AOCNP@India, 2021

Japan Brain Bank Network

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

Specially Appointed Researcher
The Brain Bank for Aging Research
Tokyo Metropolitan Geriatric Hospital and Institute of Gerontology (Cross Appointment)

Shigeo Murayama M.D. Ph.D.

I will talk about Japan Brain Bank Network. I am working with two brain bank system in Japan.

My Background

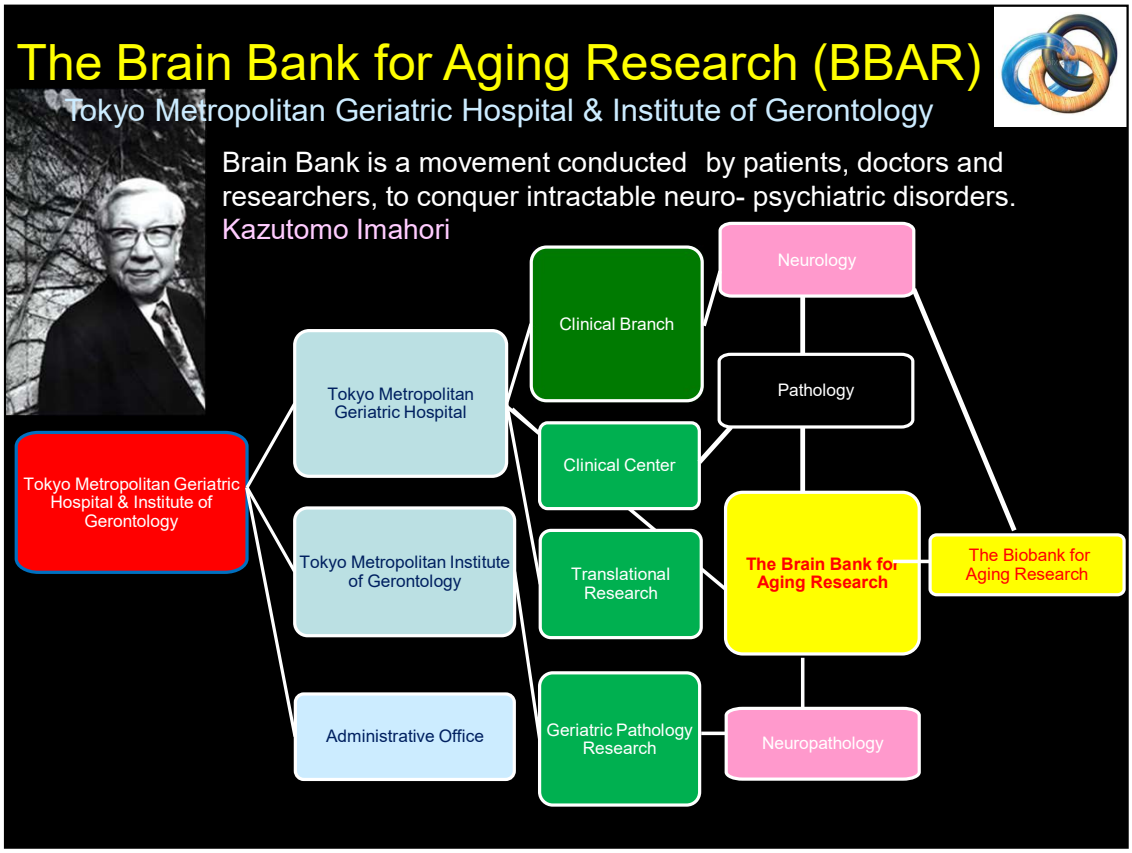
- I am a Zen master of Soto school of Zen (曹洞宗).
- I have been educated that those who have eaten food offered to Buddha（仏飯）should dedicate their life to all living creatures on earth（衆生）.
- To establish all Japan Brain Bank Network is my life work, which I interpret to be Bodhisattva line（菩薩行）.
- I will go anywhere to fulfill brain donors' will or guide doctors who want to contribute to brain banking.

My background is a buddhist priest and feels sincere respect for people in India.

COI

Honorable Member: the Japanese Societies of Neurology, Neuropathology and Dementia Research
Associate Editor, Journal of Neuropathology and Experimental Neurology
Visiting Professor: Tokushima, Hiroshima, Tokyo Medical, Doshisha and Osaka City Universities;
Neuropathology Consultant: National Center for Global Medicine, National Hospital Organization, Tokyo, Shimoshizu, Shizuoka Epilepsy and Neurology, West Hiroshima and Okinawa Hospitals; Kagawa University; Kameda, Yokohama Rosai, Toranomon, NTT East Kanto and Chikamori Hospitals

My COI is as follows. I will go anywhere to fulfill the will of brain donation.



The Brain Bank for Aging Research is defined as activity of TMGHIG funded by Tokyo Metropolitan government in collaboration of all members of our institute.

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)

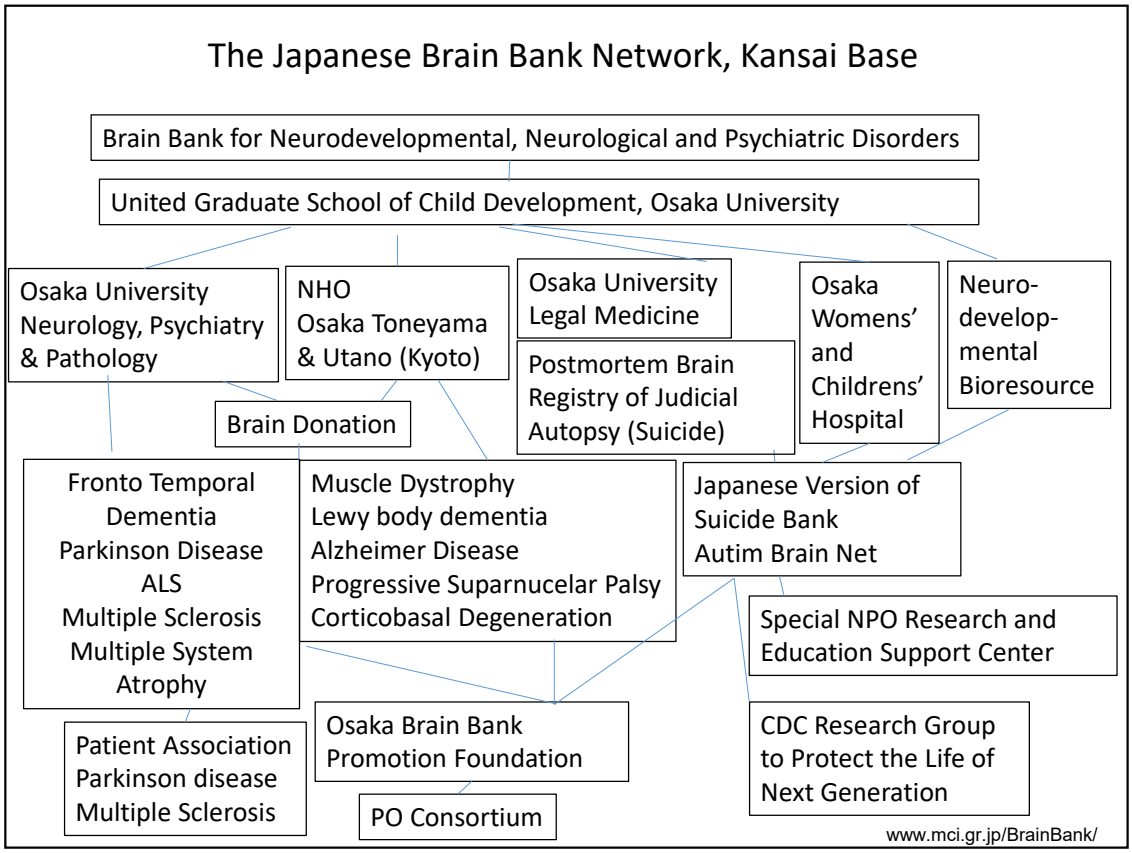
In House Cohort Resource

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

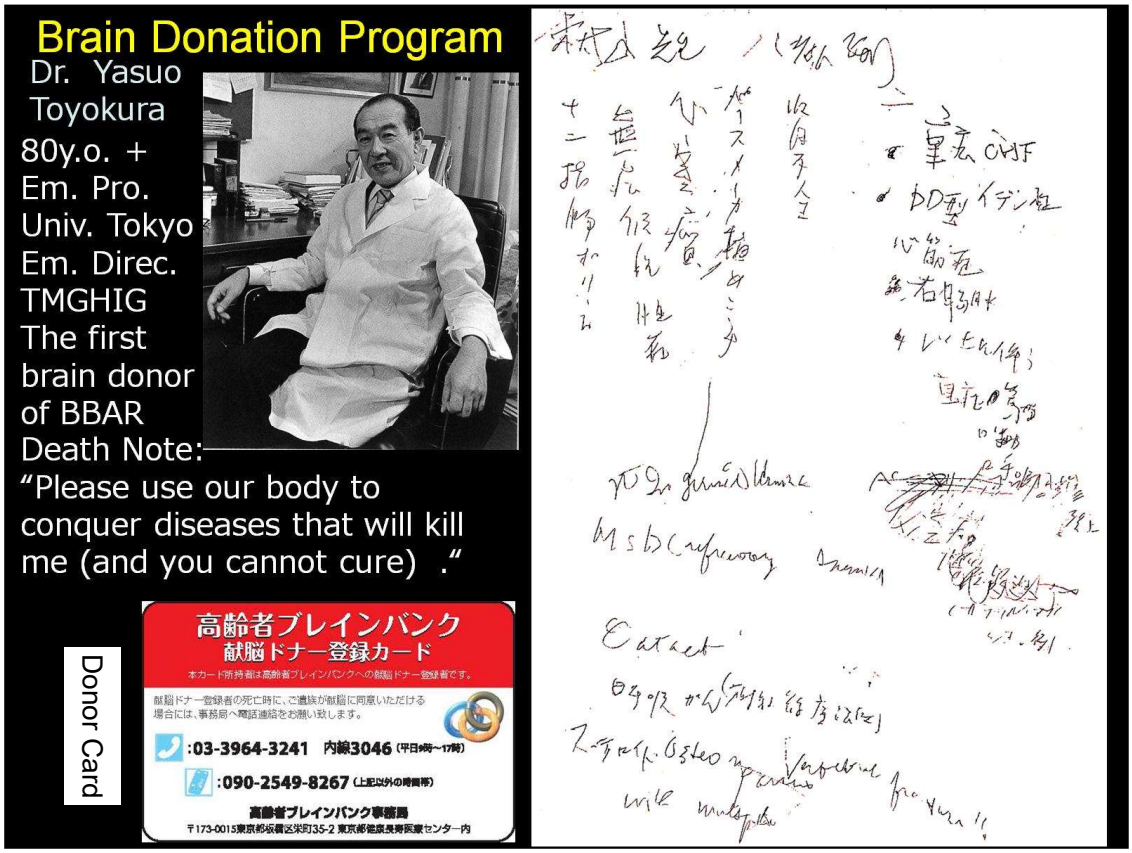
All Japan Neurological and Developmental Depository

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.

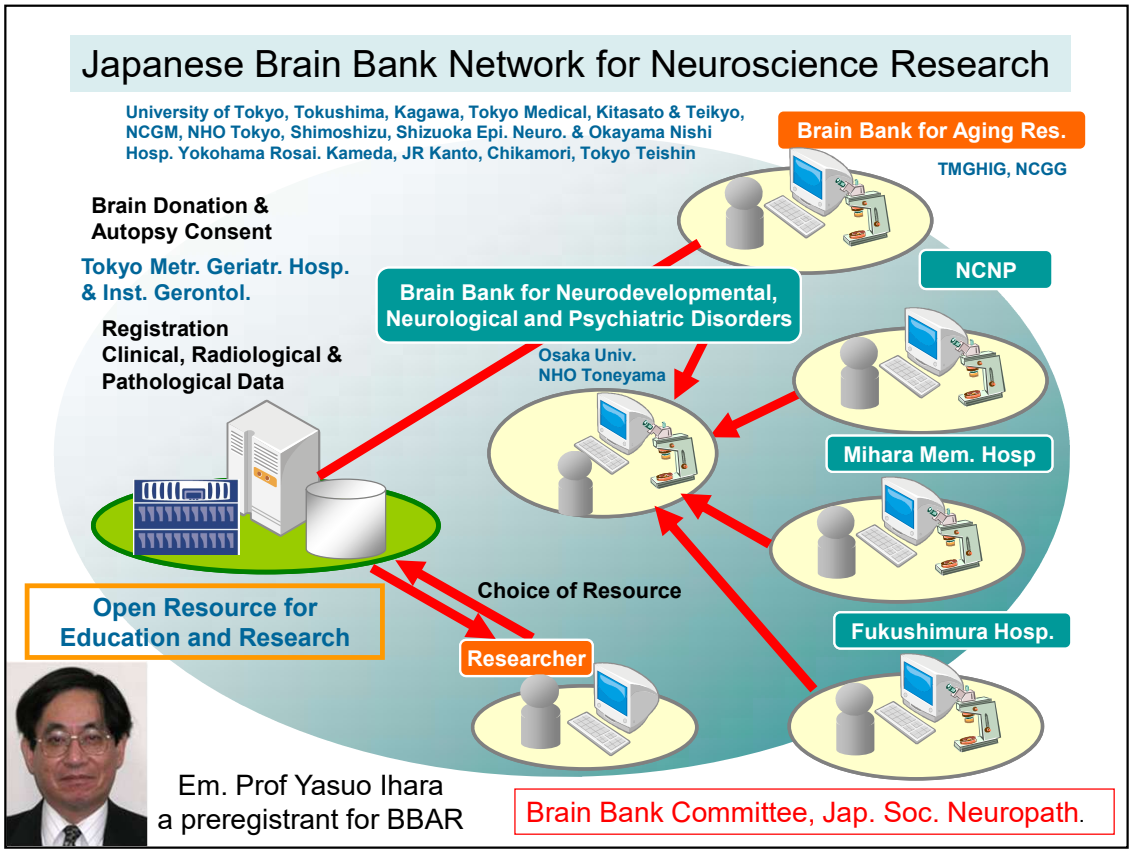


Japanese Brain Bank Network, Kansai Base was established in 2020 in collaboration with Osaka University, National Hospital Organization (NHO) and Osaka Prefectural Hospital Organization.

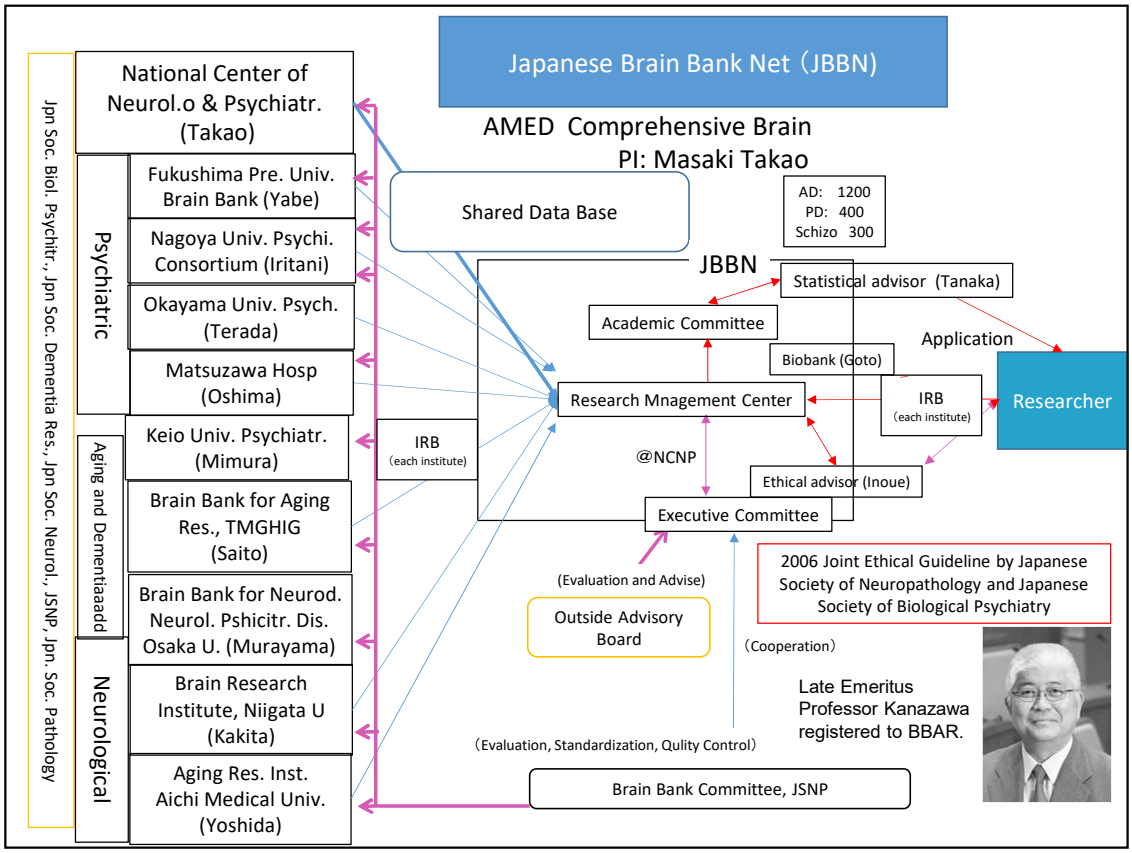


Dr. Toyokura, the Late Emeritus Professor the University of Tokyo and Emeritus President of TMGHIG was the founder of our brain donation program.

“Please use my body to cure the incurable diseases that will kill me.” He suffered from cardiomyopathy with a mutation of myosin light chain and died at age of 80 years.



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.

The Brain Bank Network										
Institute	Clinician/ Pathologist	2012	2013	2014	2015	2016	2017	2018	2019	2020
BBAR	Iwata, A./ Saito, Y.	63	39	39	45	64	52	39	36	36
NCNP	Takahashi, Y./ Takao, M.	10	10	11	9	13	18	24	14	22
Mihara	Mihara, B./ Takao, M.	29	26	15	19	23	16	19	33	18
Fukushimura	Kaneda, D./ Hashizume, Y.	36	31	27	25	25	21	25	33	40
Osaka Univ.	Mochizuki, H./ Murayama, S.					3	4	6	6	5
NHO Toneyama	Inoue, K.							18	16	12
Tokushima, U.	Izumi, Y./ Tsuneyama, K.	1	3	5	10	4	12	4	5	3
Univ. Tokyo	Kubota, A./ Ikemura, M.	28	23	22	25	26	15	17	18	21
NCGM	Arai, T./ Igari, T.	23	16	17	27	17	17	9	9	7
NHO Tokyo	Komiya, T./	5	5	2	4	3	0	1	1	1
NHO Shizuoka	Obi, T.	1	2	2	4	6	6	4	2	2
Yokohama Rosai	Imafuku, I/ Kakuta, Y.	1	6	6	8	8	4	4	4	2
Kameda	Ando, T/ Takeuchi, R.	12	10	6	9	12	10(2)	10(2)	10(2)	5(4)
Kitazato Y.	Nishiyama, K./ Ichinohe, M.	7	9	5	4	2	6	6	1	1
Mita IUHW	Iwata, N./ Aida, S.	2	3	2	0	2	1	1	2	0
Kagawa U.	Kamada, M./ Ueno, M.	2	4	3	1	1	1	2	1	0
Toranomon	Uesaka, Y./ Ito, S.		3	1	2	2	3	1	8	2
Teikyo, U.	Sonoo, M./ Uozaki, H.	3	2	2	0	4	0	4	2	0
Tokyo Teishin	Shiio, Y./ Kishida, Y.	5	2	2	3	5	3	0	3	3(2)
Tokyo Medical U.	Aizawa, H./ Kuroda, M.	1	0	0	1	0	1			
NHO E. Hiroshima	Watanabe, C./Tachiyama, Y					3	4	4	2	4	0
Osaka City Univ.	Ito, Y./ Osawa, M.			1	1	1	1	0		1	0
NHO Sagamihara	Hasegawa, I./ Yagishita, S.					8	10	18	18	17	8
NHO Okinawa	Suwazono, S./ Atami, E.					1	2	2	4	2	0
Open Resource		140	109	100	110	156	155	168	171	163
Inst. Collection （MEXT、AMED）		79	85	84	105	74	69	50	67	35

We tried to increase open brain resource for neuroscience research, in collaboration with clinicians and pathologists.

Brain Bank Registrants BBAR (Aug. 2021) : (Preregistrants: 203)

No.	Age	Gen.	Dix	Con.	Place of death/ auto.
1	80	M	Heart	S	TMGHIG
2	83	M	FAD	F	Body transfer
3	79	F	FAD	F	Brain transfer
4	69	F	CBD-PNFA/ TDP-43 type A	F	Body transfer
5	86	F	AD	F	Brain transfer
6	91	M	AD/CAA/DG/ HS-TDP-43	S	Body transfer
7	84	F	PSP	S	Body Transfer
8	89	F	(Colon Ca)	S	TMGHIG
9	84	M	CVD	F	TMGHIG
10	86	M	AD	F	TMGHIG
11	88	F	DLB	F	Body transfer
12	93	F	PD	S	TMGHIG
13	99	F	DLB	F	Body transfer
14	73	M	(肺癌)	F	Body transfer
15	111	F	NFTD	F	Body transfer
16	90	F	AD	F	Body transfer
17	97	M	NFTD/ PSP/LBD/DG	F	Body transfer
18	72	M	CVD	F	Body transfer
19	61	M	Encephalit.	F	Body transfer
20	79	M	CJD	F	Body transfer
21	83	M	Malignant ly.	F	Body transfer
22	95	F	iNPH	F	Body transfer
23	80	F	ALS	F	TMGHIG
24	78	F	PSP	F	Body transfer
25	74	M	LBD	F	Body transfer
26	79	M	AD	F	Body transfer
27	91	F	AD	F	Body transfer

No.	年齢	性別	Dix	同意	死亡場所・剖検施設
28	83	F	PSP	F	Body transfer
29	90	F	AD	S	Body transfer
30	87	F	AD	F	Body transfer
31	95	M	AGD	S	Body transfer
32	85	M	AGD	F	Body transfer
33	80	F	ALS	F	Body transfer
34	80	M	SMA	F	Body transfer
35	70	F	PSP	F	Body transfer
36	68	M	CBD	F	Body transfer
37	84	M	ALS	S	Body transfer
38	69	M	PSP	S	Brain transfer
39	86	M	PDD	F	Body transfer
40	93	M	PSP	F	Brain transfer
41	87	F	Early AD	S	Body transfer
42	77	F	AD	F	Body transfer
43	86	M	DLB/AD	F	Body transfer
44	80	M	AD/AGD	F	Body transfer
45	83	F	PSP	F	Body transfer
46	68	M	PSP	F	Body transfer
47	78	M	PSP	F	Body transfer
48	102	F	(Influ.)	F	Body transfer
49	69	M	CVD	F	Brain trasfer
50	83	F	AD/DLB	F	Body transfer
51	63	M	Cereb. Con.	F	Body transfer
52	86	M	FTLD-TDP typeC	F	Body transfer
53	89	F	CJD	F	Body transfer
54	94	M	eAD/AGD	F	Body transfer

No.	年齢	性別	Dix	同意	死亡場所・剖検施設
55	44	M	SPG11	F	Body transfer
56	78	F	AGD	F	Body transfer
57	85	M	CJD MV1	S	Body transfer
58	85	M	(renal Ca)	S	Body transfer
59	61	M	ALS	S	Brain transfer
60	86	M	(Lung Ca)	F	Body transfer
61	82	F	(CVD)	F	TMGHIG
62	85	F	PSP	F	Body transfer
63	92	M	AD	F	Body transfer
64	61	F	fCJD	F	Body transfer
65	85	F	CJD/PD	F	Body transfer
66	82	F	PSP	F	Body transfer
67	49	F	NMO	F	Body transfer
68	82	F	PSP	F	Body transfer
69	72	M	AD	F	Body transfer
70	41	F	SCA1	F	Body transfer
71	83	M	AD	F	Body transfer
72	92	M	AD	F	Body transfer
73	91	F	AD	F	TMGHIG
74	63	F	Tauopathy	F	Body transfer
75	85	M	SCA6	S	Body transfer
76	82	M	AD	S	Body transfer
77	57	M	CJD	F	Body transfer
78	86	M	Y-10227 (pending)	F	Body transfer
79	65	F	Y-10231 (pending)	F	Body transfer

Brain Bank Registrants in BBAR reached 79 among 203 preregistrants.

2020 Collaboration

www.mci.gr.jp/BrainBank/

	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.

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[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.

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

September 28, 2018
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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.

JSNP Brain Bank Committee (1986-)

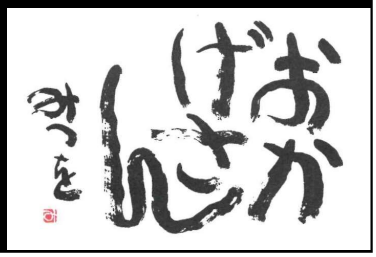
Chair: Murayama, S. (UO)

- Adachi, T. (Tottori U.)
- Ikeuchi, K. (Genome. Niigata U.)
- Izumi Y. (Neu. Tokushima U)
- Ito, K. (NP. Kyoto Pr. U.)
- Inoue, Y. (Ethis, IMSUT)
- Iritani, S. (Psy. Nagoya U.)
- Oshima, K.（Psy. Matsuzawa H.）
- Kato, T. (Psy, Riken)
- Kaneda, D. (Fukushimura H.)
- Kunii, Y. (Psy. Fukushima)
- Komori, T. (NP. TMNH)
- Kowa, H.（Neu. Kobe U.）
- Saito, Y. (NP. TMGHIG)
- Shimizu, H. (NP. Niigata U.)
- Takao, M. (Lab. NCNP)
- Tanigawa, K. (Pat. Hokkaido U.)
- Taniguchi, D.（Neu. Juntendo U.）
- Tokumaru, A. (Rad. TMGHIG)
- Nishida, N. (For. Toyama U.)
- Nishimura, H.（Pat. Kawasaki U.)
- Hasegawa, M. (Bio. Ch, TMIMR)
- Fujimura, H.（Toneyama H.)
- Furuta T (Pat. Saga U.)
- Matsumoto, H. (For. Osaka U.)
- Beck, G. (Neu. Osaka U.)
- Miki, Y (NP. Hirosaki U.)
- Yamada, M. (NP, Shinshu U.)
- Yokota, O. (Psy, Okayama U.)
- Yoshida, M. (NP, Aichi M. U.)

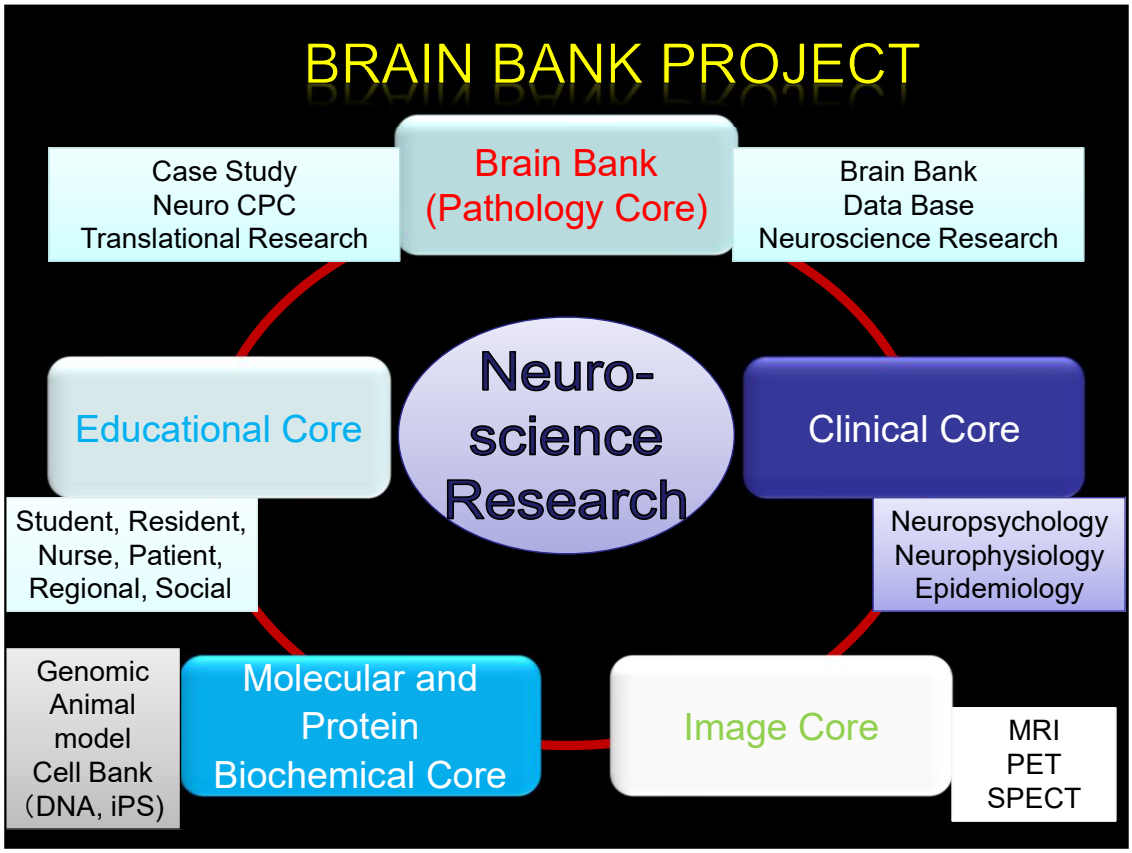
The JSNP (Japanese Society of Neuropathology) Brain Bank Committee supports JBBN and JBBNNR for quality assurance of neuropathological diagnosis. The committee covers all areas of Japan.

The philosophical background

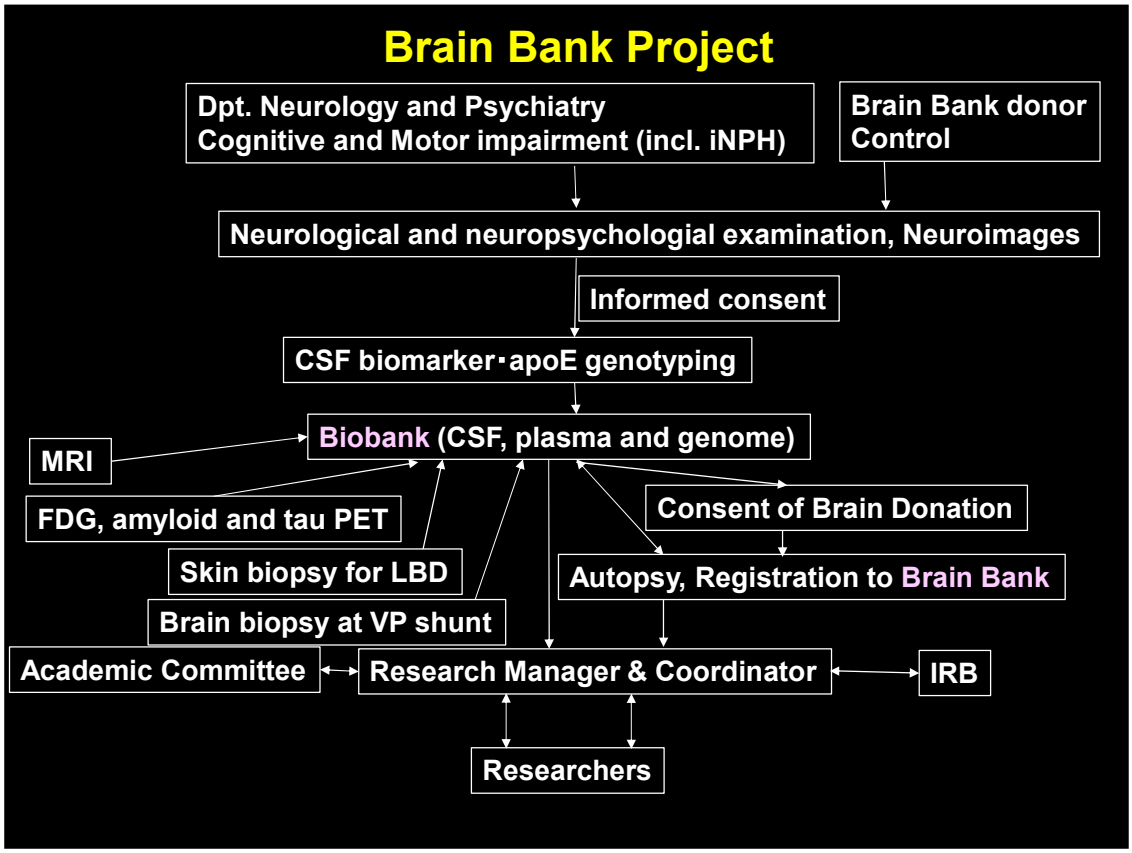
- The respect for general autopsy since Edo era for evidence- based medicine.
- The Brain Bank Committee, the Japanese Society of Neuropathology supports quality assurance of brain banking in neuropathological diagnosis, legal regulation and COI.
- Japanese tradition, “Okagesan”.



The philosophical background of brain bank is deep respect for autopsy. The brain bank committee supports brain banking for more than twenty years. Japanese tradition, “Okagesan” is based on this activity.



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



Our brain bank projet includes biobanking of CSF, plasma and gnome of living patients and controls.

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

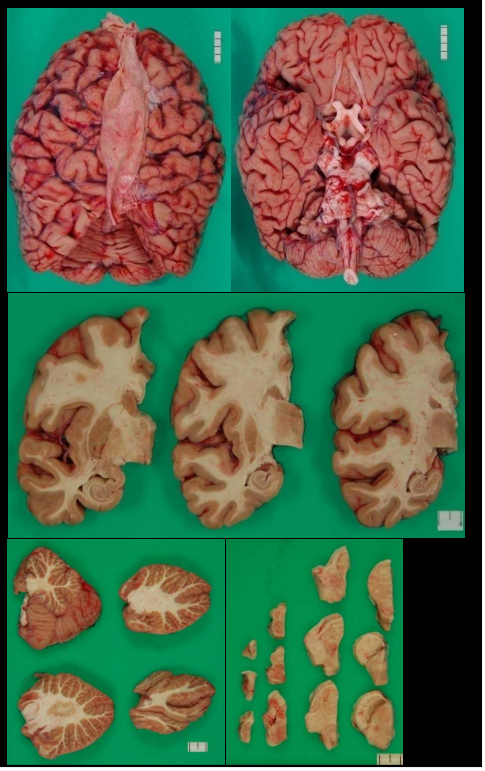
- >7000 case paraffin blocks
- BBAR Data Center: a virtual slide system for educational output.
- BBAR Internet Conference Room
  with NCNP, Osaka U., Toneyama and Fukushimura

The Brain Bank for Aging Research (BBAR) employs a full-time coordinators. All BBAR registrants' data are stored in clinical chart system with the brain bank ID. We have a resource center, carrying 24 deep freezers and paraffin blocks of more than 7000 cases.

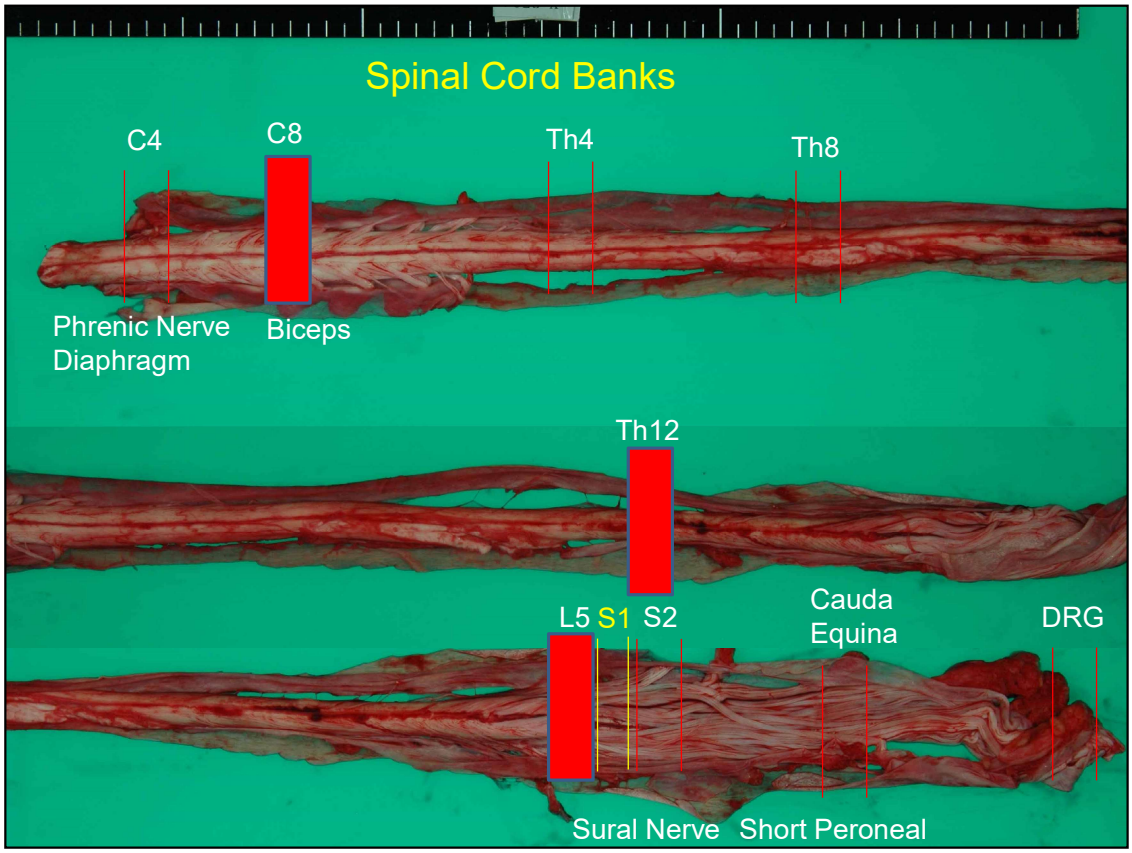
The BBAR Data Center is equipped with a virtual slide system for neuropathological education. The BBAR network conference room is connected to the National Center for Neurology and Psychiatry (NCNP), Osaka University, NHO Osaka Toneyama Medical Center and Fukushimura Brain Bank for neuropathology quality assuarance conference 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 our brain bank system, 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 at least five professionals.



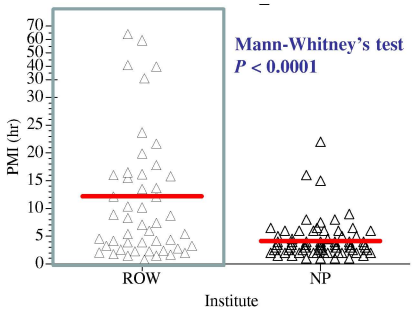
Spinal cords are recovered from all cases. After sampling for histopathological evaluations, the remaining spinal cords are frozen for biochemical and molecular studies.

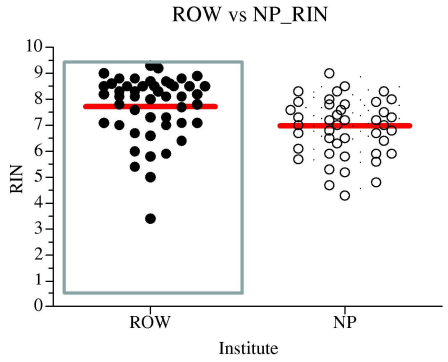
Total RNA Quality Check (Dpt. Mol. Biol. Niigata Univ. BRI)

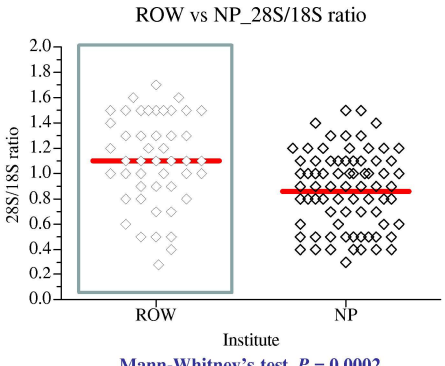
DNA & RNA Back Up

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).







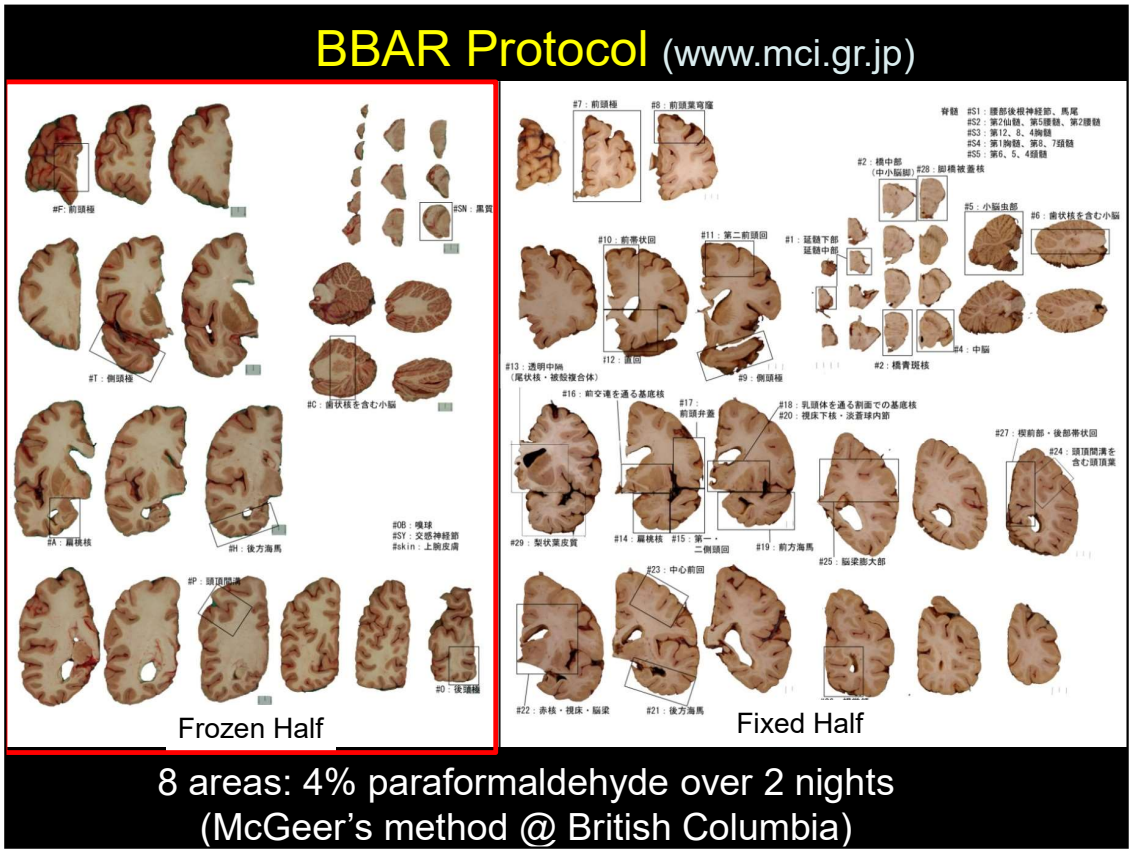
080121 (Mon)

In collaboration with the Department of Molecular Biology, the Brain Research Institute at Niigata University (BRIN), we check the RNA qualities of all cases to meet NIH requirement. Niigata works as DNA/ RNA backup bank.

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, skeletal muscle, small pieces of general organs and serum.

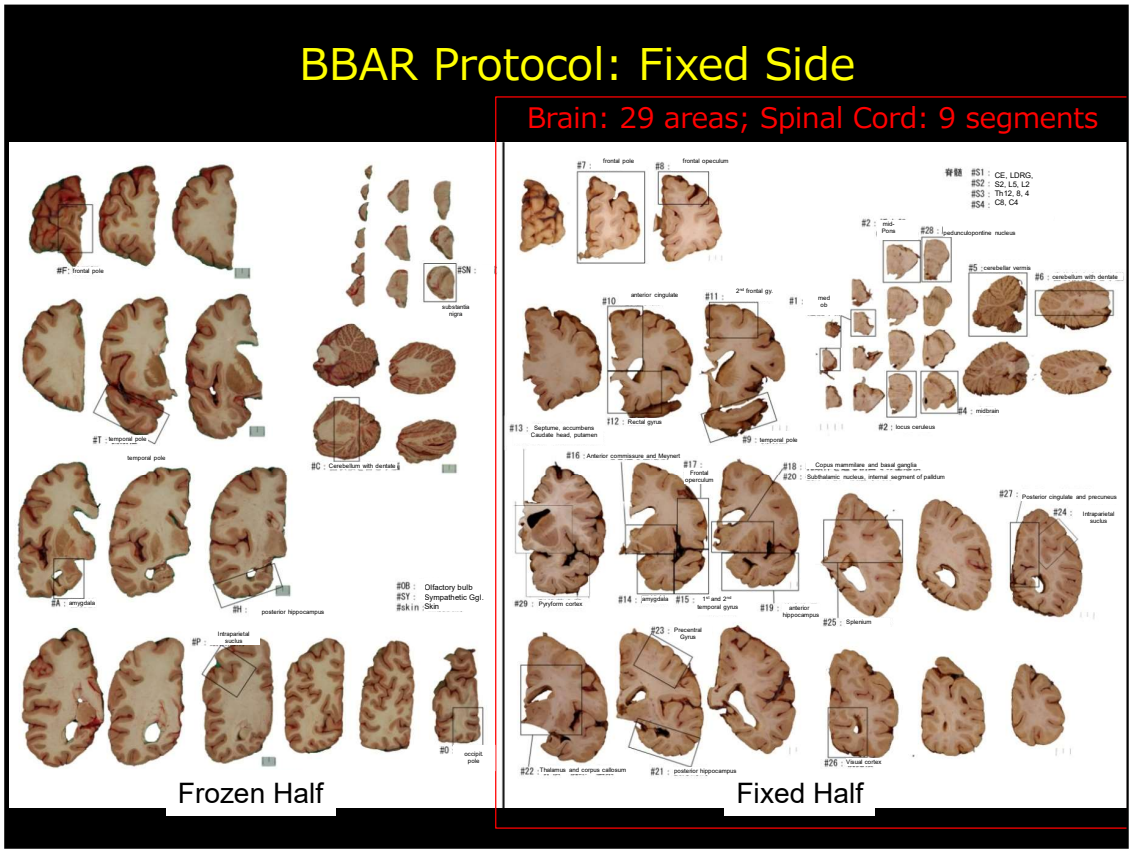


From the frozen side, eight small samples from specific anatomical areas are fixed in 4% paraformaldehyde over two nights for better correlation with studies of experimental animals.

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, connected with BBAR, NCNP, Osaka University and Toneyama Medical Center.



Tissue blocks 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

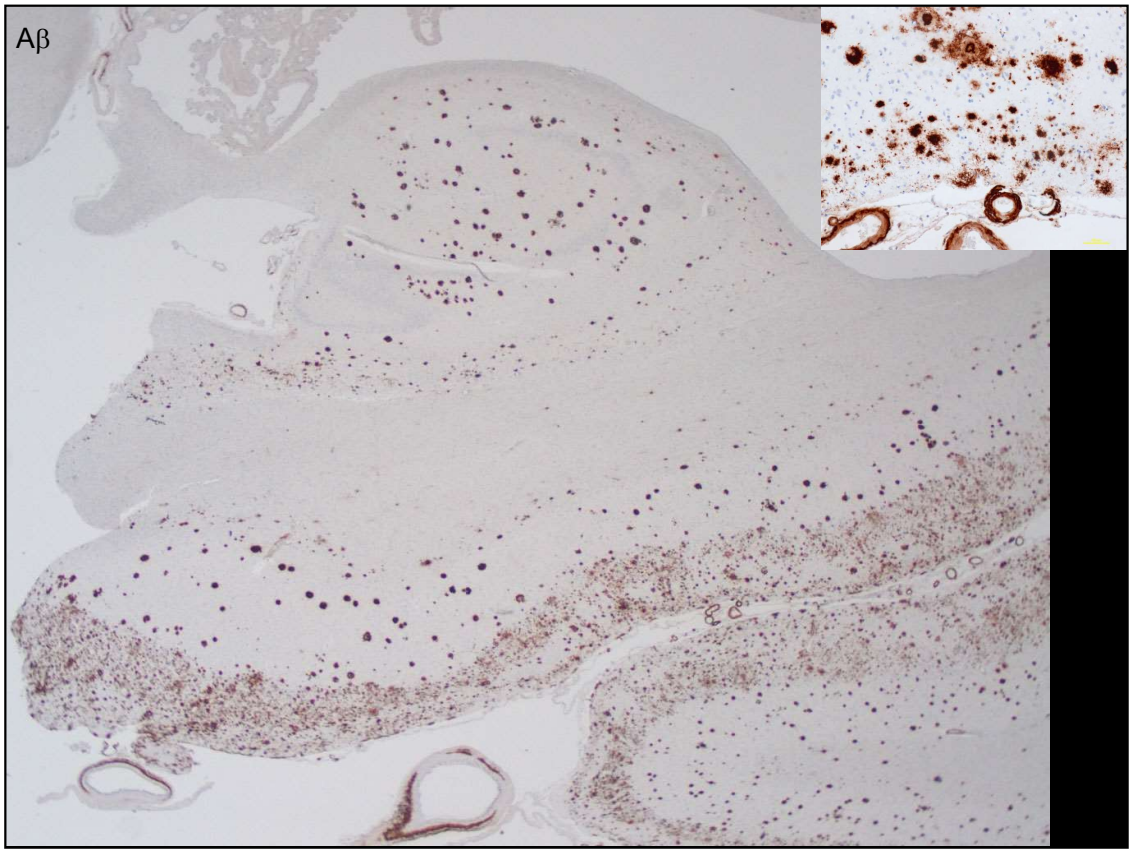
Fixed tissue resource consists of paraform- fixed tissues from a frozen half and buffered- formalin fixed tissues from a fixed half of the brain

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 (Fujirebio)	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

Immunohistochemical screenings of all autopsy cases are performed with commercially available antibodies.



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																				
Thoratic 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

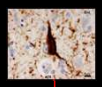
BBAR	Y96XX									
A/G	CDR	PMI	NFT	AT8	SP	CERAD	Thal	LB	LB score	DLB 3rd
93M	3	11:22	4/3	3/3	2	2	5	4	4	Limbic (amygdala predominant)
Grain	AA	AT	UD	TDP	ApoE	RIN				NPD
0.5/ 0.5	1C	1	3	T1M1S0	3/3	8.1				AD, LBD, CVDE

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 with international standards. Researchers who apply to BBAR choose samples based on this database.

DNA Resource (1,890 cases)

Braak NFT/ SP

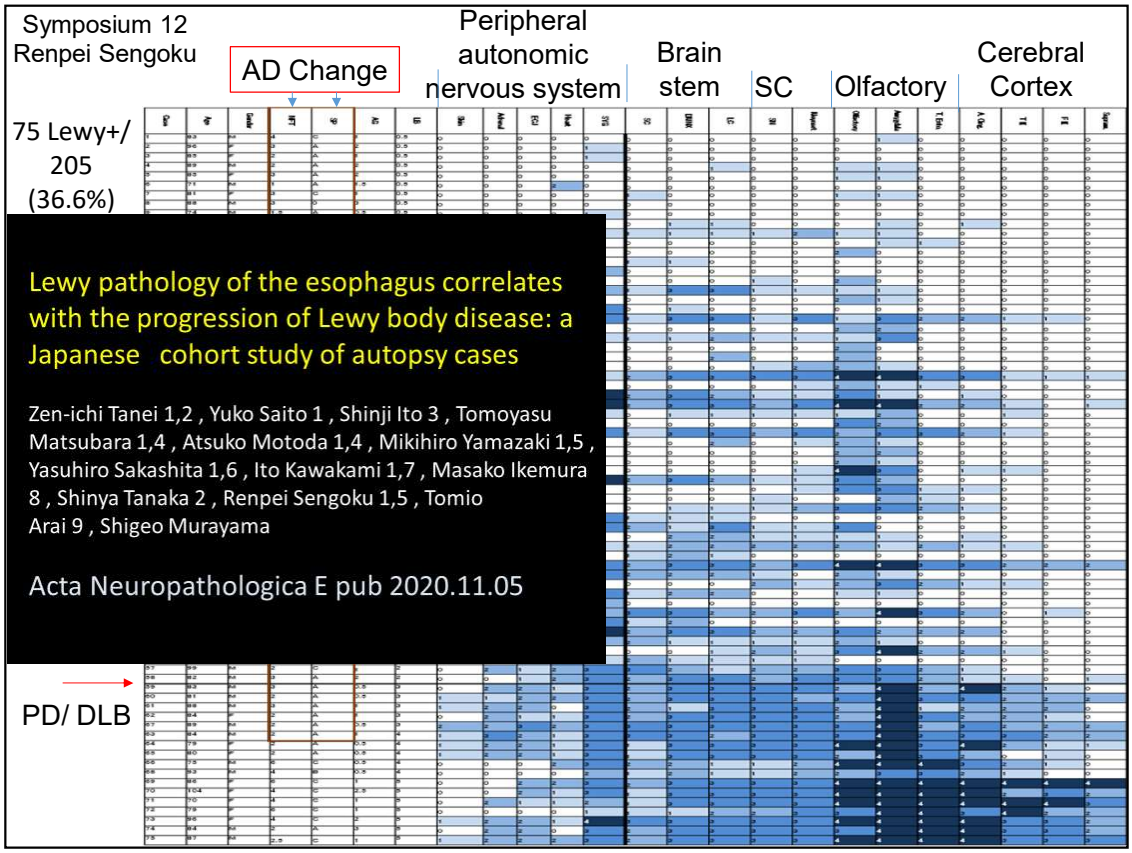


	0	I	II	III	IV	V	VI	計
0	34 66.3	314 75.8	102 81.8	46 85.6	12 85.4	1 81.0	0 -	509 77.5
A	16 75.5	350 78.0	149 83.6	74 86.2	23 88.6	1 99.0	0 -	613 80.6
B	8 76.1	169 79.9	91 82.8	70 85.6	23 91.2	2 82.0	1 94.0	364 82.4
C	3 76.0	50 79.4	51 83.0	80 84.5	80 86.6	100 86.4	40 83.9	404 84.4
計	61 70.5	883 77.7	393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

Case #
Average Age

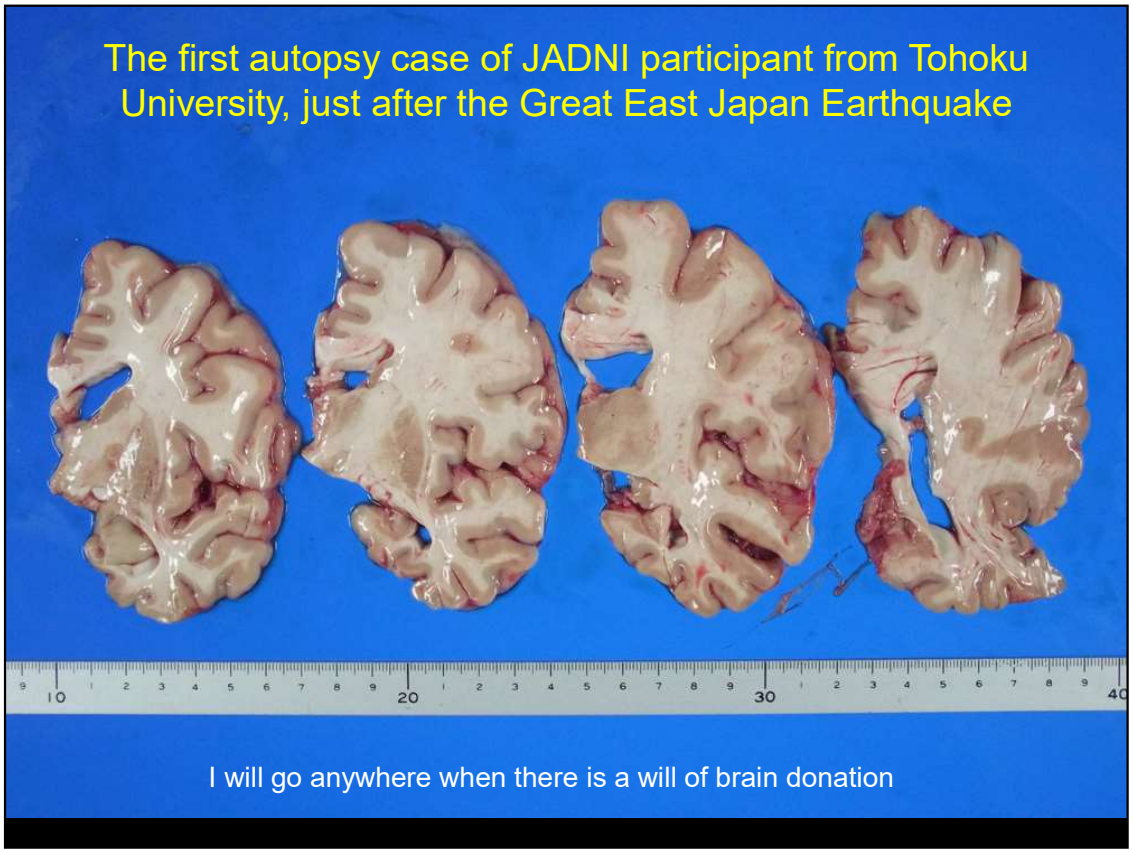
Alzheimer Disease: 220/ 1890 = 11.6%

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.



In our most recent 205 consecutive autopsy cases, 36% contained Lewy body pathology. We published the results in Acta Neuropathologica in 2020.

We establish ALS bank in collaboration with Tokushima University together with 300 control spinal cord.



I recovered 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.

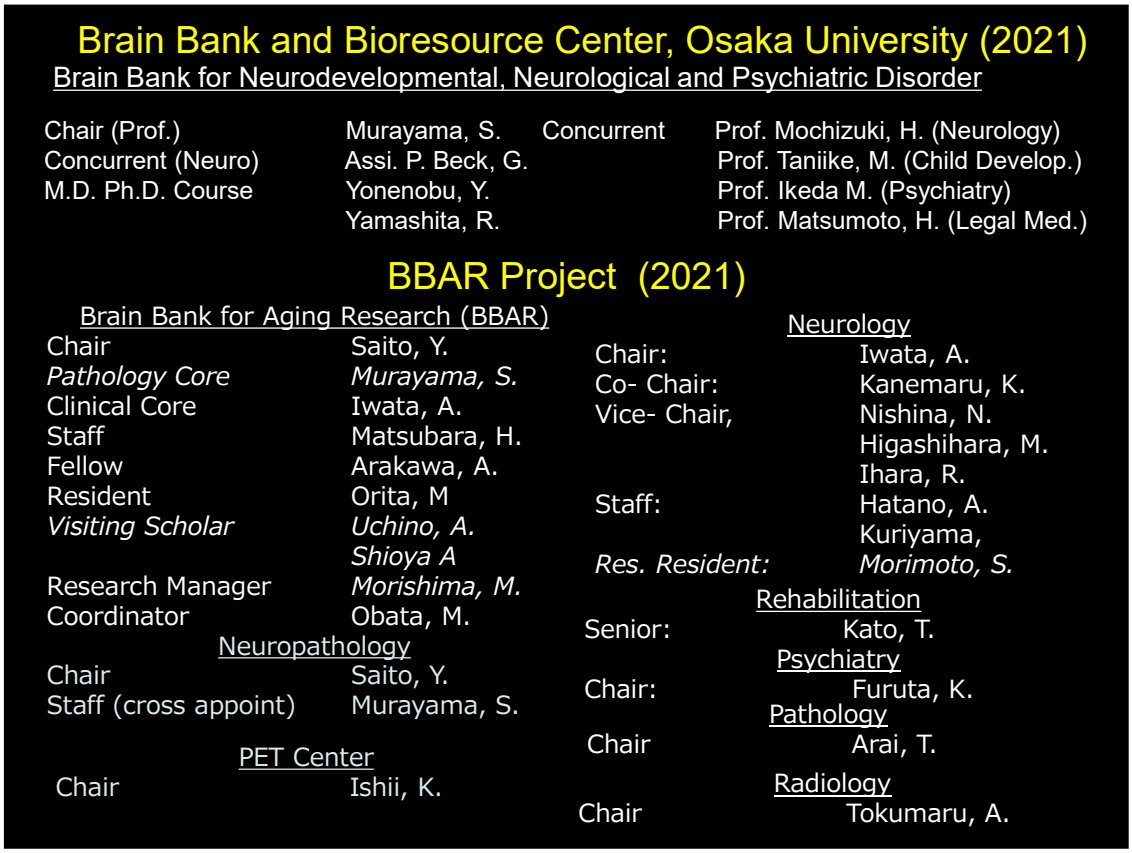
Grants in Aid from Ministry of Health, Labor and Welfare, Japan

I am a pathology core of the Japanese CJD Surveillance Committee and contribute to prion research.

International Collaboration

- Collaboration with Sydney Parkinson Disease Brain Bank funded by Michael J Fox Foundation (Prof. Halliday).
- Collaboration with Sydeney Westmead Hospital for ALS research
- Collaboration with Cambridge for atomic force microscope

We promote international collaboration.



The list of BBNNPD and BBAR members.