

DOES INFLAMMATION CONTRIBUTE TO THE DEVELOPMENT OF POST-STROKE DEMENTIA: YES

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Introduction: Stroke and the deposition of amyloid in the cerebral cortex are both known risk for developing dementia (Snowdon et al., 1997) (Leys et al., 2005). While animal models suggest that stroke induced inflammation and amyloid deposition both act synergistically (Cechetto et al., 2008), this relationship remains to be established in human stroke. We conducted a pilot study to determine the spatial and temporal relationship between amyloid deposition, microglia activation and cognitive performance in stroke-patients (see Thiel et al 2014)

Methods: 7 Patients (55-85y) with first supratentorial ischemic stroke underwent MRI-scanning and the Montreal Cognitive Assessment (MOCA) within 2 weeks and 5-7 months post stroke. Two PET-scans were performed between 5 and 7 months after the event to assess amyloid deposition (^{11}C -PIB) and microglia activation (^{11}C -[R]-PK11195). MRI was performed on a clinical 1.5T MRI scanner (Siemens Magnetom, 1mm resolution, T1-weighted, T2-weighted, and FLAIR), PET-scanning was performed on an ECAR HR+ scanner (Siemens) after a transmission scan of 10 minutes duration. Patients received 370MBq of ^{11}C -PIB and 370MBq of ^{11}C -[R]-PK11195 in separate scanning session 1-2 days apart. For the PIB-scans dynamic data acquisition started 30 minutes after injection (7 frames 600 sec each), for the ^{11}C -[R]-PK11195-PET a series of 21 dynamic scans was acquired. Images were reconstructed using filtered back-projection (Hanning filter: kernel FWHM=3 mm) after correction for attenuation, scatter and decay. Standardizes uptake value ratios (SUVR_{PIB}) for ^{11}C -PIB in global gray and white matter relative to cerebellum and uptake ratios for ^{11}C -[R]-PK11195 (SUVR_{PK}) between the stroke-affected and unaffected hemisphere gray and white matter were analyzed.

Results: Cognitive performance 5-7 months after the stroke (MOCA2) was negatively correlated with gray matter amyloid deposition (SUVR_{PIB}). This relationship remained significant even when initial cognitive performance (MOCA1) and age were entered as covariates. A multiple regression with MOCA1 and SUVR_{PIB} as independent variables explained 98% of the variance in MOCA2 (adjusted $R^2 = 0.979$, $P < 0.01$). Similarly microglia activation in the stroke-affected hemisphere white matter (SUVR_{PK}) was highly correlated with MOCA2 (after controlling for age and MOCA1, adjusted $R^2 = 0.932$, $P < 0.01$). No significant relationship was found between gray matter SUVR_{PIB} and SUVR_{PK} .

Conclusion: The results of this study in human stroke suggest that cortical amyloid deposition and post-stroke white matter inflammation independently contribute to post-stroke cognitive impairment and may thus constitute separate pathomechanisms to explain amyloid dependent and non-amyloid dependent but inflammation related cognitive decline. If confirmed in larger trials, this finding might offer possibilities for clinical intervention to prevent post-stroke cognitive decline by modulation of inflammation or amyloid deposition.

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