

Profile

Michel Ferrari: game, set, and match in headache research



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We have tennis to thank for kick-starting Michel Ferrari's career in neuroscience. After toying with the idea of becoming an aeronautical engineer or a physicist, it was a chance conversation with a fellow tennis player that resulted in Ferrari choosing a career in medicine. The tennis player was Cees Tulleken, who later became an internationally renowned professor of neurosurgery at Utrecht University in The Netherlands.

Tennis is a start-stop-start kind of game, and that theme is reflected both in Ferrari's career and his work-life balance. He has always been fascinated by the range of episodic brain disorders, in particular migraines and cluster headaches. What particularly interests him is the start-stop-start nature of how the brain switches on and off at intervals ranging from minutes to days. Likewise, Ferrari can work 70 h weeks for months, but then has no problem switching off as soon as he and his wife go on their travels, mainly in Spain and Italy.

On completing his medical degree at Leiden University Medical Centre (LUMC) in The Netherlands, and before embarking on his neurology training with the late George Bruyn at LUMC, Ferrari spent a year pursuing an interest in cerebrovascular disease at the Baylor College of Medicine, Houston (TX, USA), under Michael Welch. But as the months passed, he found himself more drawn to migraine, the other research line at Welch's lab. This also happened to be a research area close to Bruyn's heart, and on Ferrari's return to Leiden in 1981, he started a PhD on the role of serotonin in migraine.

Since 1986, Ferrari has worked as a consultant neurologist, and it was seeing two patients in his clinic in 1989 that led to one of his major research breakthroughs. In the space of a few days he treated two patients from the eastern part of The Netherlands who both had hemiplegic migraine. Although they did not seem to be related, Ferrari was convinced they had a genetic link. Around this time he met the medical geneticist Rune Frants and they decided to collaborate. After identifying and studying several extended multi-generational families with hemiplegic migraine throughout the world, they identified the first gene for migraine in 1996 (CACNL1A4) and managed to unravel the underlying pathogenetic mechanism. Later collaboration at LUMC with neurologist and biologist Gisela Terwindt and molecular neurobiologist Arn van den Maagdenberg led to the identification of several other genes and molecular mechanisms for migraine.

Welch said Ferrari's work on the genetics of migraine and population-based imaging "have been among the most important and revealing works of the last two decades".

Frants sees Ferrari's mission as "promoting multi-disciplinary collaborations between clinical and basic science

to realise real translational neuroscience to the benefit of patients and society", and it is certainly true that Ferrari's research covers many areas, including the biochemical, genetic, pharmacological, neurobiological, epidemiological, and therapeutic aspects of migraine and other episodic brain disorders. On winning the NWO Spinoza Prize in 2009 for lifetime scientific achievements (the highest scientific award in The Netherlands), Ferrari said: "You can only make breakthroughs at the borders between sciences. Biomedical scientific research is working together. This is why it is so important to speak one another's language and to respect and understand one another's work. Only then can you bridge the cultural differences between clinical specialists and fundamental researchers."

Ferrari's goal is to produce a prophylactic treatment that will prevent migraine attacks for the millions of people who get migraine around the world, but of course: "in order to achieve that, we try and understand why and how attacks begin—what the initiation mechanism of attacks are". In 2007, Ferrari became chair of the new Leiden Centre for Translational Neuroscience. He and his colleagues chose the centre's name together to reflect the fact that the ultimate aim of their laboratory research is to affect the development of new therapies for patients. Ferrari says: "The most important aspect of our research at Leiden is the translation into how much it helps patients."

Ferrari continues to rail against the myths and misconceptions that continue to surround migraine—a disorder now known to be caused by both genetic and environmental factors. He says: "What makes me really angry is that many people, and even physicians, still believe migraine is a disease of hysterical females—they don't appreciate the disability caused by the disease. Despite the fact that WHO ranks migraine as the third most disabling disease among women, and the seventh among men, they think it's 'just a headache'." He is also annoyed by the misconception that migraine is caused by stress or eating specific food: "In fact it's the other way around. During the earliest subclinical initiation phase of a migraine attack, before patients realise that an attack has started, several premonitory urges and behavioural changes occur, including feeling stressed or craving for specific food."

Since returning to Leiden, he made the conscious decision to stay in The Netherlands because he enjoys living and working there, and he can access the rest of the world quite easily. It also means that he and his team can carry out nationwide studies, supported by Dutch and international funding bodies.

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