

Head-to-head SuStaln Comparison of MRI- and Tau PET-derived Subtypes and Stages in ADNI

Gordon Zhaoqi An^{1,2}, Yunchang Xie^{1,2}, Peter R. Millar³, Carling Robinson², Taylor Pedersen², Aristeidis Sotiras⁴, Brian A. Gordon²

¹Division of Computational and Data Sciences, Washington University in St. Louis, St. Louis, MO, USA; ²Mallinckrodt Institute of Radiology, Washington University School of Medicine, St. Louis, MO, USA; ³Department of Neurology, Washington University School of Medicine, St. Louis, Missouri, USA; ⁴Department of Radiology, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania, USA,

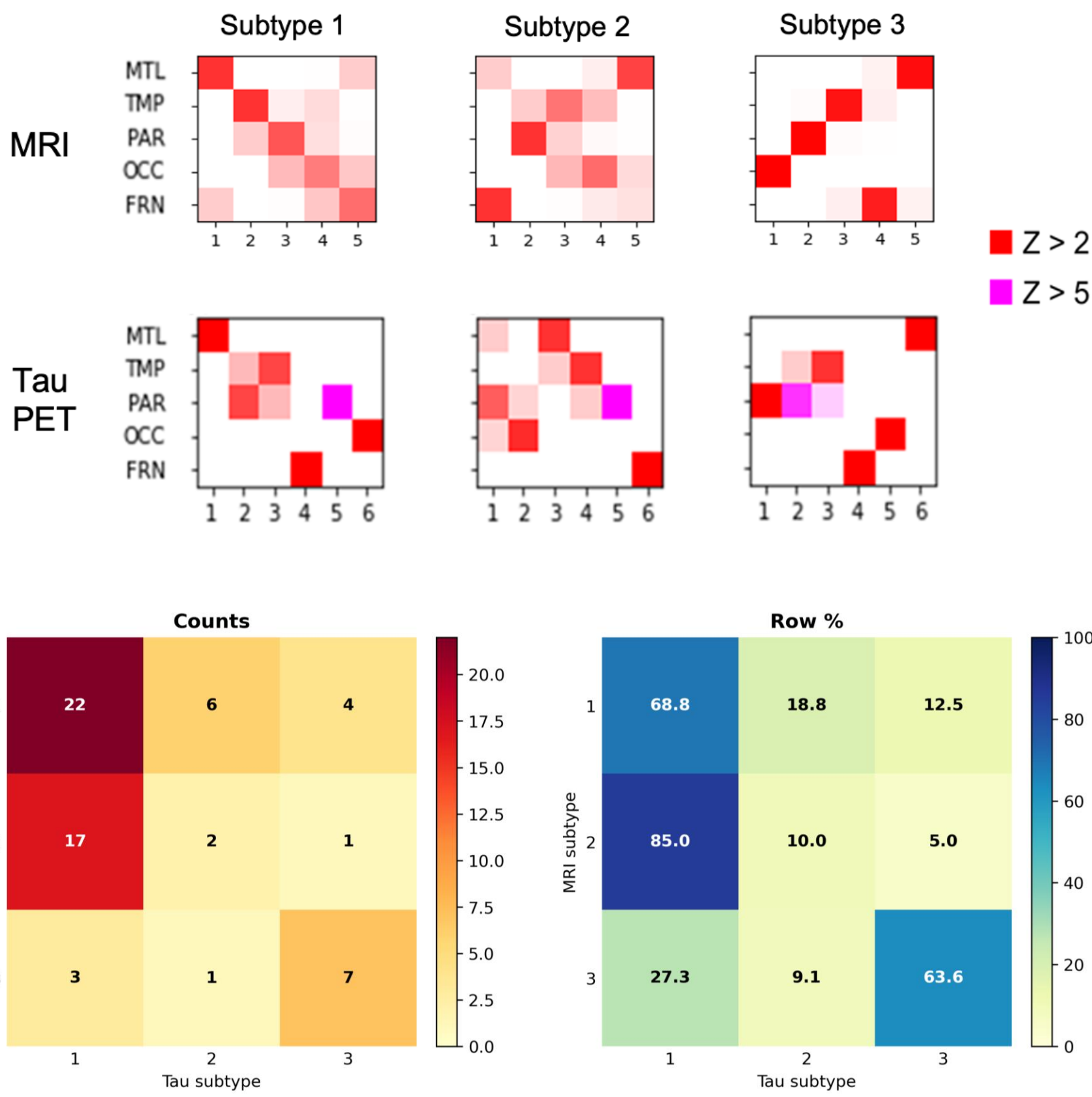
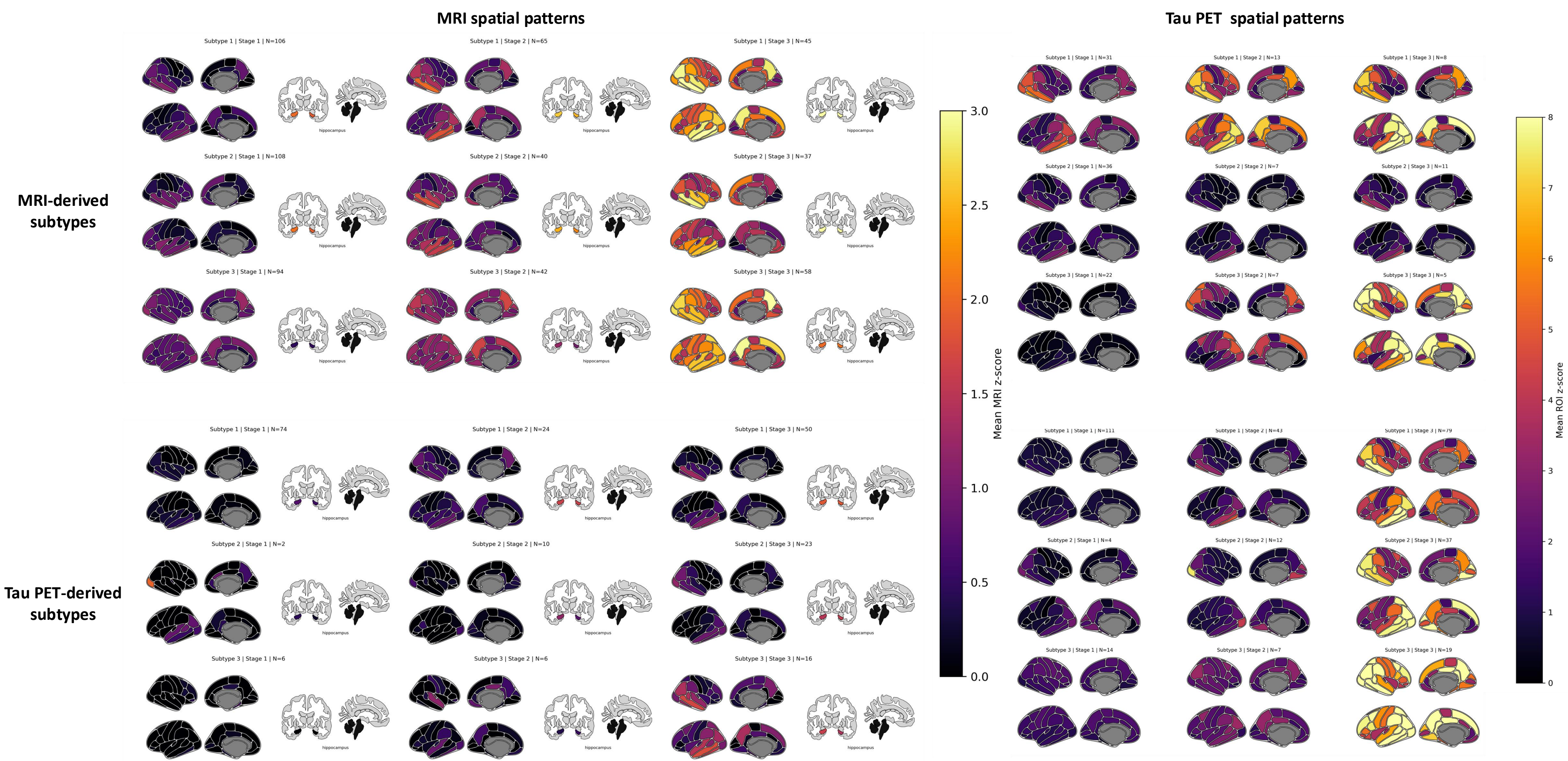
➤ Introduction

- Alzheimer's disease (AD) is biologically heterogeneous, with substantial variation in the regional expression of neurodegeneration and tau pathology.
- Structural MRI and tau PET provide complementary views of AD: MRI reflects downstream neurodegeneration, whereas tau PET more directly indexes molecular pathology.
- It remains unclear whether MRI-derived and tau PET-derived disease subtypes represent the same patient stratification axis, or whether they capture distinct but related dimensions of disease heterogeneity.

➤ Aims

- To perform a head-to-head comparison of MRI- and tau PET-derived SuStaln subtypes and stages in ADNI, evaluating:
- Spatial progression patterns within each modality
 - Subject-level subtype correspondence in matched MRI-tau PET participants
 - Clinical severity across subtype-stage groups
 - Longitudinal progression from MCI to dementia

➤ Results



Variable	Stage 0	Subtype 1	Subtype 2	Subtype 3	P
MRI					
N	1260	216	185	194	
Amyloid positive (%)	35	61	51	47	<0.001
APOE4 carriers (%)	32	61	45	46	<0.001
Age, mean (SD)	71.6 (7.3)	72.8 (8.2)	74.0 (6.9)	70.7 (7.6)	<0.001
Female (%)	54	54	33	47	<0.001
Education, mean (SD)	16.3 (2.5)	15.6 (2.6)	16.4 (2.8)	15.9 (2.9)	<0.001
MMSE, mean (SD)	28.4 (1.9)	25.4 (2.9)	26.0 (3.3)	27.1 (2.8)	<0.001
CDR-SB, mean (SD)	0.8 (1.2)	3.0 (2.2)	2.5 (2.0)	1.7 (1.7)	<0.001
Tau PET					
N	858	233	53	40	
Amyloid positive (%)	33	86	98	70	<0.001
APOE4 carriers (%)	22	48	51	40	<0.001
Age, mean (SD)	70.4 (7.1)	72.3 (6.4)	73.1 (7.4)	69.8 (6.7)	<0.001
Female (%)	51	54	57	44	0.639
Education, mean (SD)	16.6 (2.4)	16.0 (2.4)	16.2 (2.4)	15.8 (2.2)	0.008
MMSE, mean (SD)	28.6 (1.8)	25.5 (4.5)	24.8 (4.4)	25.8 (5.6)	<0.001
CDR-SB, mean (SD)	0.7 (1.4)	2.8 (3.1)	3.3 (3.8)	2.8 (3.5)	<0.001

➤ Conclusion

- Separate MRI and tau PET SuStaln models revealed heterogeneous subtype and stage structures in ADNI.
- MRI- and tau PET-derived patterns showed partial spatial correspondence, but individual-level subtype agreement was limited.
- Clinical severity and longitudinal progression analyses support the validity of subtype-stage assignments.

➤ References

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Contacts

Email: a.zhaoqi@wustl.edu Twitter/X: @Zhaoqi_An LinkedIn: www.linkedin.com/in/zhaoqi-an-066621224

➤ Future Work

- Test whether combining MRI and tau PET subtype/stage information improves prediction of clinical progression.
- Evaluate whether modality-specific stratification can improve enrichment strategies for trials targeting tau pathology versus neurodegeneration.



Gordon
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