



Amsterdam Neuroscience

Glial Fibrillary Acidic Protein and Neurofilament Light reference intervals in cognitively normal individuals



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Introduction

- Plasma neurofilament light (NfL) and glial fibrillary acidic protein (GFAP) have utility for the diagnosis and prognosis of many neurological disorders.
- Plasma NfL and GFAP concentrations are known to be influenced by non-neurological factors age, sex, body mass index (BMI), and kidney function.
- These factors may make interpretation of plasma NfL and GFAP concentrations difficult.

Methods

Type of cohort	Data from	Participants	Available covariates
Reference cohorts	NTR	Cognitively normal (n=6778)	age, sex, BMI, eGFR
	ADC	SCD Aβ- (n=510)	age, sex, BMI
	LASA	Cognitively normal (n=370)	age, sex, BMI, eGFR
	100-plus	Cognitively normal (n=300)	age, sex
Validation cohort	LLS	Cognitively normal (n=370)	age, sex, BMI

Analyses (reference intervals)

1. Fit generalized additive models for locations, shape, and scale over age
2. Add sex, BMI, and/or eGFR and use likelihood ratio test to determine added value of covariates
3. Define 50th (median), 80th, 95th, 97.5th, and 99th percentiles adjusted for relevant factors

Analysis (validation)

1. Distribution of plasma NfL and GFAP in the validation cohort are partitioned within each percentile range defined in the reference intervals
2. A X² test is used to determine if observed proportion per percentile range differs from expected proportion

Conclusion

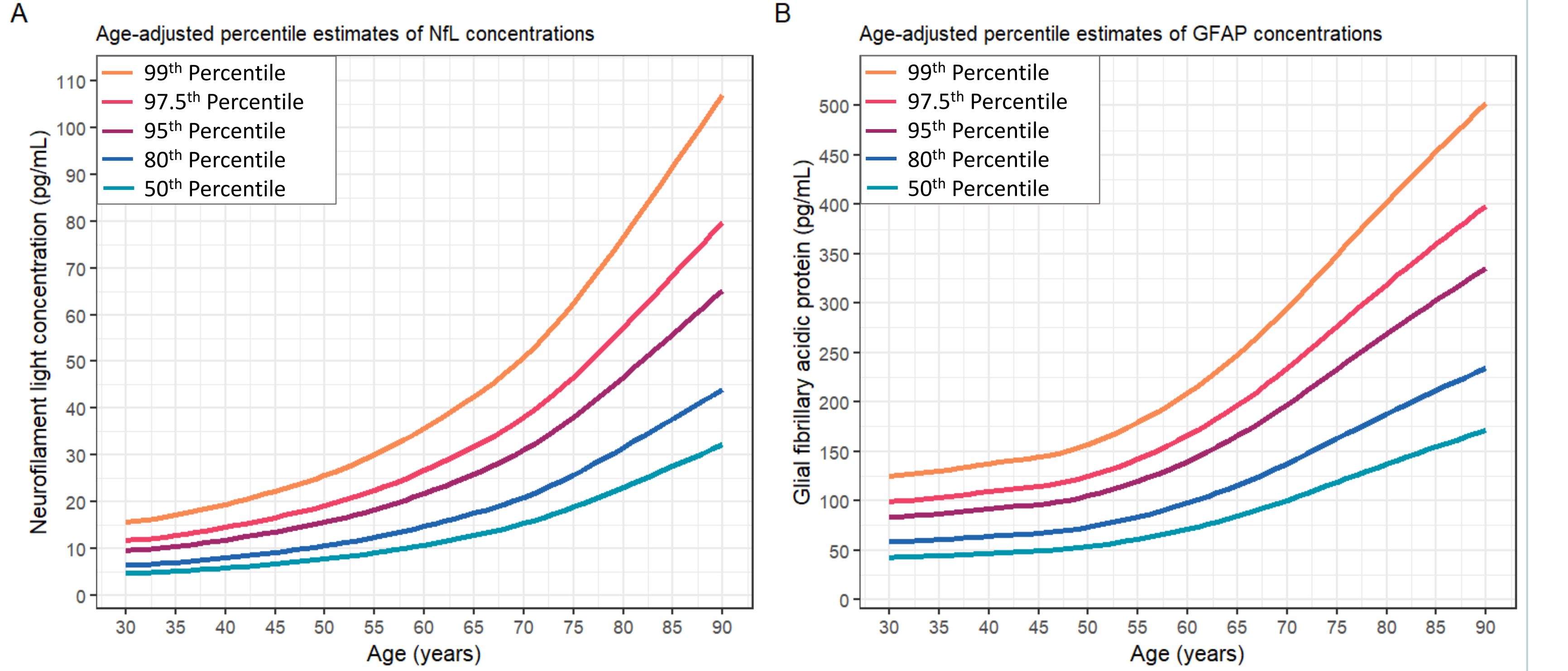
The established reference intervals can be used to identify normal or abnormal biomarker concentrations in the context of an individual’s demographic profile. This will aid the use of plasma NfL and GFAP in clinical routine for neurological diseases.

Abbreviations
ADC: Amsterdam Dementia Cohort; BMI: body mass index; eGFR: estimated Glomerular Filtration Rate; GFAP: glial fibrillary acidic protein; LASA: Longitudinal Aging Study Amsterdam; LLS: Leiden Longevity Study; NfL: neurofilament light; NTR: Netherlands Twin Register.

Aim

Develop reference intervals for plasma NfL and GFAP over age, accounting for sex, BMI, and kidney function; implement these reference intervals in a web-based app.

Results



Covariate	NfL	GFAP
BMI	↑ BMI = ↓ plasma NfL	↑ BMI = ↓ plasma GFAP
Kidney function	↓ eGFR (worse kidney function) = ↑ plasma NfL	↓ eGFR (worse kidney function) = ↑ plasma GFAP
Sex	No effect	Higher in females

Neurofilament Light (in pg/mL):

24

Glial Fibrillary Acidic Protein (in pg/mL):

150

Patient's age:

30

72

90

Sex (optional)

Female

Body Mass Index (optional):

20

estimated Glomerular Filtration Rate (in mL/min/1.73m2) (optional):

50

Case study

Patient profile: 72-year-old woman with a normal BMI (20) and moderate kidney dysfunction (eGFR 50).

Plasma NfL: 24 pg/mL

Plasma GFAP: 150 pg/mL

If sex, BMI, and kidney function are not accounted for, the percentile estimates are **83 (NfL)** and **81 (GFAP)**, which may be cause for concern.

Once accounting for covariates, percentile estimates are **67 (NfL)** and **68 (GFAP)**, much less concerning.