INTERVIEW WITH PAOLO NICHELLI
by Enrico Alleva

EA: Prof. Paolo Nichelli. You have recently published in Italian a book about "The brain and the mind" (*Il cervello e la mente,* Bologna Il Mulino). What motivated you to write about this topic?

PN: I wanted to convey what we know and what we don't about the relationships between brain and mind, and I wanted to do it in a way that could give the sense of the pathway followed by cognitive neuroscience. During my long career as a clinical neurologist, mostly interested in understanding and treating cognitive disorders, I have witnessed an explosion of instruments and methods to study the brain and its functioning. I remember my strong emotion when, in 1973, prof. Giuseppe Scotti, at that time a post-doctoral fellow at the Montreal Neurological Institute, brought us a prodigy: one of the first images of the brain obtained with a CT scanner.

EA: How was it possible to study the relationship between the brain and the mind before the invention of computed tomography and magnetic resonance?

PN: Before CT scanning of the brain, we had only two methods for diagnosing patients with neurological problems: cerebral angiography and pneumoencephalography. Angiography required to insert a contrast agent in the carotid artery. Radiographs, taken while the contrast agent circulated, showed blood vessel abnormalities due to tumors, vascular malformations, or diseases such as atherosclerosis. During a pneumoencephalogram, air was injected into the spinal subarachnoid space (a cavity filled with cerebrospinal fluid that contains the blood vessels that supply the brain and spinal cord), which permitted the visualization of the brain's ventricular system and subarachnoid spaces on X-rays. Both these procedures were dangerous for patients if not done properly.
It was obviously out of question the possibility to use them for scientific purposes. The possibility to "see" the brain *in vivo* with the CT scan opened new opportunities not only for patients with neurological diseases but also for cognitive neuroscientists.
During the following two decades, the approach to patients and to studies of the neurological basis of cognitive functions underwent a further revolution with the possibility to obtain not only detailed anatomical imaging *in vivo* with Magnetic Resonance (MRI), but also to map areas of the brain activated during different tasks with Positron Emission Tomography (PET) and functional Magnetic Resonance (fMRI). It happened that, from 1991 to 1993, I was at the NIH, in one of the laboratories that were developing fMRI techniques. I could take advantage of this opportunity and learn about the brain substrate of cognitive functions by matching functional neuroimaging studies with clinical investigations of persons with lesions or diseases of the brain. This was the great leap forward in Cognitive Neuroscience of the last three decades: the building up of converging evidence coming from clinical neuropsychology and from functional studies of normal subjects.

EA: In your book, case studies introduce new topics and chapters. Why did you choose this method?

PN: I believe that good questions allow the development of good science and that in neuroscience the best questions are those that make the move from trying to interpret patients' ailments. Also, when we try to get a sense of what is happening in the brain of a person with, for instance, a language disorder, we might have the opportunity to find out something that could be useful either for the patient we are studying or for future patients with the same disorder.

Eventually, this narrative approach could be helpful for people that are just beginning to approach neuroscience.

EA: How can brain lesions contribute to a better understanding of brain functioning?

PN: The early period of neuropsychology, before the Second World War, was characterized by anatomo-clinical correlation studies in patients. The method required analysis of a patient's performance and waiting for the autopsy the establish the correlation of impaired functions with brain areas. It involved a long process of discovery and the risk of unverifiable assumptions. Complex functions, such as auditory language comprehension, were localized to circumscribed areas of the brain. But it was impossible to generalize the findings of a single person to the population. To solve this problem, in the sixties of the last century, researchers as Henry Hécaen, Harold Goodglass and Ennio De Renzi introduced standardized testing and statistical inference methods and compared normal controls and groups of patients selected as they shared the same site of the lesion, or the same deficit. More recently, it became possible to study patients' MRI with computerized techniques (e.g., voxel-based morphometry) to relate focal differences in brain anatomy with any function of interest.
However, anatomo-clinical correlation studies can only identify the regions of the brain necessary to perform a given task, not all the network that is normally involved.
It was only with the development of neuroimaging methods that it was possible to overcome this limitation as they showed brain activity in normal subjects engaged in cognitive tasks. In the last couple of decades, further advances in MR imaging made it possible to describe also the structural and functional connectivity between cortical areas and subcortical structures. Eventually, new electrophysiological methods were added to the tools available to researchers.
It remains that progress in cognitive neuroscience requires converging evidence from different methods and that patients with brain lesions both give the impulse and take advantage of new knowledge about brain functioning.

EA: Which might be the evolution of brain mapping studies in the next few years?

PN: So far, we have tried to map on the brain the cognitive architecture as we envisage it. But the more we accumulate results of normal neuroimaging studies the more we understand that there almost no direct correspondence between a single function and a brain area. The next step will be to try to find out the operation that is performed by each area of the brain. As an example, we can take Broca's area, which recent studies found it is not only activated by language tasks but also, more generally, in detecting and representing abstract hierarchical structures regardless of modality and use.

EA: Can neuroscience be of any use in everyday life?

PN: Brain studies are important in the health field, but neuroscience is already having a great impact on everyday life, and even in everyday language. Indeed, it has become common to express feelings, thoughts, and attitudes in terms of one's dopamine, adrenaline, or serotonin levels.
Scientific concepts are typically more formal and fine-grained than common-sense concepts. Let's take as an example the word "memory". Brain studies have partitioned the concept in different ways: long-term memory, episodic memory, semantic memory, working memory, and so on. These concepts, which have a strong basis in studies of patients with brain lesions, are entering the wealth of knowledge of teachers and lecturers.
Educators might use a child's brain examination of responses to phonological tests to assess readiness to read, devise appropriate exercises, and alleviate the anxiety that arises with late readers.

The discovery of mirror neurons (a group of neurons that fire both when an animal acts and when the animal observes the same action performed by another) has changed the way we interpret social interactions and is having important effects on the rehabilitation of people with motor deficits.

EA: Is there any role of neuroscience in the judicial system?

PN: The engagement of law with neuroscience is inevitable. Indeed, the legal system depends on weighing evidence about how and why persons behaved as they did. For instance, when sentences are considered for violent offenders, judges can take into consideration what neuroscience knows about the interplay between genes and the environment affecting persons' behavior. I know at least two instances of murder where this happened, one in the United States and one in Italy. Both offenders shared the dangerous cocktail of a low MAO-A gene and negative experiences, such as child abuse, in the early years of life. This combination, which is known to be associated with sociopathy, was considered by the jury a risk factor of violent behavior and therefore capable of determining a reduced sentence. This of course doesn't mean to attribute to genes are the culprit of aggressive behavior. But, as we recognize that past life episodes can affect our character and behavior, it would be strange not to acknowledge that we also have biological constraints.

EA: Who is this book addressed to?

PN: I foresee that neuroscience can influence our lives in many more ways than in the past. Martha Farah, an eminent cognitive neuroscientist, said that this calls for an increase of "neuroliteracy". I believe that curiosity for what is happening in our brain might be the mover for stimulating this increased literacy and that presenting true stories of people with brain damage can lead readers to ask the same questions that research is trying to answer. My target readers are curious persons with no more than a school-level knowledge of human biology, and my goal is that they will find neuroscience both challenging and rewarding as I found it.

ABOUT THE AUTHOR

Paolo F. Nichelli is a senior professor of Neurology at the University of Modena and Reggio Emilia (Italy). He studied in Milan and then in Modena, where he has been director of the Clinical Neuroscience Department and dean of the Medical School. From 1991 to 1993 he has been a visiting scientist at the National Institute of Health, in Bethesda, MD (USA). His research work was mainly carried out in the field of Cognitive Neuroscience. He has published more than 250 scientific papers. He has been president of that Italian Neuropsychological Society, of which he was one of the founding members.