COMMENTARY

Obituary: Cornelius H. Vanderwolf

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ABSTRACT: C.H. Vanderwolf described motor correlates of hippocampal theta oscillations and uncovered two broad classes: atropine-sensitive and atropine-resistant rhythm with likely different behavioral and cognitive significance. © 2015 Wiley Periodicals, Inc.

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With great sadness we would like to inform the international neuroscience community that Cornelius (Case) H. Vanderwolf, our fellow neuroscientist, mentor, and dear friend passed away on June 16, 2015, of Komoka, in his 80th year. Case was born in Edmonton, Alberta in Canada and took his BSc in Psychology and Biology at the University of Alberta in 1958. He obtained his PhD from McGill University under Donald O. Hebb's supervision in 1962. These were the peak years in psychology at McGill, when several other eminent future neuroscientists studied under Hebb, including Brenda Milner, Peter Milner, James Olds, Mortimer Mishkin, and Lynn Nadel. Following completion of his PhD, Case spent a year at the California Institute of Technology with Roger Sperry (1962–1963) and another year with Konrad Akert, the Founder of the Brain Research Institute of the University of Zurich (1963–1964). These were formative years for Case, not only to learn how others thought about the major problems in brain research, but also how his own thinking departed from the existing frameworks. According to John O'Keefe, a fellow student at McGill, Case declared early on that attempts to study the neurophysiology of the mind in animals "were a real waste of time," a view he repeatedly stated in his career. Instead, students of neuroscience should examine the relationship between microscopic behavioral changes in the tradition of European ethology and brain activity. After returning to Canada, Case accepted a position in psychology at McMaster University and then moved to the University of Western Ontario in London, Ontario in 1968, where he spent the rest of his illustrious career.

The name of Case Vanderwolf is connected with important studies of the behavioral correlates of theta oscillations. As early as 1964, he was among the first investigators to carefully study the correlation between observable motor activity and brain waves. Recording from the thalamus and hippocampus of the behaving rat, he found a reliable relationship between "voluntary movement" and rhythmic (theta) EEG activity. This early paper (Vanderwolf and Heron, 1964) was followed up by a detailed account of a variety of motor behaviors and hippocampal theta oscillation (Vanderwolf, 1969). This second paper became a citation classic and Vanderwolf's most significant contribution to neuroscience. He showed that in the waking rat, hippocampal EEG is dominated by theta oscillations (6–10 Hz; for this he coined a new term, rhythmic slow activity or RSA) during locomotion, rearing, exploratory head turning, and sniffing. In contrast, in other observable behaviors such as eating, drinking, grooming, and immobility, theta is replaced by "large amplitude irregular activity" (LIA). These observations were confirmed through numerous experiments by his students and other laboratories in several species.

His descriptions have not remained unchallenged. Others believed that movement was a secondary effect, while hippocampal theta rhythm was primarily linked to attention, arousal, or sensory processing. In response to these challenges, Case and his collaborators demonstrated repeatedly that sensory stimuli may or may not induce theta oscillations, depending on whether the rat responds or not with head turning or locomotion. To simplify his behavioral descriptions but still remain within the territory of objectivity, he classified behaviors into two major categories: theta and non-theta behaviors. Because these behavioral groups largely corresponded to the voluntary and non-voluntary categories of the great English neurologist John Hughlings Jackson, Case adopted them as descriptors of hippocampal EEG. This created an interesting paradox: by adopting the term voluntary, a subjective and strongly debated philosophical term, volition became mixed with his quest for an ethology-based description of brain–behavior strategy. However, irrespective of his use of various terms, his basic description of the relationship between motor behavior and hippocampal electrical patterns has become a solid fact in neuroscience. From this firm ground, he departed to multiple directions over the years, only to return to the fundamental basics: any claim to a cause–effect relationship between cognition

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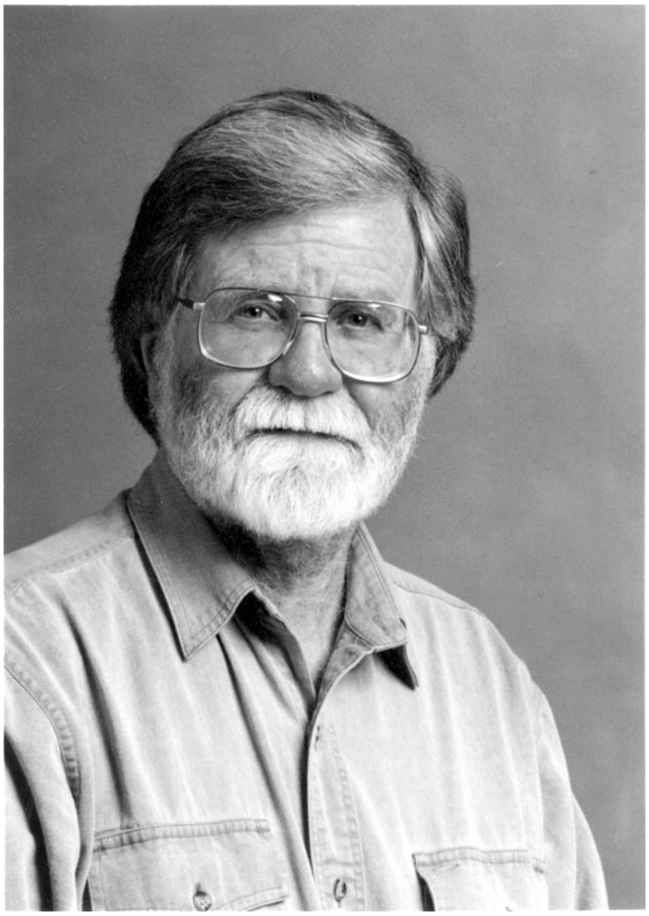

and brain activity should be carefully tested against the intermediate effects of observable behavior. Violation of this rule often leads to erroneous conclusions and such mistakes persist to this day.

Vanderwolf's second most significant finding was the discovery of two kinds of theta oscillations. Since theta oscillations during walking persist when the muscarinic-cholinergic receptor blockers atropine or scopolamine are administered systemically (atropine-resistant theta), but the same drugs can abolish slower frequency theta oscillations in anesthetized animals (atropine-sensitive theta), Case concluded that at least two pharmacologically distinct theta oscillations exist. He subsequently showed that some sensory stimuli can elicit transient theta oscillations in the immobile animal which can be abolished by atropine, but as soon as the animal begins to move, theta oscillation reemerges. Case carried out numerous pharmacological experiments in attempts to further characterize the physiological nature of the two-theta systems and generalized his observations in the hippocampus to the behavior–brain pattern relationship of the neocortex. In this approach, he used the same rigorous observational analysis as in his early works, and demonstrated repeatedly that interpretation of drug effects is possible only if intermediate variables, such as overt movement and temperature changes, can be discounted.

He summarized his several decades-long systematic studies on the electrical activity of the hippocampus and neocortex in a noteworthy monograph that remains a highly recommended text for all systems neuroscientists. In Case's own words, "perhaps the most fundamental principle to be derived from all this work is that the brain is organized to analyze sensory inputs and produce behaviors such as walking, running, manipulating objects, chewing food, drinking etc. and that it is not organized in terms of the traditional philosophical subdivisions of the mind such as sensation, attention, emotion, and motivation. This argument has the potential to transform traditional psychology, psychiatry, and the philosophy of the mind."

Case Vanderwolf can perhaps be best described as a laboratory neuroethologist with a high level of curiosity and an extreme dose of tenacity. It is remarkable that nearly all his observations were carried out on a $1'$ by $1'$ elevated platform with a spring-and-coil motor sensor attached and a pen-recorder EEG machine. He used very little statistical analysis in his works, yet his conclusions were remarkably precise and reliable. To achieve such a high level of accuracy, he performed many more experiments to "get it right" in contrast to today's standards, where obsessions about *P* values are common but there is much lesser use of common sense.

In addition to his academic achievements in the laboratory, Case Vanderwolf became serious about the quality of middle school education and devoted more than a decade of his life to improve English language education in Canada. He had a good sense of "bitter" humor and a reserved personality. He rarely attended scientific meetings and tended to avoid crowded places. On the other hand, he felt perfectly at home in the Canadian wilderness as a true outdoor individual. Nearly every summer he made his voyage to the rivers, brooks, and cascades of Northern Ontario with his canoe and he occasionally took his lucky postdocs with him to these ventures. Both of us (B.B. and G.B.) were beneficiaries of these ventures, where Case taught us how to paddle a canoe properly in rapid waters, recognize upcoming waterfalls before it was too late, pitch a tent, light fire in the rain, signal the rescue plane with smoke in case of danger, avoid close interactions with bears, and most importantly, how to appreciate and enjoy nature. Postdoc life was very different in those early days. The density of people in his lab was low, typically one or no postdoc and a single student. Although Case was busy with teaching most of the time, weekend dinners at his house were regular events where we could learn about the art of medieval cooking with bone marrow and other "exotic" ingredients. Perhaps his most creative moments were his regular long evening walks when he often shared his ideas and philosophical views with us.

With the passing of Case Vanderwolf, the Canadian as well as the global neuroscience community is losing a great personality. His name will forever be included among the list of those who made major contributions to the discovery of the brain's secrets, particularly in regards to the intricate relationship between electrical activity of the brain and behavior.