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The clinical picture and concept of ALS in 2016

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Jean-Martin Charcot was the first to describe ALS by his revolutionary clinicoanatomical method in the middle of the 19th century. In the late 20th century, on the basis of molecular markers Heiko Braak and colleagues introduced a staging method for neurodegenerative diseases which are now the basis for innovative approaches to their pathogenesis („Braak staging"). Recently, a staging system was also proposed for amyotrophic lateral sclerosis (ALS) which showed that ALS primarily affects the frontal cortex, including the motor cortex, and then sequentially spreads into subcortical structures. This staging concept can be translated into the cinical picture and offers new insights into the disease. First, it shows that ALS is not a disease restricted to motor neurons („motor neuron disease"), but rather affects mutiple systems of the central nervous system („multisystem degeneration"). Secondly, the distribution of pareses is characteristic of the „Wernicke-Mann" type of central pareses. Thirdly, in a characteristic sequence of events, ocular movements are part of the picture with frontal executive deficits showing up early. They are followed by deficits of the olivocerebellar system. The involvement of frontal structures in ALS has been suspected since the late 19th century; now we know that this has an anatomical basis which is reflected by sequential involvement of frontal lobe function. These deficits are temporally and spatially distinct from the deficits seen in behavioral FTD, suggesting the presence of two entities rather than a spectrum ranging from ALS to FTD. More surprisingly for the clinician, Braaks results show that the hippocampus is involved in late stages. Finally, successfull attempts have been made to translate the post mortem findings into the in vivo situation by using MRI and DTI by measuring the fractional anisotropy of corticoefferent tracts. This new concept of the disease does not have major therapeutical impact yet. It explains why a modifier of glutamate release like riluzole has a moderate influence on the disease; however, it opens avenues for new strategies of therapeutic modification and even prevention of the sporadic disease. It should be mentioned that the genetic subforms of ALS may be more easily therapeutically influenced. Following the example of spinal muscular atrophy (SMA), currently attempts are made to influence transcription of disease genes, such as the superoxide dismutase (SOD).

Biography

Albert C. Ludolph, MD, Professor of Neurology and Chairman of the Department of Neurology at the University Hospital and Medical Faculty of Ulm. He is also acting Director of the Academic Neuroscience Centre of the University of Ulm. 1979 –1984 resident at the Department of Neurology and Psychiatry, University of Münster FRG, 1984 – 1985 joined Deutsche Forschungsgemeinschaft: Institute of Neurotoxicology, Albert Einstein College of Medicine. 1985 - 1989 joined the Department of Neurology at the University of Münster. 1990 - 1992 has been visiting Assoc. Professor at the Center for Research on Occupational and Environmental Toxicology, Portland (Oregon). In 1996 became C4 Professor of Neurology and Chair Department of Neurology, University of Ulm. Since 2003 became the Chair of the Academic Neuroscience Center, University of Ulm. 2005 – 2009 became the Deputy Chair of the European ALS-MND-Group. Since 2009 –became Chair of the World Federation of Neurology, ALS Research and Advisory Board of Hoffmann La-Roche,and Knopp Pharma of Drug Development in ALS. In 2015 awarded Erb-Gedenkmünze of the German Society of Neurology (DGN). He is investigator in more than 40 clinical trials with total amount of Publications of 407. He has established and currently leads the ALS-Centre at the University Hospital of Ulm and directs a multidisciplinary team for ALS care, clinical and experimental research.

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