

High-Fat Feeding Alters CSF A β 42 in an ApoE4-Dependent Manner

INTRODUCTION

- High fat feeding (HFF) is a risk factor for Alzheimer's disease (AD) but this link is more tenuous in individuals with the AD risk gene APOE4 (E4)¹
- Low levels of CSF A β 42 indicate that A β 42 proteins are being trapped in plaques in the brain, a sign of Alzheimer's disease pathology²
- Long term dietary patterns are associated with changes of CSF A β 42, but this has not been studied with a single meal effect³

METHODS

- As part of the Meal and Memory study (CT# NCT03070535), 78 cognitively healthy older adults ingested high- and low-fat breakfasts (HFM & LFM, respectively, each 700 calories) 3-5 weeks apart after an overnight fast (Figure 1)
- APOE genotype and meal intake data were collected, blood samples taken at baseline and 6 time points, and CSF sample was taken 4 hours post-prandially
- APOE status was analyzed via PCR amplification
- MSD V-Plex A β Peptide Panel 1 was performed on CSF samples, 34 participants had data for both meals

Table 1. Participant demographics stratified by E4 status.

	E4 Non-Carrier	E4 Carrier
N (n female)	39 (22)	39 (22)
Age (years)	66.6 $\pm$ 6.8	64.1 $\pm$ 6.7
BMI	26.2 $\pm$ 4.1	26.4 $\pm$ 5.1
HDL (mg/dL)	61.2 $\pm$ 14.2	61.7 $\pm$ 16.3
LDL (mg/dL)	116.9 $\pm$ 27.9	122.8 $\pm$ 24.4
TG (mg/dL)	91.9 $\pm$ 36.0	83.8 $\pm$ 40.7

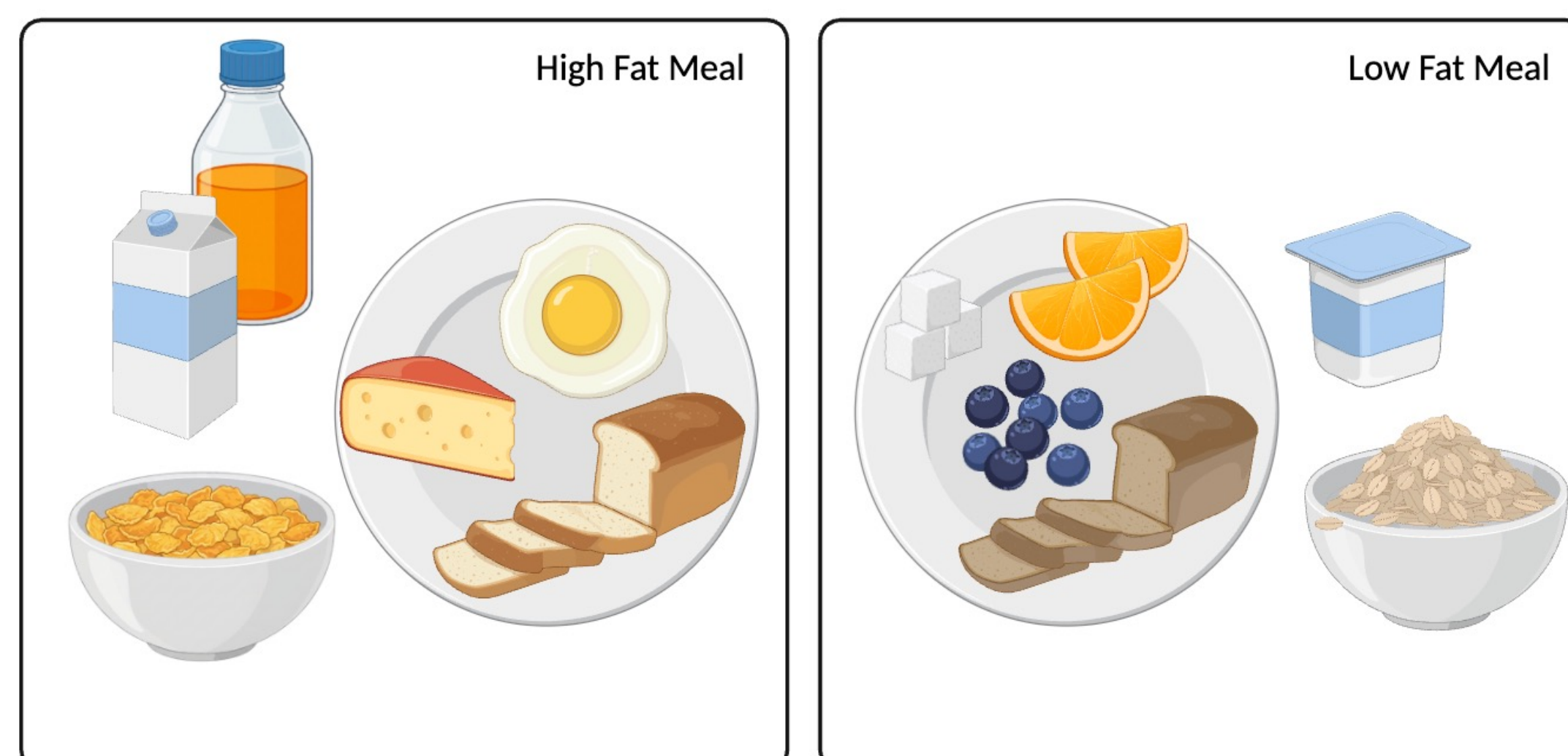


Figure 1. High-fat and low-fat breakfasts.

Table 2. ANOVA results for the effects of APOE ϵ 4 Status and Sex on CSF A β 42 levels in LFM and HFM.

Predictor	LFM		HFM	
	F Statistic	p-value	F Statistic	p-value
Sex	10.03	0.004	6.78	0.01
E4	18.63	<0.001	14.63	<0.001
Sex : E4	2.67	0.11	2.24	0.14

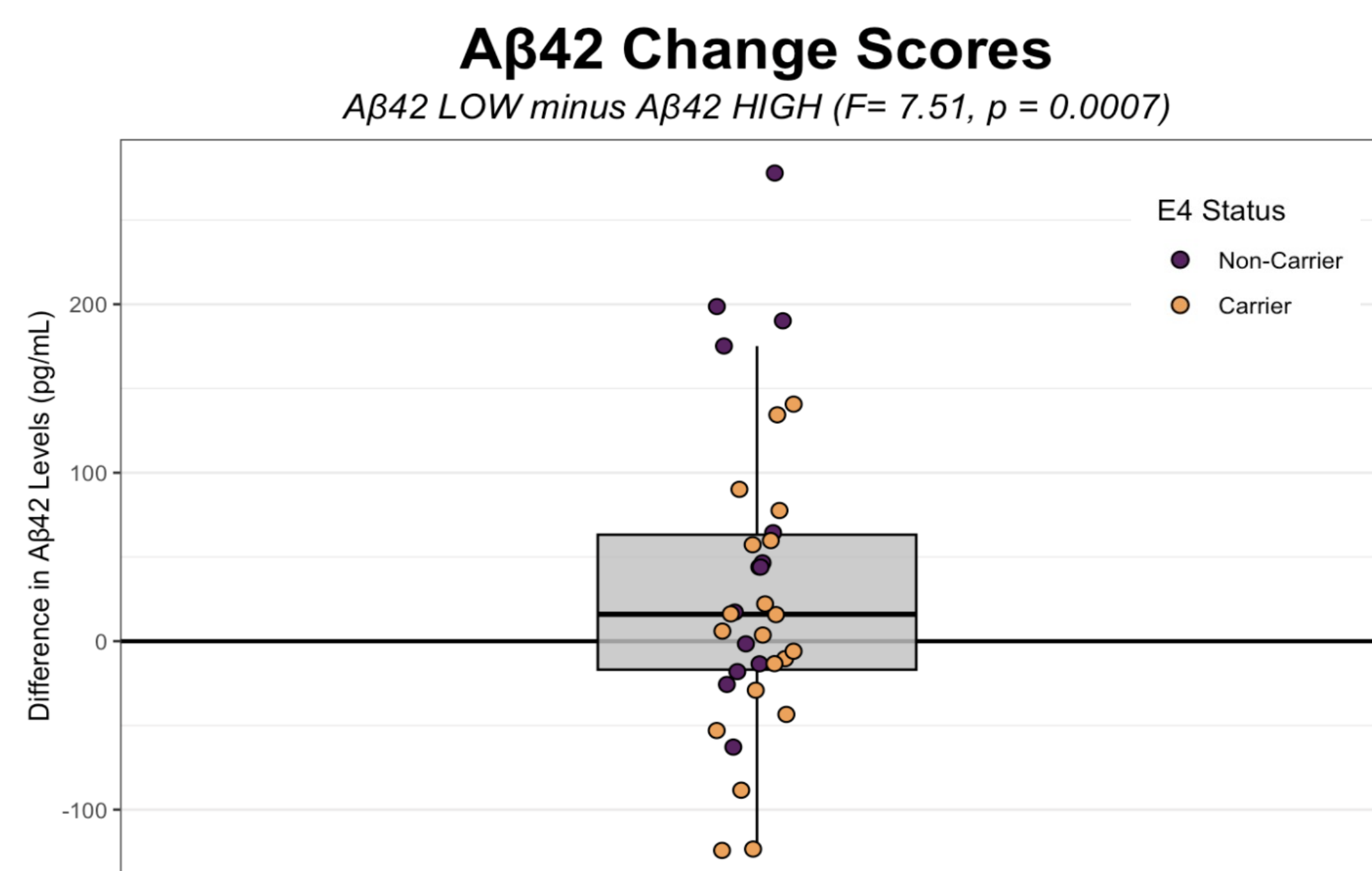


Figure 2. Boxplot showing the distribution of A β 42 change scores stratified by E4. The difference between LFM and HFM is statistically significant ($p = 0.0007$). On average, LFM produced 34.7 pg/mL more A β 42 than HFM.

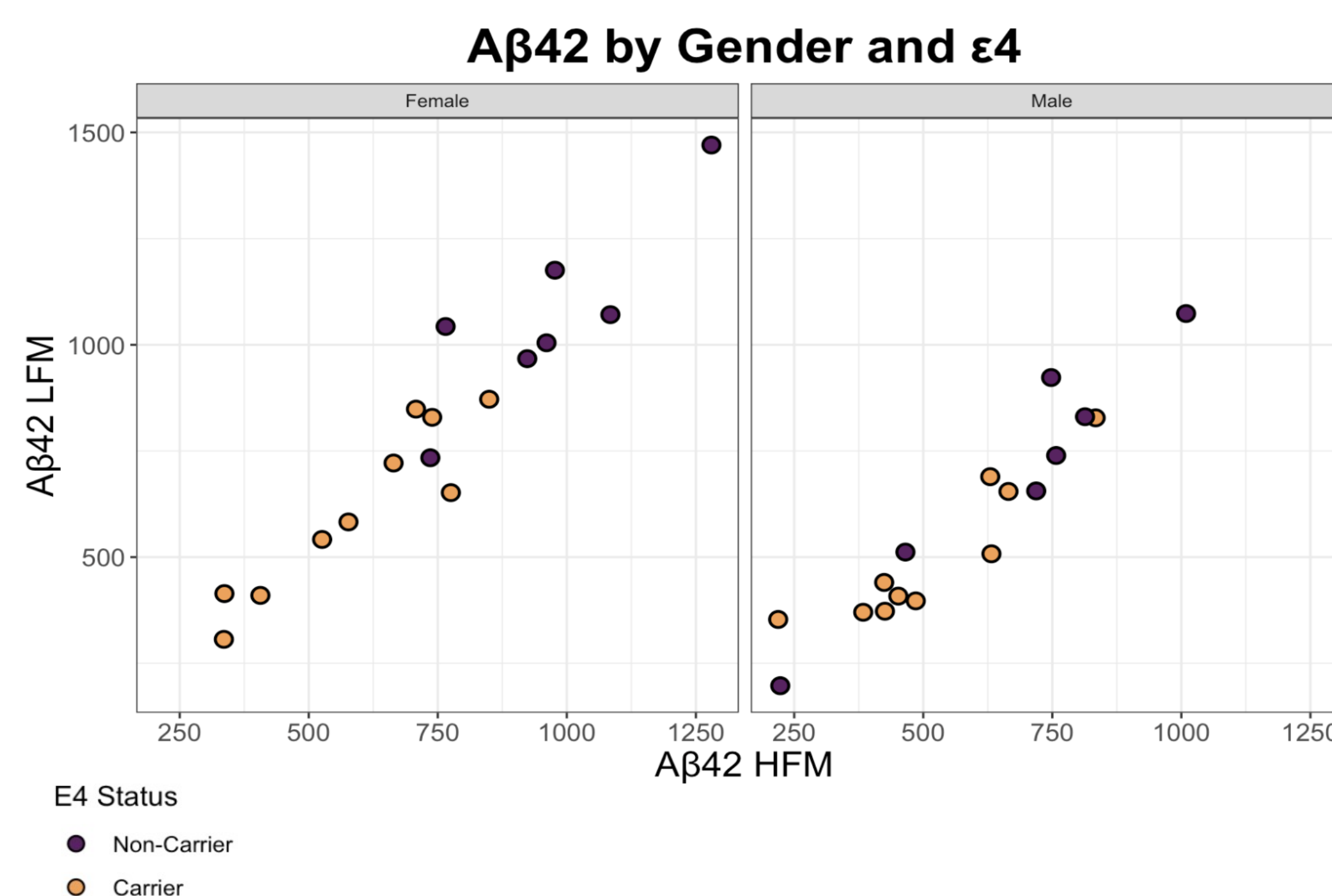


Figure 3: Relationship between A β 42 HFM and A β 42 LFM measurements stratified by gender and E4 carrier status. Scatter plots comparing A β 42 values between HFM and LFM for females (left) and males (right).

Table 3. Means and standard deviations of change scores stratified by sex and E4 status.

Sex	E4 Status	N	Ab42 Change pg/mL	
			Mean	St Dev
Female	Non-Carrier	7	105.7	114.6
	Carrier	7	28.1	78.2
Male	Non-Carrier	10	26.1	72.5
	Carrier	10	-12.5	73.4

DISCUSSION

- There was a significant difference in A β 42 between HFM and LFM (Figure 2): *Switching from LFM to HFM moved marker in more pathologic direction* (higher to lower levels).
- E4 carriers have significantly lower A β 42 levels in this study than non-carriers despite being healthy control subjects, and were less affected by meal change than E4 non-carriers.
- We show significant sex-based differences in A β 42 concentrations in this study that seemed to interact with APOE genotype: Non-carrier females had the highest change score going from LFM to HFM while E4 males had the lowest change score.

LIMITATIONS

- We did not capture a pre-intervention A β 42 sample, limiting our ability to assess true starting thresholds.
- Several participants lacked samples for both meal conditions, reducing the statistical power for paired and subgroup tests.

FINANCIAL DISCLOSURES

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