort to ensure longevity of brain banking in this research area, a decision to share resources and combine some processes with an affiliated brain bank was accorded. An inter-institutional agreement with the University of New South Wales, which houses the Sydney Brain Bank, was executed to operate collaboratively as the NSW Brain Banks (NSWB) to review requests from

*Abbreviations:* NSWBTRC, New South Wales Brain Tissue Resource Centre; DOFM, Department of Forensic Medicine; NOK, Next of Kin; UoB, Using our Brains Donor Program; ARBD, Alcohol-related Brain Damage; AUD, Alcohol-use Disorder.

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researchers and to facilitate access to this valuable resource. The NSW Brain Banks Inter-Institutional Board is the overarching body that provides governance to the NSW Brain Banks committees and panels.

### Funding

The NSWBTTC has funding from the National Institutes of Alcohol Abuse and Alcoholism and the Schizophrenia Research Institute, with infrastructure support by the University of Sydney. Each funding body shapes the focus of the brain collection and research strategy of the NSWBTTC in line with their overall objectives.

Brain banks are expensive to maintain, and understanding the actual costs is imperative to gaining long-term funding. Our recent audit of cost suggests this is AU\$ 20,000 per brain collected, a figure comparable with that previously published (Hulette, 2003). Cost recovery for access is implemented by the NSWBB using the Australian Brain Bank Network Access Policy (<http://www.austbrainbank.org.au/researchers.html>). A recent study by Albert et al. has shown that full cost recovery is not feasible and the expected revenue is between 5 and 25%, albeit toward the lower estimate if only academic research is supported (Albert, Bartlett, Johnston, Schacter, & Watson, 2014).

### Infrastructure

The NSWBTTC has recently relocated to the purpose-built research institute, the Charles Perkins Centre (CPC), at the University of Sydney (<http://sydney.edu.au/perkins/>). Although the centre's primary research foci relate to chronic systemic disorders (obesity, diabetes, and cardiovascular disease), the brain bank acts as a conduit to understanding the bi-directional relationships between the brain and these disease states. Indeed, various CPC research groups utilize brain bank material while Using our Brains (UoB) donors participate in research projects where both systemic and central phenotypic data are being collected.

### Researchers

A major aim of this facility is the promotion of post-mortem human brain tissue for neuroscience research. Traditionally, tissue banks and collections have been used to study morphological aspects of disease. The value of these studies is clear; however, further advances in our knowledge can be gained by coupling histological studies with techniques that examine functional aspects of tissue such as "omics" studies – proteomics, genomics, transcriptomics, and metabolomics (Sutherland, Sheedy, & Kril, 2014). Gaining feedback from researchers via annual evaluations allows the review of methods undertaken and those proposed for future use.

The NSWBTTC provides not only access to tissue but also experience in the application of research techniques which can assist researchers with their studies and help troubleshoot projects. This is an important interaction as many researchers have developed their skills using animal models. The availability of tissue samples to refine methods using human tissue is invaluable and allows for better use of the collection. Details of the NSW Brain Banks (NSWBB) may be accessed at <https://nswbrainbank.org.au/>. Guidelines for the researcher are available on this site. Principal and co-investigators who utilize tissue are invited to serve on the Tissue Review Panel that assists the NSWBB Scientific Review Committee to assess applications.

### Donor programs

Brains donated to the NSWBTTC come from two sources. The first is the New South Wales Department of Forensic Medicine (DOFM) (equivalent to the Medical Examiners office), that receives all sudden, unexpected, accidental, institutional, or violent deaths from the greater Sydney region (~5 million people). Approximately 60% of the next of kin contacted consent to brain donation (Glaw et al., 2009). This source provides the majority of alcoholic cases as well as controls.

The second source is prospectively consented and characterized brain donors. Here, members of the community are encouraged to donate their brains by joining our Using our Brains (UoB) donor program. This source provides cases with variable alcohol consumption and variable co-existing illnesses. Staff share the 24 h 'on call pager' for brain collection of donors who have consented through this program.

The 'Using our Brains' brain donor program has encountered positive community support. Maintaining contact is important from the initial consent process, allowing a relationship to be built with the donor and their family, which aids in longitudinal data collection. Donors are invited to participate in a variety of allied research projects, and data sharing from these studies enhances the overall program.

### Methods

NSWBTTC staff attend the DOFM daily and assess the reports of death to the coroner for potential donations using exclusion and inclusion criteria. They then call the next of kin of the deceased person to discuss the donation and consenting process.

Potentially suitable cases are donors who are over the age of 18 with no developmental or neurological disorders, infections or disease such as HIV or hepatitis C, and no history of substance dependence/abuse (except for alcohol and/or nicotine). Those that have died as a result of significant head injury or have undergone assisted ventilation for more than 24 h or that have had a poor agonal status due to other causes are excluded from the collection.

The consenting process requires initially obtaining a recorded verbal consent and later written consent from the senior next of kin of the deceased. Written consent is required from the case pathologist, the coroner, and designated officer (an authorized person appointed by the Australian Department of Health responsible for tissue and organ donation from a deceased person). Using our Brains donors have pre-consented to the donation process, including consent from their next of kin and therefore only require written consent from a designated officer for the donation to proceed.

Brains are prepared at the time of autopsy by technicians trained in anatomical dissection. The NSWBTTC brain collection protocol (Fig. 1) ensures that the maximum range and number of specimens become available to researchers. Both fresh-frozen and formalin-fixed tissue is collected and stored with the fixed hemisphere being cut at 3 mm by a rotary slicer to allow whole and regional brain volumetric analysis. The regions dissected from the fixed and frozen hemispheres (Table 1) are evidence-based and updated to reflect the current research zeitgeist. In particular, fixed blocks of commonly requested regions are paraffin-embedded at approximately 3 weeks, providing a uniform source of tissue for immunohistochemical studies. Additional regions can be requested, subject to Scientific Review Committee approval, but tissue storage times will vary as per time of donation.

Gross anatomical examination is performed by a neuropathologist with neurohistopathological characterization primarily performed using H&E-stained sections with additional stains including

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