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CURIOUS PAOLA VISITS LU NEUROSCIENCE DAY

FOTO: Kennet Ruona

BY JENS PERSSON - Much like Curious George, the famed prying monkey from the world of children's books, Paola Arlotta conveys an unbridled inquisitiveness. Not for bananas and the like, but for the human brain. Growing up in the seaside town of Trieste, Italy, she would always try to figure out how the world around her worked. Questions regarding basic principles of nature and biology would occupy her young mind. While she didn't grow up in an academic home her parents would always encourage her curiosity and later her pursuing a career in academia. Today, that knack for problem solving has brought her to an associate professorship in stem cell regenerative biology at Harvard University. In May she visited Lund University's Neuroscience Day to talk about her latest discoveries

When asked about the cerebral cortex, her main object of research, her eyes light up as her voice gains in intensity.

- What attracted me to the cerebral cortex are a number of things. First of all, it's unbelievably complex. There are so many different cell types that come together to form this very complex circuitry, which at the end underlie the very essence of human behavior. It is the cerebral cortex that makes it possible for us to have this conversation and be human, really. The cortex we have is also fundamentally different from every other mammal in the world, let alone other organisms that don't even have a one. So, how did we get this incredible part of our brain, how is it made during development and how did we get it through evolution? These are question that really drive me in my work and something that never bores me. I could just study this forever.

One of her main lines of research has an undeniable futuristic quality to it. It concerns the development and study of brain organoids, networks of neurons that have self-organized into a "mini-brain", about the size

of a grain of rice. The term "mini-brain", which has been thrown around a lot since the first paper on brain organoids was published in 2013, can be somewhat misleading. The article, by Lancaster et. al., rather describes the development of tiny three-dimensional fragments that mimic natural processes occurring inside the human brain. That discovery in itself is impressive enough, one might argue. At least that is what Palo Arlotta thought when she first laid eyes on the paper.

- It was a major splash when this atricle was first published. It really was incredible and the images that they showed were so beautiful. When I first looked at these images I was like; Oh, my goodness, they look so much like a very early fetal human or mouse brain. Naturally, the paper garnered a lot of interest and a lot of people in the field picked up this protocol and started to modify in different ways to try to evolve it to fit different models.

One of them was Paola. Her lure towards this new way of studying the human brain has all to do about getting as close as possible to the real thing, nature's own blueprint. If we are to understand the true mechanisms of early brain development, the study of singular neurons in a dish is simply not enough. What the brain organoids might be able to offer is a more truthful imitation of the natural surroundings that neurons experience in an actual living brain. For scientists to have access, in a dish, to the live communicative circuitry of the brain, not only between neurons, could represent a major step forward. Admittedly, it is early days yet but these miniscule brain models should represent an exciting alternative for studying early brain development, disease modeling and drug screening. Quite simply, these organoids offer more than the sum of their parts and could, in the longer term, lead to a deeper understanding of the human experience.

- Looking through the microscope we can see that what we have here is not only the cell type, but also the actual architecture of the tissue surrounding it. This is something that you don't get when you take embryonic stem cells and direct them to differentiate into neurons. The brain organoids are to a larger extent a result of a natural self-organizing process. This is important because there are many components during human development that are at play in the development of the brain, it's not only the cell-intrinsic mechanism within each cell that specify their fate, it's the activity of the circuitry that they form, it's the fact that you have to have the right diversity of cell types and so on.

- Looking forward, I think that more complex aspects of higher order circuit function may be modeled within these organoids, for example learning. This may be a controversial opinion, but I don't see why not? I like to think about stuff that might challenge what is thought to be possible.

Making a Change for Women in Science

Another area where Paola is challenging long-held conventions is that of women in science. Or rather, the lack of women in leading positions within the STEM-fields: science, technology, engineering and math. Together with a host of women in science, and men, she is part of the 'Initiative on Women in Science and Engineering' (IWISE), aiming to not only spark women's interest in science but help them compete and excel in their careers. Susan Solomon, CEO of the New York Stem Cell Foundation, who convened the first panel meeting last year, recently told Reuters that STEM fields are "too critical to leave behind half the nation's brainpower."

The 28 members of IWISE have already produced a number of tangible initiatives that can help women advance in science. They range from proposals aiming to raise awareness on gender equity among academic institutions to more direct suggestions where funding is tied to how well universities perform in promoting these issues. Generating real change in areas that carry long-standing structural and cultural connotations sometimes demand not only carrots, but also a stick. Unsurprisingly, the most forceful stick identified by the IWISE-group is money. That is why their most talked about suggestion is a report card where academic institutions will be annually evaluated on a set of quantifiable criteria. Based on the institutions' scores they will be assigned a gender equality grade. Paola Arlotta tells me that the IWISE Working Group is hoping to get different funding agencies to start implementing the report card when evaluating grant applications.

- Our hope is that this could become a key element in deciding whether academic institutions could, or could not, receive funding from certain foundations. A lot of these funding agencies are linked to each other quite closely, they talk to each other, and they obey similar principles. Now we hope to convince multiple private funding agencies to agree that less funding will go to institutions where their scorecard shows a bad grade. I believe if you are successful in tying these incentives to money it should be a powerful way to highlight issues of gender balance and affect positive change.