

Calne D B, Teychenne P F, Claveria L E, Eastman R, Greenacre J K & Petrie A. Bromocriptine in Parkinsonism. *Brit. Med. J.* 4:442-4, 1974.
[Department of Medicine (Neurology), Royal Postgraduate Medical School, Hammersmith Hospital, London, England]

This paper describes the initial use of bromocriptine in Parkinson's disease. Bromocriptine was the first of a subsequently large series of ergot derivatives that behaved as artificial dopamine agonists. Previous dopaminomimetic therapy had employed levodopa, which required conversion to dopamine by the enzyme dopa decarboxylase. Since cerebral dopa decarboxylase is decreased in Parkinson's disease, bromocriptine had a theoretical advantage over other treatment. [The *SCI*[®] indicates that this paper has been cited in over 235 publications.]

Donald B. Calne
Division of Neurology
University of British Columbia Health
Sciences Centre Hospital
Vancouver, British Columbia V6T 1W5
Canada

May 19, 1987

Bromocriptine was developed by E. Flückiger and colleagues¹ to suppress plasma concentrations of prolactin. Swedish researchers² subsequently showed that it behaved as a dopamine agonist in animals. We tested its possible application to Parkinson's disease in a double-blind study on small groups of patients, and efficacy was clearly established. The main practical benefit that stemmed from this discovery was the introduction of a drug with a therapeutic index comparable to levodopa but a different profile of adverse effects.³

Levodopa causes dyskinesia and after some years there are profound fluctuations in response over the course of a day. In contrast, bromocriptine causes less dyskinesia, and efficacy is more sus-

tained after each dose; however, bromocriptine induces more frequent and severe psychiatric side effects than levodopa. Now both drugs are commonly used together—a logical approach first suggested in 1983.⁴ Bromocriptine played a crucial role in the series of observations that led to the subcategorization of dopamine receptors into two types.⁵ The full implications of these developments are likely to emerge over the next few years, with the advent of drugs that selectively stimulate D1 or D2 receptors and are suitable for human use.⁶

The discovery of bromocriptine's anti-Parkinson efficacy stemmed from a combination of circumstances including an international "club" of neuropharmacologists whose interest in dopamine can reasonably be described as obsessive. Also relevant was a fortuitous friendship with Walter Aellig, then a young clinical pharmacologist involved in the development of new compounds at Sandoz in Basel. He had trained, together with me, for two years at University College Hospital in London, under the guidance of Desmond Laurence.

Bromocriptine is the first dopamine agonist to be introduced into routine clinical use. Undoubtedly, many new molecules with varied profiles of dopamine receptor activation will follow. In addition to their application to Parkinson's disease, drugs that increase dopaminergic transmission have an important place in the management of prolactinomas. The role of bromocriptine as a selective D2 agonist has allowed important conclusions to be drawn concerning the clinical manifestations of inadequate and excessive drive to this category of dopamine receptor (parkinsonism and schizophrenia, respectively).

1. Flückiger E & Wagner H. 2-Br- α -ergokryptin; Beeinflussung von Fertilität und Laktation bei der Ratte (Effects of bromocriptine on murine fertility and lactation). *Experientia* 24:1130-1, 1968. (Cited 175 times.)
2. Corrodi H, Fuxe K, Hökfelt T, Lidbrink P & Ungerstedt U. Effect of ergot drugs on central catecholamine neurons: evidence for a stimulation of dopamine neurons. *J. Pharm. Pharmacol.* 25:409-12, 1973. (Cited 490 times.)
3. Thorner M O, Flückiger E & Calne D B. *Bromocriptine. A clinical and pharmacological review.* New York: Raven Press, 1980. 181 p. (Cited 75 times.)
4. Calne D B. Current views on Parkinson's disease. *Can. J. Neurol. Sci.* 10:11-5, 1983.
5. Keibarian J W & Calne D B. Multiple receptors for dopamine. *Nature* 277:93-6, 1979. (Cited 1,310 times.)
6. Karobath M. The pharmacology of CY 208-243. A CNS active dopamine-1 receptor agonist. (Calne D B, Fahn S, Goldstein M & Marsden C D, eds.) *Symposium on Parkinson's disease.* New York: Raven Press. (In press.)