

Synaptic SNAP25 and VAMP2 levels in temporal cortex and plasma

Sandra O Tomé ^{1,2} ; Steffi De Meyer ²⁻⁴; Bas Lahaije ¹; Jeroen Vanbrabant ⁵; Charlotte Lambrechts ⁵; Julie Goossens ⁵; Eugene Vanmechelen ⁵; Christine Von Arnim ⁶⁻⁷; Markus Otto ⁸⁻⁹; Koen Poesen ³; Dietmar Rudolf Thal ^{1,10}; Rik Vandenberghe ^{2,11}.

1. Laboratory of Neuropathology, Department of Imaging and Pathology and Leuven Brain Institute, KU Leuven, Leuven, Belgium; 2Laboratory for Cognitive Neurology, Department of Neurosciences, Leuven Brain Institute, KU Leuven, Leuven, Belgium; 3. Laboratory for Molecular Neurobiomarker Research, Department of Neurosciences, Leuven Brain Institute, KU Leuven, Leuven, Belgium; 4. Neurochemistry Laboratory, Department of Laboratory Medicine, Amsterdam UMC, Amsterdam, The Netherlands; 5. Fujirebio Europe NV, Ghent, Belgium; 6. Department of Neurology, University of Ulm, Ulm, Germany
7. Department of Geriatrics, University Medical Center Gottingen, Gottingen, Germany ; 8. Department of Neurology, Ulm University, Ulm, Germany; 9. Department of Neurology, Martin-Luther University, Halle (Saale) Germany ; 10. Department of Pathology, University Hospitals Leuven, Leuven, Belgium; 11. Department of Neurology, University Hospitals Leuven, Leuven, Belgium.



BACKGROUND

- Synaptic markers such as the presynaptic protein synaptosomal-associated protein 25 (SNAP25) have shown an association with synaptic degeneration and cognitive decline in Alzheimer’s Disease (AD).
- Evidence for a role of vesicle-associated membrane protein 2 (VAMP2) on synapse degeneration remains limited.

What is the relationship between brain and plasma SNAP25 and VAMP2 levels in neuropathologically-confirmed AD patients?

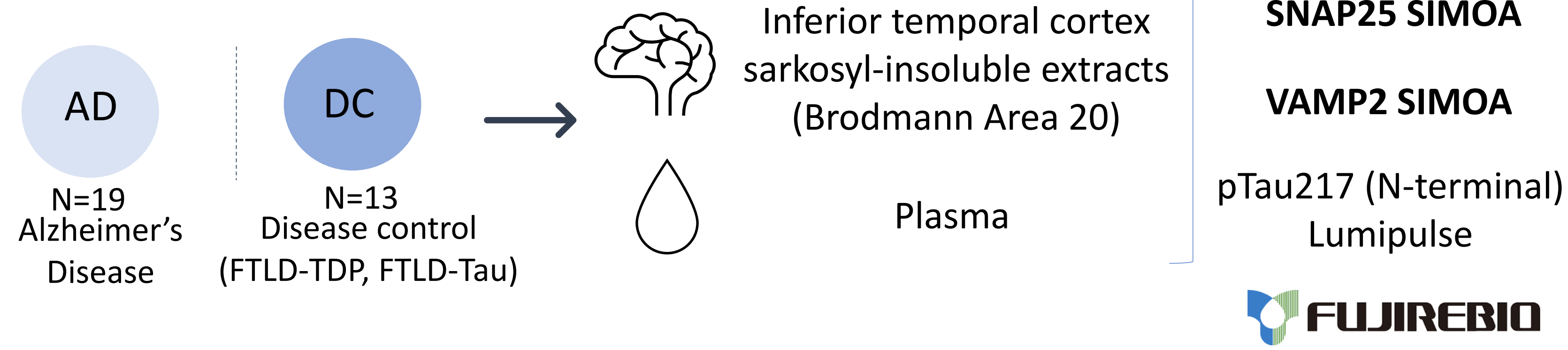
COHORT CHARACTERIZATION

Characteristic	AD	DC	P
No. (%)	19 (59)	13 (41)	
Age at sampling, years	67 ± 8, 51 to 83	65 ± 13, 37 to 86	0.60
Time interval (TI), years	6 ± 3, 0 to 10	4 ± 2, 1 to 8	0.020
Female, No. (%)	8 (42)	4 (31)	0.78
APOEε4 carriers, No. (%)	9 (47)	0 (0)	0.0043
PMI, hours	24 [12], 6 to 72	24 [12], 9 to 72	0.77
Aβ phase 0/1/2/3/4/5, No.	0/0/0/0/1/18	6/4/2/0/1/0	<0.0001
Braak NFT stage 0/I/II/III/IV/V/VI, No.	0/0/0/1/1/5/12	2/7/3/1/0/0/0	<0.0001
CERAD score 0/1/2/3, No.	0/2/8/9	11/1/1/0	<0.0001
Braak LBD stage 0/1/2/3/4/5/6, No.	11/2/0/1/2/1/2	12/0/0/1/0/0/0	0.29
LATE-NC stage 0/1/2/3, No.	0/0/9/10	13/0/0/0	<0.0001
CAA stage 0/1/2/3, No.	1/2/12/4	11/1/0/0	<0.0001
GVD stage 0/1/2/3/4/5, No.	1/1/0/4/5/8	9/2/1/1/0/0	0.00048
CDR score at time of death 0/1/2/3, No.	0/2/4/13	0/0/2/11	0.41
MMSE score at blood sampling	10 [20], 3 to 23	10 [18], 5 to 23	0.95
Neuropathologic diagnoses	AD (n=19), LATE-NC (n=19), Lewy Body disease (n=8), FTLT-TDP Type C (n=1)	FTLTD-TDP type A (n=4), type B (n=2), type C (n=2), Type D (n=2); FTLT-tau: PSP (n=1), CBD (n=1), Pick’s (n=1), AGD (n=1)	

Table 1 – Characteristics of dementia patients stratified for diagnosis. Continuous data are expressed as mean ± standard deviation, range when normally distributed in both groups and median [IQR], range when not. Categorical data are expressed as No. (%). Comparisons between cohort subgroups were made using either unpaired t-tests (normal data), Mann–Whitney U-tests (non-normal data) or χ2 tests (categorical data). Abbreviations: AD, Alzheimer’s disease; PART: primary age-related tauopathy; CERAD: Consortium to Establish a Registry for Alzheimer’s disease; CAA, cerebral amyloid angiopathy; CDR, clinical dementia rating; DC, non-AD disease controls; GVD, granulovacuolar degeneration; LATE-NC, limbic-predominant age-related TAR DNA-binding protein 43 encephalopathy neuropathologic change; LBD, Lewy body disease; MMSE, mini-mental state examination; NFT, neurofibrillary tangle; PMI, postmortem interval;

METHOD

Neuropathologically-characterized cases



BRAIN, BUT NOT PLASMA LEVELS OF SNAP25 AND VAMP2 STRONGLY CORRELATE WITH EACH OTHER

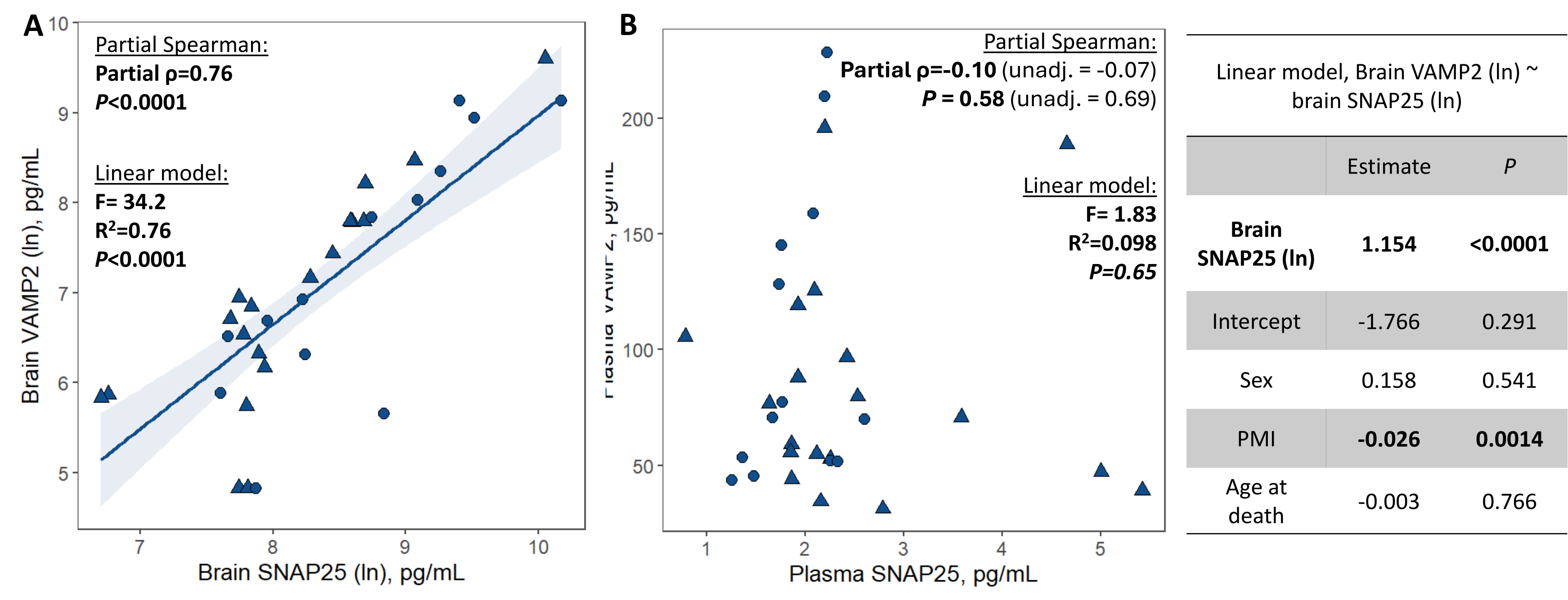


Figure 2 - Scatterplots show the associations between brain SNAP25 and brain VAMP 2 (A) in the temporal cortex and between plasma SNAP25 and plasma VAMP2 (B). The solid line in A indicates the fitted linear model smooth term with the shaded area representing the 95% confidence interval. Analyses were corrected for age, sex, time interval between plasma sampling and death, and PMI.

BRAIN SNAP25 CORRELATES WITH PLASMA PTAU217, Aβ PHASE AND PMI

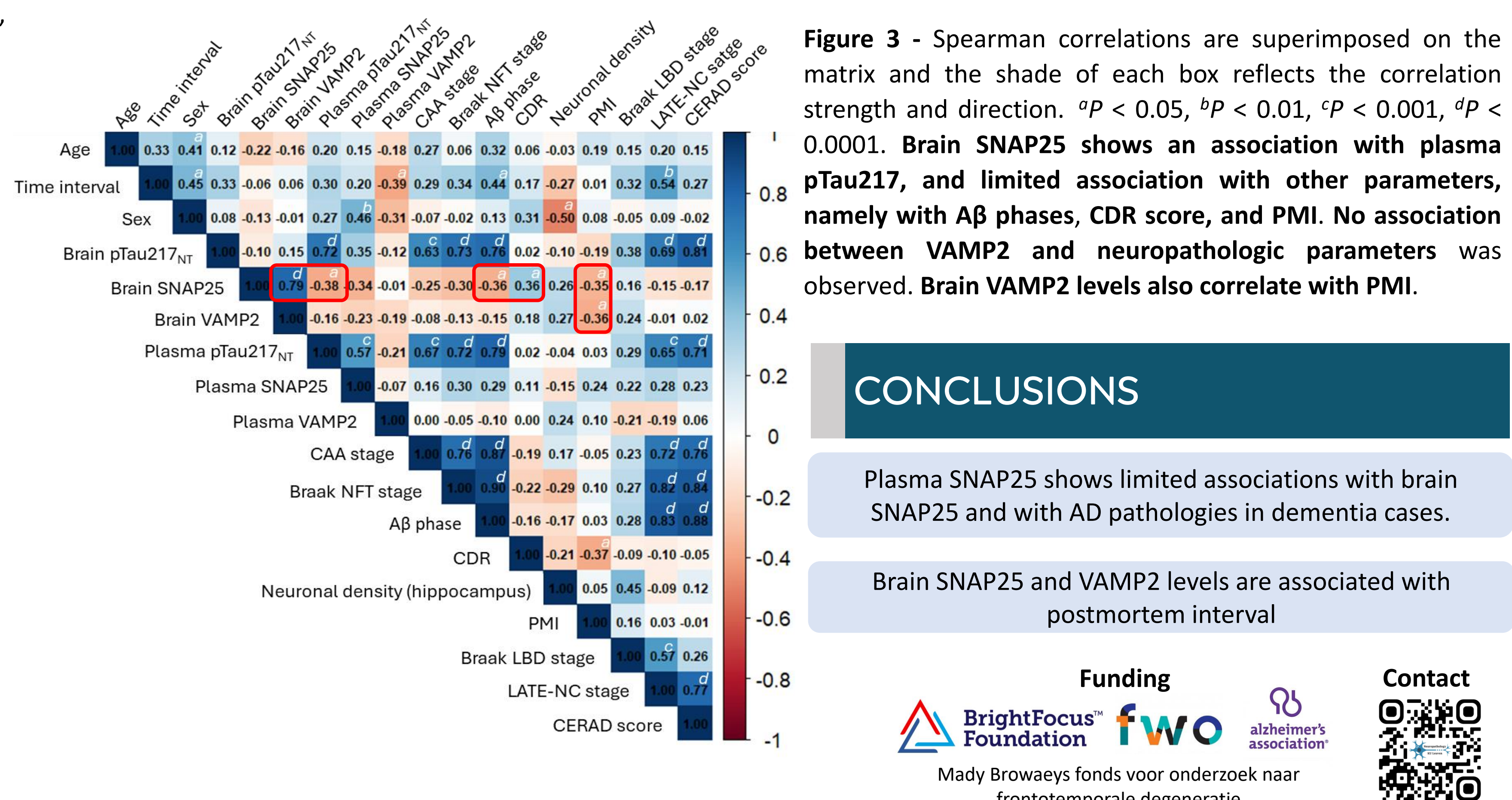


Figure 3 - Spearman correlations are superimposed on the matrix and the shade of each box reflects the correlation strength and direction. ^aP < 0.05, ^bP < 0.01, ^cP < 0.001, ^dP < 0.0001. Brain SNAP25 shows an association with plasma pTau217, and limited association with other parameters, namely with Aβ phases, CDR score, and PMI. No association between VAMP2 and neuropathologic parameters was observed. Brain VAMP2 levels also correlate with PMI.

CONCLUSIONS

Plasma SNAP25 shows limited associations with brain SNAP25 and with AD pathologies in dementia cases.

Brain SNAP25 and VAMP2 levels are associated with postmortem interval

SNAP25 SHOWS MODEST ASSOCIATION IN PLASMA VS. BRAIN

