

A. D. (Bud) Craig, Jr. (1951–2023)

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Bud Craig, an outstanding neuroscientist, died on 15 July 2023 at age 71. Bud made unique contributions to the fields of pain and interoception, challenging major dogmas and offering powerful explanations for various phenomena including central pain and the subjective awareness of feelings, with great implications for our understanding of consciousness.

Arthur Dewitt Craig, Jr., colloquially known as Bud Craig, earned a BSc in mathematics in 1973 at Michigan State University, after which he switched to graduate studies in neurophysiology, with a PhD thesis on spinal sensory processing, under Daniel Tapper at Cornell University. In 1978, as a postdoctoral fellow with Harold Burton at the Washington University School of Medicine, St. Louis, Missouri, Bud initiated studies of the projections of spinal lamina I pain- and temperature-responsive neurons, a theme to which he would devote a large part of his career.

In 1981, Bud moved to Germany to join Robert Schmidt's Institute of Physiology, first in Kiel and from 1983 in Würzburg. With Klaus-Dietrich Kniffki, Bud showed that lamina I spinothalamic tract neurons consisted of three distinct populations, responding specifically to mechanical or thermal (heat) nociceptive stimuli, to cooling, or to cooling as well as to nociceptive stimuli¹. These seminal findings laid the ground for Bud's future work in which he explained the role of these distinct populations² and how pain and temperature interact.

In 1986, Bud returned to the United States to direct the Atkinson Pain Research Laboratory at the Barrow Neurological Institute, Phoenix, Arizona, with a decisive switch to macaque monkeys. Most critically, while previous works had concluded that the spinothalamic tract terminates in the same nuclei as those receiving innocuous tactile information and projecting to the somatosensory cortex, Bud showed that the main termination field in primates was distinct and, in fact, adjacent to the



basal part of the ventromedial nucleus, which receives taste and visceral information from the solitary tract nucleus. He showed that this region, which he named the posterior portion of the ventromedial nucleus, contained the same three populations of neurons as in the spinal lamina I and, critically, that it projects to the insular cortex³, similarly to the basal ventromedial nucleus. He showed that the insula encodes both the bodily localization and the intensity discrimination of pain and temperature sensations. All pieces fell into place: while the somatosensory pathways are exteroceptive, providing mechanoreceptive and proprioceptive information needed for musculoskeletal control, pain and temperature pathways are interoceptive, signaling information about the physiological status of the body in direct relation to the autonomic control of homeostasis. This major paradigm shift resolved the long-standing paradox, as pointed out by Head and Holmes in 1911, that lesions of the somatosensory cortex, while producing extensive sensory loss, fail to abolish the sensation of pain. It also explained why pain was rarely elicited by the stimulation of the cortical surface in Penfield's classical studies of the 1930s.

Bud further demonstrated spinothalamic lamina I neurons that were specifically activated by histamine⁴, thus unraveling a specific pathway for itch. Using the thermal grill

illusion, in which touching spatially interlaced warm (40 °C) and cool (20 °C) bars produces a painful burning sensation, Bud showed that while both cooling-specific and multireceptive spinothalamic lamina I neurons are activated by the cool stimulus, the response of the former but not the latter neurons is attenuated by the warm stimulus⁵. These findings imply that cold normally inhibits the activity of the multireceptive nociceptive neurons, and when this inhibition is mitigated, pain appears. Bud suggested that such impaired inhibition could be the basis for central pain⁶, a largely treatment-resistant condition occurring after lesions of the CNS.

In the later part of his career, Bud focused on the insular cortex. He identified the dorsal posterior insula as the primary interoceptive cortex⁷ and proposed a new model in which re-representations of interoception in the anterior insula integrate salient multimodal activities into a subjective 'material me', substantiating awareness⁸. In a seminal neuroimaging study, he showed that human brain activity correlates with graded cooling stimuli in the dorsal posterior insula whereas the subjective rating of intensity correlates with activation in the anterior insula⁹. He further supported his model by showing that the anterior insula is critical for epileptic ecstatic auras, for fluid intelligence and for the perception of time.

Bud left to science a game-changing legacy. He radically changed our understanding of pain. His demonstration of a primate-specific interoceptive afferent pathway and his redefinition of Sherrington's interoception explosively revived the field and put the insula on the map after it had been long ignored. His unique insight on consciousness, a phenomenon long considered elusive and beyond comprehension, is inspiring a wealth of new studies. His outstanding achievements are even more remarkable considering that they were mostly done entirely by himself, hands-on, or with a small number of collaborators.


While Bud had a demanding and uncompromising attitude to science, he was also a very warm person and loyal to his friends. He loved classical music, history, language and research on nearly every subject. He loved outdoor life and spent years hiking throughout Arizona and the Bavarian Alps, and enjoyed early-morning walks to appreciate the glorious Arizona sunrise. In the last years of his life, while Bud managed the deleterious impact of a decade-long multiple sclerosis with his splendid intellect and enthusiasm remaining intact, his powers waned. It was with a heroic effort, and with the help of his loving wife Lora, that

he managed to finish his monograph¹⁰, which can be seen as his scientific testament. It is no less than a masterpiece and a must-read for anyone interested in neuroscience.

We who have had the privilege to work with Bud remember him with deep affection.

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