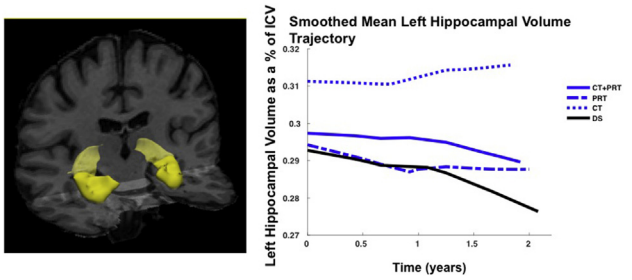

Figure 1. Render of hippocampi from FreeSurfer segmentation (left). Lowess plot of left hippocampal volume as a percentage of ICV (right). The lowess plot shows predicted values of left hippocampal volume from LME model. Sliding window data fraction was set to 0.9.

Table 1

Significance difference in rate of change between	BL-FU1 p	DF	F value	BL-FU1-FU2 p	DF	F value
H1 - DS and all training groups	0.349	75.3	0.89	**0.025**	155.1	4.70
H2 - DS and CT	0.119	40.1	1.84	**0.027**	84.4	5.10
H3 - DS and PRT	0.183	36.1	2.54	**0.027**	80.8	5.04
H4 - PRT and CT	0.369	39.0	0.83	0.585	72.2	0.30
H5 - PRT+CT and DS	0.573	39.1	0.32	0.114	82.9	2.02

Background: Cognitive and physical exercise may reduce risk of dementia in mild cognitive impairment (MCI) but the underlying mechanisms are poorly understood. The SMART is a longitudinal randomised controlled trial that compares the benefits of isolated and combined progressive resistance and computerised cognitive training in MCI. Previously, we revealed therapeutically relevant structural and functional brain changes immediately after training cessation[1], however, no effects were found on hippocampal structure. Here, for the first time, we investigate the ongoing impact of training on hippocampal anatomy 12-months after cessation using linear mixed effects (LME) models to account for imperfect timing and missing data. **Methods:** Eighty six community-dwelling participants aged ≥55 with MCI were randomised into 4 training groups; 1- Combined computerised cognitive and progressive resistance training (CT+PRT), 2- PRT and Sham CT (PRT), 3- Sham PRT and CT (CT), 4- Double Sham (DS). Training consisted of 2x1.5hours/week for 6-months. Cognitive and MRI assessments were carried out at baseline (BL), 6-months (F1) (directly after training) and 18-months (F2) from BL. Whole-brain T13DTFE MR images were automatically processed with the longitudinal FreeSurfer analysis pipeline. Longitudinal hippocampal volume was analysed with a freely available LME Matlab tool, modelled as % of BL volume. A linear time x group interaction was selected as the main contrast of interest in a comprehensive model controlling for covariates (sex, education, age). **Results:** Five alternate hypotheses tested for group x time interactions between BL->F1 and BL->F1->F2 (**Table 1**). LME models showed significant differences in left (but not right) hippocampal atrophy rates for either training intervention compared to DS across the entire 18-month follow-up period. There were no differences in hippocampal trajectories between PRT or CT, nor between combined training and the DS. **Conclusions:** Meta-analysis in MCI and Alzheimer's confirm a faster rate of atrophy in the left hippocampus compared to the right[2]. Our findings of preserved left but not right hippocampal volume due to training may therefore have implications for combating neurodegeneration. Further work is needed to determine if such training-related benefits are linked to improved memory and cognitive outcomes long term. References: 1-C. Suo, et al. Molecular Psychiatry. 2016.21:1633–1642 2-F. Shi et al. Hippocampus. 2009. 19:1055–1064.

IC-03-02 [^{11}C]PK11195 PET IN ALZHEIMER'S DISEASE AND PROGRESSIVE SUPRANUCLEAR PALSY: THE NIMROD STUDY

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Background: Neuro-inflammation plays a significant role in the pathogenesis of Alzheimer's disease and progressive supranuclear palsy. Here we test whether the intensity and regional distribution of neuro-inflammation differs between these disorders and controls; and whether neuro-inflammation relates to disease severity. **Methods:** We used the radiotracer [^{11}C]PK11195 with positron emission tomography and kinetic modeling to compare regional [^{11}C]PK11195 binding in 16 patients with Alzheimer's disease pathology (including amyloid-positive mild cognitive impairment), 16 with progressive supranuclear palsy, and 13 controls. We correlated [^{11}C]PK11195 binding with clinical variables and C-reactive protein. **Results:** [^{11}C]PK11195 binding in the medial temporal lobe and occipital-parietal cortex was increased in Alzheimer's disease patients, relative to both progressive supranuclear palsy patients and controls. Progressive supranuclear palsy patients showed elevated [^{11}C]PK11195 binding in the thalamus, putamen, and pallidum relative to controls. [^{11}C]PK11195 binding in the pre-cuneus correlated *negatively* with episodic memory in Alzheimer's disease, while [^{11}C]PK11195 binding in the pallidum, midbrain, and pons correlated *positively* with disease severity in progressive supranuclear palsy. **Conclusions:** The magnitude and distribution of neuro-inflammation, indexed by [^{11}C]PK11195, differed between Alzheimer's disease and progressive supranuclear palsy, and mirrored the established neuropathological distribution for each disease. In both Alzheimer's disease and progressive supranuclear palsy, disease severity correlated with neuro-inflammation in the regions most closely associated with principal neuropathological markers including tau aggregates. Immunotherapeutic strategies targeting neuro-inflammation may be a useful strategy in slowing the progression of these neurodegenerative disorders.

IC-03-03 REGARDLESS OF THEIR LOCATION, WHITE MATTER HYPERINTENSITIES ARE ASSOCIATED WITH ADVANCED BRAIN AGING THROUGHOUT ADULTHOOD IN THE STUDY OF HEALTH IN POMERANIA

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Background: White matter hyperintensities (WMH) have shown to be associated with increased risk of dementia. However, studies reporting the association of specific WMH locations with brain aging and dementia are scarce. We sought to investigate the association of WMH appearance in predefined anatomical brain regions and cardiovascular risk with brain atrophy patterns related to brain aging (BA), throughout adulthood in the general population, leveraging state of the art pattern analysis methods and structural equation modeling. **Methods:** We delineated WMH using a fully automated segmentation method in a large population-based sample (n=2,367) covering most of the adulthood life span (range 20-90 years, median=53 years), from the Study of Health in Pomerania, Germany. We automatically quantified WMH volume within four anatomical WM regions of interest i) frontal, ii) parietal -temporal, iii) deep structures including fornix and internal capsule and iv) occipital, using a multi-atlas segmentation method. Using machine-learning methods, we calculated the SPARE-BA score, a subject-specific index that captures and quantifies age-related brain atrophy patterns. The Framingham cardiovascular disease risk score (CVD-RS) was used to summarize the individual cardiovascular risk profile. We used four structural equation models independently; we modelled the SPARE-BA index as dependent variable, age as independent variable as well as CVD-RS and WMH volume within each region of interest as mediators. **Results:** Structural equation modeling showed that the age effect on brain aging patterns captured by the SPARE-BA score was mediated by WMH volume in frontal (8.7% Variance explained (VE), P<0.0001), parietal-temporal (9.5% VE, P<0.0001), deep WM structures including fornix and internal capsule (2.8%, VE, P<0.0001) and occipital (6.6% VE, P<0.0001) regions. The cardiovascular risk score was associated with WMH in frontal (P<0.0001), occipital (P<0.0001) and parietal-temporal (P<0.0001) regions but not in deep structures. **Conclusions:** Our results indicate that, regardless of their location, WMH might accelerate the brain aging process throughout adulthood in the general population as a result of vascular risk factors, but also independent of them. Preventive strategies against WMH could help to delay brain aging.

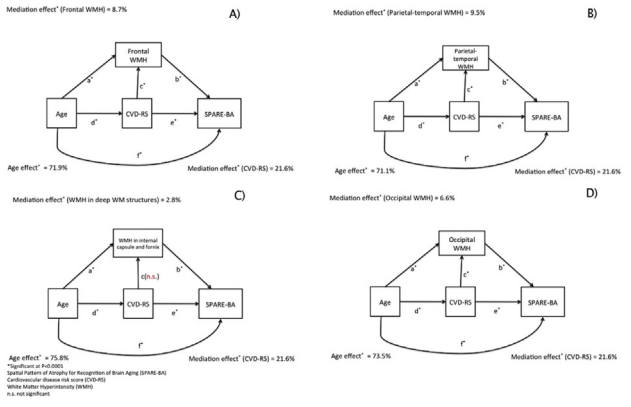

Figure 1. Four structural equation models showing potential causal association of regional WMH in the A) frontal, B) parietal -temporal, C) deep structures including fornix and internal capsule and D) occipital regions, with brain aging patterns of atrophy (SPARE-BA) across the adulthood life span from the SHIP sample (range 20-90 years, median = 53 years).

IC-03-04

WHITE MATTER HYPERINTENSITIES IN GENETIC FRONTOTEMPORAL DEMENTIA: A GENFI STUDY

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Background: Around a third of frontotemporal dementia (FTD) is caused by mutations in three main genes: progranulin (*GRN*),

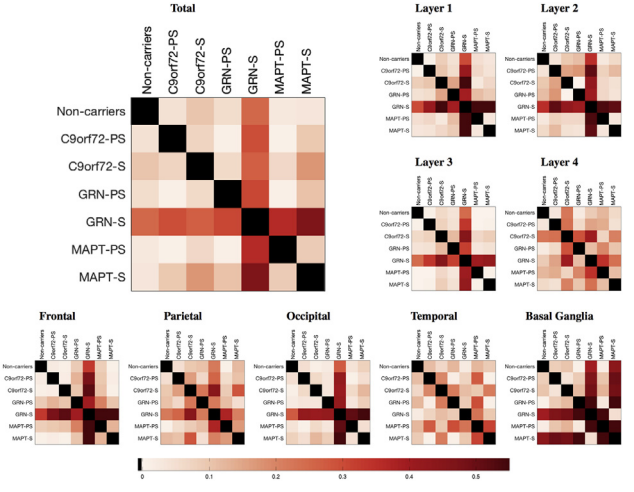

Figure 1. Effect sizes of observed differences between groups at local (layers and lobes) and global scales; PS - Presymptomatic ; S - Symptomatic.