



Functional MR Imaging at 3.0 T versus 1.5 T: A Practical Review

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- Signal-to-noise and contrast-to-noise ratio
Signal-to-noise ratio
Contrast-to-noise ratio
- Field tests: direct comparisons of 1.5 T and higher fields for functional imaging
Greater extent and strength of activation
Success stories of high-field MR imaging
- Potential gains and tradeoffs of high-field imaging

- Susceptibility artifacts*
- Imaging time*
- Acoustic noise*
- Specific absorption ratio*
- Statistical analysis and modeling*
- Clinical functional imaging
- Summary and discussion
- References

Since 1999, when 3.0 T MR imaging scanners were approved by the US Food and Drug Administration (FDA) for imaging studies of humans, the numbers of available devices has been rising steadily [1]. The main interest in higher magnetic fields stems from the fact that signal-to-noise ratio (SNR) increases with the field strength, allowing greater sensitivity to contrasts of interest, including functional blood oxygen level dependent (BOLD) contrasts, and higher spatial resolution. Although the availability of higher field scanners has driven new progress in functional neuroimaging, most studies are still performed on more widely available 1.5 T machines. A PubMed search in June 2005 revealed a ratio of 180 to 970 functional MR imaging studies conducted on 3.0 T and 1.5 T, respectively. This article reviews recent comparisons of research and clinical functional imaging for 1.5 T and 3.0 T, emphasizing advantages and disadvantages

of the two field strengths. The article also details technical issues associated with the field strength, including how theoretically anticipated improvements associated with high field strength can be offset by practical considerations.

The main physical reason for going to higher field strength in anatomical MR imaging is the increased SNR, which can be beneficial in itself or traded against decreased imaging time or voxel size. As more experience is gained in functional MR imaging at 3.0 T and higher, however, it turns out that there are also rather complex physiological dependencies that are much less obvious and cannot be assessed easily by physical laws. The dynamic contrast-to-noise ratio (CNR) of the BOLD effect, which is from a statistical point of view more important than SNR in functional magnetic resonance imaging (fMRI) experiments, may depend on the part of the brain imaged, the functional paradigm,

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the local tissue microstructure, the local magnetic field distortions, the local and surrounding blood vessel distribution, scanner noise, chemical shifts, and other influences that each have the potential to interact with field strength. In surveying the literature of direct comparisons of 1.5 T with 3.0 T and higher fields, the authors found that it is virtually impossible to clearly separate out the effects of field strength alone. The fact that scanner hardware and pulse sequences have improved over time and that 3.0 T scanners have on average more advanced hardware than 1.5 T scanners contribute to the complexity of this topic. Yet, from many carefully conducted fMRI experiments, there are an increasing number of experimental findings that can be attributed mainly to effects of field strength.

The purpose of this article is to review some of the main results and, rather than provide definite answers, to give the neuroscientist a feel for how functional MRI depends on magnetic field strength. It concentrates on 1.5 T and 3.0 T fields, but also includes some important results obtained on 4.0 T magnets. Since MRI techniques, as well as FDA and International Electrotechnical Commission (IEC) standards, differ profoundly for higher fields, fields larger than 4.0 T are not covered. Before reviewing some field studies, the authors describe the concepts of SNR and CNR with focus on BOLD-dependent fMRI. Then, potential gains and trade-offs of imaging at high fields are discussed, and, finally, the emerging application of clinical functional imaging is reviewed.

Signal-to-noise and contrast-to-noise ratio

Greater SNR and CNR are the main motivations for scanning at higher field strengths. Whereas SNR is only slightly tissue-dependent, CNR depends on the tissue properties and is the more important quantity with respect to detecting functional activations in the brain. For these reasons, each quantity is described separately.

Signal-to-noise ratio

The SNR typically is used to compare imaging hardware and data acquisition methods. Roughly, it is defined as the mean signal divided by the standard deviation of the noise. Sometimes correction factors are used to account for the fact that the noise distribution is non-Gaussian. Signal and noise usually are measured by comparing signal from different regions of interest, for example mean tissue signal versus the standard deviation of the background signal in areas that are not affected by ghosting. Another way to measure SNR is to acquire two consecutive images and subtract the intensities afterwards. The SNR then can be

computed from a single region of interest and applied to one of the images and the difference image. An overview about the different ways to measure SNR is given by McRobbie and colleagues [2].

The noise components are background noise, generated by the scanner, coil noise, motion-related noise, physiologic noise, partial volume effects, flow artifacts, and physical errors caused, for example, by a nonequilibrium average spin state at the beginning of an fMRI sequence. Central to fMRI, however, is the SNR of the time series data of single voxels and the stability of the signal over time.

fMRI is more susceptible to noise than many other neuroscience methodologies, because the random variation of the BOLD activation can reach or exceed the level of the signal even in a blocked design [3]. In high-field MR imaging, the physical equipment and coil noise become less important relative to physiological noise, the latter one depending on signal strength itself. Furthermore, in fMRI one is interested in the BOLD signal and contrast, which are not accessible by phantom studies. Therefore, many phantom studies provide only limited information about fMRI relevant noise [3]. Parrish and colleagues [4] provide a recipe to compute the necessary minimum SNR to detect functional activations in dependence of given relative signal change, significance (t value or correlation coefficient), and power of the test. As an example, for a typical blocked design paradigm with 5% error probability and 95% detection rate or power, and expected 2% BOLD signal change, the required minimum SNR is about 34.

The dependence of SNR on magnetic field strength has two physical contributions, the signal from the receiver coil and the signal from the nuclear spin system. When only noise generated by the coil is considered, the dependence on the field strength B_0 is $\text{SNR} \sim B_0^{7/4}$ [5,6]. This contribution is not dominant in high-field imaging, however, because the patient resistance is much greater than the coil resistance. In high fields, the following consideration dominates the coil noise contribution. The signal intensity is both proportional to the number of excited spins and the voltage induced by each spin. For imaging at body temperature, both the number of excited spins and the induced voltage are proportional to the magnetic field. This results in a quadratic signal intensity dependency on the magnetic field. When all noise comes from a phantom sample, noise is proportional to the magnetic field. From this it follows that a doubling of field strength causes a doubling of SNR [7,8].

On the other hand, BOLD-fMRI is based on susceptibility effects of deoxygenized hemoglobin, which are also more prominent in higher fields

and may cause a larger expected signal change [9]. Taking this into account, one would expect an even more increased SNR if the relaxation times T_1 , T_2 , and T_2^* are assumed to be constant.

In practice, however, the relaxation times change. T_1 increases, and T_2 and T_2^* decrease with field strength. For example, T_1 increases with field strength about 30% for 3.0 T versus 1.5 T, and for spin echo experiments, the relaxation rate $1/T_2$ depends in a quadratic way on the field strength [10]. Krüger and colleagues [11] gave a recent overview about these dependencies and performed a thorough quantitative comparison between 1.5 T and 3.0 T fMRI of the brain. For this kind of quantitative comparison, it is important that echo time (TE) is adjusted to the corresponding T_2^* values in gray matter at 1.5 T and 3.0 T, or, if other values are preferable to maximize the signal, that the ratios of TE to T_2^* for both field strengths are kept equal. Also, the Ernst angle is affected, and thus the optimal flip angle should be scaled accordingly [11–14]. Typical values in cortical gray matter are [11] $T_2^* = 65$ milliseconds and 49 milliseconds for 1.5 T and 3.0 T, respectively, suggesting imaging parameters of TE = 40 milliseconds and 30 milliseconds, and $\alpha = 67^\circ$ and 64° , respectively. For BOLD imaging, one should adjust the imaging parameters to the values for gray matter only. Fera and colleagues [15] present a thorough study in which TE was varied over a broad range in functional imaging experiments, confirming a decreased optimum TE at 3.0 T.

Contrast-to-noise ratio

In functional MR imaging, CNR usually refers to time series properties of voxel intensities rather than to the comparison of intensity in different regions of interest as in anatomical MR imaging. To make a clear distinction, it is sometimes called functional or dynamical CNR, or even functional SNR. An overview about functional CNR, including the design of studies to optimize it, is given by Huettel and colleagues [16]. Because there are few comparative studies of functional imaging using cerebral blood flow changes or diffusion, this article only focuses on the most widely used BOLD effect. The BOLD contrast relies on the interplay between cerebral blood flow, cerebral metabolic rate of oxygen, and blood volume, among other parameters [9,17–22].

A useful quantity is the maximal functional CNR for fully relaxed BOLD imaging [8], $\Delta S/N$. It can be computed from measurements of the apparent transverse relaxation rates of the baseline and the activated states. The BOLD contrast $\Delta S/N$ depends on the strength of the main magnetic field. This is because the bulk magnetic susceptibility difference

between blood containing paramagnetic deoxy-hemoglobin and surrounding diamagnetic tissue increases with the main magnetic field strength, creating larger MR signal changes between baseline and activated states. There are many physiological factors that may influence the functional CNR, and the optimal field strength for performing fMRI experiments has been a matter of some debate [23,24].

Numerous studies have reported a higher CNR in fMRI studies performed at higher field strengths [11,15,25–27]. For example, in optimized gradient echo imaging experiments at 0.5 T, 1.5 T, and 4.0 T, Gati and colleagues [8] found that on the one hand the SNR increased linearly with field strength, whereas there was a complex relationship of functional CNR with tissue structure [17]. The maximally calculated BOLD contrast increased less than linearly in voxels containing vessels larger than the voxel itself and greater than linearly in voxels containing a mixture of capillaries and draining veins or venules with a diameter less than that of the voxel. The latter is the more relevant contrast for fMRI, given the desirability of tissue BOLD response for an accurate localization of brain function. Similarly, Ugurbil and colleagues [28,29] found, by comparing human brain scans at 1.5 T and 4.0 T, that the higher field provides increased contribution from the venules and the capillaries, which again favors fMRI at higher fields. This result is also in agreement with early studies from Menon and colleagues [30] at 4.0 T.

Krüger and colleagues [11] also found a tissue dependence of the gain in CNR, again for the benefit of functional imaging. CNR in venous vessels increased sublinearly with field strength, but CNR in activated areas increased 2.2-fold, again outperforming the theoretical results obtained under pure physical considerations. Looking alone at functional CNR and extrapolating these results, one could conclude that for the highest spatial or temporal resolution, one should operate at the highest available magnetic field strength. In one of the earliest of these studies by Turner and colleagues [25], it was found that in and primary visual cortex, image contrast over time was 7% at 1.5 T and 28% at 4.0 T during photic stimulation. It was concluded that this superproportional increase is because of an increased importance of susceptibility differences between deoxygenated and oxygenated blood. This result was later questioned by Krüger and colleagues [11] who related it partly to using coils with different spatial sensitivities. This points toward a general difficulty in direct comparisons of CNR and SNR. There are few studies where all imaging and technical parameters besides the field strength are kept constant. Nevertheless, it is worth

examining direct comparisons of functional activations at different field strength, which is covered in the next section.

Field tests: direct comparisons of 1.5 T and higher fields for functional imaging

Numerous groups have studied the relative benefits of functional imaging at different field strengths by directly comparing the results from typical experiments on two different MR systems. These studies provide the most straightforward data regarding the relative benefits of different field strengths for functional neuroimaging, and suggest real advantages for higher field strengths in terms of the extent and strength of activation observed, and the spatial resolution that can be achieved.

Greater extent and strength of activation

Two measures of the relative sensitivity of a functional mapping experiment are the voxel-wise significance of activation and mean cluster size of activated voxels during tasks that engage specific brain regions. In such experiments, activity throughout the brain specifically associated with stimulation in a particular sensory modality (eg, seeing patterns or listening to sounds) or engaging in a particular motor or cognitive task (eg, finger tapping or rehearsing strings of digits) is determined by inferential statistical tests. When the site of neural activity is established by existing research (eg, activity in primary motor cortex should be related to finger tapping), the strength and extent of activation reflect the sensitivity of the instrument to this neural activity.

If greater SNR at higher fields is traded for greater spatial resolution, it seems odd to state that a larger extent of activation is indicative of greater sensitivity. However, one also must consider the influence of local autocorrelation. Activity observed in fMRI tends to reflect responses in relatively large regions, and there is a tendency for adjacent neurons to have correlated firing patterns. Thus, to some degree, extent and strength of activation as measured by the value of inferential tests necessarily are related. A more sensitive instrument will give higher values for a statistical test for the same real correlation. Thus, peak activations will have higher values, but lower levels of activity in surrounding tissue that may be subthreshold at one field strength will cross statistical thresholds at higher field strength.

The results of direct comparisons at different field strengths generally have shown increased sensitivity at higher field strengths. For example, in a simple finger tapping task, Yang and colleagues [26] found that average cluster size of activated voxels was

70% larger, and average t score was 20% greater in a 4.0 T experiment as compared with 1.5 T experiment. Fera and colleagues [15] found, again in a finger tapping task, that the number of pixels and t score values were 59% and 18% higher, respectively, at 3.0 T than at 1.5 T, an improvement that was much lower than the observed 100% to 110% increase in SNR at 3.0 T. What makes this study unique is that the authors varied TE over a broad range. They also varied the receiver bandwidth and found that it affected the BOLD sensitivity only marginally. This result is interesting, because the receiver bandwidth directly determines the expected image SNR.

The main advantage of the finger tapping task is the reliability and strength of activity in motor cortex associated with finger movements. In the Yang and colleagues study, extent and strength of activation were determined by examining the BOLD response within a predefined anatomical region. Most cognitive neuroscience research involves less neatly circumscribed anatomical regions, however, and a more relevant measure of sensitivity is the extent and strength of typical activations in whole-brain analyses.

To this end, Krüger and colleagues [11] examined responses to a simple visual stimulation paradigm and a timed finger tapping task using whole-brain analysis techniques more typical of cognitive neuroscience research. They found an increase in the number of activated voxels between comparable 1.5 T and 3.0 T systems of 36 to 44% in the primary motor and visual cortices, respectively. More specifically, they discovered that the gain in functional SNR depends on whether the images are acquired in a fully relaxed way or, as more realistic for functional imaging, with a shorter repetition time (TR). Between 1.5 T and 3.0 T the average gain in the brain was only 1.7 in the fully relaxed condition but 2.2 in images with a realistic TR of 1.5 seconds. They explain this finding with the fact that the physiological noise depends on signal strength and becomes a larger fraction of the total noise at 3.0 T. The ratio of physiological noise against thermal plus systematic noise is about 0.67 in 1.5 T and 1.14 in 3.0 T. To deal with this, the signal strength and the fraction of physiological noise on the total image noise can be manipulated by varying the flip angle. Generally, T1 increases in higher fields, and saturation effects in functional sequences counteract the gain in SNR for sequences with TR much smaller than T1.

Krasnow and colleagues [31] used a suite of tasks involving visual processing, working memory, and emotional processing. In the visual task, which consisted of flashing checkerboards, they found an increase in the number of active voxels in striate

and extrastriate regions of visual cortex. Okada and colleagues [32] showed similar results in an anatomically defined region of interest in calcarine sulcus. As these regions are known from numerous neuroimaging and neurophysiological studies to be engaged by a wide range of visual stimuli, the increased extent of activation at higher field strength is taken to be evidence of a more accurate representation of functional activity. In the working memory task, greater extent and higher Z scores were observed throughout a broad network of regions known from previous neuroimaging research to play a role in working memory, including frontal, parietal, and cerebellar cortices. Results for the emotion processing task did not differ between the two field strengths.

Hoenig and colleagues [27] compared activity in a series of tasks typical of cognitive neuroscience research at 1.5 T and 3.0 T. They focused on the motor decision component of three disparate tasks: lexical decision, semantic decision, and letter identification. Their tasks were designed so that half of all responses would be made with the left and right hands. Common areas of activation across tasks requiring a motor decision (relative to a verbal fluency baseline) and between field strengths were SFG and M1. They found that the overall mean cluster size in motor decision paradigms was 60% to 80% higher, and t scores for peak activations were 30% higher at 3.0 T [11]. Some novel regions of activity also were observed at higher field strength.

There are few studies directly addressing the payoff of sensitivity and specificity, for example by looking at receiver operating characteristic (ROC) curves. In a preliminary multi-institutional study of the reproducibility of fMRI, Zou and colleagues [33] found that field strengths of both 3.0 T and 4.0 T were better than 1.5 T, yielding more activation and less variability in terms of sensitivity and specificity. Sensitivity was defined as the true activation fraction of activated voxels, whereas specificity was defined as the true nonactivation fraction of nonactivated voxels. For example, at 3.0 T, the mean sensitivity per subject ranged 0.58 to 0.76, while the mean specificity ranged 0.99 to 1.00. At 1.5 T, however, the mean sensitivity only ranged from 0.42 to 0.69, while the mean specificity ranged from 0.95 to 1.00. In other words, at 1.5 T, one not only detects less activation, but the activation that is detected is less reliable. These differences may look small, but for hypothesis testing and in view of type I errors, a specificity of 0.95 is much worse than a specificity of 0.99. The ROC curves demonstrated moderate to high classification accuracy, which was generally higher at 3.0 T and 4.0 T than at 1.5 T.

A discussion of statistical aspects would be incomplete without mentioning experiments concerning the reproducibility of activations. In a comparative study of visual activations, Miki and colleagues [34] found that activation of the visual cortex was observed in all subjects, and activation of lateral geniculate nucleus also was detected in four of the five subjects. The ratio of overlapping activated voxels in the first and second acquisition was 0.81. The authors concluded that reproducibility of visual activation using fMRI at 4.0 T is acceptable, and the results from 4.0 T scanners show reliability similar to those at 1.5 T. A similar reproducibility study, using a finger opposition task, has been performed by Tegeler and colleagues [35].

Success stories of high-field MR imaging

Thus far studies have been considered in which high field strength enhanced the ability to observe activity readily observable at lower field strengths. A main consequence of an increased SNR and CNR at higher fields is that the image resolution can also be increased. SNR of a single voxel is proportional to its volume; thus, a doubled SNR means that the voxel volume can be half as large without losing sensitivity. The partial volume effect, meaning that the signal in a voxel constitutes a mixture of signals from different tissue types, like gray and white matter or different cortical columns, is decreasing accordingly.

The increased sensitivity, and particularly the spatial resolution available with higher field strengths, enables researchers to observe novel phenomena [22]. For example, in their battery of motor decision tasks, Hoenig and colleagues [27] found several areas activated only in 3.0 T but not in 1.5 T. Specifically, activity in supplementary motor area (SMA), which seems to play a role in motor-related decision making was found only at higher field strength. In addition to its greater sensitivity, the higher spatial resolution possible at high fields opens up the possibility of observing functional activity at the level of hyper-columns or potentially single columns of neurons, providing the possibility of observing activity of functional units on a scale more compatible with how the brain is thought to be organized.

Maldjian and colleagues [36] could identify the sensory somatotopic organization of individual digits using sensory stimulated fMRI at 4.0 T. They took advantage of the increased SNR at 4.0 T; previous attempts to recover the well-known fact of a somatosensory organization at 1.5 T showed only limited success.

Numerous groups have reported functional imaging of human ocular dominance columns at 4.0 T

[37,38]. Cheng and colleagues [37] used a combination of a 4.0 T scanner and small surface coil to obtain very high (less than 0.5 mm) resolution, and they were able to resolve the differential responses to left or right eye stimulation in the V1 area, which agreed with postmortem cytochrome oxidase studies.

These seminal papers were the first to show the feasibility of fMRI at the cortical columnar resolution, and it seems that this is only possible at high fields. Liu and colleagues [39] were able to identify patches of V1 preferentially sensitive to one or the other eye on 1.5 T, albeit on a much lower resolution than what would be necessary for resolving cortical columns. The high spatial resolution available at higher fields also has enabled investigation of the lateral geniculate nucleus, in thalamus, from its topographic organization [40] to its specific response properties and modulation by attention [41,42]. Further accomplishments of fMRI at higher fields, like single-trial fMRI, which avoids averaging of signals with its associated information loss, are given by Ugurbil and colleagues [22].

The studies reviewed here lead to a strong conclusion. Both the number of activated voxels and the sensitivity increase consistently with the field strength, and hard-to-detect functional parcellations of the cortex can be detected more easily in higher fields. The following section explores the physical and technical considerations that pose limits on the relative benefit of higher-field scanning, and considers some new techniques that may allow practitioners to take fuller advantage of the potential gains.

Potential gains and tradeoffs of high-field imaging

There are further aspects that should be considered when comparing fMRI at different field strengths. Some of them like imaging time can be traded against each other or against SNR, whereas others like acoustic noise, cannot.

Susceptibility artifacts

Susceptibility artifacts result from abrupt changes in magnetic susceptibility that occur across tissue–air and tissue–bone interfaces, for example the air-filled sinuses and the brain parenchyma [43]. These artifacts give rise to geometric and intensity distortions, and intravoxel signal dephasing, and therefore, signal dropout. In higher fields, the effected brain regions spread out and suffer from stronger intravoxel dephasing or even a total signal loss, in particular for long TE [11]. Signal dropout is more serious for gradient echo planar

imaging (EPI), as used for fMRI, than for spin echo EPI.

There is one study so far that compares the extent of these artifacts in a region of strong signal dropout onto fMRI sensitivity at 1.5 T and 3.0 T [31], concentrating on the amygdala. It was found that susceptibility induced signal dropout was slightly larger at 3.0 T (12%) versus 1.5 T (9%).

There are different methods to overcome high-field intravoxel decoherence in EPI imaging. Some require new pulse sequences or come at the cost of increased scan time, like *z* shimming [44–47], spiral sequences [48], and radiofrequency (RF) pulse excitation with nonlinear phase responses [49–52]. Others are based on simply optimizing prescription parameters. Sorensen [53] reports very good results by simply decreasing the slice thickness to decrease the voxel size. Chen and colleagues [3] optimize signal by using optimal voxel sizes and slice orientations for 1.5 T and 3.0 T. Slice orientation can be optimized by first measuring the dominant susceptibility field gradient in the region of interest (eg, the amygdala) and then by choosing the frequency encoding direction parallel to the field gradient measured from each subject.

Spiral-in/out data acquisitions [48] showed superior performance with respect to signal dropout in a recent comparison for 1.5 T and 3.0 T imaging [54]. The spiral-in/out sequence acquires one image before the echo time and a second image after the echo time. Weighted averaging of the two images then provides a time series with reduced susceptibility dropout in frontal and medial temporal regions and increased SNR in regions of uniform cortex. Another way to reduce these artifacts is multi-shot EPI. As was found by Menon and colleagues [55], multi-shot EPI improves BOLD fMRI at high magnetic field strengths.

Geometric distortions can be reduced by multi-shot EPI, by field map approaches [56–59], or by reversed gradient methods [60–65] for signal acquisition. In the reversed gradient method, phase encoding gradients are applied twice, at the second time with reversed polarity. In functional imaging, by alternating gradients in each repetition, this can be accomplished without elongating the sampling interval. Fig. 1 demonstrates the latter approach.

The performance of many of the methods, however, depend on the specific region of the brain to which they were optimized, and the full potential of these methods for fMRI in the whole brain has not been explored and represents an active field of research [67].

Imaging time

One theoretical advantage of higher field strength is that acquisition times can be shorter in 3.0 T com-



Fig. 1. Reversed gradients to reduce geometric distortions at 3.0 T. Application of the reversed gradient method to reduce susceptibility induced geometric distortions at 3.0 T to EPI images of the brain (A–D). (A) An EPI image with parameters set to enhance distortion for demonstration purposes. (B) Same with reversed gradients. (C) The combined image. (D) Anatomical control image. Application of the reversed gradient method to reduce susceptibility induced distortions at 3.0 T to EPI images of the brain in a preliminary study of a functional sequence [66] without and with alternating gradients (E, F, respectively). For this slice, only in the reversed gradient method imaging sequence were ipsilateral right-hand- finger-tapping task activations detected in the cerebellum (F).

pared with 1.5 T. Theoretically, as Takahashi and colleagues [68,69] argue, because SNR doubles in the higher field and increases with the square root of the number of averaged images, the imaging time to get the same SNR at 3.0 T should be only a quarter of the time needed at 1.5 T. One could ask whether acquiring a larger number of images to increase the SNR and CNR in 1.5 T would provide an advantage equivalent to doubling field strength. However, turning this argument around, one can see that this is not a feasible strategy.

In practice, imaging time is determined primarily by the longitudinal relaxation time T_1 of the tissue (which increases in 3.0 T, as mentioned before), because in many applications, a single acquisition is sufficient. For example, Duewell and colleagues [70] compared T_1 and T_2 values in anatomical scans of the knee at 1.5 T and 4.0 T, and found that, depending on tissue, the T_1 values increased up to 56%. T_2 values were 10% to 20% shorter in all tissues, but did not affect image contrast. The longer T_1 relaxation time at higher fields should be accounted for by using a longer TR to achieve the same CNR [27]. This would impair the temporal resolution during data acquisition, however. If TR is kept fixed, the repetition time becomes relatively shorter (as compared with T_1), penalizing the BOLD sensitivity at 3.0 T. In fMRI, the repetition rate is determined mostly by T_1 (and the flip angle), diminishing these advantages in scan time. Thus, the theoretical value of a quarter scan time is not achieved, and in practice the gain in SNR often is used to get a better resolution and only slightly reduced scan time [71].

Acoustic noise

The acoustic noise generated by Lorentz forces on the gradient coils because of rapid gradient switching increases with magnetic field strength. This problem is most severe for EPI-based imaging as

used in fMRI. Ravicz and colleagues [72] performed acoustic noise measurements at 1.5 T and 3.0 T for EPI sequences, and found that the high-field scanner produces significantly louder noise (an increase in 15 dB), mainly attributable to the EPI readout gradients. This can hamper imaging with auditory stimuli considerably, as the authors' own experience with experiments on speech perception shows. Using a clustered spiral sequence in a study of eight subjects, the authors found only weak activation of Heschl's gyrus (A1) for a simple speech versus silence contrast [Fig. 2]. These results agree with data from Gaab and colleagues (submitted for publication), who only observed activity in primary auditory cortex when a very sparse imaging protocol with one volume every 12 seconds was used. In a continuous scanning condition, no activity was observed in this region, although other auditory areas did show activity relative to silent baseline for complex sounds.

Aside from passive noise attenuation, there are other means to reduce the influence of scanner noise. In a study of attentional modulation of the human auditory cortex at 1.5 T, Petkov and colleagues [73] had success with masking the scanner noise with white noise at a sound pressure level that subjectively matched the scanner noise. It is believed that in this way the frequency scatter of loud sounds can be attenuated.

Another way is to reduce the noise at the source before it is produced. There are currently two main approaches now: the design of silent gradients and the switching off of EPI gradients. For the former, there have been numerous reports demonstrating the use of smoothed gradient waveforms to eliminate higher harmonics that are produced by trapezoid waveforms (eg, the SIMEX pulse sequence [74]). In the latter possibility, called ISSS (interleaved silent steady state), the EPI readout gradients are switched off during the silent period, but the

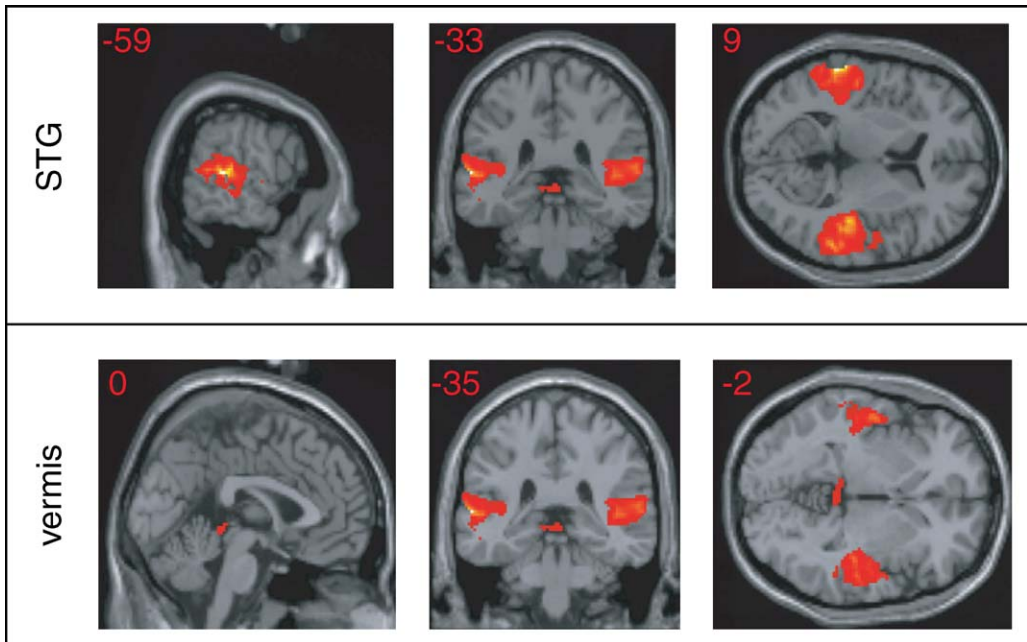


Fig. 2. Speech—silence activations. Areas of greater activation for speech than silence, measured for eight subjects at 3.0 T. Note the lack of activity in Heschl's gyrus (*top*), likely the result of stimulation by the acoustic noise of the scanner. *Abbreviation:* STG, superior temporal gyrus. (From Zevin JD, McCandliss BD. Dishabituation of the BOLD response to speech sounds. *Behav Brain Funct* 2005;1(1):4; with permission.)

silent RF excitation pulses are kept unchanged to maintain longitudinal magnetization equilibrium [75]. This method was found to be a promising alternative to sparse imaging, in which data acquisition is preceded by a silent interval without EPI readout trains or RF pulses, during which the auditory stimuli are presented, and there are neither EPI readout trains nor RF pulses [76].

Specific absorption ratio

Because the specific absorption ratio (SAR) of the RF field scales with the square of field strength, RF deposition is more limiting at higher fields [77]. With advanced scanner technology and pulse sequence design, however, SAR limits place only minor restrictions on, for example, the number of sections that can be acquired in one scan. The higher SAR, however, may limit the straightforward applicability of sequences designed for 1.5 T, and there is a learning curve one needs to navigate [78]. Overall, SAR considerations do not impose much of a practical constraint on fMRI, because EPI has inherently low SAR compared with spin echo sequences.

Statistical analysis and modeling

Although not directly field dependent, the statistical processing of functional MR imaging data

becomes more and more refined, and one may believe that improved statistical tools may compensate somewhat for imaging at lower field strengths. The general trend is to take more prior knowledge about the signal to be expected into account, thus increasing the sensitivity of statistical tests for BOLD activation. An improved statistical analysis may be able to overcome the limitations of a lower magnetic field to some degree. One prominent approach is the general linear model [79–81], which takes account, for example, of a known hemodynamic response function and time delays, and can integrate other nuisance factors, such as the influence of breathing, in a quite flexible way.

The general linear model can be refined by using other concepts like an improved smoothing of the signal for a more accurate estimation of cluster shape [82,83] (Tabelow and colleagues, submitted for publication, 2006), or unknown hemodynamic delays [84]. BOLD modeling, and, therefore, statistical significance of activation may be improving by a better understanding of the BOLD effect and other effects related to neuronal activity. For example, a phenomenon called the initial dip was used to increase spatial resolution of functional activation effectively [85]; this was used in monkey studies at 4.7 T [86]. The reason for the failure to detect the initial dip in some studies with field

strengths of 1.5 T or lower may be that low-field measurements are not sufficiently sensitive to deoxyhemoglobin concentration changes in cortical capillaries [87].

No matter how much statistical processing and modeling of the BOLD effect improves, however, the limitations in SNR and CNR in lower magnetic fields are unlikely to be completely overcome. Because any averaging of signal causes a loss of information, and neuroscientists are striving for an ever higher resolution, the authors believe that imaging at higher fields will open new possibilities. This process may not end before the smallest length scales of capillary blood flow are reached, if not even new markers of neuronal activity emerge.

Clinical functional imaging

fMRI is becoming a routine tool in clinical applications like presurgical planning [88] or neuropsychologic evaluation. Presurgical fMRI can be used to localize motor, sensory, and language-control areas [89], and it has been used to study cerebral reorganization in tumor patients [90]. In presurgical planning of tumor resection [91–93], it is important to have a high test power to avoid false-positive (in particular in the lesion) and false-negative (in particular outside the lesion) activations. False-negative activations (ie, there is no activation visible at locations where it should be) are of particular concern in brain tumor resection.

Because of the clinical circumstances, usually simple-to-understand and strong activation paradigms are used, such as finger tapping, word rhyming, or picture naming. Motion, fatigue, and degree of cooperation may play a more significant role in patients than in normal volunteers participating in well-controlled neuroscience studies. These circumstances sometimes even render the detection of activated areas in simple and strong activation paradigms difficult. This is even more serious as the sensitivity of fMRI measurement directly affects the detectability and reproducibility of the activation area, which will affect clinical decisions strongly. Nakai and colleagues [94] performed a comparative study between 1.5 T and 3.0 T using a sequential finger tapping paradigm in healthy volunteers. They found that the detectability of the premotor area, the supplementary motor area, and the ipsilateral sensorimotor area showed significant improvement at 3.0 T, whereas detectability of the contralateral sensorimotor area was about equal. The authors, however, point out the adverse effect of susceptibility distortions, in particular at 3.0 T. Nevertheless, they conclude that fMRI at 3.0 T has greater potential for detecting neuronal activation as a functional network, and emphasize

that the difference in detectability between different motor areas, which is dependent on the field strength, must be taken into account when considering the application of fMRI for surgical planning or evaluation of neurological symptoms.

The evaluation of functional activations relies on the overlay onto anatomical images and can be only as good as the anatomical images. For this reason, decisions about scanning patients at 1.5 or 3.0 T cannot be considered on the basis of functional imaging quality alone. Magnetic field inhomogeneity induced distortions are greater for higher fields, rendering a coregistration of EPI-based functional images to the anatomy more difficult or imprecise. There is another drawback of high-field imaging; it has been observed frequently that the white/gray matter contrast in 3.0 T is diminished considerably compared with 1.5 T. The reason is because at 3.0 T, the relaxation rates of gray and white matter become more similar. This is a non-negligible drawback, in particular for neuroscience studies that involve quantification of the anatomy as well, for example, volumetric studies where automated segmentations of brain compartments are performed. Another point to consider is the chemical shift artifact. At 3.0 T, it doubles in size and needs to be corrected by means that can considerably decrease SNR. Shapiro and colleagues [71], however, mention that in practice and with advanced technology, this issue is only of minor importance.

On the other hand, pathologic abnormalities often can be detected better at higher fields. For example, Keiper and colleagues [95] conducted a detailed comparison of the detection of white matter abnormalities in multiple sclerosis and found a clear superiority in the detection rate at 4.0 T versus 1.5 T. Nobauer and colleagues [96] report a significant increase of contrast between brain tumors and surrounding tissue in 3.0 T compared with 1.5 T, for two different anatomical sequences [1].

To summarize, in clinical fMRI there are certain drawbacks and pitfalls that arise, in particular in anatomical imaging. Many of these drawbacks have been overcome recently by a better design of pulse sequences and hardware [77]. Taking this aspect into account, one can conclude that clinical fMRI at 3.0 T is advantageous over scanning at 1.5 T.

Summary and discussion

Functional BOLD imaging depends in a complex way on the main magnetic field strength. Neither the signal intensity nor the signal extent depend in a direct way on the field strength. Rather, many issues affecting experiments at different field

Table 1: Summary of advantages and disadvantages of functional MR imaging at 1.5 and 3.0 T

Property	1.5 T	3.0 T
SNR	–	+
Dynamical CNR	–	+
White/gray matter CNR	+	–
Extent of activation	–	+
Strength of activation	–	+
Resolution	–	+
Imaging time	–	+
Susceptibility artifacts	+	–
Chemical shift artifact	+	–
Specific absorption ratio	+	–
Acoustic noise	+	–

The table should not be read in a too dogmatic way, because some disadvantages at 3.0 T can or could be overcome in the future or already are compensated for by technical improvements, such as stronger gradient systems in 3.0 T magnets.

+ = advantageous.

– = disadvantageous.

strengths have to be taken into account. There are direct factors, like signal-to-noise and BOLD contrast-to-noise ratios, and more indirect factors like altered relaxation rates and artifacts, and very indirect factors, like the effects of acoustic noise on an auditory experiment, or the generally more advanced technology available for newer 3.0 T scanners. Table 1 summarizes the main results as obtained by various authors.

There is, however, one general advantage of higher fields dominating the consideration: the increased signal-to-noise and functional contrast-to-noise ratios. At higher field strength, the BOLD effect is more pronounced in capillary tissue, closer to the expected true functional activity, and relatively more suppressed in venous tissue. This fact favors 3.0 T fMRI beyond what is expected based on purely physical considerations. As MR imaging techniques develop, other problems may be solved in the future like the correction for susceptibility induced artifacts and the acoustic noise problem. Another rather pragmatic point is that few MR imaging devices are used solely for functional imaging, meaning that their purchase often has to be justified by clinical usage. In addition to the clear advantages for functional imaging, there are some clinical anatomical advantages as well, such as rendering some tumor and white matter abnormalities. Taking everything together, the authors believe it can only be beneficial to concentrate future research activities on functional imaging at 3.0 T or higher fields.

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