Tidsskriftet Tidsskrift for Den norske legeforening

Per Andersen

OBITUARIES

LEIF GJERSTAD

VIDAR JENSEN

IVER ARNE LANGMOEN

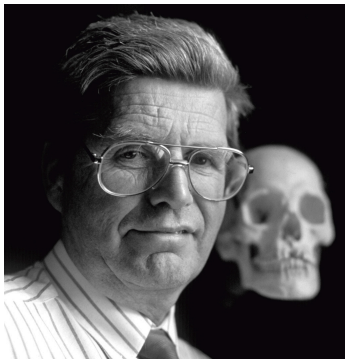
TERJE LØMO

EDVARD INGJALD MOSER

MAY-BRITT MOSER

JOHAN FREDERIK STORM

JON STORM-MATHISEN



'Per Andersen uncovers the brain' – picture from the front page of the Aftenposten evening edition, Saturday 9 April 1988, which carried an interview with Per Andersen on

memory and learning in connection with the Research Council's Research Award and five-year grant for studying memory processes. Photo: Tor G. Stenersen, Aftenposten, reproduced with permission.

Per Andersen's death on 17 February 2020 at the age of 90 marked the end of an era. 'New generations of doctors and researchers need to learn about and be inspired by his important contributions, not only as an internationally renowned neuroscientist, but also as a tireless and highly capable communicator and a source of inspiration', says Are Brean, Editor-in-Chief of the Journal of the Norwegian Medical Association.

Per Andersen's work spanned from the infancy of neurophysiology in the 1950s, when he helped pioneer the electrophysiological mapping of the brain's neural network, 'electro anatomy', involving the localisation of inhibitory and excitatory synapses on the nerve cells, to the 2000s with synaptic-level learning and functional effects of molecular changes in neurotransmitter receptors and other membrane proteins. The Royal Society put it like this: '... his discoveries shaped our understanding of neural circuitry' (1).

Per Oskar Andersen was born in Oslo on 12 January 1930, the oldest of four children. He learnt through the words and deeds of both his parents that knowledge is the be-all and end-all, and they made sure that all their children received a good education. Per started his medical studies at the University of Oslo, where, in his role as *prosector minor* at the Anatomical Institute, he was asked to provide guidance for other students and where he took his first steps towards a great career in brain research.

Per's doctoral work was carried out in the Neurophysiological Laboratory, which had been established at the Anatomical Institute by Birger Kaada in the 1950s under the inclusive, forward-looking and paternal gaze of its Head, Jan B. Jansen. Per's background from the Oslo School of Neuroanatomy founded by Jan B. Jansen and Alf Brodal, which set the tone for all research into the structures of the brain throughout most of the 20th century, gave him a unique approach to the understanding of function. Theodor Blackstad's work on the neural connections in the hippocampus (part of the cerebral cortex) and how neural pathways terminate in different zones was also important. Per's dissertation was old-school, based on his series of single-author original articles, 'Interhippocampal Impulses I–IV', published in Acta Physiologica Scandinavica in 1959–60. It has influenced all subsequent work on the interpretation of how electric fields spread in the neural tissue, and our understanding of communication between different parts of the brain.

After being awarded his 'doctor medicinae' degree in June 1960, Per sought out the most prominent research circle on the international scene. With the help of Jansen and Brodal, he gained the attention of Sir John C. Eccles in Australia, and was awarded a Rockefeller Fellowship. Per and his family flew out to Canberra where they stayed for two high-paced years, from 1961 to 1963, with twice-weekly experiments with Eccles from 8 am till 2 am, and eight articles

published in Nature. While Per was there, Eccles was awarded the Nobel Prize for his identification of synaptic mechanisms based on experiments conducted in the spinal cord. His work with Per led Eccles to study the brain itself. Among other things, they showed that inhibitory synapses from basket cell axons, strategically placed on the cell body of pyramidal cells, control the signals from the cerebral cortex. This was the first time that an inhibitory neuron and its synapses had been identified in the brain. The results were published in Nature in 1963, followed in the same issue by an article by Blackstad, which used electron microscopy to demonstrate the inhibitory synapses. In another Nature article that same year, Andersen and Eccles showed that a similar principle applies in the cerebellum (another area where Per brought specialist expertise from Oslo). When Per returned to Norway in 1963 and gave a talk about his stay in Canberra, he said: 'I learnt a lot about physiology, and taught them a bit about anatomy.' Eccles later said (to Roger A. Nicoll): 'Per helped navigate me through the foramen magnum!'

Back in Oslo, Per set up his own research group and championed the work to build the Neurophysiological Institute (now a part of the Institute of Basic Medical Sciences) at the University of Oslo. He became prosektor (Associate Professor) in 1963, dosent (Reader) in 1968 and Professor in 1972, until he was awarded emeritus status on retirement in 2000. Important contributions from Per's group include i) functional neural connections and networks, including the location and structure of excitatory neuronal terminals in the hippocampus (2), ii) plasticity changes in synaptic strength, particularly activity-induced long-term potentiation (LTP) discovered by Terje Lømo in Per's laboratory in 1966 (3–5), and iii) the hippocampal slice preparation for in vitro studies of how nerve cells work (6), based on Per's discovery that the main projections of nerve fibres, *the trisynaptic circuit*, are organised in lamellae across the longitudinal axis of the hippocampus (7), allowing the circuitry to be preserved within a thin transverse slice (longitudinal projections connect the slices in vivo). This preparation remains a key tool in neurophysiology, and we tend to forget what a radical idea and innovation it represents. Long-term potentiation is now a well-established mechanism of learning and memory storage and it is the subject of a large field of research, in which Per held a leading role. His work on neural connections forms an important premise for many discoveries, including the Nobel Prize-winning discovery by Edvard Moser and May-Britt Moser of grid cells in the hippocampus region. Insights from these and other studies based on Per's work shaped the development of modern neurophysiology and have remained pillars of the field (1). It is also interesting to read his own thoughts about his life as a researcher (8).

Several of the early articles did not list Per Andersen as a co-author. This may seem surprising today, but in those days the tradition was not for groups leaders to be named as co-author, even if they had supervised and laid the foundation for the research activities and ideas. Per's leadership style was modelled on that of Jan B. Jansen, with considerable freedom balanced by responsibility, where the unwritten rule was for everyone to take responsibility for making full use of their capabilities. The result was an enthusiastic, creative and egalitarian research group in which each individual enjoyed a large degree of independence. At the same time, Per ensured that the focus would always

remain on critical thinking, healthy scepticism, intense discussions and a commitment to high standards. And once Per had accepted you as a student and co-worker, you could count on his full support. Eric Kandel (Nobel Laureate in 2000) writes: 'He was one of the great leaders of our field and he mentored many people who are now contributing importantly to brain science. His loss will be felt for a long time by many of us.' Per's infectious enthusiasm and extensive insights made him a sought-after speaker in international fora and gave him a vast network of contacts among eminent neuroscientists all over the world. He played an important role in establishing a European network for research in neuroscience through the setting up of the Federation of European Neuroscience Societies (FENS), the European Journal of Neuroscience and various EU programmes. Per may well have won more fame and acclaim abroad than in Norwegian research circles. He was enormously appreciative of being part of the global 'family' of likeminded knowledge-seekers. He was a social being at heart, and with his wife Kari he extended many invitations to his home and to his holiday house in Hemsedal – or trips aboard his ocean-going boat, which he had built from scratch. He took the world's most eminent researchers skiing and introduced them to Norwegian traditions. This hospitality left its mark and provided much inspiration for his guests as well as his students, who were included in the network. Per became our door-opener to the world.

Per retained his sense of curiosity throughout his life. He enjoyed finding out what things are and how they work, and he took delight in his students' achievements. He was fair-minded and was always ready to stand up for anybody who became a victim of injustice. Per also had a competitive instinct, and took care to celebrate his lab's successes. Whenever an article had been accepted, the sherry glasses would come out. His expectations were clear. When the institute moved from central Oslo to Gaustad in 1990, there was competition in-house to be the first to get results in the new laboratories. 'And we must always beat the Swedes', he said, jovially thumping his hands together and bursting into a loud laugh. He was actually really fond of the Swedes, and the feeling was mutual. Tomas Hökfelt writes: 'He was an unusually fine human being, a brilliant researcher and a charismatic lecturer. He was extremely generous to us here at KI [Karolinska Institutet]. We could always rely on him whenever Sten [Grillner] and I held our researcher training courses. And the students loved him. We all thought of Per as a dear friend.'

Per was also a role model in his work to popularise medical knowledge. All of Norway came to know him thanks to his televised series of conversations with Per Øyvind Heradstveit, broadcast by the NRK in 1980 and entitled 'Your fantastic brain'. He was a media resource and a willing and highly-valued speaker in a variety of fora.

Per Andersen won much recognition in the way of research awards (Anders Jahre's Prize for Young Medical Researchers 1967, the Fridtjof Nansen Prize for Outstanding Research 1972, Norwegian Research Council's Award 1988, Fondation Ipsen Neuronal Plasticity Prize 1993, Eric K. Fernström's Nordic Prize 1995, the Lundbeck Fund Scientific Prize 1996), honorary doctorates (Universität Zürich 1988, Karolinska Institute 1998) and appointments to science academies all over the world (Norwegian Academy of Science and

Letters 1980, Royal Norwegian Society of Sciences and Letters 1988, Academia Europaea 1989, Royal Swedish Academy of Science 1991, National Academy of Sciences 1994, The Royal Society 2002). He was also a Commander of the Royal Norwegian Order of St. Olav (1997).

Per was ill towards the end of his life, but he was cared for at home, where he shared meals and music with Kari, who was by his side for 65 years. Per and Kari had four children and six grandchildren, of whom they were immensely proud.

Per was a phenomenal inspiration and role model. Few people will meet someone as engaging, inspiring, fearless and visionary as him. We did, and are immeasurably grateful for the privilege. Now he is gone, and we are left with the memories of a great man. Per was a giant in Norwegian and international science, and he played an essential part in securing Norway's strong position within the field of neuroscience.

Quotes for which no source is given in the text are personal communications to Jon Storm-Mathisen. On behalf of Per Andersen's students.

LITERATURE

1. The Royal Society. Per Andersen. https://royalsociety.org/people/per-andersen-10994 Accessed 19.4.2020.

2. Andersen P, Blackstad TW, Lömo T. Location and identification of excitatory synapses on hippocampal pyramidal cells. Exp Brain Res 1966; 1: 236–48. [PubMed][CrossRef]

3. Lømo T. Frequency potentiation of excitatory synaptic activity in the dentate area of the hippocampal formation (XII Scandinavian Congress of Physiology, Turku 1966). Acta Physiol Scand 1966; 68 (suppl 277): 128.

4. Bliss TV, Lømo T. Long-lasting potentiation of synaptic transmission in the dentate area of the anaesthetized rabbit following stimulation of the perforant path. J Physiol 1973; 232: 331–56. [PubMed][CrossRef]

5. Andersen P. Long-lasting facilitation of synaptic transmission. Ciba Found Symp 1977; 58: 87–108. [PubMed]

6. Skrede KK, Westgaard RH. The transverse hippocampal slice: a well-defined cortical structure maintained in vitro. Brain Res 1971; 35: 589–93. [PubMed][CrossRef]

7. Andersen P, Bliss TV, Lømo T et al. Lamellar organization of hippocampal excitatory pathways. Acta Physiol Scand 1969; 76: 4A–5A. [PubMed]

8. Andersen P. Per Andersen. I: Squire LR, red. The History of Neuroscience in Autobiography. San Diego, CA: Academic Press 2004: 2– 38.

Publisert: 15 June 2020. Tidsskr Nor Legeforen. DOI: 10.4045/tidsskr.20.0353