



Cover illustration
Hippocampal granule cells (nuclei, green) lose expression of calcium- and activity-regulated proteins such as calbindin (pink) in a mouse model of Alzheimer's disease. (Courtesy of L. Mucke.)

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NEURODEGENERATION

On 4 November 2006 it will be 100 years since Alois Alzheimer gave his first lecture on a patient with "a peculiar disorder of the cerebral cortex". The late Auguste D. had suffered from dementia during the last years of her life, and in her brain Alzheimer had discovered protein plaques, neurofibrillary tangles and atherosclerotic changes. These features came to define what is now known as Alzheimer's disease.

Since then, we have learned much about a wide variety of neurodegenerative disorders, and there seem to be some remarkable parallels between them. It is clear that plaques and other atypical protein assemblies are a hallmark of several such disorders, including Parkinson's disease and Huntington's disease, but their significance is still hotly debated. In addition, the failure of neuronal networks and the death of neurons have been implicated in the pathogenesis of various neurodegenerative disorders, as have certain cellular processes such as protein degradation and mitochondrial biology. And, although prion disease may seem to be the odd one out owing to its infectious nature, emerging evidence suggests that several of its peculiarities may also feature in Alzheimer's disease.

We hope that this Insight will offer the reader an exciting, up-to-date guide to the mechanisms and themes that underlie the development of different neurodegenerative diseases. Some of the views expressed may be controversial, but as Alzheimer said, "excessive reservations and paralysing despondency do not help the sciences to advance". What is needed is "a healthy optimism that cheerfully searches for new ways to understand, as it is convinced that it will be possible to find them".

We are indebted to our authors, reviewers and advisors for their considerable efforts in producing a stimulating collection of reviews on various aspects of neurodegenerative disease.

Marie-Thérèse Heemels
Senior Editor

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