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Abnormal tau in amyloid PET negative individuals

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Main aim: Investigate the characteristics of individuals with biomarker evidence of tauopathy but without β amyloid (Aβ) (A-T+) in relation to individuals with (A+T+) and without (A-T-) evidence in AD

Analysis #1: Demographics
Analysis #2: Tau levels at Braak1, Braak34, Braak56, meta-ROI
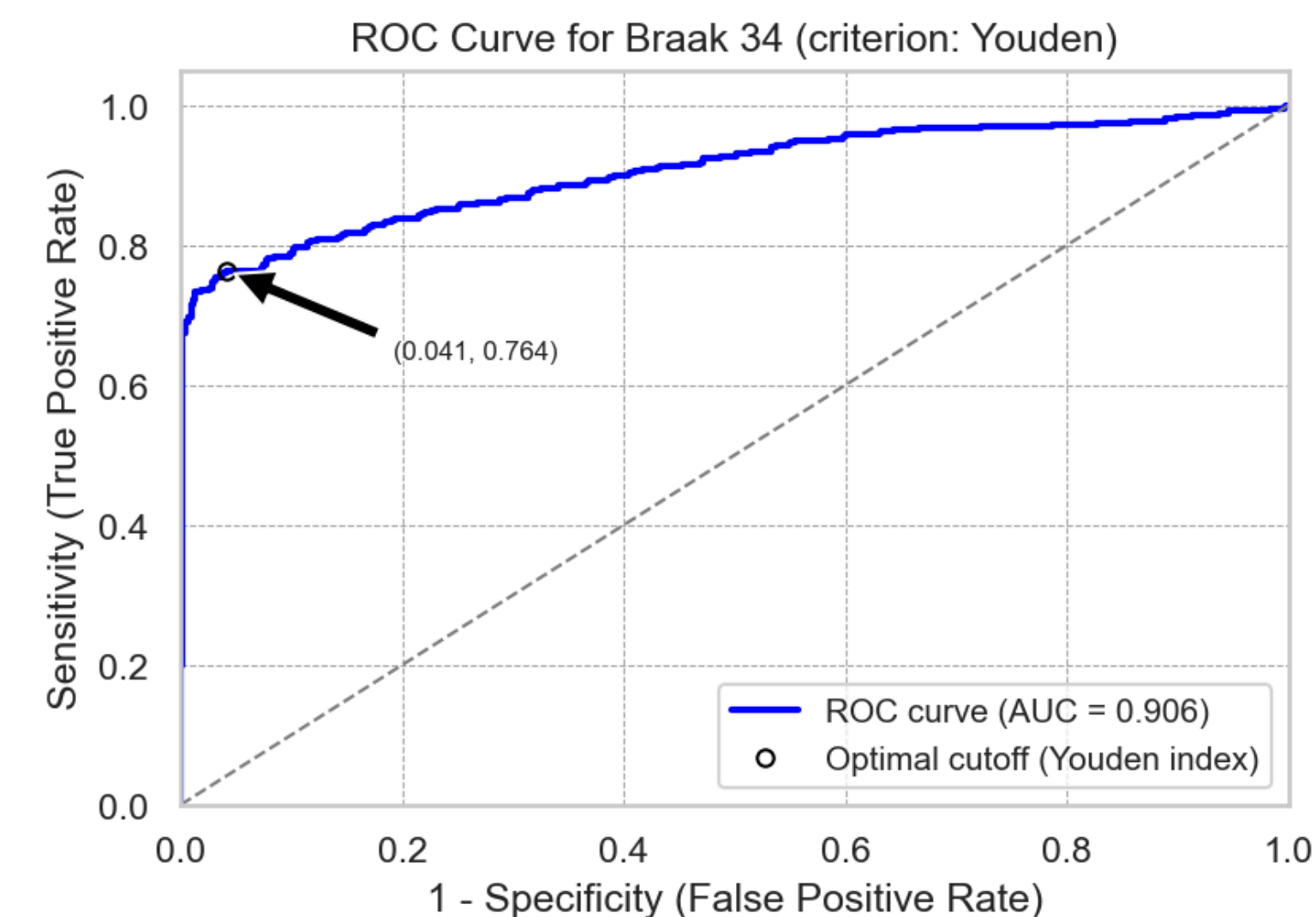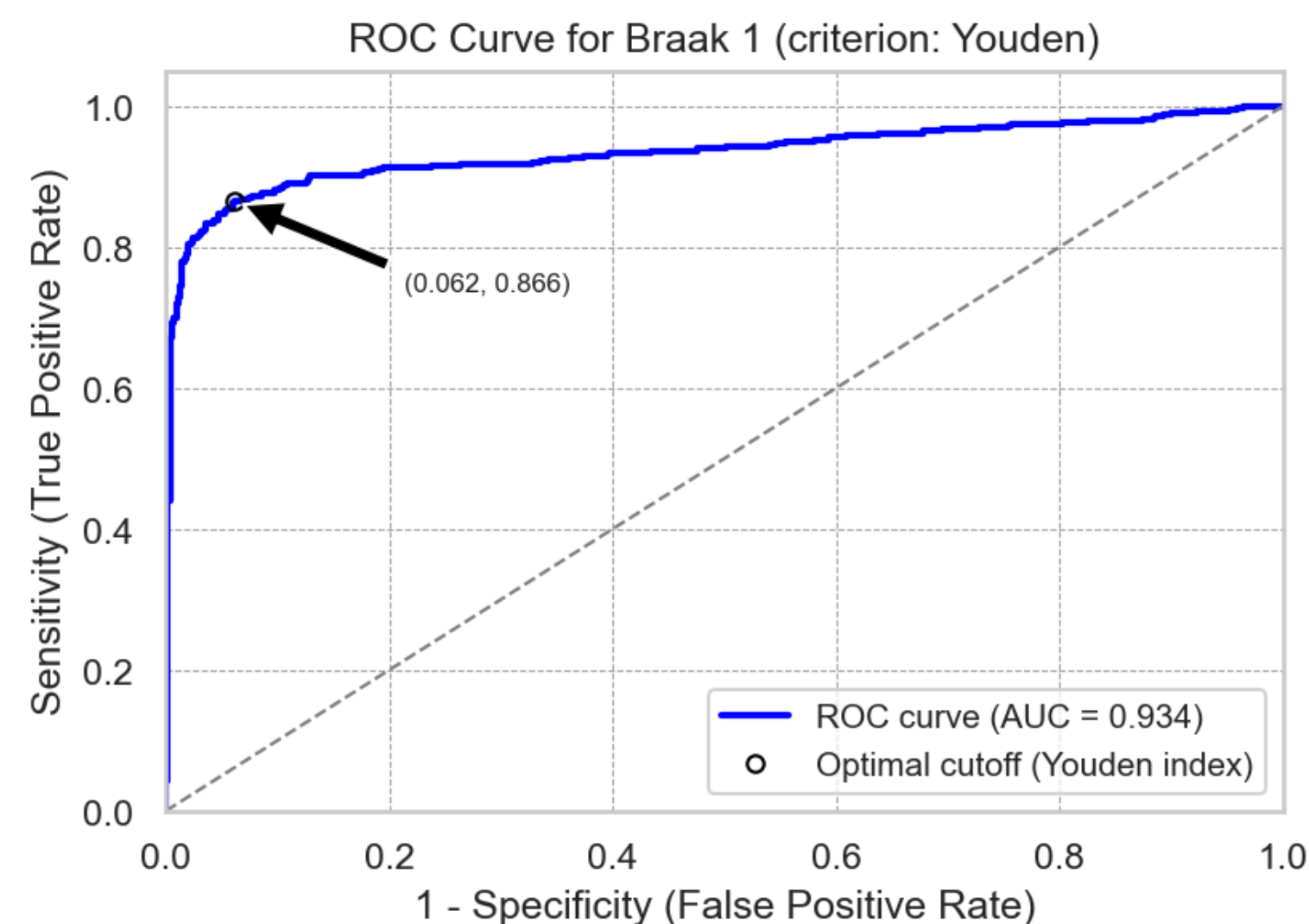**Analysis #3**: Tau deposition topography and hemispheric asymmetry

Analysis #0: Grouping & cutoffs

Calculated cut-offs using Youden index:
- Braak 1: 1.316
- Braak 34: 1.209

Participants grouped based on either Braak 1 or Braak 34 > cut-off
- A-T-: 585
- A-T+: 66
- A+T+: 505

Toomas Erik Anijärv, 13/4/24
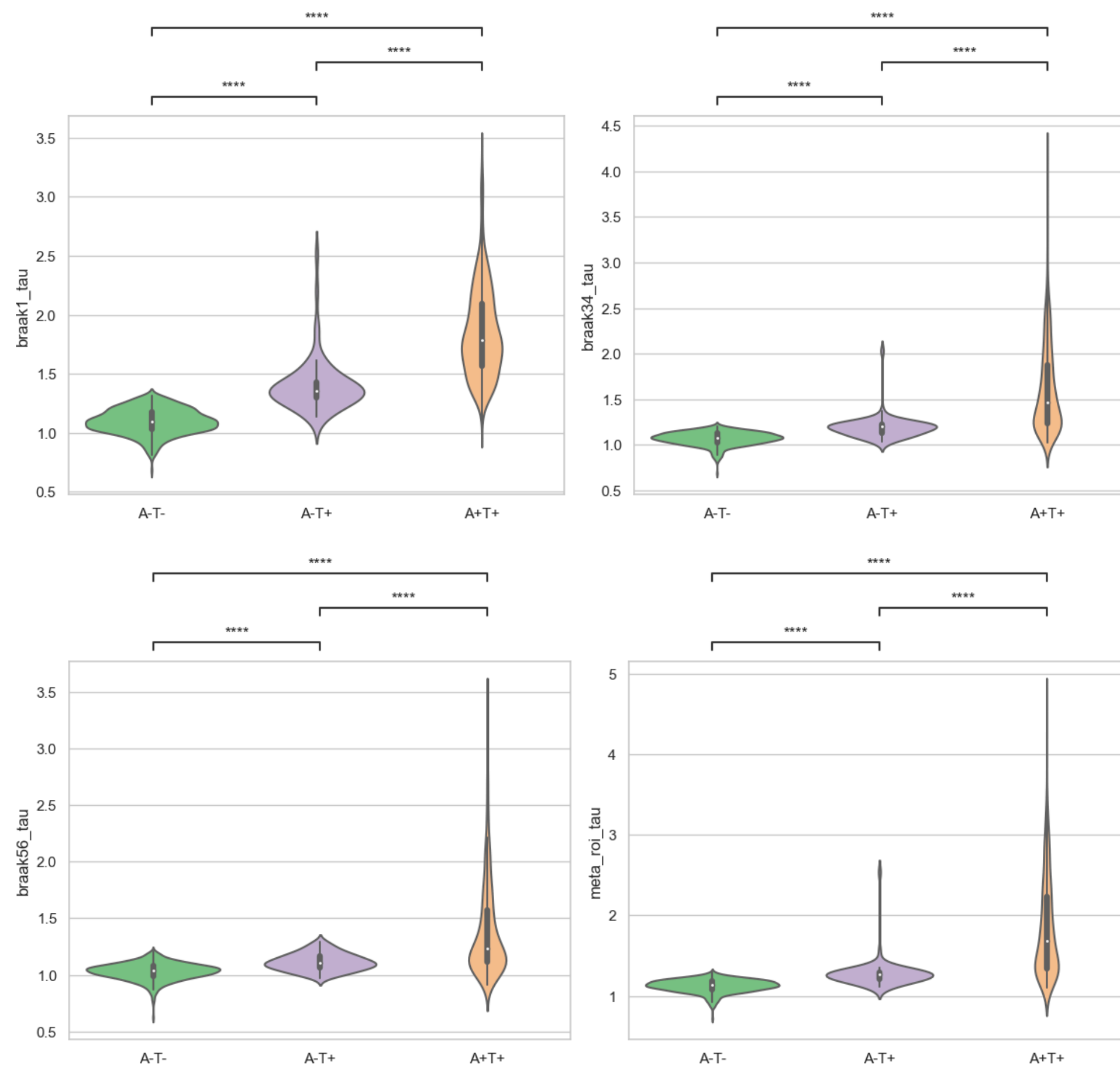
Analysis #1: Demographics
Partially replicated

Original vs replication results:
- Education wasn't different between any groups
- Hippocampal volume wasn't different between A-T- and A-T+
- Ptau was different between A-T- and A-T+

Analysis #2: Tau levels at Braak1, Braak34, Braak56, meta-ROI
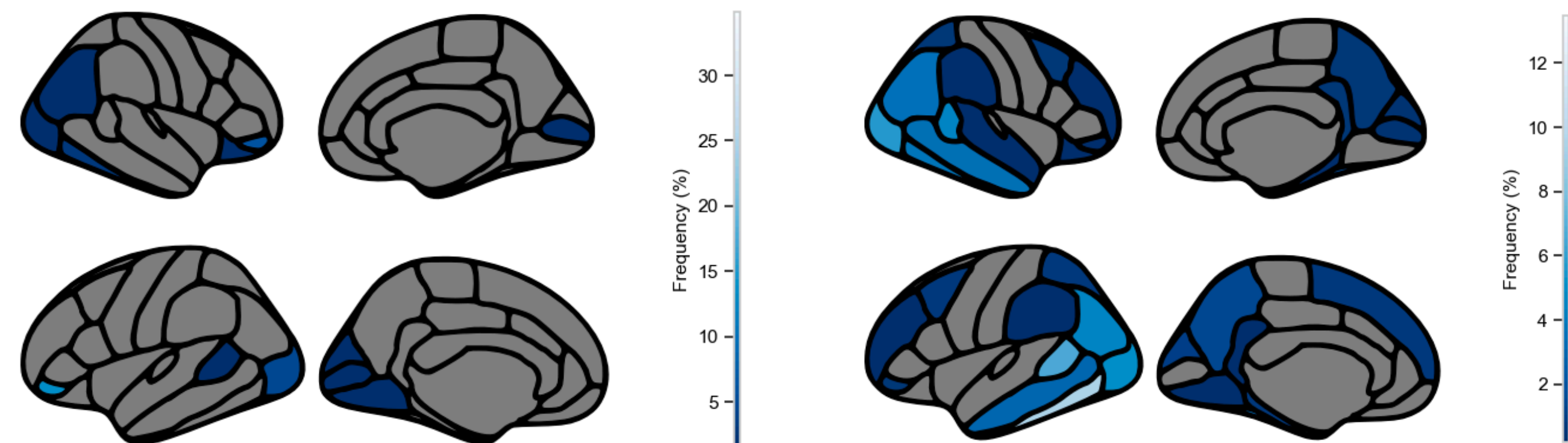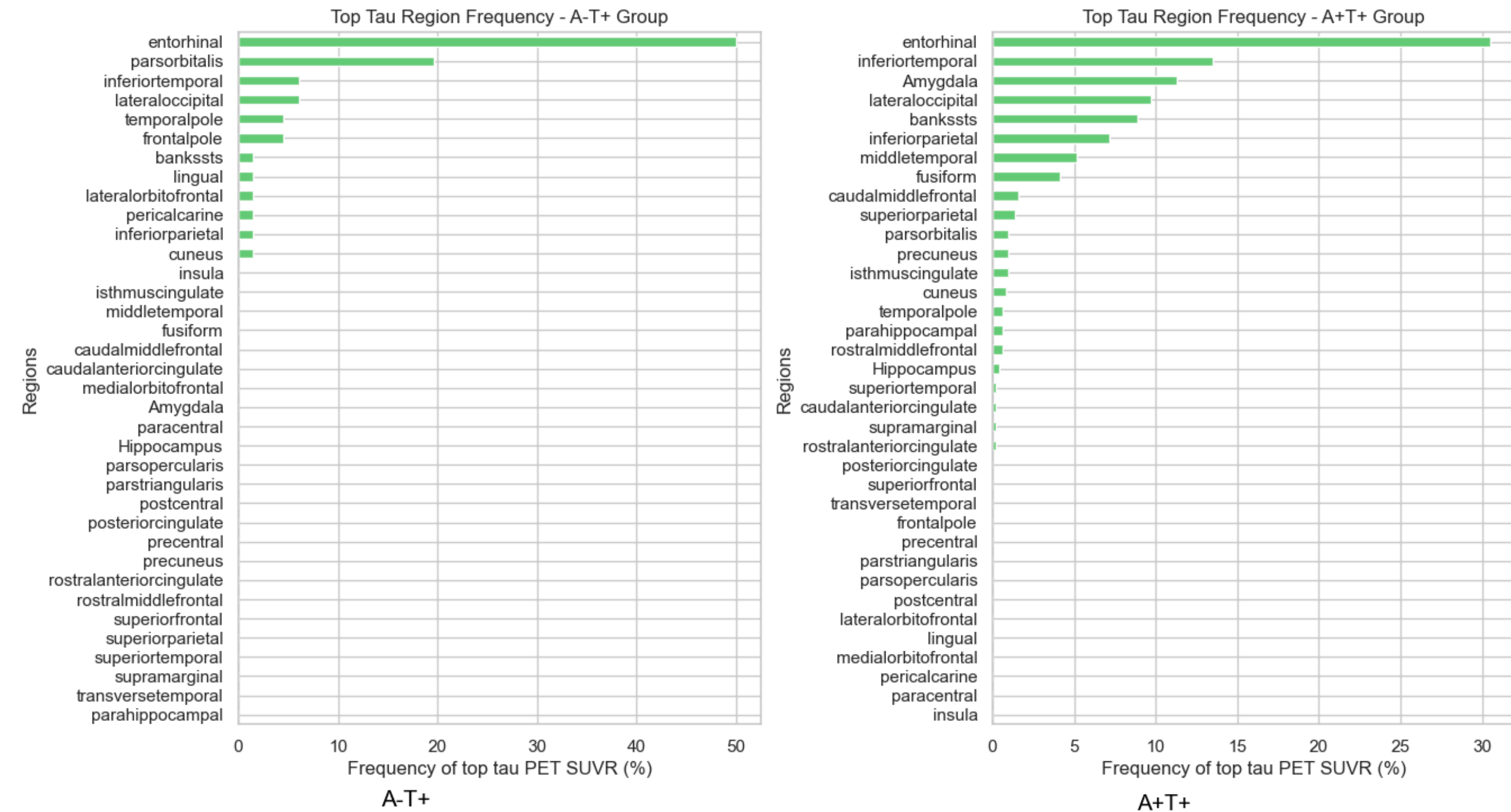## Successful replication

Analysis #3: Tau deposition topography
Replication proved different patterns of tau deposition

Original vs replication results:
- Indeed the A+T+ has more widespread distribution of tau, but similar top tau region between A-T+ and A+T+ is entorhinal cortex, not amygdala

	A-T- (n=585)	A-T+ (n=66)	A+T+ (n=505)	p1	p2	p3
Age	66.03 (10.34)	74.55 (8.77)	73.35 (7.20)	<0.001[a,b]		
Female	313 (53.5%)	34 (51.5%)	280 (55.4%)	0.733		
Education	12.82 (3.47)	12.77 (3.66)	12.61 (4.15)	0.655		
Diagnosis				<0.001		
NL	486 (83.1%)	48 (72.7%)	108 (21.4%)			
CI	99 (16.9%)	18 (27.3%)	397 (78.6%)			
APOE ε4 carrier	200 (34.2%)	10 (15.2%)	355 (70.3%)	<0.001		
MMSE	28.70 (1.50)	28.61 (1.26)	24.33 (4.53)			<0.001[b,c]
Hippocampal volume	3733.04 (489.90)	3406.00 (505.02)	3065.65 (480.55)		<0.001[b]	
Amyloid PET						
Centiloid	-7.25 (6.04)	-5.48 (6.72)	81.46 (34.27)		<0.001[b,c]	
CSF						
Ptau-181	41.92 (18.04)	57.33 (33.68)	182.39 (100.50)		<0.001[a,b,c]	
Ab42	2037.12 (744.66)	2308.52 (905.44)	898.65 (319.35)		<0.001[b,c]	
Ab42/Ab40	0.11 (0.02)	0.11 (0.02)	0.05 (0.01)		<0.001[b,c]	

p1: ANOVA, Kruskal-Wallis, or chi-square
p2: ANCOVA adjusted by age, sex, and diagnosis
p3: ANCOVA adjusted by age, sex, and education.

Tukey posthoc analysis was conducted in p1 and Bonferroni posthoc analysis was conducted in p2 and p3.

a: $p < 0.05$ between A-T- and A-T+
b: $p < 0.05$ between A-T- and A+T+
c: $p < 0.05$ between A-T+ and A+T+