D-SERINE DEGRADATION IN HUMAN BRAIN: CORRELATION WITH SCHIZOPHRENIA.

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D-Serine has been shown to be a major endogenous coagonist of the NMDA receptors. Accumulating evidence suggests that NMDA receptor hypofunction contributes to the symptomatic features of schizophrenia. D-serine degradation can be mediated by the enzyme D-amino acid oxidase (DAAO). The possible involvement of D-serine in the etiology of schizophrenia is further suggested by the association of the disease with single nucleotide polymorphisms in the DAAO and its regulator (G72). The present study aims to further elucidate whether the DAAO activity is altered in schizophrenia. Specific DAAO activity was measured in postmortem cortex samples of controls and patients groups. The mean DAAO activity was two-fold higher in the schizophrenia patients' group compared with the control group. Furthermore neuroleptics users group (including bipolar disorder patients) had higher DAAO activity. In contrast there was no correlation between DAAO activity and age, age of onset, duration of disease, pH of the tissue and tissue storage time and no effect of gender, cause of death and history of alcohol and substance abuse. In mice either chronic exposure to antipsychotics and acute administration of NMDA receptor blocker MK-801 did not change DAAO activity. These findings provide indications that D-serine availability in the nervous system may be altered in schizophrenia because of increased D-amino acid degradation. Supported by CAEN-ISN, FAPERJ, CNPq and FUJB. Key words: D-serine, DAAO, schizophrenia.