FNDS NEWS

Mark Hallett: Celebrating 40 Years of Service and Pioneering Work in Neuroscience

Interview with Mark Hallett, MD
By Michael Romeo

"You know, there are people who have stuck with exactly the same topic most of their career. I kept changing topics!" With a career spanning over 40 years, summarizing Dr. Mark Hallett's life's work is a daunting task. But it is a challenge that even Mark himself admits is difficult.

Following Mark's announcement of his retirement from the National Institutes of Health in December 2022, I had the pleasure of talking to him about his career, legacy, and the future of FND research and treatment. Mark may be retiring from his long-standing position at the NIH, but his passion for understanding the brain remains unwavering. "I've retired from NIH, but I am not retiring from my interests. I certainly will continue to think and read about different problems in brain function. There's plenty of unpublished work and our group is quite busy with that. I've sort of aligned myself with a number of different people in different places at NIH and elsewhere and lending help with different things. I'm happy to advise people even though I don't want to be on the frontlines to do any of the work."

Talking with Mark Hallett is like meeting the young man he was in the 1970s, with his unwavering enthusiasm and eagerness to solve the mysteries of the brain. It's hard to imagine him slowing down anytime soon. "I'm trying to take off more time to read some books, which I haven't had a lot of time to do. But there's so much to do and so much to think about. At the moment, I'm still stuck on free will. That's where a lot of my interests are. I still have things going on, for example, the physiology of dystonia. That was the major topic we were dealing with in the laboratory before I shifted to functional neurological disorders. I am still doing some work in essential tremor. I'm finding that I have my hands in a variety of different things that I haven't given up, but the thing that really interests me is still volition and free will."

With over 40 years of federal service and 38 with the National Institute of Neurological Disorders and Stroke, Mark built his career focusing on movement disorders, motor learning, neuroplasticity, and brain stimulation. His interest in FND arose from two factors. Firstly, he noticed many patients in his clinic suffering from functional movement disorders who were not receiving adequate attention, diagnosis, treatment, or care. NIH's lack of research and funding prompted him to investigate this field further. Secondly, he was intrigued by the idea that patients could exhibit movements that appeared voluntary but were experienced as involuntary. This led him to question the nature of voluntariness and the underlying physiology of motor control.

In October 2003, Mark gathered a group of his colleagues and physiologists interested in functional movement disorders. "When I saw that there wasn't anything being published, and no one seemed to understand it, that led me to decide we would study it. I thought it would be worthwhile getting people together who were interested in the topic to talk about it." Twenty years on, it is hard to keep up with the torrent of research from around the world.

LOOKING BACK

Mark had a few different possible career paths, including astronomy, psychiatry, neurosurgery, general medicine, and (if his father had his way), ophthalmology. However, it was by chance that Mark happened to be inspired by the early work of Sigmund Freud which then led him to study neurology. I asked him what Freud would make of the advancements in the current understanding of FND.

"I think he would be very pleased by what we have learned because the evidence appears to show that there are a number of basic physiological things going on. One of them certainly seems like an abnormality of the limbic system. There is very good evidence for the overactivity of the amygdala. And it seems to me that, and there's good reason for why it appears to happen, for example, the early childhood trauma and the abnormal development of the amygdala, you have this abnormality of the underlying emotional structure of the brain. I think that that fits in with at least the early Freudian theories."

Of course, Freud's legacy wasn't the only legacy that Mark pursued. He is grateful for the support and guidance of great minds such as Norman Geschwind, C. Miller Fischer, and David Marsden. "Absolutely. Yes, I was very lucky in that regard. I have a whole series of marvelous teachers. I sort of built on their work."

So, what does Mark regard as his legacy?

"I think the legacy to some extent, of course, is in the people that I've trained because I think that it's the people who carry on the work and the ideas. But I guess the overarching thing would be the application of physiology to problems in brain physiology, brain mechanisms that we can take tools such as EEG, EMG, Neuroimaging, TMS and non-invasive brain stimulation of various sorts, to be able to get objective measures of the way the brain is doing its various things, both normally and pathologically. I think that kind of application has led us to a lot of good insights. So, I suppose it's that kind of process which may be a sort of a legacy."

So, were there any moments Mark felt particularly proud of? With such a long and varied career, it was a difficult question to answer!

"Yeah, it is difficult. There are people who have stuck with exactly the same topic for most of their careers. I kept changing topics. So, there are a number of things in different areas which I think are important. For example, even back to the fellowship work I did with David Marsden in trying to understand the pathophysiology of myoclonus. This work has stood pretty much as a foundation for our understanding of myoclonus ever since we did it back there in 1975-76. I'm continually asked to give lectures on myoclonus, and I'm still using some of the same slides that I used in the 70s."

"One of the stories that I tell from time to time, is the role of the cerebellum in adaptation learning, which, I think is a very important aspect of how people learn things. We did an experiment, which is a popular experiment in psychology, where you put prism glasses on people, and you shift the visual world to one side. At first people point incorrectly, but then adapt. When you take the glasses off, they point in the opposite

direction. So, we wanted to know if you made a lesion anywhere in the brain, would it compromise that particular phenomenon. We had no idea of what the situation would be. We found it was only lesions of the cerebellum where there was a problem with that. So, we said, "Yes" this type of learning, which is adaptation learning, is related to the cerebellum. Now, I thought that was an important finding. And, of course, this was a very long time ago and in those days, people had paper reprints. If you're old enough to know that we used to get piles of reprints, and you'd get postcards from people wanting to get a print of it. I ordered hundreds of paper copies of it, but we got almost no requests for anything. I was so disappointed. No one seemed to read to the paper or understand it. About ten or 15 years later, Tom Thatch who was a cerebellar neuroscientist repeated the experiment slightly differently and found the same result (as Mark's study). And then, all of a sudden it became a popular topic, and people recognised that it was an important issue. Now I think it's a standard part of understanding cerebellum adaptation learning that we had identified very early on, but no one recognised it. It was something way ahead of its time."

"There are a few fundamental findings that my group has made over the years that have been major steps forward such as the trans-modal plasticity of the brain. And that was something we found by accident. We were looking into the physiology of how blind people read Braille. What we found is that when blind people read Braille, they activate their visual cortex. So, it turns out that they rewired their brain, and that somatosensory input goes to the visual cortex. The visual cortex is not used for vision because they are blind. The brain utilises the visual cortex to help analyse the somatosensory information. Well, that was the first example of plasticity in the brain, where information in one modality goes into another modality of the brain. So that was another major observation that we had made. That one has now been studied by lots of people over the years. So, over the years, we've occasionally come across some very important foundational principles."

LOOKING FORWARD

With FND research evolving at a phenomenal pace, I asked Mark what he regards as some of the challenges and questions that the FND Society will need to address. Mark suggests that "the most important thing is getting better treatments. We really need to get better at that. I think that will likely require some more understanding of the basic pathophysiological processes of the brain." However, he adds that there are far greater challenges beyond the scope of the FND society. "Some of the most important issues I think that have been uncovered are probably not ones we can even deal with as a professional society." He adds, "For example, society's problems overall such as early childhood trauma. It's a very important factor. Can we improve, or can we get rid of early childhood trauma or reduce that? What can we do about peace in the world? I don't think we will be able as a (FND) Society to solve that. One of my concerns is, knowing what we know about early childhood trauma and its effects on people thirty years later. What's going to happen to the children that have been through the pandemic now? All the stresses they've had growing up, and how resilient they will be when they're in their 30's and 40s. That's a concern. Then there are the children growing up in the Ukrainian war. A similar thing. There's a lot of big questions which will be very difficult to answer."

Mark will continue in an emeritus position at NIH. He plans to take some well-earned R&R to travel, but he also looks forward to continuing to publish manuscripts over the next few years. Despite his retirement, he

maintains a commitment to research in the scientific community. "I like beaches and going to the beach. But I can't do that all day long!"

Mark's retirement from NIH marks the end of a remarkable career spanning four decades of pioneering work in neuroscience. His contributions to the study of motor control, movement disorders, neuroplasticity, brain stimulation, and the development of the Functional Neurological Disorder Society have transformed our understanding of these complex disorders. We are deeply grateful for his 40 years of service to the National Institutes of Health and his tireless dedication to improving patient care. We wish him all the best in his well-deserved retirement, knowing that he will continue to inspire future generations of neuroscientists with his work and passion for the field.