The Brain Bank Project
to conquer intractable disorders-
Asian- Oceanian Network

Specially Appointed Professor,
Brain Bank for Neurodevelopmental,
Neurological and Psychiatric Disorders,
United Graduate School of Child Development,
Osaka University

Shigeo Murayama M.D. Ph.D.

My Background

- I am a Buddhist priest of Soto school of Zen (曹洞宗).

- I have been educated that those who have eaten food offered to Buddha（仏飯）should dedicate their life to all living creatures on earth（衆生）.

- To establish all Japan Brain Bank Network is my life work, which I interpret to be Bodhisattva line（菩薩行）.

- I will go anywhere to fulfill brain donors' will or guide doctors who want to contribute to brain banking.

My background a buddhist.

COI

President, the Asian Oceanian Society of Neuropathology,
Vice President: the International Society of Neuropathology,
Honorable Member: the Japanese Societies of Neurology,
Neuropathology and Dementia Research
Associate Editor, JNEN
Visiting Professor: Tokushima, Hiroshima, Tokyo Medical,
Doshisha and Osaka City Universities;
Neuropathology Consultant: NCGG, Kagawa University;
NHO Tokyo, Shimoshizu, Shizuoka Epilepsy and Neurology,
West Hiroshima and Okinawa Hospitals; Kameda,
Yokohama Rosai, Toranomon, NTT East Kanto and
Chikamori Hospitals

My COI.

The Brain Bank for Aging Research (BBAR)

TMGHIG

Resources consisting of consecutive autopsy cases from a general geriatric hospital & all Japan depository of rare neurological and developmental disorders (http://www.mci.gr.jp/BrainBank)

In House Cohort Resource

1. Paraffin blocks and glass slides (1972.5–)
   for Clinical, Radiological and Pathological Research 7418
   >2. Frozen neocortex and body tissues (1995.1–)
   for Molecular Research: 2,415
   >3. Frozen half brains (2001.7–)
   for Neuroscience Research: 1,102

All Japan Neurological and Developmental Depository

In collaboration with Brain Bank for Neurodevelopmental, Neurological and Psychiatric Disorders (BBNNPD)
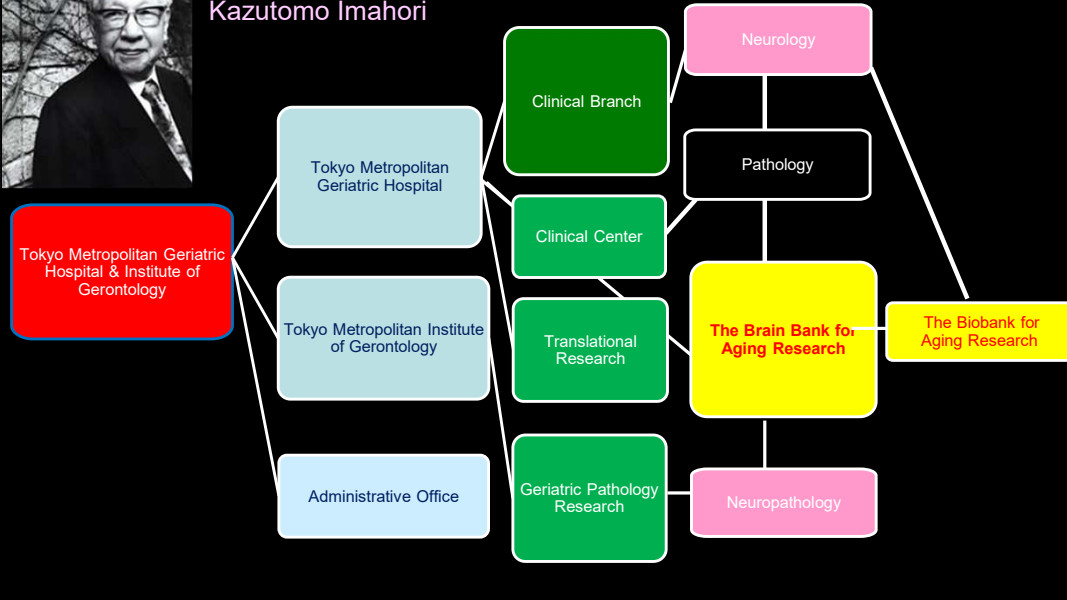
The Brain Bank for Aging Research has been accumulating paraffin blocks of brain and body tissues since 1972, frozen small pieces of brain and body tissues since 1995 and frozen half brains, spinal cords and peripheral autonomic nervous tissues since 2001. We are also responsible for all Japan depository of rare intractable neurological disorders.

The Brain Bank for Aging Research is a cooperative center of both the hospital and the research institute and supported by the Departments of Neurology and Neuropathology.

2020 Collaboration

	PI	Institute	Research theme
1	Ikeuchi, K.	NIBR	apoE4 and aging brain
2	Kuwano, R.	NIBR	miRNA editing in Alzheimer brain
3	Toda, T.	Kobe Univ.	Genomic pathology of neurological disease
4	Nishimura, M.	Mol. Neurosci. Shiga Med. Univ.	Novel protein in human aging
5	Hasegawa, M.	Tokyo Metro. Inst. Med. Sci.	CSF early biomarker of AD
6	Ono, M.	Pharm. Shiga Med. Univ.	Estrogen receptor in AD
7	Hisanaga, S.	Tokyo Metro. Univ.	Tau phosphorylation in tauopathy
8	Takahashi, Y.	Neurol. NCNP	Immunocytochemistry of ALS
9	Yamanaka, K.	Enviro. Res. Nagoya Univ.	Novel biomarker in neurodegeneration
10	Ito, M.	TMGHIG	SiRNA in argyrophilic grain disease
11	Okamura, N.	Tohoku Pharm. Univ.	Pet ligand for tau and alpha- synuclein
12	Miyasaka, T.	Life Sci. Doshisha Univ.	Imaging mass spectroscopy of human brain
13	Tanaka, M.	Riken	DISC1 and neurodegeneration
14	Tsuji, S.	Neurol. UT	Genomic screening in neurodegeneration
15	Ishikawa, K.	Neurol. TMDU	Genomic screening of ACA
16	Iwata, A.	Neurol. UT	Epigenetics of ALS
17	Tokumaru, A.	Raidiol. TMGHIG	White matter change in MRI
18	Hattori, N.	Neurol. Junten. Univ.	Genomic screening of PD
19	Kwak, S.	Neurol. UT	RNA editing in ALS
20	Kubo, S.	Neurol. Junten. Univ.	Back ground pathology of early LBD
21	Okazawa, H.	Neuropath. TMDU	Proteomic analysis of neurodeneratiion.
22	Kokubo, Y.	Mie Univ.	ALS/PDC Kii
23	Higuchi, M.	NIRS	alpha- synuclein ligand
24	Honma, N.	Patho. Toho Univ.	Estrogen receptor in AD
25	Hashimoto, Y.	Fukushima Med. Univ.	Glycosylation in AD
26	Sengoku, R.	Neurol. TMGHIG	Pathology of olfactory plate
27	Hashimoto, K.	Psy. Res. Cntr. Chiba Univ.	Lipid metabolism in PD
28	Saito, Y.	Life Sci. Doshisha Univ.	anti- oxidant DJ1 in LBD
29	Kato, T.	Riken	Neuropathology of depression
30	Nagata, N.	Animal Radiol. UT	L-PGDS in NPH
31	Kabuta, T.	NCNP	Chaperone- mediated autophagy
32	Sato, N.	NCGG	DM and demntia
33	Ri, M.	Juntendo Univ.	CHCHD2 gene in neurodegeneration
34	Ishii, K.	Pet Center TMGHIG	Neuropathology of tau imaging
35	Imaizumi, K.	Hiroshima Univ.	ER stress
36	Nagai, Y.	Osaka Univ.	exome analysis of in vivo proteostasis
37	Araki, I.	NCNP	BACE1 and synapse degeneration in AD
38	Yamagoshi, T.	NCGG	Salivary gland in aging
39	Kameyama, A.	AIST	Glycomics in aging
40	Ishigami, A.	TMGHIG	Citrulinated protein as an early biomarker of AD
41	Suhara, T.	NIRS	Dynamic pathology of amyloid- negative dementia
42	Ishiura, H.	Neurol. UT	High grade genome study of neurodegeneration

BBAR provided its resource to 42 laboratories in 2020.

2020 publication

[1] Hamaguchi T, Sakai K, Kobayashi A, Kitamoto T, Ae R, Nakamura Y, Sanjo N, Arai K, Koide M, Katada F, Harada M, Murai H, Murayama S, Tsukamoto T, Mizusawa H, Yamada M: Characterization of Sporadic Creutzfeldt-Jakob Disease and History of Neurosurgery to Identify Potential Iatrogenic Cases. Emerg Infect Dis 2020, 26:1140-6.

[2] Hamaguchi T, Sanjo N, Ae R, Nakamura Y, Sakai K, Takao M, Murayama S, Iwasaki Y, Satoh K, Murai H, Harada M, Tsukamoto T, Mizusawa H, Yamada M: MM2-type sporadic Creutzfeldt-Jakob disease: new diagnostic criteria for MM2-cortical type. J Neurol Neurosurg Psychiatry 2020.

[3] Hata S, Hu A, Piao Y, Nakaya T, Taru H, Morishima-Kawashima M, Murayama S, Nishimura M, Suzuki T: Enhanced amyloid-beta generation by gamma-secretase complex in DRM microdomains with reduced cholesterol levels. Hum Mol Genet 2020, 29:382-93.

[4] Hideshima M, Beck G, Yamadera M, Motoyama Y, Ikenaka K, Kakuda K, Tsuda H, Nagano S, Fujimura H, Morii E, Murayama S, Mochizuki H: A clinicopathological study of ALS with L126S mutation in the SOD1 gene presenting with isolated inferior olivary hypertrophy. Neuropathology 2020, 40:191-5.

[5] Imai M, Tanaka M, Sakata M, Wagatsuma K, Tago T, Toyohara J, Sengoku R, Nishina Y, Kanemaru K, Ishibashi K, Murayama S, Ishii K: Metabolic Network Topology of Alzheimer's Disease and Dementia with Lewy Bodies Generated Using Fluorodeoxyglucose Positron Emission Tomography. J Alzheimers Dis 2020, 73:197-207.

[6] Ishigaki K, Akiyama M, Kanai M, Takahashi A, Kawakami E, Sugishita H, Sakaue S, Matoba N, Low SK, Okada Y, Terao C, Amariuta T, Gazal S, Kochi Y, Horikoshi M, Suzuki K, Ito K, Koyama S, Ozaki K, Niida S, Sakata Y, Sakata Y, Kohno T, Shiraishi K, Momozawa Y, Hirata M, Matsuda K, Ikeda M, Iwata N, Ikegawa S, Kou I, Tanaka T, Nakagawa H, Suzuki A, Hirota T, Tamari M, Chayama K, Miki D, Mori M, Nagayama S, Daigo Y, Miki Y, Katagiri T, Ogawa O, Obara W, Ito H, Yoshida T, Imoto I, Takahashi T, Tanikawa C, Suzuki T, Sinozaki N, Minami S, Yamaguchi H, Asai S, Takahashi Y, Yamaji K, Takahashi K, Fujioka T, Takata R, Yanai H, Masumoto A, Koretsune Y, Kutsumi H, Higashiyama M, Murayama S, Minegishi N, Suzuki K, Tanno K, Shimizu A, Yamaji T, Iwasaki M, Sawada N, Uemura H, Tanaka K, Naito M, Sasaki M, Wakai K, Tsugane S, Yamamoto M, Yamamoto K, Murakami Y, Nakamura Y, Raychaudhuri S, Inazawa J, Yamauchi T, Kadowaki T, Kubo M, Kamatani Y: Large-scale genome-wide association study in a Japanese population identifies novel susceptibility loci across different diseases. Nat Genet 2020, 52:669-79.

[7] Kakuda N, Yamaguchi H, Akazawa K, Hata S, Suzuki T, Hatsuta H, Murayama S, Funamoto S, Ihara Y: gamma-Secretase Activity Is Associated with Braak Senile Plaque Stages. Am J Pathol 2020, 190:1323-31.

[8] Kameyama M, Ishibashi K, Toyohara J, Wagatsuma K, Umeda-Kameyama Y, Shimoji K, Kanemaru K, Murayama S, Ogawa S, Tokumaru AM, Ishii K: Voxel-based morphometry focusing on medial temporal lobe structures has a limited capability to detect amyloid beta, an Alzheimer's disease pathology. Aging (Albany NY) 2020, 12.

[9] Kitano T, Sakaguchi M, Yamagami H, Ishikawa T, Ishibashi-Ueda H, Tanaka K, Okazaki S, Sasaki T, Kadono Y, Takagaki M, Nishida T, Nakamura H, Yanase M, Fukushima N, Shiozawa M, Toyoda K, Takahashi JC, Funatsu T, Ryu B, Yoshioka D, Toda K, Murayama S, Kawamata T, Kishima H, Sawa Y, Mochizuki H, Todo K: Mechanical thrombectomy in acute ischemic stroke patients with left ventricular assist device. J Neurol Sci 2020, 418:117142.

[10] Koshi-Mano K, Mano T, Morishima M, Murayama S, Tamaoka A, Tsuji S, Toda T, Iwata A: Neuron-specific analysis of histone modifications with post-mortem brains. Sci Rep 2020, 10:3767.

[11] Moriguchi S, Takahata K, Shimada H, Kubota M, Kitamura S, Kimura Y, Tagai K, Tarumi R, Tabuchi H, Meyer JH, Mimura M, Kawamura K, Zhang MR, Murayama S, Suhara T, Higuchi M: Excess tau PET ligand retention in elderly patients with major depressive disorder. Mol Psychiatry 2020.

[12] Nagano S, Jinno J, Abdelhamid RF, Jin Y, Shibata M, Watanabe S, Hirokawa S, Nishizawa M, Sakimura K, Onodera O, Okada H, Okada T, Saito Y, Takahashi-Fujigasaki J, Murayama S, Wakatsuki S, Mochizuki H, Araki T: TDP-43 transports ribosomal protein mRNA to regulate axonal local translation in neuronal axons. Acta Neuropathol 2020, 140:695-713.

[13] Omura T, Motoyama R, Tamura Y, Nonaka K, Tanei ZI, Shigemoto K, Tokumaru AM, Murayama S, Arai T, Araki A: Meningoencephalitis caused by masked mastoiditis that was diagnosed during a follow-up in an elderly patient with diabetes mellitus: A case report. Geriatr Gerontol Int 2020, 20:500-1.

[14] Schweighauser M, Shi Y, Tarutani A, Kametani F, Murzin AG, Ghetti B, Matsubara T, Tomita T, Ando T, Hasegawa K, Murayama S, Yoshida M, Hasegawa M, Scheres SHW, Goedert M: Structures of alpha-synuclein filaments from multiple system atrophy. Nature 2020, 585:464-9.

[15] Serisawa S, Hirao K, Sato T, Ogawa Y, Kanetaka H, Enomoto M, Shimizu S, Sakurai H, Sakashita Y, Murayama S, Hanyu H: Adult-onset neuronal intranuclear inclusion disease showing markedly high phosphorylated tau protein levels in cerebrospinal fluid. Geriatr Gerontol Int 2020, 20:793-5.

[16] Tanaka H, Homma H, Fujita K, Kondo K, Yamada S, Jin X, Waragai M, Ohtomo G, Iwata A, Tagawa K, Atsuta N, Katsuno M, Tomita N, Furukawa K, Saito Y, Saito T, Ichise A, Shibata S, Arai H, Saido T, Sudol M, Muramatsu SI, Okano H, Mufson EJ, Sobue G, Murayama S, Okazawa H: YAP-dependent necrosis occurs in early stages of Alzheimer's disease and regulates mouse model pathology. Nat Commun 2020, 11:507.

[17] Uchino A, Nagai M, Kanazawa N, Ichinoe M, Yanagisawa N, Adachi K, Nanba E, Ishiura H, Mitsui J, Tsuji S, Suzuki K, Murayama S, Nishiyama K: An autopsy case of GM1 gangliosidosis type II in a patient who survived a long duration with artificial respiratory support. Neuropathology 2020.

[18] Yoshinaga S, Yamanaka T, Miyazaki H, Okuzumi A, Hiyama A, Murayama S, Nukina N: Preserved proteinase K-resistant core after amplification of alpha-synuclein aggregates: Implication to disease-related structural study. Biochem Biophys Res Commun 2020, 522:655-61.

[19] Zhang W, Tarutani A, Newell KL, Murzin AG, Matsubara T, Falcon B, Vidal R, Garringer HJ, Shi Y, Ikeuchi T, Murayama S, Ghetti B, Hasegawa M, Goedert M, Scheres SHW: Novel tau filament fold in corticobasal degeneration. Nature 2020, 580:283-7

[20]. Tanei, S., Saito, Y., …Murayama, S.: Lewy pathology of the esophagus correlates with the progression of Lewy body disease: a Japanese cohort study of autopsy cases: Lewy pathology of the esophagus correlates with the progression of Lewy body disease: a Japanese cohort study of autopsy cases. Acta Neuropath in press

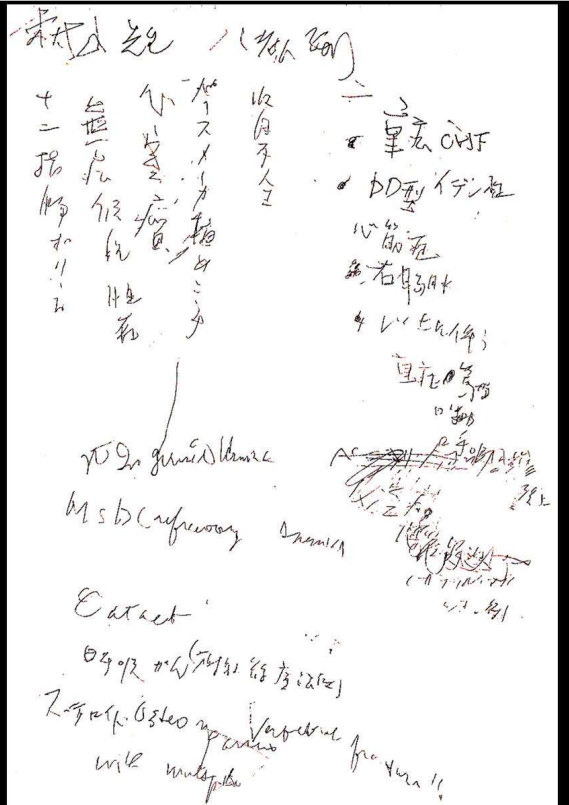We published 20 English original peer- reviewed papers in 2020.a

Brain Donation Program

Dr. Yasuo Toyokura
80y.o. +
Em. Pro. Univ. Tokyo
Em. Direc. TMGHIG
The first brain donor of BBAR

Death Note: "Please use our body to conquer diseases that will kill me (and you cannot cure) ."

Donor Card

高齢者ブレインバンク
献脳ドナー登録カード
本カード所持者は高齢者ブレインバンクへの献脳ドナー登録者です。

献脳ドナー登録者の死亡時に、ご遺族が献脳に同意いただける場合には、事務局へ電話連絡をお願い致します。

☎ :03-3964-3241　内線3046 (平日9時～17時)
📱 :090-2549-8267 (上記以外の時間帯)

高齢者ブレインバンク事務局
〒173-0015東京都板橋区栄町35-2 東京都健康長寿医療センター内

Late Eameritus Professor Toyokura, the University of Tokyo and Emeritus President of TMGHIG was the founder of our brain donation program.

"Please use my body to establish the path to cure the incurable diseases that will kill me." He suffered from cardiomyopathy with a mutation of myosin light chain.

Preregistered donors who fulfilled their will (2019/5) : preregistrants: 160

No.	Age	Gen.	Dix	IC	Place of death	No.	Age	G	Dix	IC	Place of Death	No.	Age	G	Dix	IC	Place of Death
1	80	M	(CCM)	S	FTMGHIG	21	83	M	CFNS lymphoma	F	Outside Hosp.	41	87	F	Early AD	S	Nursing
2	83	M	FaAD	F	Outside Hosp.	22	95	F	iNPH	F	Home	42	77	F	AD	F	Outside Hosp.
3	79	F	FaAD	F	Outside Hosp.	23	80	F	ALS	F	TMGHIG	43	86	F	DLB+AD	F	Outside Hosp.
4	69	F	CBD-PNFLA/TDP-43 type A	F	Outside Hosp.	24	78	F	PSP	F	Outside Hosp.	44	80	M	AD、DG	F	Outside Hosp.
5	86	F	AD	F	Brain transfer	25	74	M	LBD	F	Outside Hosp.	45	83	F	PSP	F	Outside Hosp.
6	91	M	AD/CAA/DG/HS TDP-43 typeA	S	Outside Hosp.	26	79	M	AD	F	Outside Hosp.	46	68	M	PSP	F	Outside Hosp.
7	84	F	PSP	S	Outside Hosp.	27	91	F	AD	F	Outside Hosp.	47	78	M	PSP	F	Outside Hosp.
8	89	F	(colocn CA)	S	TMGHIG	28	83	F	PSP	F	Outside Hosp.	48	102	F	Influenza Enc.	F	Outside
9	84	M	CVD	F	TMGHIG	29	90	F	AD	S	Outside Hosp.	49	69	M	CVD	F	Brain Transfer
10	86	M	AD	F	TMGHIG	30	87	F	AD	F	Outside Hosp.	50	83	F	AD、DLB、AGD	F	Outside Hosp.
11	88	F	F	F	Outside Hosp.	31	95	M	ADG	S	Nursing	51	63	M	pending	F	Outside Hosp.
12	93	F	PD	S	TMGHIG	32	85	M	ADG	F	Outside Hosp.	52	86	M	pending	F	Nursing
13	99	F	DLB	F	Outside Hosp.	33	80	F	ALS	F	Outside Hosp.	53	89	F	pending	F	Outside Hosp.
14	73	M	(Lung CA)	F	Outside Hosp.	34	80	M	SMA	F	Outside Hosp.	54	94	M	pending	F	Nursing
15	111	F	NFTD	F	Nursing	35	70	F	PSP	F	Outside Hosp.	55	44	M	pending	F	Outside Hosp.
16	90	F	AD	F	Outside Hosp.	36	68	M	CBD	F	Nursing	56	78	M	pending	F	Nursing
17	97	M	NFTD / PSP/LBD/DG	F	Nursing	37	84	M	ALS	S	Nursing						
18	72	M	CVD	F	Nursing	38	69	M	PSP	F	Brain Transfer						
19	61	M	Encephalitis	F	Outside Hosp.	39	86	M	PDD	F	Outside Hosp.						
20	79	M	CJD	F	Outside Hosp.	40	93	M	PSP	F	Brain Transfer						

Preregistered donors reach 160, 56 of whom fulfilled their will.

September 28, 2018
@
The Brain Bank for Aging Research
Tokyo Metropolitan Geriatric Hospital &
Institute of Gerontology
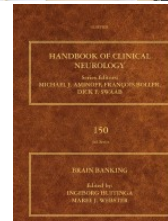
In 2018, BBAR organized the international brain bank symposium. Professor Huitinga, the director of Netherland Brain Bank edited Brain Bank Chapter of the Handbook of Clinical Neurology.

The Japanese Brain Bank Network, Kansai Base

Brain Bank for Neurodevelopmental, Neurological and Psychiatric Disorders

United Graduate School of Child Development, Osaka University

Osaka University Neurology, Psychiatry & Pathology

NHO Osaka Toneyama & Utano (Kyoto)

Osaka University Legal Medicine

Postmortem Brain Registry of Judicial Autopsy (Suicide)

Osaka Womens' and Childrens' Hospital

Neuro-developmental Bioresource

Brain Donation

Fronto Temporal Dementia Parkinson Disease ALS Multiple Sclerosis Multiple System Atrophy

Muscle Dystrophy Lewy body dementia Alzheimer Disease Progressive Suparnucelar Palsy Corticobasal Degeneration

Japanese Version of Suicide Bank Autim Brain Net

Special NPO Research and Education Support Center

Patient Association Parkinson disease Multiple Sclerosis

Osaka Brain Bank Promotion Foundation

CDC Research Group to Protect the Life of Next Generation

PO Consortium

www.mci.gr.jp/BrainBank/

The Kansai Base, The Japanese Brain Bank Network was established in 2000 in collaboration with Osaka University, National Hospital Organization (NHO) and Osaka Prefectural Hospital Organization.

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Japanese Brain Bank Network for Neuroscience Research

University of Tokyo, Tokushima, Kagawa, Tokyo Medical, Kitasato & Teikyo, NCGM, NHO Tokyo, Shimoshizu, Shizuoka Epi. Neuro. & Okayama Nishi Hosp. Yokohama Rosai. Kameda, JR Kanto, Chikamori, Tokyo Teishin

Brain Bank for Aging Res.

TMGHIG, NCGG

Brain Donation & Autopsy Consent

Tokyo Metr. Geriatr. Hosp. & Inst. Gerontol.

Registration Clinical, Radiological & Pathological Data

Brain Bank for Neurodevelopmental, Neurological and Psychiatric Disorders

Osaka Univ. NHO Toneyama

NCNP

Mihara Mem. Hosp

Fukushimura Hosp.

Open Resource for Education and Research

Choice of Resource

Researcher

Em. Prof Yasuo Ihara a preregistrant for BBAR

Brain Bank Committee, Jap. Soc. Neuropath.

BBNNPD and BBAR form the core of the Japanese Brain Bank Network for Neuroscience Research, funded by MEXT, collaborating with the National Center of Neurology and Psychiatry (NCNP), Mihara Memorial Hospital and Fukushimura Hospital. Dr. Yasuo Ihara, a preregistered brain donor for BBAR and Emeritus Professor, the University of Tokyo, has been contributing to this frame from the beginning.
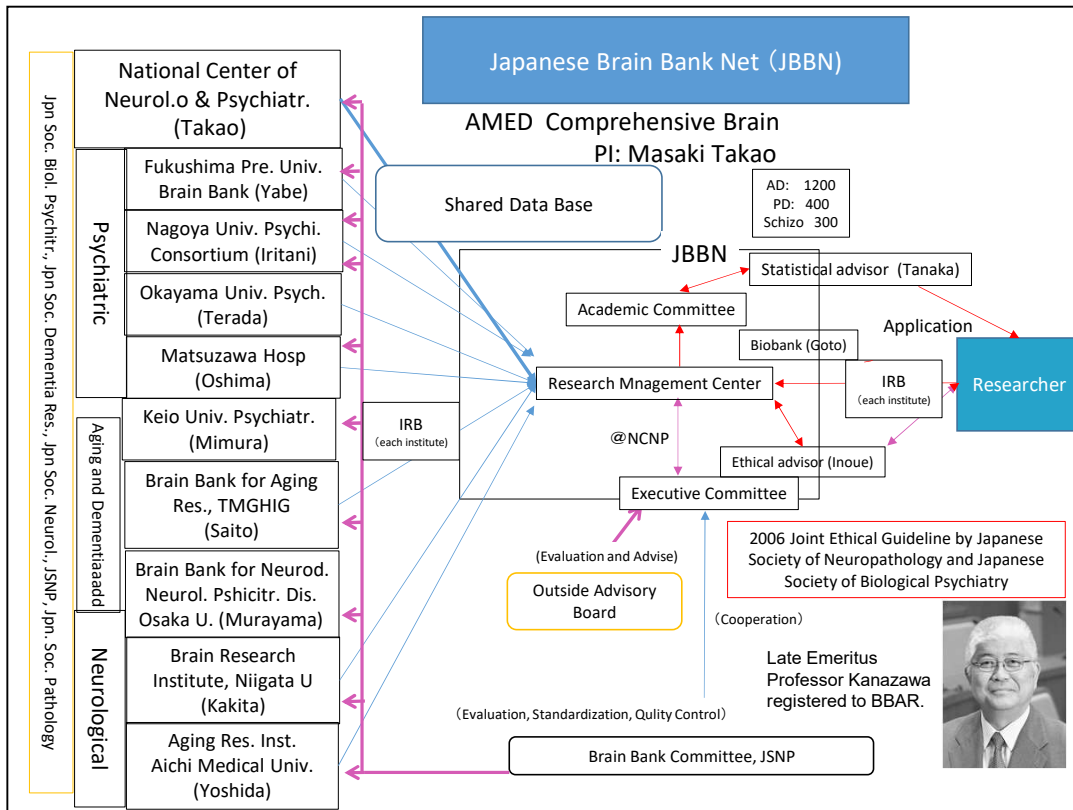
Japan Brain Bank Net (JBBN) is funded by AMED, first in 2016 and renewed in 2021. Dr. Masaki Takao, the director of NCNP Brain Bank is PI. BBAR takes responsibility for aging and dementia and BBNNPD for suicide and pediatric registry. The establishment of JBBN was Emeritus Professor Kanazawa's dream, who was registered to BBAR on January 21, 2016, just before the start of JBBN.

JSNP Brain Bank Committee (1986-)
Chair: Murayama, S. (UO)

- Akatsu, H. (Ger. Fukushimura H.)
- Fujimura, H. (Neu.Toneyama H.)
- Hasegawa, M. (Bio. Ch, TMIMR)
- Ikeuchi, K. (Genome. Niigata U.)
- Inoue, Y. (Ethis, IMSUT)
- Iritani, S. (Psy. Nagoya U.)
- Ito, K. (NP. Kyoto Pr. U.)
- Kakita, A. (NP. Niigata U.)
- Kato, T. (Psy, Riken)
- Izumi Y. (Neu. Tokushima U)
- Kaneda D (Fukushimura)
- Komori, T. (NP. TMNH)
- Kowa, H.(Neu. Kobe U.)
- Kunii, Y. (Psy. Fukushima)
- Mochizuki, H. (Neu. Osaka U.)
- Tanigawa, K. (Pat. Hokkaido U.)
- Nishimura, H. (Pat. Kawasaki U.)
- Oshima, K. (Psy. Matsuzawa H.)
- Saito, Y. (NP. TMGHIG)
- Takao, M. (Lab. NCNP)
- Takanashi, M.(Neu. Juntendo U.)
- Tokumaru, A. (Rad. TMGHIG)
- Wakabayashi, K (NP. Hirosaki U.)
- Yamada, M. (NP, Shinshu U.)
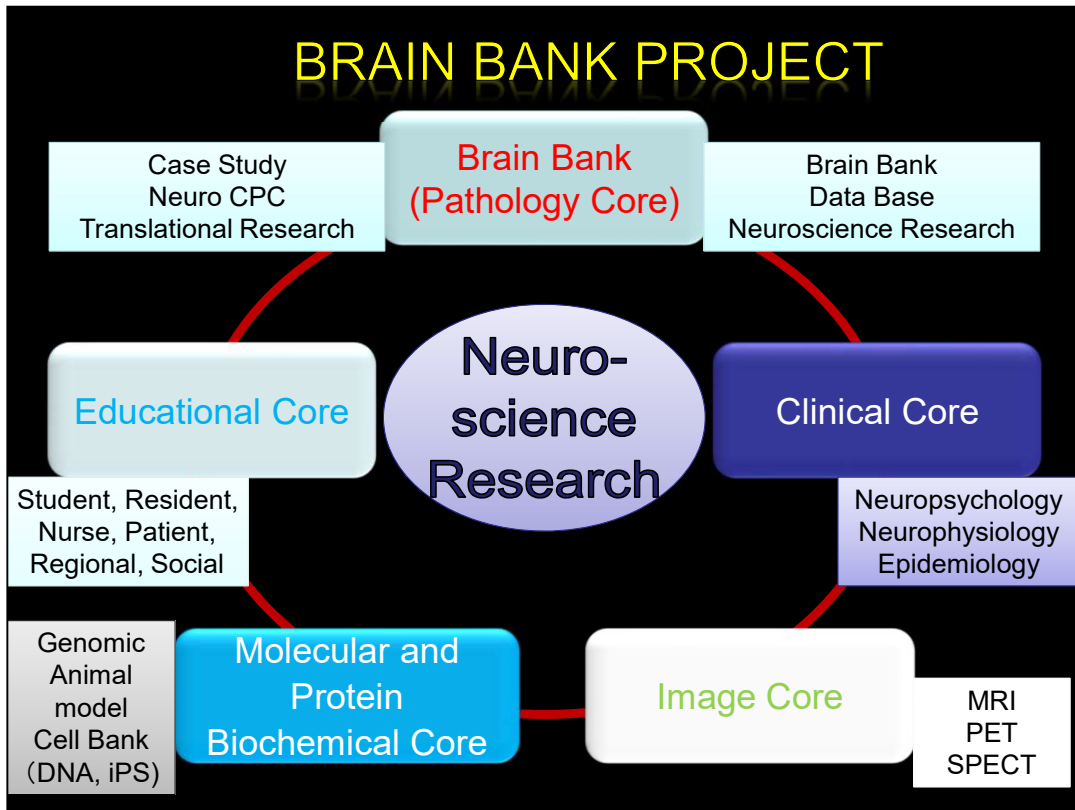- Yokota, O. (Psy, Okayama U.)
- Yoshida, M. (NP, Aichi M. U.)

The JSNP (Japanese Society of Neuropathology) Brain Bank Committee supports JBBN and JBBNNR for quality assurance of neuropathological diagnosis. Underlined names denote diagnostic neuropathologists for JBBN, and those in blue denote members of JBBNNR.

The philosophical background

- The respect for autopsy since Edo era.
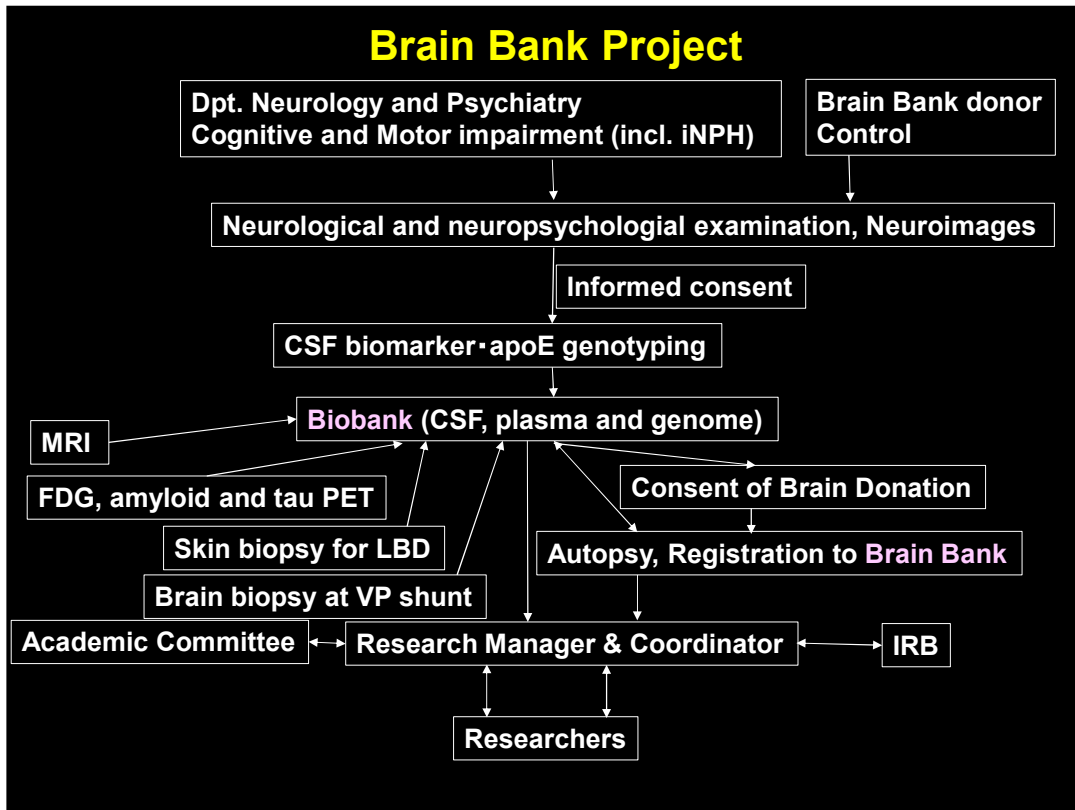- Medical positivism.
- The Brain Bank Committee, the Japanese Society of Neuropathology guarantees quality assurance of brain bank from the points of neuropathological diagnosis, legal regulation and COI.
- Japanese tradition, "Okagesan".
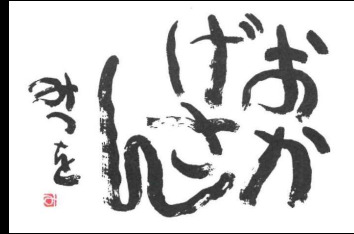
The philosophical background of brain bank is picked up.

The BBAR follows the framework of Alzheimer Disease Research Coordinating Center in US.

Brain Bank Project

Dpt. Neurology and Psychiatry Cognitive and Motor impairment (incl. iNPH) → Brain Bank donor Control → Neurological and neuropsychologial examination, Neuroimages → Informed consent → CSF biomarker・apoE genotyping → Biobank (CSF, plasma and genome)

MRI → Biobank
FDG, amyloid and tau PET → Biobank
Skin biopsy for LBD → Biobank
Brain biopsy at VP shunt → Biobank
Biobank → Consent of Brain Donation → Autopsy, Registration to Brain Bank

Academic Committee ↔ Research Manager & Coordinator ↔ IRB
Research Manager & Coordinator ↔ Researchers

From 2017, BBAR extended its research support to include biobanking of CSF, plasma and gnome of living patients and control volunteers.

BBAR Resource Center

- A full time coordinator.
- All BBAR records stored in our digital clinical chart system with Brain Bank ID.
- BBAR Resource Center:
  24 deep freezers, including one for a national prion back- up bank
- >7000 case paraffin blocks
- BBAR Data Center: a virtual slide system for educational output.
- BBAR Internet Conference Room
   with NCNP, OU, NHO Toneyama and Fukushimura

The Brain Bank for Aging Research (BBAR) employs a full-time and a part- time coordinators. Our registrants' data are all stored in clinical chart system with the brain bank ID. We have a resource center, carrying 22 deep freezers and paraffin blocks of more than 7000 cases.
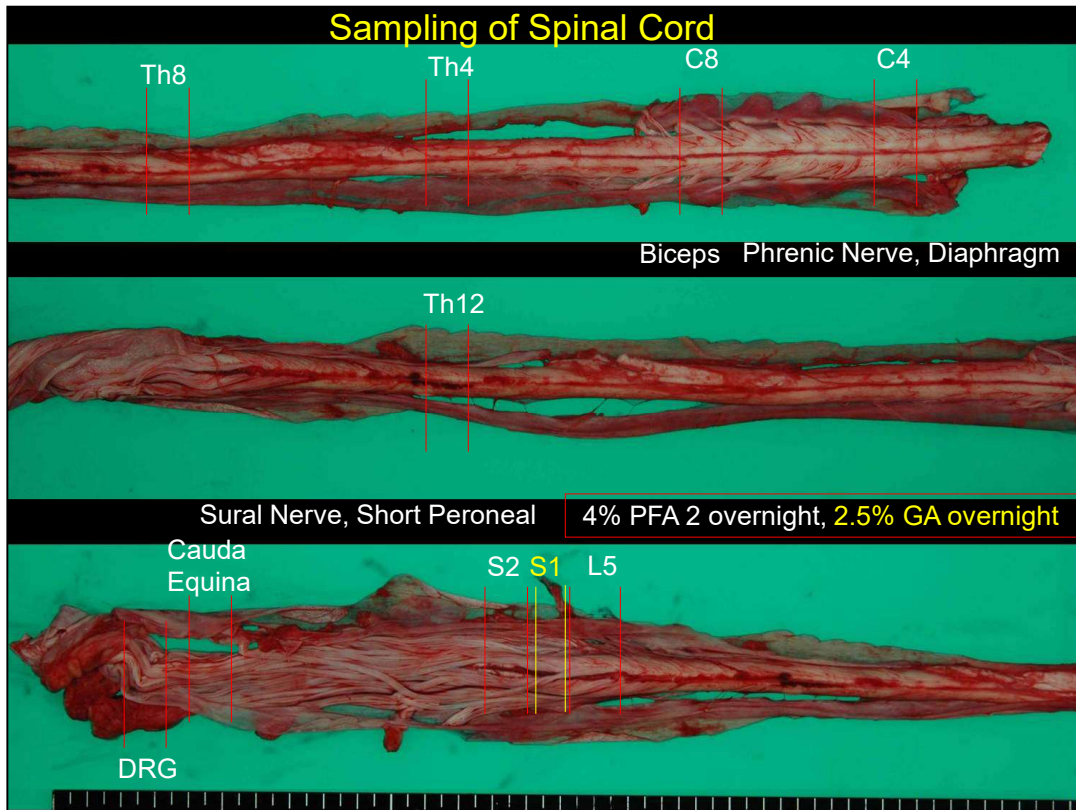
The BBAR Data Center is equipped with a virtual slide system for neuropathological education. The BBAR network conference room is connected to the National Center for Neurology and Psychiatry (NCNP), Osaka University, NHO Osaka Toneyama Medical Center and Fukushimura Brain Bank for neuropathological conferences once a week.

Autopsy of Brains

- Each case is handled by an attending brain bank doctor (neuropathologist) and a technician (specially trained), in collaboration with an attending general pathologist and two technicians.

- The attending brain bank doctor determines the frozen side.

- The doctor forms 8mm-thick serial coronal slices of the brain, 5mm- thick serial sagittal slices of the cerebellum and 5mm- thick axial slices of the brain stem.

- The technician takes photos and freezes tissues immediately.
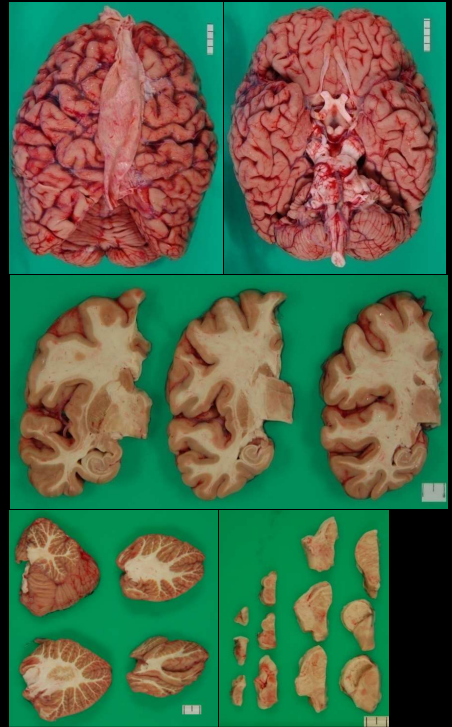
In BBAR, each autopsy is conducted by a general pathologist, an autopsy technician and a laboratory technician, in collaboration with a neuropathologist and a brain bank technician (2). Thus, every autopsy is handled by five professionals.

Sampling of Spinal Cord

Th8   Th4   C8   C4

Biceps   Phrenic Nerve, Diaphragm

Th12

Sural Nerve, Short Peroneal   4% PFA 2 overnight, 2.5% GA overnight
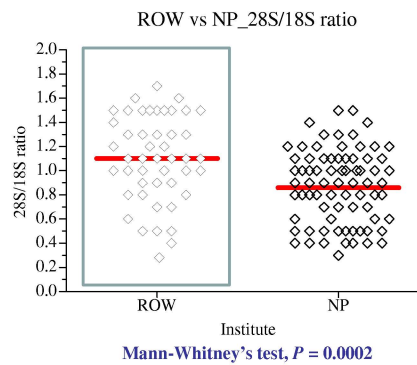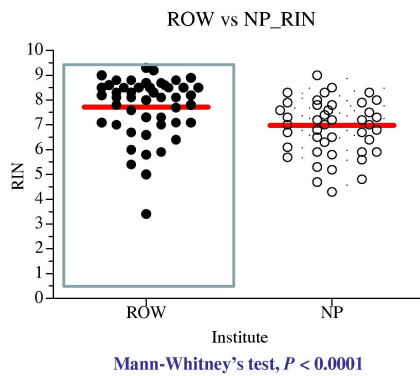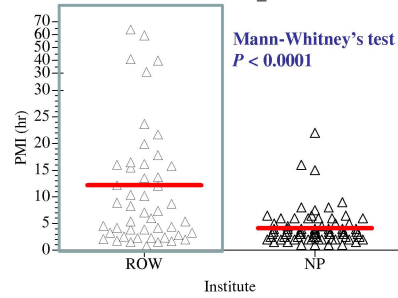
Cauda Equina   S2 S1 L5

DRG

Spinal cords are recovered from all cases. After sampling for histopathological evaluations, the remaining spinal cords are frozen for biochemical and molecular studies.

Total RNA Quality Check (Dpt. Mol. Biol. Niigata Univ. BRI)

DNA & RNA Back Up

BBAR (N=48: ROW) vs Control (N=78: NP)

RNA Quality of BBAR is better than rapid autopsy control, probably due to a very short cooling interval (interval between death and transfer to a refrigerator).

Mann-Whitney's test
$P < 0.0001$

ROW vs NP_RIN

Mann-Whitney's test, $P < 0.0001$

ROW vs NP_28S/18S ratio

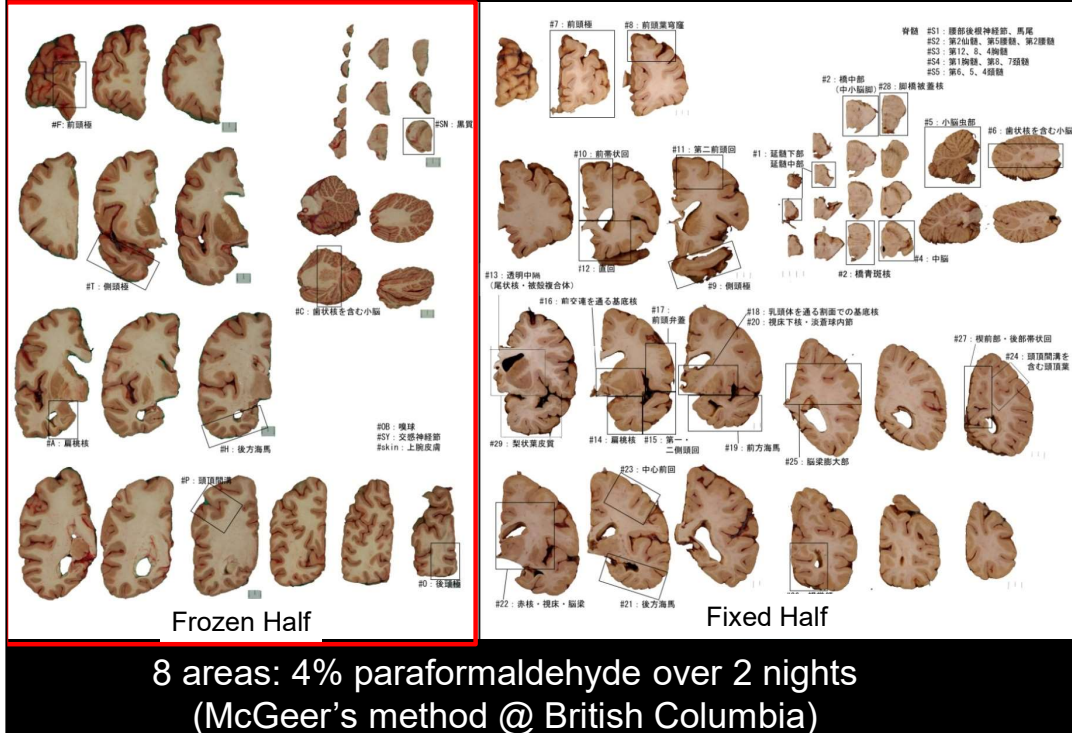Mann-Whitney's test, $P = 0.0002$

080121 (Mon)

In collaboration with the Department of Molecular Biology, the Brain Research Institute at Niigata University (BRIN), we check the RNA qualities of all cases. Our cases present better quality than specimens of a a reference institute. ApoE genotyping is determined for every case. DNA and RNA are stored in BRIN to back up BBAR.

BBAR Resource (Frozen)

- Half brain after sampling small pieces of tissues for weak fixation.
- Entire spinal cord, after sampling the segments for pathological evaluation.
- Peripheral autonomic nervous system: sympathetic ganglia, esophago- columnar junction, heart, skin and olfactory plate.
- Skeletal muscle: biceps brachii (for the study of sarcopenia)
- General organs: small pieces of liver, kidney, lung, esophagus
- Serum (stored in the hospital laboratory).

Frozen resource includes half brain, entire spinal cord, peripheral autonomic nervous system and skeletal muscle.

BBAR Protocol (www.mci.gr.jp)

Frozen Half

Fixed Half

8 areas: 4% paraformaldehyde over 2 nights
(McGeer's method @ British Columbia)

From the frozen side, eight small samples from specific anatomical areas are fixed in 4% paraformaldehyde over two nights. The fixation simulates perfusion followed by overnight fixation protocol that is applied to experimental animals.

Brain Cutting (1972.5.1-)

In collaboration of Neurology, Neuropathology, Psychiatry, Pathology and Rehabilitation, connected via internet.

Brain Cutting is an important activity for diagnosis and education, with BBAR and NCNP connected by internet. Emeritus Professor Kinuko Suzuki, Department of Pathology (Neuropathology), the University of North Carolina at Chapel Hill joins the conference after she returned to Japan.
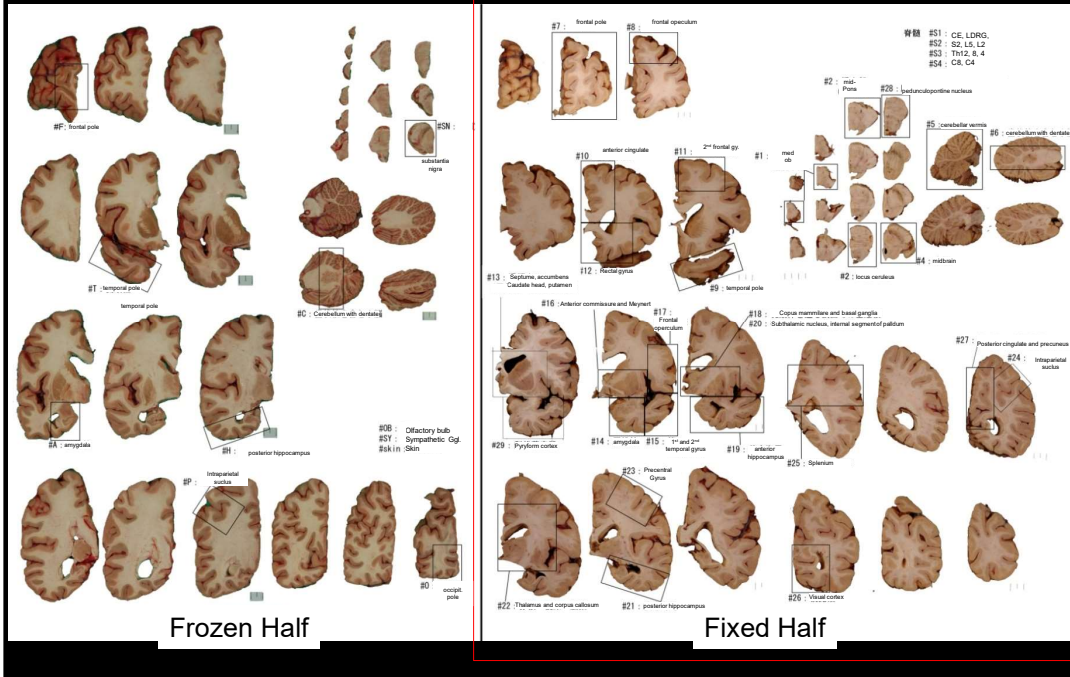
Tissue sections were obtained from a fixed side, in compliance with CERAD requirements, DLB Consensus Guideline, and Braak's recommendation that requires evaluation of bilateral amygdala and hippocampi.

BBAR Protocol: Histological Examination.

Internationally Standardized
Neuropathological Diagnostic Method

Paraffin block of >7,000 cases
easily accessible

Library

We have been accumulating glass slides and paraffin blocks in the BBAR
Resource Center.

BBAR Resource (Fixed)

- 4% paraformaldehyde over two nights, one half for paraffin embedding and another half preserved in 20% sucrose PBS+0.1% NaN3

- Brain: frontal, temporal and occipital poles, intraparietal sulcus, anterior amygdala, posterior hippocampus, midbrain, dentate nucleus, olfactory bulb

- Spinal Cord: C4/8, T4/8/12, L5, S2

- Peripheral ANS: sympathetic ganglia, esophago-columnar junction, anterior wall of the left ventricle of the heart, skin, olfactory plate, biceps brachii

- 20% buffered formalin for 7-13 days

- Half brain, body organs

Fixed tissue resource consists of weakly stained tissues from a frozen half and formalin fixed tissues from a fixed half of the brain

Staining

Routine： H.E., K.B.
Special： Gallyas-Braak, methenamine silver,
Elastica Masson, Congo red, thioflavin S
Immunohistochemistry with automatic stainer（Ventana）

Epitope	Antibody	Clone
Aβ11-28aa	12B2 (IBL)	monoclonal
phosphorylated tau	AT8 (Innogene)	monoclonal
3R/ 4R tau	RD3/ RD4	monoclonal
phosphorylated α- synuclein	psyn64 (Wako)	monoclonal
Ubiquitin	Sigma	polyclonal
Phosphorylated TDP43	PSer409/410	monoclonal
FUS/ TLS	Sigma	polyclonal

Systematic screenings of unbiased consecutive autopsy cases are performed with commercially available antibodies.

Aβ
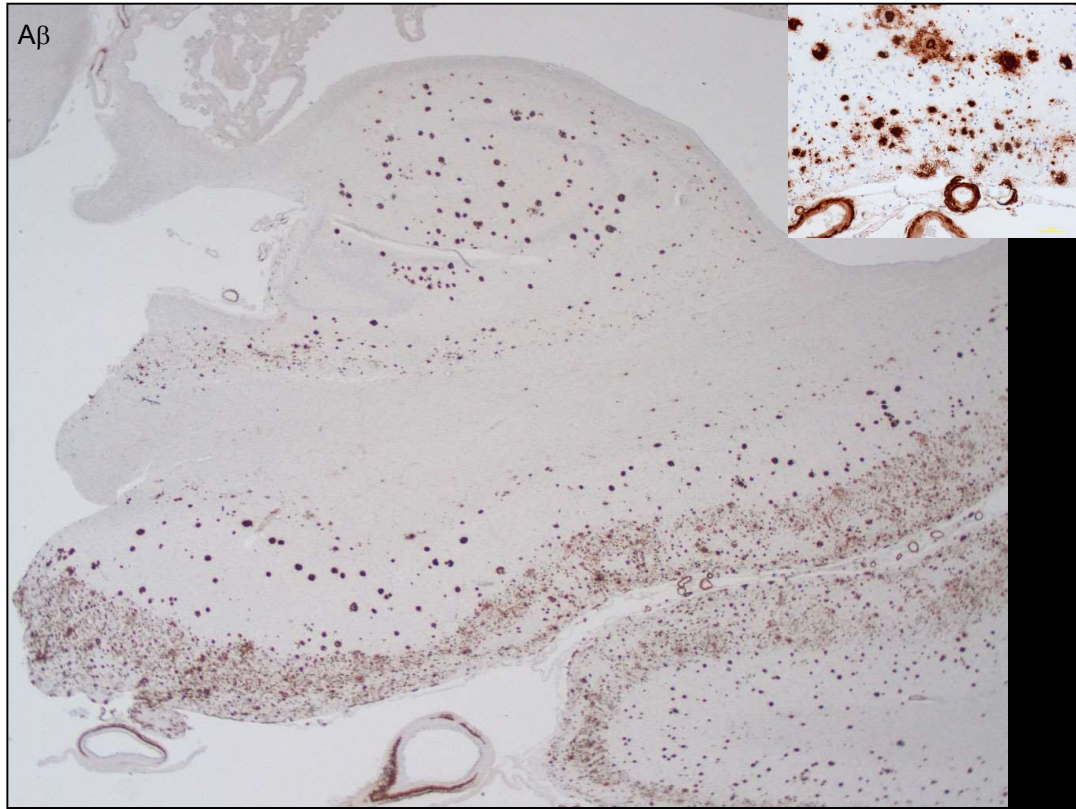
A section of hippocampus fixed in 4% paraformaldehyde presented numerous A-beta (11-28)- immune- positive deposits in the parenchyma and the walls of vessels.

P & CNS Screening ⟵ tau ⟶ Lewy TDP ⟵ Aβ ⟶																				
Y-9□7□	PT	NFT	GT	NT	NP	AG R	AG L	AT TSA	AT BLA	Psyn R	Psyn L	TDP -43	DP R	DP L	CP R	CP L	A/V R	A/V L	CCAA R	CCAA L
Sympathetic ganglion										o										
Dorsal root ganglion																				
Spinal cord																				
Sacral anterior horn																				
Sacral posterior horn																				
Intermediate zone (Sacral)										o	o									
Lumbar anterior horn												o								
Lumbar posterior horn																				
Lumbar anterior column																				
Lumbar lateral column										o	o									
Lumbar posterior column																				
Thoracic anterior horn																				
Thoracic posterior horn																				
Intermediolateral N. (Thoracic)										o										
Cervical anterior horn	o			o																
Cervical posterior horn																				
Medulla oblongata																				
Dorsal motor N. of vagus										o										
Hypoglossal N.																				
Inferior olivary N.																				
Pons																				
Pontine N.																				
Locus ceruleus										o										
Subceruleus																				
Pedunculopontine N.																				
Midbrain																				
Oculomotor N.																				
Edinger-Westphal N.																				
Pars compacta of SN	o			o						o	o									
Periaqueductal gray matter																				
Cerebellum																				
Cerebellar cortex													o		o		o			
Cerebellar white matter																				
Dentate N.																				
Interbrain / Basal ganglia																				
Broca's diagonal band																				
Hypothalamus																				
Nucleus basalis of Meynert	o			o																
Accumbens N.																				
Caudate N.																				
Putamen													o		o					
Ext. globus pallidus																				
Int. globus pallidus																				
Claustrum																				
Subthalamic N.																				
Thalamus																				
Allocortex (Rhinencephalon/Limbic)																				
Olfactory bulb periphery										o										
Anterior olfactory N.										o										
Piriform cortex (frontal)																				
Piriform cortex (temporal)																				
Amygdala	o	o		o		o	o	o	o	o			o		o					
Uncus / Ambient gyrus	o	o		o		o	o					o								
Dentate gyrus	o	o	o	o																
Hippocampus CA4	o	o	o	o																
Hippocampus CA3	o	o	o	o																
Hippocampus CA2	o	o	o	o						o										
Hippocampus CA1	o	o	o	o								o	o		o					
Subiculum	o	o	o	o		o	o					o								
Presubiculum																				
Entorhinal	o	o	o	o								o								
Transentrhinal	1	1	o	1						o										
Insular cortex																				
Anterior cingulate gyrus																				
Temporal pole (medial)																				
Cerebral neocortex (isocortex)																				
Temporal pole (lateral)																				
T4	o	o	o	o																
T2	o	o	o	o									o		o		o			
Fronatal pole													o		o		o			
F2																				
Supramarginal gyrus													o		o		o			
Visual association cortex																				
Striate area													o		o		o		o	
Primary motor cortex																				

We screen all cases immunohistochemically. Blue highlights denote the peripheral autonomic nervous system, and the orange rectangle, the spinal cord.

BBAR Degenerative Pathology Database

BBAR	Y96XX									
A/G	CDR	PMI	NFT	AT8	SP	CERAD	Thal	LB	LB score	DLB 3rd
93M	3	11:22	4/3	3/3	2	2	5	4	4	Limbic (amygdala predominant)
Grain	AA	AT	UD	TDP	ApoE	RIN				NPD
0.5/ 0.5	1C	1	3	T1M1S0	3/3	8.1				AD, LBD, CVDE

A/G age/ gender
CDR (clinical dementia rating):   0-3
PMI: postmortem interval
NFT (tangle: Braak Stage):   0-6
AT8 (tangle: AT8 Stage)   0-6
SP (senile plaque: Braak Stage):   0-3
CERAD   0-3 (0- C)
Thal (amyloid Thal Stage)   0-5
Lewy (Lewy body, BBAR Stage):   0-5
DLB score (DLB 1st Consensus Guideline)
DLB 3rd (DLB 3rd Consensus Guideline)
Grain (argyrophilic grain, Saito Stage):   0-3
AA (amyloid angiopathy, BBAR Stage):   0-3
AT (astrocytic tangle):   0-3
UD (ubiquitinated dots):   0-3
TDP (TDP-43 proteinopathy, temporal, medulla and spinal)   0-3
ApoE (apoE genotyping)
RIN (RNA intergrity number)
NPD: neuropathologic diagnosis (AD: Alzheimer disease; LBD: Lewy body disease; CVDE: embolic infarct)

Each case is evaluated using international standards. Researchers who apply to BBAR choose samples based on this database.

DNA Resource (1,890 cases)

Braak NFT/SP	0	I	II	III	IV	V	VI	計
0	34 / 66.3	314 / 75.8	102 / 81.8	46 / 85.6	12 / 85.4	1 / 81.0	0 / -	509 / 77.5
A	16 / 75.5	350 / 78.0	149 / 83.6	74 / 86.2	23 / 88.6	1 / 99.0	0 / -	613 / 80.6
B	8 / 76.1	169 / 79.9	91 / 82.8	70 / 85.6	23 / 91.2	2 / 82.0	1 / 94.0	364 / 82.4
C	3 / 76.0	50 / 79.4	51 / 83.0	80 / 84.5	80 / 86.6	100 / 86.4	40 / 83.9	404 / 84.4
計	61 / 70.5	883 / 77.7	393 / 82.9	270 / 85.4	138 / 87.6	104 / 86.4	41 / 84.1	1890 / 80.9

Case # / Average Age

Alzheimer Disease: 220/ 1890 = 11.6%

DNA resources represent progressive accumulation of tangles and plaques. We adopt Braak NFT Stage equal to or more than IV and SP Stage C for diagnosis of Alzheimer disease or Alzheimer dementia in 2011 NIA- AA classification.
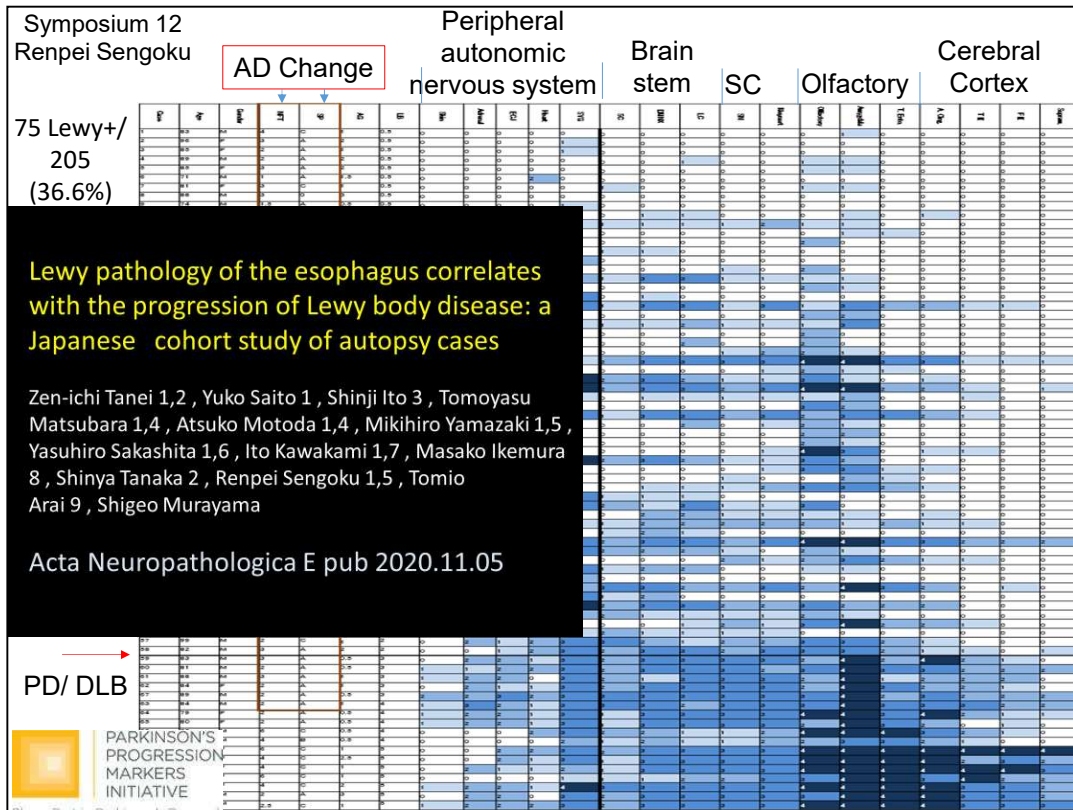
In our most recent 205 consecutive autopsy cases, 36% contained Lewy body pathology. In 2014- 2016 we received funding from the Michael J Fox Association as a Lewy body disease body bank.

47 ALS/ MND Brain and Spinal Cord Resource (with 300 frozen control spinal cord)
Westmead detecting upper motor neuron sigh for early diagnosis of ALS

徳島大学、ビハーラ花の里病院剖検を広島西医療センターで行う体制の元、筋萎縮性側索硬化症脳・脊髄バンクを高齢者ブレインバンクに構築しています。健康長寿医療センター脳神経内科東原医長は2年間豪シドニーWestmead研究所で上位運動ニューロンの二発磁気刺激による神経生理検査法を取得し、帰国後前頭側頭型認知症・筋萎縮性側索硬化症（ALS）クリニックを立ち上げました。豪は医療費ゼロシーリングで、病理解剖が制限されており、剖検による確認を、Westmeadとの共同研究として開始予定です。

The first autopsy case of JADNI participant from Tohoku University, just after the Great East Japan Earthquake
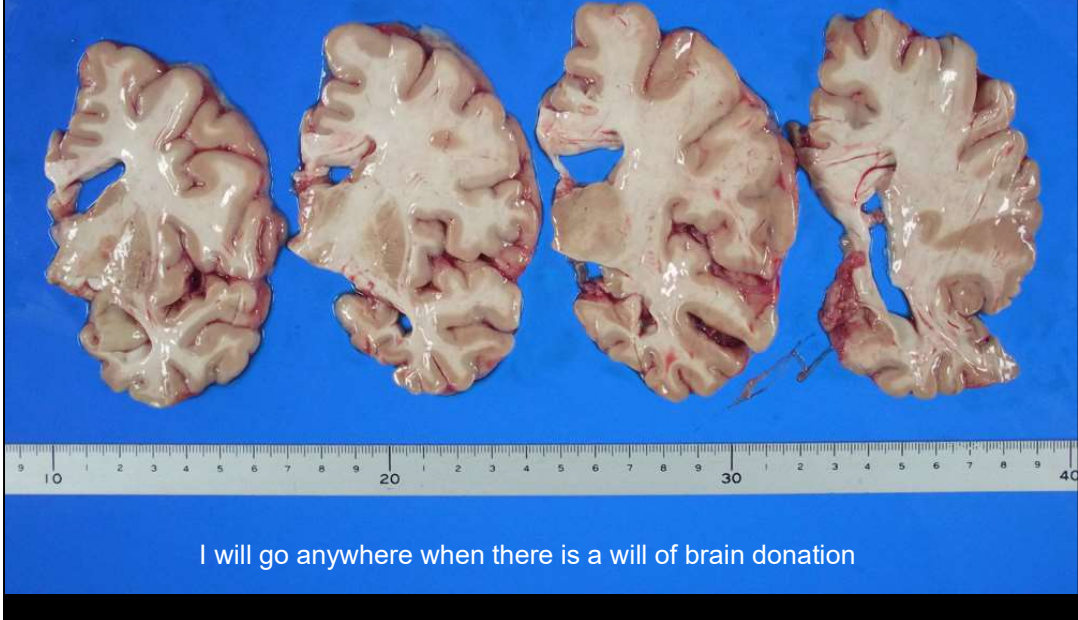
I will go anywhere when there is a will of brain donation

This is the first JADNI participant autopsy from Tohoku University. The autopsy was done just after the Higashinippon Earthquake**,** and I went to Tohoku University to recover this brain.

CJD Surveillance Commitee Pathology Core

- To promote autopsies of prion disease.

- To receive autopsies of outside cases.

- To report to the committee on autopsy- proven prion cases (pathology route)

- Quality control of pathological findings of registered cases.

- To establish a national prion back- up bank.

- To study natural course of prion disease.

Grants in Aid from Ministry of Health, Labor and Welfare, Japan

BBAR is the pathology core of the Japanese CJD Surveillance Committee and contribute to prion research.

International Collaboration

- MOU with Seoul University (Prof. Park) for Korean Brain Bank
- MOU with National Neuroscience Institute of Singapore for Neuronal Intranuclear Inclusion Body Disease
- Collaboration with Sydney Parkinson Disease Brain Bank funded by Michael J Fox Foundation (Prof. Halliday).
- Collaboration with Sydeney Westmead Hospital for ALS research

BBAR promotes international collaboration.

Brain Bank and Bioresource Center, Osaka University (2021)

<ins>Brain Bank for Neurodevelopmental, Neurological and Psychiatric Disorder</ins>

Chair (Prof.)	Murayama, S.	Concurrent	Prof. Mochizuki, H. (Neurology)
Concurrent (Neuro)	Assi. P. Beck, G.		Prof. Taniike, M. (Child Develop.)
M.D. Ph.D. Course	Yonenobu, Y.		Prof. Ikeda M. (Psychiatry)
	Yamashita, R.		Prof. Matsumoto, H. (Legal Med.)

BBAR Project (2021)

<ins>Brain Bank for Aging Research</ins>

Chair	Saito, Y.
Pathology Core	*Murayama, S.*
Clinical Core	Iwata, A.
Staff	Matsubara, H.
Fellow	Arakawa, A.
Resident	Orita, M
Visiting Scholar	*Uchino, A.*
	Shioya A
Technician	*Harada, M.*
Research Manager	*Morishima, M.*
Coordinator	Obata, M.

<ins>Neuropathology</ins>

Chair	Saito, Y.
Staff (cross appoint)	Murayama, S.

<ins>PET Center</ins>

Chair	Ishii, K.

<ins>Neurology</ins>

Chair:	Iwata, A.
Co- Chair:	Kanemaru, K.
Vice- Chair,	Nishina, N.
	Higashihara, M.
	Ihara, R.
Staff:	Hatano A
Res. Resident:	*Morimoto, S.*
Resident	*Kimura, T.*

<ins>Rehabilitation</ins>

Senior:	Kato, T.

<ins>Psychiatry</ins>

Chair:	Furuta, K.

<ins>Pathology</ins>

Chair	Arai, T.

<ins>Radiology</ins>

Chair	Tokumaru, A.

The list of BBNNPD and BBAR members.