



Let's connect!

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BACKGROUND

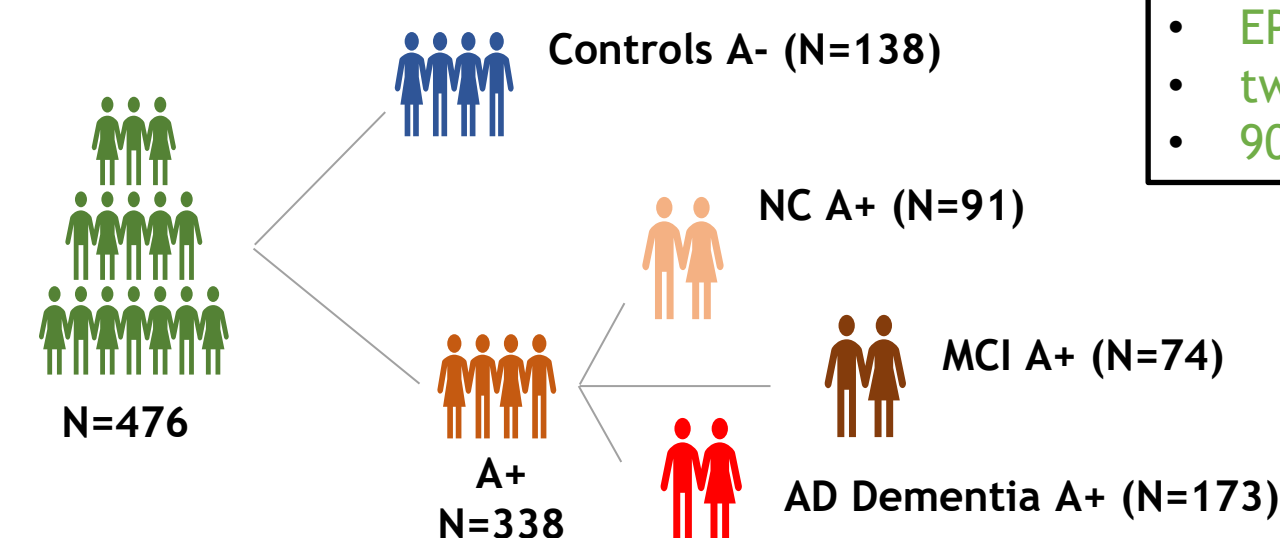
- Hypertension is a modifiable vascular risk factor linked to Alzheimer's disease (AD)¹, yet the relationship with AD pathophysiology remains unclear.

AIM

What molecular processes in the CSF proteome are associated with hypertension, and do these associations differ by sex and/or CSF amyloid and tau status?

METHODS

1 Cohort description



Alzheimer centre studies:
• ADC (n=377)
• EPAD (n=49)
• twin (n=29)
• 90+ (n=21)

2 Data processing

CSF proteomics

Untargeted · mass spectrometry · proteins with >20% missing excluded

Hypertension classification

SBP ≥140 or DBP ≥90 mmHg · hypertensive n=301 · normotensive n=175

3 Data analysis

Linear regression

Hypertension × CSF protein levels · interaction by sex, AT biomarker group, and APOE genotype

Stratified analyses

Repeated analyses · Stratified results for sex, AT biomarker group, and APOE genotype

GO pathway enrichment

Molecular process characterisation · FDR correction

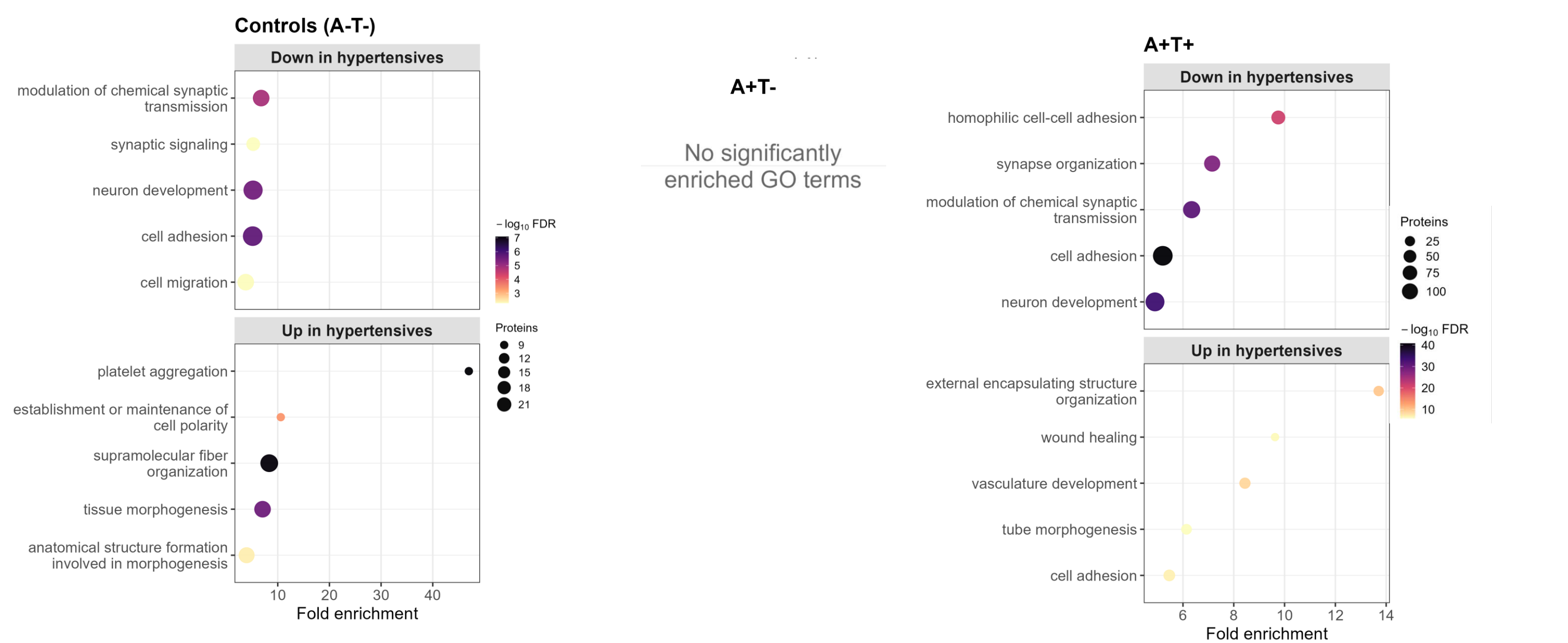
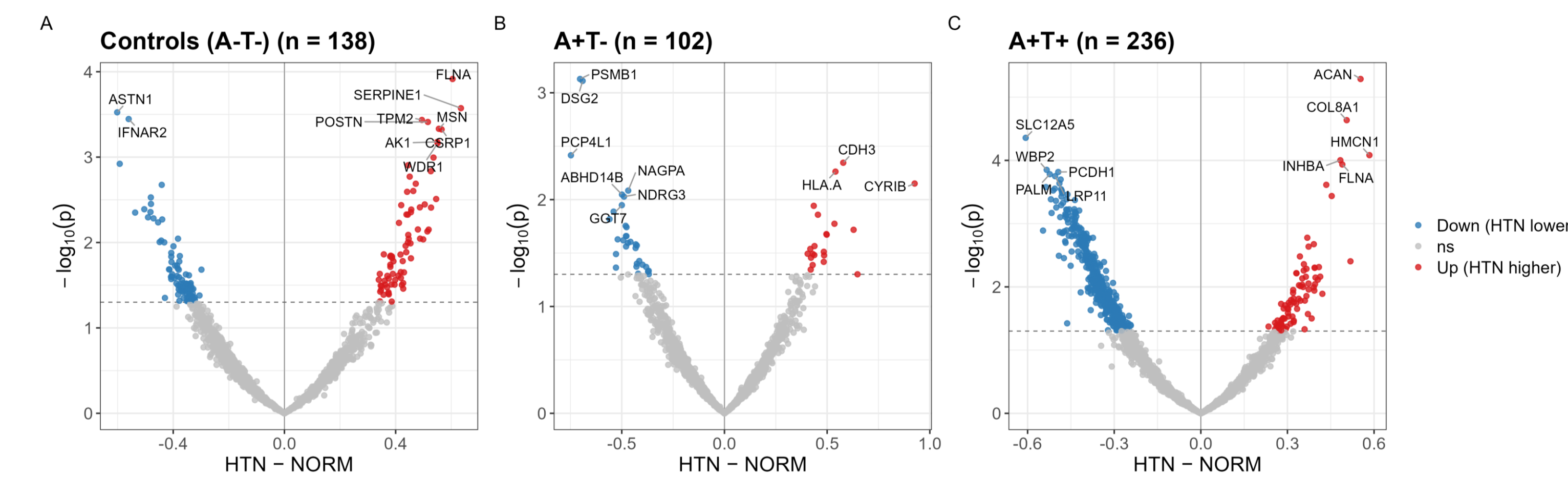
RESULTS

Characteristic	Overall N = 476 ¹	Normotensive N = 175 ¹	Hypertensive N = 301 ¹	p-value
Age	65.6 (9.5)	63.3 (9.5)	66.9 (9.2)	
Sex				0.385
f	222 (46.6%)	77 (44.0%)	145 (48.2%)	
m	254 (53.4%)	98 (56.0%)	156 (51.8%)	
Diagnosis				0.039
Control	138 (29.0%)	62 (35.4%)	76 (25.2%)	
Dementia	173 (36.3%)	51 (29.1%)	122 (40.5%)	
MCI	74 (15.5%)	26 (14.9%)	48 (15.9%)	
NC	91 (19.1%)	36 (20.6%)	55 (18.3%)	
APOE ε4 carrier				0.696
Non-carrier	202 (44.1%)	77 (45.3%)	125 (43.4%)	
Carrier	256 (55.9%)	93 (54.7%)	163 (56.6%)	
Unknown	18	5	13	
Antihypertensive medication				<0.001
Unknown	129 (28.0%)	30 (18.1%)	99 (33.7%)	
Known	16	9	7	
Amyloid/tau profile				0.054
A+t-	102 (21.4%)	36 (20.6%)	66 (21.9%)	
A+t+	236 (49.6%)	77 (44.0%)	159 (52.8%)	
Control	138 (29.0%)	62 (35.4%)	76 (25.2%)	

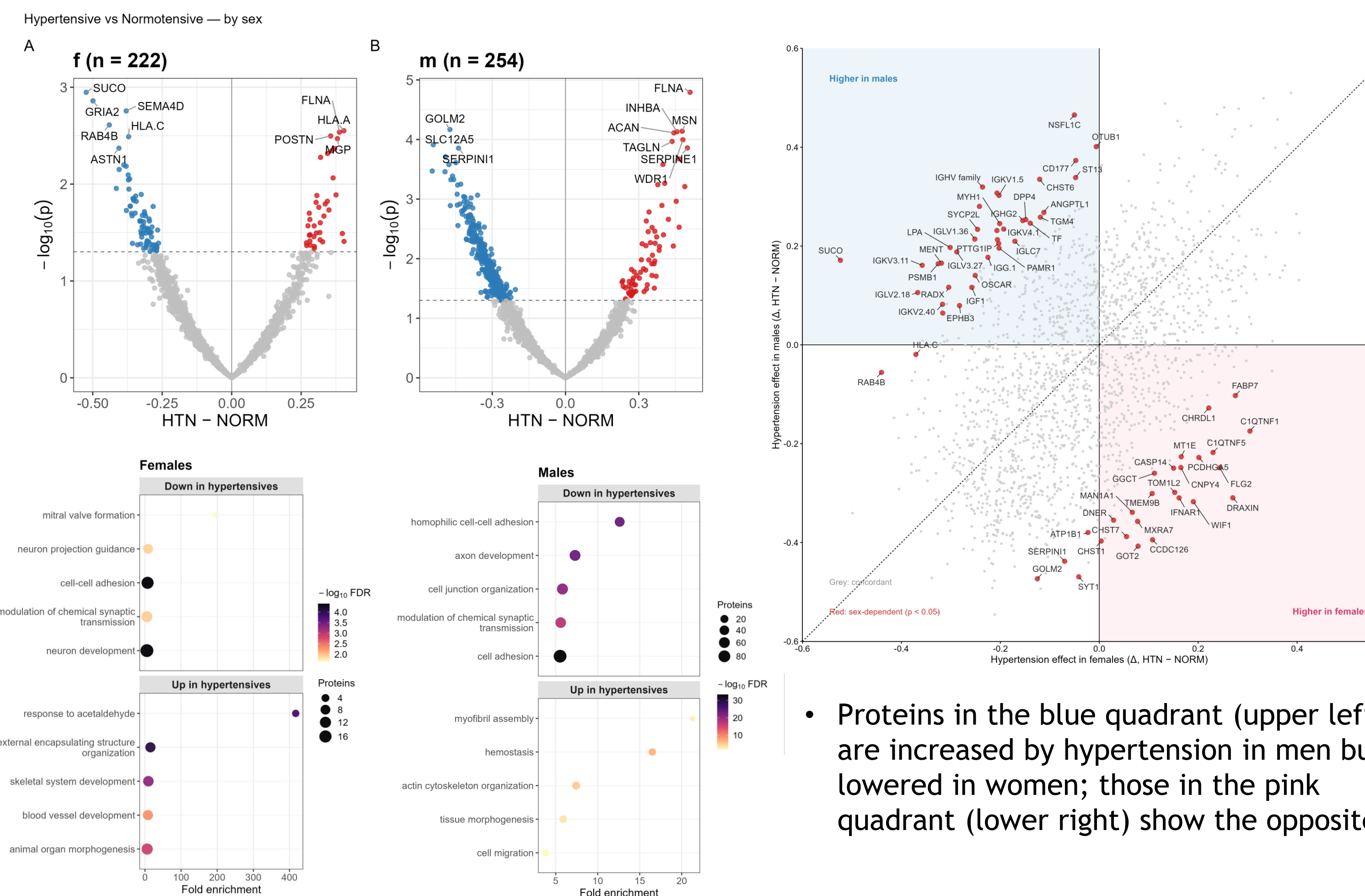
¹Mean (SD); n (%)

RESULTS

- Interaction effects of hypertension on CSF protein levels across amyloid/tau biomarker groups

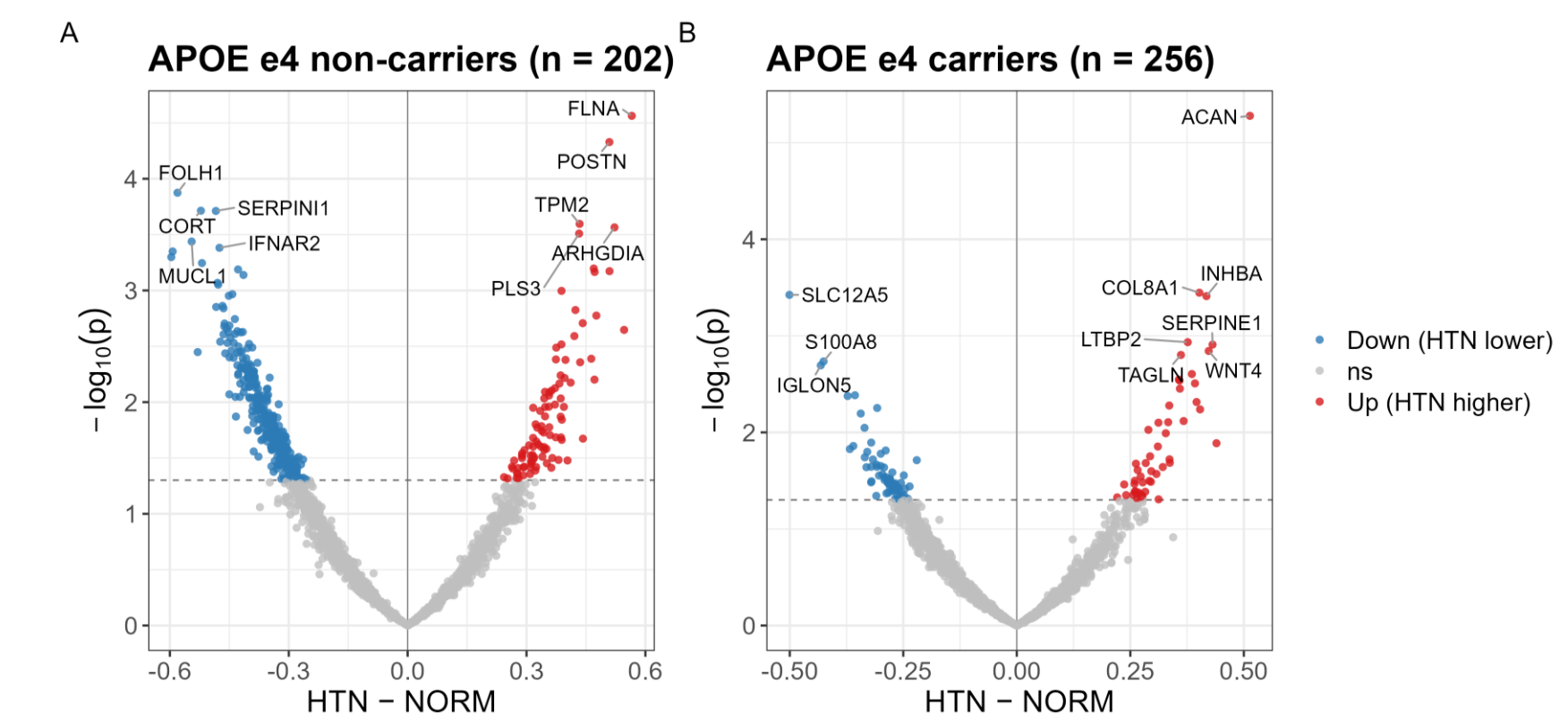


- Hypertension-associated protein changes are more pronounced in males. Most proteins respond concordantly across sexes, while a sex-dependent subset ($p < 0.05$) reverses direction.



RESULTS

- Interaction effects of hypertension on CSF protein levels across APOE ε4 carriers and non-carriers



CONCLUSION

- Hypertension is associated with alterations in the CSF proteome, with the strongest effects observed in individuals with abnormal amyloid and tau biomarkers (A+T+).
- Several hypertension-related protein changes differ by sex and APOE ε4 status.
- These findings provide insight into potential molecular pathways linking hypertension to AD, supporting the importance of hypertension as a modifiable risk factor and a potential target for early interventions in AD.

- Proteins in the blue quadrant (upper left) are increased by hypertension in men but lowered in women; those in the pink quadrant (lower right) show the opposite.