Suppression of Levodopa-Induced Dyskinesias by an NMDA Receptor Antagonist in MPTP-Treated Monkeys

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Objective. To evaluate the effect of NMDA receptor antagonists on dyskinesias complicating the response to long-term levodopa therapy.

Background. Dopaminergic mechanisms are influenced by the extensive glutamatergic innervation of the basal ganglia; blockade of NMDA receptors may thus affect both the anti-parkinsonian effects and the dyskinetic complications of levodopa.

Methods. Six monkeys (*Macaca mulatta* and *fascicularis*) were given MPTP intravenously until stable parkinsonism was

attained. Animals were then treated with oral levodopa daily until dyskinesias appeared. LY235959, a competitive NMDA antagonist, was administered subcutaneously in 0.5-, 1-, 3-, and 5-mg/kg doses, each three times, in combination with the minimal subcutaneous dose of levodopa/benserazide that induced moderate dyskinesias. Vehicle combined with levodopa served as the control. Animals were scored every 20 minutes by direct examination and subsequent videotape analysis by a blinded examiner.

Results. LY235959 (3 mg/kg) abolished oral dyskinesias and diminished by 70% choreic and dystonic limb dyskinesias ($p < 0.01$) induced by levodopa. The quality of "on" states was unchanged compared with levodopa plus vehicle. Lower doses of LY235959 failed to significantly affect levodopa-induced dyskinesias; the highest dose (5 mg/kg) increased dystonic movements.

Conclusions. Blockade of NMDA receptors may improve motor responses to levodopa during long-term therapy, ameliorating dyskinetic complications while maintaining the beneficial effects on parkinsonian symptoms.

Corrections

In the 47th Annual Meeting Program of the American Academy of Neurology (*Neurology* 1995;45[suppl 4]), abstract number 1011P was mistakenly withdrawn. It is printed below. In abstract number 335P, an error appeared in the title. The abstract, with the corrected title, is reprinted below. The editors apologize for the errors.

1011P

Anti-Ri Paraneoplastic Syndrome in Association With Primary Lung Carcinoma

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Objective. To describe the first case of paraneoplastic anti-Ri antibody syndrome in association with a primary lung tumor.

Background. Anti-Ri is an anti-neuronal nuclear antibody associated with a paraneoplastic syndrome usually including opsoclonus and ataxia. It has most often been described in association with breast and gynecological malignancies.

Methods. A previously healthy 65-year-old woman presented with a 4-month history of progressive gait ataxia, opsoclonus, and startle myoclonus. Initial brain imaging, cerebrospinal fluid studies, and systemic malignancy screen were negative. Paraneoplastic antibody studies yielded a 1:7,680 anti-Ri antibody titer. Serial screens for systemic malignancy were performed.

Results. Nine months after the onset of symptoms, a chest CT showed a small right hilar mass. Open biopsy revealed a non-small-cell lung carcinoma. Chemotherapy was initiated and the patient's neurological symptoms improved.

Conclusion. Paraneoplastic syndromes have traditionally been associated with specific malignancies. A variety of tumor types may have the potential to express antigens that are linked with CNS neurons. This case suggests that the search for malignancy in paraneoplastic syndromes should not be limited to specific tumor types.

335P

Evaluation of the Glutamate Antagonist Remacemide Hydrochloride in Huntington's Disease

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Objective. To evaluate the effect of short-term treatment with remacemide, a glutamate antagonist, on motor characteristics of Huntington's disease (HD).

Background. Evidence from excitotoxic animal models of HD suggests that glutamate receptor antagonists may exert anti-choreic effects. Remacemide is a non-competitive, N-methyl-D-aspartate (NMDA) ion channel blocker, which has not previously been evaluated in patients with neurodegenerative disorders.

Design/Methods. Thirty-one (18M/13F) ambulatory HD patients were randomized in double-blinded fashion to receive low-dose remacemide (200 mg per day), high-dose remacemide (600 mg per day) or placebo for 4 weeks. Tolerability and safety were the primary outcome measures. Oculomotor function, rapid alternating movements, chorea, and dystonia were assessed by a standardized rating scale.

Results. Twenty-nine subjects completed the study; two subjects in the high-dosage group withdrew, one because of poor compliance and another due to nausea and vomiting. Baseline clinical characteristics were comparable among treatment groups. Subjects in the low-dose (200 mg per day) group showed a 1.6 ± 3.7 point improvement in scores of maximal chorea compared with a 1.1 ± 2.4 point worsening in the placebo group. No other changes in motor performance were found, and no differences between high-dose remacemide and placebo were demonstrated.

Conclusions. The glutamate antagonist remacemide hydrochloride is well tolerated and may exert short-term anti-choreic effects in HD patients. A larger and longer-term trial is warranted to further characterize the tolerability and potential efficacy of this agent.

Study supported by Fisons Pharmaceuticals.

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Karl Kieburtz, M. McDermott, F. J. Marshall, et al.
Neurology 1995;45;1417-1417-b
DOI 10.1212/WNL.45.7.1417-b

This information is current as of July 1, 1995

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