γ-Hydroxybutyrate in Narcolepsy

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Broughton and Mamelak [1] recently reported the successful use of oral γ-hydroxybutyrate (GHB) in the treatment of narcolepsy. Treatment not only improved the continuity of night sleep but also reduced the number of daytime sleep attacks and cataplexy. The drug was very well tolerated. We wish to record our own less successful experience with intravenous GHB in narcoleptics to emphasize the very different clinical effects of oral and intravenous administration of the drug.

Four patients with severe narcolepsy and cataplexy gave informed consent and were given GHB, 25 mg per kilogram of body weight, by slow intravenous drip; on a separate occasion they received a single-blind infusion of saline. All other drugs were discontinued 24 hours before either GHB or saline was given. Saline injection did not alter the severity of narcolepsy or cataplexy in any subject. GHB caused drowsiness, slurred speech, ataxia, and nystagmus for 1 to 2 hours in all subjects, with reduction in mean dominant electroencephalographic frequency from 8 to 9 Hz down to 3 to 6 Hz. One patient was unrousable for 30 minutes, with frequent sleep apnea, and three had visual hallucinations with euphoria and disinhibition. During this period of reduced awareness, frequent cataplectic attacks occurred in two patients with loss of muscle tone and tendon reflexes. Three subjects developed orofacial dyskinesia, limb chorea, or dystonic foot postures. Sleep attacks and cataplexy were more frequent and severe after GHB than after saline in all patients for 24 hours.

GHB given intravenously in a dose of 60 mg per kilogram has been used widely as an adjunct in anesthesia, but it causes variable sedation and recently has fallen from use. Side effects in humans have been infrequent [2]; primates given the very high dose of 200 mg per kilogram intravenously may develop myoclonus but not tonic-clonic seizures [4]. The physiological role of the GHB occurring naturally in mammalian brain is unknown; there appears to be very little conversion to γ-aminobutyric acid [3]. Since GHB given intravenously causes a high incidence of distressing symptoms in narcoleptic patients, further investigation of the agent should be confined to the oral route.

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Staging in Reye Syndrome

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In the August 1980 issue of the *Annals* (Ann Neurol 8:202, 1980), Dr Trauner responded to Dr Tomasi's letter on Reye syndrome and referred to my chapter "Clinical experience with Reye's syndrome" in Pollack JD (ed): Reye's Syndrome (New York, Grune & Stratton, 1975, pp 3–14). I believe she has incorrectly interpreted our staging of patients. Having devised the protocol with Dr Huttenlocher, I was using his staging and not that of Lovejoy. Our stage III is not equivalent to the Lovejoy stage III. Furthermore, we were not using intracranial monitoring. Mortality rate at this hospital from 1973 through 1976 was 52%. Since mid-1977 we have been monitoring and using mannitol more judiciously, and the mortality rate of children requiring monitoring is now 18%. I do not believe it is helpful to use our early study to compare outcome with an entirely different approach to treatment.

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Amantadine in Essential Tremor

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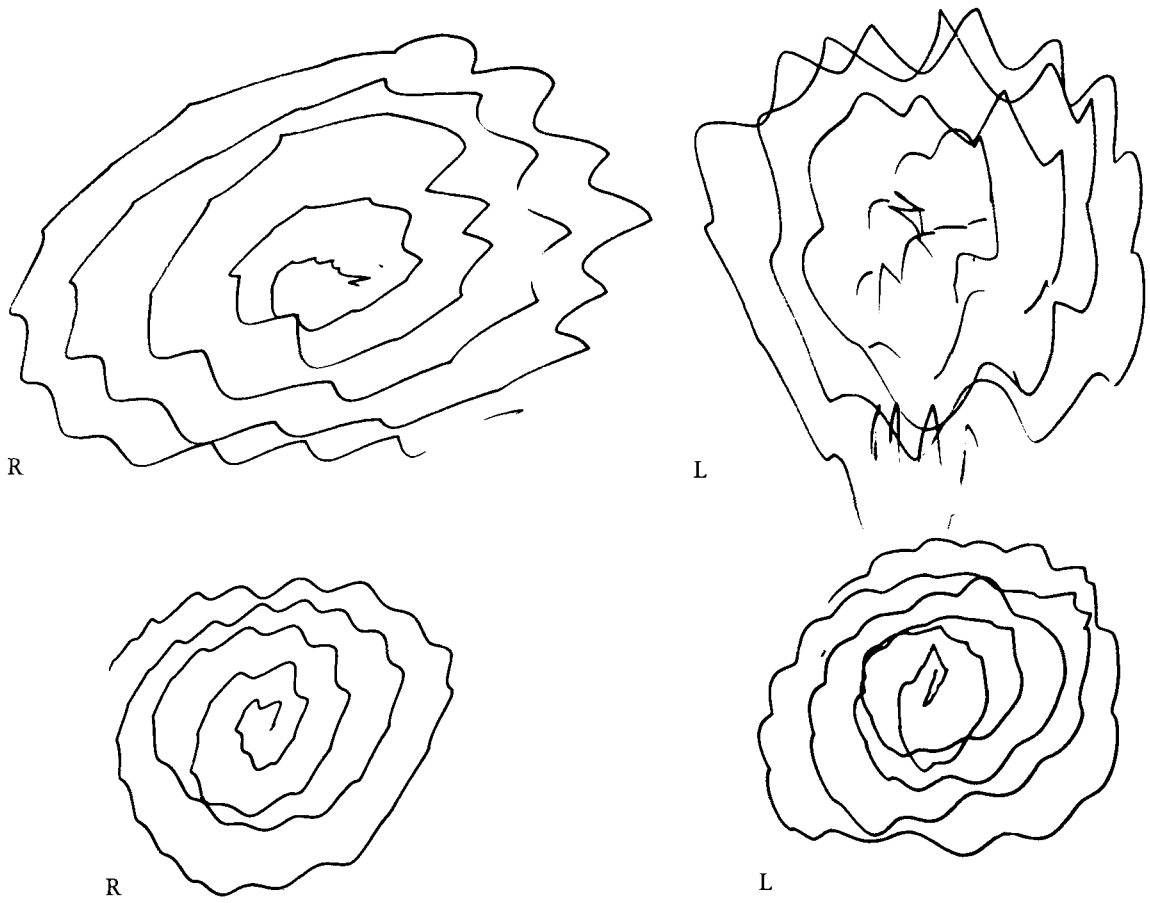
Amantadine hydrochloride, NF (Symmetrel), is a synthetic antiviral agent which has shown beneficial effect in Parkinson disease, drug-induced extrapyramidal disorders, and postherpetic neuralgia. The drug was found to improve tremors in 15 out of 26 patients with essential tremor (Critchely E: Clinical manifestations of essential tremor. J Neurol Neurosurg Psychiatry 35:365–372, 1972).

Amantadine was administered to 8 men with essential tremor with a mean age of 64 years. No other antitremor drugs were used, and the average duration of follow-up was 16 weeks. The dosage of the drug was 100 mg twice daily in 5 patients, 200 mg twice daily in 1 patient, and 100 to 200 mg twice daily in the remaining 2 patients. The effect of the treatment was assessed by clinical examination and by comparison of the Archimedes spiral of each unsupported hand recorded before and following treatment.

Tremor improved in 5 of the 8 patients (Figure), while it got worse in 2 and no change occurred in the other. No side effects attributable to the drug were encountered.



Effect of amantadine, 100 mg twice daily, in essential tremor: Archimedes spiral by unsupported hand recorded before (top) *and following* (bottom) *treatment.* (R = *right hand;* L = *left hand.)*

Amantadine is of limited value in the treatment of essential tremor but a drug to be considered when propranolol is contraindicated or ineffective.

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Palatal Myoclonus Responding to Carbamazepine

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We recently observed a rare example of palatal myoclonus occurring in the setting of active central nervous system syphilis with tabes dorsalis. The woman had been well until May, 1979, when she developed a sudden period of unconsciousness that lasted for several hours and was followed by amnesia, euphoria, and uncontrolled logorrhea. Attacks of involuntary movements affecting the lower jaw, tongue, and pharynx began six weeks later, occurring ten to twenty times a day and lasting 10 to 20 seconds each. On examination she was alert, euphoric, and demented. She had Argyll Robertson pupils and a continuous, rhythmic contraction of the soft palate bilaterally with a frequency of 120 to 200 per minute. Paroxysms of rhythmic contractions of the posterior pharyngeal wall, tongue, and lower jaw appeared intermittently. Both these involuntary movements were observed during sleep.

Laboratory data showed a positive serological test for syphilis and *Treponema pallidum* hemagglutination titer in the blood, the latter in a dilution of 5,120. The cerebro-