

Dementia in PD is Due to Diffuse Lewy Body Disease

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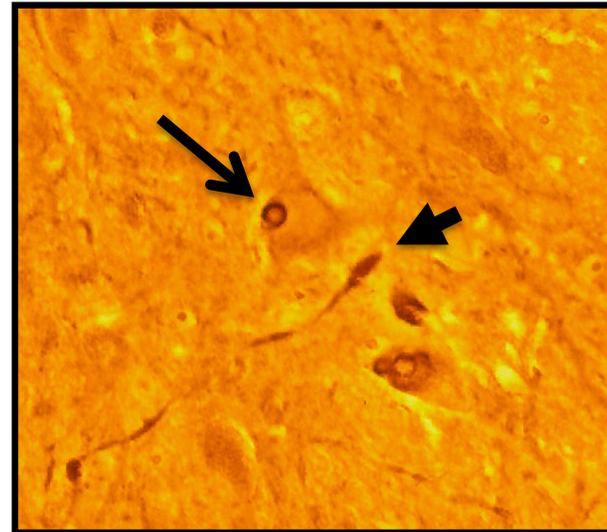
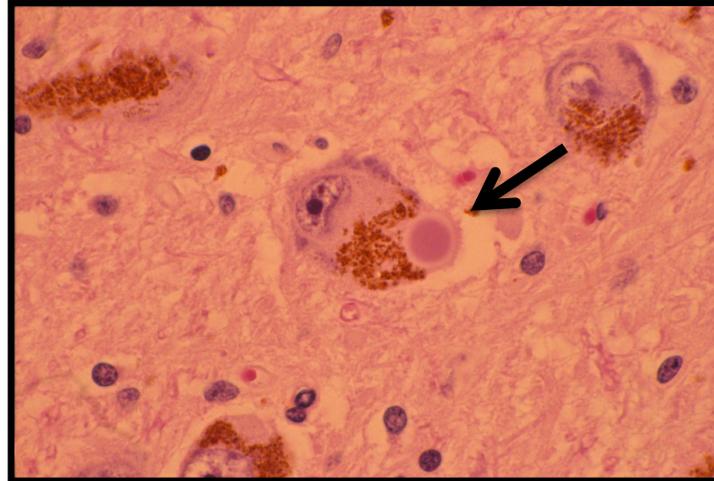
Overview

- **What is “Diffuse Lewy Body Disease”?**
 - ◆ define Lewy related pathology (LRP)
 - ◆ Braak staging of LRP
 - ◆ define “diffuse” Lewy body disease
- **What is PDD?**
- **Is dementia due to coexistent AD?**
- **Is neocortical LRP associated with dementia in PDD?**
 - ◆ Is it presence of diffuse LRP or severity?



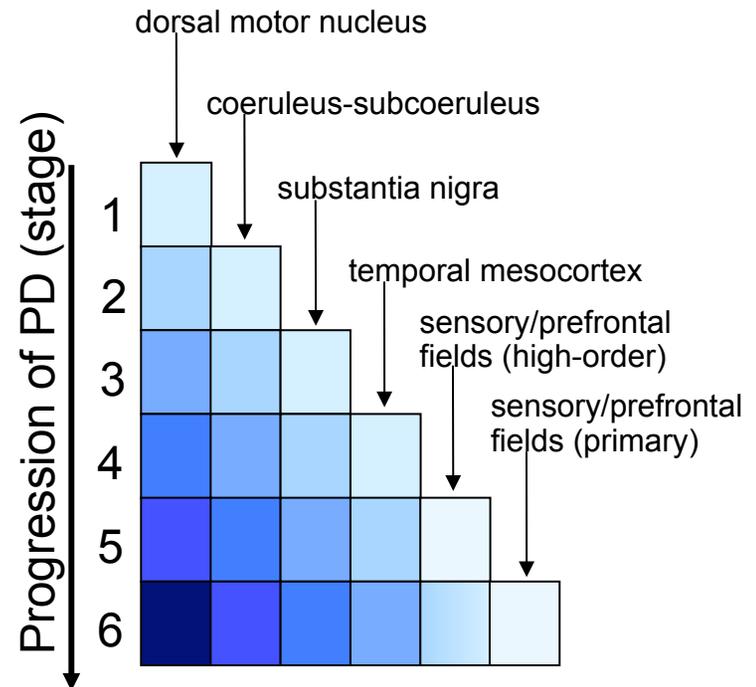
What is Lewy Related Pathology (LRP)?

- **Classic Lewy bodies**
- **Alpha-synuclein immunopositive inclusions and neurites**



Braak Staging of LRP

- Examination of “incidental” and PD cases with SNCA antibodies
- Proposed “stages” of LRP anatomic progression



(intensity of color represents degree of degeneration)



What is “Diffuse Lewy Body Disease”?

- Involvement of LRP in all three major anatomic regions “+”
 - ◆ brainstem
 - ◆ limbic
 - ◆ neocortical
 - ◆ “more” diffuse



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What is PDD?

2007 Clinical Diagnostic Criteria

- **Diagnosis of PD**
- **Dementia syndrome within the context of established PD**
 - **impairment in more than one cognitive domain**
 - **decline from premorbid level**
 - **deficits severe enough to impair daily life**



What is PDD?

Interpretation of Neuropathologic Studies

- **Case selection**
 - ◆ PD precedes dementia onset (“1 year rule”)
- **Neuropathology**
 - ◆ SNCA immunohistochemistry
 - ◆ Up to date AD pathologic criteria
 - ❖ Braak stage IV or greater neurofibrillary tangles
 - ❖ CERAD neuritic plaque density \geq moderate



Is Dementia in PDD due to Coexistent AD?

Study	# PDD	# AD positive
Hurtig Neurology '00	22	7 (32%)
Apaydin Arch Neurol '02	12	1 (8%)
Aarsland Ann Neurol '05	18	0
Braak Neurology '05	79	2 (3%)
Galvin Neurology '06	34	13 (38%)
TOTAL	165	23 (14%)



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Is Dementia in PDD due to Coexistent AD?

Study	# PDD	# AD positive	# LRP positive
Hurtig Neurology '00	22	7 (32%)	22 (100%)
Apaydin Arch Neurol '02	13	1 (8%)	12 (92%)
Aarsland Ann Neurol '05	18	0	18 (100%)
Braak Neurology '05	79	2 (3%)	NA
Galvin Neurology '06	34	13 (38%)	32 (94%)
TOTAL	165	23 (14%)	84 (97%)



Is Neocortical LRP associated with Dementia?

Two Community Sample Studies

- **Honolulu-Asia Aging Study (HAAS)**
 - ◆ 285 autopsies
 - ◆ logistic regression for AD/Vascular/Cortical LB/HS & dementia
 - ◆ odds ratio for cortical LB = 2.17
- **Adult Changes in Thought (ACT)**
 - ◆ 221 autopsies
 - ◆ Multivariate log-linear regression for AD/Vascular/Cortical LB/AA & dementia
 - ◆ odds ratio for cortical LB = 5.08



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Is Neocortical LRP Associated with Dementia in PDD?

- **Hurtig, Neurology 2000**
 - ◆ 20 PD & 22 PDD
 - ◆ 41/42 with cortical LRP

		Cortical Lewy Body Score			
<i>Dementia</i>	<i>0</i>	<i>1</i>	<i>2</i>	<i>3</i>	
Yes, n (%)	0 (0)	2 (9)	13 (59)	7 (32)	
No, n (%)	1 (5)	17 (85)	2 (10)	0	



Is Neocortical LRP Associated with Dementia in PDD?

- Apaydin, Arch Neurol 2002
 - ◆ 12 PD & 8 PDD

<i>Region</i>	<i>PDD Mean (SD)</i>	<i>PD Mean (SD)</i>	<i>p value</i>
Neocortex	2.3 (2.4)	0.2 (0.2)	.002
Limbic cortex	6.9 (4.5)	0.7 (0.7)	> .001
Amygdala	17.5 (18.2)	1.5 (1.9)	.006
Substantia nigra	5.7 (2.5)	3.3 (2.1)	.05



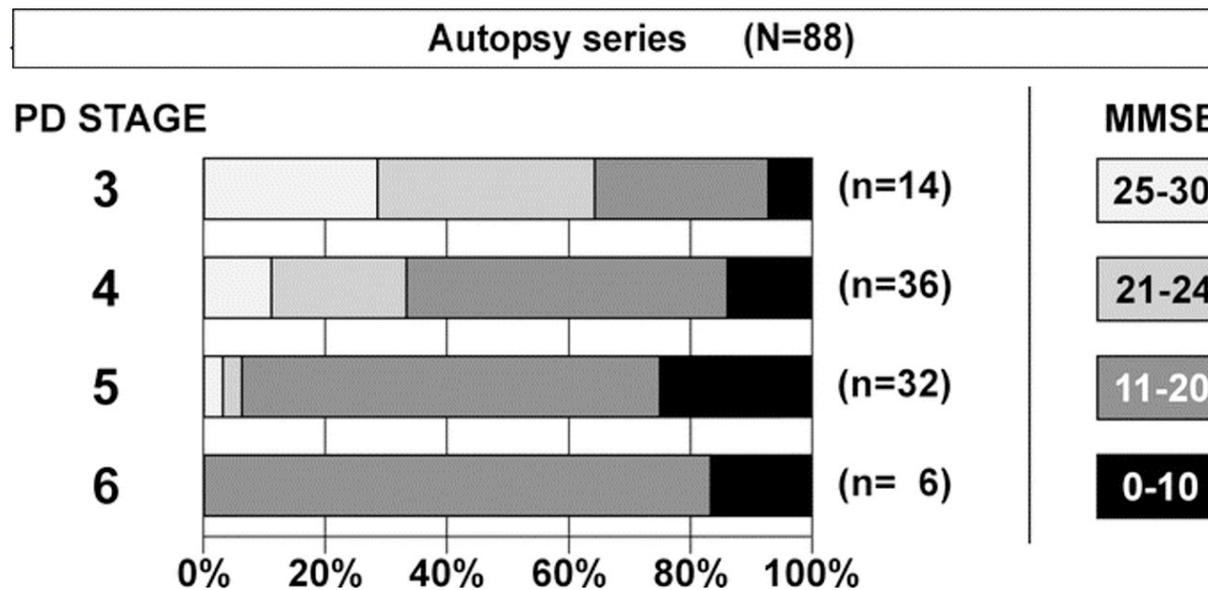
Is Neocortical LRP Associated with Dementia in PDD?

- **Aarsland, Ann Neurol 2005**
 - ◆ **community-based study of PD**
 - ◆ **4 PD & 18 PDD**
 - ◆ **LRP total score**
 - ◆ **Only LRP score significantly associated with rate of cognitive decline**



Is Neocortical LRP Associated with Dementia in PDD?

- Braak, Neurology 2005
 - ◆ 9 PD & 79 PDD



Conclusion

- Is dementia due to coexistent AD? **No**
- Is presence of any neocortical LRP associated with dementia in PDD? **No**
- *Is it presence of “more” diffuse LRP associated with dementia? **Yes!***

