

- 1 Villeneuve, S., Reed, B. R., Madison, C. M., Wirth, M., Marchant, N. L., Kriger, S. et al. (2014). Vascular risk and Abeta interact to reduce cortical thickness in AD vulnerable brain regions. *Neurology*, 83, 40-47.
Notes: OBJECTIVE: The objective of this study was to define whether vascular risk factors interact with beta-amyloid (Abeta) in producing changes in brain structure that could underlie the increased risk of Alzheimer disease (AD). METHODS: Sixty-six cognitively normal and mildly impaired older individuals with a wide range of vascular risk factors were included in this study. The presence of Abeta was assessed using [(11)C]Pittsburgh compound B-PET imaging, and cortical thickness was measured using 3-tesla MRI. Vascular risk was measured with the Framingham Coronary Risk Profile Index. RESULTS: Individuals with high levels of vascular risk factors have thinner frontotemporal cortex independent of Abeta. These frontotemporal regions are also affected in individuals with Abeta deposition, but the latter show additional thinning in parietal cortices. Abeta and vascular risk were found to interact in posterior (especially in parietal) brain regions, where Abeta has its greatest effect. In this way, the negative effect of Abeta in posterior regions is increased by the presence of vascular risk. CONCLUSION: Abeta and vascular risk interact to enhance cortical thinning in posterior brain regions that are particularly vulnerable to AD. These findings give insight concerning the mechanisms whereby vascular risk increases the likelihood of developing AD and supports the therapeutic intervention of controlling vascular risk for the prevention of AD
- 2 Villeneuve, S., Reed, B. R., Wirth, M., Haase, C. M., Madison, C. M., Ayakta, N. et al. (2014). Cortical thickness mediates the effect of beta-amyloid on episodic memory. *Neurology*, 82, 761-767.
Notes: OBJECTIVE: To investigate the associations among beta-amyloid (Abeta), cortical thickness, and episodic memory in a cohort of cognitively normal to mildly impaired individuals at increased risk of vascular disease. METHODS: In 67 subjects specifically recruited to span a continuum of cognitive function and vascular risk, we measured brain Abeta deposition using [(11)C] Pittsburgh compound B-PET imaging and cortical thickness using MRI. Episodic memory was tested using a standardized composite score of verbal memory, and vascular risk was quantified using the Framingham Coronary Risk Profile index. RESULTS: Increased Abeta was associated with cortical thinning, notably in frontoparietal regions. This relationship was strongest in persons with high Abeta deposition. Increased Abeta was also associated with lower episodic memory performance. Cortical thickness was found to mediate the relationship between Abeta and memory performance. While age had a marginal effect on these associations, the relationship between Abeta and cortical thickness was eliminated after controlling for vascular risk except when examined in only Pittsburgh compound B-positive subjects, in whom Abeta remained associated with thinner cortex in precuneus and occipital lobe. In addition, only the precuneus was found to mediate the relationship between Abeta and memory after controlling for vascular risk. CONCLUSION: These results suggest strong links among Abeta, cortical thickness, and memory. They highlight that, in individuals without dementia, vascular risk also contributes to cortical thickness and influences the relationships among Abeta, cortical thickness, and memory
- 3 Villeneuve, S., Massoud, F., Bocti, C., Gauthier, S., & Belleville, S. (2011). The nature of episodic memory deficits in MCI with and without vascular burden. *Neuropsychologia*, 49, 3027-3035.
Notes: This study measured episodic memory deficits in individuals with mild cognitive impairment (MCI) as a function of their vascular burden. Vascular burden was determined clinically by computing the number of vascular risk factors and diseases and neuroradiologically by assessing the presence and severity of white matter lesions (WML). Strategic memory processes were measured with free recall and temporal contextual memory tasks requiring self-initiated retrieval. Nonstrategic memory retrieval processes were appraised with a five-choice recognition procedure. Results showed that MCI participants with high vascular burden displayed impairment of strategic memory processes, whereas MCI participants with no

vascular burden showed impairment of both strategic and nonstrategic memory processes. A similar pattern was found whether vascular burden was measured using a clinical index of vascular risk profile or whether it was measured neuroradiologically by assessing the extent and severity of subcortical WML. However, the effect of WML on memory differed as function of level of education, used here as a proxy for cognitive reserve. Among participants with MCI, those who had higher education and no WML were the least memory impaired. The study also examined memory as a function of whether patients later progressed to dementia after a three-year follow-up. When examining progressors' performance, strategic and nonstrategic processes were both impaired in progressors with no concomitant vascular conditions, whereas progressors with a high vascular burden showed less impairment of nonstrategic than strategic processes. Overall, results indicate that the presence of vascular burden in MCI is associated with selective impairment of strategic memory processes

- 4 Villeneuve, S., Belleville, S., Massoud, F., Bocti, C., & Gauthier, S. (2009). Impact of vascular risk factors and diseases on cognition in persons with mild cognitive impairment. *Dementia and Geriatric Cognitive Disorders*, 27, 375-381.

Notes: BACKGROUND/AIM: To investigate the impact of vascular burden (assessed by the number of vascular risk factors and diseases) on the cognition of persons with amnesic mild cognitive impairment (aMCI). METHODS: This study included 145 participants; 68 meeting criteria for amnesic single-domain or multiple-domain MCI and 77 matched controls. Four cognitive domains were assessed: executive functions, processing speed, episodic memory and general cognitive functioning. RESULTS: A larger vascular burden among aMCI is correlated with lower performance in the executive domain. In addition, persons with aMCI with high vascular burden were more frequently of the multiple domain subtype, whereas persons with no vascular burden were more frequently of the single domain subtype. CONCLUSION: Our findings suggest that the combined effect of multiple vascular risk factors and diseases increases the amount of executive impairment in persons with aMCI. Vascular burden may play an important role in the heterogeneity of aMCI by impairing cognitive functions other than memory