Inflammation may amplify effect of genetic risk variants for schizophrenia

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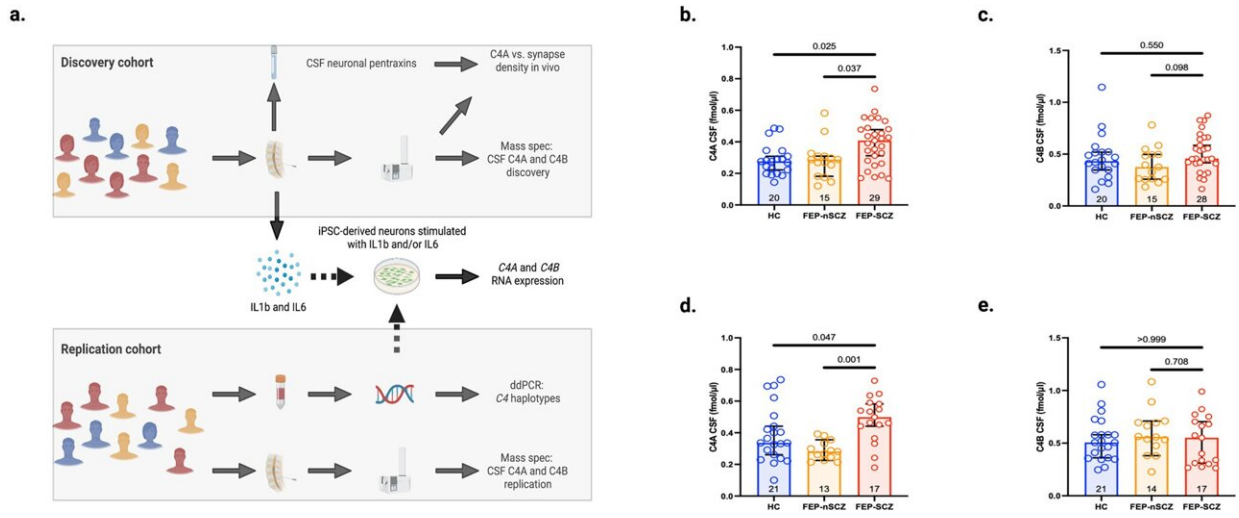

Cerebrospinal fluid levels of C4A are increased in patients with first-episode psychosis who develop schizophrenia. a Overview of the study design. b In the discovery cohort (KaSP), patients with first-episode psychosis (FEP) who developed schizophrenia (FEP-SCZ; n = 29) displayed significantly higher cerebrospinal fluid (CSF) C4A concentrations as compared to healthy controls (HCs; n = 20) or patients with FEP who did not develop SCZ (FEP-nSCZ; n = 15) (HCs: 0.28 fmol/ul; 95% confidence interval [CI] = 0.24–0.33, FEP-nSCZ: 0.29 fmol/ul; CI = 0.22–0.35, FEP-SCZ: 0.41; CI = 0.34–0.45, adjusted P [FEP-SCZ vs. HCs]=0.025, adjusted P [FEP-SCZ vs. FEP-nSCZ]=0.037). c CSF C4B concentrations were similar across groups (HCs [n = 20]: 0.43 fmol/ul; CI = 0.36–0.57, FEP-nSCZ [n = 15]: 0.38 fmol/ul; CI = 0.30–0.49, FEP-SCZ [n = 28]: 0.46 fmol/ul; CI = 0.44–0.58, adjusted P [FEP-SCZ vs. HCs]=0.550, adjusted P [FEP-SCZ vs. FEP-nSCZ]=0.098). d In the replication cohort (GRIP), patients with FEP-SCZ (n = 17) displayed significantly higher CSF C4A concentrations as compared to HCs (n = 21) or patients with FEP-nSCZ (n = 13)

(HC: 0.34 fmol/ul; CI: 0.31–0.47, FEP-nSCZ: 0.28 fmol/ul; CI: 0.25–0.33, FEP-SCZ: 0.50 fmol/ul; CI: 0.41-0.56, adjusted P [FEP-SCZ vs. HCs]= 0.047, adjusted P [FEP-SCZ vs. FEP-nSCZ]=0.001), while (e) CSF C4B concentration were similar across groups (HCs [n = 21]: 0.51 fmol/ul; CI = 0.44–0.63, FEP-nSCZ [n = 14]: 0.56 fmol/ul; CI = 0.47–0.72, FEP-SCZ [n = 17]: 0.55 fmol/ul; CI = 0.41–0.65, adjusted P [FEP-SCZ vs. HCs]=0.999, adjusted P [FEP-SCZ vs. FEP-nSCZ]=0.708). Bar graphs represent medians and error bars represent 95% CIs. Data were analyzed using Kruskal–Wallis H tests followed by post-hoc tests. Significance was set to P