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Seeman P. Brain dopamine receptors. *Pharmacol. Rev.* 32:229-313, 1980.
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The discovery of the antipsychotic/dopamine receptor in 1974 and the vast growth of dopamine receptor data resulted in a need for a single-place source to obtain the information readily. The central rôle of dopamine receptors in such psychomotor diseases as schizophrenia and Parkinson's disease may account for the frequent citations. [The *SCI*® indicates that this paper has been cited in more than 1,200 publications.]

The Mushrooming World of Dopamine Receptors

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Since hallucinations and delusions in schizophrenia and psychosis are controlled by dopamine receptor-blocking drugs, and since the immobility of Parkinson's disease is alleviated by dopamine receptor stimulants, dopamine receptors are of considerable clinical and research interest. Possibly this explains the many citations to this review.

My wife, Mary, a psychiatry resident at Manhattan State Hospital in 1962, encouraged me to start schizophrenia-related research during my graduate studies at Rockefeller University with George Palade. I later chose to search for the brain's antipsychotic receptor. We found this receptor in 1974-1975 using radioactive dopamine[1] or radioactive haloperidol.[2,3] The finding was based on the fact that the tissue binding of either of these radioactive compounds was inhibited by 1 nanomolar haloperidol. This was the concentration known to exist in the cerebrospinal fluid of haloperidol-medicated psychotic patients. Although I named this antipsychotic receptor "the neuroleptic/dopamine receptor,"[4] it was later rechristened as the dopamine D2 receptor.[5] This work[1-3] provided the first direct evidence that antipsychotic drugs acted on dopamine receptors, since animal work had difficulty settling which of the many catecholamine receptors were selectively blocked by these drugs.[6,7]

Like rabbits, dopamine receptors soon rapidly multiplied in name and number.[8] Although Milt Titeler suggested that a review be written solely on our own lab data, I felt it essential to analyze the mushrooming world literature on these receptors (then appearing at 200 papers per year), in order to determine which of these "rabbits" might be identical. The work devoured a year of my life, but my wife said it was good occupational therapy and must have demonstrated something to our three sons.

This review is convenient to cite because it contains references to the chemistry of dopamine agonists and antagonists, as well as to the biology and extensive pharmacology of dopamine receptors. It also provided a receptor model for medicinal chemists.

The review served as only one small step in the research strategy of seeking a possible biological basis for schizophrenia. The D2 receptors appear abnormal in structure and are elevated in the schizophrenic brain,[9] particularly on the left side.[10]

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4. **Seeman P, Lee T, Chau-Wong M & Wong K.** Antipsychotic drug doses and neuroleptic/dopamine receptors. *Nature* 261:717-9, 1976. (Cited 400 times.)
5. **Kebabian J W & Calne D B.** Multiple receptors for dopamine. *Nature* 277:93-6, 1979. (Cited 1,900 times.)
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8. **Titeler M, Weinreich P, Sinclair D & Seeman P.** Multiple receptors for brain dopamine. *Proc. Nat. Acad. Sci. USA* 75:1153-6, 1978. (Cited 100 times.)
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10. **Farde L, Wiesel F-A, Stone-Elander S, Halldin C, Nordstrom A-L, Hall H & Sedvall G.** D_2 dopamine receptors in neuroleptic-naive schizophrenic patients. A positron emission tomography study with [^{11}C]raclopride. *Arch. Gen. Psychiat.* 47:213-9, 1990.

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