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D-serine effects in a schizophrenia patient positive for anti NMDAR antibodies

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Since anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis was first described a decade ago, the family of disorders associated with antibodies (AB) against neuronal surface antigens is one of the most rapidly expanding categories of neurologic disease. We hypothesized that: 1) anti-NMDAR-ABs seropositive patients can be identified among chronic treatment-resistant schizophrenia patients having atypical disease characteristics; and 2) treatment with D-serine (DSR), which acts *in vivo* as NMDAR co-agonist at the NR1 receptor subunit will be beneficial for the patients. Out of 17 DSM-IV-diagnosed schizophrenia patients, a 67 yr old female patient hospitalized since age 27 was seropositive for both IgG and IgM anti-NR1 AB isotypes. There was no evidence of other diseases, including malignancy. Brain MRI revealed non-specific cortical FLAIR/T2 signal hyperintensities and cEEG showed extreme delta brush (EDB) events. The patient entered a 6 wk clinical trial with DSR in doses increased gradually from 1.5 to 4 g/day. This treatment was well tolerated and resulted in increased DSR serum levels from 0.93 to 103.1 μM. No side effects were registered. Positive and Negative Syndrome Scale (PANSS) symptom clusters improved and PANSS total score decreased by 34%. The quality of life of the patient, as assessed by schizophrenia quality of life scale (SQLS) improved considerably (37% total score reduction). At 6 wks, cEEG showed significant reduction of EDB-type activity. This pilot investigation: 1) supports the hypothesis that a subgroup of treatment-resistant patients diagnosed with schizophrenia may suffer from an NMDAR-related autoimmune disorder; and 2) indicates that DSR may represent a novel type of treatment for these patients.

Biography

Uriel Heresco-Levy is a Full Professor of Psychiatry at Hadassah Medical School, Hebrew University and Director of the Psychiatry Department at Herzog Memorial Hospital, Jerusalem, Israel. He is a Member of the European College of Neuropsychopharmacology (ECNP) and Fellow of Collegium International Neuro-Psychopharmacologicum (CINP). He has conducted pioneer clinical trials with N-methyl-D-aspartate receptor (NMDAR) modulators, including glycine, D-serine and D-cycloserine and has published extensively on the role of NMDAR-mediated neurotransmission and D-serine in neuropsychiatric disorders. He is the inventor of patents focusing on the use of NMDAR-neurotransmission pharmacomodulation in Parkinson's disease, major depressive disorder and autoimmune NMDAR encephalopathies.

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