Abstract

Background: Neuroactive steroids (NAS) are exogenous or endogenous compounds that act in the central nervous system through genomic and non-genomic ways. They affect neurotransmitter systems by interactions with various receptors. They play role in variety of neuronal proceses such as maturation, protection, signaling or plasticity, thus their role in etiopathogenesis of psychiatric disorders inclouding schizophrenia is studied.

Aims: The primary aim was to analyze levels of NAS in patients, their siblings and healthy controls groups and to examine whether altered NAS levels may be considered as an endophenotype of psychotic disorders. The secondary aims were to verify cognitive deficit as an endophenotype of psychosis and to examine interactions of NAS with cognitive domains.

Methods: Study sample consisted of 1) patients with first episode of psychosis, 2) healthy siblings of the patients, and 3) matching healthy controls. Psychosis was verified or excluded by Mini international neuropsychiatric interview (M.I.N.I.). Scale of prodromal symptoms was used to asses subtreshold psychotic symptoms in healthy siblings. Study procedures included administration of a battery of neuropsychological tests assessing six cognitive domains and examination of NAS plasma levels [cortisol (CORT), 11-deoxycorticosterone (DOC), testosterone (TEST), dehydroepiandrostendione (DHEA), dihydrotestosterone (DHT), and progesterone (PROG)]. For comparison of age, education, NAS and cognitive domain between groups we used Kruskal-Wallis test epsilon2, Dunn test for post hoc analysis, Benjamini-Hochbergs metod for P value adaptation. Interaction in cognition and NAS were assessed by nonparametric analysis of covariance (ANCOVA). Statistics was run on software R v. 3.3.2.

Results: A total of 67 subjects were analyzed (16 patients, 22 siblings, and 29 controls). The Kruskal–Wallis test revealed significant group differences in CORT levels ($p < 0.01$), TEST ($p < 0.01$), and DHT ($p < 0.001$); no difference was found in PROG, DHEA, and DOC. Significant group differences were found in most of the cognitive domains; the patients had the lowest scores. All cognitive domains, except for attention, were affected by the NAS levels. CORT levels of patients correlated with speed of processing ($r = 0.55$) and working memory ($r = 0.52$), while PROG levels correlated with abstraction ($r = -0.63$). In siblings, there was a negative correlation between TEST levels and verbal memory ($r = -0.51$) and PROG with attention ($r = -0.47$).

Conclusions: Higher levels of cortisol and testosterone in siblings are consistent with high-risk states for psychosis. Study limitations (small sample size and administration of antipsychotic medication) did not allow us to establish unequivocally NAS as an endophenotype. Our results verified that specific domains of cognitive deficit (abstraction and verbal memory) can be considered as an endophenotype of psychosis. Multiple interactions between NAS and cognitive functioning, particularly memory functions, were observed.