behavioral supersensitivity to dopamine agonists develops following striatal dopamine denervation, imaging of neuroleptic binding sites on nondisrupted striatal tissue using radiolabeled spiperone has not yet provided insight into the mechanism responsible for such phenomena.

References

- Bennett JP Jr, Wooten GF: Dopamine denervation does not alter in vivo ³H-spiperone binding in rat striatum: implications for external imaging of dopamine receptors in Parkinson's disease. Ann Neurol 19:378-383, 1986
- Kuhar MJ, Murrin C, Malouf AT, Klemm N: Dopamine receptor binding in vivo. The feasibility of autoradiographic studies. Life Sci 22:203–210, 1978
- Laduron PM, Janssen PFM, Leysen JE: Characterization of specific *in vivo* binding of neuroleptic drugs in rat brain. Life Sci 23:581-586, 1978
- Leslie CA, Bennett JP Jr: ³H-Spiperone binds selectively to striatal D2 dopamine receptors *in vivo*: a kinetic and pharmacological analysis. Brain Res (in press)
- Perlmutter JS, Raichle ME: In vitro or in vivo receptor binding: where does the truth lie? Ann Neurol 19:384–385, 1986

Naloxone in Gilles de la Tourette's Syndrome

N. Gadoth, MD, C. R. Gordon, MD, DSc, and J. Streifler, MD

We read with interest the letter by Sandyk [2] and would like to add our experience. Dr. Sandyk has reported on transient abatement of tics in a patient with Gilles de la Tourette syndrome (GTS) treated with naloxone. Based on observations from two patients [1, 2], he postulated the possible role of the endogenous opioid system in GTS. However, to quote Sandyk, "... both over- and underactivity of the opioid system ..." can account for the previous reports.

We studied a 26-year-old man with a 20-year history of progressive multiple tics accompanied by vocalization, echolalia, and coprolalia. For the past 3 years, he has been treated with haloperidol, clonidine, pimozide, tiapride HCl, and carbamazepine, with only partial or transient relief. At the time of examination he had been drug-free for several months. Head shaking, facial tics, grimacing, lingual protrusion, and vocalizations were evident and could be counted easily. In a simple blind trial, 3 ml of saline or 3 ml of saline containing 1.2 mg of naloxone was administered intrave-

| Effect | of Salin | e or Na | loxone | Admir | nistration |
|--------|------------|---------|--------|-------|------------|
| in To | urette's S | yndrom | e | | |

| Symptoms | Saline | Naloxone |
|--|--------|----------|
| No. of vocalizations | 333 | 133 |
| No. of head shaking | 235 | 165 |
| No. of facial tics, grimacing, or lingual protrusion | 607 | 962 |
| Total | 1,175 | 1,260 |

nously. The patient's behavior was recorded on videotape, and later the film was evaluated by three observers.

The number of vocalizations, head movement, facial grimacing, and tongue protrusion was counted from the recordings for the 50-minute periods following the separate saline and naloxone administrations. It can be seen from the Table that, although there is some variation in the number of a particular symptom between the naloxone and saline periods, the total number of tics was not affected by naloxone.

We observed no beneficial effect on the number or severity of tics in our patient with classic severe GTS.

Department of Neurology Beilinson Medical Center Petah Tiqva 49 100 Israel

References

- Gillman MA, Sandyk R: Gilles de la Tourette syndrome—effect of analgesic concentrations of nitrous oxide. Br Med J 288:114, 1984
- Sandyk R: The effects of naloxone in Tourette's syndrome. Ann Neurol 18:367-368, 1985

Dysarthria–Clumsy Hand Syndrome and Cerebellar Hemorrhage

E. P. Roy, III, MD, Robert W. Keefover, MD, Jack E. Riggs, MD, and Gary D. Marano, MD*

Initially described by Fisher [2] in 1967, the dysarthriaclumsy hand syndrome has been associated with lesions in the pons [2, 4] and internal capsule [1, 3]. A cerebellar lesion producing this syndrome, though not previously reported, is not unexpected and was even predicted by Fisher. We describe a patient with the dysarthria-clumsy hand syndrome associated with a small, deep cerebellar hemorrhage.

A 57-year-old right-handed hypertensive man was admitted with a one-day history of slurred speech and clumsiness of the right hand. On the evening prior to admission, he noted the abrupt onset of slurred speech. There was no associated alteration of consciousness, dizziness, nausea, dysphagia, visual changes, aphasia, weakness, or numbness. The next morning, his speech remained slurred and he noticed that his right hand was clumsy while attempting to write.

On admission, his blood pressure was 140/86. He was alert with intact cognitive functioning. His speech was fluent but dysarthric. There was no aphasia. Pupil responses; visual fields; eye movements; facial strength and sensation; tongue, palate, and swallowing movements; limb sensation; muscle strength and tone; and deep tendon reflexes were normal. There was no pronator drift. The right hand exhibited decreased facility with finger tapping and rapid alternating movements. There was no extremity dysmetria or gait ataxia. The toes were down-going on plantar stimulation.



Unenhanced cranial computed tomographic scan demonstrating a small, deep right cerebellar hematoma.

Cranial computed tomographic scan on admission demonstrated a small, deep right cerebellar hemorrhage (Figure). Brainstem sections were normal. The patient was discharged two days later, with mild improvement in his speech and right hand function. Cranial magnetic resonance imaging done $7\frac{1}{2}$ weeks later showed a small residual defect in the same region of the cerebellum. Two months following admission, the patient's speech remained dysarthric but his right hand symptoms had resolved.

This case further illustrates the concept that the dysarthriaclumsy hand syndrome is not a distinct clinicopathological entity, but rather a clinical syndrome associated with pathological lesions at various sites, including the pons, internal capsule, and cerebellum.

Department of Neurology and *Radiology West Virginia University Medical Center Morgantown, WV 26506

References

- Donnan GA, Tress BM, Bladin PF: A prospective study of lacunar infarction using computerized tomography. Neurology 32:49-56, 1982
- Fisher CM: A lacunar stroke: the dysarthria-clumsy hand syndrome. Neurology 17:614-617, 1967
- 3. Spertell RB, Ransom BR: Dysarthria-clumsy hand syndrome produced by capsular infarct. Ann Neurol 6:263-265, 1979
- Tuhrim S, Yang WC, Rubinowitz H, Weinberger J: Primary hemorrhage and the dysarthria-clumsy hand syndrome. Neurology 32:1027-1028, 1982

Naloxone Reverses the Inhibition by Sodium Valproate of GABA Transport Across the Deiters' Neuronal Plasma Membrane

H. Hydén,* A. Cupello,† and A. Palm*

 γ -Aminobutyric acid (GABA) can diffuse through a GABAreceptive membrane such as that of the Deiters' neuron in the rabbit. This was assessed by our group by studying the passage of GABA as a function of its "extracellular" concentration [4]. This mechanism is extremely efficient, suggesting that it may be mainly responsible for removal of GABA from synaptic clefts [2]. This process is inhibited (by 57%) by the anticonvulsant drug sodium valproate (VPA) at concentrations higher than those corresponding to the therapeutic range [3] and also by met 5-enkephalin [1].

In a clinical case report, Steiman and associates [5] communicated that an accidental overdose of sodium valproate was successfully treated with the opioid antagonist naloxone. Our experimental data indicate that VPA and met 5-enkephalin have a similar effect on GABA diffusion through a GABA-receptive membrane. The question thus arose: Do they interact with the same site, in some way coupled to the GABA postsynaptic diffusion mechanism [1]? If so, the site should be an opioid receptor and the VPA effect should be antagonized by low concentrations of naloxone. This mechanism might explain why naloxone was effective in the case cited above.

To investigate this possibility, we used the experimental model described in detail elsewhere [3, 4], in which a single Deiters' neuronal membrane, microdissected from the rabbit brainstem, separates two microchambers (M_1 and M_2). We studied the passage of [³H]GABA, 0.2 mM in Earle's bal-

Effects of Various Agents on GABA Diffusion through the Rabbit Deiters' Neuronal Membrane

| Agent | Passage of GABA (moles/ μ m ² × sec) ^{a,b} |
|---|---|
| Control | $\frac{1.01 + 0.17 \times 10^{-14}}{(7)}$ |
| 2.4 mм VPA | $\begin{array}{l} 0.44 \pm 0.05 \times 10^{-14}; \\ p^{\rm c} < 0.0001 \ (6) \end{array}$ |
| 2.4 mM VPA + 10^{-9} M naloxone | $0.85 \pm 0.08 \times 10^{-14};$ NS ^c ; $p^{\rm d} < 0.0001$ (4) |
| $2.4 \text{ mM VPA} + 10^{-7} \text{ M naloxone}$ | $0.86 \pm 0.04 \times 10^{-14};$ NS ^c ; $p^{d} < 0.0001$ (3) |

^aNumber in parentheses refers to the number of experiments. ^bAll values are \pm standard deviation.

^cCompared with control.

^dCompared with the 2.4 mM VPA value.

GABA = γ -aminobutyric acid; VPA = sodium valproate; NS = not significant.