Imaging Science

Measuring Activity and Structure in the Human Brain

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Recent developments in magnetic resonance technologies have stirred much interest in analytical methods designed to help us visualize and understand the significance of the various types of MR measurements. Some of the new methods yield information about brain structure, while others inform us about brain function. The technologies and analytical methods have added enormously to our knowledge of how the brain mediates thought and behavior; they are also finding their way into many clinical applications.

The best-known of the new methods is functional magnetic resonance imaging. Introduced by Ogawa and his colleagues, fMRI measures spatial variations in blood oxygenation levels across the brain. The oxygenation levels, in turn, are correlated with neural responses. An excellent introduction to fMRI can be found in [3]; for a more recent, relatively advanced review of the relation between neural signals and fMRI measurements, see [4].

The original applications of fMRI were designed under the assumption that the signals would be weak and that we would be able to formulate only the most basic of questions: Which part of the brain is active as subjects perform a given perceptual task? To increase the statistical power of the method, the first generation of experimental designs compared group averages. This approach spurred the development of a variety of mathematical techniques for aligning brain structures in different individuals in order to compare signals in the transformed areas, and for modeling the signals and noise to provide more reliable statistical processing.

In recent years, however, it has become clear that simply detecting the presence or absence of fMRI signals is only the beginning. It is possible, for example, to measure signals in individual subjects, to measure the size and responses of major brain structures, and to compare one individual with another. The ability to make measurements in an individual, and to compare that individual's measurements with the population norms, has become an essential part of clinical evaluation.

Our group has contributed to the development of this type of analysis, often called computational neuroimaging (see [5]), by examining responses and structures in the visual pathways. The primary visual cortex, the major projection zone for signals from the retina, is located in the posterior portion of the brain (see Figure 1). The responses in the primary visual cortex are organized as a spatial map of the visual field, with the right visual field represented in the left hemisphere and the left visual field in the right hemisphere. The central portion of the visual field (fovea) projects to a very large section of the cortex, located around the posterior-most point of the cortex (occipital pole). Increasingly peripheral portions of the visual field send their signals to increasingly anterior regions, as shown in Figure 1.

Using modern technologies and analytical methods, we can measure these maps in individual human brains in a one-hour experiment. We can then compare the properties of the maps from normal and diseased individuals, such as individuals who have lost retinal function. This makes it possible to measure the consequences of various peripheral diseases, such as the loss of signals from the retina and other input failures, on cortical organization.

A second MR technique, diffusion tensor imaging, provides another valuable measurement of the brain. While fMRI provides information about brain signals, DTI provides insight about the properties of brain structures. DTI has been particularly important in determining which parts of the brain are connected to one another. Readers might imagine this topic to be well understood; in fact, however, measurements of the connections within the brain's large fiber tracts, usually called white matter, are very difficult to obtain. DTI measures the
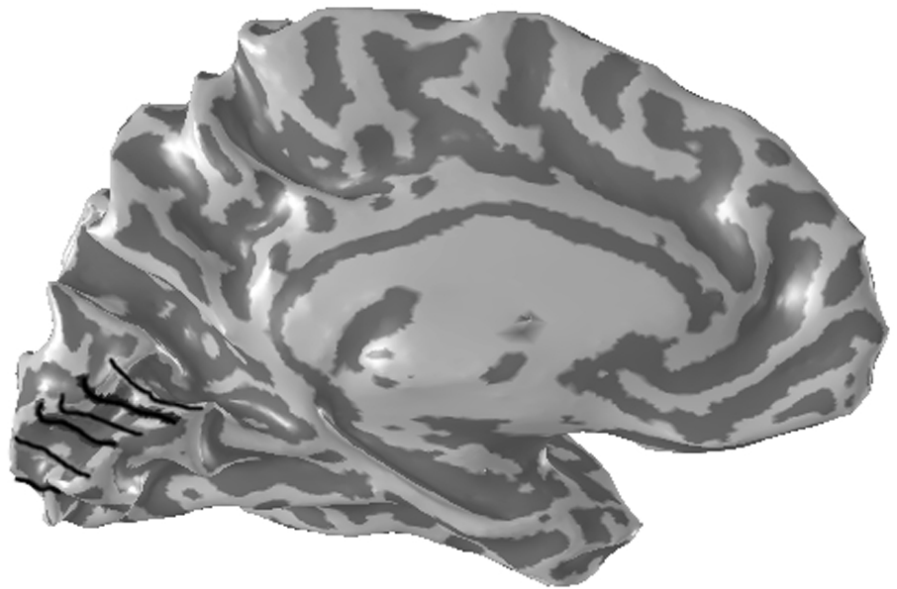

Figure 1. *Functional MRI can be used to measure visual maps in the human cortex. This medial view of the cortex shows measurements of the iso-eccentricity bands in the human brain using the methods described in [5]. Each black line indicates a cortical strip that responds best to stimuli at increasing eccentricity (from posterior to anterior: 0.5, 1, 2, 4, 8, 16 degrees). The image of the brain is made by finding the boundary between the white matter and the gray matter, forming a surface tessellation, and then smoothing the tessellation. The light and dark shading indicates whether the original surface was a sulcus (dark) or a gyrus (light).*

local diffusion of water within the brain, and these local diffusion paths inform us generally about the orientation of large fiber tracts. Using algorithms pioneered by several groups to interpret these local measurements, researchers can trace the trajectory of the larger fiber tracts in the white matter tissue [1,2,6].

The image in Figure 2 shows our estimates of the fiber tracts in a part of the brain in which fractional anisotropy (a measure of the directionality of fibers) differs in children who read well and those who read poorly. The location, identified in earlier studies, is revealed by DTI to be at the confluence of three distinct fiber bundles.

The development of MR measurement modalities and the accompanying analytical tools has opened up many new possibilities. Scientists are now measuring structure and function in the awake-behaving human brain (in contrast with similar measures performed in anesthetized monkeys); these

Figure 2. *Diffusion tensor imaging permits us to identify the locations of major fiber bundles in the human brain. This image shows a region within the white matter of the brain that is at the confluence of three major fiber bundles, shown in three shades of gray. The quality of children's reading performance is correlated with several of the properties of these three fiber bundles.*

data were completely hidden from us fifteen years ago. As might be expected for a new discipline, there have been both advances and retreats along the way. Collaborative work between neuroscientists, engineers, physicists, mathematicians, and statisticians has made the measurements and analysis possible. The ability to measure these properties of the brain, for the first time, will surely be a good thing in the end. And there is every reason to believe that new modalities will continue to emerge, offering new opportunities to deepen our understanding.

References

[1] P.J. Basser, S. Pajevic, C. Pierpaoli, J. Duda, and A. Aldroubi, *In vivo fiber tractography using DT–MRI data*, Magn. Reson. Med., 44:4 (2000), 625–632.

[2] T.E. Conturo, N.F. Lori, T.S. Cull, E. Akbudak, A.Z. Snyder, J.S. Shimony, R.C. Mckinstry, H. Burton, and M.E. Raichle, *Tracking neuronal fiber pathways in the living human brain*, Proceedings of the U.S. National Academy of Science, 96:18 (1999), 10422–10427.

[3] S.A. Huettel, A.W. Song, and G. McCarthy, *Functional Magnetic Resonance Imaging*, 1st ed., Sinauer Associates, Sunderland, Massachusetts, April 1, 2004.

[4] N. Logothetis and B. Wandell, *Interpreting the BOLD signal*, Ann. Rev. Physiol., 66 (2204), 735–769.

[5] B. Wandell, *Computational neuro-imaging of human visual cortex*, Ann. Rev. Neurosci., 10:22 (1999), 145–173.

[6] R. Xue, P.C.M. van Zijl, B.J. Crain, M. Solaiyappan, and S. Mori, *In vivo three-dimensional reconstruction of rat brain axonal projections by diffusion tensor imaging*, Magn. Reson. Med., 42:6 (1999), 1123–1127.

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