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TREATMENT WITH GLUTAMATERGIC DRUGS IN THE RESISTANT SCHIZOPHRENIA

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Introduction: The neurodevelopmental hypothesis defends the existance of factors that would cause an early impairment on the normal brain development. The neurodegenerative hypothesis proposes the existance of later and progressive pathological phenomena, responsible of the appearance of clinical manifestations and changes on neuroimaging. Both hypotheses would be complementary. Neurodevelopment is completed during adolescence. Within this period, these deficts on executive functions would become apparent, reflecting a neurodevelopmental impairment. Glutamate is the main excitatory neurotransmitter, present throughout the normal postnatal brain development and maduration. In schizophrenic patients and unaffected relatives, a glutamatergic hypofunction has been found and so, an alteration of the dopaminergic mesocortical limbic and nigrostriatal pathways.

Objectives: Usage of molecules that are capable of reversing the glutamatergic hypofunction would be potentially benefitial for either positive or negative symptomathology in schizophrenia.

Method: We have performed a review of several clinical trials (on humans and animals) using glutamatergic drugs alone and combined with neuroleptics to diminish behavioural disturbances related to NMDA blockage.

Results: Usage of glycine binding site agonists (glycine, D- cicloserine, D-serine) has been proposed. D-serine is effective both as monotherapy and combined with neuroleptics. D-cicloserine is not effective on negative symptoms. Usage of high doses of oral glycine (30-60mg a day) on its own has not shown any clinical change but there is an improvement on negative and positive symptoms if combined with neuroleptics.

Conclusion: Nowadays, there is no glutamatergic agonist used in schizophrenia treatment. Out of the three previously mentioned drugs, only D-serine has shown some efficacy.

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