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REVIEW ARTICLE

Human Brain Banking as a Convergence Platform of Neuroscience and Neuropsychiatric Research

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ABSTRACT

Neuropsychiatric disorders affect hundreds of millions of people and their families worldwide. Many studies have used human postmortem brain samples to decipher the molecular framework of these diseases. These studies uncovered brain-specific genetic and epigenetic patterns using high-throughput sequencing techniques. Therefore, determining the best way to collect human postmortem brain samples, analysing such a large amount of sequencing data, and interpreting these results are critical to advancing the field of neuropsychiatric sciences. By collecting postmortem/biopsied neural tissues and information about the diseases and life of donors, human brain banks support the observation and research of human brain sciences. Furthermore, the construction of large-scale brain banks has promoted the exploration of human brain morphology and function, development and ageing, as well as the mechanism of many neuropsychiatric diseases, which progressively reveal the normal mechanism of human brain activities and lead the direction of the prevention and treatment of neurological diseases. This article introduces the significance of human brain tissue bank construction and the current situation of the human brain tissue bank worldwide, as well as an overview of neurology or neuroscience advanced by using human brain samples.

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The research focused on human brains is essential to increase our understanding of neuropsychiatric disorders, not only in terms of disease pathogenesis but also to translate research on molecular mechanisms in disease models to novel treatments for human beings (Samarasekera et al., 2013). To meet researchers' demands, human brain banks have been established worldwide, and networks have been set up both in developing and developed countries. These networks have enabled a more focused approach to the study of neuropsychiatric disorders, with individual banks specialising in specific disorders and donor programs in clinical trials or population-based cohorts (Samarasekera et al., 2013).

The Alzforum (https://www.alzforum.org) is a nonprofit that provides information regarding human brain banks that have been constructed worldwide (https://www.alzforum.org/brain-banks). A total of

144 human brain banks were included: 81 brain banks in the United States, 16 brain banks in the United Kingdom, 10 brain banks in Australia, 7 brain banks in Germany, 4 brain banks in France, 3 brain banks in Canada, 3 brain banks in the Republic of Korea, 3 brain banks in Spain, 2 brain banks in Austria, 2 brain banks in Finland, 2 brain banks in Italy, 2 brain banks in Mexico, 1 brain bank in China, 1 brain bank in Greece, 1 brain bank in Hungary, 1 brain bank in India, 1 brain bank in Japan, 1 brain bank in the Netherlands, 1 brain bank in New Zealand, 1 brain bank in South Africa, and 1 brain bank in Sweden (Table 1). It is worth noting that the United States, the European Union, and Australia have established the brain bank consortium (Ma et al., 2019).

For example, the National Institutes of Health (NIH) established a specialised agency, the NeuroBioBank (NBB), to support and coordinate the National Brain Tissue Bank and to serve as a central point of access to the world-class collections of its six biorepositories: University of Miami Brain Endowment Bank, University of Maryland Brain and Tissue Bank, Harvard Brain Tissue Resource Center, the Human Brain and Spinal Fluid Resource Center, Mt. Sinai Brain Bank, and Brain Tissue Donation Program at the University of Pittsburgh (https://neurobiobank.nih.gov/about/#network). In addition, the BNE (BrainNet Europe) Consortium consists of nineteen European Brain Banks distributed in the United Kingdom, France, Germany, Spain, Italy, Denmark, Greece, Austria, Finland, Iceland, Sweden, Hungary, and other countries (Ma et al., 2019). The BNE Consortium was funded by the European Commission's Sixth Framework Program for the Life Sciences Project (LSHM-CT-2004-503039) to provide high-quality human brain samples, carry out quantitative research on human brain nucleic acids, proteins, and neurochemicals, and explore the normal working principles and disease mechanisms of the human brain (Ma et al., 2019). The BNE Consortium required members to adopt a unified and standardised procedure for brain sampling, preservation, and essential pathological detection and promoted the sharing of brain tissue resources to support collaborative neuroscience research in Europe and the rest of the world (Ma et al., 2019). In addition, the UK Brain Banks Network established a coordinated national network of UK brain tissue resources (banks) for researchers to use, including Cambridge Brain Bank, Edinburgh Brain Banks, London Neurodegenerative Diseases Brain Bank, Manchester Brain Bank, Multiple Sclerosis and Parkinson's Tissue Bank, Newcastle Brain Tissue Resource, Oxford Brain Bank, Queen Square Brain Bank for Neuropsychiatric Disorders, Sheffield Brain Tissue Bank (SBTB), and South West Dementia Brain Bank (https://brainbanknetwork.ac.uk/BrainBank/BrainBanks).

Development of human brain banks in China

Unlike developed countries, China's human brain bank has remained preliminary over decades (Ma et al., 2019). However, joint efforts since 2012 have substantially promoted this critical frontier of brain bank construction in China to support high-quality research into major neuropsychiatric, psychiatric, and developmental brain diseases affecting the Chinese people (Ma et al., 2019). First, the Standardised Operational Protocol for brain banking in China was published in 2019 after extensive collaboration among domestic and international experts over several years of continuous effort (Ma et al., 2019; Qiu et al., 2019). Second, three specific human brain banking conferences have been held to strengthen the scholarly consensus and coordinate multi-institutional efforts on brain bank construction in China (Ma et al., 2019). In 2014, the first international workshop focused on brain bank construction was held in Changsha and Beijing. Professor Shumin Duan proposed establishing multiple banking centers and developing shared protocols and databases accessible to all researchers (Ma et al., 2019). Following this initiative, a second workshop was held in Beijing at Peking Union Medical College in 2016, and then a third workshop was held in Hangzhou at Zhejiang University in 2018 (Ma et al., 2019). All these meetings consisted of thematic presentations on topics covering the role of human brain banking in basic and translational neuroscience, the status of brain banking across the world, and current research findings in the areas of neuropsychiatric, and neurodevelopmental brain diseases (Ma et al., 2019). To date, China has already been establishing a nationwide brain bank alliance, the China Brain Bank Consortium, led by the National Human Brain Bank for Development and Function, Institute of Basic Medical Sciences Chinese Academy of Medical, Sciences Peking Union Medical College and National Health and Disease Human Brain Tissue

AMERICA				
Brain Banks	**Location**	**Website**	**Details**	**Samples**
NIH-funded NeuroBioBank	United States	https://neurobiobank.nih.gov/	An open-access network of six established brain banks in the United States that stores samples covering neurological, neuropsychiatric, and neurodevelopmental diseases and disorders with good clinical information and neuropathology, as well as normal controls.	N/A
Mayo Clinic Brain Bank	Rochester, MN, United States	https://www.mayo.edu/research/departments-divisions/department-neuroscience-florida/brain-banks/mayo-clinic-brain-bank	Collected over 3,000 cases of Alzheimer's disease, 2,000 cases with Lewy body disease, nearly 2,000 cases of tauopathies, and a growing collection of frontotemporal dementia and ALS cases with well clinical information and neuropathology, as well as normal controls.	> 9,000 specimens
Harvard Brain Tissue Resource Center	Belmont, MA, United States	https://hbtrc.mclean.harvard.edu/	Collected over 9,000 donated brains with well clinical information and neuropathology information, as well as normal controls, and distributed over a hundred thousand samples, both United States nationally and globally.	> 9,000 specimens
Human Brain Collection Core (HBCC)	Rockville, MD, United States	https://www.nimh.nih.gov/research/research-conducted-at-nimh/research-areas/research-support-services/hbcc	Collected human brain tissue and blood samples from deceased individuals diagnosed with mental illnesses such as schizophrenia, depression, bipolar disorder, substance abuse disorder, and those who died by suicide, as well as from individuals without a history of mental illness	> 1,000 specimens
UCSF Neurodegenerative Disease Brain Bank (NDBB)	San Francisco, CA, United States	https://memory.ucsf.edu/research-trials/professional/neurodegenerative-disease-brain-bank	Established in 2008 and serves as a repository for nervous system tissue donated for research purposes. NDBB is committed to advancing the understanding of neurodegenerative disease by (1) performing comprehensive neuropathological characterisation of participants who participated in clinical research during life and (2) providing tissue to leading investigators worldwide.	N/A
EUROPE				
Brain Banks	**Location**	**Website**	**Details**	**Samples**
BrainNet Europe	Munich, Germany	https://cordis.europa.eu/project/id/503039	A network of 19 established brain banks across Europe that stores samples covering neuropsychiatric disorders with good clinical information and neuropathology information, as well as normal controls.	N/A
Netherlands Brain Bank	Amsterdam, Netherlands	https://www.brainbank.nl/brain-tissue/availability/	An open-access brain bank that collected human brain tissue of donors with a variety of neurological and psychiatric disorders but also of nondiseased donors.	> 4,000 specimens
Brains for Dementia Research, Wolfson Centre for Age-Related Diseases	London, United Kingdom	https://www.kcl.ac.uk/research/brains-for-dementia-research	Established in 2007 to promote brain donation and develop a network of brain tissue banks to facilitate research into dementia.	N/A
UK Brain Banks Network	Medical Research Council, Bristol, United Kingdom	https://brainbanknetwork.ac.uk/BrainBank/BrainBanks	A coordinated national network of UK brain tissue resources (banks).	

Table 1. Human brain banks around the world. *(Continues)*

ASIA				
Brain Banks	**Location**	**Website**	**Details**	**Samples**
National Human Brain Bank for Development and Function	Beijing, China	http://anatomy.sbm.pumc.edu.cn/brain-bank/	As national resource platform, support and lead China's brain science research, and make positive contributions to maintaining brain health and defeating brain diseases.	> 500 specimens
National Human Brain Bank for Health and Disease	Hangzhou, Zhejiang, China	http://zjubrainbank.zju.edu.cn/index	Collected and stored more than 300 human whole brain samples, covering common neuro-psychiatric and psychiatric diseases and Control whole brain samples without brain disease.	> 300 specimens
Central South University Brain Bank	Changsha, Hunan, China	https://xysm.csu.edu.cn/	A member of the China Brain Bank Consortium.	N/A
Fudan University Brain Bank	Shanghai, China	https://shmc.fudan.edu.cn/	A member of the China Brain Bank Consortium.	N/A
Tiantan Hospital Capital Medical University Brain Bank	Beijing, China	https://bjtth.org/	A member of the China Brain Bank Consortium.	N/A
Hebei Medical University Brain Bank	Shijiazhuang, Hebei, China	https://www.hebmu.edu.cn/	A member of the China Brain Bank Consortium.	N/A
Anhui Medical University Brain Bank	Hefei, Anhui, China	https://www.ahmu.edu.cn/	A member of the China Brain Bank Consortium.	N/A
Guiyang Medical University Brain Bank	Guiyang, Guizhou, China	https://gmc.edu.cn/	A member of the China Brain Bank Consortium.	N/A
Brain Bank for Aging Research	Tokyo, Japan	https://www.tmig.or.jp/eresearch/a23.html	For aging and dementia and construction of Geriatric Neuroscience Data Base.	N/A
Human Brain Bank	Karnataka, India	https://thenimhansbrain-bank.in/brain-bank/	A resource organisation to procure precious human nervous tissue for neurobiological research	> 715 specimens
AUSTRALIA/OCEANIA				
Brain Banks	**Location**	**Website**	**Details**	**Samples**
Victorian Brain Bank	VIC, Australia	https://florey.edu.au/science-research/scientific-services-facilities/victorian-brain-bank	Supports research into the study of brain disorders by providing tissue to researchers.	N/A
MS Research Australia Brain Bank	NSW, Australia	https://msbrainbank.org.au/progress/	Over 2260 people with MS have registered their interest and more than 930 have consented to their tissue.	> 80 specimens
NSW Brain Bank Network	Australia	http://www.nswbrain-banknetwork.org.au/		N/A
Schizophrenia Research Institute	NSW, Australia	https://www.neura.edu.au/discovery-portal/asrb/	Collects and links genetic, clinical, neuro-psychological and brain imaging information from over 1,000 individuals with schizophrenia and healthy controls.	> 1,000 specimens
Sydney Brain Bank	NSW, Australia	https://www.neura.edu.au/sydneybrainbank/	Hold brain tissue from over 700 donors with diverse neuropathology including Alzheimer's disease, Lewy body disease, motor neuron disease, Huntington's disease, frontotemporal lobar degeneration, multiple system atrophy.	> 700 specimens
Neurological Foundation of New Zealand Human Brain Bank	AUK, New Zealand	https://neurological.org.nz/what-we-do/neurological-foundation-human-brain-bank/	Received more than 700 brains, and brain tissue samples from over 300 donors with neurosurgical operations.	> 700 specimens
AFRICA				
Brain Banks	**Location**	**Website**	**Details**	**Samples**
Tygerberg Hospital	Cape Town, South Africa	http://www.trauma.org/index.php/resources/elective/352/		N/A

Table 1. Human brain banks around the world.

Resource Center, Zhejiang University, and other members, including Shanghai Medical College Fudan University, Xiangya School of Medicine of Central South University, Beijing Tian Tan Hospital Capital Medical University, Hebei Medical University and so on. The mission of the China Brain Bank Consortium is to advance basic and translational human brain research by providing donors clinical biometrics, brain/tissue/fluid samples, and primary neuropathological documentation (Ma et al., 2019). The China Brain Bank Consortium also aims to serve as a knowledge-integration and broadcasting organisation for public education and policy decision-making to improve neuropsychiatric and neurodevelopmental brain disease research and, ultimately, the brain health and life of the Chinese people (Ma et al., 2019).

Human brain tissue as a cornerstone of neuroscience

To help researchers review the history of the development of research and make further contributions to future research in the brain field, a total of 7172 articles were retrieved from the Web of Science database using the following strategy: "Topic = postmortem brain", and publication years were between 2012 and 2021. Fig. 1A shows the Number of articles published from 2012 – 2021. The total citations of articles published from 2012 – 2021 are shown in Fig. 1B. The distribution of research focus of 7172 articles between 2012 and 2021 were unevenly distributed, mainly focused on neuroscience, neurology, biochemistry, molecular biology, psychiatry, and behavioural sciences (Fig. 1C). The use of

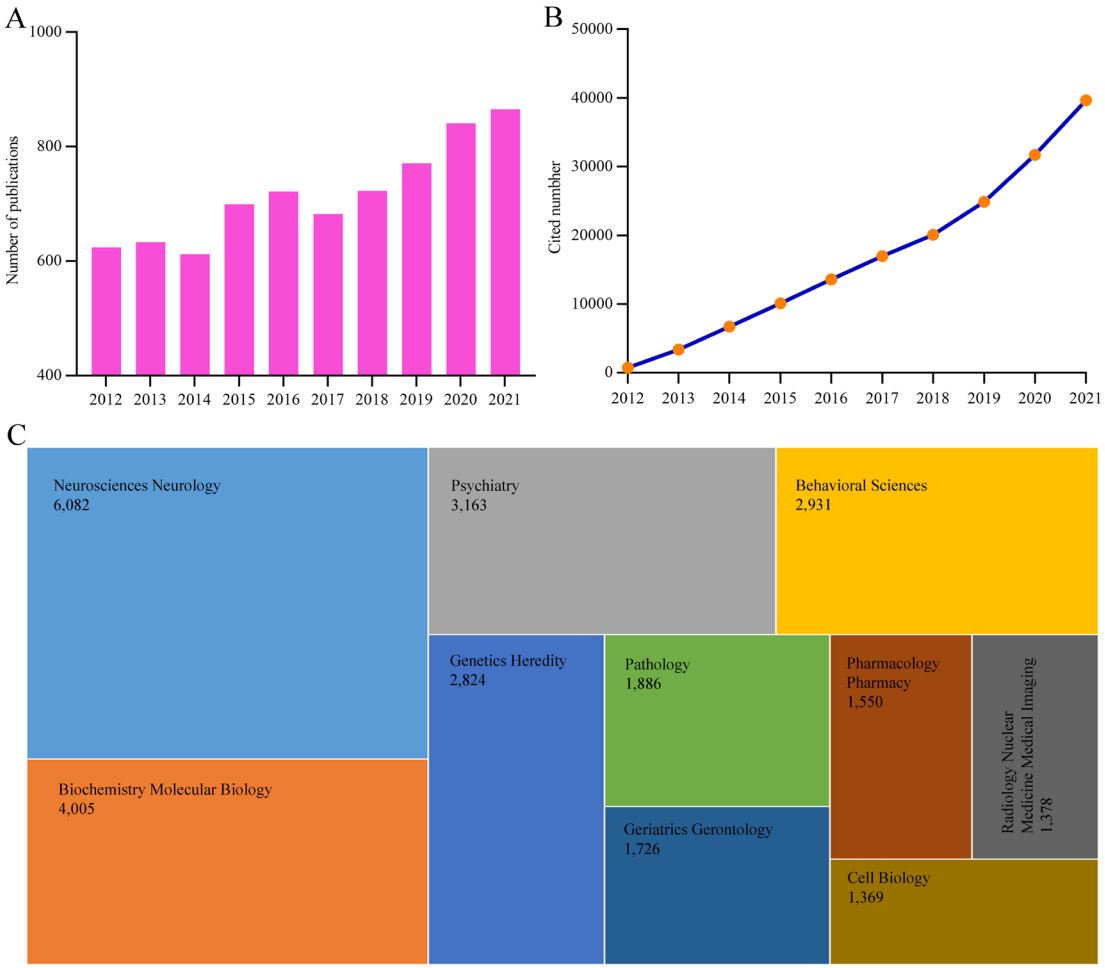

Figure 1. Analysis of articles citing postmortem brain between 2012 and 2021. **A:** Number of articles published from 2012 – 2021. **B:** Citation analysis of articles published from 2012 – 2021. **C:** Research foci of articles citing postmortem brain in 2012 – 2021.

postmortem human brain materials has given insights into brain differences in health-related to age, sex, sexual orientation and human brain diseases, from neurodegenerative diseases and neuroendocrine disorders to psychiatric disorders, especially Alzheimer's disease, Parkinson's disease, schizophrenia and bipolar disorder.

Utilising human brain tissue sections from dementia patients, argyrophilic senile plaques and neurofibrillary tangles (NFTs) of the cerebral cortex were found by Alois Alzheimer in 1906 (Alzheimer, et al., 1995; Morris & Salmon, 2007). Dementia, which is characterised by the deposition of argyrophilic senile plaques and NFTs in the brain, was named Alzheimer's disease (AD) (Montine et al., 2012). A spate of molecular neurobiology research identified inheritable mutations of the APP gene directly responsible for familial AD (Campion et al., 1999). In single-transgenic or double-transgenic animal models (Tg animal) of APP mutations of familial AD (Borchelt et al., 1997; Carlson et al., 1997; Games et al., 1995), the histopathological progression of cerebral amyloid-β (Aβ) deposition was reproduced, and the synaptic damage, neuronal loss and memory impairment of the AD patients can again be found in the animal models of AD, but NFTs, the major neuropathological features of AD brain, cannot be reproduced in the Tg animals (Pang et al., 2022; Sanchez-Varo et al., 2022; Sasaguri et al., 2017). The information that was obtained from the collected human brain tissues was indispensable for uncovering the mechanisms of neuropsychiatric disorders. Without well-preserved human brain tissues that were a standardised collection and had perfect clinical information, understanding the agents of neuropsychiatric disorders would have been impossible.

In recent years, more knowledge of neuropsychiatric disorders has been obtained from cultured cells, brain organoids and Tg animals with the progress and application of new technologies. Over the years, Tg animal models and cell research have overshadowed human tissues, especially brain or other nerve tissues (Duyckaerts et al., 2008; Webster et al., 2014). Animal models and cellular experiments have many advantages, such as ease of manipulation, convenience for longitudinal studies, more observations performed in living animals, and gene knockout and transgene experiments. Cellular culture and animal models cannot always mimic every aspect of human disease, especially mental and neuropsychiatric disorders (Duyckaerts et al., 2008). For example, monogenic and biogenic APP-based AD mouse models involving mutant APP or mutant APP and presenilin (PS) 1 or presenilin 2 gene expression model the typical amyloid-β (Aβ) accumulation of familial and sporadic AD in humans, but neuropathological changes in NFTs have not been found (Carlson et al., 1997; Duyckaerts et al., 2008; Sanchez-Varo et al., 2022; Sasaguri et al., 2017; Webster et al., 2014). Although current Tg-mice of AD models reproduce the Aβ plaques that were described in human AD brains to some extent, the morphological variety and diversity of Aβ plaques are wider in human samples. According to current studies, Aβ, tau, and ApoE are key molecules in AD (Borchelt et al., 1997; Borchelt et al., 1996; Fryer et al., 2005; Funato et al., 1998; Gessel et al., 2012; Lewis et al., 2001; Lewis et al., 2000; Maruyama et al., 2013). Nevertheless, AD research has benefited from various transgenic mice, such as the function, metabolism and behaviour of critical molecules relevant to AD. For example, Nav1.1 hypofunction has been observed in mouse models of AD (Corbett et al., 2013; Hamm et al., 2017), and the effect of Aβ amyloid on Nav1.1 phenotypic consequences should be reviewed and validated in future studies. However, the genes and proteins of Aβ, tau, and ApoE differ between rodents and humans in their sequences, pathogenicity or number of isoforms expressed.

PD is a neurodegenerative disorder that affects approximately 1.5% of the global population over 65 years of age, the hallmark feature of which is degeneration of the dopamine (DA) neurons in the substantia nigra pars compacta (SNc) and the consequent striatal DA deficiency (Brichta et al., 2013; Nussbaum & Polymeropoulos, 1997; Pringsheim et al., 2014; Rodriguez-Oroz et al., 2009). From human patients with familial PD, researchers found the first PD-linked gene *SNCA*, code synuclein alpha (α-syn), which is a member of the synuclein family and the main component of Lewy bodies (Chan et al., 1998; Farrer et al., 1998; Munoz et al., 1997; Nussbaum & Polymeropoulos, 1997; Zareparsi et al., 1998). Although there is currently no cure for PD, multiple mutations of PD-related genes were found, such as three missense mutations (encoding

the substitutions A30P, A53T, and E46K) of the *SNCA* gene of familial PD (Chan et al., 1998; Farrer et al., 1998; Munoz et al., 1997; Zareparsi et al., 1998), mutations of the *PARKIN* gene of familial PD and some young-onset sporadic PD patients (Abbas et al., 1999; Hattori et al., 1998; Kitada et al., 1998; Lucking et al., 2000), mutations (G2019S and R1441C) of the *LRRK2* (Leucine rich repeat kinase 2) gene of the late-onset autosomal dominant inherited form of PD (Di Fonzo et al., 2005; Funayama et al., 2005; Gilks et al., 2005; Nichols et al., 2005; Zimprich et al., 2004), and mutations of the *PINK1* (*PTEN Induced Putative Kinase 1*) gene or *DJ-1* gene in early-onset PD (Abou-Sleiman et al., Wood, 2004; Bonifati et al., 2005; Deng et al., 2005; Healy et al., 2004; C. Klein et al., 2005; McInerney-Leo et al., 2005; Rogaeva et al., 2004; Valente et al., 2004). Genetic animal models of PD can better understand the mechanisms underlying the genetic forms of PD (Beal, 2001; Blesa et al., 2012; Blesa & Przedborski, 2014; Chesselet & Richter, 2011; Metzger & Emborg, 2019). However, the neuropathology and behavioural phenotypes of PD animal models are often quite different from the human condition (Hinkle et al., 2012; Rathke-Hartlieb et al., 2001; Sanchez et al., 2014). Thus, transgenic models of animals with mutated genes observed in familial PD patients are insufficient to reproduce the final neuropathological features of PD. In most populations, the known pathogenic mutations of SNCA, Parkin, PINK1, and DJ1 are infrequent and can only explain a minor part of all PD cases (Hinkle et al., 2012; Rathke-Hartlieb et al., 2001; Sanchez et al., 2014).

Similar to AD and PD, it seems that many neuropsychiatric disorders, such as Parkinson's disease (PD), schizophrenia, and bipolar disorders, may be specific to humans, have no real equivalent, or are unknown in animals. Neuropsychiatric disorders often have subjective symptoms and a variety of neuropathological changes in the brain, which are unique challenges for animal models of CNS disorders. Even though the technology of cell and tissue culture from postmortem tissue was discovered more than 40 years ago (Macpherson et al., 1985), it has rapidly evolved in recent decades (Dimos et al., 2008; Ebert et al., 2009; Israel et al., 2012; Marchetto et al., 2010; X. Qian et al., 2016; Soldner et al., 2009; Takahashi et al., 2007). The discovery of induced pluripotent stem cells (iPSCs) from cultured fibroblasts, which can be redifferentiated into various cell types, such as neurons, has allowed scalable testing of neurodegeneration-associated genes and therapeutic agents entirely in human systems (Ebert et al., 2009; Israel et al., 2012; Marchetto et al., 2010; Qian et al., 2016; Soldner et al., 2009). Neurons that are currently created from iPSCs have been applied to study the underlying mechanisms of spinal muscular atrophy, amyotrophic lateral sclerosis, AD and schizophrenia (Choi et al., 2014; Egawa et al., 2012; Israel et al., 2012; Lee et al., 2009; Marchetto et al., 2010; Mariani et al., 2015; Miller et al., 2013; Moore et al., 2002; X. Qian et al., 2016; Soldner et al., 2009; Zhang et al., 2013). With the rise and use of new technologies such as brain organoid culture, cell and tissue culture from autopsy materials has occurred for psychiatric research. Cultured brain organoids from human postmortem tissue have been used to study complex neuropsychiatric diseases such as AD, frontotemporal dementia (FTD), PD, motor neuron disease and schizophrenia with neurodegeneration (Di Lullo & Kriegstein, 2017; Eiraku et al., 2011; Eiraku et al., 2008; Jo et al., 2016; Kawada et al., 2017; Lancaster et al., 2013; Mellios et al., 2018; Monzel et al., 2017; Nakano et al., 2012; Pasca et al., 2015; X. Y. Qian et al., 2018; Stachowiak et al., 2017). Brain organoid culturing offers a promising avenue to study the underlying genetic mechanism of neuropsychiatric disorders. Brain organoids or cerebral organoid cultures, which are three-dimensional (3D) cultures, have more precise neural layering and identity and allow tuning and generation of regional brain tissue structures such as cerebral, hypothalamus, midbrain, cerebellar, and hippocampal-specific organoids that enable elucidation of regional pathological mechanisms specific to more complex neuropsychiatric disorders (Hor et al., 2018; Kawada et al., 2017; Muguruma et al., 2010; Sakaguchi et al., 2015). iPSCs or brain organoids obtained by postmortem tissue can offer a unique advantage in terms of gene expression profiles and epigenetic properties of neurons. The gene expression profiles and epigenetic properties of human postmortem brain tissue allow further validation of the accuracy of iPSC-derived neurons or brain organoids. Furthermore, iPSCs or brain organoids from postmortem tissue also create methods to study the postmortem abnormalities observed in vitro and in vivo.

Brain bank advancing neuropsychiatric disease studies

Collecting human brains has a pivotal role in understanding the biological basis of the brain and neuropsychiatric diseases. The knowledge of the brain essence and nervous system disease is inseparable from the direct study of human brain material. The human brain bank collects postmortem or biopsied human nerve tissue samples of donors, including antemortem illness and life information, and shares samples and attendant demographic and clinical data with qualified researchers worldwide for research on neuroscience and neuropsychiatric diseases (Deep-Soboslay et al., 2011; Rademaker et al., 2018; Neshika Samarasekera et al., 2013; L. Wang et al., 2019). The human brain bank s a scientific platform to support the direct observation and research of health and disease brain tissue. Transcriptomics, proteomics, and lipidomics are applied to study the neuropathology mechanism of neuropsychiatric diseases and to search for new clinical therapeutic targets. The human brain, which is a total export of molecular omics (proteomics, transcriptomics, and genomics), histocytology, neuropathology, imageology, and neuropsychiatry in clinical neuroscience, will provide conditions and opportunities for revealing the workings of the brain and the mechanisms of neuropsychiatric disease. Animal models of neuropsychiatric disorders or cell and tissue culture will confirm new findings from human brain tissues. At the same time, data from animals or cells and tissue must also be validated on human brain tissue. In addition, with the traditional use of human brain samples for histopathological studies, many new approaches and methods are being developed for basic and translational neuroscience research by testing brain samples.

High levels of the fibrillogenic Aβ1-42 peptides were found to be preferentially deposited in the brains of AD patients (Borchelt et al., 1996; Iwatsubo et al., 1994). Since the 1990s, mutations in the APP, PSEN1, and PSEN2 genes are responsible for Aβ deposition in the early-onset autosomal dominant familial forms of AD (Borchelt et al., 1996; Citron et al., 1992; Ertekin-Taner, 2010; St George-Hyslop et al., 1987). Genome-wide association studies (GWASs) confirmed APOE as a genetic risk factor for late-onset AD (LOAD). In addition to APOE, the Alzheimer Disease Genetics Consortium (ADGC) and other researchers further reported nine novel LOAD susceptibility loci, including CR1, CLU, PICALM, BIN1, EPHA1, MS4A, CD33, CD2AP and ABCA7, by using genome-wide association studies (GWASs) (Hollingworth et al., 2011; Naj et al., 2011). These novel disease loci of AD identified in the recent large disease GWAS may uncover the pathophysiology of LOAD. Combined brain gene expression endophenotype and disease GWAS results revealed that the LOAD SNPs at the CLU and MS4A loci influence brain gene expression of CLU and MS4A4A genes, and additional variants within the arbitrary 100 kb cis-region also influence brain expression of CLU and ABCA7 (Allen et al., 2012). Brain expression changes in CLU, MS4A4A and ABCA7 may partly explain the LOAD risk association at these loci (Allen et al., 2012). By measuring the expression levels of transcripts in brain samples from the cerebellum and temporal cortex of autopsied subjects with AD, a combined assessment of expression and disease GWAS reported that 2,980 cerebellar cisSNP/transcript level associations (2,596 unique cisSNPs) were significant in both AD and non-AD (Zou et al., 2012). A recent assessment of postmortem human brain tissue revealed that upregulation of histone acetyltransferases H3K27ac and H3K9ac in the lateral temporal lobe was linked to disease pathways in AD by dysregulating transcription- and chromatin-gene feedback loops with an integrated multiomics approach (Nativio et al., 2020). An epigenome-wide association study with the histone 3 lysine 9 acetylation (H3K9ac) mark revealed that tau protein burden broadly affects histone acetylation in the aged and AD human brain (H. U. Klein et al., 2019). The human microglial transcriptome and genetic analysis of postmortem brain samples obtained from the Netherlands Brain Bank (NBB) and the Neuropathology Brain Bank showed associations with microglial expression of USP6NL for Alzheimer's disease and P2RY12 for Parkinson's disease (Lopes et al., 2022). High-throughput integrative transcriptome expression analyses of postmortem brain tissue indicated that the complement pathway plays a crucial role in the protective effect of *APOE* ε2 on AD (Panitch et al., 2021). STMN2, which encodes a stathmin family protein, is a key regulator functionally connected to known PD risk genes (Wang et al., 2019), and both bipolar disorder and schizophrenia revealed convergent

changes in cortical astrocytes and fast-spiking parvalbumin interneurons (Toker et al., 2018). Transcriptome data from 1,865 brain samples showed that the edited site in the 3′-UTR of *SYT11* may influence SYT11 protein levels in aged and AD human brain tissue (Ma et al., 2021). Synaptic transmission deficits of AD were first discovered in the 1970s when reductions in cholinergic markers were observed in the brains of patients diagnosed with AD (Bowen, Smith, White, & Davison, 1976). Several studies have revealed a series of synaptic protein changes in various types of dementia by using the postmortem human brain (Bereczki et al., 2018; Bereczki et al., 2016; Francis et al., 2019; Vallortigara et al., 2014; Vallortigara et al., 2016; Whitfield et al., 2014). Structural variants (SVs) that are essential sources of genetic diversity have been linked to many diseases, such as AD. Using 1,760 whole genomes from aged and AD individuals, 170,996 SVs were discovered. Quantitative trait locus (SV-xQTL) analyses revealed that more than 3,200 SVs were associated with at least one molecular phenotype in postmortem brain tissues, such as histone modifications, gene expression, splicing and protein abundance (Vialle et al., 2022).

Conclusions and future directions

In the past ten years, there have been significant developments in regulatory frameworks governing brain banking in China and the world, especially methods for optimising tissue collection and the range of neuropathological techniques available for analysing brain tissue. These novel findings in genomic, transcriptomic, proteomics and epigenomic studies of the brain highlight the potential of stored brain tissue to advance our understanding of significant scientific and clinical questions (Allen et al., 2012; Colantuoni et al., 2011; Ertekin-Taner, 2010; Hollingworth et al., 2011; H. U. Klein et al., 2019; Lopes et al., 2022; Naj et al., 2011; Nativio et al., 2020; Panitch et al., 2021; Qi et al., 2022; Toker et al., 2018; Vialle et al., 2022; Q. Wang et al., 2019; Xiong, Ge, & Ma, 2019; Zou et al., 2012). With the application of new technologies such as single-cell RNA sequencing, the application potential of human brain tissue stored in brain banks will be further enhanced. It is anticipated that basic translational studies of human brain tissue will be promoted with further scientific advances, specifically in animal models of neuropsychiatric diseases or cell culture models.

Brain tissue from spontaneous donations is predominantly from end-stage disease, and information on the disease at earlier stages is uncommon. Control tissues are required to support neuroscience research. Although more than enough people are willing to donate their brains to scientific research, recruitment of control cases is still problematic and restricted. Very few national programs or organisations focus on obtaining healthy control brains. Participants in longitudinal cohorts should be encouraged to donate. The advantages of donations from participants in this cohort are the wide range of clinical information available (including MRI data, genetic data, biomarkers and cognitive function), detailed information on lifestyle and comorbidities, and the potential to obtain samples from patients who are likely to die early in the disease.

Fetal and infant brain collection is an important and challenging direction for brain collection. At most human brain banks, donated human brains come from older people and are suitable for research into neurodegenerative diseases. Nevertheless, for neurodevelopmental disorders such as autism, SCZ, and intellectual disabilities, fetal and infant brain samples are essential for researching the causes of the disorders. Only a few banks have prenatal samples, and the sample size is comparatively limited.

Many nervous system diseases are systemic, and researchers are increasingly interested in obtaining tissue samples other than those of the brain. Therefore, samples from the appendix, colon and intestines may yield new insights. The immune system plays a role in diseases such as multiple sclerosis and AD and other neurodegenerative diseases, so the availability of blood, immune cells or immune organs can be significant.

The ultimate measure of the success of a professional brain bank is the outcome and quality of the research conducted on preserved brain samples. Progress is likely to be driven by collaborative networks that promote brain banks, which will increase sample sizes for research on rare neuropsychiatric diseases, develop generally applicable standards for postmortem brain tissue research and share ideas to maximise the potential of storing brain tissue as a valuable research resource.

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Conflict of interest

There are no potential conflicts in this research's financial and material support.

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