

Propagation of Neurodegenerative Proteins in Human Aging

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ABSTRACT

Introduction:

Age-related neurodegenerative pathology presents relatively high incidence and extent, with certain symptomatic threshold for each pathogenic protein. The aim of this study was to provide full profile of Alzheimer pathology and Lewy body-related alpha synucleinopathy (LBAS) in human aging population in addition to other neurodegenerative proteins

Method:

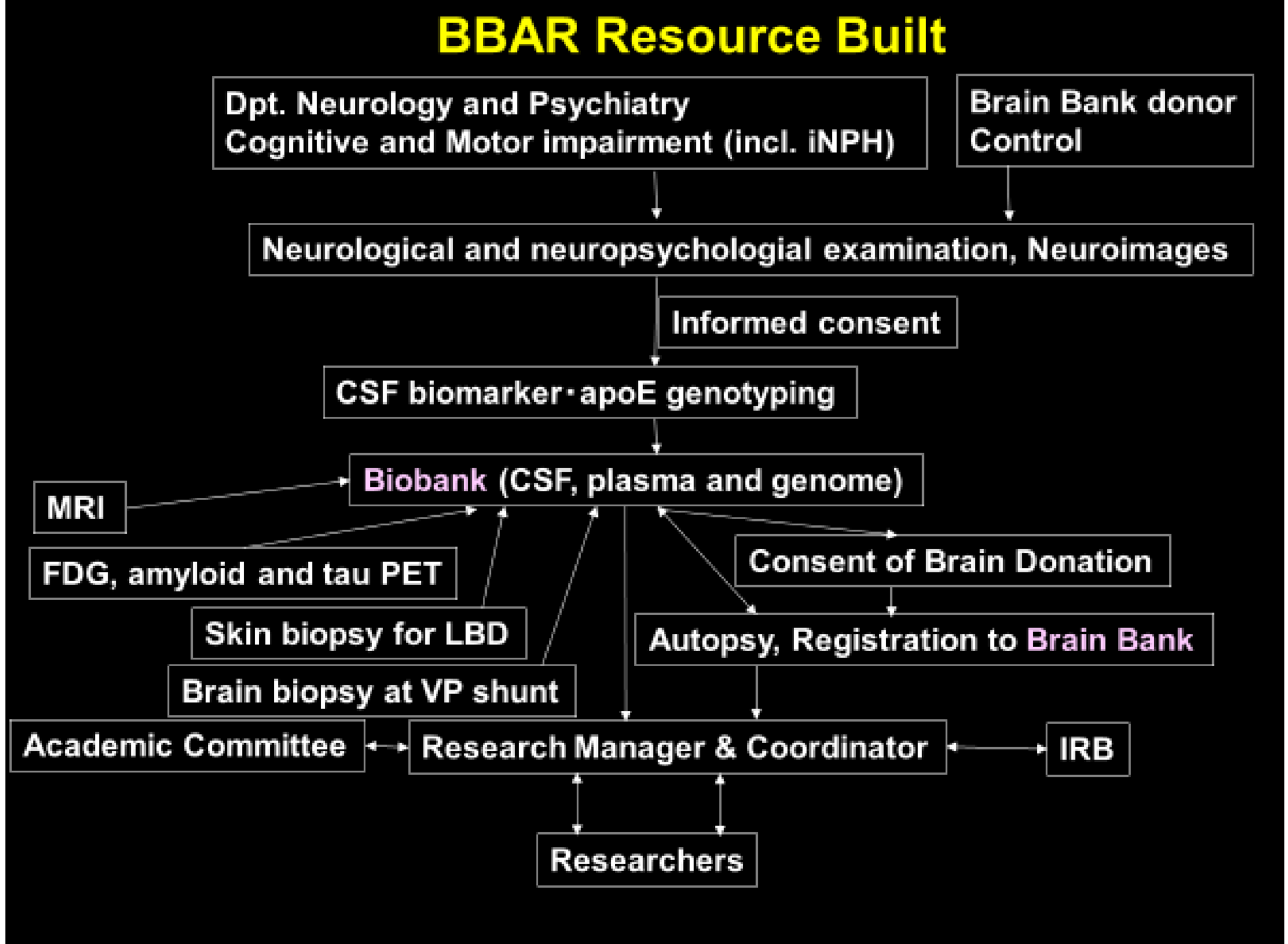
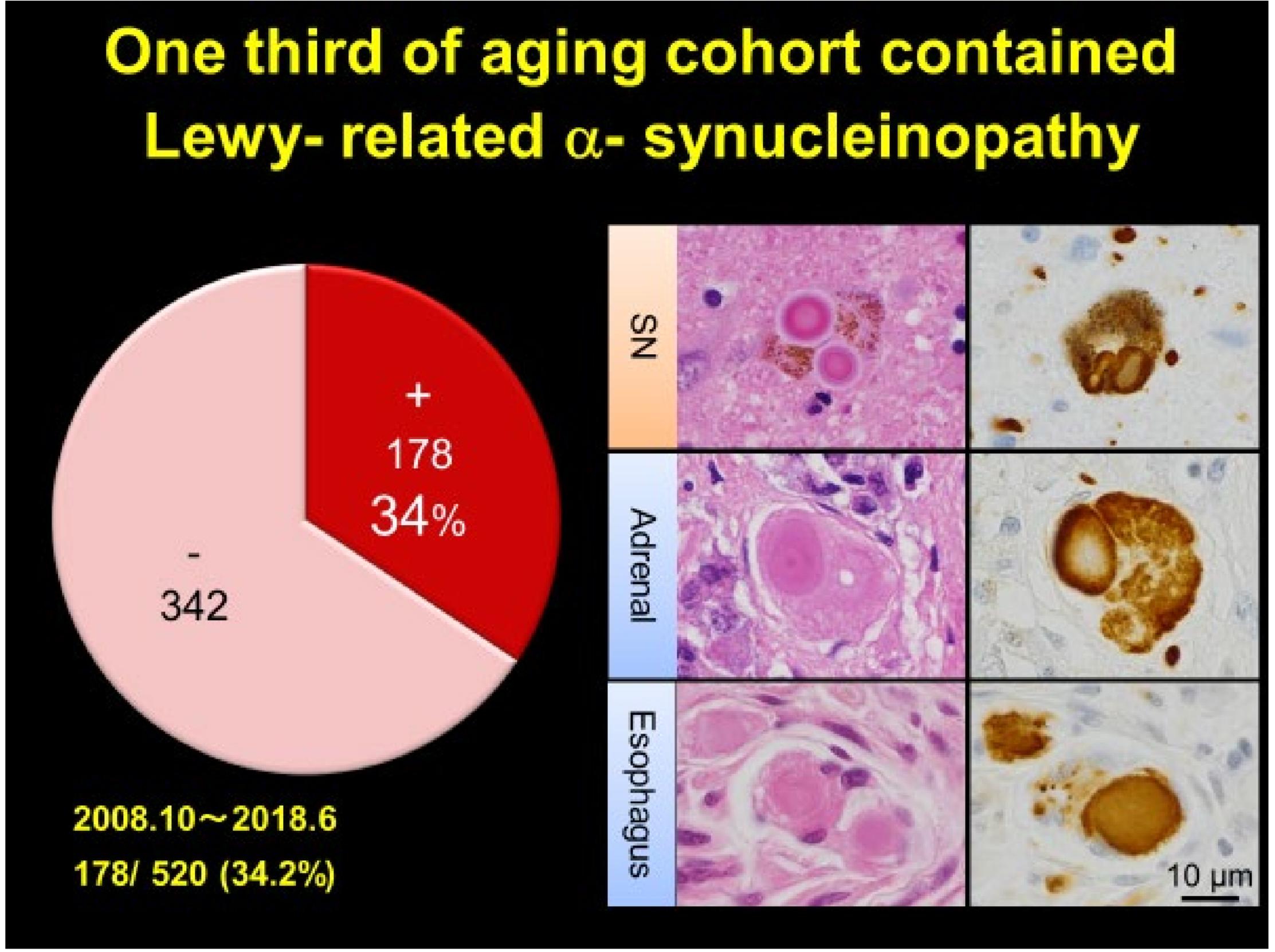
The Brain Bank for Aging Research (BBAR) consists of consecutive autopsy cases of a general geriatric hospital, which supports an aging cohort of Tokyo Metropolitan suburban area. The registration to BBAR was based on the first kin of relatives' informed consent with or without patients' living will. The tissues were processed following BBAR method which was uploaded to www.mci.gr.jp/BrainBank/. We have screened not only the brain and spinal cord, but also the peripheral nervous system (PNS) of all the registered cases to BBAR immunohistochemically. The antibodies employed include antibodies against Abeta, phosphorylated (p) tau, p-synuclein (psyn), p-TDP43 and ubiquitin.

Results:

Among the 520 cases registered to BBAR from October 2008 to July 2018, 178 cases (34%) contained Lewy body pathology either in the PNS and/ or the central nervous system (CNS). 47 out of the 178 cases fulfilled diagnostic criteria of Parkinson disease (PD) with (PDD) or without dementia, dementia with Lewy bodies (DLB) or pure autonomic failure (PAF). The most predilection site of Lewy body (LB)- related alpha-synucleinopathy (AS) was sympathetic ganglia in PNS and olfactory bulbs in CNS. In the earliest stage of Lewy body disease, these two sites were independent as was previously reported. PNS had strong connection with brain stem in contrast to olfactory bulbs with limbic system. We classified incidental LB disease (LBD) to preclinical (Stage 0.5 and 1) and prodromal stage (Stage 2) with or without loss of pigmentation in substantia nigra. Preclinical LBD could be recognized in 24 cases, of lesser frequency than preclinical, prodromal and clinical AD, which roughly represents 20%, 10% and 10% of the registered cases.

Discussion & Conclusion:

This data provides basic information about the propagation of LBAS in human aging. Our brain bank will provide research resource for mechanistic research of age-associated multiple proteinopathy, including Abeta, tau, alpha-synuclein and TDP43.



The Brain Bank for Aging Research (BBAR)

TMGHIG, NCGG

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

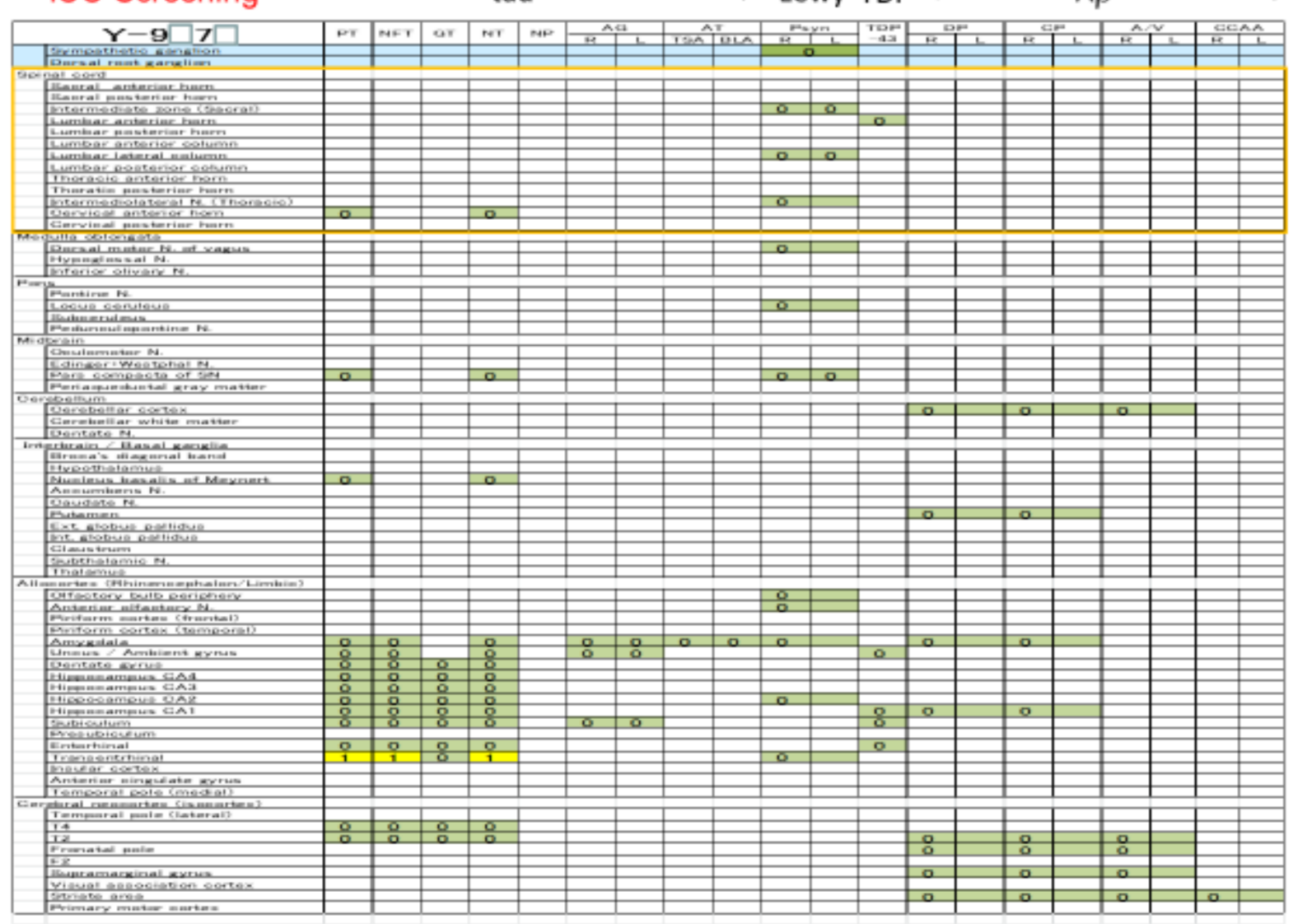
In House Cohort Resource

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

All Japan Neurological and Developmental Depository

BBAR YISex	PMI	NFT	SP	CERAD	Thal	LB	LB score	DLB-3rd			
A/G	ADR	NFT	SP	CERAD	Thal	LB	LB score	DLB-3rd			
93M	3	11222	4/3	3/3	2	2	5	4	4	4	Limbic Lesion
Grain	AA	AT	UD	TDP	ApoE	RIN					NPD
0.5/	1C	1	3	T1M150	3/3	8.1					AD, LBD, CVD

A/G age/gender, CDR (clinical dementia rating), PMI (postmortem interval), NFT (tangle; Braak Stage), AT (astrofibrillary state), SP (senile plaque; Braak Stage), Thal (amyloid Thal Stage), Lewy (Lewy body; BBAR Stage), DLB score (DLB 3rd Consensus Guidelines), Grain (argyrophilic grain; Saito Stage), AA (amyloid angiopathy; BBAR Stage), AT (astrofibrillary state), UD (ubiquitinated dots), TDP (TDP-43 proteinopathy; temporal, medulla and spinal), ApoE (apoE genotyping), RIN (RNA integrity number), NPD (neuropathologic diagnosis; AD: Alzheimer disease; LBD: Lewy body disease; CVD: embolic infarct)



No COI for this presentation.