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Revealing Form and Function with Brain Imaging

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Form and Function. The phrase appears often in English, sometimes modified to specify that "form *follows* function". This rubric is attributed to Louis Sullivan, a renowned architect of the late 19th century (the "father of the sky scraper"), especially famous as a mentor to Frank Lloyd Wright, who professed the same rule. Other industrial specialties, such as automobile and home product design, software formulations, robotics, evolutionary biology, paleontology, and more, tout the same. In such diverse areas and more, there is recognition of the intimate relations, at times the oneness, of form (structure) and function.

Here we turn our attention to the brain, specifically to the early developing brain. Most of us understand the immaturity of the newborn human brain and the extra fragility and vulnerability of the incompletely-formed brain of prematurely born infants. The early-stage brain is often considered to be a major symbol, if not the actual target, of NIDCAP practice. Understandably, many consider developmental care as "brain care" in which early brain growth and development is both protected and actively supported by providing physical, behavioral, and emotional contexts that channel healthy brain maturation. This is a kind of mantra in the world of developmental care, including among NIDCAP practitioners.

It's one thing to profess the special relation of developmental care on brain development. It is another thing to see it. But how can we look into a baby's brain and see structural health and proper functional capabilities or the opposite? How do we see into the brain and its development? Remarkably, there are now numerous ways "to image" the brain. In this article we offer a friendly guide to a popular imaging technology, magnetic resonance imaging (MRI), and two of its most popular modalities: structural MRI and functional MRI (also known as fMRI). We do this to take you a little deeper into the technical side of these methods. As we describe how they work, it will clarify what they tell us. Understanding this should deepen your appreciation of the relations among science, engineering, and many important practices in contemporary health care – including those in the Newborn Intensive Care Unit.

Structural and functional MRI are captured from the same device - the giant tube in which a patient is positioned, where high tech hardware cranks, rumbles, and whirs. As you will note, the same electromagnetic processes are employed. Yet structural MRI displays form, while fMRI displays function. Despite the intimate interdependence of form and function, these two kinds of imaging are different in process and in use.

First, let's consider the structural MRI as it is applied to brain imaging. MRI technology acts on and takes measures from some of the smallest imaginable elements in the brain – the nucleus of individual hydrogen atoms, most of which are part of the water in and around all brain cells. The nucleus of a hydrogen atom is a single proton, and the hydrogen proton nucleus spins on its magnetic axis (imagine our planet Earth spinning on its axis). When a brain is exposed to a strong magnetic field of an MRI scanner, the protons' axes shift from random orientations to lining up in a common orientation. While temporarily arranged in the same orientation, these charged axes create a directional magnetic vector. The scanner then adds radio waves that sweep over the magnetic vector, deflecting it and causing it to resonate. The dynamics of this *nuclear magnetic resonance* can be read as radio frequency (RF) pulses, and these are the signals that are captured, quantified, and spatially organized by computer wizardry into detailed gray scale images.

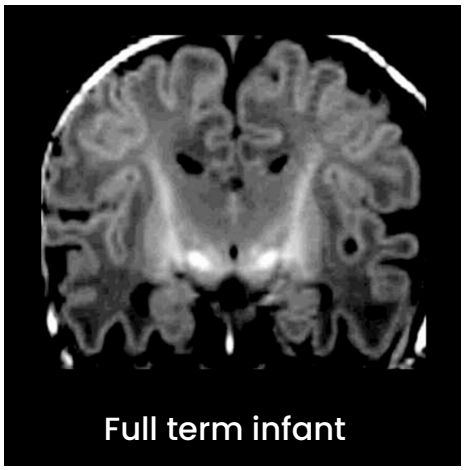

Figure 1. *A coronal view with structural MRI of a full term infant*

With awesome precision, the strength of the magnetic field can be manipulated, and with each change in energy, the axes of nuclei at differ-

ent depths are altered and measured. This produces images of successive "slices" across the brain, at any angle or depth! We can see form revealed, often in exquisite detail. Figure 1 is an example. MRI can be similarly applied all over the body and has revolutionized many kinds of medical diagnoses and analyses. Again, structural MRI reveals form. No physiology, no function is exposed.

Now we turn to fMRI for brain imaging. Function is "up front" in fMRI thanks to the use of the magnetic properties of hemoglobin, depending on whether it is bound to oxygen molecules or not. When hemoglobin is bound to oxygen, it is repelled by magnetic fields (diagmagnetic) and when hemoglobin is unbound to oxygen, deoxyhemoglobin is attracted to magnetic fields (paramagnetic).

Increased neuronal firing in a particular area of the brain as part of its involvement in some sensory, motor, cognitive or physiological activity brings a concomitant increase in energy demand in the activated region. Oxygen is an essential part of the biochemical pathways of such metabolic activity. The arteries and minute capillary branches that perfuse the networks of the activated neurons will respond to increases of local cellular activity by dilating. Such dilation increases local blood flow to the active areas, thereby meeting the larger demands for oxygen and glucose.

As with the structural MRIs described earlier, the effects of RF waves on the magnetic fields become the signal detected by the fMRI. A special measure is used, called the Blood-Oxygenation Level Dependent response (or BOLD). The BOLD signal is a change (increase or decrease) in the proportion of oxyhemoglobin relative to deoxyhemoglobin. The *contrast* between the oxygenation from its prior baseline is the signal. In other words, this

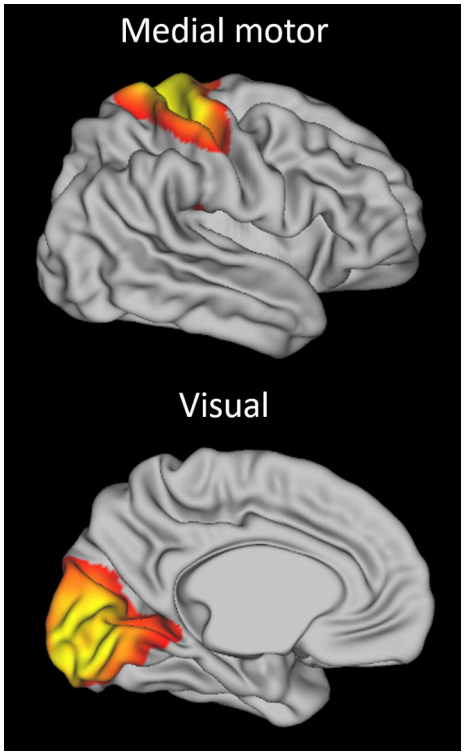

Figure 2. *Functional maps for a group of term neonates as measured by fMRI*

method does not directly reference neuronal activity, nor does it measure the oxygen itself. Rather, the BOLD signal identifies areas where there are relative changes in oxygenated hemoglobin presumed to correspond to the immediate metabolic needs of the neurons. Sophisticated analyses of these signals can achieve remarkable spatial resolution, mapping active areas about 1mm in size. These are displayed as maps of contrasting increases or decreases in regional activities, shown as graded changes in terms of color-coded nodes on a brain image. Dynamic brain function can thus be spatially portrayed by area, by network, or by structure. Figure 2 shows contrasting activities measured on the motor cortex and another image showing contrasting activities in a deeper, visual region.

We have merely scratched the surface of the creative combination of physics, chemistry, cell physiology, and systems neuroscience that has yielded a variety of imaging modalities. Beyond the technical tour de force represented in the use of magnetic resonance imaging is a panorama of applications. Because disease conditions usually include an increase in water content, MRI is suited for localizing some diseases. Brain function depends on brain structures large and small. MRI-based methods are used globally across the brain and microscopically on increasingly smaller scales of function.

Clinically, brain imaging is used to recognize early conditions of damage or malformation to predict outcomes and, significantly, to identify when and where therapeutic interventions can be applied. Brain imaging has revolutionized basic research as well. The tens of thousands of research papers describing insights gleaned from seeing brain structures within a living body as well as mapping dynamic functions have shaped entire new areas of neuroscience.

We hope to contribute at least one more *Developmental Observer* column on brain imaging, next focusing on applications suitable for newborns, including those born prematurely, for these babies present special challenges – and invite extra benefits from the knowledge gained on seeing the processes of brain development in the context of NIDCAP practice.

Unlike previous columns from the Science Desk, this one is not a commentary on a target article, but is an essay that in some ways, one side of a conversation. As such, we invite responses or questions. If this brief introduction to brain imaging inspires questions or comments, please contact us. We will gladly incorporate your input into a future essay – or simply answer your email.
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