Glycine and D-serine improve the negative symptoms of schizophrenia


Are glutamate receptor agonist drugs effective for people with schizophrenia?

METHODS

Design: Systematic review with meta-analysis.

Data sources: Studies were identified using the Cochrane schizophrenia group’s trial register, BIOSIS Inside, CENTRAL, CINAHL, EMBASE, MEDLINE, and PsychINFO plus handsearches in contact with investigators.

Study selection and analysis: Eligible studies were double blind randomised controlled trials (RCTs) of NMDA, AMPA, or kainate glutamate receptor agonist (glutamatergic) drugs in people with schizophrenia, with a trial duration of more than two weeks. Random and fixed effect models were used to carry out meta-analysis.

Outcomes: Global response (Clinical Global Impression scale [CGI]), Global Assessment Scale (GAS), negative symptoms (Assessment of Negative Symptoms), and cognitive deficiencies (PANSS cognitive subscale).

MAIN RESULTS

Eighteen RCTs met inclusion criteria. The glutamatergic drugs investigated were D-cycloserine (7 RCTs), glycine (7 RCTs), and D-serine (3 RCTs); all were used in combination with antipsychotic medication. Glycine and D-serine significantly reduced the negative symptoms of schizophrenia, but there was no significant difference between D-cycloserine and placebo (glycine or D-serine vs placebo, n = 132, SMD = 0.66, 95% CI −1.02 to −0.29, p = 0.0004; D-cycloserine vs placebo, n = 119, SMD = −0.11, 95% CI −0.48 to 0.25; p = 0.6). There was no significant improvement in cognitive deficiencies with glycine or D-serine, and no consistent evidence of improvement in global response compared with placebo (cognitive deficiencies: glycine or D-serine vs control, n = 80, WMD = −2.79, 95% CI −6.17 to 0.60, p = 0.11; global response: glycine vs placebo, dichotomous measures, n = 53, RR = 0.48, 95% CI 0.15 to 1.49; p = 0.2; glycine vs placebo continuous measure (GAS), n = 35, WMD = −3.87, 95% CI −7.69 to −0.05; p = 0.05; D-serine vs placebo, continuous measure (CGI), n = 49, WMD = −0.89, 95% CI −1.87 to −0.09, p = 0.07).

CONCLUSIONS

Glycine and D-serine improve negative symptoms, but not cognitive deficiencies or global response in people with schizophrenia in the short term.

NOTES

All of these studies investigated short term treatment (≤12 weeks) with glutamatergic drugs and may not be applicable to long term treatment for people with schizophrenia.

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Sources of funding: The Wilhelm and Else Stockmann Foundation and special government funding (EVO).

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