by her mother, who continued on the same dose of clozapine. The baby had normal developmental milestones, except for speech. She began to use consonants m, k, p, and b at the age of 1 year and started using combined syllables, like ba-ba and da-da, at the age of one-and-a-half years. At the age of 2 years she spoke only six to eight words. She would speak only 12 to 15 words until the age of 3 years and she also exhibited stuttering. Even intervention by a speech therapist did not render better results. At the age of 4, she acquired speaking skills in small sentences by joining two or three words, and she would repeat small sentences that she heard. By the end of 5 years, she gained normal fluent speech. Relevant investigations including audiometric analysis were within normal limits. ENT examination ruled out local pathology. There was no history of impaired mother-child relationship, familial phonological disorder, or bilingual environment.

Comment

Most probably, this baby fulfills the criteria of phonological disorder or may have exhibited delayed onset of speech. At least 3% of preschool children present with this disorder of unknown origin, which is often referred as developmental or functional.[3] In my case, the patient was treated only with clozapine throughout her pregnancy. However, it is difficult to draw conclusions that speech difficulty in this child is a possible consequence of pre- and postnatal exposure to clozapine or a consequence of maternal mental illness because schizophrenia in the mother implies an increased risk for poor perinatal outcome.[4] Further studies should address the magnitude of neurodevelopmental difficulties with clozapine.

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Is There a Role for Valproic Acid in the Treatment of Catatonia?

SIR: Catatonia is a complex neuropsychiatric disorder, with various medical and psychiatric etiologies, that presents with autism, rigidity, motor immobility (motor signs of catatonia), as well as uncontrollable anxieties, emotional lability, and compulsive emotions (affective signs of catatonia).[1] Catatonia has been treated successfully with GABAergic agents, such as lorazepam and ECT. Research shows that several treatments with ECT in rats increase gamma-aminobutyric acid (GABA) levels in the CNS.[2] We present a case where valproic acid was used successfully in the treatment of catatonia.

Case Report

"Ms. G" was a 46-year-old woman with a history of alcohol dependence who possibly suffered from a mood disorder for years based on her biopsychosocial history; however, she was never treated for her mood disorder. She presented with motor as well as affective signs of catatonia on multiple admissions to various hospitals within a span of 4 months. She was treated with benzodiazepines with improvement in catatonic motor signs. Ms. G was placed on various antipsychotics for her catatonic affective symptoms, which failed to improve, with her motor signs invariably returning. She was transferred to our institution for further evaluation and after several weeks with no improvement was placed on a regimen of valproic acid, 1000 mg, and within 3 to 4 days her catatonic symptoms dissipated. The patient was discharged on this regimen with no subsequent catatonic episodes.

Comment

Case reports using valproic acid in the treatment of catatonia successfully have documented neuroimaging studies showing a GABA-A receptor density reduction in the brains of catatonic patients.[2] These data further support a GABAergic deficit in catatonic patients. The relationship between catatonia and mood disorders is well established, where approximately a quarter to half the patients with catatonia also meet criteria for a mood disorder.[3] Plasma GABA levels have also been noted to be low in approximately 40% of patients with mood disorders, which further supports the hypothesis of a GABAergic deficit in catatonia and bipolar disorder.[4] Extrapolating from the above, we suggest that GABA modulation may be a significant factor involved in illness ranging from mood disorders to catatonia. The number of patients with catatonic schizophrenia has declined, yet the number of

patients with catatonia associated with mood disorders has remained stable.[3] This may, in part, be due to use of antipsychotics and involvement of a GABAergic mechanism (animal studies have shown GABA modulation of GABA receptors in animals treated on antipsychotics for a period of time).[5] This may support a greater preponderance for GABAergic deficit in mood disorder patients then in schizophrenia patients. The mechanism is not clear on how valproic acid works, but it is clear that it increases CNS GABA. Studies have shown that valproic acid enhances GABA level and neuronal GABA responsiveness. The use of valproic acid should be considered an option for treatment of catatonic patients, particularly those with mood disorders.

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Stimulating Research: A Prospective, Randomized, Double-Blind, Sham-Controlled Study of Slow Transcranial Magnetic Stimulation in Depressed Bipolar Patients

SIR: Patients with bipolar disorder may spend more than half of their lives experiencing depression.[1] Unfortunately, antidepressant treatment may adversely affect the overall course of bipolar illness, increasing the rates of rapid cycling and inducing chronic depressive states.[2] Menkes et al.[3] showed that slow (F≤1 Hz) repetitive transcranial magnetic stimulation (rTMS) applied to the right dorsolateral prefrontal cortex (DLPFC) proved to be safe and effective in the treatment of unipolar depression. This exploratory study explores safety and efficacy, in bipolar depression.

Case Report

We studied five type I bipolar disorder depressed patients on a stable mood stabilizer regimen without antidepressant treatment. Four subjects were randomly assigned to receive active rTMS, and one was assigned to sham rTMS. Patients were maintained on their medications: lithium (N = 2), risperidone (N = 1), quetiapine (N = 1), divalproex (N = 1), and lamotrigine (N = 1). One patient was on two medications. Treatments were performed using a 9 cm circular coil connected to a Cadwell MES-10 stimulator (Cadwell Laborties, Kennewick, Wash). The coil was placed over the right DLPFC, and 100 consecutive stimuli of slow (1 Hz) rTMS were delivered at 95% of motor threshold. The treatments were scheduled twice a week for four consecutive weeks. Subjects were blind to treatment assignment. The 21-item Hamilton Depression Rating Scale (HAM-D) and Young Mania Rating Scale (YMRS) assessed clinical response weekly for 4 weeks and again 2 weeks after termination of treatment. The rating investigator was blind to treatment assignments.

The active group had three women and one man (average age = 44 years); the placebo subject was a man (45 years old). At the end of the study, subjects receiving rTMS showed greater improvement than the placebo-treated subject. However, throughout the first 4 weeks there was no difference between the groups. One of the subjects did not complete the study. The unequal randomization precluded statistical analysis. There was no evidence of any manic induction as all patients maintained a YMRS = 3. Side effects included unusual feeling, fatigue, memory problems, facial myoclonus, peripheral illusions, flu symptoms, sleep disturbance, dizziness, sore throat, headache, and balance disturbance. The placebo subject reported confusion, dry mouth, and myoclonus.

Comment

This exploratory study suggests that slow right DLPFC rTMS may be beneficial in depressed bipolar patients. The continued improvement from Week 4 to Week 6 suggests this treatment has effects that persist after treatment cessation and that larger future studies of slow rTMS should be extended to 6 weeks' duration, with an increased frequency of administration.

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