

Substance use influences brain structural remodeling in young adulthood



Anna Jacobsen, MSc

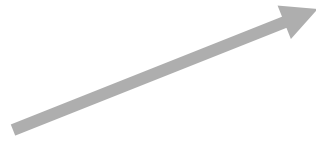
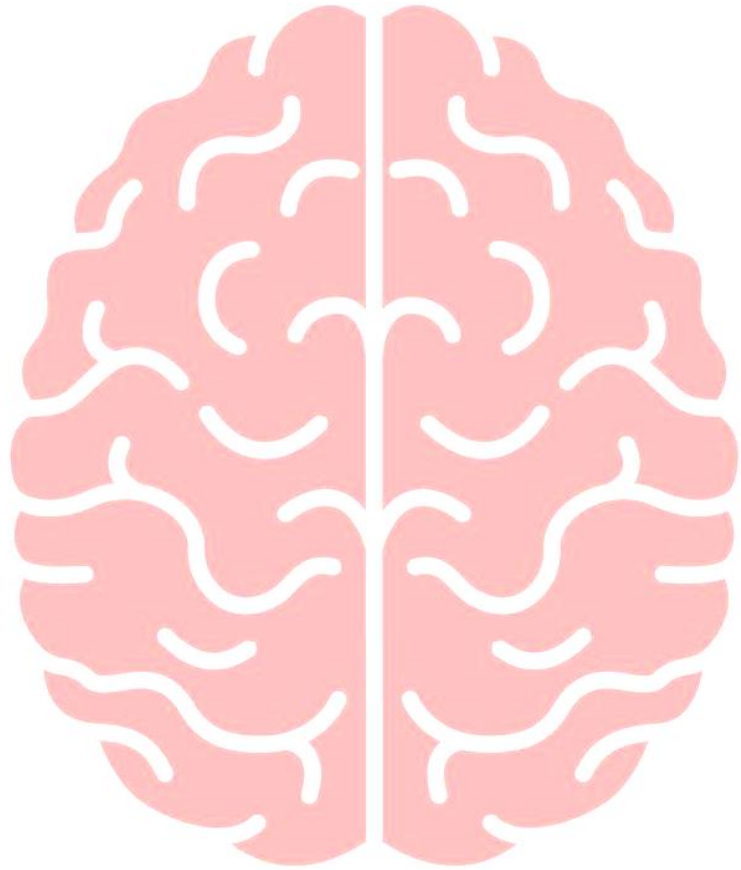


University Hospital
of Psychiatry
Zurich

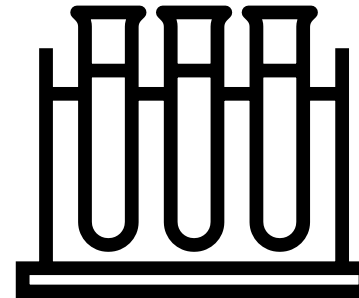
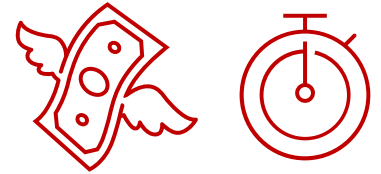


Universität
Zürich^{UZH}

How do we quantify **brain health**?

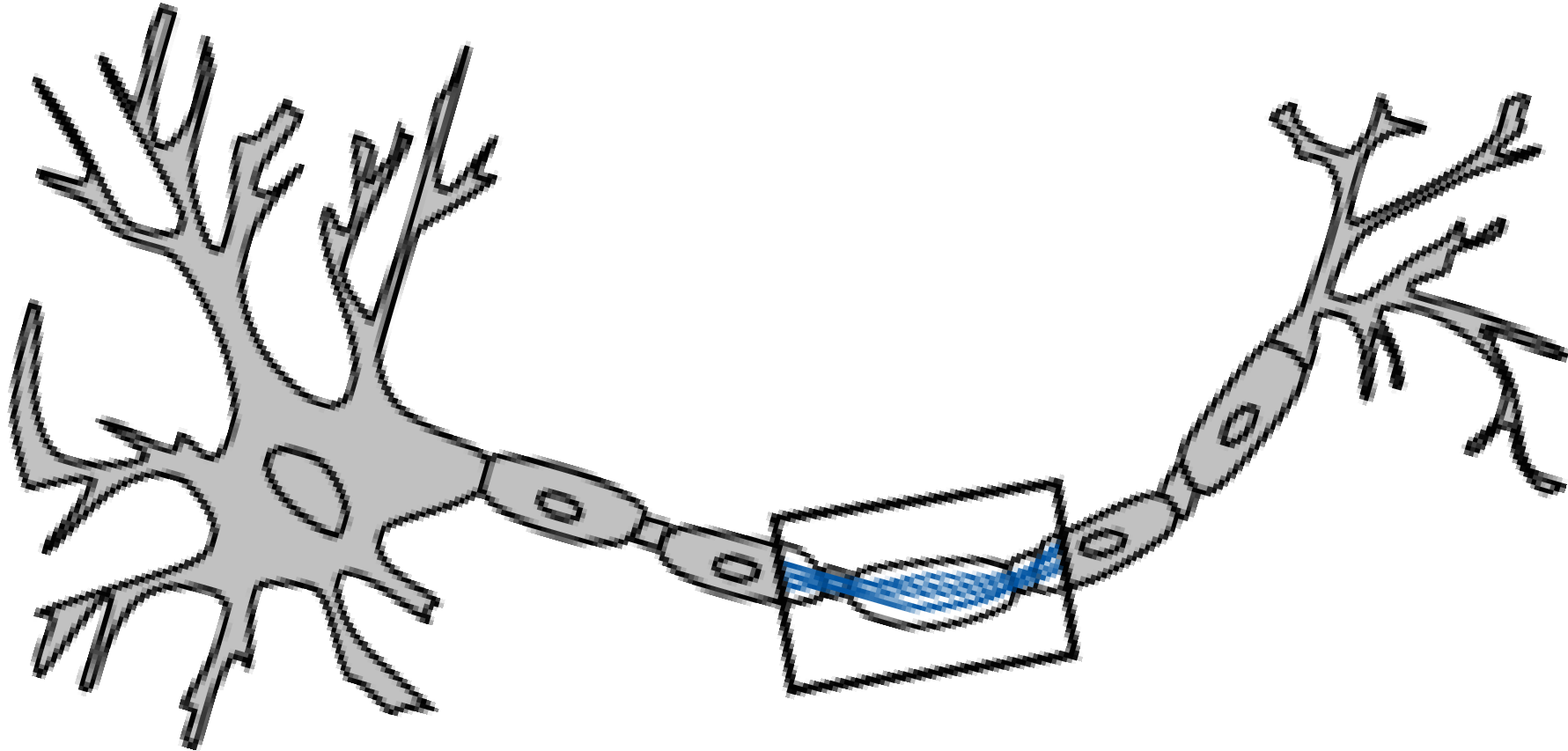


MRI scans

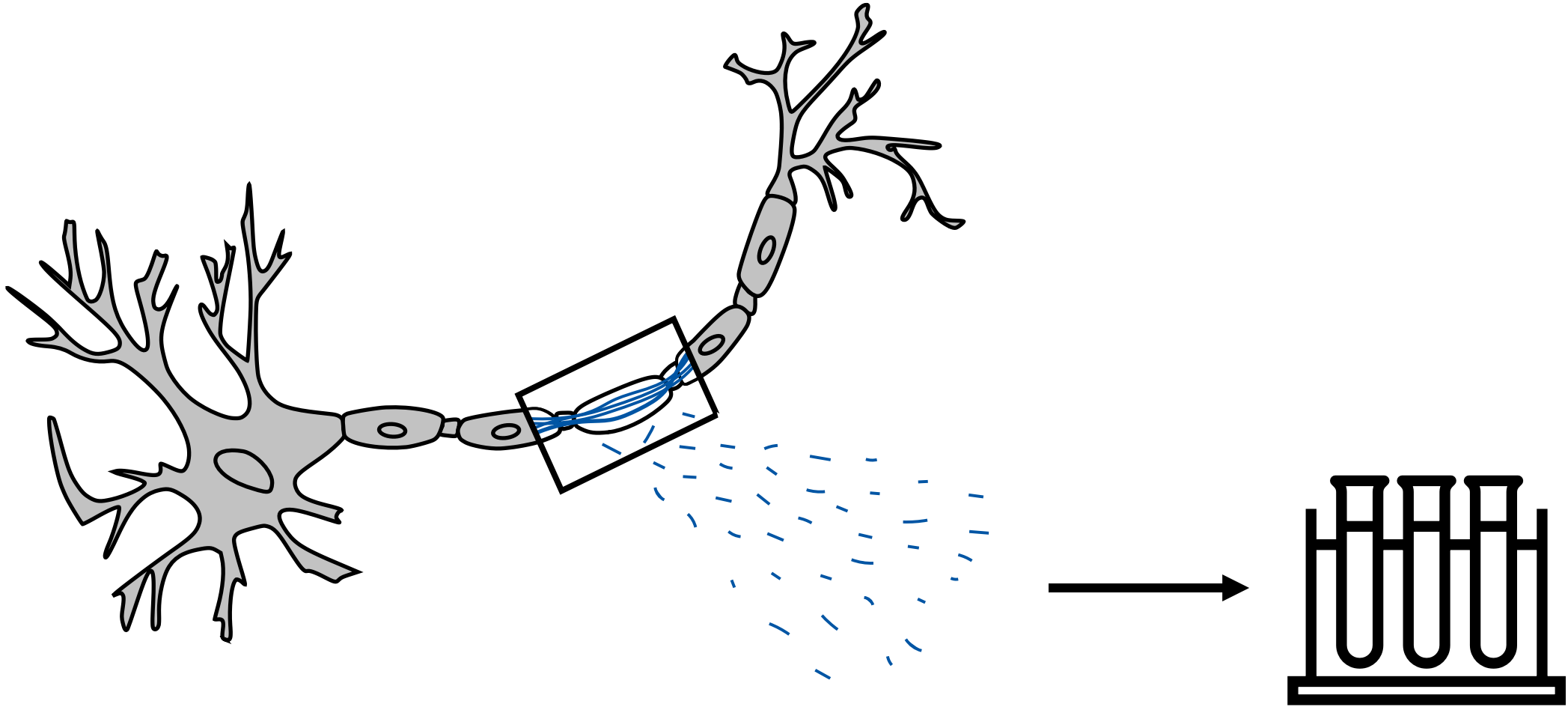


Blood tests...?

Neurofilaments provide structural support to neurons

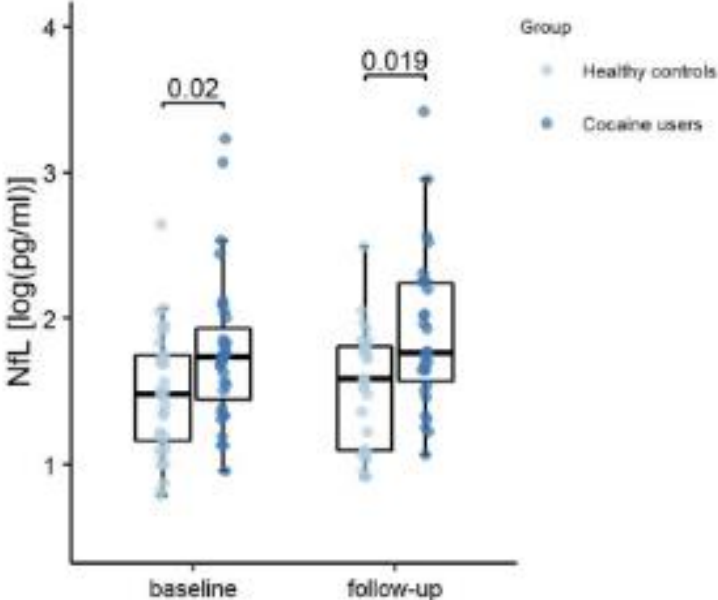


Neurofilament light chain (**NfL**) is measured in blood



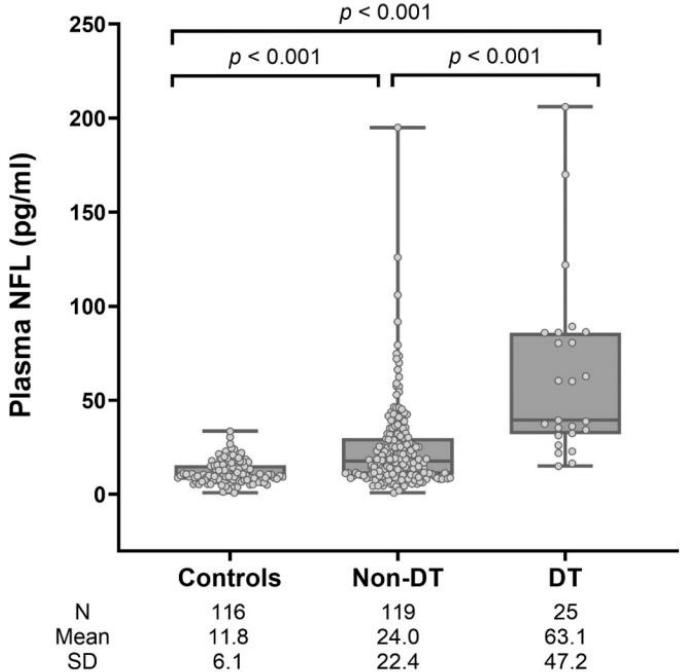
Elevated blood NfL associated with poor substance use disorder outcomes in adults

Chronic cocaine users



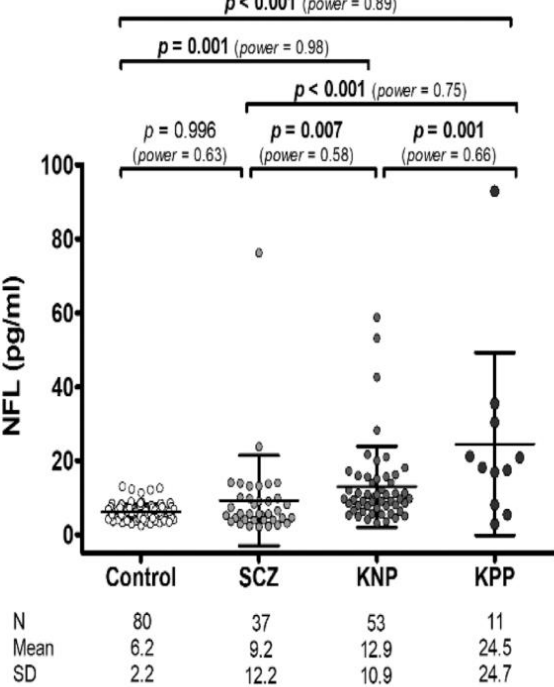
Bavato et al. *Molecular Neurobiology* (2023)

Alcohol users with delirium tremens



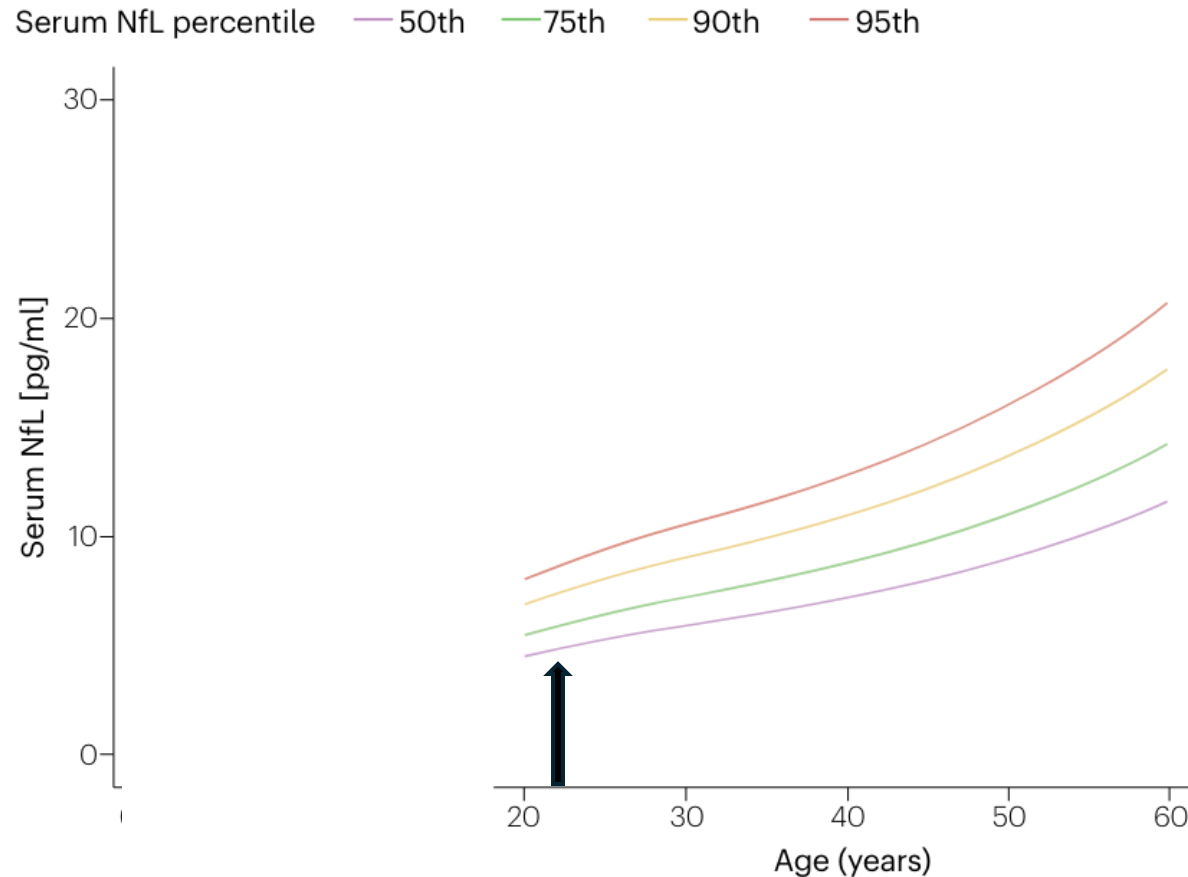
Hou et al. *Progress in Neuro-Psychopharmacology and Biological Psychiatry* (2025)

Ketamine users with psychosis



Chung et al. *Asian Journal of Psychiatry* (2024)

NfL levels change across the lifespan

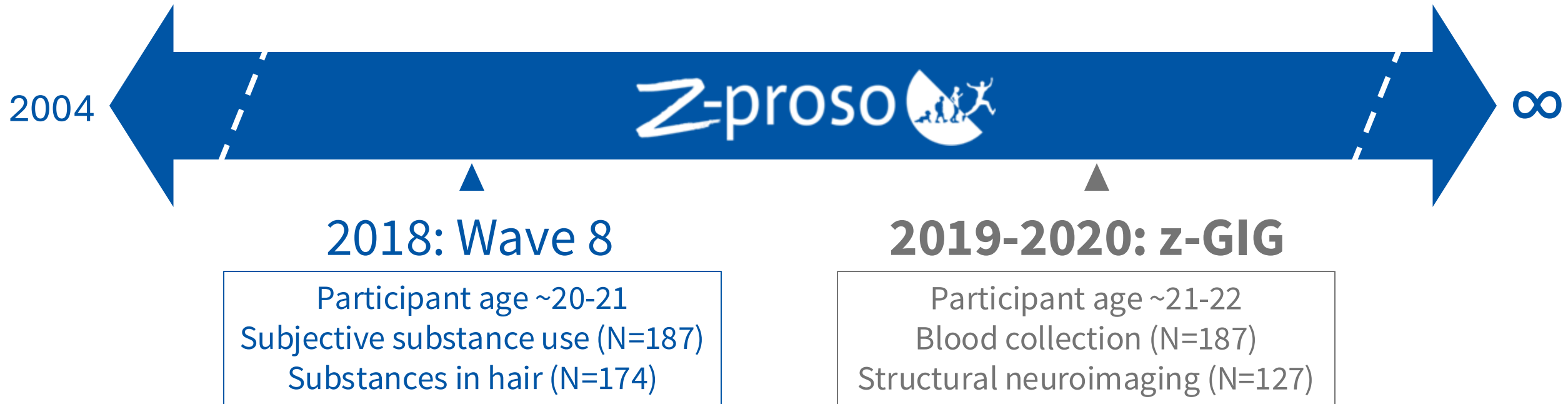


Khalil et al. *Nature Reviews Neurology* (2024)

Fig. 3 | Age-related percentiles for serum NfL. Curves were generated by the use of a generalized additive model for location, scale and shape to model the non-linear association of serum neurofilament light chain (NfL) concentration with age in healthy individuals aged 0–20 years (left) and 20–65 years (right)^{16,97}. Reproduced with permission from ref. 97, Elsevier.

z-GIG cohort:

z-proso subsample with neurobiological measures



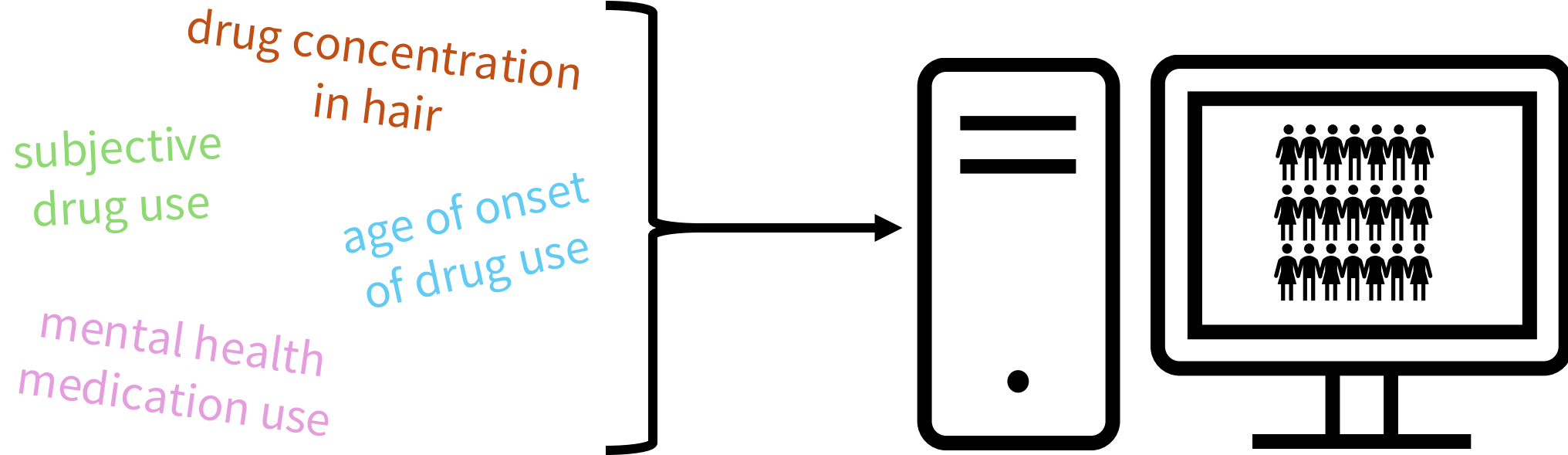
Research question #1:

How does **substance use**
influence peripheral NfL
levels in early adulthood?



Characterizing substance use patterns

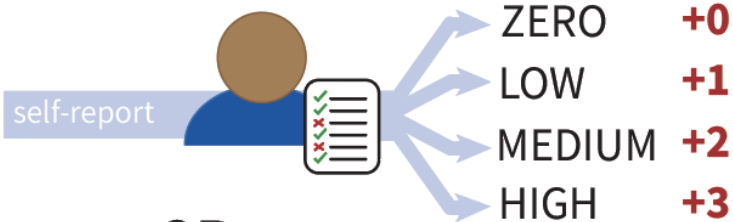
100+ substance use variables!



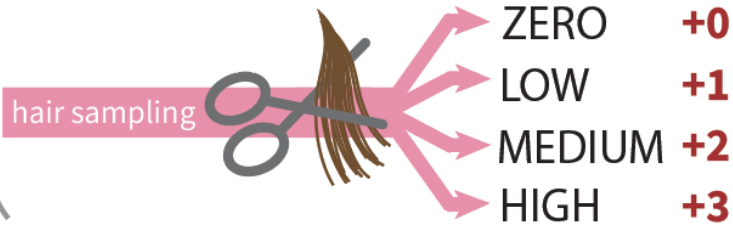
Propensity score weighting
to capture individual behavior

SUBSTANCE USE *SUMMARY SCORES*

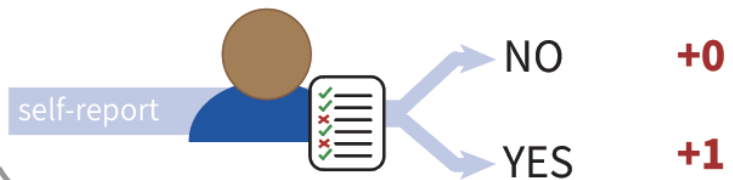
3-month substance use



OR



12-month substance use



Age of first substance use



Alcohol: liquor, beer/wine/alcopop

Tobacco: cigarettes

THC: THC, CBN

CBD: CBD, cannabis substitutes

Serotonergic drugs:

LSD, psilocybin, MDMA (ecstasy), 2C

Stimulants:

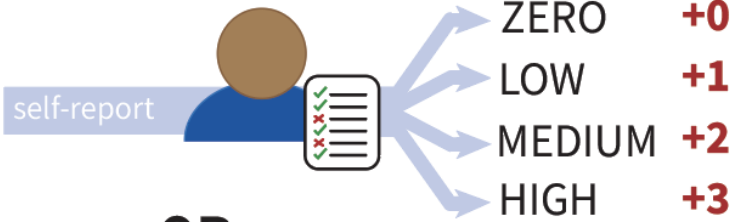
cocaine, methamphetamine, methylphenidate

Opioids:

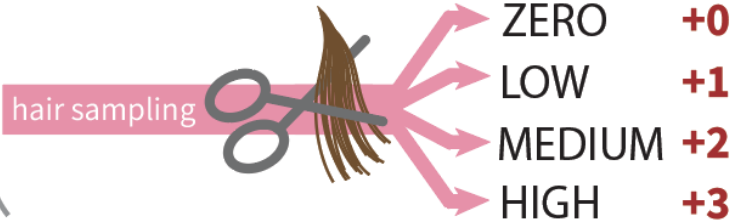
codeine, fentanyl, tramadol, pethidine, morphine,
hydromorphone, oxycodone, oxymorphone,
dextromethorphan

SUBSTANCE USE *SUMMARY SCORES*

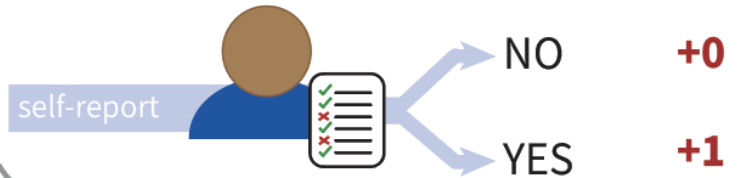
3-month substance use



OR



12-month substance use



Age of first substance use



SUBSTANCE USE *PROPENSITY SCORES*

TREATMENT

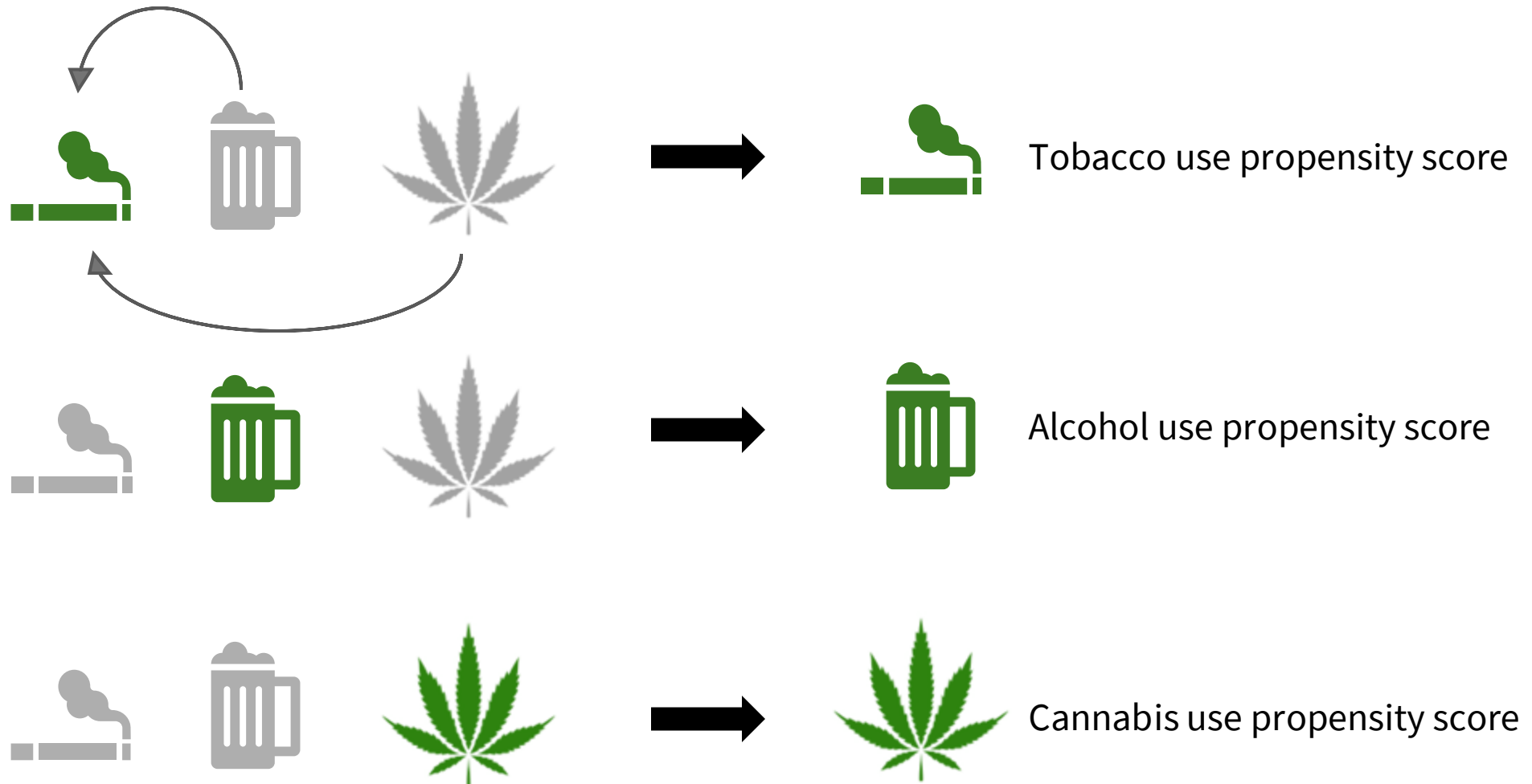


ZERO
LOW
MEDIUM
HIGH

CONFOUNDERS

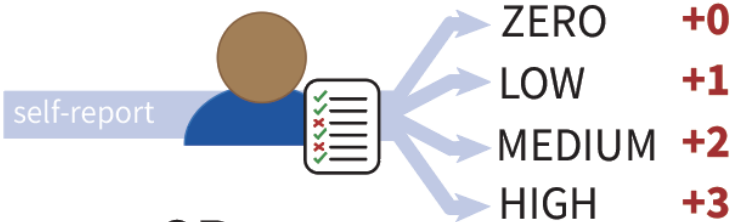


Propensity scores describe individual likelihood to use one drug class *given use of all other drug classes*

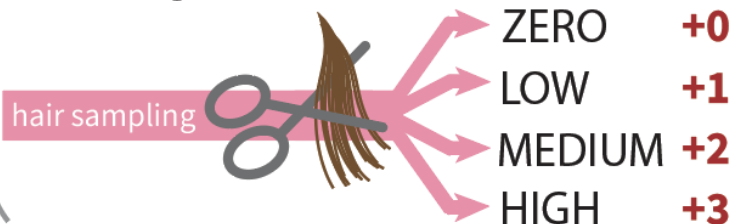


SUBSTANCE USE *SUMMARY SCORES*

3-month substance use



OR



12-month substance use



Age of first substance use



SUBSTANCE USE *PROPENSITY SCORES*

TREATMENT



ZERO
LOW
MEDIUM
HIGH

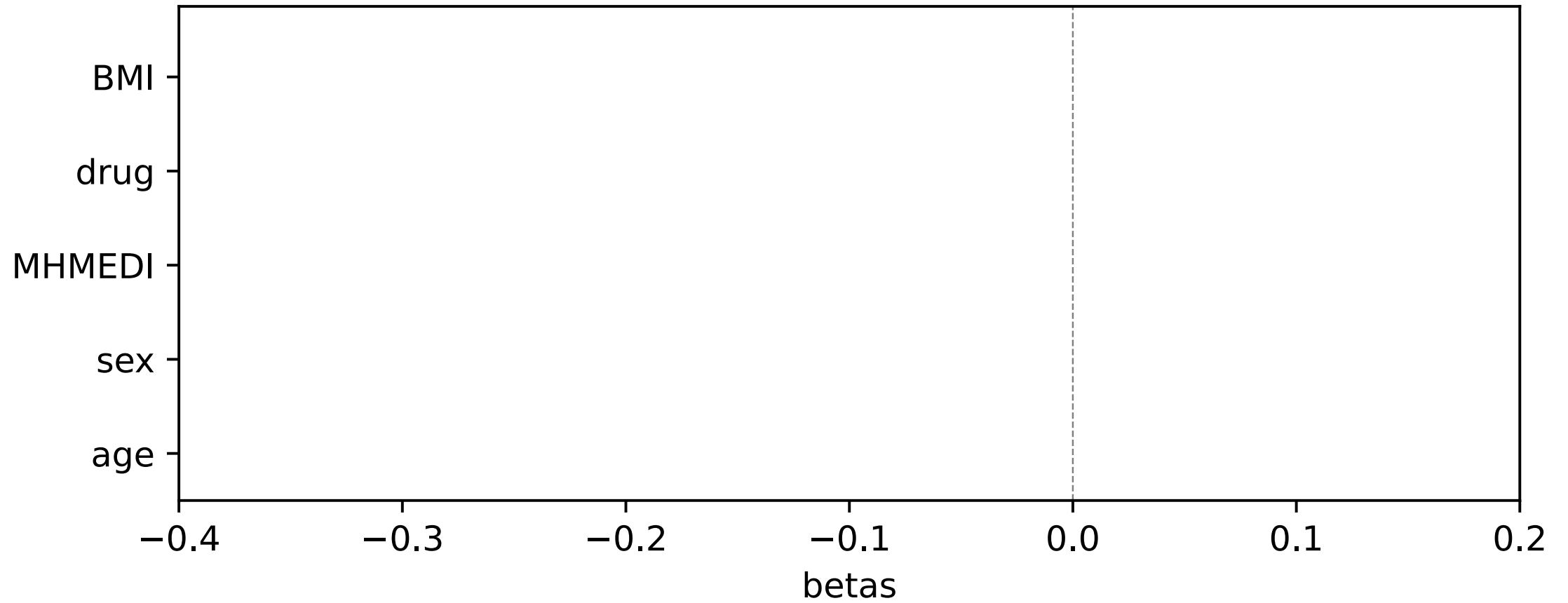
CONFOUNDERS



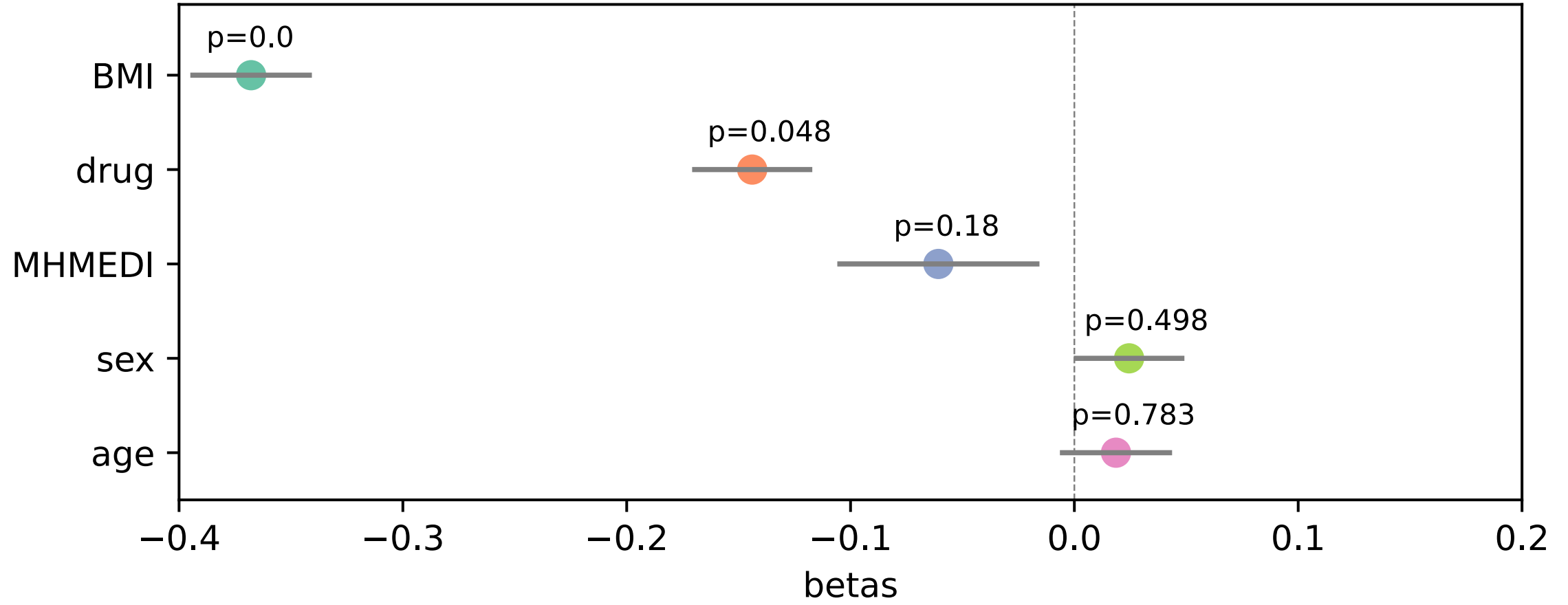
*INVERSE PROBABILITY WEIGHTED
LEAST SQUARES LINEAR REGRESSION*



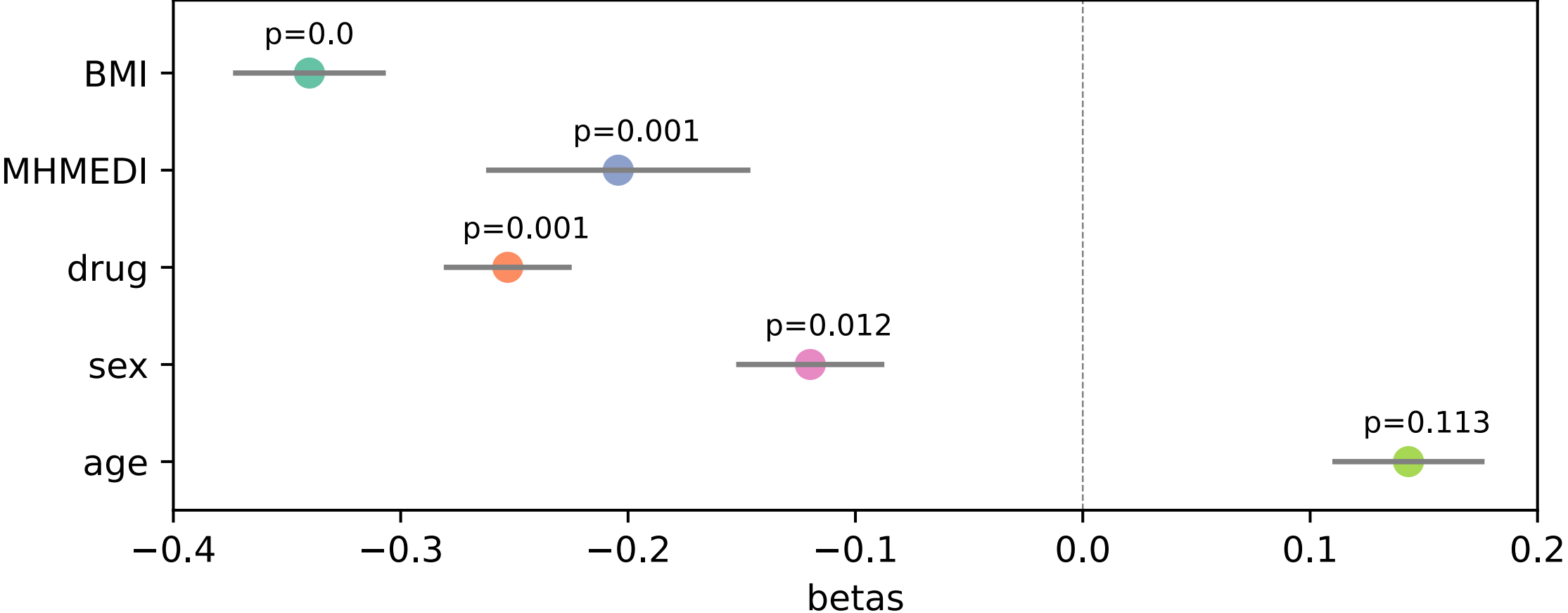
Predicting NfL with serotonin use ($R^2 = 0.3236$, AIC=152.0)



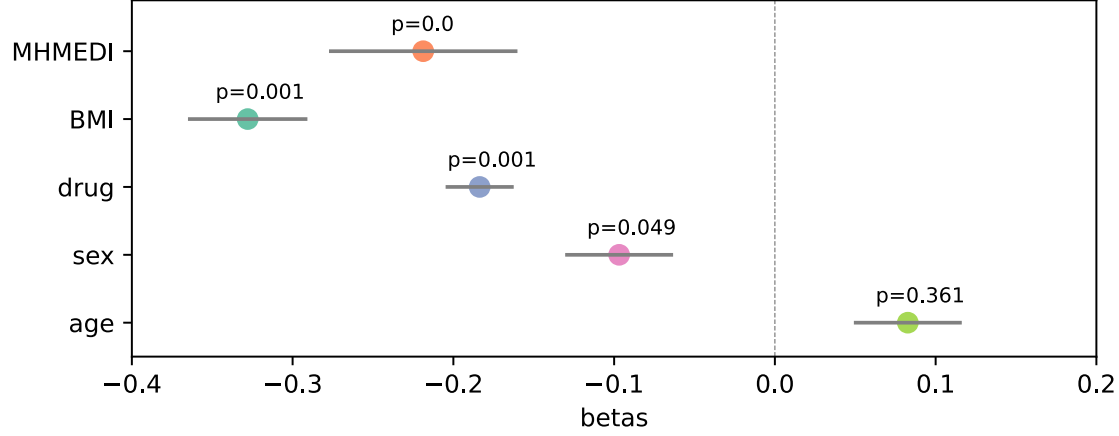
Predicting NfL with stimulants use ($R^2 = 0.1571$, $AIC=157.0$)



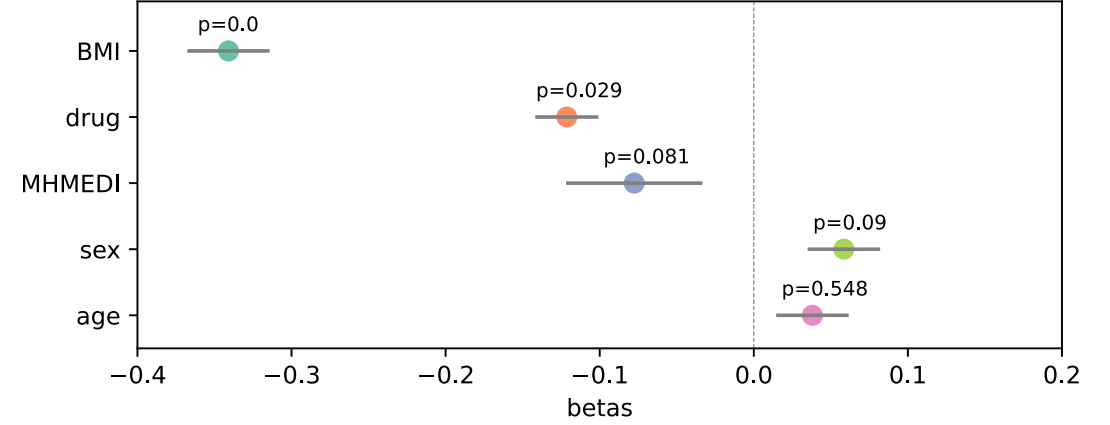
Predicting NfL with THC use ($R^2 = 0.2532$, $AIC=274.0$)



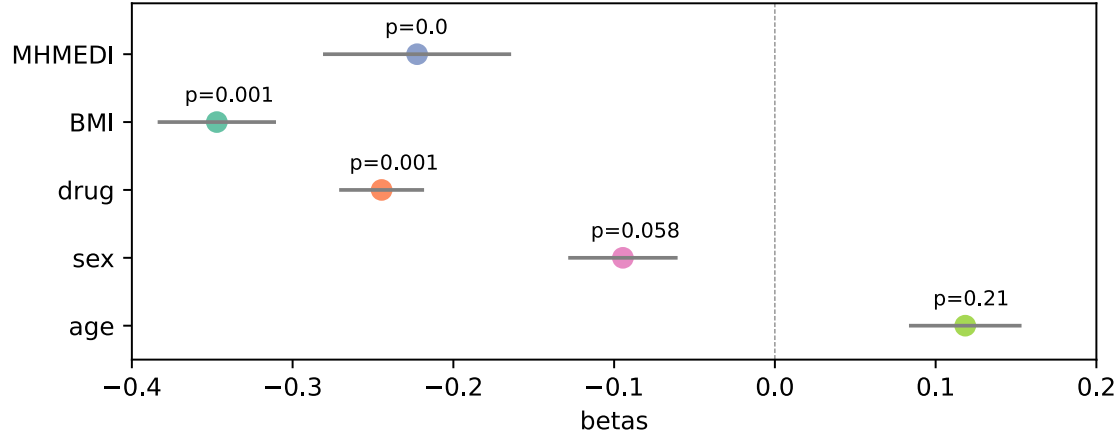
Predicting NfL with serotonin_stimulants_THC use ($R^2 = 0.2322$, AIC=304.0)



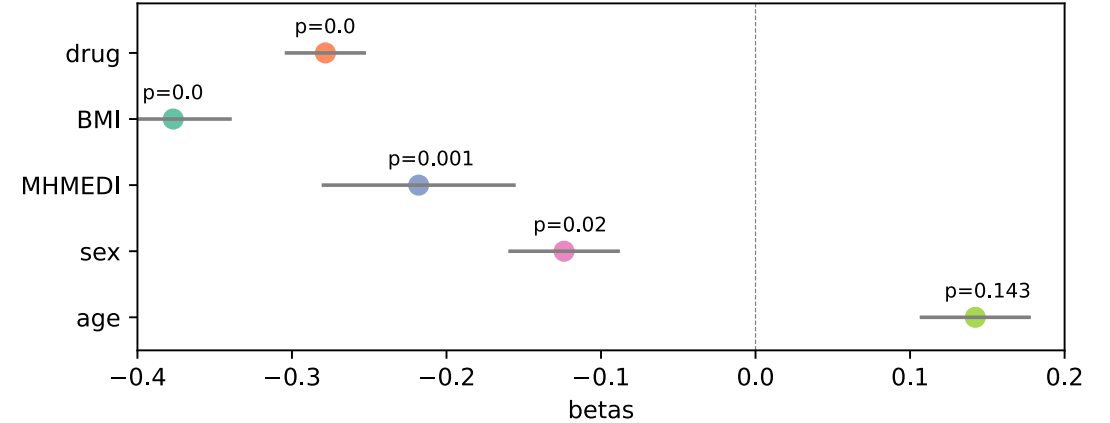
Predicting NfL with serotonin_stimulants use ($R^2 = 0.1632$, AIC=167.0)



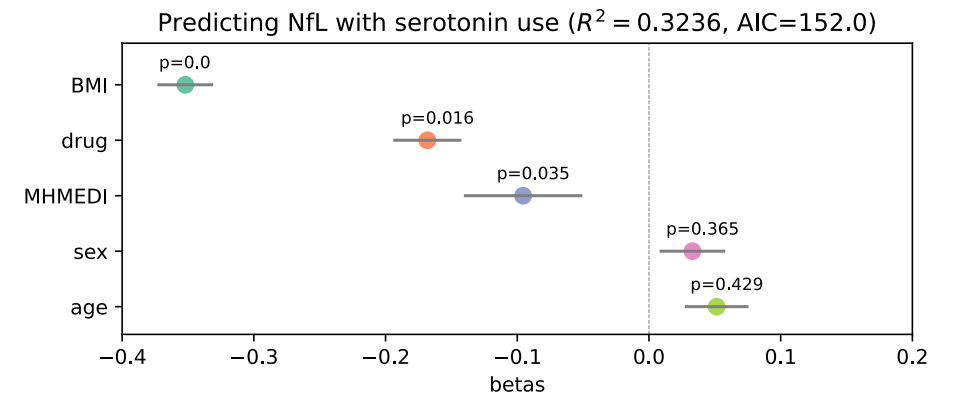
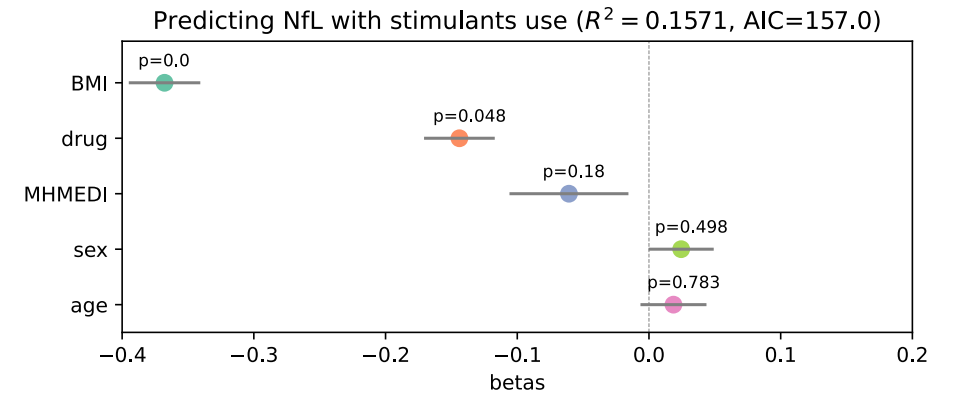
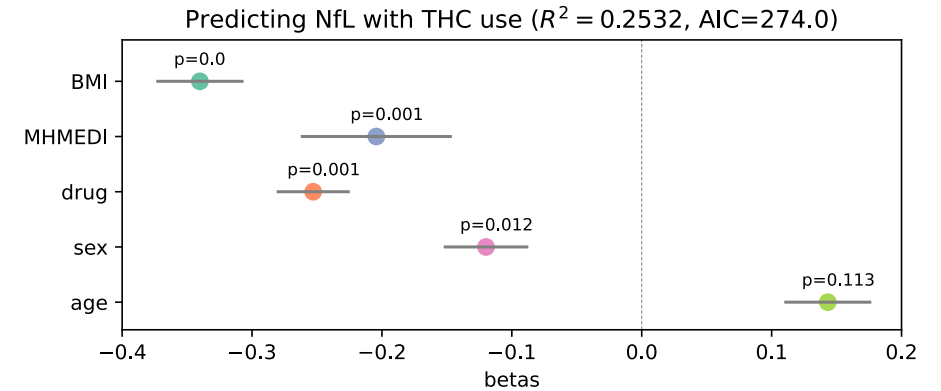
Predicting NfL with stimulants_THC use ($R^2 = 0.2435$, AIC=304.0)



Predicting NfL with serotonin_THC use ($R^2 = 0.295$, AIC=328.0)



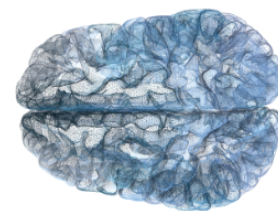
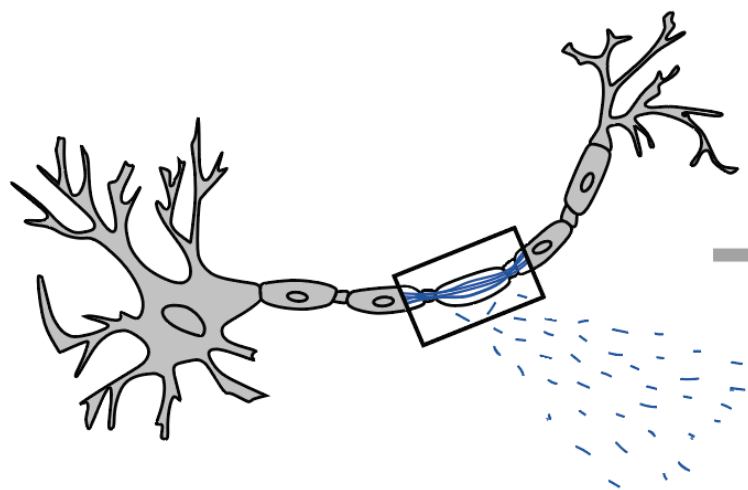
**Increased substance use
is associated with slightly
lower peripheral NfL
levels in early adulthood**



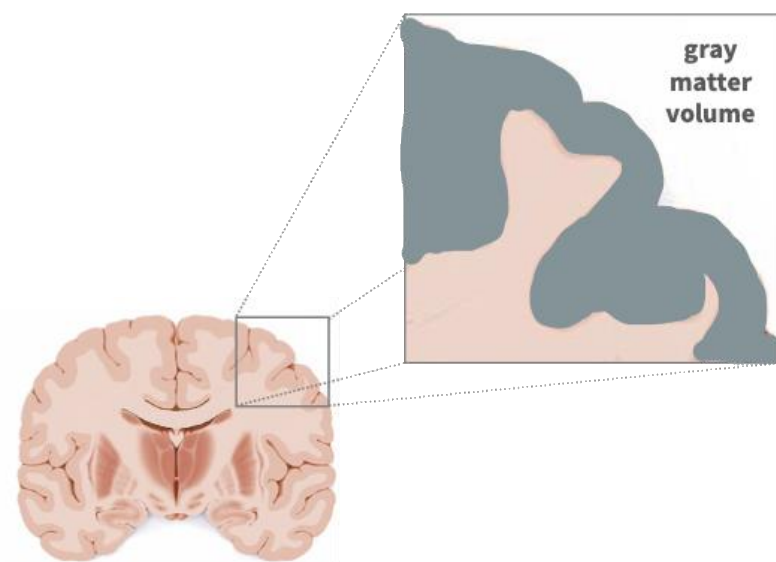
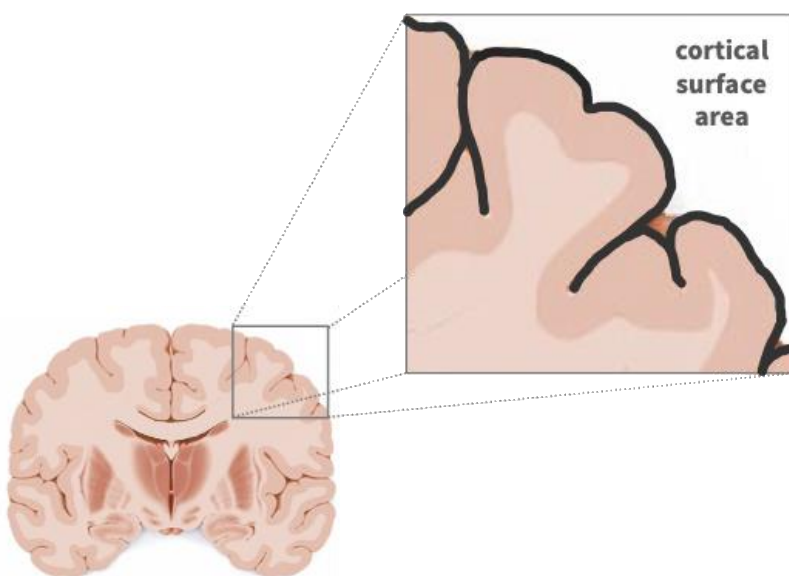
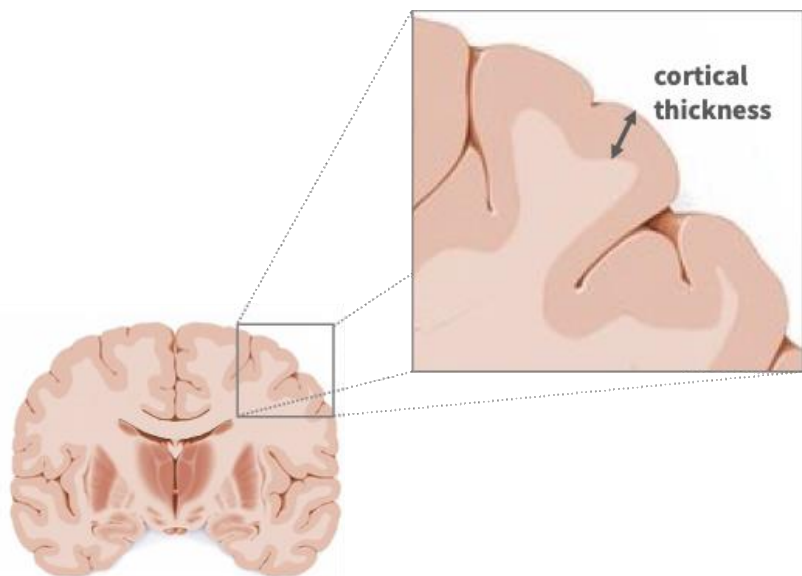
Research question #2:

How do peripheral NfL levels relate to structural neuroimaging measures in early adulthood?

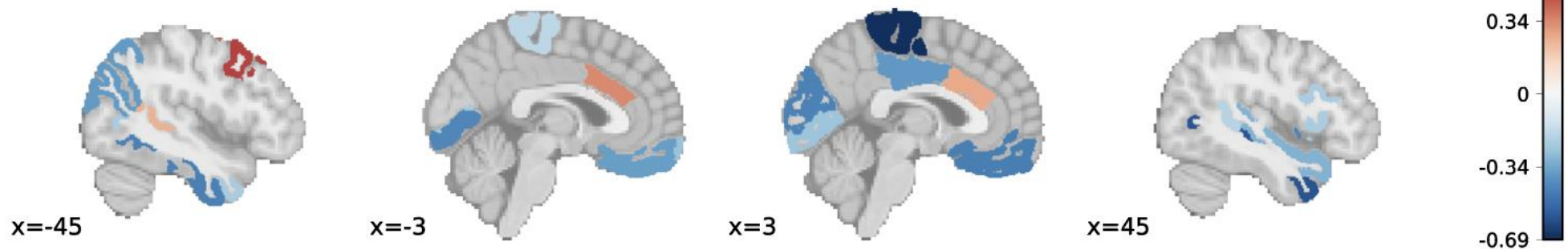




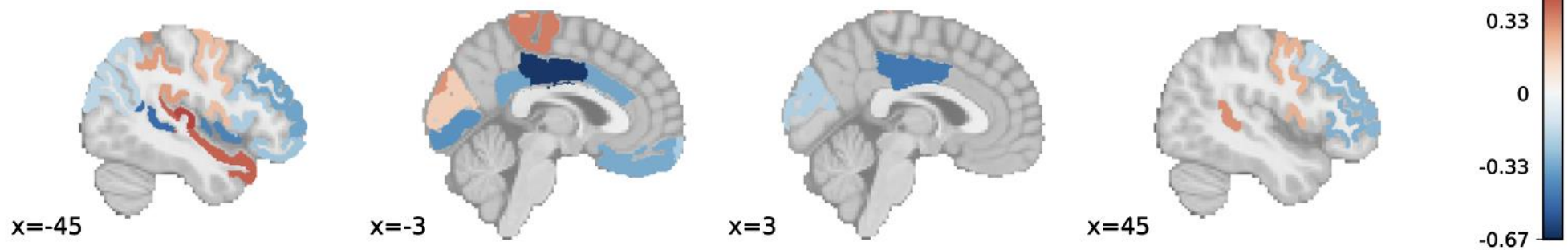
FreeSurfer



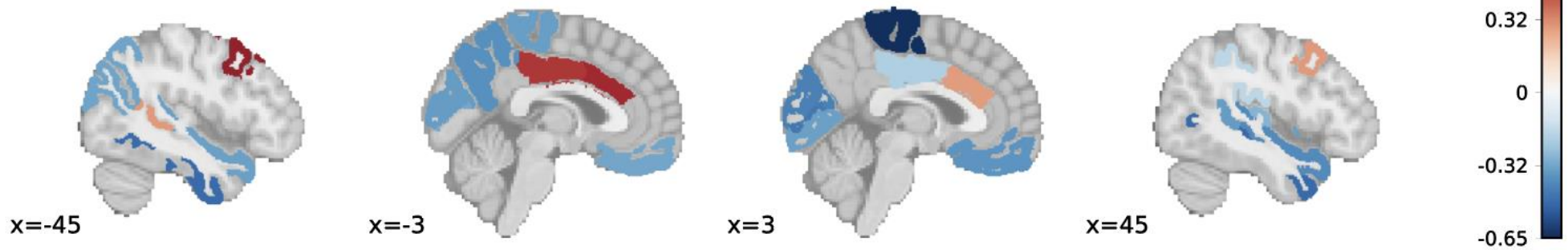
Gray matter volume



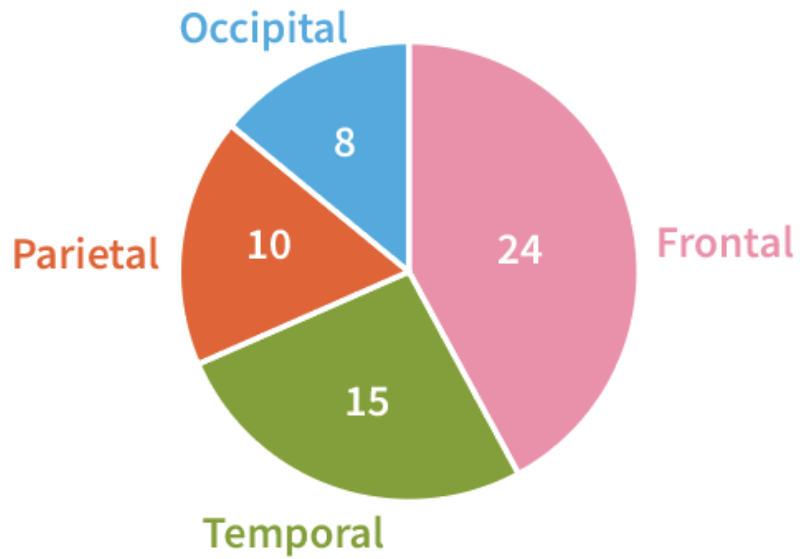
Cortical thickness



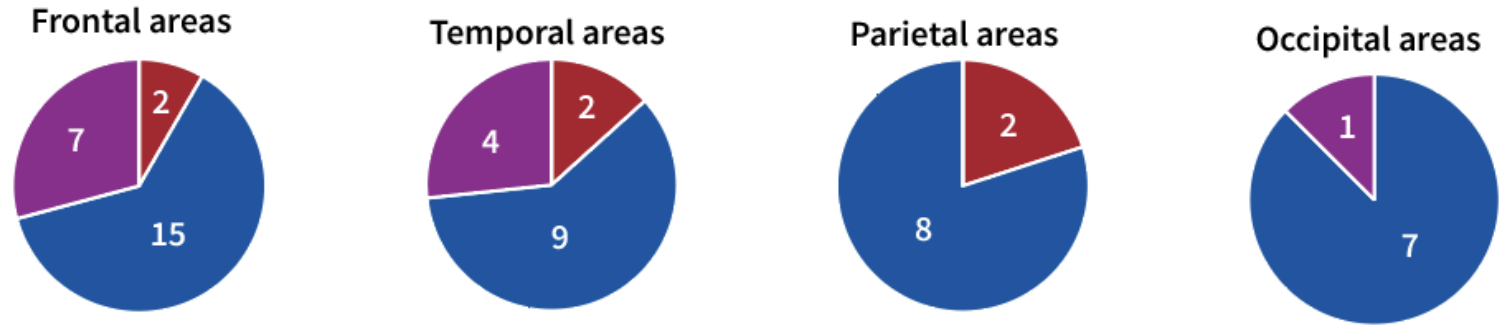
Cortical surface area



Brain areas associated with NfL



Directionality of associations with NfL



Mixed correlations with NfL across different structural measures for the same area

All structural measures in one area correlated positively with NfL

All structural measures in one area correlated negatively with NfL

**Higher peripheral NfL levels
are associated with
predominantly decreased
gray matter structural
metrics in early adulthood**



Gray matter structures shrink in young adulthood

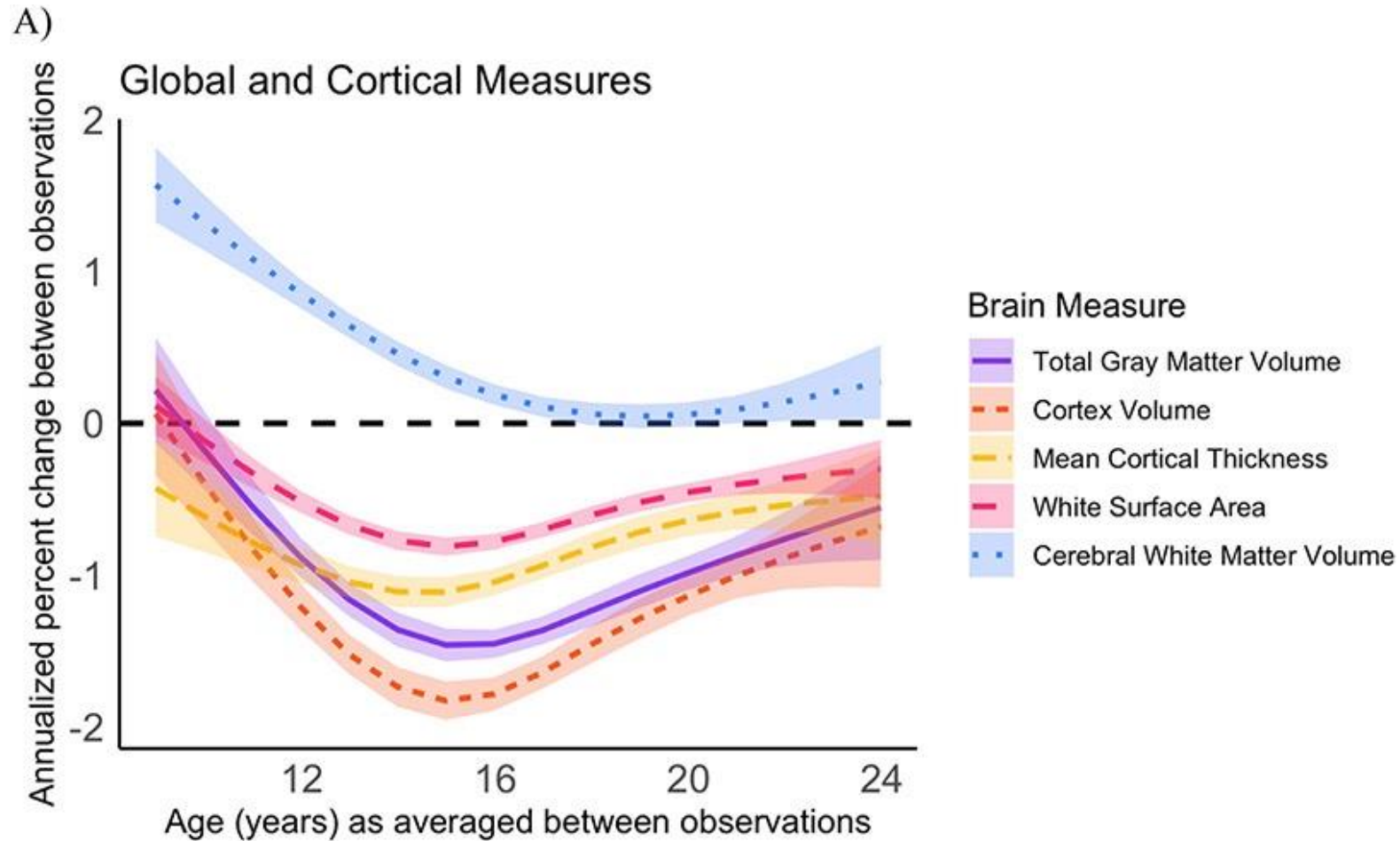
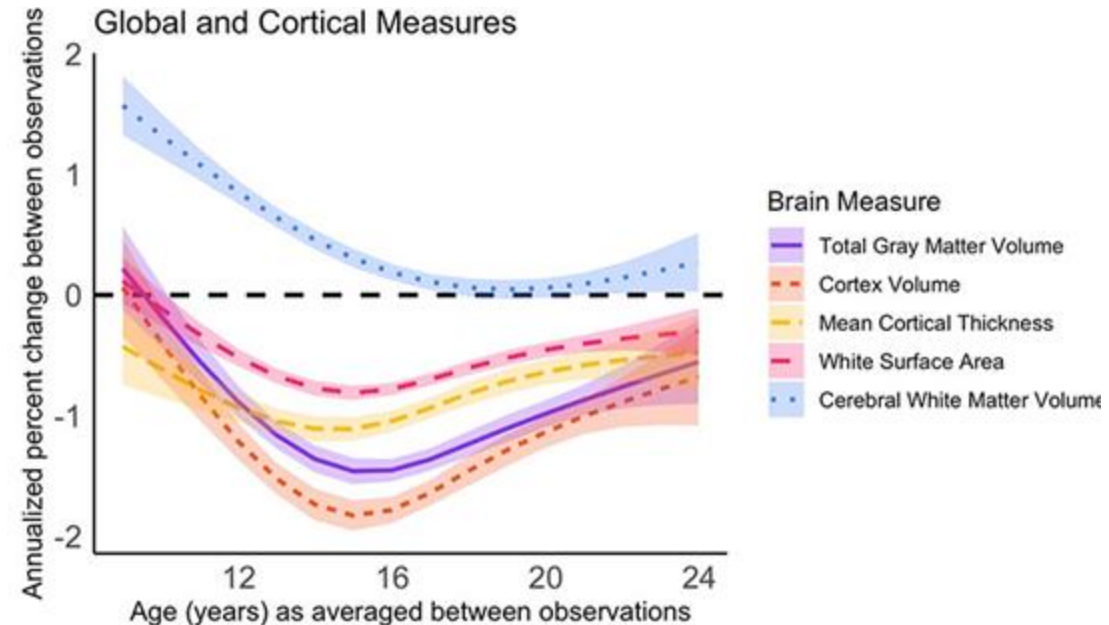
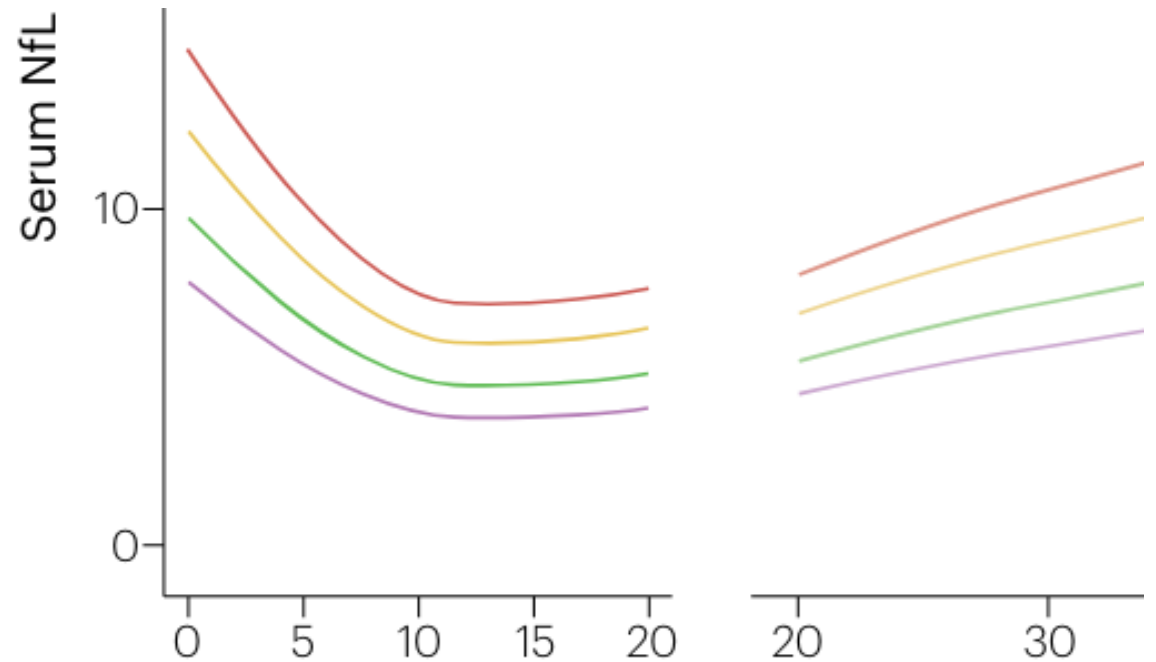


Fig. 4 – Mills et al.
NeuroImage (2021)

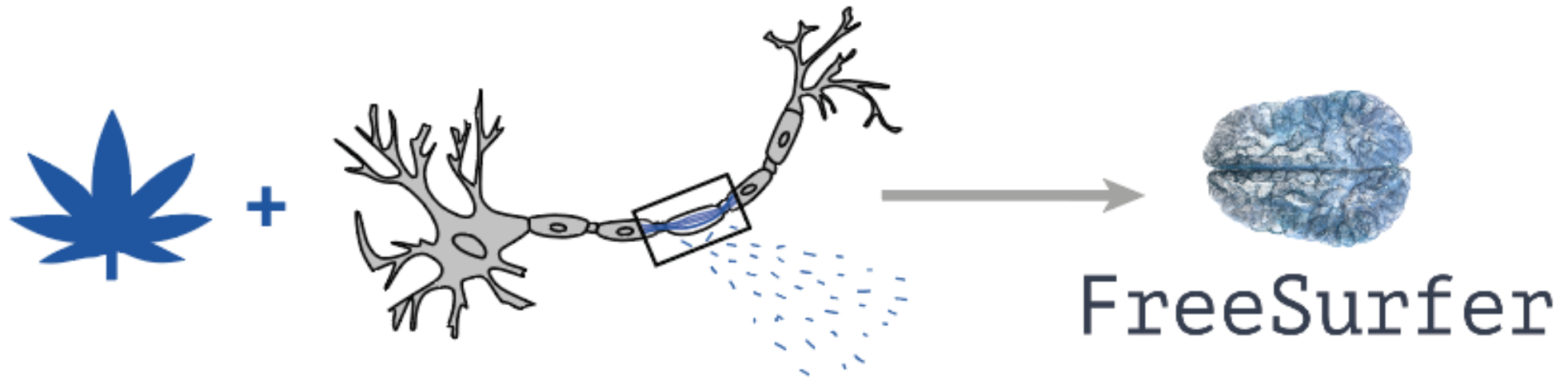
Peripheral NfL levels in early adulthood reflect brain development which may be influenced by substance use



Research question #3:

How do peripheral NfL levels and substance use relate to structural neuroimaging measures in early adulthood?





Stay tuned...

Thank you for your attention!



Dr. Denis Ribeaud
Dr. Manuel Eisner
Dr. Lilly Shanahan



Prof. Todd Hare
Dr. Michael Shanahan
Mirjam Habegger
Jens Heumann



Jens Kuhle
Aleksandra Maleska

Experimental Pharmacopsychology and Psychological Addiction Research



Prof. Dr. Boris Quednow



Francesco Bavato, MD



Lena Mehnert, MSc



Clarissa Janousch, PhD



Lukas Eggenberger, MSc