Neurons in the primary visual cortex of primates respond preferentially to visual stimuli from one eye. A large number of electrophysiological studies in nonhuman primates have demonstrated that these eye preferences are organized into vertical columns, with all neurons in a column sharing the same preference (Figure 8.6). The presence of ocular dominance columns in human visual cortex was verified using postmortem cytochrome oxidase staining in the early 1980s. Vascular responses have been shown by optical imaging to be localized within these columns, so hemodynamic techniques like fMRI could, in principle, map the columnar structure of the primary visual cortex. However, in humans the transition from one ocular dominance column to another occurs over about 1 millimeter of cortex, near the limit of spatial resolution for fMRI.

An early attempt to distinguish ocular dominance columns using fMRI was reported by Menon and colleagues in 1997. They used a FLASH pulse sequence on a high-field (4 T) scanner to acquire very-high-resolution (547 μm by 547 μm) images parallel to the calcarine sulcus in the primary visual cortex. On such slices, ocular dominance columns will often be oriented perpendicularly to the slice plane. The visual stimulus was a large red light-emitting diode (LED). To ensure monocular stimulation, subjects were instructed to open and close one eye at a time in a blocked pattern. The authors used a binocular stimulation condition to identify voxels corresponding to primary visual cortex. For each such voxel, they compared the relative

**ocular dominance**
The degree to which a given neuron in the visual cortex responds more to stimuli presented to one eye than to stimuli presented to the other eye.

**T₂* blurring**
Distortions in T₂* images that result from having a data acquisition window that is sufficiently long that significant T₂* decay occurs over that interval.

In a later study conducted in 2001, Cheng and colleagues investigated whether dominance patterns measured using fMRI were stable across multiple sessions. They also used high-field (4 T) fMRI, but with a multishot gradient-echo echo-planar pulse sequence. Very-high-resolution voxels were used (470 μm by 470 μm). It is worth emphasizing that these high-resolution studies present a different set of challenges than standard fMRI. For example, here the authors acquired each slice through a series of 32 successive excitation pulses, resulting in a total time between successive volumes of nearly 10 s, even though only three slices were acquired. This multishot technique reduced the data acquisition time needed for each excitation, which in turn reduced T₂* blurring, which results from
the $T_2^*$ decay that occurs during the acquisition window. To understand $T_2^*$ blurring, remember that data acquisition (e.g., filling $k$-space) takes time, about 40 ms for a typical $64 \times 64$ image and much longer for very-high-resolution images. During this acquisition window, the spins are continuously undergoing $T_2^*$ decay, so if the window is very long compared to the $T_2^*$ value of the tissues being imaged, there will be virtually no signal toward the end of the acquisition window. This significant decay process can cause blurring for BOLD images, especially those that acquire an entire slice at very high resolution following a single excitation.

As a result of the long acquisition time, the authors also used very long block intervals of 2 minutes of monocular stimulation interleaved with 1 minute of darkness. Comparing the patterns evoked by monocular stimulation provided strong evidence for ocular dominance columns in primary visual cortex, notably in areas where the calcaneal fissure ran parallel to the imaging plane, but not in areas identified with the secondary visual cortical area, V2 (Figure 8.8A–D). The mean width of columns was about 1.1 mm, consistent with the results from both earlier postmortem staining and from Menon and colleagues’ study. Replicability analyses re-

**Figure 8.7** Early results suggesting the identification of ocular dominance columns in visual cortex using fMRI. Shown in (A) are voxels in human primary visual cortex that responded predominantly to stimulation from one eye or the other. Arrows in (B) indicate transitions between nearby voxels within the calcarine cortex. Voxels responding mostly to left-eye stimulation are shown in red, while voxels responding mostly to right-eye stimulation are shown in blue. In-plane voxel dimensions are approximately 0.5 mm on a side. (From Menon et al., 1997.)

**Figure 8.8** Ocular dominance columns in visual cortex. These results show repeatable measurements of ocular dominance columns across two sessions. The same subject participated in two sessions, shown in panels A and C. Note that the outlines of the areas of ocular dominance from the first session (B) correspond well to the results from the second session (D). (From Cheng et al., 2001.)
BOX 8.2 (continued)

vealed that the observed patterns were significantly correlated for a given subject both between two experiments within the same session and across two different sessions.

The mapping of ocular dominance columns provides an example of the potential of very high-resolution fMRI. It has obvious value as a technical demonstration and will undoubtedly spur additional improvements in both pulse sequence design and image acquisition hardware. But does it add to the understanding of the brain? At first glance, these studies merely replicate a phenomenon that was first demonstrated in animals more than four decades ago and in humans more than two decades ago. The existence of ocular dominance columns was never in question, regardless of the outcome of the fMRI studies. Nevertheless, fMRI can provide an important contribution through the in vivo study of the human visual system, in contrast to in vitro or animal studies. For example, a topic of considerable interest is the presence or absence of attentional influences upon early visual processing. Understanding whether spatial attention influences activity in dominance columns will provide information about the organization of the visual system. It is important to emphasize that here, as in many areas of neuroscience, fMRI provides a source of information about the brain that can complement results derived from other techniques.

normalization The transformation of MRI data from an individual subject to match the spatial properties of a standardized image, such as an averaged brain derived from a sample of many individuals.

Many aspects of brain function vary over the spatial range of fMRI. Brain regions identified by cytoarchitectonic features, such as used by Brodmann in 1909, generally are several centimeters in size. While the visual cortex includes much of the occipital lobe, along with pathways extending into the temporal and parietal lobes, individual functional regions within the visual cortex extend in size from a few millimeters to a centimeter or more. Subcortical nuclei such as the caudate, putamen, and thalamus all are sufficiently large to encompass multiple fMRI voxels. Nevertheless, many aspects of brain structure, including both horizontal cortical layers and vertical cortical columns, exist on a much smaller scale and are very difficult to address using fMRI.

While this discussion has focused on effects of data acquisition upon spatial resolution, choices made in experimental analysis are also important. A common preprocessing step explicitly reduces spatial resolution by smoothing fMRI data using a three-dimensional Gaussian filter of several voxels in width (see Chapter 10). Typical smoothing parameters can increase the effective voxel size to $6 \times 6 \times 6$ mm or greater. Note that such a voxel contains more than 3 times the volume of a voxel 4 mm on a side, and 27 times the volume of a voxel 2 mm on a side. While smoothing can reduce spatial resolution, it can improve the validity of statistical tests and comparisons across subjects. Other analysis steps also reduce spatial resolution, albeit not as obviously as spatial smoothing. Any comparison across subjects will reduce spatial resolution, since subjects will differ in their anatomical structure. In addition, algorithms for transforming subjects to a common stereotaxic space, a process known as normalization, further reduce spatial resolution due to the difficulty in matching a person's individual anatomy to a stereotaxic template.

The decision to use anatomically based region-of-interest analyses has implications for spatial resolution as well. In an ROI analysis, the basic spatial unit changes from a single voxel to a region containing many voxels. Obviously, the ability to identify differences between adjacent voxels is lost, and thus spatial resolution is greatly reduced. However, to the extent that the chosen regions accurately map onto functional divisions within the brain, the functional resolution of the data may be greatly increased by sig-