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### Title

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## HIGH SENSITIVITY C-REACTIVE PROTEIN (HSCRP) LEVELS ARE A SIGNIFICANT PREDICTOR OF FUNCTIONAL CAPACITY ABILITIES IN SCHIZOPHRENIA

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**Background:** Schizophrenia is a heterogeneous disorder characterized by impaired cognition and poor functional outcomes. C reactive protein (CRP), a serum marker associated with inflammatory states, has been shown to be elevated in schizophrenia. The aim of this study was to determine whether inflammation associated with high sensitivity CRP (hsCRP) levels was related to executive functioning or functional capacity deficits in schizophrenia using a well characterized sample.

**Methods:** We assessed high sensitivity CRP (hsCRP) levels, executive functioning (Delis Kaplan Executive Functioning System - DKEFS) ability, and functional capacity (UCSD Performance Based Skills Assessment-Brief - UPSA-B) in 114 clinically stable adults with schizophrenia or schizoaffective disorder and 99 age-matched healthy comparison subjects (HCs).

**Results:** People with schizophrenia had elevated hsCRP levels ( $t = -3.9$ ,  $p < .001$ ,  $d = .625$ ), poorer executive functioning performance ( $t = 11.1$ ,  $p < .001$ ,  $d = -1.5$ ), and functional capacity deficits ( $t = 8.6$ ,  $p < .001$ ,  $d = -1.2$ ) compared to HCs. Higher hsCRP levels were significantly correlated with poorer executive functioning in HCs ( $r(71) = -.246$ ,  $p = .039$ ) but not in people with schizophrenia ( $r(88) = -.030$ ,  $p = .778$ ). Lower total UPSA-B scores were correlated with higher hsCRP levels in schizophrenia ( $r(86) = -.255$ ,  $p = .018$ ) but not in HCs ( $r(71) = -.154$ ,  $p = .200$ ). Hierarchical linear regressions were performed to model the relationships between hsCRP and executive functioning or functional capacity. After accounting for significant demographic (race, education level) and lifestyle factor (BMI, HDL level, current smoking status) correlates; hsCRP levels were a significant predictor of total UPSA-B scores independent of diagnosis ( $\Delta R^2 = .024$ ,  $\Delta F = 4.1$ ,  $p = .046$ ). HsCRP levels did not predict executive functioning composite scores in people with schizophrenia or HCs over and above lifestyle factors ( $\Delta R^2 = .009$ ,  $\Delta F = 1.5$ ,  $p = .231$ ).

**Conclusion:** These data suggest that demographic and lifestyle independent factors may contribute to the relationship between hsCRP levels and functional capacity. The relationship between hsCRP and executive functioning deficits is largely moderated by lifestyle factors in this study. Future studies may help elucidate the potential neurotoxic effects of hsCRP and metabolic dysfunction on cognitive or functional decline in schizophrenia.

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