
DISTINCT MOLECULAR PHENOTYPES IN MALE AND FEMALE SCHIZOPHRENIA PATIENTS

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In schizophrenia, sex differences related to age of onset, course of illness and response to antipsychotic treatment may be mirrored by differences in the underlying molecular pathways. We attempted to increase our understanding of these phenomena by carrying out multiplex immunoassay profiling of 95 serum molecules using samples from 4 independent cohorts of male and female first episode antipsychotic naive schizophrenia patients (n=133) and matched controls (n=133). The concentrations of 16 molecules associated with hormonal, inflammation and growth factor pathways showed significant sex differences in schizophrenia patients compared with controls. In line with the numerous sex differences reported in schizophrenia, our findings included alterations in the levels of several hormones, including elevated free and total testosterone in female patients and concomitant sex differences in sex hormone binding globulin and prolactin concentrations. We also found higher levels of thyroxine binding globulin and seven inflammatory markers in male schizophrenia patients only, raising the possibility that some aspects of the widely-reported immunological abnormalities in schizophrenia may be specific for males. Several of these markers showed sex-specific associations with positive and negative syndrome scale (PANSS) scores and changes in concentration after 6 weeks of treatment with antipsychotics. Finally, we also evaluated overlapping and distinct sex-specific biomarkers for schizophrenia, Asperger syndrome, major depressive disorder and bipolar disorder. We propose that future studies should investigate the common and sex-specific aetiologies of schizophrenia, as the current findings suggest that different therapeutic strategies may be required for male and female patients.