

EDITORIAL

India Gets a Seat at the Table of Human Brain Cartography

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In this Special Issue, *The Journal of Comparative Neurology* is proud to bring to the scientific community a monumental contribution that comes not from the usual Western power players in the business of generating knowledge about the brain, but from an unexpected newcomer. The contribution is DHARANI, a freely accessible, digital, micrometric-resolution, three-dimensional atlas of the developing fetal human brain, currently available for five gestational ages during the second trimester, and the newcomer is what is shaping up to become a new player at the high-stakes table of human brain map-making: the Sudha Gopalakrishnan Brain Center (SGBC) of the Indian Institute of Technology Madras, the Indian equivalent of the Allen Institute of Brain Science in the United States.

Five hundred years ago, Europeans expanded the conceptual boundaries of the world that they could represent in their minds by navigating into unknown waters, whilst updating their maps of lands and seas: charts that depicted side by side on paper what they experienced side by side in the world. The word comes from *mappa*, the word in medieval Latin for the table napkin or cloth upon which those maps would be unrolled and examined. The *mappa mundi* was thus the flat napkin-like representation of the world.

Maps of the brain, in the form of illustrations that depict the spatial arrangement of the structures that form a brain, have existed for at least 500 years, ever since humans began to suspect that the intricate contents of our minds had something to do with the particular arrangement of that bloody soft matter that we carry inside our skulls (Scatliff and Johnston 2014). Keeping a record of the brains that one sees is no longer an issue; nowadays, humans carry in their pockets the technology that allows for the direct capture and later observation of images of brains exposed to study. Moreover, any laboratory with a decent microscope can produce beautiful images of whole thin sections of mouse brains by stitching together a handful of snapshots—for, seen through

an objective high-powered enough that individual neurons can be observed, even the tiny mouse brain does not fit whole through the lenses.

Modern brain map-making is something else entirely, which goes beyond simple image capturing and representation. The brain, unlike the surface of the planet, is a complex three-dimensional structure, whereas our practical means to represent and observe it remain two-dimensional, like in the original *mappas*. Capturing the intricacies of the anatomical organization of the human brain thus requires cutting it into series of very thin sections which can then be stained for contrast (for, cut thin, brain tissue is transparent, with hardly any visible features), placed into a system of Ptolomaic coordinates (or no navigation, mental or physical, will be possible), observed for features that can be described and later identified by others (or the images are of no more than just that: images), and then, finally, organized systematically into a stack that reconstructs the third dimension of that brain. That systematic stack of maps is an atlas.

The Allen Institute for Brain Science released in 2006 the Allen Brain Atlas, a fully digital (and digital-only) compendium of maps of expression of more than 21,000 genes in the adult mouse brain, generated at the combined cost of 41 million dollars over 3 years (Brill 2006). Ten years later, the institute published, in *The Journal of Comparative Neurology*, the Allen Human Brain Reference Atlas (Ding, Royall, and Sunkin 2016), in an unprecedented 350-page stand-alone issue. That was an atlas of a single adult female human brain hemisphere subjected to a combination of magnetic resonance imaging and diffusion tensor imaging, followed by cutting into slabs, sectioning each slab into a series of 50 micron-thick slices, processing the slices for histology, then delineating their anatomy and annotating known brain structures. The entire enterprise took five years from start to finish, producing an opus of 1356 plates, 106 of which annotated in their 862 brain structures.



FIGURE 1 | Left, Allen Human Brain Atlas image of the adult human brain, level 28a (Figure 17 in Ding, Royall, and Sunkin 2016). Right, DHARANI image of fetal human brain at 22 gestational weeks, A-P level 1.32 mm (Verma et al. 2024).

Of course, feats of such monumental magnitude cannot be achieved through standard competitive funding opportunities awarded to independent laboratories. Although it now operates on competitively acquired federal and private grants, the Allen Institute for Brain Science was launched in 2003 with a 100-million dollar donation by Microsoft co-founder and philanthropist Paul G. Allen, followed by an additional 300 million in 2012. Through the Institute, those funds were geared toward the goal of generating freely available data on the brain that could not be obtained otherwise, and that would catalyze brain research in multiple fronts. Those were the funds that led to the completion of the Allen Human Brain Reference Atlas.

Enter DHARANI, which stands for “A 3D Developing Human-brain Atlas Resource to Advance Neuroscience Internationally”, and pays tribute to the Hindu goddess of the Earth and of beginnings—like the developing brain. Mapping something that changes over time, such as the developing brain, poses the additional challenge to map-making of identifying and keeping track of structures as they first form, then grow and morph into their adult configuration. Charting a developing brain thus takes map-making into even more complex and expensive waters.

It is no wonder, then, that DHARANI, the second human brain atlas that *The Journal of Comparative Neurology* presents to the scientific community, was delivered by a brain research center created with the single specific purpose of mapping the human brain on a cellular level through its entire lifespan, powered by a large-scale multi-disciplinary effort in the fields of science, technology, computing, and medicine. That research center is the SGBC, launched as a joint initiative of the Office of the Principal Scientific Adviser of the Government of India and

private philanthropists Kris and Sudha Gopalakrishnan in the top-ranked technology institution in India, the Indian Institute of Technology Madras.

DHARANI is now the largest publicly accessible digital dataset of the human fetal brain, created with less than 1/10 of the initial funds that powered the Allen Brain Atlas, and with a technology platform that was entirely custom-made in India between 2020 and 2022, during the COVID pandemic. Featuring 5132 plates of developing human brains at gestational weeks 14, 17, 21, 22, and 24, 466 of which fully annotated to cover ~500 brain structures as they form (Figure 1), DHARANI is freely available as an online resource for scientists around the globe at <https://brainportal.humanbrain.in/publicview/index.html>.

The Indian Institute of Technology Madras thus joins the Allen Brain Institute, and India joins the United States, at the table of human brain cartography, where large sums are invested in the name of providing humankind with freely available atlases of the available knowledge about the structures that compose the human brain. Besides extending DHARANI to include more developmental ages, the SGBC is currently adding region-specific cell types to the database, and in the future will include developmental trajectories of brain structures revealed by three-dimensional morphometry.

Importantly, while DHARANI calls itself an atlas, it is in actuality the beginnings of a meta-atlas, something for which there is not even a word yet. Just like an atlas is a series of maps, in a flip-chart of sorts that allows the browser to reconstitute the three dimensions of a brain in their mind, what lies ahead, as DHARANI continues to grow, is an atlas of atlases: a platform to

visualize the brain, in all its complex glory, as it morphs into its adult self.

Data Availability Statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

Peer Review

The peer review history for this article is available at <https://publons.com/publon/10.1002/cne.70005>

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