

Serum C-reactive protein is linked to cerebral microstructural integrity and cognitive function

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Objective: C-reactive protein is a marker of inflammation and vascular disease. It also seems to be associated with an increased risk of dementia. To better understand potential underlying mechanisms, we assessed microstructural brain integrity and cognitive performance relative to serum levels of high-sensitivity C-reactive protein (hs-CRP).

Methods: We cross-sectionally examined 447 community-dwelling and stroke-free individuals from the Systematic Evaluation and Alteration of Risk Factors for Cognitive Health (SEARCH) Health Study (mean age 63 years, 248 female). High-field MRI was performed in 321 of these subjects. Imaging measures included fluid-attenuated inversion recovery sequences for assessment of white matter hyperintensities, automated quantification of brain parenchyma volumes, and diffusion tensor imaging for calculation of global and regional white matter integrity, quantified by fractional anisotropy (FA). Psychometric analyses covered verbal memory, word fluency, and executive functions.

Results: Higher levels of hs-CRP were associated with worse performance in executive function after adjustment for age, gender, education, and cardiovascular risk factors in multiple regression analysis ($\beta = -0.095$, $p = 0.02$). Moreover, higher hs-CRP was related to reduced global fractional anisotropy ($\beta = -0.237$, $p < 0.001$), as well as regional FA scores of the frontal lobes ($\beta = -0.246$, $p < 0.001$), the corona radiata ($\beta = -0.222$, $p < 0.001$), and the corpus callosum ($\beta = -0.141$, $p = 0.016$), in particular the genu ($\beta = -0.174$, $p = 0.004$). We did not observe a significant association of hs-CRP with measures of white matter hyperintensities or brain atrophy.

Conclusion: These data suggest that low-grade inflammation as assessed by high-sensitivity C-reactive protein is associated with cerebral microstructural disintegration that predominantly affects frontal pathways and corresponding executive function.

Abbreviations: CRP = C-reactive protein; DTI = diffusion tensor imaging; FA = fractional anisotropy; FLAIR = fluid-attenuated inversion recovery; GMF = gray matter fraction; hs-CRP = high-sensitivity C-reactive protein; ROI = region of interest; SEARCH = Systematic Evaluation and Alteration of Risk Factors for Cognitive Health; TE = echo time; TI = inversion time; TR = repetition time; WM = white matter; WMF = white matter fraction; WMH = white matter hyperintensities.

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Supplemental data at www.neurology.org

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