

Short-term intra-individual stability assessment of 110 plasma neurobiomarkers



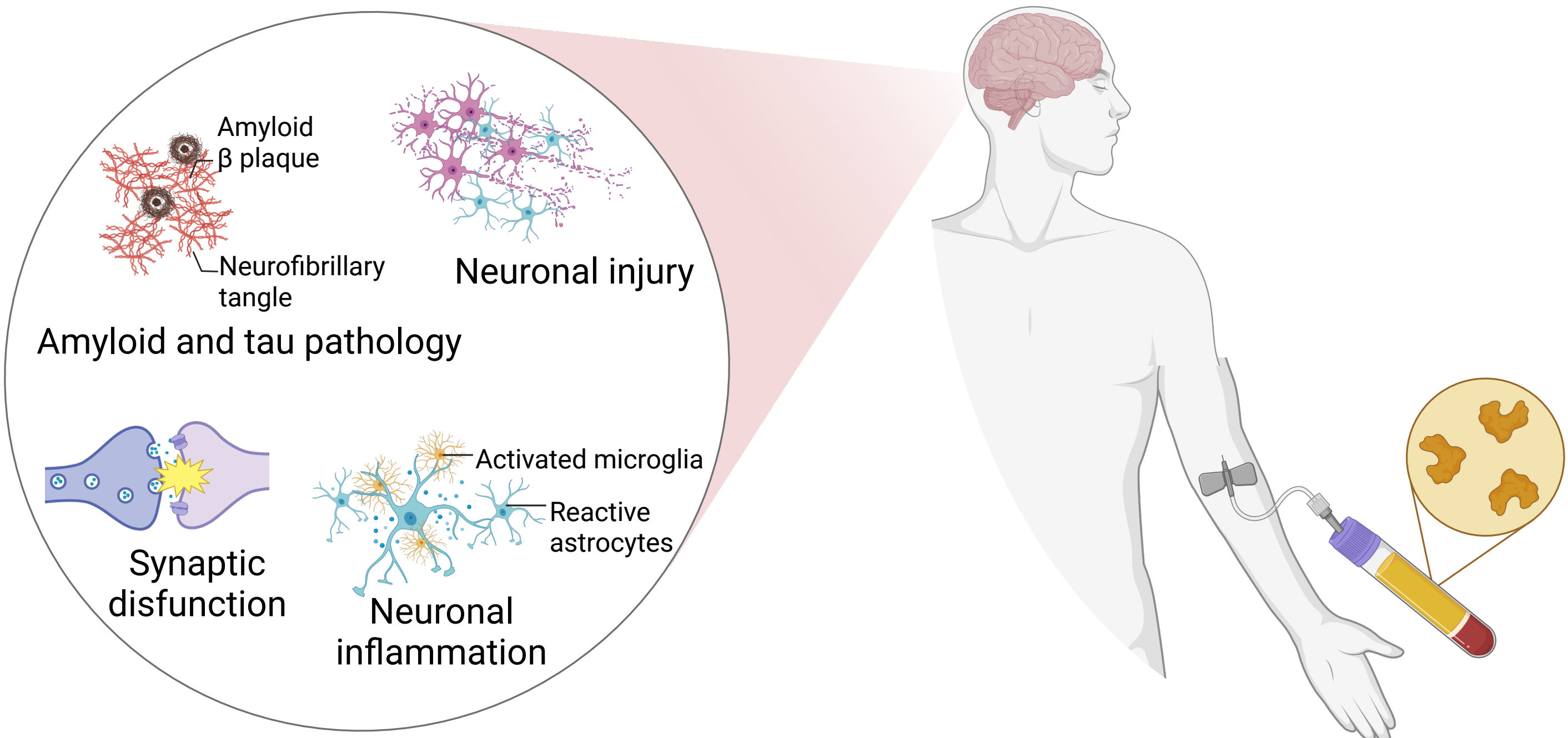
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INTRODUCTION

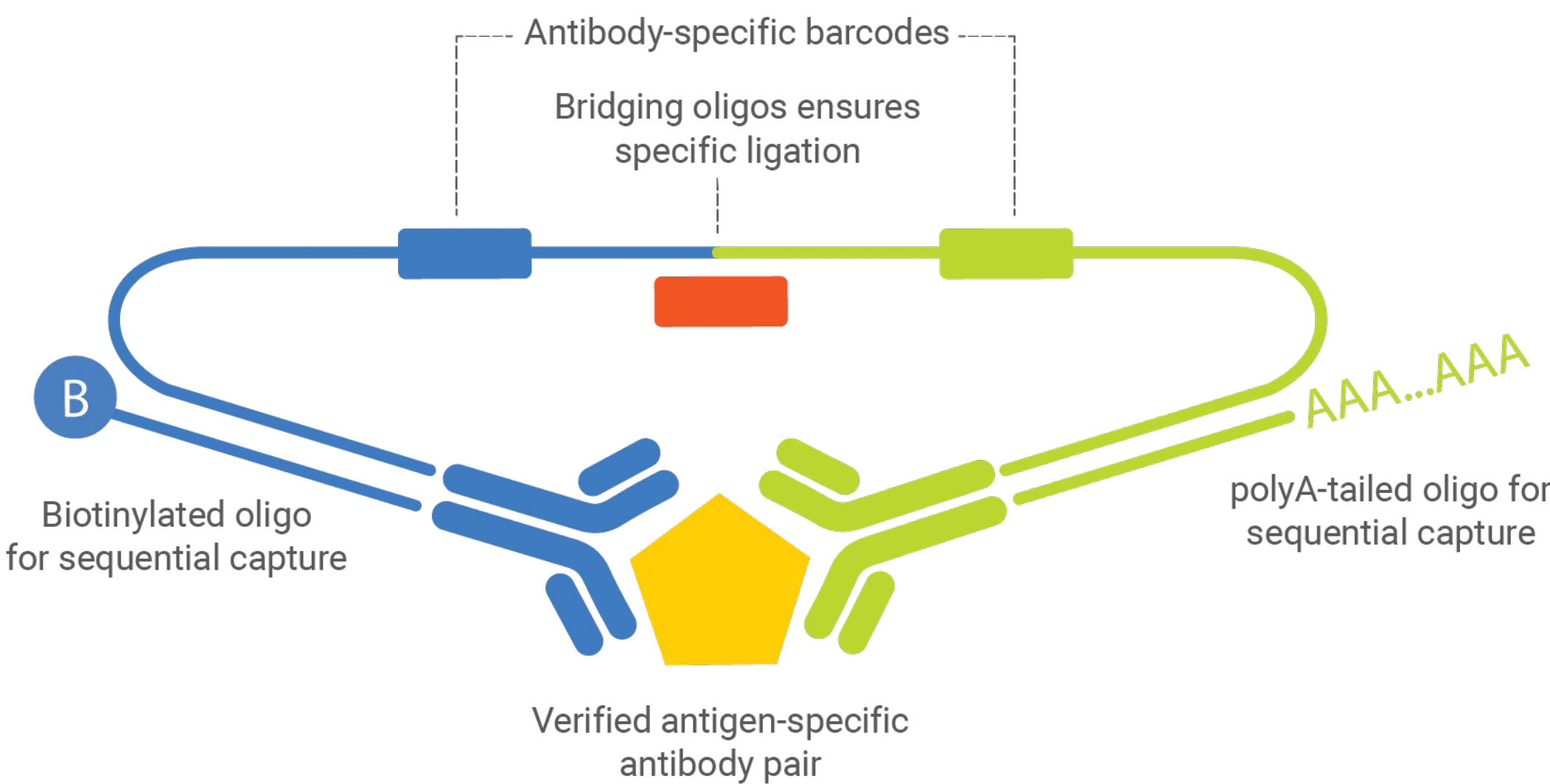
Blood-based biomarkers are minimally invasive alternatives to cerebrospinal fluid (CSF) biomarkers for diagnosis of Alzheimer's disease (AD). Their accessibility enables frequent sampling to monitor progression and treatment effects. To recognize meaningful changes in biomarker levels over time, disease-related shifts must be distinguished from normal biological fluctuations. We assessed short-term intra-individual variability of plasma biomarker levels, using a multiplex panel covering p-Tau isoforms and markers of amyloid and tau pathology, neuroinflammation, neuronal injury, and synaptic dysfunction.



METHODS

Blood samples were collected from 32 individuals, including equal numbers of cognitively healthy participants and those with positive CSF AD biomarkers. Half underwent blood draws on five consecutive days, the other half at weekly intervals over one month. 131 plasma markers were measured using the NULISaseq™ CNS Disease Panel (Alamar Biosciences).

110 markers that passed stringent detectability filtering were included for analysis. For each marker, intra-individual variation ranges (IIR) across timepoints were calculated per individual, with median IIR (mIIR) across individuals reported to quantify biomarker variability.



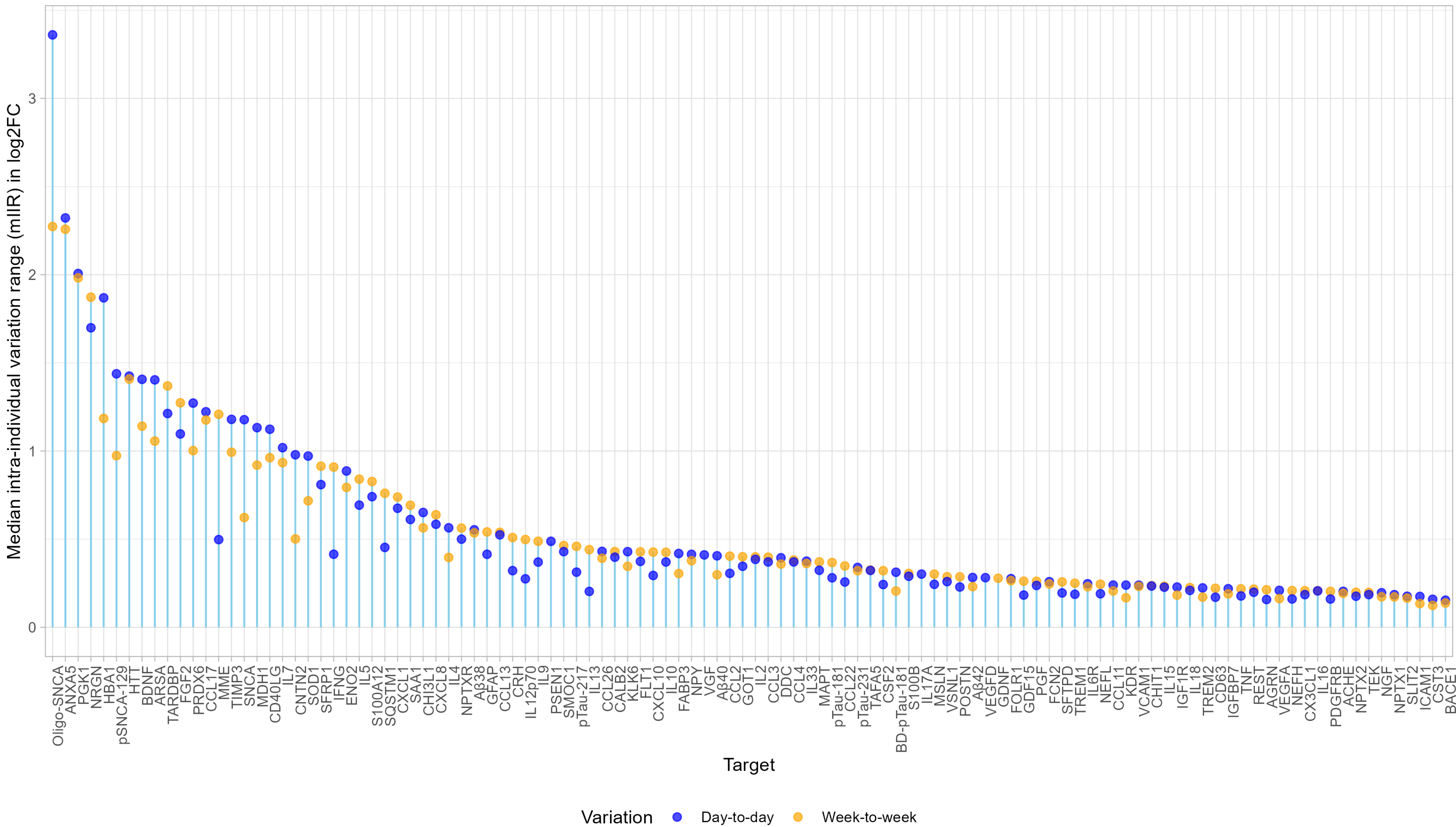
CNS 120 DISEASE PANEL

AMYLOID & TAU PATHOLOGIES			SYNUCLEIN & SYNAPTIC			VASCULAR & METABOLISM	
Abeta38 (aβ38)	CD63	pTau181	AGRN	IL6R (IL6Ra)	SNCB (β-Syn)	FLT1 (VEGF R1)	PGK1
Abeta40 (aβ40)	CST3	pTau181-BD*	ARSA	MDH1	SOD1	HBA1; HBA2	POSTN
Abeta42 (aβ42)	IGFBP7	pTau217	BDNF	NGF	TDP43	KDR (VEGF R2)	PTN
ACHE	KLK6	pTau217-BD*	DDC	Oligo-SNCA (Oligo-α-Syn)	pTDP43-409	MME	SAA1
APOE	PSEN1	pTau231	FABP3	PARK7	UCHL1	PDGFRB	VEGF-A
APOE (APOE4)	SFRP1	pTau231-BD*	FOLR1	pSNCA-129	VGF	PGF(PLGF)	VEGF-D
BACE1		totalTau	HTT	SNCA (α-Syn)	VSNL1 (VILIP-1)		
BASP1		totalTau-BD*					

NEURODEGENERATION		INFLAMMATION			
ANXA5	NPTX2	CCL2 (MCP1)	CSF2 (GM-CSF)	IL4	PRDX6
CALB2	NPTXR	CCL3 (MIP1a/CCL3)	CX3CL1 (Fractalkine)	IL5	RUVBL2
CNTN2	NPY	CCL4 (Mip1b/CCL4)	CXCL1 (GROa)	IL6	S100A12
ENO2	NRGN	CCL11 (Eotaxin)	CXCL8 (IL8)	IL7	S100B
FGF2 (FGF basic)	PDLIM5	CCL13 (MCP4)	CXCL10 (IP-10)	IL9	SFTPD
GDI1	REST	CCL17 (TARC/CCL17)	FCN2	IL10	SLIT2
GDNF	SMOC1	CCL22 (MDC)	GDF15	IL12A/IL12B (IL-12p70)	TAF45
GOT1	SNAP25	CCL26 (Eotaxin-3)	GFAP	IL13	TEK (Tie-2/TEK)
MSLN	SQSTM1	CD40LG (CD40L/TNFSF5)	ICAM1	IL15	TIMP3
NEFH	UBB	CHI3L1 (YKL40)	IFNG (IFN-gamma)	IL16	TNF (TNF-a)
NFL	YWHAG	CHIT1	IGF1R	IL17A	TREM1 (sTREM1)
NPTX1	YWHAZ	CRH	IL1B (IL-1 beta)	IL18	TREM2
		CRP	IL2	IL33	VCAM1 (CD106)

Median intra-individual range in log2 fold change (log2FC) for 124 plasma biomarkers; day-to-day variation (blue) and week-to-week variation (orange) are shown separately. Day-to-day and week-to-week biomarker stability were highly concordant when comparing the median intra-individual ranges across all plasma biomarkers (Pearson $r = 0.93$, $p\text{-value} < 2 \times 10^{-16}$)

RESULTS



OUTLOOK

Our study evaluates short-term biological variation across a large panel of plasma neurobiomarkers. These results offer essential reference data to distinguish disease-associated changes from normal fluctuations, supporting the selection and interpretation of plasma biomarkers for disease monitoring and clinical trials.



Amsterdam Neuroscience

