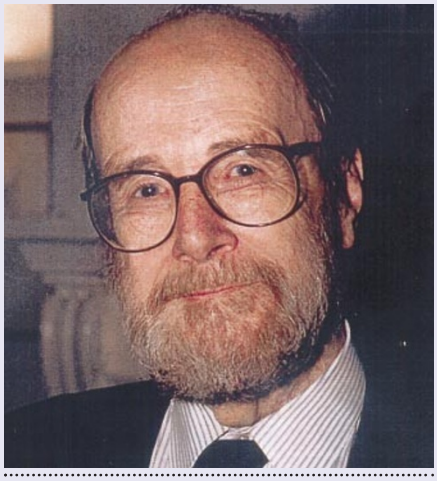
Obituary

Patrick D. Wall (1925–2001)



Neurobiologist who transformed the study of pain

Major advances in biomedicine — such as the decoding of the human genome — increasingly depend on the application of ever more complex technologies, the harnessing of large teams of scientists and technicians, and the acquisition and management of huge budgets. Some of the most successful contemporary biomedical scientists are really like chief executive officers of large multinational corporations, more involved in managing and delegating than in experimenting or thinking. Patrick David Wall, who died on 8 August aged 76, was the antithesis of this kind of scientist.

Wall's major scientific contributions were twofold. First, he was integral in transforming the investigation of pain into a key area of modern neurobiology, one that is fully amenable to study at the molecular, cellular and systems levels. And second, he recognized that the ability of the nervous system to change — its plasticity — is fundamental to its function, both in normal circumstances and in disease.

Wall studied medicine at Oxford University during the Second World War, moving shortly afterwards to the United States. There, during brief sojourns at Yale, Chicago and Harvard, he mastered the art of electrophysiology and interacted with many of the major figures in the then new field of neuroscience. Afterwards, he settled for some years at the Massachusetts Institute of Technology. It was here that his fundamental work on pain and neuronal plasticity evolved, culminating in the seminal 'spinal gate control theory', which he developed with Ron Melzack and published in 1965. This theory basically proposes that there is a gating system in the central nervous system that determines when and how much pain we feel from an injury. It offers an explanation for why similar injuries can produce widely different sensations of pain, depending on whether a gate in the spinal cord opens or is blocked in response both to the pattern of input it receives and to influences from the brain.

In the late 1960s, Wall returned to Britain to lead the cerebral functions research group at University College London. It was here, and during his repeated visits to Israel, where he worked at the Hebrew University in Jerusalem, that he first argued and then showed that there are different types of pain. The pain that helps to protect us from tissue injury — for example, the sensation that we feel when we touch a hot pan that makes us move our hands away quickly — is quite different from the pain that arises when tissue is inflamed or nerves are damaged. Moreover, these two types of pain, the physiological and the pathological, involve different neurobiological mechanisms.

Before then, all pain was seen as the result of activation of a specific neuronal system — the 'pain pathway'. The intensity and duration of pain were thought to be determined only by the intensity and duration of the peripheral stimulus. But Wall recognized that pain is a sensory experience that shows a complex relationship to many different kinds of stimuli, some extrinsic and some intrinsic. A peripheral stimulus that would be expected to produce pain might not do so in some circumstances. Equally, a stimulus that would commonly be experienced as innocuous could, if nerves are damaged, elicit exquisite pain.

In studying this complex relationship, Wall investigated how damage to a peripheral nerve changes the excitability of nerve fibres — which begin to fire spontaneously — as well as the functional connections that they make. He also investigated the role of inhibitory systems in controlling the transfer of information in the nervous system. He recognized that a decrease in inhibition as well as increase in excitability of the nervous system is fundamental to many types of long-lasting pain.

In short, the unifying theme of much of Wall's work was his desire to decry the simple cartesian notion of a fixed pain system that connects the peripheral tissues with the seat of conscious awareness in the brain. He also wanted to expose the complex events that lead to the varied feelings of discomfort and hurt that we call pain. Although he attacked many modern molecular approaches to the study of pain as forms of 'molecular phrenology' — what he saw as the ridiculous search for a pain gene — this approach is, ironically, beginning to validate his views by revealing the complexity of reactions to different types of injury. Pain involves change at many levels, from gene expression to activation of the brain's cortical region.

Wall also maintained that success in treating patients suffering from chronic pain requires an understanding of the underlying mechanisms, rather than trial-and-error therapies. One of his greatest strengths was that he recognized that pain is a personal experience that has to be studied in patients. He made important contributions to new approaches for managing pain, and actively encouraged the setting up of the hospice movement.

Wall's power as a scientist arose from his ideas, from his dedication to experiments — which he always conducted himself — and from his ability to communicate his thoughts in a way that enthralled, and sometimes appalled, all who listened to him or read his work. He enthralled because of his extraordinary capacity to translate dry scientific observations into a story that could be understood and wondered at. And he appalled because he was always willing to flout perceived wisdom and to expose, without any token of pseudocivility, what he saw as stupidity or charlatanism.

He also lacked the caution we usually expect of an experimentalist: he was always willing to use his data as a platform to develop his ideas. Yet these ideas were well thought out, and based on a deep understanding of neurobiology, uncanny intuition, and an insight into what the data mean in a larger context. This capacity to think deeply about his findings, rather than just catalogue them, meant that his interpretations always seemed to be ahead of the data. This enraged some of his competitors, but Pat saw that as a compliment. He was both an extraordinary scientist and a forceful individual, whose powerful political convictions and personal eccentricities made him one of a kind.

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