

Blood biomarkers of Alzheimer’s disease and olfactory-related brain volumes associated with 15-year trajectories of odor identification

Javier Oltra¹, Grégoria Kalpouzos¹, Ingrid Ekström¹, Benoît Jobin², Janina Seubert³, Martina Valletta¹, Maria Larsson⁴, Johannes Frasnelli⁵, Davide Liborio Vetrano¹, Giulia Grande¹, Erika J. Laukka¹

¹Aging Research Center, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet and Stockholm University; ²Department of Neurology, Massachusetts General Hospital; ³Division of Psychology, Department of Clinical Neuroscience, Karolinska Institutet; ⁴Gösta Ekman Laboratory, Department of Psychology, Stockholm University; ⁵Department of Anatomy, Université du Québec à Trois-Rivières

Background

Olfactory decline is a sensitive marker of brain health. Longitudinal studies tracking progressive smell deterioration are scarce, and few investigations have integrated Alzheimer's disease (AD) biomarkers and structural brain measures to examine potential underlying mechanisms.

Methods

- Sample:** 287 older adults (dementia-free at baseline, mean baseline age = 69 years, age range: 60–88 years) from the Swedish National Study on Aging and Care in Kungsholmen (SNAC-K) MRI cohort.
- Dependent variable:** annual average change in odor identification up to 15 years assessed using Sniffin’ Sticks test.
- Independent variables:** baseline serum AD-related biomarkers (Aβ42/40, t-tau, p-tau181, ptau-217, NfL, GFAP) and volumetric measures of the olfactory brain network.
- Covariates:** sex, education, APOE ε4 status, anemia, chronic kidney disease, obesity, and cardiovascular disease.
- Data analyses:** linear mixed models (LMM), penalized regression (LASSO, 80/20 train-test split), mediation models and structural equation models.

Figure 1 Key predictors of odor identification decline identified by LASSO regression

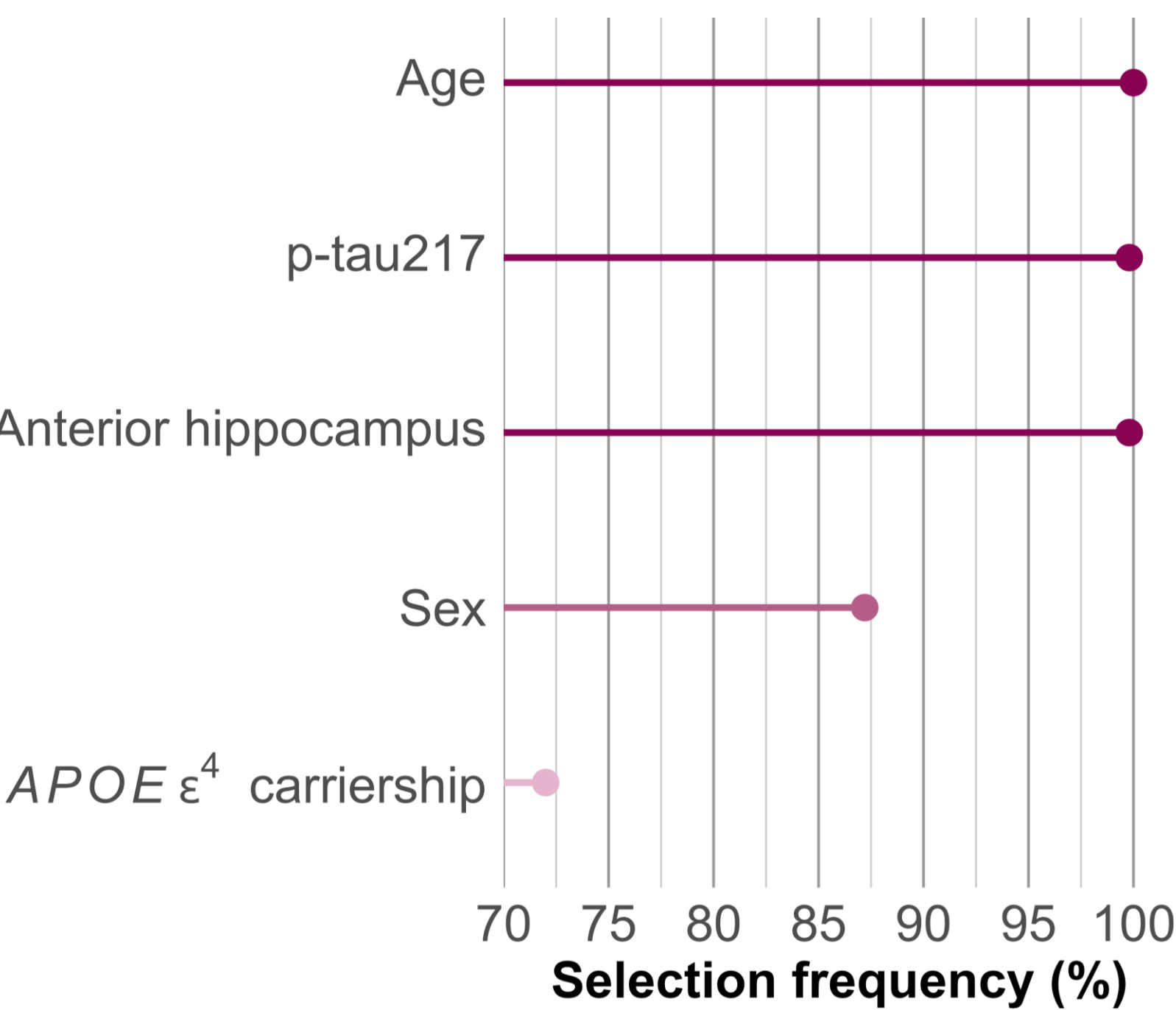


Table 1 Predictive performance of the LASSO model

Metric	Value	95% CI
r (pred-obs)	0.438	0.333, 0.539
Pooled RMSE	0.142	0.129, 0.156
Pooled R ²	0.192	0.099, 0.276

BOX 1 Other variables associated with odor identification decline (LMM).

- Blood biomarkers: GFAP.
- Brain volumes: amygdala, entorhinal cortex, posterior hippocampus, anterior and posterior piriform cortex.

Conclusions

The results support a link between the morphometry of the brain olfactory network and subsequent olfactory decline in aging. The association with AD biomarkers was largely driven by individuals who later received a dementia diagnosis, reinforcing the link between olfactory impairment and being on the path to dementia.

Figure 2 Fluid biomarkers and brain volumes mediate the relation between age and odor identification decline

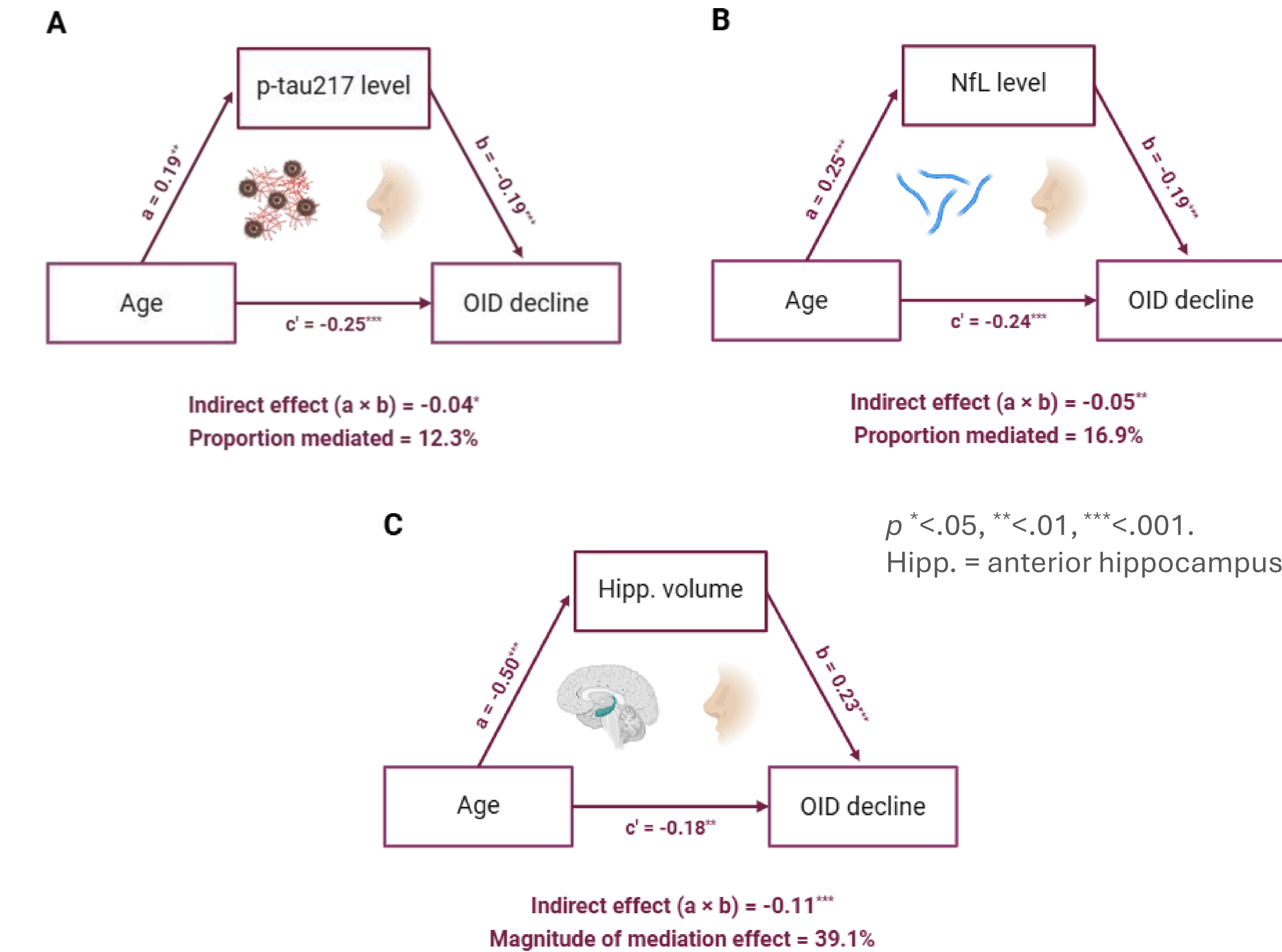
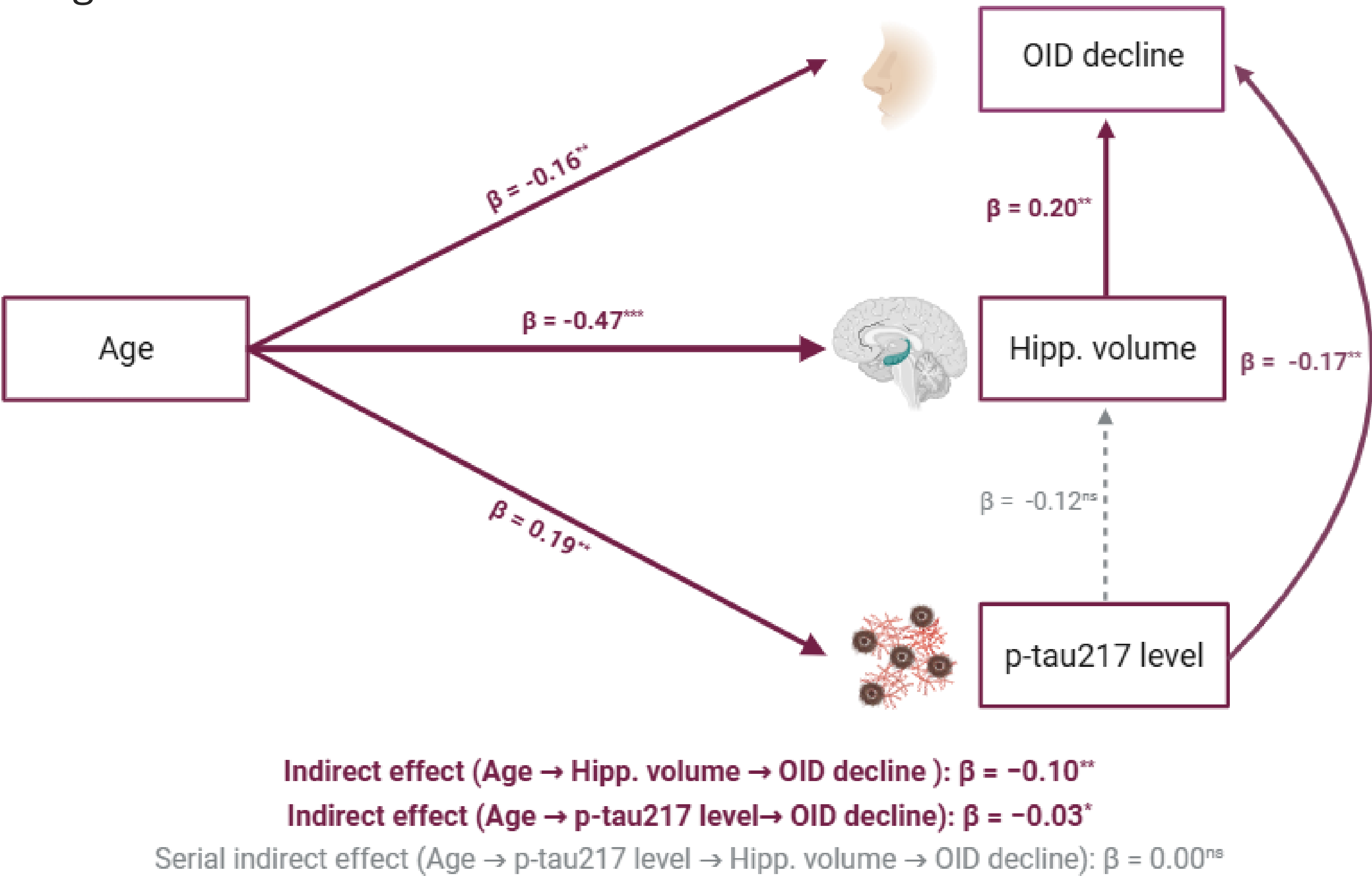


Figure 3 AD-pathology and hippocampal volume independently mediate the relation between age and odor identification decline



Javier Oltra | Postdoctoral Researcher
Division of Clinical Geriatrics | Aging Research Center (ARC)
Department of Neurobiology, Care Sciences and Society (NVS)
javier.oltra@ki.se

