Norwegian neuroscience research began with Fridtjof Nansen 130 years ago, accelerated from the 1950s and has now been honoured with the greatest prize of all for fundamental discoveries about how the brain works

Nobel Prize in Physiology or Medicine 2014

May-Britt and Edvard I. Moser share this year's Nobel Prize in Physiology or Medicine with John O'Keefe of University College London. It is the first time this prize has gone to Norway. The award is special too because the Norwegian laureates are unusually young and are a married couple. They received the award for their studies on the sense of place – they investigated how rats can tell where they are and where they have been, and how they navigate through their surroundings. The story began in London around 1970, when O'Keefe showed that cells in the hippocampus react selectively to whereabouts a rat finds itself in space. At each place the rat visits, electrical nerve impulse activity is recorded, but any single neuron («place cell») is active at only one of these places.

When May-Britt and Edvard I. Moser began their own research in newly established positions in Trondheim after completing valuable years of training and doctorates with Per Oskar Andersen at the Institute of Neurophysiology, University of Oslo, they had to ask themselves: What shall we focus on? In the hippocampus, the chances of major breakthroughs might have seemed small. Place cells had already been discovered. The importance of the hippocampus for learning and memory, an essential prerequisite for the sense of place, was well established. But what about the entorhinal cortex, a harder to access and more complicated part of the cortex with what was at the time a virtually unknown function? The entorhinal cortex is the target area for all sensory information from primary sensory cortices and almost the only route into the hippocampus for information about conditions inside and outside the body.

They could hardly have made a better choice. Important things had to happen in that area, and whoever got there first with suitable methods had to find something. By inserting electrodes into the entorhinal cortex of awake rats moving freely around in an enclosure, the Nobel laureates discovered single cells that fired whenever the rat was at not just a single location, but at any of several locations in that enclosure. On a map of the enclosure, these locations gave rise to an unexpected pattern in which each formed the corners of triangles that tessellated across the entire space, so that together they formed a grid («grid cells») (1). Other cells were soon shown to react to other signals: head direction (head direction cells), the rat's speed of movement (speed cells), and signals from walls and other obstacles in the enclosure (border cells). This information is stored in the networks of neurons through changes at the contact points between them (synaptic plasticity), in such a way that the original pattern of impulse activity can be reproduced later on. Together these patterns represent the areas that the rat has previously been in.

These findings have made it possible to search for and identify corresponding mechanisms in humans. As a result, we can now (partly) explain how we can find our way around in a familiar room in the dark. Nevertheless, some landmarks are also required, for example a bedside table, as these serve to anchor the map we have in our brains to the room in which we find ourselves. Subsequently, this information, in the form of nerve impulses from peripheral sensory organs, will tell us how we are moving relative to the map and guide us through the room (pathway guidance). The results also help us to understand how we remember objects, facts, words and events (semantic memory) and can place these in space and time (episodic memory), since such mental processes seem to rely on the same kind of processing and to some extent the same network as our sense of place (2).

Taking new steps is important in research. Grid cells would not have been discovered had the rats not been allowed to explore a much larger space than was typical at the time. It was this that made it possible to establish that the entorhinal cortex is the primary location of the sense of place. It was also the entorhinal cortex, and not the hippocampus, that was particularly affected in the famous «memory-less» patient HM, based on post-mortem material.

Some believe that the Nobel Prize should be awarded for the discovery itself – others can concern themselves with the follow-up work. The Committee in Stockholm seems to have taken into account both aspects. It is almost unbelievable what the Nobel laureates have managed to build up in Trondheim in the space of a few years, going from nothing to an extremely active research environment with almost 100 employees. The commitment and vision of the Norwegian University of Science and Technology, which made this possible, must be commended. Also important was that the laureates went abroad early on, established close contacts with the best, including O'Keefe, and benefited from their support while they established themselves in Trondheim.

The environment attracts outstanding researchers from all over the world. They like it there, and not just because of the research, but also because the Mosers attach great importance to taking care of their employees and making them feel at home. The experimental animals are also taken good care of, and are readily shown to visitors and to the media. This sort of thing contributes to good research results – results that are published regularly in leading international journals. Since 2002 alone, the Nobel laureates have published 31 papers in *Science*, *Nature* and *Nature Neuroscience*, besides a large number in other leading journals.

How does one manage such a large research environment? From what I hear, the laureates have mastered that too. They cannot possibly participate directly in all the experiments, but they keep up to date with everything that goes on, plan projects, interpret the results, write, and direct the whole enterprise. Thus, no doubts can arise as to who deserves the award – the laboratory head or their co-workers who performed the experiments – as has been the case with some previous Nobel Prizes.

Fridtjof Nansen was Norway's first neuroscientist. Many years then passed before the threads were picked up again by Jan B. Jansen and Alf Brodal in Oslo in the 1930s. They laid the foundations for Norway's strong position in the neurosciences. Progress accelerated from the 1950s as new methods, more resources and younger generations came along. Inspired by the environments they came from, they themselves became the inspiration for new generations and academic communities. The Nobel Prize in Physiology or Medicine for 2014 is a brilliant result of this development, which encom-

passes both basic research and considerable recruitment into Norwegian neurology. Today many groups in Norway conduct first-class research in neuroscience. May economics, politics and recruitment ensure its successful continuation.

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The author has completed the ICMJE form and declares no conflicts of interest.

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