

**In Memoriam: Oleh Hornykiewicz (1926-2020) by Mary and Philip
Seeman**

The two of us first heard of Oleh Hornykiewicz during our internship at Harper Hospital in Detroit (1960-61). The causes of Parkinson's disease were not known at the time but Oleh, conducting autopsies in Vienna, discovered a deficiency of dopamine in patients who died with Parkinson's. He studied the brains of people who had died of other neurological diseases – their dopamine levels were intact. He studied many brains and came to the breakthrough realization that the absence of dopamine was specific to Parkinson's disease. He administered L-dopa to Parkinson's patients and, almost miraculously, they were able to move again.

The two of us were excited because we were interested in dopamine as well, not by its absence but, rather, by its excess neurotransmission in psychotic states. A Dutch pharmacologist, Jacques van Rossum, had earlier suggested that schizophrenia might be associated with supersensitive dopamine receptors – not that there was an abundance of dopamine in schizophrenia (to mirror its deficiency in Parkinsonism) but that putative neuronal dopamine receptors, which hadn't yet been discovered, were supersensitive or overreactive to dopamine.

We were anxious to “talk dopamine” with Oleh and, luckily for us, in 1967 all three of us were hired by the University of Toronto. His recruitment was a major coup for the Departments of Psychiatry and Pharmacology.

A cherished early memory is a dinner we attended at the Toronto home of Oleh and his wife Christina soon after our arrival. We didn't, in fact, talk about dopamine but, instead, argued about the pros and cons of abortion on demand and stood by while Oleh showed off their newly purchased dishwasher. Nobody else at the dinner had a dishwasher yet – they were just becoming fashionable. Oleh was very proud of his stacking ability, about the number of dishes his machine could accommodate if you stacked it properly (they had a lot of dishes because they had four

children). You could tell by listening to the account of his dish experiments that he was a meticulous researcher, that he proceeded by formulating hypotheses, devising ways of testing the hypotheses and not taking results for granted until they proved themselves correct over and over.

With time, Oleh and Phil held many dopamine discussions on both diseases, Parkinson's and schizophrenia, and collaborated together on several dopamine projects. Oleh provided post-mortem tissues from Parkinson brains, while Philip, who by then had discovered dopamine D2 receptors, pursued the issue of supersensitivity. They often argued about the meaning of their various discoveries but arguing with Oleh was a pleasure; he was logical, commonsensical, lucid, ultimately convincing.

In the year before Oleh returned to his beloved Vienna, Phil was proud to show him evidence for elevated numbers of supersensitive dopamine D2HIGH receptors in 25 different animal models of psychosis, later confirmed in schizophrenia patients by Kubota, Nagashima, Takano et al. (2017) using positron emission tomography. Oleh, at the time, was invested in a norepinephrine model of schizophrenia but, always open to proof, he finally believed what he saw.

At the Brain Research Institute in Vienna, Oleh continued dissecting brains and, in 1979, received the prestigious Wolf Prize in Medicine for his work on L-dopa. In his 2004 book, *The History of Neuroscience in Autobiography*, he wrote:

“Today, it is generally agreed that the initiation of the treatment of Parkinson's disease with L-dopa represented one of the triumphs of pharmacology of our time. L-dopa's unprecedented success proved, for the first time, that therapeutic neurotransmitter replacement in a chronic, progressive, degenerative brain disease (until then regarded as basically untreatable) was indeed possible. This provided, apart from the benefit to the patients, a stimulus for analogous studies of many other brain disorders, both neurological and psychiatric. As John Hardy (National Institutes of Health, Bethesda) put it in a recent letter to me, ‘L-dopa's discovery was the defining finding for transmitter-based therapeutics.’”

John Hardy was correct. Oleh's discovery led to the establishment of brain tissue banks all over the world, including in Toronto. His work in brain science has been a catalyst for neurology and psychiatry research the world over.

Oleh and Phil continued their dopamine discussions whenever Oleh returned to Toronto (he kept his appointment at the University of Toronto and commuted back and forth until 1992).

Oleh also wrote in his 2004 book:

“..my family and I, still count the 10 years we spent in Toronto as among the happiest years of our life together. The people who were so generous and hospitable, the excellent colleagues, the friendly neighbors, and the easy way to raise children all contributed to our feeling happy and very much at home in Canada. And then there was, again, the allure of nature: intense, boundless, and bountiful.”

In between times, Oleh and Phil corresponded by e-mail. During the last year their conversations veered away from talking “shop” to discussing Vienna subway cars. In his 90s, Oleh still travelled by subway and was unhappy about people eating on the subway and leaving behind empty pizza cartons.

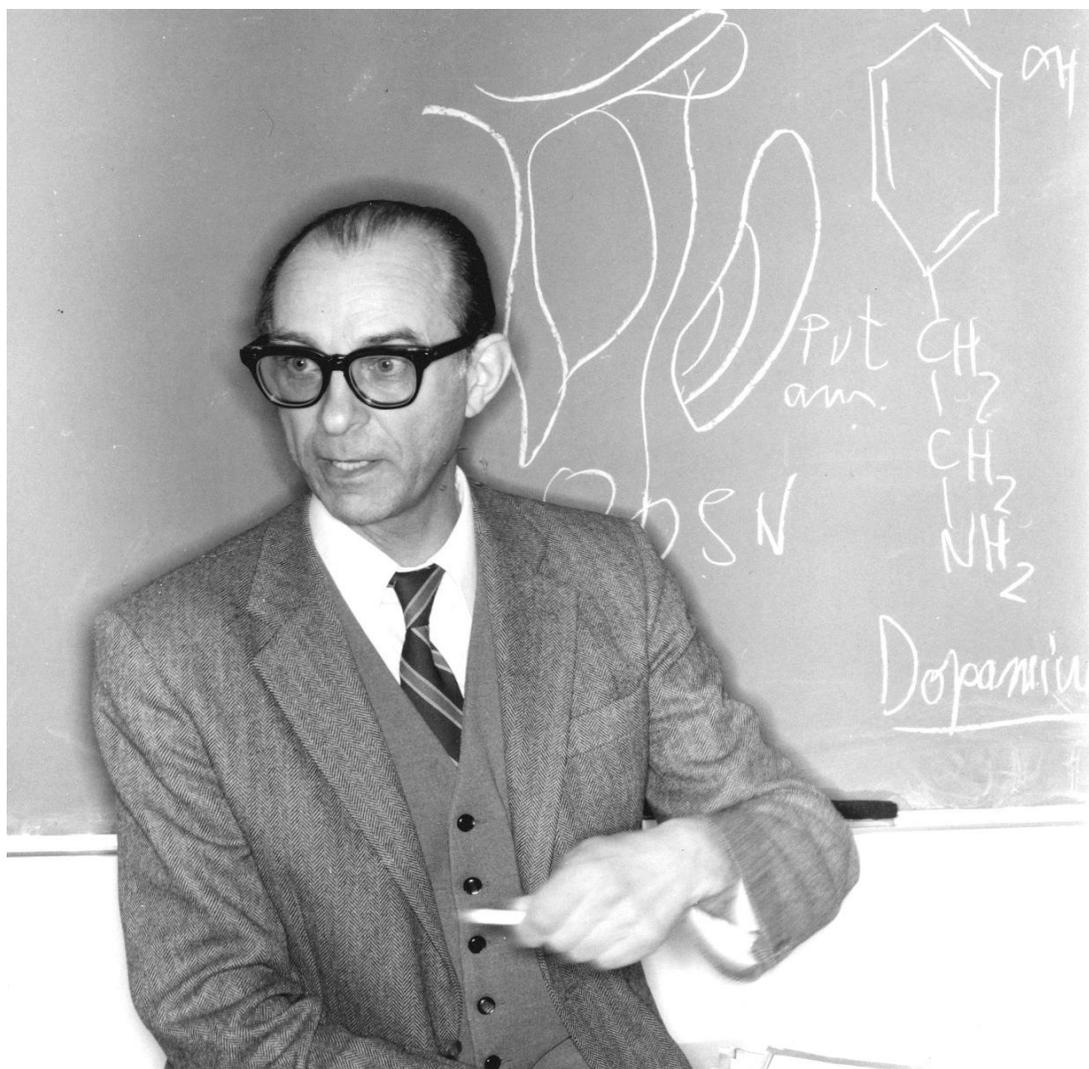
Oleh was not only a brilliant experimentalist. He was first a humanist, interested always in the vagaries of human behavior.

We will miss him.

References:

Hornykiewicz O. The History of Neuroscience in Autobiography. 2004; 4:240-81.

Kubota M, Nagashima T, Takano H, Kodaka F, Fujiwara H, Takahata K, Moriguchi S, Kimura Y, Higuchi M, Okubo Y, Takahashi H, Ito H, Suhara T. Affinity states of striatal dopamine D2 receptors in antipsychotic-free patients with schizophrenia. *Int J Psychopharmacol.* 2017; 20(11):928-35.



Dr. Oleh Hornykiewicz (1926-2020) during the late 1970s teaching about dopamine and the brain's basal ganglia at the Clarke Institute of Psychiatry in Toronto. Photo courtesy of the Centre for Addiction and Mental Health (CAMH) Toronto Archives. Photo received by John Court.

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