



17-20
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2025
Napoli

70° CONGRESSO
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SIGG
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Università degli
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di **SCAMPIA**



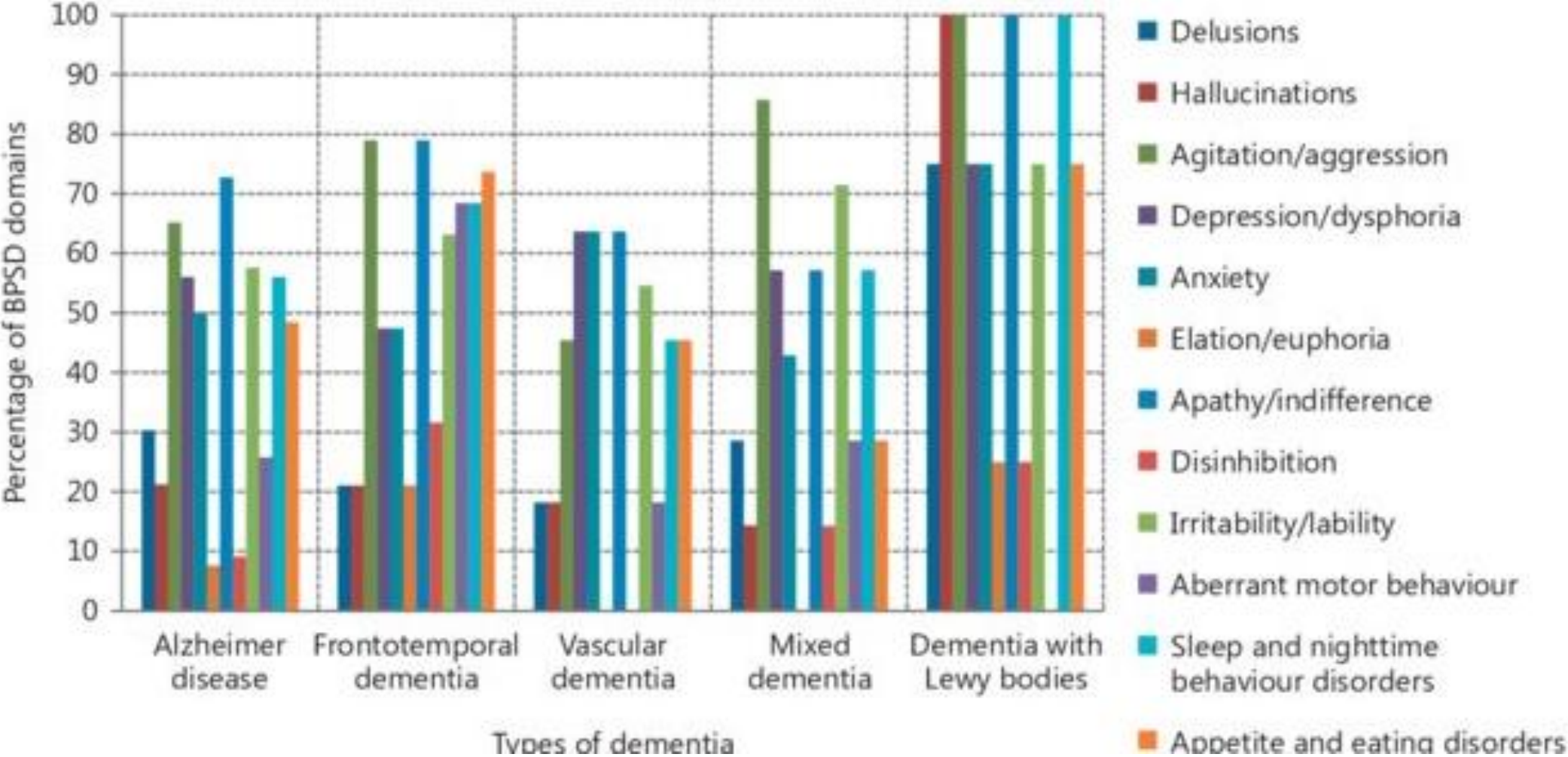
BPSD NELLA DEMENZA

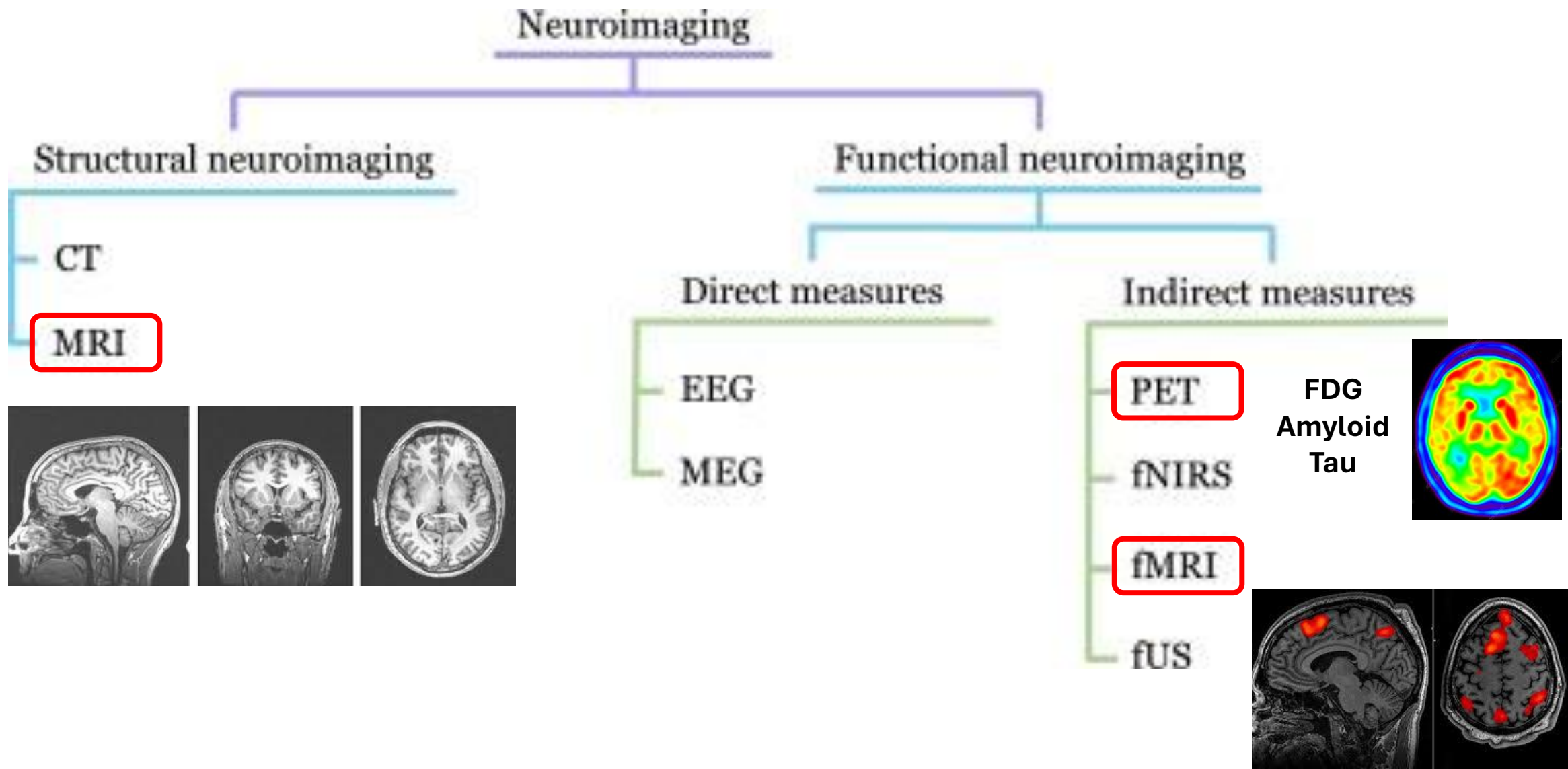
Nuove evidenze dall'imaging



Grazia Daniela Femminella
Dipartimento di Scienze Mediche Traslazionali
Università degli Studi di Napoli Federico II

BPSD in dementia subtypes





Imaging of BPSD in dementia: what for?

Diagnostic Aid



Imaging is useful for differentiating dementia subtypes and uncovering contributing pathologies

Understanding Neurobiology



Neuroimaging provides insight into the neural basis of BPSD, helping link clinical symptoms to underlying neuropathology, improving our understanding of why these behaviors occur

Guiding Management



While no scan can directly “diagnose” BPSD, imaging can influence care plans (for example, finding significant vascular changes may prompt aggressive CV risk factor control to alleviate BPSD).

Diagnostic Aid



Neuropsychi idiopathic ne

Prevalence (%) of neu
 with iNPH and AD

Symptoms

At least 1 symptom

Delusion

Hallucination

Agitation

Depression

Anxiety

Euphoria

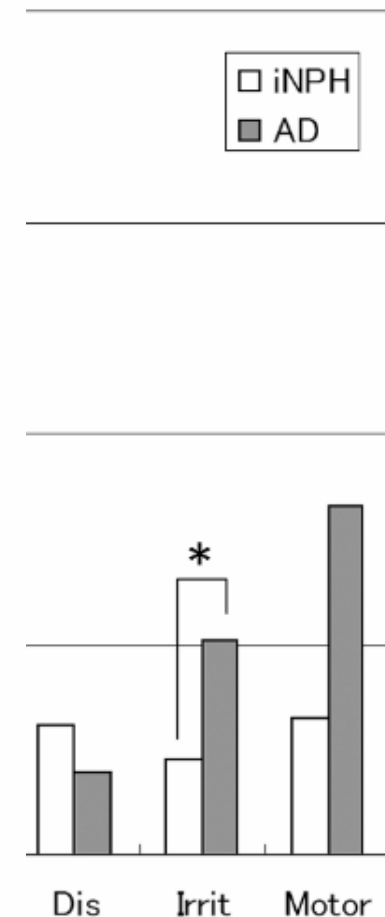
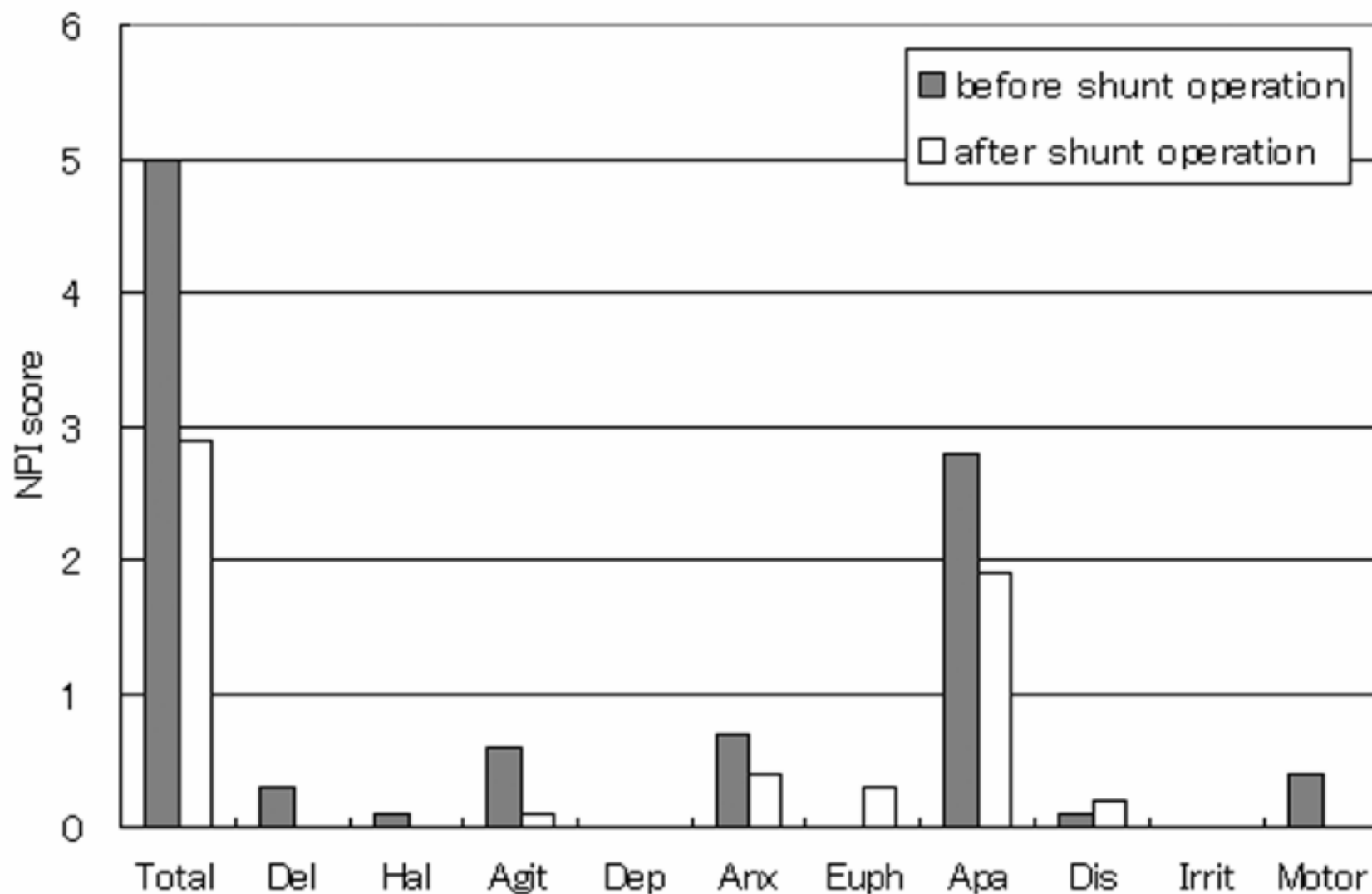
Apathy

Disinhibition

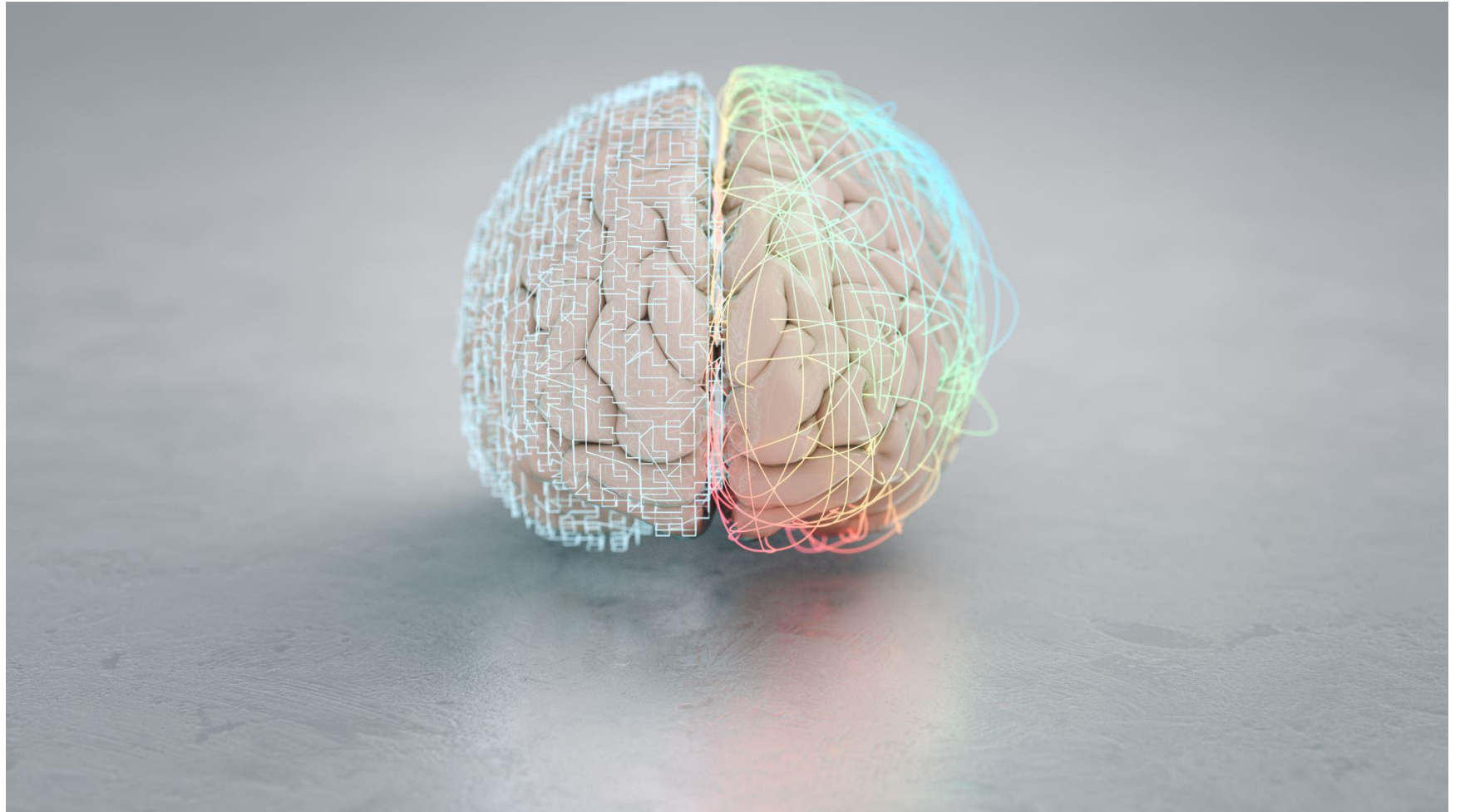
Irritability

Aberrant motor activi

iNPH = idiopathic n
 = Alzheimer's diseas



Understanding Neurobiology



ORIGINAL ARTICLE

Medial temporal lobe atrophy is independently associated with behavioural and psychological symptoms in Alzheimer’s disease

José María GARCÍA-ALBERCA,¹ Mercedes FLORIDO,¹ Marta CÁCERES,¹ Alicia SÁNCHEZ-TORO,¹ José Pablo LARA² and Natalia GARCÍA-CASARES³

- 46 patients with Alzheimer’s disease
- MTA and WMH rated with visual scales

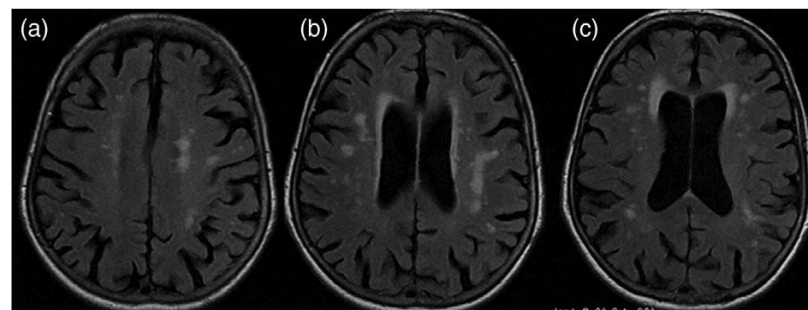
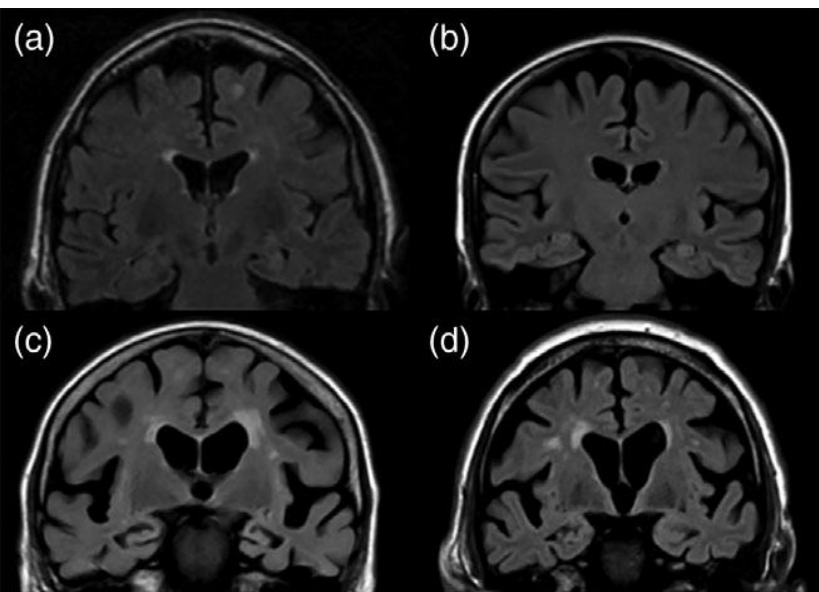


Table 4 Binary logistic regression analysis of individual BPSD and significantly associate variables

BPSD item	Significant independent variables	OR	95%CI	P-value
Apathy	Total MTA	1.605	1.017–2.533	0.042
Disinhibition	Total MTA	0.607	0.376–0.982	0.042

The table only shows the significant independent variables. BPSD, behavioural and psychological symptoms of dementia; CI, confidence interval; MTA, Medial temporal atrophy; OR, odds ratio.

Brain Volume Predicts Behavioral and Psychological Symptoms in AD

Frontal: Ax, A, D, Ag, H, Dp, Amb, Irr, Ad

- Anterior Cingulate cortex: H, D, Amb
- Middle Cingulate cortex: Ag
- Posterior Medial Frontal cortex: Ag
- Superior Medial gyrus: H, Amb
- Precentral gyrus: Ax, Dp
- Superior Frontal gyrus: Ag, Irr
- Middle Frontal gyrus: A, Ag, H, Ad
- Inferior Frontal gyrus: Amb, H
- Rectal gyrus: Amb
- Orbits-Frontal cortex: H, Amb

Parietal: Ax, Dp, Ag

- Precuneus: Ax, Ag
- Postcentral gyrus: Dp
- Superior Parietal lobule: Dp
- Angular gyrus: Dp

Occipital: Ax,

- Middle Occipital
- Inferior Occipital
- Calcarine sulcus
- Cuneus: A

Subcortical: H

- Caudate nucleus: H
- Thalamus: H

Temporal: H, E, Di

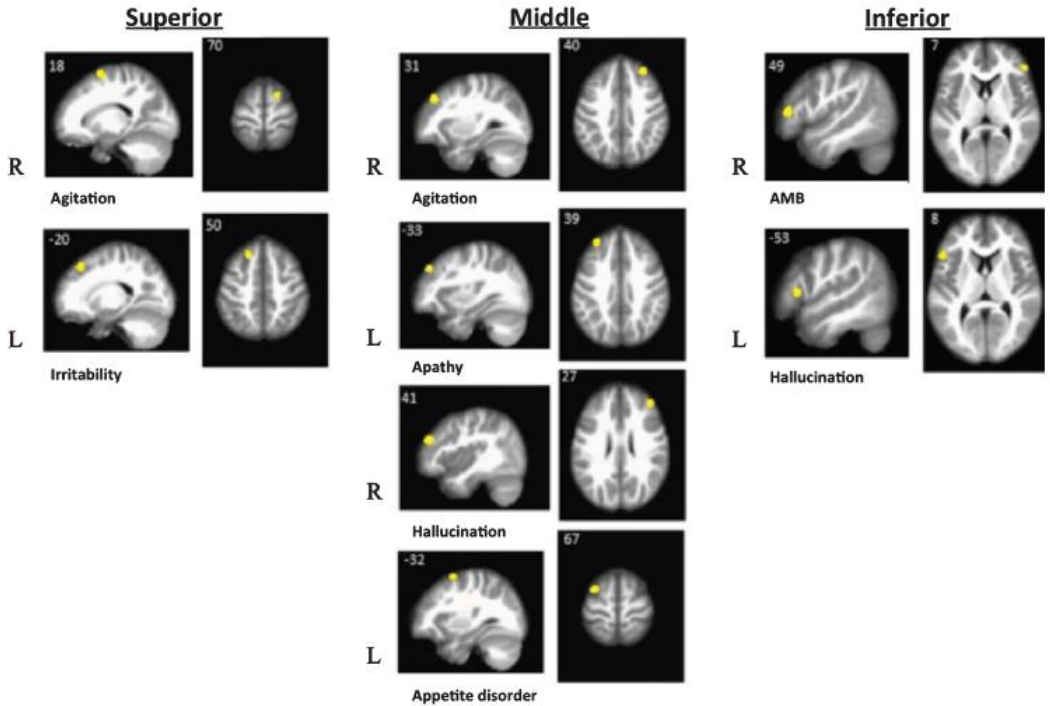
- Middle Temporal gyrus: H, E
- Inferior Temporal gyrus: Di

Cerebellum:



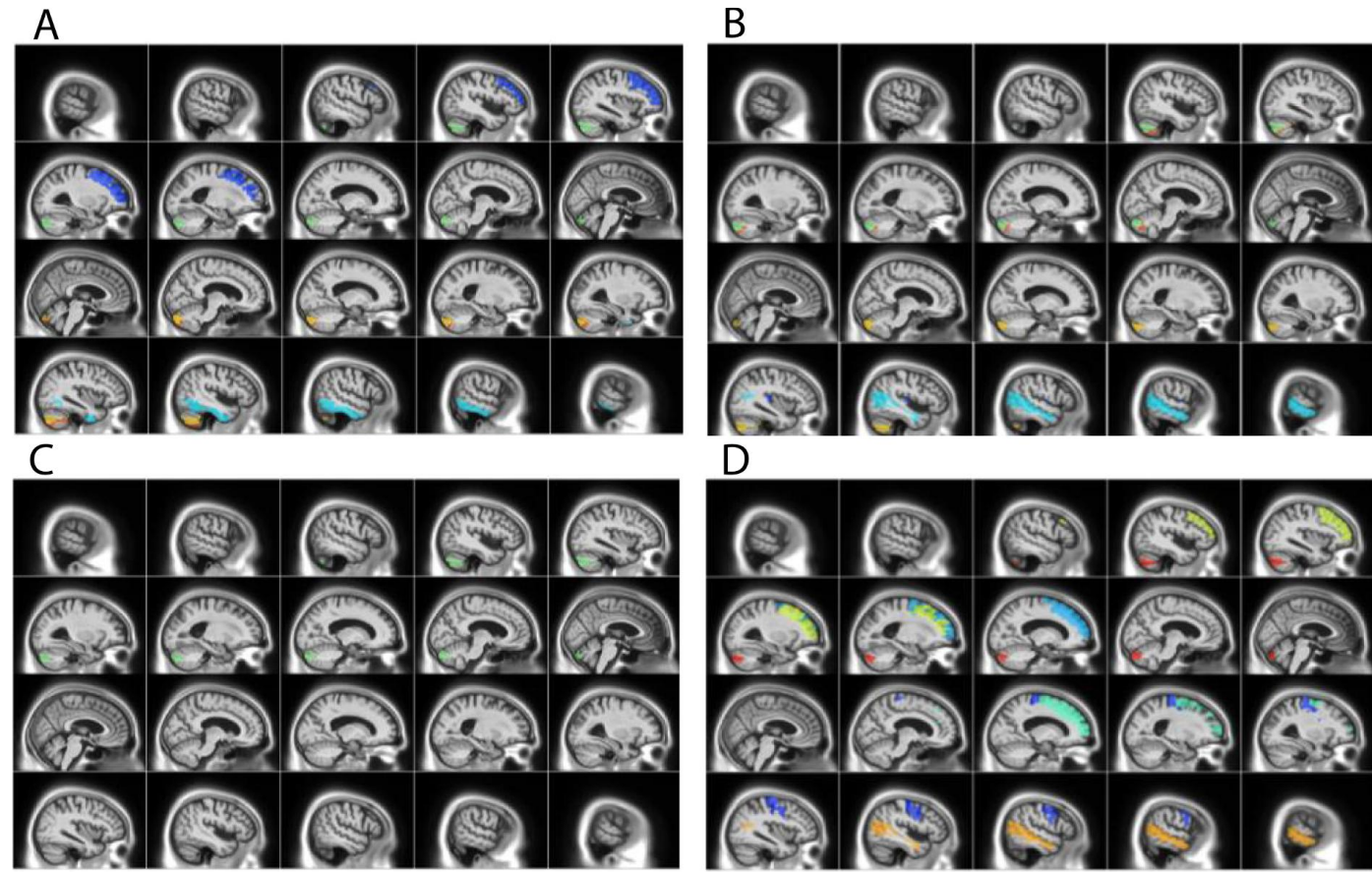
252 patients with mild AD followed up for 18 months

Frontal gyrus



D, delusions; A, apathy; Dp, depression; Ag, agitation; H, hallucinations; Ax, anxiety; Amb, aberrant motor behavior; Di, disinhibition; Irr, irritability; Ad, appetite disorders; E, euphoria; S, sleep disorders.

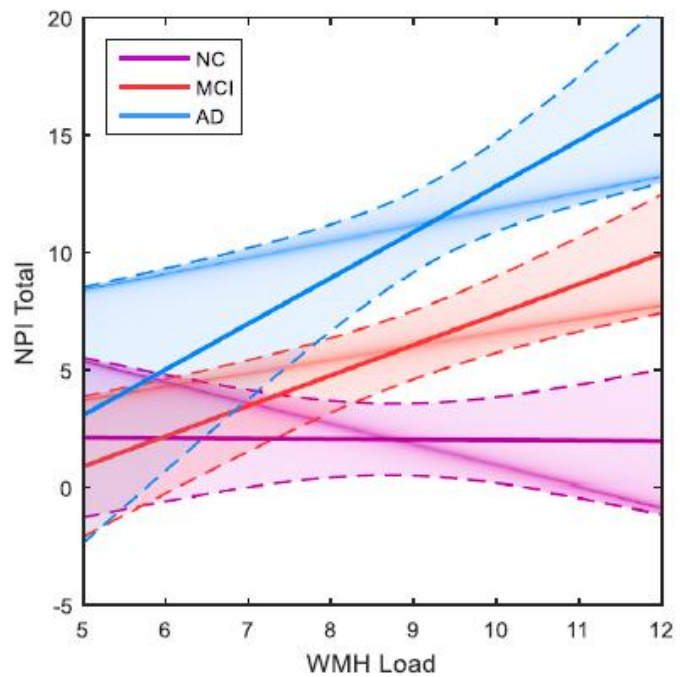
Grey matter atrophy and WMH volume contribute to BPSD subsyndromes in MCI and AD



Hyperactivity	Psychosis	Affective	Apathy
L middle frontal gyrus L Cerebellum Crus2	L Heschl's gyrus L Cerebellum 7b L Cerebellum Crus2	L Cerebellum Crus2	L Frontal middle gyrus L Frontal superior gyrus L Cerebellum Crus2
R Inferior Temporal gyrus R Cerebellum 7b R Cerebellum Crus2	R Middle Temporal gyrus R Cerebellum Crus2		R Frontal superior gyrus R Temporal middle gyrus R Precentral gyrus

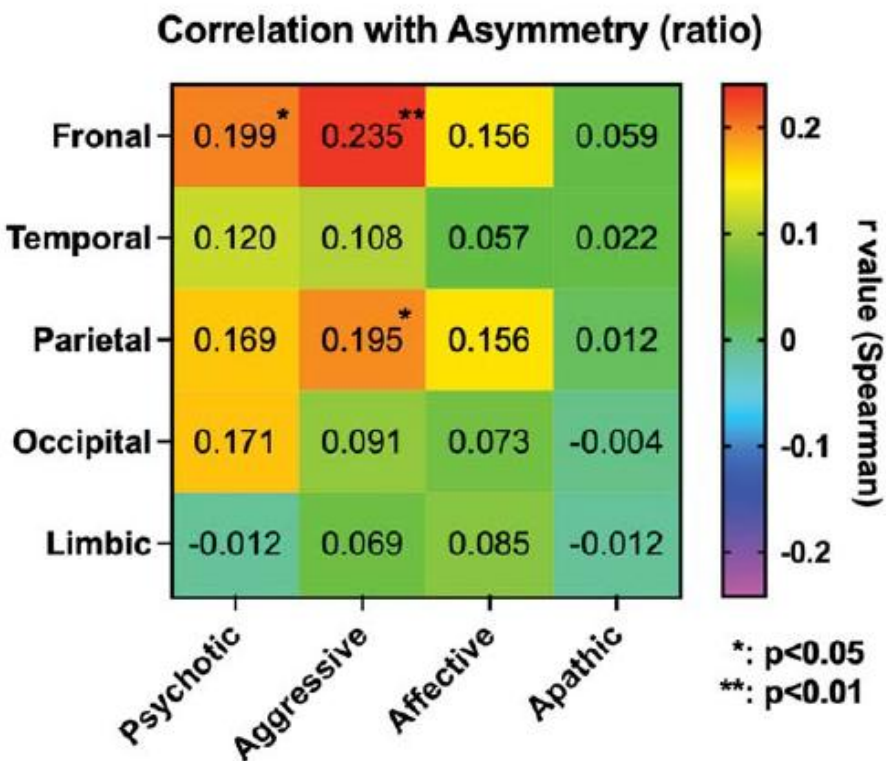
121 AD, 315 MCI and 225 NC from ADNI

A) hyperactivity B) psychosis C) affective and D) apathy subsyndromes



Examining Frontal Lobe Asymmetry and Its Potential Role in Aggressive Behaviors in Early Alzheimer's Disease

121 mild AD cases from Japanese dataset



Comparison of brain asymmetry ratios in AD patients with and without aggressive NPS

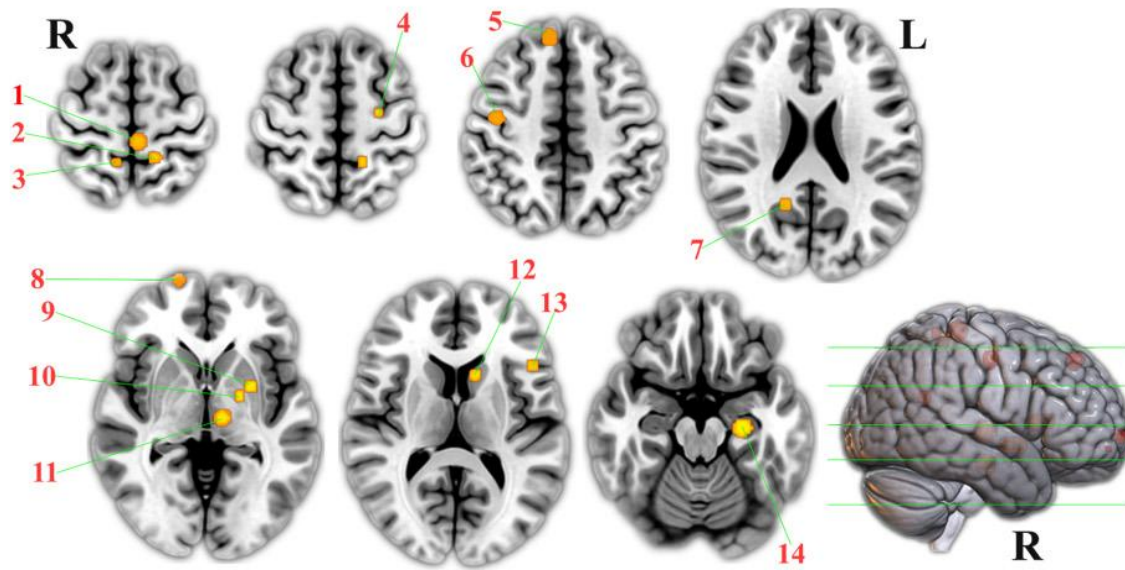
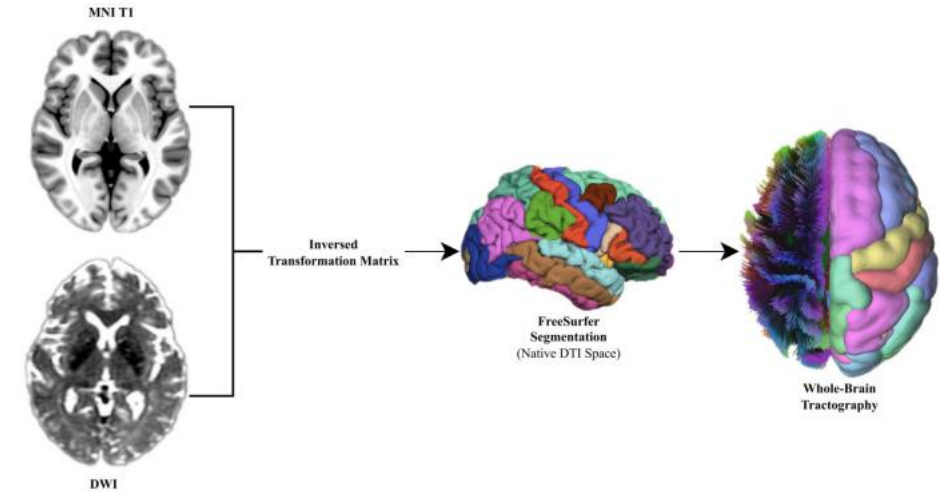
Asymmetry (ratio)	Aggressive NPS (+)	Aggressive NPS (-)	<i>p</i>
Frontal lobe	1.03 ± 0.032	1.01 ± 0.032	0.029*
Temporal lobe	0.984 ± 0.080	0.973 ± 0.093	0.482
Parietal lobe	1.027 ± 0.058	1.016 ± 0.075	0.409
Occipital lobe	1.01 ± 0.082	1.01 ± 0.076	0.954
Limbic lobe	1.06 ± 0.067	1.07 ± 0.092	0.532

* $p < 0.05$.

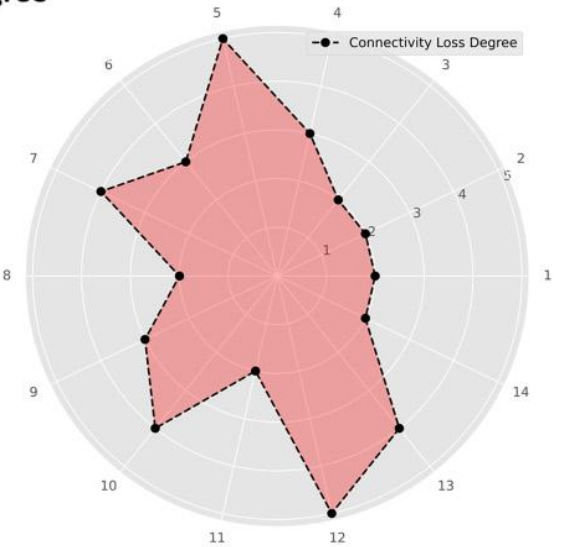
Asymmetry Ratio: volume of the left hemisphere divided by the volume of the right hemisphere (Left/Right volume)

Structural WM connectivity loss in MCI subjects with BPSD

- 12 MCI with NPS (MCI+) and 49 without NPS (MCI-), along with 35 HC
- Voxel-based morphometry and tract-based spatial statistics were employed to identify structural and microstructural alterations

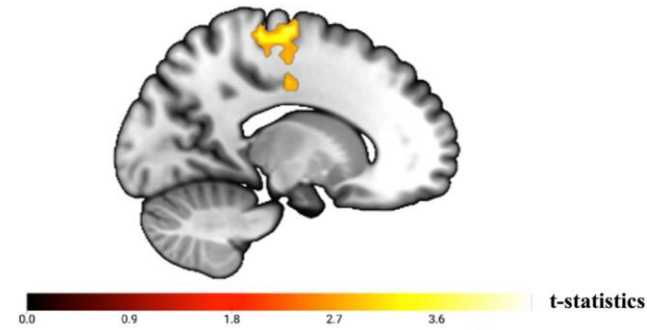
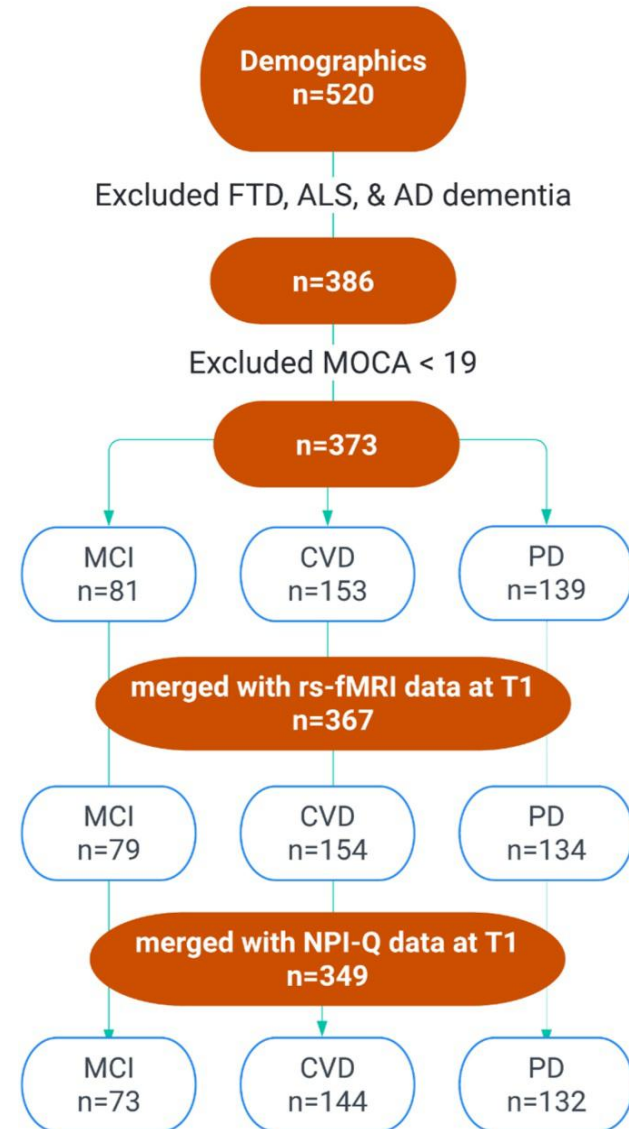


	Brain Regions	Connectivity Loss Degree
1	Paracentral lobule and sulcus	2
2	Left-Precuneus	2
3	Right-Precuneus	2
4	Left-Precentral gyrus	3
5	Left-Superior frontal gyrus	5
6	Right-Postcentral gyrus	3
7	Right-Parieto-occipital sulcus	4
8	Transverse frontopolar gyri & sulci	2
9	Left-Putamen	3
10	Left-Caudate	4
11	Left-Thalamus-Proper	2
12	Left-Pallidum	5
13	Left-Inferior frontal gyrus	4
14	Left-Hippocampus	2



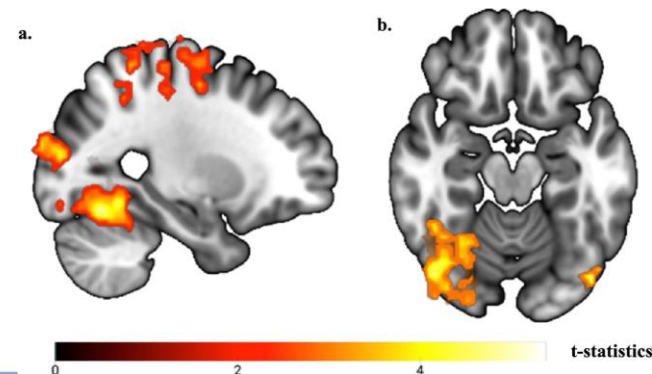
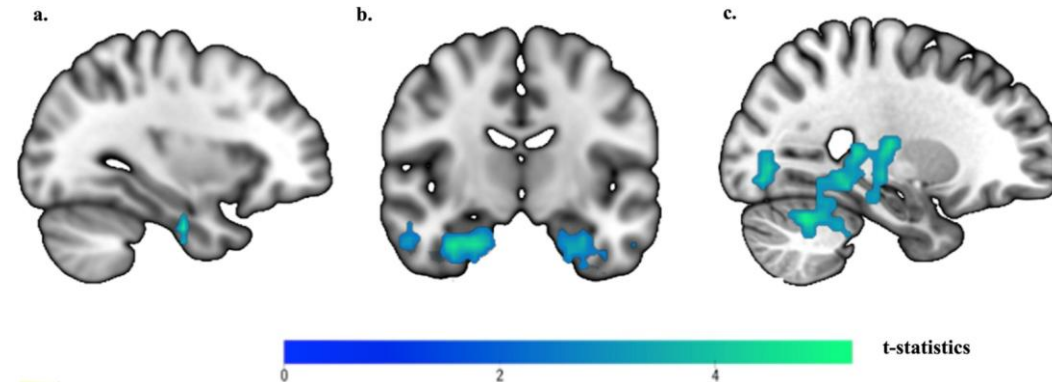
BDSD and Brain Functional Connectivity in Patients With MCI, CVD and PD

ONDRI Baseline data- Visit 01



Significant positive association between **nighttime behavior** and FC between anterior salience network and precentral gyrus (sensorimotor network) in **MCI**

Significant negative associations between **anxiety** and FC (a) within dorsal DMN, (b) within ventral DMN, and (c) between right executive control network and left hippocampus in **CVD**



Significant positive associations between **nighttime behavior** and FC between (a) right executive control network and precuneus (DMN); (b) left ECN and fusiform gyrus in **PD**



Anxiety and irritability are associated with greater amyloid deposition in cognitively impaired elderly people

657 participants including 230 HC, 308 MCI and 119 AD subjects form the ADNI cohort; regional amyloid deposition evaluated with ¹⁸F-florbetapir PET

Partial Spearman's correlations coefficients between neuropsychiatric inventory symptoms score and ¹⁸F-florbetapir standard uptake value ratio (SUVR) in cerebral regions of interest in each population. Correlation coefficient are presented with p value in brackets with "*" for significant results

¹⁸ F-florbetapir cortical uptake	Frontal	Cingulate	Parietal	Temporal	Cortical summary index (SUVR)
<i>Total population</i>					
NPI hallucination	0.077 (0.049)*	0.079 (0.042)*	0.081 (0.038)*	0.09 (0.020)*	0.078 (0.044)*
NPI anxiety	0.102 (0.009)*	0.083 (0.034)*	0.072 (0.064)	0.073 (0.061)	0.099 (0.010)*
NPI irritability	0.089 (0.022)*	0.085 (0.029)*	0.087 (0.025)*	0.076 (0.051)	0.093 (0.017)*
<i>MCI group</i>					
NPI anxiety	0.126 (0.027)*	0.104 (0.070)	0.094 (0.101)	0.074 (0.196)	0.14 (0.013)*
<i>AD group</i>					
NPI irritability	0.175 (0.059)	0.175 (0.058)	0.201 (0.029)*	0.117 (0.209)	0.149 (0.109)

Neuropsychiatric symptoms and their neural correlates in individuals with mild cognitive impairment

Nataschia De Lucia,¹  Giovanni Carbone,² Benedetta Muzii,³ Nicola Ferrara,² Giuseppe Rengo,^{2,4} Nelson Mauro Maldonato,¹ Grazia Daniela Femminella,^{2,5}  and Alzheimer's Disease Neuroimaging Initiative*

- 233 MCI and 305 NC from the ADNI-3 cohort
- Neuropsychological assessment, volumetric MR brain scan, and Flortaucipir PET for in vivo assessment of regional tau deposition
- 61.4% MCI subjects showed at least one BPSD, with the most prevalent ones being depression (26.1%), irritability (23.6%), and sleep disturbances (23.6%)
- Posterior cingulate cortex volume was the only predictor of global neuropsychiatric burden in this MCI population

Table 3. Normalized Flortaucipir SUVR with partial volume correction in MCI patients with and without behavioral symptoms

	MCI+ (N = 143)		MCI- (N = 90)		COHENS' D
	Mean	SD	Mean	SD	
Middle Frontal Cortex, bilateral	1.62	0.35	1.65	0.37	0.08
Orbitofrontal Cortex, bilateral	1.69	0.27	1.72	0.22	0.12
Amygdala, bilateral	1.63	0.58	1.56	0.48	0.13
Hippocampus, bilateral	1.34	0.24	1.36	0.25	0.08
Anterior cingulate cortex, bilateral	1.31	0.19	1.35	0.22	0.19
Posterior cingulate cortex, bilateral	1.44	0.29	1.43	0.30	0.03
Striatum, bilateral	1.47	0.18	1.51	0.21	0.20
Braak 3-4 regions, combined	1.59	0.34	1.61	0.39	0.05
Braak 5-6 regions, combined	1.59	0.27	1.62	0.30	0.10

Table 4. Regional brain volumes (mm³) in MCI patients with and without behavioral symptoms

	MCI+ (N = 143)		MCI- (N = 90)	
	Mean	SD	Mean	SD
Middle Frontal Cortex, bilateral	38,420.4	4832.4	38,829.3	4315.8
Orbitofrontal Cortex, bilateral	26,161.8	2591.5	26,755.4*	2337.8
Amygdala, bilateral	2927.2	588.9	3022.4	566.2
Hippocampus, bilateral	7535.5	1124.4	7653.4	937.7
Anterior cingulate cortex, bilateral	7768.4	1291.9	7731.6	1399.3
Posterior cingulate cortex, bilateral	5537.7	843.7	5847.6*	808.0
Striatum, bilateral	19,552.4	2579.0	19,380.8	2457.9

*Significantly different from MCI + at $p < 0.05$.

Neural Basis of Anxiety in Dementia With Lewy Bodies




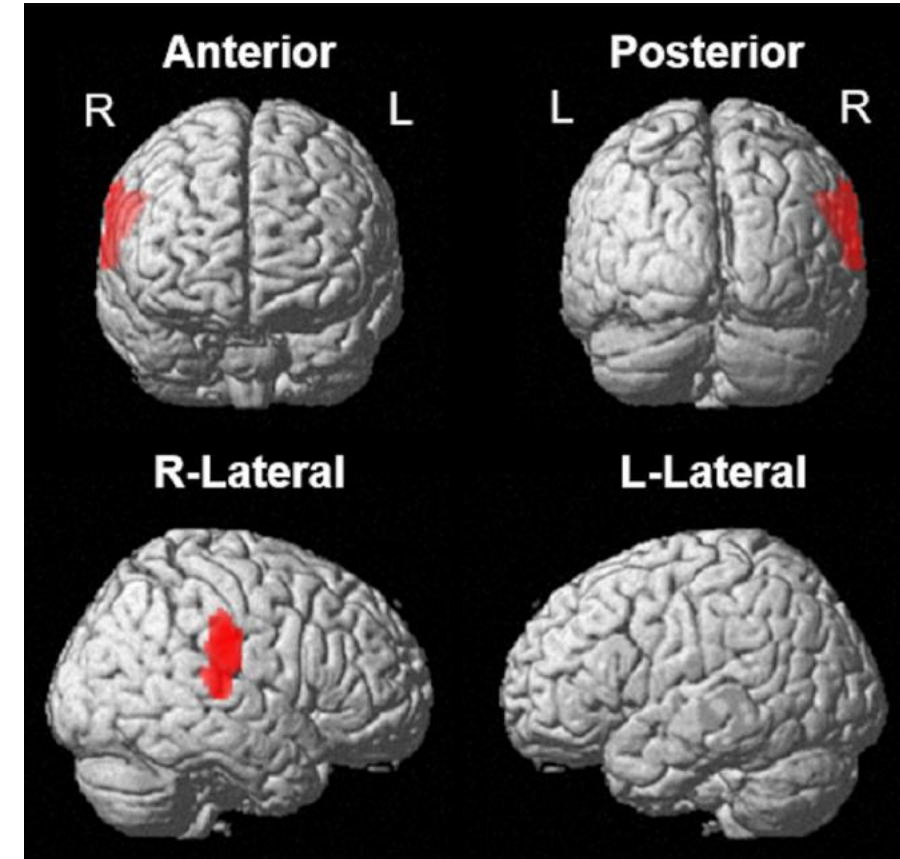
Naohiro Kimura^{1,2} | Yoshihiro Chadani¹ | Ryo Kawai¹ | Ryoko Fujito¹ | Hideki Kanemoto^{3,4}  | Ryuichi Takahashi⁵  | Tetsuo Kashibayashi⁵ | Shunichiro Shinagawa⁶ | Kenji Tagai⁶ | Kazunari Ishii⁷  | Manabu Ikeda³ | Hiroaki Kazui¹

TABLE 2 | Comparison of the incidence of the 4 core clinical features between Anxiety+ and Anxiety- groups in DLB.

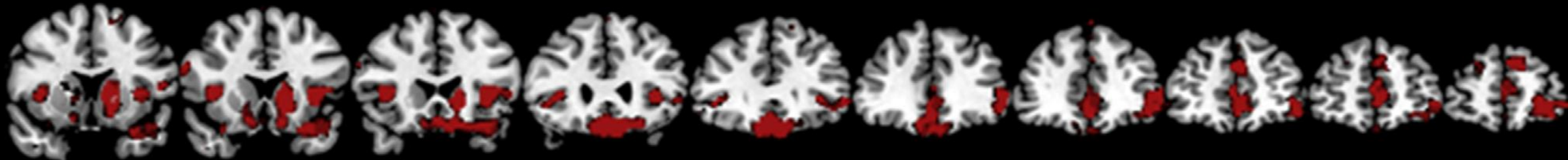
	Whole N = 40	Anxiety+ N = 14	Anxiety- N = 26	p value
Fluctuating cognition	55.0%	78.6%	42.3%	0.046
Visual hallucinations	65.0%	71.4%	61.5%	0.730
REM sleep behavior disorder	35.0%	42.9%	30.8%	0.501
Parkinsonism	47.5%	50.0%	46.2%	1.000

- 40 patients with probable DLB
- 35% had significant anxiety
- The NPI anxiety score was significantly negatively correlated with regional cerebral blood flow in the right supramarginal gyrus in patients with DLB, evaluated with SPECT

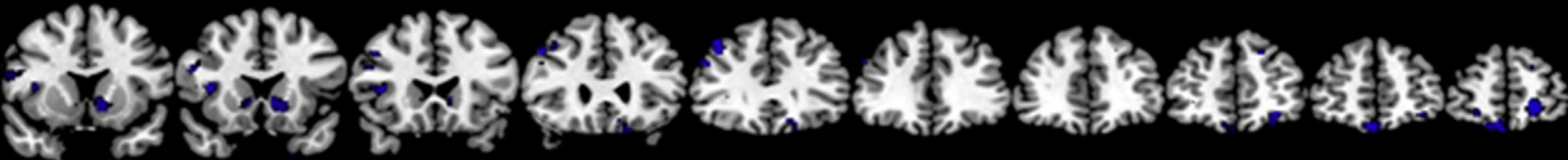


Apathy in Alzheimer's disease and frontotemporal dementia

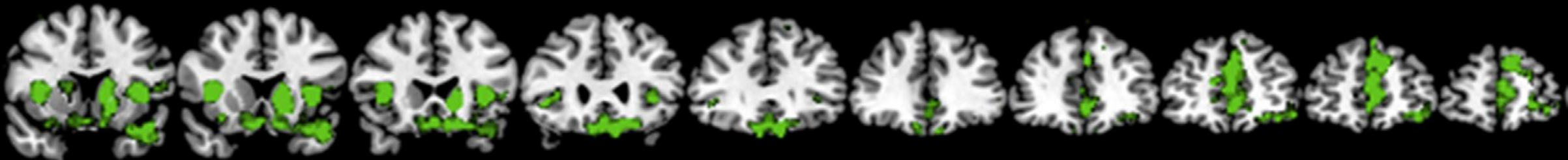
Affective apathy



Behavioural apathy



Cognitive apathy

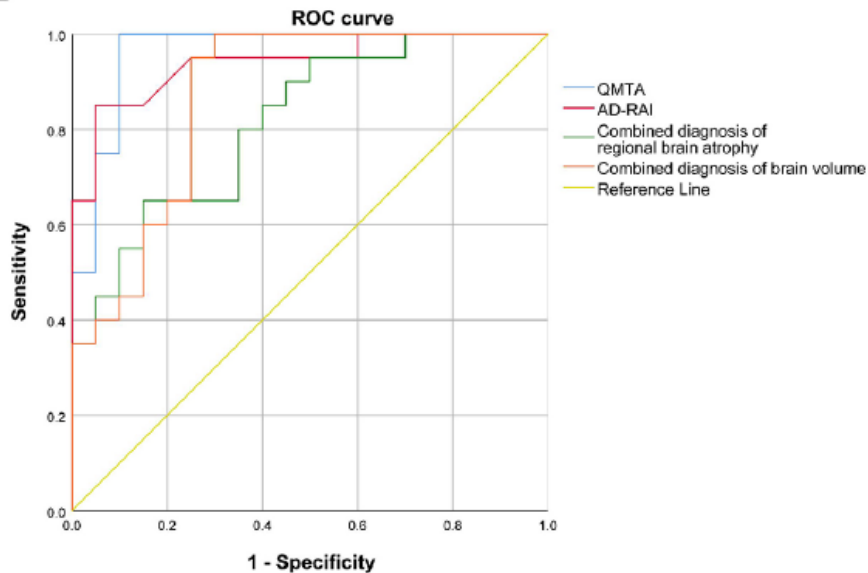


Evaluation of AccuBrain-based MRI quantitative analysis in diagnosing Alzheimer's disease and assessing behavioral and psychological symptoms of dementia

Huixian Lu¹ · Caixia Xu¹ · Jiaquan Liang¹

120 participants divided into AD (n=40), MCI (n=40), and HC (n=40)

Brain MRI data were analyzed using the AccuBrain system to quantify AD Resemblance Atrophy Index (AD-RAI), Quantitative Medial Temporal Atrophy (QMTA), hippocampal volume, and white matter hyperintensities



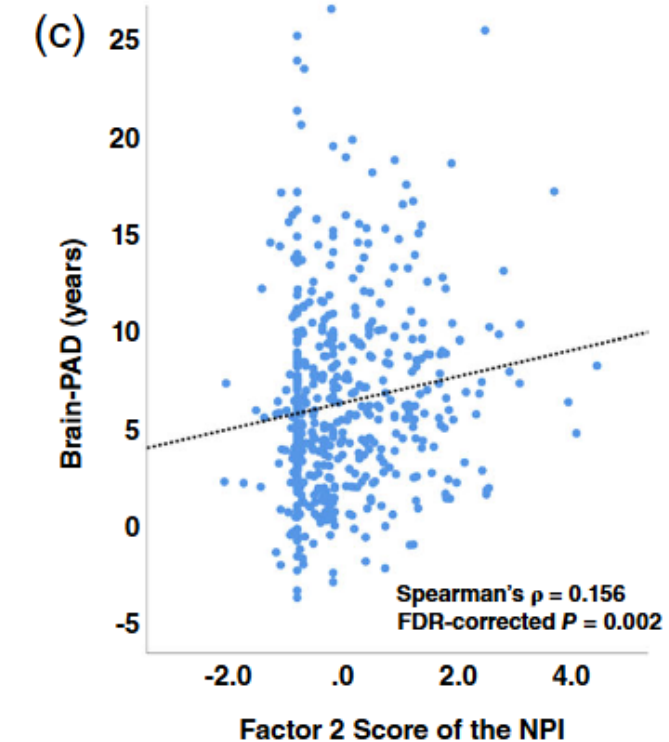
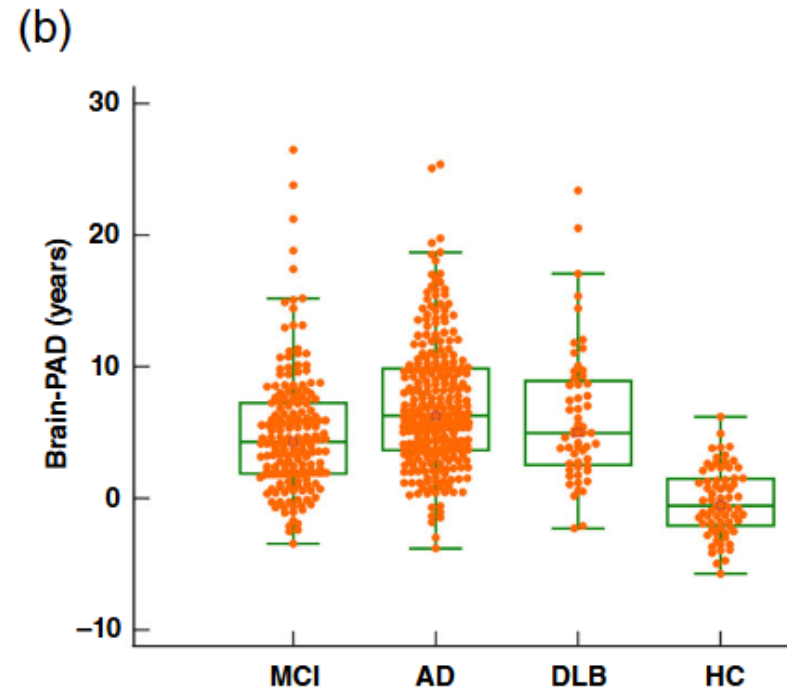
QMTA showed the highest diagnostic accuracy for identifying patients with BPSD, with an AUC of 0.960, a sensitivity of 95.0%, and a specificity of 90.0%

Table 3 Imaging quantitative analysis between BPSD and Non-BPSD groups

	Non-BPSD (n=20)	BPSD (n=20)	t	P
MMSE (score)	20.6±2.68	18.55±2.21	2.636	0.012
MocA	19.45±2.14	18.65±2.66	1.048	0.301
FAQ	17.6±5.02	18.3±4.43	0.468	0.643
NPI (score)	2.75±0.91	3.8±0.83	3.804	0.001
Fazekas score				
PVWML	0.6±0.5	0.65±0.59	0.289	0.774
DWML	0.5±0.51	0.65±0.49	0.946	0.35
AD-RAI	0.73±0.18	1.09±0.18	6.338	<0.001
QMTA	0.38±0.17	0.76±0.13	7.858	<0.001
Brain volume				
Hippocampal volume	0.41±0.09	0.31±0.05	4.355	<0.001
Caudate nucleus volume	0.21±0.03	0.2±0.04	0.590	0.558
Amygdala volume	0.16±0.06	0.11±0.07	2.425	0.020
White matter hyperintensities (mm ³)	4405.6±290.96	4608.7±3.95	3.121	0.003
Regional brain atrophy (ICV%)				
Temporal lobe atrophy (%)	28.35±4.91	33.17±5.7	2.867	0.007
Frontal lobe atrophy (%)	47.35±10.24	48.73±11.19	0.407	0.686
Parietal lobe atrophy (%)	44.18±7.01	48.98±7.37	2.112	0.041
Cingulate gyrus atrophy (%)	19.23±3.7	20.13±3.95	0.744	0.462
Occipital lobe atrophy (%)	19.03±3.16	21.08±3.38	1.982	0.055
Insular atrophy (%)	23.15±3.71	26.31±4.13	2.547	0.015

Apathy and depression are associated with higher brain-age in MCI and early dementia

- 499 individuals with diagnoses of amnesic MCI (n = 185), early AD (n = 258) or DLB(n = 56)
- Brain-age prediction model using 694 healthy brain MRIs
- NPI scores subdivided into : (i) Agitation and Irritability, (ii) Depression and Apathy,(iii) Delusions and Hallucinations, and (iv) Euphoria and Disinhibition
- PAD= predicted age difference



All groups showed significantly increased brain-PAD: 4.3 years in MCI, 6.3 years in AD, and 5.0 years in DLB

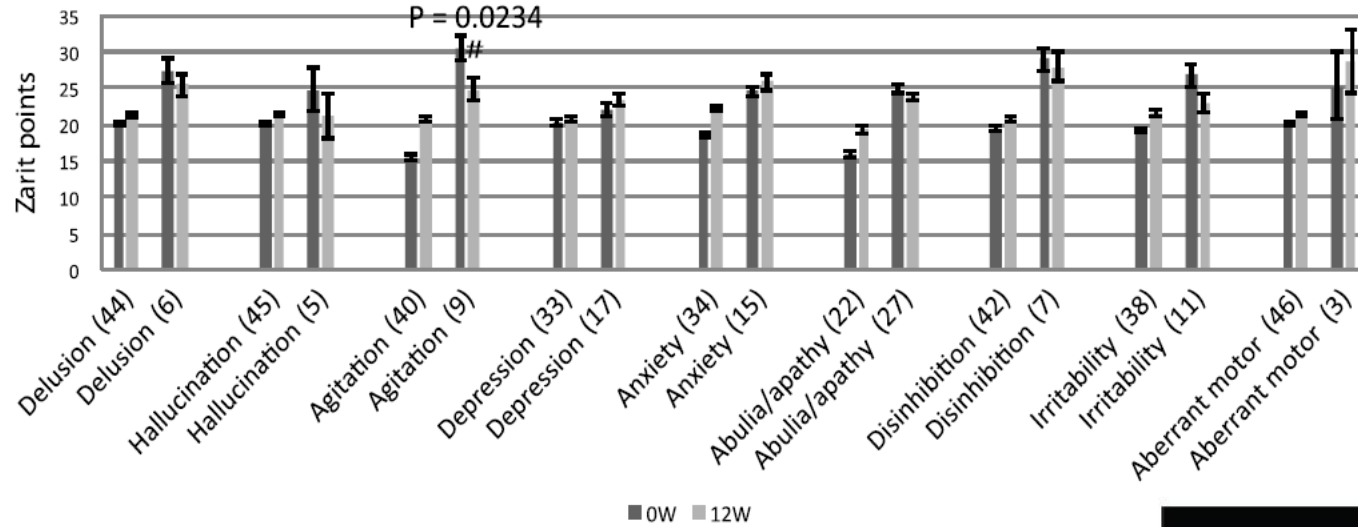
Positive correlation between brain-PAD and the depression/apathy factor (Spearman's $r = 0.156$, $p = 0.002$)

Guiding Management



Galantamine for BPSD in Alzheimer's Disease

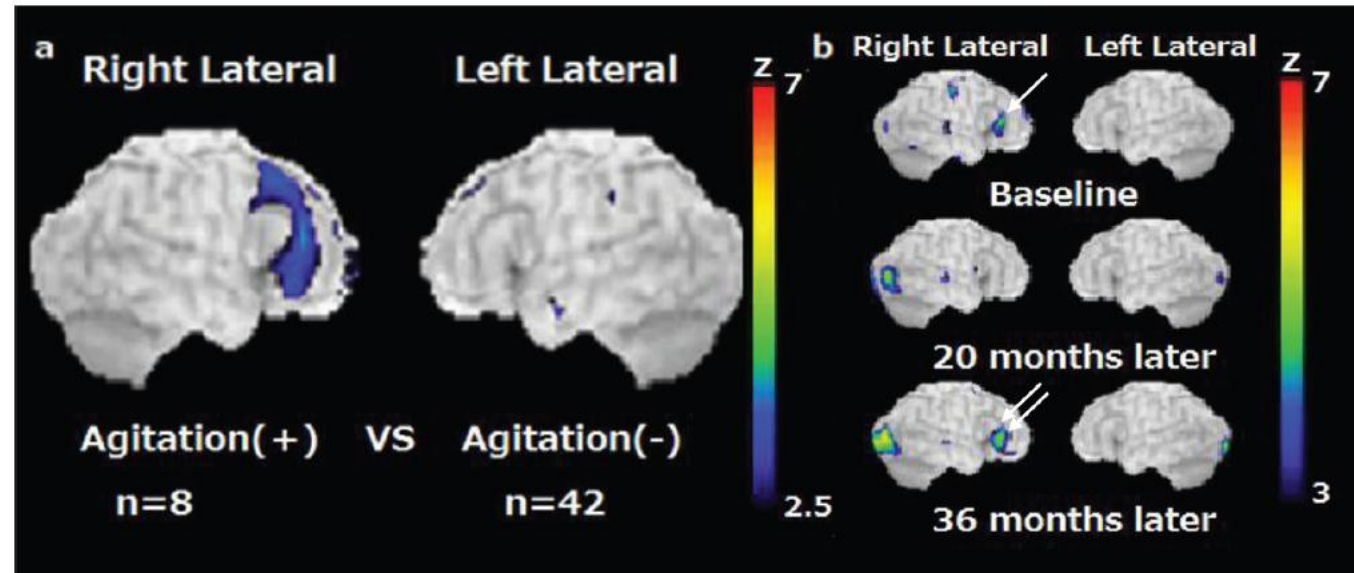
The changes in the NPI subscale sores and Zarit points



- 50 patients with mild AD for 12 weeks
- Evaluated with Neuropsychiatric Inventory (NPI) and Japanese version of the Zarit Caregiver Burden Interview (ZBI)

A. The group with agitation exhibited an increase in rCBF in the right lateral prefrontal cortex compared with that without agitation.

B. Change in rCBF SPECT in a patient with agitation
The increased area in rCBF in the right lateral frontal lobe disappeared after 24 mg galantamine treatment for 20 months. After 36 months, it reappeared



Conclusions

- ✓ Compared to the significant progress that has been made in the field of cognitive symptoms in dementia, the neuroimaging findings of BPSD are less consistent, particularly in terms of the affected brain regions.
- ✓ This discrepancy may be due to differences in neuroimaging modalities or analytical methods, the fact that BPSD can change over time, and/or the subjective nature of BPSD assessments.
- ✓ A better understanding of the cognitive and neuroanatomical mechanisms of neuropsychiatric symptoms in dementia could help develop more targeted and effective treatment options

Thank You!