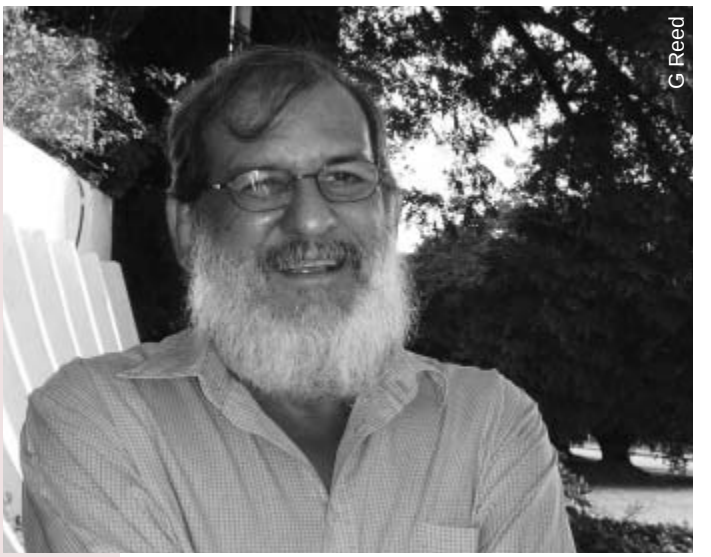
Riding the Brainwaves of Cuban Science: Pedro Valdés Sosa, MD, PhD

Vice Director for Research and Director of Neuroinformatics Cuban Neuroscience Center, Havana

By Gail Reed, MS & Julián Torres


G Reed

Pedro Valdés spent his childhood in Chicago, Illinois, USA, where he says his love of science began. After his family returned to Cuba in 1961, he studied medicine, received his PhD in biological sciences, and in 1990 at the age of 40, founded the Cuban Neuroscience Center with a group of young scientists that included his brother Mitchell, now the Center's Director. Since then, the Center has accumulated an impressive record developing patented neuroimaging diagnostic equipment for national use and export, a nationwide infant screening program for hearing loss, and the Cuban Brain Mapping Project, among other pioneering efforts. The Center's recruitment of new graduates keeps the median age of its professionals at 28, and its scientists are the island's most widely published outside of Cuba.

Dr Valdés' research appears frequently in international journals, including the Philosophical Transactions of the Royal Society (UK), for which he was Guest Editor in May 2005. He is a full professor at the Higher Institute of Medical Sciences of Havana, a member of the Cuban Academy of Sciences and coordinates the Center's national network of neurophysiology laboratories. *MEDICC Review* interviewed Dr Valdés at his offices at the Cuban Neuroscience Center in Havana.

MEDICC Review: **Tell us about the evolution of Cuban neuroscience and the Neuroscience Center itself.**

Pedro Valdés: Our neuroscience is rooted in the convergence of several factors, based fundamentally on the development of public health in Cuba during the last four decades. As you know, major investments were made in Havana's Scientific Pole in the 1980s, involving a series of institutions whose main purpose has been to apply the advances of science to population health and, secondarily, to make those applications available to other countries – especially in the developing world. (See Evenson D, Cuba's Biotechnology Revolution. *MEDICC Review*. 2007; Winter 10(1):8-10.)

In the case of neuroscience, our takeoff was also linked to the design and building of the country's first micro-computer (PC) in 1970 – when it was very difficult for Cuba to access this kind of technology. This was about the same time the first generation of biomedical researchers was being trained at CNIC. Along the way, we've had the good fortune to receive valuable international cooperation: in fact, the first equipment we worked with was donated by Dr Erwin Roy John of New York University. And the embryo of what is now the Cuban Neuroscience Center was created with people like Drs Thalia Harmony of Mexico, Bjorn Holgrem of Sweden and Ruth Urbá of Chile.

We wanted to develop computerized equipment to analyze electrical brain signals, and eventually create instruments for early diagnosis of neurological, psychiatric, and developmental disorders. At the time, there were only five research groups in the world who shared those same objectives. Early results included equipment prototypes and finally, in 1982, MEDICID-03 was developed, our first digital EEG for export –in this case to Mexico. The group that designed MEDICID-03 baptized it "Arturito" – Spanish phonetics for "R-2 D-2," the Star Wars robot, because of its boxy shape, lights, and buttons.

Since then, five generations of this equipment have been designed and produced, expanding functional capabilities along different lines under the Neuronic trademark, and earning the European Union's certification for sale in Europe – the only Cuban equipment to date that has attained this distinction. We're now exporting to 18 countries.

But of course, the main use is still here at home in the 57 neurophysiology laboratories all across Cuba, where the equipment is used to study hearing loss, epilepsy, dementia and other degenerative disorders of the central nervous system, cerebrovascular disease, trauma, vertigo, and tumors, among other conditions. The MEDICID line has allowed us to launch national screening programs for such problems as hearing loss.

MEDICC Review: **The Neuroscience Center also has teaching responsibilities, correct?**

Pedro Valdés: Yes, with the adoption of clinical neurophysiology as a field of medical study in Cuba, the Center has taken on primary responsibility for human resource development in this specialty.

We teach both traditional and digital techniques, and have trained hundreds of specialists to staff the national neurophysiology laboratory network I just mentioned. All professionals working in those labs must first be certified by the Center.

We also offer a master's degree, and we're now preparing a doctoral program in neurosciences with several profiles, including clinical neuroscience, basic neuroscience, neuroinformatics, and cognitive neuroscience.

MEDICC Review: **Early detection of hearing loss: how did you decide to take this on and why is it so important?**

Pedro Valdés: We began working on this in 1970 at the request of the Ministry of Education. Teachers were finding children in their classrooms with undetected hearing loss, and so the Ministry asked us what could be done to diagnose this condition earlier, since it can lead to severe psychological problems and, of course, learning difficulties.

There are critical periods for development of brain activity. For example, language development takes place during the first two years of life – influenced by both genetic and environmental factors. Noam Chomsky and others have written extensively on this subject. A loss of hearing of course influences the child's ability to develop language.

In 1983, we began screening infants-at-risk at three months of age with Cuban-designed and manufactured AUDIX equipment. AUDIX uses evoked potentials for objective screening. This relies on auditory stimulus, designed to evoke response in the brain, measuring electronically whether a person hears or not. Of course, this is ideal when the person – in this case an infant – is unable to cooperate, unable to say "yes, I can hear that" or "no, I can't."

Dr John at New York University, who collaborated with us, was a pioneer in the field of digital analysis of nervous system activity. We were also glad to have cooperation from Dr Terry Picton at the University of Toronto, who used steady state response to develop audiograms.

Our next step is to institute universal screening of infants at birth. Virtually all births in Cuba occur in hospitals, and so this makes the screening more feasible logistically. There are still some hurdles, but we are moving in this direction. As far as we know, the only country currently carrying out this kind of universal screening is Qatar, but they have a rather small population, and the births take place in a single hospital.

The Center and our national hearing loss studies are also playing a role in the national program to fit children who are both blind and deaf with cochlear implants. As of November 2007, 108 children had received the implants. Eventually, we hope to offer a Cuban-designed and manufactured implant for this program.

MEDICC Review: **And the Center is involved in a number of studies on learning disabilities among Cuban children…**

Pedro Valdés: Yes, this is a combined effort between the Ministry of Public Health and the Ministry of Education. In several studies, we found that 13%-14% of school-aged children have some form of learning disability. Within this group, we find greater prevalence of attention deficit hyperactivity disorder (ADHD), but we also find dyslexia, dyscalculia, etc. We're now studying the basis of dyscalculia and finding specific cerebral alterations associated with it and with dyslexia.

But social, family, and environmental factors play into this, as well as the biological ones. There is a complex relationship between vulnerable genes and social determinants, which cries out for an integrated approach to these problems.

MEDICC Review: **Which leads us to the Cuban Brain Mapping Project.**

Pedro Valdés: That's the backbone now for everything else we're doing. Internationally, the Human Brain Mapping Project has been spearheaded by the International Consortium for Brain Mapping. This is the neuroscience equivalent of the Human Genome Project. However, this study only includes developed countries, with core research sites in the United States, Germany, and Canada and partner sites in the UK, Finland, France, the Netherlands, and Australia. So the mere fact that Cuba is working on this is important for the developing world.

At the same time, you have to realize that globally, 34% of the disability-adjusted life years (DALYs) – or years of "healthy" life lost – are due to brain disorders; whether psychiatric, neurological, or child development. Yet, their diagnosis is extremely difficult due to the complexities and variations among different people's brains, even within the normal range. Thus, the use of informatics opens up new opportunities for developing instruments to detect even subtle changes that allow for early diagnosis of a number of pathologies. The place to begin is to map the normal brain.

We are pursuing three lines of work in this field, leading to the use of brain mapping to study learning disabilities, mild cognitive impairment (as a predictor of Alzheimer's) and other disorders. First is the Cuban Human Brain Atlas, from birth through old age, which we're developing as a normative instrument to define ranges of the normal brain. As far as we know, this is the first combination of functional and structural neuroimaging in a single atlas. Second, we are working to create instruments for active screening and early diagnosis of various pathologies. And third, we aim to create quantitative instruments for improving clinical trials. Along the way, we will be comparing our results to those of the international Human Brain Mapping Project.

MEDICC Review: **At what stage is the Cuban Brain Mapping Project now?**

Pedro Valdés: We are working with a cohort of 495 individuals, selected after informed consent, among a random sampling of 1,574 individuals in the catchment area of one community polyclinic in La Lisa Municipality, Havana City Province. Those persons were excluded who had some pathology, and at this point we are working primarily with persons from 14-60 years of age.

We have applied neuroimaging techniques (EEG and MRI) to each subject, as well as conducted interviews and clinical examinations. We have begun to correlate these results with some of the disabilities and disorders I've mentioned, but we still have a ways to go. Shortly, we will be expanding the study cohort to include older persons and children.

Our goal is to finish the first edition of the atlas within the next year; and obtain the first diagnostic instruments within the next two.

We've been greatly encouraged by reactions from leaders of the International Consortium, such as Dr Alan Evans of the McConnell Brain Imaging Centre in Montreal. We have exchanged visits with his institution, and are now cooperating on a number of levels. This spring, we're launching the Latin American Human Brain Mapping Project under the auspices of the Pan American Health Organization (PAHO) and World Health Organization (WHO), involving Dr Evans and representatives of various Latin American countries.

MEDICC Review: **Much has been made of the philosophical-scientific divide between psychiatry, psychology, and neuroscience. What are your thoughts on this?**

Pedro Valdés: Yes, and this has led to further fragmentation that, in my view, is counterproductive. In public health, we have to be able to measure quality of life, and for that, the nervous system is essential. Psychiatry, psychology, social work – all these are critically important for understanding how the human brain functions. Interestingly, Freud's "master plan" was to try to discover how the brain's circuitry worked as a clue to discover why people act the way they do. When he found that the level of science at the time wouldn't allow him to do that, he went as far as he could to treat disorders with psychotherapy. Now, we are closing the circle once again.

Both psychiatry and neuroscience have begun to evolve towards each other in important ways, and I believe this integration will become more important over time.

Two examples illustrate the complexities of the relationship among biology, genetics, lifestyle, and environment. First we have the famous "juggler's study" in which it was proven that acquisition of a new skill can actually thicken the cortex. And then we had an interesting case here in Cuba: we received a car crash victim from Colombia. The accident destroyed two fusiform areas of the brain that mediate recognition of faces, normally allowing us to recognize facial features as belonging to people we know. So he couldn't recognize anyone, at least on the conscious level. However, when he was shown familiar faces, his prefrontal lobes – the home for emotions – did indeed react to faces of people he knew. To us, this amounted to objective evidence of the subconscious.

So the various disciplines are not so far apart from each other. A comprehensive approach is crucial to solving the brain's riddles, especially the ones offering clues to better health outcomes in both the developing and developed world.

To generate a more holistic approach, the WHO has adopted the single term "brain disorders" to qualify a host of conditions, and to obligate us to look at this problem in its real – and very serious – magnitude.