Spiral K-space MR Imaging of Cortical Activation

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Brain function can be mapped with magnetic resonance (MR) imaging sensitized to regional changes in blood oxygenation due to cortical activation. Several MR imaging methods, including conventional imaging and echo-planar imaging, have been successfully used for this purpose. The authors investigated spiral k-space MR imaging, implemented with an unmodified 1.5-T clinical imager, for imaging of cortical activation. A gradient-echo, spiral k-space imaging method was used to measure activation in the primary visual cortex (number sequence task), primary motor cortex (fist-clenching task), and prefrontal cortex (verbal fluency task). Comparison of conventional and spiral k-space imaging in the visual and motor cortex, in which signal-to-noise ratio, voxel size, and imaging time were matched, showed that artifacts were reduced with the spiral k-space method, while the area and degree of activation were similar. The number of sections that could be imaged in a fixed time interval was increased by a factor of four with this implementation of spiral k-space imaging compared with conventional imaging.

Index terms: Brain function, 10.918 • Brain, MR, 10.121412 • Functional studies • Image processing • Pulse sequences • Rapid imaging

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Abbreviations: PET = positron emission tomography, S/N = signal-to-noise ratio, 2DFT = two-dimensional Fourier transform.

REGIONAL CHANGES in blood oxygenation resulting from cortical activation enable magnetic resonance (MR) imaging to be used as a tool for noninvasive mapping of human brain function (11-14). These changes in blood oxygenation are presumed to result from a decoupling of blood flow and oxygen metabolism in activated cortical tissue (5). Since deoxygenated hemoglobin is paramagnetic and fully oxygenated hemoglobin is diamagnetic, deoxygenated hemoglobin can serve as an endogenous MR contrast agent, the presence of which leads to a transverse relaxation (1.6,7). Accordingly, activation can cause small changes in MR signal intensity on T2- and T2*-weighted images.

Although many of the first demonstrations of MR imaging of cortical activation with the deoxymyoglobin effect were conducted with high-speed echo-planar imaging devices (2,4,8), cortical activation has also been demonstrated with conventional two-dimensional Fourier transform (2DFT) imaging (9) at 1.5 T (10-12) and higher field strengths (3,13). There is substantial appeal in using conventional techniques for functional MR imaging: These techniques are easy to use and, since they require no specialized hardware, can be used with nearly any high-field-strength clinical MR imager. These techniques can also routinely achieve high resolution (<2 mm in plane) and demonstrate limited geometric distortion due to magnetic field inhomogeneity.

High-spatial-resolution functional imaging has proved useful for detailed mapping along the narrow cortical ribbon (11). Imaging of small areas of activation (14), and reducing partial-volume effects (15). The primary disadvantages of conventional imaging techniques are that imaging times can be rather long when the number of sections is large and activation images are often corrupted by artifacts resulting from a variety of physiologic processes (16). We estimate that as many as one-third of our conventional functional MR imaging data sets have been corrupted by these artifacts, which include low-spatial-frequency bands of apparent activation and deactivation, edge artifacts, and flow-related artifacts.

Figure 1 shows the difference between two axial T2*-weighted 2DFT images through the primary motor cortex during a fist-clenching task. Here, T2* weighting was achieved with a long TE gradient-echo technique. The "true" area of activation-related change was determined as the area of statistically
significant change on a set of 10 difference images. Low-spatial-frequency banding and edge artifacts are also apparent. When imaging multiple sections, it is desirous to interleave acquisitions because the theoretical signal-to-noise ratio (S/N) per unit imaging time is better than that with sequential acquisition. However, we have also found that artifacts in 2DFT imaging worsen with increased TR, limiting the ability to take advantage of this potential gain in S/N. Many artifactual areas of activation can be eliminated by averaging several trials and by using post-processing procedures such as parametric statistical analysis on a pixel-by-pixel basis (e.g., the Student t test) (17) and split-half reliability testing (see Materials and Methods) (14). Nonetheless, these artifacts can certainly reduce statistical power and make negative findings uninterpretable. In the present study, we examined spiral k-space imaging, which in our early work was found to be more robust with regard to these artifacts than conventional imaging (18).

- MATERIALS AND METHODS

Spiral K-space Imaging

The spiral k-space imaging method (19–22) was studied as a possible solution to the main disadvantages of conventional functional MR imaging: artifacts and a severe trade-off between imaging time and the number of sections to be imaged. In conventional, or 2DFT, imaging, k-space is sampled over time, with samples acquired one line at a time in a rectilinear fashion. In spiral k-space imaging, k-space is sampled along spiral trajectories that are typically defined by an Archimedean spiral. This is achieved by means of time-varying gradient magnetic fields. While it is possible to generate low-resolution spiral images in a single excitation, interleaving spiral k-space trajectories from multiple excitations can be used to reduce gradient power requirements and improve spatial resolution (22).

Figure 2 shows sample spiral k-space gradient waveforms and four interleaved trajectories in k-space. These gradients were designed to numerically trace the desired trajectory without exceeding gradient rise time and maximum strength constraints. While the image reconstruction procedure is non-standard and was performed off-line on a workstation, our implementation required no special-purpose imager hardware. As was observed for projection-reconstruction imaging (23), the nature of motion and other artifacts in spiral k-space imaging is somewhat different from that of 2DFT imaging, offering the prospect for reduced artifacts in functional MR imaging. Additionally, spiral trajectories begin at the origin in k-space and no gradients are applied before acquisition, which makes the technique fully compensated with respect to in-plane flow and motion. These trajectories also have the property that all gradient moments periodically return to zero (22), which makes the trajectory well behaved with regard to motion and flow for high spatial frequencies as well.

Raw data from the spiral acquisitions are transferred to a Sun Sparcstation (Sun Microsystems, Mountain View, Calif.) for image reconstruction with use of convolution gridding (24,25). For off-resonance spins, spiral k-space imaging demonstrates a blurred point spread function, which in this study was corrected with a method requiring a map of resonant frequencies (26). These corrections have been integrated with the image reconstruction program. In this method, the sampled data are segmented according to the time after the excitation at which each sample was acquired, each segment is reconstructed, and the off-resonance correction is applied in the image domain for the average acquisition time of the data in that segment. In our implementation, the nominal time for each segment was 5 msec. Full-resolution frequency maps are determined for each imaging section from the phase difference between two images acquired with different gradient TE's. Acquisition of these maps typically takes less than 30 seconds and is implemented as part of the preacquisition tuning and calibration procedures. Effects of off-resonance acquisition may also be corrected with automatic deblurring methods that do not require field maps (27).

Activation Studies

Both spiral k-space imaging and conventional imaging were used to show activation in the primary visual cortex and the primary motor cortex. So that the degree of activation and artifact with these two methods could be compared, attempts were made to match as many relevant parameters as possible, al-
though it was difficult to match all parameters. Those that were matched to within 10% included total imaging time, TE, section thickness, field of view, in-plane resolution, data sampling window length, number of signals acquired, and theoretical S/N for gray matter. While the sample density variations in spiral acquisitions and differences in the shape of the acquisition pattern (rectangular vs circular) were accounted for in the S/N calculations, T2* decay during the acquisition period was neglected. In calculating theoretical resolution, the effect of the acquisition pattern and of T2* decay (which weights the high spatial frequencies) was neglected. Additionally, the spiral sequence used 3 seconds of excitation before data acquisition to minimize the effect of the dynamic approach to steady state.

Pulse sequence parameters for 2DFT imaging were TR msec/TE msec = 100/36; field of view, 128 x 256 matrix, no averaging, 4-7-mm section thickness, 25° flip angle, spoiling applied. 16-msec data sampling window, and 13-second acquisition time. Images were acquired with frequency encoding (readout) in both possible directions in all but one case. Our previous experience indicated that first-order gradient moment nulling resulted in only a minor reduction in flow artifacts and had no effect on low-spatial-frequency banding and other artifacts seen in functional MR imaging. As a result, no moment nulling was included in the sequence. Pulse sequence parameters for spiral k-space imaging were 500/36. 240-mm field of view, 170 x 170 matrix (circular pattern), no averaging, 4-7-mm section thickness, 45° flip angle, rephasing (no spoiling). 16-msec data sampling window, 20 interleaved spiral trajectories, and 13-second acquisition time. The flip angle for both methods was chosen to be approximately equal to the Ernst angle [28] for gray matter (T1 = 1,200 msec was assumed). A single 5-inch (12.7-cm) surface receive coil was positioned over the occipital pole for improved S/N during the visual activation experiments. For motor activation, either a pair of 5-

inches surface coils or a pair of 3-inch (7.6-cm) surface coils were positioned parallel to each other at the sides of the head.

The primary visual cortex was stimulated with single characters (digits subtending 2.5° by 5°) presented at a rate of 1 Hz in either the lower-left or lower-right quadrants of the visual field. Small character stimuli, such as these, are commonly used in electrophysiologic studies [29] and have more recently been used in a study using functional MR imaging [14]. The subject was asked to monitor a sequence of numbers for deviations in the ascending numeric sequence (eg, the first 8 in 1234867812...) and to respond by pressing a button. The stimuli were presented in an alternating fashion in the lower-left and lower-right visual fields. These two conditions were subtracted to identify areas of activation in the right and left visual cortices.

The primary motor cortex was stimulated by means of a fast-clenching task in which the subject smoothly opened and closed his or her fist at an approximate rate of one every 1.5 seconds; a resting condition was used as a control. In one case, fist clenching of the opposite hand was used in place of the resting condition. In these experiments, imaging with the pulse sequence parameters listed above began approximately 10 seconds after the beginning of each condition. Each condition was repeated 10 times, and images of activation were calculated by using maps of the average difference in image intensity, the percentage difference in image intensity, and the Student t test [15] applied on a pixel-by-pixel basis.

**Data Analysis**

Conventional and spiral k-space imaging methods were compared by means of measurements of area and degree of activation and of image variance not related to activation. We defined a region of activation as a set of contiguous pixels exceeding a certain level of statistical significance for intensity, as deter-
Figure 3. Activation in primary visual cortex with a single character in the visual field. 
(a) T1-weighted image of coronal section near occipital pole. (b-d) Average difference images obtained with (b) spiral k-space acquisition, (c) 2DFT with left-to-right phase encoding, and (d) 2DFT with superimposed phase encoding. Ghost images of the sagittal sinuses are seen in c (arrow). The table lists measurements of the area and degree of activation of the two regions of activation indicated by the arrows in b.

Determined by application, on a pixel-by-pixel basis, of the group Student t test. In each section, we identified regions of activation that were evident with both imaging methods to reduce the possibility that artifacts would be included in the analysis. Once a region of activation was identified, the area of activation was calculated from the number of pixels in that region of activation that exceeded specified levels of statistical significance as determined with the t test calculations ($P < 0.05; t > 1.73; P < 0.005; t > 2.85$). The degree of activation in each region was determined by means of the average percentage difference in that region. To prevent bias introduced by using different areas of activation for the calculation, the region over which the percentage difference was calculated was identical with both imaging methods and was defined by the union of the statistically significant areas ($P < 0.05$) in each region. To determine the amount of variance in the activation maps not related to activation, an average difference image was generated by averaging activation-activation difference images with control-control difference images for each section studied. This image, therefore, had the same noise and artifact characteristics as the average activation-control difference images, but without any regions of activation. The standard deviation of the average difference was calculated over the entire brain area for each section and was normalized by the average image intensity over the same area. This quantity provided the measure of variance that could be expected with each method in a manner that was independent of the activation-related changes.

**Frontal Cortex Activation**

Because of the high level of artifacts, we had little success in applying conventional imaging to frontal cortex activation. Here we report the results of the spiral k-space method applied to functional imaging in the frontal cortex during a verbal fluency task. The spiral k-space method has also been applied in the frontal cortex to a working memory task, reported elsewhere (30). With functional positron emission tomography (PET), verbal fluency tasks have been found to cause activation in the left inferior frontal cortex in right-handed subjects (31). Other verbal tasks have also been used to localize activation to roughly the same area with both functional PET (32) and functional MR imaging (33,34). In the verbal fluency task in the present study, subjects were given a category (eg, animals) and were asked to generate and speak aloud words belonging to that category at a rate of once every 2 seconds. Two control conditions were chosen for this task: a repeat condition, in which subjects simply repeat words presented to them visually, and a resting condition. The subject’s head was first immobilized with a surgical vacuum pillow. A 10-spiral implementation was then used to generate images of medium resolution (128 x 128 matrix over a 240-mm field of...
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* Sum of two areas of activation.
' Five subjects, 17 areas of activation.

Each condition in the task lasted 60 seconds, during which imaging was performed, and each condition was repeated 40 times. During the 60-second imaging interval, images were acquired at an average rate of one every second at six section locations. Shimming was not performed, although off-resonance correction (25) was used.

Areas of activation were identified with the split-half t test procedure (14), in which images of the paired t test are calculated for each of the first and second halves of each experiment and only areas of activation that are statistically significant in both halves are considered. Time series plots of signal intensity and percentage difference calculations were made for regions of interest.

**RESULTS**

Spiral k-space and conventional 2DFT imaging were applied to the imaging of cortical activation in five subjects. Two subjects with the visual stimuli and three with the motor stimuli. In these subjects, 17 distinct areas of activation were identified, of which 13 were in several distinct areas of the visual cortex. Figure 3 shows differences images of a representative coronal section through the occipital pole with spiral k-space imaging and 2DFT imaging with phase encoding in the left-right and superior-inferior directions. The difference images were calculated as the average difference in signal intensity between the 10 images in the active state and the 10 images in the control (inactive) behavioral state. For the two areas of activation identified with arrows in Figure 3, measurements of the summed areas of activation and the percentage difference in activation were obtained and are listed in the Table. Note the projected ghost image of the sagittal sinus causing false areas of activation in Figure 3c. The background (non-activation) standard deviations were calculated from an average difference image calculated from activation-activation and control-control difference images and are also listed in the Table.

Figure 4 shows difference images of a representative coronal section through the primary motor cortex with spiral k-space imaging and 2DFT imaging with phase encoding in the left-right and superior-inferior directions. Low-spatial-frequency banding artifacts are present on the 2DFT functional maps that are not present on the spiral maps. These artifacts are apparent as vertically and horizontally oriented bands in Figure 4c and 4d, respectively. Measurements of activation in the primary motor cortex (arrow, Fig 4b) and background standard deviations are listed in the Table. The Table also lists the average calculated area of activation, the area-weighted average of the percentage difference, and the average background standard deviation for spiral k-space and 2DFT imaging.

Activation of the frontal cortex with the verbal fluency task was imaged with the spiral k-space method. Figure 5a shows an oblique coronal section through the frontal cortex slightly anterior to the genu of the corpus callosum, in which pixels highlighted in white show activity with the verbal fluency task. For the region in the inferior left cortex identified with an arrow, a plot of signal intensity versus time for the verbal fluency and rest conditions is shown in Figure 5b. One experimental block consists of 10 images obtained during the word-generating task and then 10 images obtained in the resting state, with the block repeated seven times. Changes in signal intensity occur after every group of 10 images. The percentage change in signal intensity was 8.1% between the generating and resting conditions. Between the repeat and resting conditions in the same region, the percentage change in signal intensity was 3.2% over the same region. The apparent drift in signal intensity is due, we suspect, to subject motion over the course of the experiment.

**DISCUSSION**

Examination of Figures 3 and 4 indicates that the area and degree of activation were similar for spiral k-space and conventional 2DFT imaging. This qualitative observation is largely confirmed by measurements of area and degree (percentage difference) of activation given in the Table for Figures 3 and 4 and the average of all identified areas of activation. On average, the area and degree of activation are larger with the spiral k-space method, although a paired statistical comparison of area and degree did not result in a statistically significant difference between the imaging methods. This is the expected result, since the theoretical S/N and T2* weighting are nearly the same for the two methods.

Different gradient-echo imaging methods will result in similar S/N values, provided that the voxel volume in-plane resolution...
Figure 4. Activation in primary motor cortex with a fist-clenching task. (a) T1-weighted image of coronal section through primary motor cortex. (b-d) Average difference images obtained with (b) spiral k-space acquisition, (c) 2DFT with left-to-right phase encoding, and (d) 2DFT with superoinferior phase encoding. The Table lists measurements of area and degree of activation for the region of activation indicated by the arrow in b.

Figure 5. Activation in prefrontal cortex with a verbal fluency task. (a) T1-weighted image of an oblique coronal section slightly anterior to the genu of the corpus callosum. Areas of activation identified by the split-half t test procedure (see text) are shown in white as an overlay. (b) Time series plot of signal intensity during verbal fluency task (V) and rest (R) for the region in the lower-left prefrontal cortex (arrow in a).

\[ S/N = \frac{C}{\sqrt{TR}} \frac{(1-e^{-TR/T1})}{(1+e^{-TR/T1})} \]

where C is a scaling constant. This relationship as-
Figures 3 and 4 demonstrate that spiral k-space imaging results in a reduced level of artifacts compared with conventional 2DFT imaging. This was confirmed by measurement of artifacts (Table). Both low-spatial-frequency artifacts and flow-related artifacts were reduced. This was confirmed with a paired statistical comparison (t test) in which the standard deviation of the background was found to be reduced with spiral k-space imaging ($P < .025$ [df = 14]). This also confirms our experimental findings, in that spiral k-space imaging appeared more robust, with fewer artifacts and false areas of activation, than conventional imaging. With spiral k-space imaging, we have also had greater success in identifying expected areas of activation (e.g., distinct regions of activation in the first three processing stages of the visual system) and have found that fewer data sets have to be discarded because of artifacts.

There are a variety of reasons artifacts are reduced with spiral k-space imaging. A degree of motion robustness arises from the inherent flow and motion compensation of this acquisition method. This is important because any induced phases arising from blood flow, cerebral spinal fluid, and brain motion (35,36) can cause artifacts on functional maps. Another factor that may have reduced flow artifacts in our study was the spiral pulse sequence had a longer TR, which reduced the effects of wash-in of pulsatile flow, particularly in large vessels. In other studies, we found that first-order gradient moment nulling applied to 2DFT imaging led to some reduction in flow ghosting, although it had little influence on the troublesome low-spatial-frequency banding and on edge artifacts. The reduction in flow ghosting in spiral acquisition, therefore, does not completely explain the reduction in artifacts, since these other artifacts could not be attributed to blood flow. Additionally, the low-spatial-frequency artifacts in 2DFT imaging were found to be sensitive to TR, becoming more pronounced with longer TR. In our work with multiple-section 2DFT imaging, this factor steered us toward sequential, short TR acquisitions and away from section-interleaved, long TR acquisitions, which have superior S/N. Other properties of the acquisition method may also influence artifacts. For example, the spiral acquisition method has greater sampling density at the origin in k-space, which effectively provides extra averaging of signal fluctuations at the important low spatial frequencies. Finally, the nature of the artifacts that result from data inconsistency is different for spiral trajectories than for 2DFT sampling. These inherent properties may make spiral trajectories robust to signal variations in much the same way that projection-reconstruction imaging was found to have low levels of motion artifacts (23).

We found that except for the nature and size of image artifacts, the area and degree of activation were similar on activation images generated with the two very different data acquisition methods. This is a strong indication that activation-related changes are not a function of imaging method, but rather are a function of the pulse sequence and image parameters such as resolution, S/N, and TE. Since S/N can be made nearly equal with different gradient-echo imaging methods over a fixed imaging interval, the choice of imaging method can be made with regard to issues such as artifacts and number of sections that are desired in a given imaging interval.

Activation in the prefrontal cortex was imaged with the spiral k-space technique by using a verbal fluency task. Of particular note is that this study was performed with a conventional clinical MR imager and involved a pre-education that did not require shimming of the main magnetic field. The percentage change in signal intensity was consistent with other reported results of func-

**Figure 6.** S/N for a fixed imaging interval in a gradient-echo sequence plotted as a function of TR. This plot assumes that imaging is performed with excitation at the Ernst angle, the T1 of the tissue of interest is 1200 msec (gray matter), and that the length of the data acquisition window, the voxel size, and overall imaging time remain constant.
ational MR imaging in an active language task (32). The area demonstrating activation was also consistent with those in other studies involving verbal tasks in which both PET and functional MR imaging were used. We were unable to duplicate this success with conventional MR imaging because of the high level of artifacts.

In summary, imaging of cortical activation was demonstrated in the primary visual cortex, primary motor cortex, and prefrontal cortex with spiral k-space imaging. Like conventional MR imaging, the spiral k-space method can achieve high resolution and can be implemented with a standard clinical MR imager. Compared with conventional 2DFT imaging, a measure of artifacts—the standard deviation of difference images with no expected activation-related changes—was found to be lower with spiral k-space imaging. The number of sections that could be simultaneously examined was also substantially larger with the spiral k-space method. As expected, the calculated area of activation and the percentage change in signal intensity were roughly the same with the two imaging methods, indicating that activation-related changes may be largely independent of imaging method and are probably more closely related to S/N and voxel dimensions.

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