

## Neurofilament light chain (NfL) and cognitive performance in selected siblings from the CATSLife study

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### INTRODUCTION

Neurofilament light chain (NfL) is elevated with neurological disease, e.g., multiple sclerosis, Alzheimer's disease [1]. NfL is a marker of axonal integrity, and positively related to the degree of damage [1]. NfL variations among healthy young adults may relate to executive function performance [2]. We evaluated NfL in siblings who differed on *APOE* genotype and associations with IQ and general cognitive ability (GCA) in a pilot sample of adults 28-37 years in the Colorado Adoption/Twin Study of Lifespan behavioral development and cognitive aging (CATSLife).

### METHODS

- N = 34 (14 sibships with 2+ sibs);
  - 3 Full sibling sets, 4 incomplete sibships,
  - 5 DZ pairs, 6 MZ pairs
  - 44% female
  - Age = 30.87 years (SD=3.13; range 28-37 years)
  - All self-reported as white, non-Hispanic
- Selected on health and/or *APOE* E4 status
  - Neuroinflammatory health conditions (N = 5)
  - APOE* genotype:
    - 18 Non-E4, 16 E4 carriers
- Quanterix Simoa assays of neurofilament light (NfL)
  - Measured in duplicate

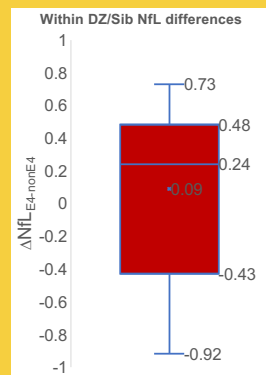
### RESULTS

- NfL distribution: 1.3 - 22.3 pg/ml
- MLM regression of log-transformed NfL, accounted for sibling type suggests NfL higher in
  - Cases (health conditions), Males, Age, & *APOE* E4 carriers (see Table 1)
  - 7 Discordant DZ/Siblings for *APOE* E4 show a tendency for higher NfL [Median = .24; exp(.24) = 1.27 pg/ml] (see Figure 1).
- MLM analysis of FSIQ suggests trend significance for E4 x NfL ( $p = .0659$ ) [c.f. Figures 2C & 3].
- MLM analysis of GCA suggests trend significance for main effect of NfL ( $p = .0963$ ) (c.f. Figure 2B).

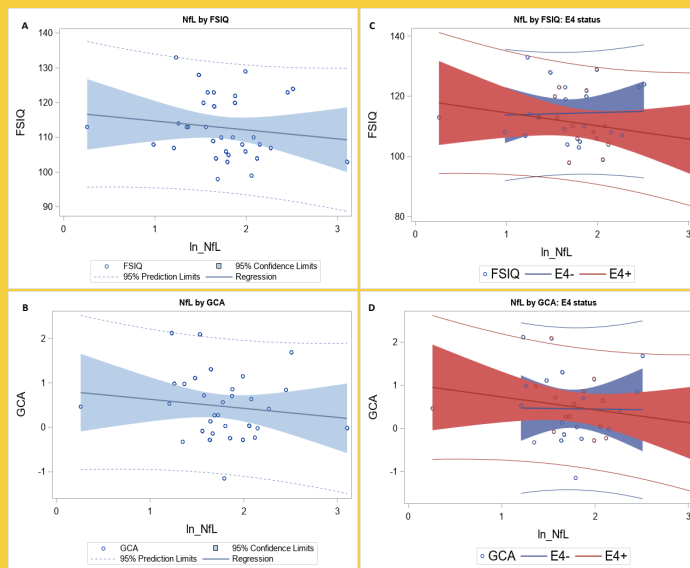
In a pilot study, we observed patterns of higher NfL in Males, with Age, and *APOE* E4 (Table 1, Figure 1). Higher NfL corresponds with lower general cognitive ability (GCA) & Full Scale IQ, especially in *APOE* E4 carriers (Figure 2).

**Table 1. Expected values of ln(NfL), adjusted for sibling type.**

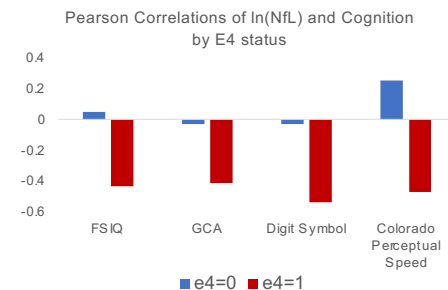
Effect	B	SE	Exp(B)
Intercept	1.60	0.16	4.97
Age	0.02	0.03	1.02
Male	0.25	0.16	1.29
Case	0.09	0.22	1.09
E2	-0.09	0.28	0.91
E4	0.17	0.17	1.18



**Figure 1.** Within DZ/Sibling differences in ln(NfL) between *APOE* E4 carriers and non-carriers (N=7 pairs).



**Figure 2.** (A, B) Higher ln(NfL) is associated with lower Full Scale IQ (FSIQ) and general cognitive ability (GCA); (C, D) *APOE* E4 carriers show stronger relationship of NfL with FSIQ and GCA.



**Figure 3.** Correlations of ln(NfL) and cognition are stronger among *APOE* E4 carriers ( $r$ 's = -.42 to -.54) than non-E4 carriers ( $r$ 's = -.03 to .25), partialled for age, sex, case status. Digit Symbol and Colorado Perceptual Speed are consistent in effect with GCA and FSIQ.

### DISCUSSION

- Our preliminary associations with general ability and speed are in keeping with Beste et al. (2019) [2] who observed that lower NfL was associated with better cognitive performance on a go/no-go task.
- In this pilot study, the observed NfL associations with general cognitive ability, and IQ, particularly among *APOE* E4 carriers, suggests NfL may be a salient biomarker of cognitive functioning by early- to mid-adulthood.

### FINANCIAL DISCLOSURE

NIH AG046938

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### REFERENCES

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