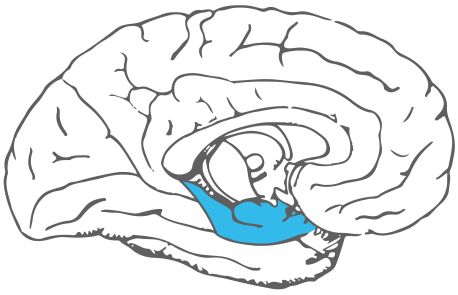
Functional imaging of the human medial temporal lobe

A neuroscientist's guide to fMRI pulse sequence optimization

Matthias Nau
Kavli Institute for Systems Neuroscience
Centre for Neural Computation, NTNU, Trondheim, Norway
Email: matthias.nau@ntnu.no

May 15, 2020



Abstract

Functional magnetic resonance imaging of the medial temporal lobe is difficult due to its proximity to air cavities and distance to the MRI head coil. This guide discusses these challenges and recommends prodecures to optimize echo-planar imaging sequences and improve data quality.

Contents

OSF - http://doi.org/10.17605/osf.io/cqn4z

1 Why this guide and for whom is it?

Functional magnetic resonance imaging (fMRI) measures human brain activity non-invasively and is a 'workhorse' technique in cognitive neuroscience. One intensively studied region is the medial temporal lobe (MTL). It comprises the hippocampus, amygdala, entorhinal cortex and perirhinal cortex, and supports a wide range of perceptual and mnemonic functions. Unfortunately, it is also among the regions most difficult to image with fMRI. Its anteroventral parts are especially subject to strong distortions, signal loss and low temporal signal-to-noise ratios (tSNR) and it requires special dedication and care to get a good signal. This guide provides tips and tricks about optimizing gradient-echo echo-planar (EPI) sequences for studies of the MTL and discusses how the individual sequence parameters affect data quality. With this, I hope to help future generations of students to get the most of their precious scanning time, and that it triggers discussions from which I hope to learn myself. This simply is the guide I wish existed when setting up new EPI-sequences in the group of Christian F. Doeller.

I am not an MR-physicist, and this guide is not for MR-physicists, it is for those biology, psychology & medical students that are about to start an fMRI-study, with only limited understanding of pulse sequences and data quality measures. The lessons learned here build on many hours of scanning, quality checks, online searches and reading. The conclusion is perhaps little surprising, but it is an important one: There is no free lunch! An 'all-round carefree' sequence does not exist and improving the data on one end, often affects it at another.

If you want to study hippocampal subfields, a small voxel size is important. If you want to analyze the global connectivity of the amygdala, a big field of view (FOV) could help. Often you cannot have both and your choice influences other factors such as tSNR or artifacts. Thinking about your requirements carefully before scanning, and understanding how your choice of sequence affects the data, will greatly benefit your study later on.

I adapt and update this guide from time to time. If you have suggestions or comments, but especially if you disagree with anything, please approach me.

2 Background learning material

This guide assumes that you have a basic understanding of the key terms and parameters of an MRI pulse sequence. If the terms 'TR & TE', 'slice package' or 'multiband' do not mean anything to you, there are some great books [1, 2] and online resources that will get you started. If you want to look up a term, here is an MRI Glossary by Savoy and Jovicich. I highly recommend checking out the amazing online blogs that are around (e.g. practicalfmri.blogspot.com, mriquestions.com, technicalfmri.blogspot.com to mention a few). Also, Remi Gau made a great list of online learning material. If you are interested in MRI of the hippocampus, its subfields and the MTL in general, check out the Hippocampal Subfields Group, who work on a harmonized segmentation protocol for hippocampal and parahippocampal subregions [3].

3 Why is the medial temporal lobe so difficult to image?

There are at least three major problems in gradient-echo echo-planar imaging (EPI) that are not unique to, but often most severe in the MTL.

Distortions
MRI localizes voxels based on their resonance frequency. In an ideal world, the static B0-field of an MRI-scanner is the same for all voxels and does not affect this frequency. In reality, the B0-field is not perfectly homogeneous and some voxels' B0 deviates from the one used to calibrate the RF-pulse exciting these voxels. If so, the voxels resonate at the 'wrong' frequency and will ultimately be mislocalized [4, 5]. This is called a susceptibility artifact and it gets more pronounced at the boundaries between air and tissue where the field is most inhomogeneous. Unfortunately, just below the MTL there are big air cavities, which make it very sensitive to distortions [6].

Signal loss
Another susceptibility artifact is signal loss or 'drop out'. If the B0-field is inhomogeneous, it varies not only across voxels, but also within a voxel, causing it to resonate at many frequencies. This can lead to phase-interference when reading the signal from that voxel, ultimately resulting in the signal being lost. This is also called 'voxel dephasing'. Again due to its proximity to air cavities, the MTL is often strongly affected by such signal loss [6, 7].

Low temporal signal-to-noise ratio (tSNR)
The mean signal intensity of a voxel divided by its temporal standard deviation is *the* currency for any type of fMRI study. As discussed below, there are various ways of reducing distortions and signal loss, unfortunately many of them penalize tSNR (as well as the related contrast-to-noise ratio [8]). Sequences optimized for the MTL typically seek to reduce susceptibility artifacts, often leading to low tSNR values and lower statistical power.

4 Exploring pulse sequence parameters

Let's look at sequence parameters and some hardware options and how they affect the three problems introduced above. Please note that I refer to gradient-echo echo-planar imaging (GRE-EPI) at 3T by default (but see section 7 for a comparison to ultrahigh-field fMRI).

Slice package

Three things are important here: field of view, spatial resolution and tilt. The bigger your field of view and the more voxels are in it, the longer it will take to acquire each volume. For whole-cerebrum (wc) coverage, not including the cerebellum, usually a slice package of at least 200×200×130 mm is necessary to accommodate most participants.

I typically aim at having relatively short TRs (∼1000 ms) to resolve fast events and to increase the number of volumes per event to get a good estimation of the hemodynamic response function (HRF) [9, 10]. Without multi-slice imaging (multiband (MB)/simultaneous multislice (SMS)) and with wc-coverage, this would require the voxels to be quite large (>3.5mm). MB/SMS reduces the TR drastically by acquiring multiple slices simultaneously, allowing you to shrink the voxel size to around 2 mm and still get wc-coverage. To resolve hippocampal subfields, you want a voxel size no bigger than 1.5 mm isotropic (also see the 'in-plane resolution' section below). In that case, you will probably need to sacrifice coverage and focus your field of view on the MTL directly or have a long TR. Always add >2-3 slices below the MTL to not have it at the edge of the slice package.

Once you defined your slice package, you need to choose its orientation relative to the participant's head. Importantly, distortions occur mostly along the phase-encoding direction. The slice tilt defines your phase-encoding direction relative to the head, which in turn affects susceptibility artifacts. Optimizing tilt can hence greatly affect your data quality [7, 11]. A positive slice tilt (Fig. 1), that is the anterior edge of the slice points towards the chest [7], aligns your slices parallel to the MTL (e.g. along the hippocampal long axis).

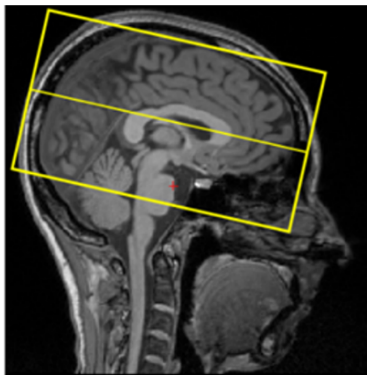


Figure 1: Positive slice tilt

If you choose a positive tilt (Fig. 1), use an anterior to posterior (A>>P) phase-encoding, as this has been shown to reduce susceptibility artifacts and improve MTL BOLD sensitivity (Fig. 2, [7], also see [11, 12]). Avoid the oral cavities here and do not tilt the slices more than ∼40°. Otherwise you will most likely cut off the nose and risk a strong phase wrapping artifact, meaning that the nose wraps around to the back of the head, potentially occluding parts of the occipital or parietal lobe. For the same reason you generally do not want the object you are scanning to be larger than your field of view. Knowing this, do you see a problem in Fig.1?

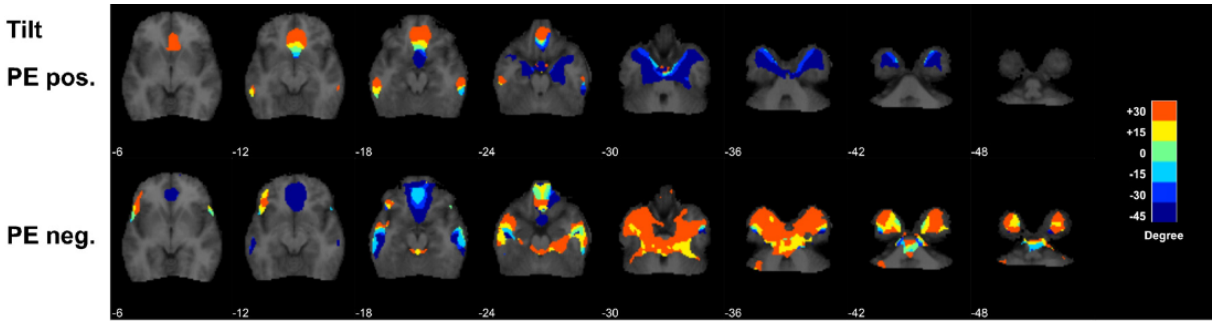


Figure 2: Optimal tilt and phase encoding direction at 3T. For the MTL, a positive tilt is best for anterior to posterior (A>>P) phase-encoding. PE pos. and PE neg. denotes positive (P>>A) and negative (A>>P) phase encoding direction. Colors denote the optimal slice package tilt in degrees. Figure adapted from [7].

By scanning only one pilot participant with several slice tilts, you will learn a lot about your sequence. It is also a great example of how optimizing a simple parameter can improve your data substantially. Keep in mind however that optimizing tilt for the MTL can lead to stronger distortions in other areas such as the ventromedial prefrontal lobe (Fig. 2). A promising direction to reduce costly piloting are recently proposed automated EPI-optimization methods [13]. They use previously acquired field maps to simulate and minimize the effect of e.g. gradient polarity and slice tilt on susceptibilty artifacts. This does not (yet) generalize across scanners, but you could re-purpose field maps (>30) for this your group has acquired in previous studies to make future piloting more efficient.

Echo time (TE)

Keep the TE short, but not too short. Typically, the longer your TE is, the stronger the susceptibility artifacts will be. To shorten the TE, you could increase the bandwidth (which penalizes tSNR) or use parallel imaging such as GRAPPA, ARC or SENSE [12, 14, 15] at moderate acceleration (∼2-fold) [16]. If the TE is too short however, i.e. the echo occurs earlier than ∼15-20ms after excitation, the T2 signal did not have time to decay much before it is read out. This leads to a suboptimal signal amplitude and ultimately low tSNR. The sensitivity to BOLD is maximal when the TE equals the T2*-decay time constant, which differs across regions [17].

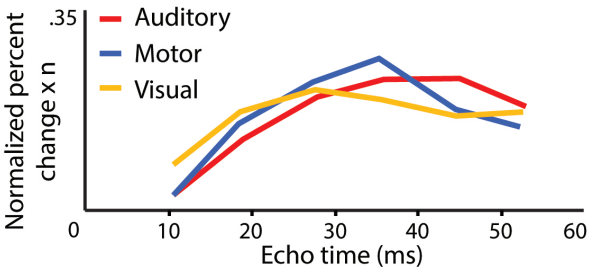


Figure 3: The effect of echo time (TE) on BOLD sensitivity. The optimal TE differs across regions (depicted are the auditory-, motor- and visual cortex). Data from [17].

The T2* decay is slower for cortical grey matter (∼66ms) than for deeper gray matter, such as the putamen (∼31ms) [18]. Others report the optimal TE to be 25-30 ms in visual cortex and 35-40 ms in auditory and motor cortices (Fig. 3) [17]. The optimal TE might also vary across the lifespan. If you scan infants for example, longer TE's are better [19]. Importantly, if you scan elderly participants such as patients with Alzheimer's disease, be aware that some regions in the brain accumulate iron across the lifetime [20]. Iron induces voxel dephasing and signal loss, complicating the comparison of BOLD effects between young and old. Keep this in mind when checking data quality. Optimize your TE for the elderly, even if you additionally scan a group of younger participants.

To me, TE's of around 25 ms seem to be a good compromise between distortions and sensitivity for studies of the MTL in a typical (student) population. You might end up scanning a TE that does not maximize the tSNR fully, but your data will be less distorted. In many cases, this is still worth considering, simply because a region of interest (ROI) with lower tSNR is still better than an ROI that misses most voxels entirely due to distortions and drop-out (also see chapter 'Quality assessment and artifacts'). If you do not see strong distortions in your data, you could afford taking a longer TE (∼30-35 ms).

Importantly, while parallel imaging like GRAPPA does reduce the TE and distortions, it also comes at a cost. It is quite sensitive to head motion occurring during the reference scan in the beginning and it decreases SNR. If you use GRAPPA, a super simple life-hack to reduce head movements is to attach medical tape on both sides of the head coil and across the participant's forehead after placing the cushioning but before putting on the front piece. This gives participants gentle feedback about their own movements, many of which are not aware that they moved. It reduces movements during scanning to some degree at basically no cost (but not comparable to head cast or bite bar solutions). Amazingly, there is a paper about this now [21]. Side note: Always check your ROIs overlaid on the functional images, not on the structural T1 scan.

A potential alternative to GRAPPA for reducing the TE is partial Fourier imaging (pF). It reduces acquisition time by recording only parts of k-space and relying on the k-space symmetry to reconstruct the rest. Because this reconstruction is not perfect however, this introduces

additional spatial smoothness and even increases drop out. In my hands, it did not improve MTL-signal quality and clearly worsened dropout. Read more about pF here.

Repetition time (TR) and multi-slice imaging

Multi-slice imaging MB/SMS enables to sample multiple slices simultaneously, which greatly accelerates your acquisition. But how much can you accelerate? As mentioned above, pulse sequences with short TR's produce more images, providing a better HRF-estimation, and often lead to higher statistical power [9, 10]. After testing many settings for the cmrr-multiband- and the Siemens SMS-package in combination with other factors such as GRAPPA, I recommend what Siemens and others had recommended anyway. Do not accelerate more than 6-fold overall! If you do not need a super short TR, accelerate less ($\leq$4-fold). Keep in mind that this might depend on the type of head coil you use (I refer to the Siemens 32-channel head coil) and that MB/SMS and IPAT/GRAPPA interact. With wc-coverage and a decent in-plane resolution this still gives you a TR between 1-1.5 s. Notably, there are amazing fMRI studies with ultrashort TR's of below 100 ms, these however usually use only very few slices and examine high-tSNR regions (e.g. [22]). Even with a long TR you can resolve quite fast events (with enough data) [23].

Importantly, MB/SMS can lead to two problems. The first one is noise amplification [24], an increase in the temporal standard deviation of a voxel. This problem becomes stronger with distance to the head coil, making the MTL particularly vulnerable. The second problem is an artifact called slice-leakage [24, 25]. Here, the signal of one slice leaks into other simultaneously acquired slices (Fig. 4), leading to false positive activations across the brain [13,14]. This is critical because your nice cluster in hippocampus might actually originate somewhere else. To quantify this problem in your data, you could compute the 'L-factor', a metric that quantifies slice leakage [25, 26].

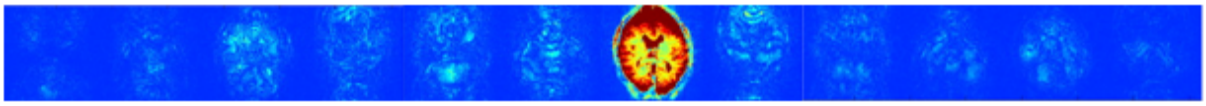


Figure 4: Slice leakage. Depicted are 12 simultaneously acquired slices (MB/SMS = 12). For very high multiband accelerations, you risk leakage of the signal of one slice into all other simultaneously acquired slices [25]. Color code depicts the L-factor, the fractional signal cross-contamination per slice. Figure adapted from [10].

Higher acceleration factors lead to more false positive activations [27]. You can reduce this problem drastically by using the Split Slice-GRAPPA image reconstruction technique [28, 24]. I did not yet compare these different reconstruction methods, but the benefit is obvious (Fig. 5).

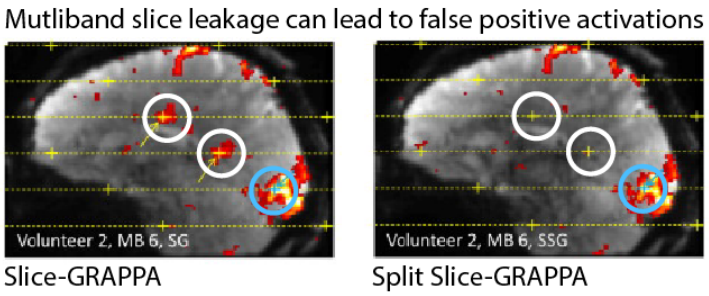


Figure 5: Mutlislice imaging (mutliband/SMS) can lead to false positive activations due to slice leakage. The signal of one slice (blue circle) leaks into other slices that were simultaneously acquired (yellow lines), leading to false positive activations (white circles). Split Slice-GRAPPA reconstruction reduces this problem [28]. Figure adapted from [27].

Generally, if you use MB/SMS with an interleaved acquisition, make sure the number of slices divided by the MB/SMS factor equals an odd number (Fig. 6). For example, 10 slices and SMS = 2 (10/2 = 5) is better than 12 slices and SMS = 2 (12/2 = 6). If it is an even number, the slice groups can interfere with each other and create artifacts.

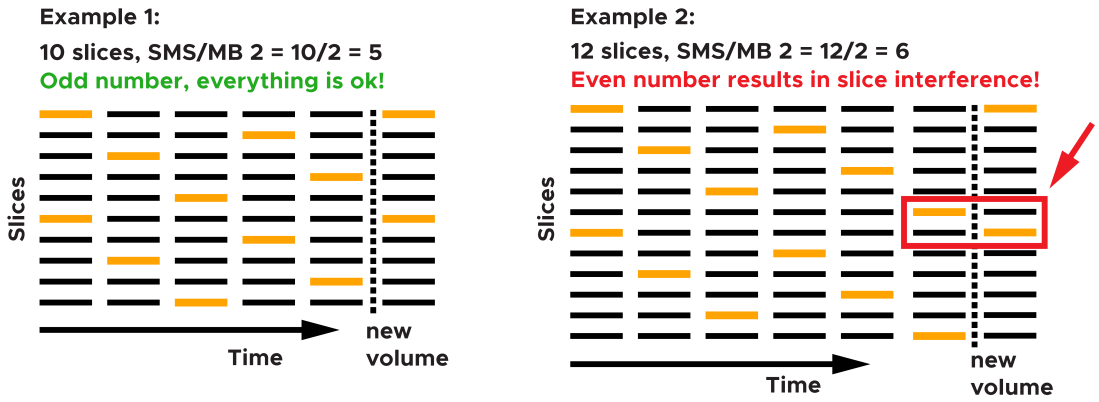
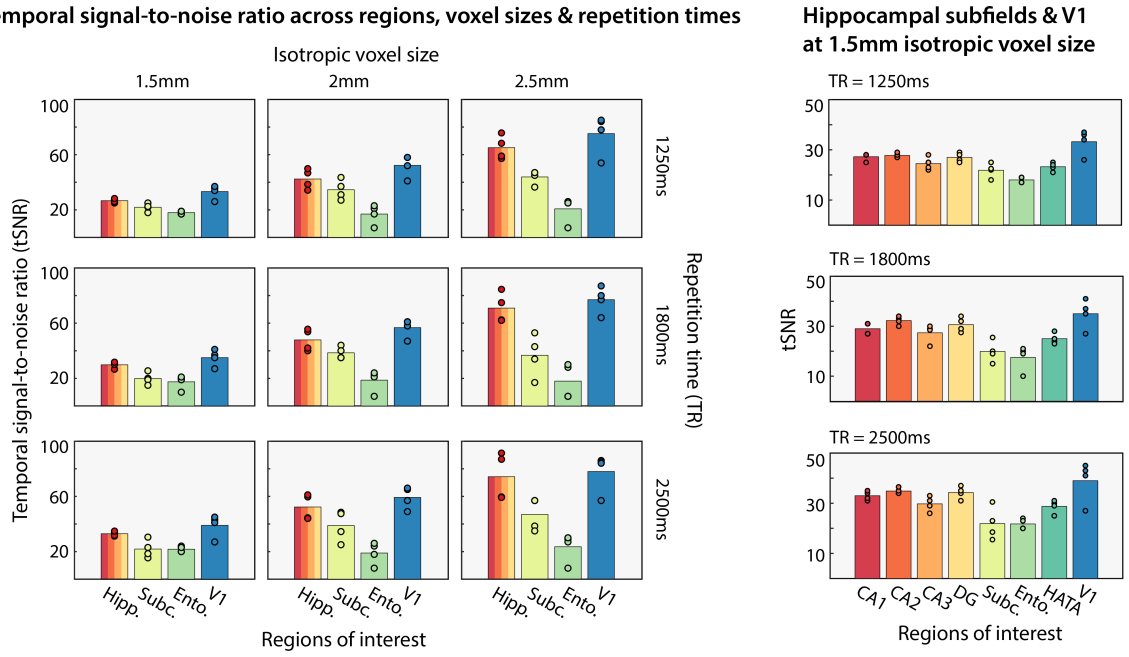


Figure 6: Number of slices divided by the MB/SMS factor must equal an odd number for interleaved acquisition.

Side note: when you adjust the TR of your sequence, do not forget to adjust the flip angle as well. The optimal angle is called 'Ernst angle' and can be calculated here: mritoolbox.com/ErnstAngle. Small deviations from the Ernst Angle are ok, but aim to get it as close as possible since your signal intensity depends on it. If your desired flip angle cannot be reached with the pulse you defined, which is called 'RF-clipping', try to increase the pulse duration (which might unfortunately also increase your TR).

In-plane resolution

Increasing in-plane spatial resolution can decrease voxel-wise tSNR and increases the readout time. Longer readout time in turn leads to stronger distortions. If you require a voxel size smaller than ∼1.5mm at 3T, you will most likely have to sacrifice coverage/field of view to keep the readout time short. With 2-2.5mm voxels however you get enough voxels to perform multivariate analyses in areas such as the entorhinal cortex or hippocampus (>200 voxels), while still covering the entire cerebrum at a short TR. In theory, larger voxels should lead to higher tSNR because more signal is averaged and noise is reduced. This is true for most areas, specifically if the B0-field is homogenous. However, since drop out occurs due to inhomogeneity in the B0 within a voxel, increasing the voxel size can actually lead to more phase-interference in regions with B0-field inhomogeneity, resulting in stronger signal loss and hence lower average tSNR and amplitude in an ROI (see for example the entorhinal cortex in Fig. 7). In the MTL, larger voxels do therefore not automatically lead to higher tSNR. In fact, if you have strong signal loss in your data, reducing the voxel size can help to recover the signal by increasing in-plane resolution or decreasing slice thickness.



3T-MRI Skyra, 32ch. headcoil. 2D-EPI, MB = 4, TE = 26ms, pF = 7/8, positive tilt, viewing task, ~7min each. Data realigned & slice-time-corrected, Juelich ROIs: Hippocampus (CA1,2,3,DG), subicular complex, entorhinal cortex, hippocampus-amygdala-transition area (HATA) & early visual cortex (V1)

Figure 7: tSNR of MTL-regions and V1 at 3 voxel sizes and 3 TRs. Four participants performed a viewing task for 7minutes per protocol. Flip angles were aligned to the Ernst angle. In most regions, tSNR increased with increasing voxel size and (slightly) with TR. In entorhinal cortex, individual voxels gain tSNR with increasing voxel size, but drop out is increased and counteracts a net-gain on ROI level. Note that all sequences shown here use partial Fourier imaging, which I do not recommend using for the MTL, and that preprocessing (e.g. unwarping, smoothing and denoising) can further boost tSNR drastically.

Interestingly, smoothing high resolution data improves the tSNR more than acquiring larger voxels (Fig. 8). In my hands, smoothing 1.5mm data of V1 with a kernel of 2.5mm led to 1.3x higher tSNR than acquiring the same data with a 2.5mm voxel size. This effect is even stronger in regions sensitive to dephasing such as the entorhinal cortex, in which smoothing led to an impressive 2.9x higher tSNR than acquiring the data at a lower (smoothing-kernel-equivalent) resolution. If you see strong drop out in your MTL data, try to decrease your voxel size.

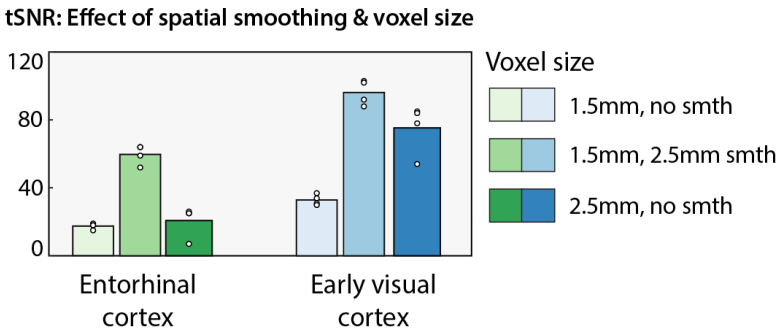


Figure 8: Effect of smoothing and voxel size on tSNR. Smoothing high-resolution data leads to higher ROI-average tSNR than acquiring larger but smoothing-equivalent voxels. This effect is especially strong in regions that are sensitive to dephasing such as the entorhinal cortex. Same data (n = 4 participants) as in Fig. 7

Bandwidth

While the term can mean two things, the transmitter bandwidth and the receiver bandwidth, by default it describes the latter. The receiver bandwidth refers to the range of frequencies that are read-out per pixel in the 2D-slice plane (e.g. 1500hz/pixel). It basically describes with how many 'bits' the signal is recorded. Increasing the bandwidth reduces distortions and drop out (even around metal parts) and allows for shorter TE's and TR's. It however also increases the amount of noise that is recorded, in turn leading to a decrease in tSNR. Therefore, keep the bandwidth low for the first pilot sequence and try to reduce susceptibility artifacts by other means (e.g. moderate GRAPPA acceleration to shorten the TE, optimizing the slice tilt, unwarp your data...). If you are still not happy with the result, then start increasing the bandwidth. Side note: the transmitter-bandwidth defines the slice thickness (broader spectrum means more protons resonate). To find an excellent overview by J. Graessner about bandwidth [29] please click here.

Head coil

In addition to the sequence parameters discussed above, there are also hardware factors to be considered. An important one is your choice of head coil. The more coil elements in a head coil, the smaller each individual element is. The size of a coil element, determines its depth sensitivity, with larger coils receiving signals from deeper structures in the brain. The 32-channel head coil provides a good compromise between spatial resolution and tSNR in deep structures like the MTL. Notably, if a voxel size of >3 mm is sufficient for your study, it can be better to use

a 20- or 12-channel head coil since the mean signal amplitude in deeper structures tends to be higher than with 32-channels [30]. However, only change to fewer channels if it does not cost you tSNR, which is typically higher on head coils with more channels [31](Fig. 9). This is true also for deep structures like the cerebellum, for which tSNR has been reported to increase by 40 percent on the 32- compared to the 12-channel head coil [30]. Since other factors such as e.g. voxel size play a more important role for tSNR (Fig. 9, [31]), I suggest to use the 32-channel head coil for your pilot scans and, once you have a favorite sequence, test it on the 12-, 20- or 64-channel head coil as well. Click here to find a nice blog-article related to this.

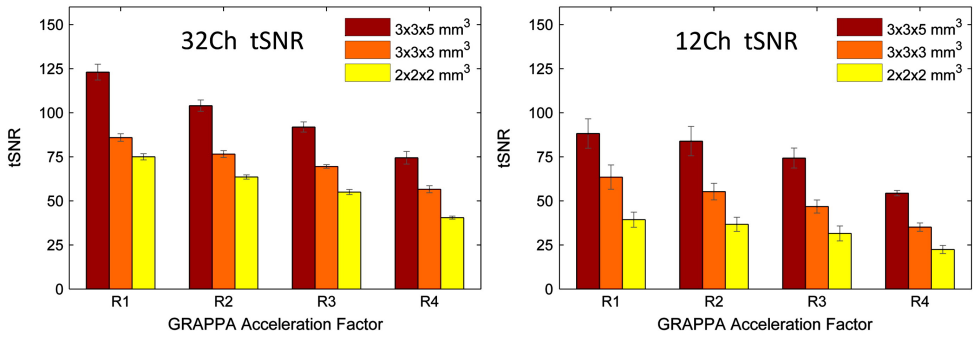


Figure 9: tSNR (average across several gray matter ROIs) as a function of head coil (12-channel vs. 32-channel), voxel size and GRAPPA acceleration factor. tSNR increases with voxel size and number of head coil channels, but decreases with increasing GRAPPA factor. Figure adapted from [31]

Shimming

When you place an object in a magnetic field it will induce inhomogeneities in that field. This happens also when you put a participant in the scanner. Shimming describes a set of techniques to compensate for these inhomogeneities. There are several different types of shimming. First, most of modern scanners automatically adjust the current in dedicated coils at the beginning of each scan session to minimize above effects. The shim protocol the scanner uses depends on the tissue type. This is why you specify the tissue type before scanning e.g. by setting the tissue type to 'brain'. If you want to ensure that one area in particular is being shimmed well, you can define a shim box: a local 3D-cube ROI to be placed around the MTL. The currents in the coils will then adjust to be optimal not for the entire brain but for this region in particular. The brain can be quite asymmetric for some people. If you use a shim box, make sure that both hemispheres of the MTL are fully included. Use a localizer scan with multiple slices to be sure. Finally, a technique called z-shimming adds an additional shimming pulse to your sequence, which can be used in combination with your 'real' images to recover lost signal [7, 11]. Due to the added pulse however z-shimming makes your sequence slower. Never scan without shimming. If you can, use a shim box. If you can afford a slower image acuisition, a moderate z-shim pulse can work well for you.

5 Quality assessment and MR-artifacts

Once you have a few different pilot sequences, you want to know how well they perform. Find below how to do a simple quality assessment. This does not replace proper control checks of the scanner by experts, but it will give you a quick idea of performance.

- Scan each of your sequence settings with the same pilot subject(s) for about 10 minutes (same duration, not the same number of TR's). Acquire a structural T1 scan. Ideally, you want a participant with a big head to be sure everybody else will fit too.
- Preprocess these data the same way you would preprocess your final data. At the very least, realign your images, create a meanEPI and tSNR image and coregister everything to the T1. Segment the T1 to get grey- and white matter masks as well as a global in-brain mask.
- Overlay your meanEPI on the T1 and/or the gray matter mask on the meanEPI (e.g. using itk-SNAP). Naturally, you want these images to overlap as much as possible. In reality, it will never be perfect. Search for mismatches between the meanEPI and the T1. If you find any, zoom in and double-check if there is grey matter still (but distorted) or if it is lost (drop out). Definitely zoom in on the MTL and check carefully. Distortions can be factored in on the ROI level, drop out cannot.
- Calculate the spatial signal-to-noise ratio (sSNR) for your ROIs using the meanEPI image. It is the average signal intensity of the ROI divided by the standard deviation of intensities across voxels. The higher sSNR, the better. By doing this, you can also identify areas that are partially affected by drop out (often those with very low sSNR).
- Coregister your favorite brain atlas to the T1 (e.g. the Juelich atlas) and compare the tSNR in a couple of regions across the brain as well as across sequences. The best sequence is the one for which the tSNR is highest and most similar across regions. The tSNR determines your minimal effect size and the minimal scan duration to detect it [32], so make sure your sequence and study design allow you to detect your expected effects (Fig. 10).
- Many software packages classify voxels using a voxel intensity cut-off and segment the brain based on the distribution of intensities across voxels. While tSNR is more critical than absolute amplitude for fMRI, make sure you do not lose voxels in the MTL only because they do not surpass the amplitude threshold of the software you plan to use (a common problem for entorhinal cortex for e.g. SPM defaults).
- Search through the meanEPI and the tSNR image and look for artifacts (Fig. 11). You will find a list of the common ones below, along with some tips on how to deal with them.

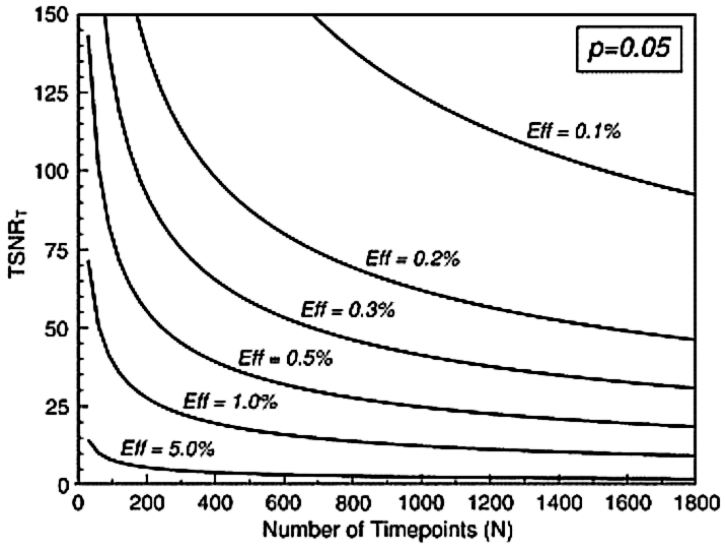


Figure 10: The tSNR and the scan duration determine the minimal effect size (Eff) you can expect to find. Depicted is the (theoretical) relationship between these factors for a liberal p-threshold (p = 0.05). Figure adapted from [32].

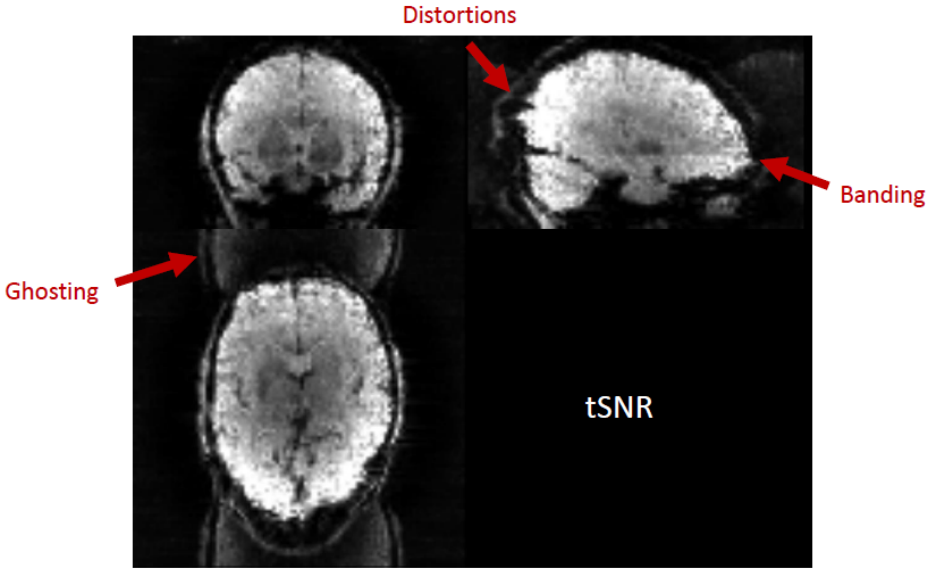


Figure 11: MR-artifacts. Depicted is the tSNR image of one participant for a poorly performing sequence, showing strong distortions, a strong Nyquist ghost and mutliband-banding

Distortions & drop out

Distortions and drop out and the influence of different sequence parameters are discussed throughout the guide. In short, to reduce distortions, try lowering the TE and/or the in-plane resolution and optimize the slice tilt first. Applying a moderate z-shim gradient pre-pulse can also recover tissue affected by distortions and drop out [7, 11].

Moreover, always try to correct distortions during the preprocessing, for example via the widely supported B0-field map correction. It requires you to perform an additional scan for each participant, but it is quick and all major fMRI software packages support it ('Unwarping' in SPM, 'FUGUE' in FSL...). Since distortions mainly follow the phase-encoding direction with a magnitude that depends on the TE, this method utilizes the voxel shift at two different TE's to reconstruct where the voxel must have been at a hypothetical TE = 0.

While the approach above is still the most widely used one, there are better options around. For example, rather scan a few extra volumes with your own functional sequence (∼1 minute) but reverse the phase-encoding direction (e.g. P>>A instead of A>>P) [33, 34]. In these extra images, the distortions will fall into the opposite direction compared to your functional images of interest. Create one meanEPI for your actual data and one for these extra scans. Then, use the FSL-function 'TOPUP', AFNI's 3dQwarp with the '-plusminus' option or CMTK to compute and correct the distortions. Such reverse-gradient correction techniques tend to work better than a classical field map (Fig. 12) [35].

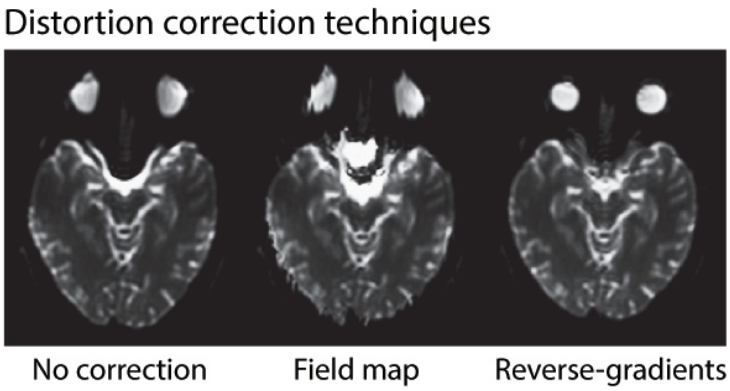


Figure 12: EPI-image distortions without correction (left), field map corrected (middle) and reverse-gradient corrected (right). Figure adapted from [35]

This guide focuses on gradient-echo sequences, which are still the most widely used sequences to date. They typically give you a stronger BOLD signal and higher acquisition speeds (shorter TR's) than spin-echo sequences. However, the latter have one advantage: spin-echo sequences are robust against voxel dephasing and are hence less prone to signal loss. For above-mentioned reasons, I nevertheless recommend piloting gradient-echo sequences first.

Nyquist ghost

In EPI, odd and even lines in k-space are sampled with opposite read gradients, making it necessary to reverse the direction of every other line before image reconstruction. Unfortunately, the two echoes with opposite gradient are sometimes not perfect mirror versions of each other and the timing of the switching gradients is not always perfect (because the machine is not). During image reconstruction, such timing differences can lead to errors in the estimated signal phase, ultimately resulting in a second image shifted/phase-offset relative to the main image [36, 37]. This is called the Nyquist- or N/2-ghost.

If you see ghosting in your meanEPI or the tSNR image, make sure it does not overlap with the brain. If so, this can severely confound your data, especially if participants move and the two overlaid images move relative to each other. As long as the ghost does not overlap with the brain, there are several methods to correct for it (e.g. [38] for recent work). Many of them require an additional calibration scan (for an overview and comparison see e.g. [39]). You can quantify the severity of ghosting using the ghost-to-signal ratio (GSR) and compare it across your epi-sequences. For each sequence, do the following steps.

- Mask 1: take the whole-brain mask (e.g. from the segmentation step).
- Mask 2: Circular-shift it by n/2-voxels along the phase encoding direction. Then, remove overlap with mask 1.
- Mask 3: Make an ROI for out-of-brain & out-of-ghost voxels
- Calculate mean intensities for these three masks across voxels and time
- GSR = (Mask 1 - Mask 3)/Mask 2 Ghosting often occurs when there are technical problems with the MR-scanner or the head coil. Ask your local support to double-check if the ghosting is severe.

Banding

Multiband/SMS imaging can lead to a surprisingly common artifact. It is visible as sudden intensity difference between slices and is often referred to as 'banding' (Fig. 11), see github-discussion here. In my experience, it is often times more pronounced in the tSNR image than in the meanEPI, so make sure to check those carefully. To reduce it, first try an 'ascending' or 'descending' slice order instead of 'interleaved'. If that does not help, increase the pulse duration (which will unfortunately lead to stronger drop out and longer TRs and TEs).

To be extended

6 One sequence to rule them all?

Many labs try to establish a standard sequence, which they trust and use for multiple studies. Having this sequence does make sense for similar study designs, if your task design or objectives differ, it clearly does not. Think about your own requirements carefully before scanning and adapt the sequence accordingly. This guide does not cover different task designs in detail, but as a start it can help to see what sequence parameters other studies have used. Below, you find the T2*-sequence parameters of a few studies examining MTL activity, taken from the published articles. For quick overview, I indicated the objectives and analyses with simplified tags.

3T-sequences:

- **Baldassano et al., 2017** [40]: Hidden-Markov model, movie watching, event-segmentation.
  TR = 1500 ms, TE = 28 ms, voxel size 3×3×4mm, flip angle 64, 27 slices, FOV 192×192 mm.

- **Bellmund et al., 2018** [41]: Multivariate, pre-post design, picture viewing.
  TR = 2270 ms, TE = 24 ms, flip angle = 85°, voxel size = 1.5×1.5×1.5mm, 40 slices, FOV = 210×210mm.

- **Brunec et al., 2018** [42]: Temporal autocorrelation analysis, virtual navigation.
  TR = 2000 ms, TE = 30 ms, voxel size = 3.5×3.5×5.0mm flip angle = 70 degrees, FOV = 200 mm. Base resolution = 64×64, 30 axial slices.

- **Constantinescu et al., 2016** [43]: Univariate, movie stimulus-outcome judgement.
  TR = 3000 ms, TE = 30 ms, flip angle = 87°, voxel size = 3×3×3mm. 45 slices. FOV = 192mm.

- **Córdova et al., 2019** [44]: Image viewing, relational attention task
  TR = 2000 ms, TE = 37 ms, voxel size 1.5×1.5×1.5mm, flip angle = 71°, 27 slices perpendicular to the hippocampal long-axis.

- **de Voogd et al., 2018** [45]: Univariate, 2-back-task /w & /wo eye movements.
  TR = 2200 ms, TE = 9.4, 21, 33, 44 and 56 ms (multi-echo), GRAPPA factor = 3; flip angle, 90°; slice matrix size, 64×64; slice thickness: 3.0 mm; slice gap: 0.51 mm; FOV: 212×212 mm; bandwidth: 2604 Hz/px; echo spacing: 0.49 ms, 35 axial slices, 1.5T.

- **Dimsdale-Zucker et al., 2018** [46]: Multivariate, object-recognition, HPC subfields.
  TR = 2010 ms, TE = 25 ms, multiband factor = 2, voxel size = 1.5×1.5×1.5mm. Field of view = 216 mm, image matrix = 144×152, flip angle = 79°, bandwidth = 1240 Hx/pixel, partial phase Fourier = 6/8, parallel imaging = GRAPPA factor 2 with 36 reference lines, 52 slices.

- **Garvert et al., 2017** [47]: Repetition suppression, stimulus detection & memory task.
  TR = 3010 ms, TE = 70ms, voxel size = 3×3×2mm, 1mm gap, 43 slices tilted by 30° relative to the rostro-caudal axis and a local z-shim with a moment of -0.4 mT/m ms was applied to the orbitofrontal cortex region.

- **Julian et al., 2018** [48]: Univariate, eye movements.
  TR = 1000 ms, TE = 25 ms; multiband factor = 4, voxel size = 2×2×2 mm; flip angle = 45°, FOV = 192°, matrix size = 96×96, 78 slices.

- **Kaplan and Friston, 2018** [49]: Univariate, memory-guided decision making.
  TR = 3360 ms, TE = 30 ms, voxel size 3×3×2mm, field of view, 64×72 mm, 48 slices tilted 45°.

- **Kim and Maguire, 2018** [50]: Repetition suppression, spatial & object memory task.
  TR = 3080 ms, TE = 30 ms, voxel size = 3×3×3mm, matrix size = 64×74, z-shim gradient moment of -0.4 mT/m ms, 44 transverse slices angled at -30°.

- **Kok and Turk-Browne, 2018** [51]: Inverted encoding, same-or-different detection task.
  TR = 1000 ms, TE = 32.6 ms, voxel size = 1.5×1.5×1.5 mm, multiband factor 6, flip angle = 55°, 60 slices, partial volume parallel to hippocampus.

- **Montchal et al., 2019** [52]: Univariate, video & image viewing, temporal judgment task
  TR = 2500 ms, TE = 26 ms, voxel size = 1.8×1.8×1.8mm, Flip angle = 70°, 33 slices acquired as a partial axial volume and without offset or angulation, FOV = 180×65.8×180mm.

- **Nau et al., 2018** [53]: Univariate, eye movements.
  TR = 1000 ms, TE = 34 ms, multiband factor = 6, voxel size = 2×2×2 mm, flip angle = 60°, FOV = 210×210 mm, 66 slices, base resolution 104×104.

- **Schuck and Niv, 2018** [23]: Multivariate/decoding, 1-back task /w rule-switching.
  TR = 3000 ms, TE = 27 ms, voxel size 2×2×2mm, flip angle = 80°, 53 slices, FOV = 192 mm, GRAPPA factor = 3, positive tilt = 30°.

- **Stangl et al., 2018** [54]: Univariate, virtual navigation.
  TR = 1500 ms, TE = 30 ms, voxel size = 2×2×2mm, 24 slices, FOV = 216 mm, flip angle = 80°.

- **Zeithamova et al., 2018** [55]: Multivariate, reward encoding task.
  TR = 2000 ms, TE = 31 ms, multiband factor = 3, voxel size 1.7×1.7×1.7mm, flip angle = 73°, GRAPPA Factor = 2, base resolution: 128×128, 72 slices.

7 Comparison: 3T vs. 7T fMRI

Ultrahigh-field (UHF) scanning is not fundamentally different from scanning at lower field strength. Many of the challenges and recommendations are conceptually the same (for review see e.g. [56, 57, 58])). The main benefit of using a higher field strength is that your tSNR and observable BOLD signal increases compared to 3T, and so does statistical power [59]. In motor cortex for example, the relative BOLD signal change related to button presses has been shown to be ∼3% at 1.5T, ∼4% at 3T and ∼7% at 7T [60]. In rodents, scanning at 15.2T showed BOLD signal changes of ∼11% [61]. Because the effects observed in the MTL at 3T are typically much smaller than in motor cortex (often ∼0.5%), higher field strength has the potential of making so far infeasible task designs possible. In addition, at higher field strength, the contribution of small blood vessels to the observed BOLD signal is stronger, the one of larger vessels smaller than at 3T. In turn this leads to improved spatial specificity [62]. A great advantage over 3T

is that the increase in tSNR allows you to decrease the voxel size to scan at submillimeter resolution [63], resolve e.g. hippocampal subfields [64] and approximate cortical layers [65]. To give an idea of what you can expect, Fig. 13 depicts the tSNR across regions for one of our (preprocessed) task-based 7T data sets with 0.9mm isotropic voxels and a 3D-EPI sequence. In entorhinal cortex and hippocampus, we observed a tSNR of ∼25 and ∼40 respectively [66].

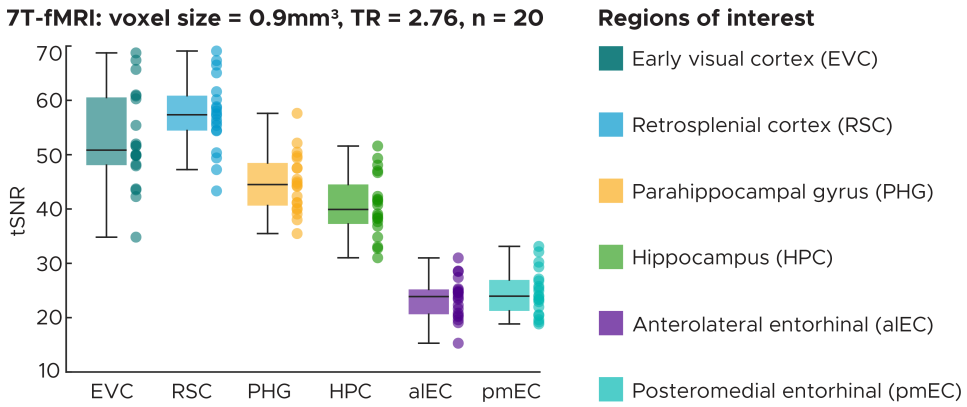


Figure 13: Temporal signal-to-noise ratio (tSNR) across regions at 7T-fMRI. Data from Navarro Schröder et al. 2015 [66]. Following 3D-pulse sequence [67] was used on a 32-channel head coil: voxel size = 0.9mm iso., TR = 2.76s. TE = 20ms, flip angle = 14°, PE-acceleration = 4, 3D acceleration = 2. Data were preprocessed (realigned, unwarped, smoothed with 2.7mm & ICA-denoised with FSL FIX). This figure should only help to give an idea of the ballpark of tSNR other studies report. Your tSNR depends on the scanner hardware, sequence and preprocessing.

However, not everything is better at higher field strength. As field strength increases, frequency offsets and field inhomogeneities get amplified, leading to stronger distortions on whole-brain level. These field inhomogeneities also amplify within-voxel dephasing, inducing stronger and larger signal loss [18]. Again, these problems are unfortunately especially severe in the MTL. Luckily, most of the strategies to reduce susceptibility artifacts still work, but they need even more careful adjustment and control. For the MTL, shim well [68] and keep the TE very short to reduce distortions and drop out as much as possible. This is not a problem at 7T because short TE's lead to stronger relative BOLD signal change at higher field strength than at lower field strength [60, 69]. You will see that on average most MTL studies therefore used shorter TE's at 7T (see below) compared to 3T (see above). Definitely pilot some TE's [e.g. 16, 20 & 24ms] to find the optimal one. If you can, use a multi-echo sequences and use it for signal denoising. This boosts tSNR especially at 7T drastically [69]. I would try to not use iPAT/GRAPPA acceleration due to its motion sensitivity, or with a maximal 2-fold acceleration. Be aware that a shorter TE unfortunately also reduces the sensitivity in well shimmed regions in the neocortex, but that is a price worth paying if you get a good MTL signal instead. Even more important than at 3T is the acquisition of reverse-gradient data or a field map for later unwarping. If you use the reverse-gradient method [34], make sure to sample enough images for each participant to obtain a stable meanEPI (>10). Many 7T facilities will also have dielectric pads: pillows filled with conductive materials, which help to homogenize the B0 field, boost the signal and reduce distortions. You can put them inside the head coil on the sides of the participants neck

(the closer to the MTL, the better). If you do, make your participants aware of potential local tissue heating. The specific absorption rate (SAR) becomes spatially more heterogeneous at higher field strength [58], meaning that some focal spots of tissue can absorb more energy than intended. Your head coil is designed to not exceed an internationally regulated SAR, but anecdotal evidence suggests that dielectric pads can amplify this problem. At 7T and above, many users want to scan at higher spatial resolution. Luckily, reducing the voxel size and slice thickness helps to reduce drop out because the within-voxel field inhomogeneities (and hence voxel dephasing) become less dominant. Especially at smaller voxel sizes (<1.5mm), a faster TR has been shown to increase task-based BOLD contrasts and decoding performance, interestingly despite a decrease in tSNR [70]. I did not test this for the MTL at 7T, but it should in principle hold true. Try it out! Start piloting a TR of ∼1.5-2s and try to keep the SMS/MB acceleration low (≤3-fold). With increasing field strength and smaller voxel size also physiological noise becomes more dominant. Make sure to acquire breathing and heart rate measures to later correct potential confounds (e.g. using the PhysIO Toolbox [71]) and perform even more conservative motion correction. As mentioned above, many of the challenges you will face are similar to a 3T-sequence, so keep sections 4 & 5 in mind. On a practical note: when designing your experiment, know that UHF studies often have strict limits on maximal scanning time. Below, you will again find T2*-EPI sequence parameters used in other 7T-studies examining MTL regions such as the entorhinal cortex, hippocampus and amygdala.

7T-sequences:

- **Hodgetts et al. 2017** [72]: Univariate, scene/face/object viewing task
  TR = 2000 ms, TE = 25 ms, voxel size 1.2×1.2×1.2mm, flip angle 90°, 30 slices, FOV 192×192 mm, bandwidth = 1562 Hz/px, echo spacing 0.72 ms, partial Fourier: 6/8, GRAPPA factor = 2.

- **Maass et al. 2015** [73]: Multivariate/decoding, visual associative memory task
  TR = 2000 ms, TE = 22 ms, voxel size 0.8×0.8×0.8mm, flip angle 90°, FOV 205×205 mm, bandwidth = 1028 Hz/px, echo spacing 1.1 ms, partial Fourier: 5/8.

- **Navarro Schröder et al., 2015** [66]:Univariate & connectivity, virtual navigation.
  TR = 2756 ms, TE = 20 ms, voxel size 0.9×0.9×0.92mm, flip angle 14°, 96 slices, FOV 210×210 mm, 3D-EPI, PE-acceleratio = 4, 3D acceleration = 2, 32-channels.

- **Shah et al. 2018** [74]: Functional connectivity analysis, resting-state.
  TR = 1000 ms, TE = 24 ms, voxel size 2×2×2mm, 64 slices, FOV 192×192 mm, MB/SMS = 4.

- **Sladky et al. 2018** [75]: Univariate, emotion discrimination & face viewing task
  TR = 1400s, TE = 23, voxel size 1.5×1.5×1mm, 78 slices, flip angle = 62°, 32-channel head coil.

- **Suthana et al. 2015** [76]: Univariate, visual associative memory task
  TR = 3000 ms, TE = 19 ms, voxel size 1×1×2mm, flip angle 90, 21 slices, FOV 200×200 mm, echo spacing 1.2 ms, GRAPPA factor = 3.

- **Theysohn et al., 2013** [77]: Univariate, visual associative memory task
  TR = 2050 ms, TE = 25 ms, voxel size 2.5×2.5×2mm, flip angle 70°, 50 slices, FOV 230×230 mm, bandwidth = 2090 Hz/px, echo spacing 0.56 ms, GRAPPA factor = 2, 8-channels.

8 Conclusion

I hope this guide helped you to better understand some of the sequence parameters and that you feel more confident in testing the impact of some of them on your data yourself. If you do, test these parameters within the same pilot participants before you start your study. There is no perfect sequence that will always give you what you want and the choice of parameters very much depends on your study objectives. Having said this, if I had to put my 3T-recommendation into a nutshell, this would be it:

Top priorities are avoiding drop out and maximizing tSNR. Keep the TR as short as possible without inducing artifacts. Do not MB/SMS-accelerate more than 6-fold. If you use GRAPPA, keep it low (2-fold). Keep the TE at around 25 ms. Use a voxel size of 2 mm isotropic or less. Use a positive slice tilt. Use the 32-channel head coil. Keep the bandwidth low. Correct distortions with the reverse-gradient method. Always check for artifacts.

Acknowledgements

I thank Joshua B. Julian and Tobias Navarro Schröder for joint sequence tests and along with Dörte Kuhrt and Ingrid F. Syversen for helpful comments on an earlier version of this guide. I thank Christian F. Doeller for his support as well as the Kavli Institute for Systems Neuroscience - Centre for Neural Computation for kindly sponsoring the figure permission fees. Thank you to everyone who commented on version 1 of this guide online and helped to make it better.

9 References

[1] Huettel S.A., Song A.W., and Sunderland G.M. (2015) Functional Magnetic Resonance Imaging. Third Edition. Q. Rev. Biol. 90, 455-455

[2] Poldrack R.A., Mumford J.A. and Nichols T.E. (2011) Handbook of Functional MRI Data Analysis. Cambridge University Press.

[3] Wisse, L.E.M. et al. (2017) A harmonized segmentation protocol for hippocampal and parahippocampal subregions: Why do we need one and what are the key goals? Hippocampus 27, 3-11

[4] Jezzard, P. and Clare, S. (1999) Sources of distortion in functional MRI data. Hum. Brain Mapp. 8, 80-85

[5] Farzaneh, F. et al. (1990) Analysis of T2 limitations and off-resonance effects on spatial resolution and artifacts in echo-planar imaging. Magn. Reson. Med. 14, 123-139

[6] Olman, C.A. et al. (2009) Distortion and Signal Loss in Medial Temporal Lobe. PLoS ONE 4, e8160

[7] Weiskopf, N. et al. (2006) Optimal EPI parameters for reduction of susceptibility-induced BOLD sensitivity losses: A whole-brain analysis at 3 T and 1.5 T. NeuroImage 33, 493-504

[8] Welvaert, M. and Rosseel, Y. (2013) On the Definition of Signal-To-Noise Ratio and Contrast-To-Noise Ratio for fMRI Data. PLoS ONE 8, e77089

[9] Feinberg, D.A. et al. (2010) Multiplexed Echo Planar Imaging for Sub-Second Whole Brain FMRI and Fast Diffusion Imaging. PLoS ONE 5, e15710

[10] Ugurbil, K. et al. (2013) Pushing spatial and temporal resolution for functional and diffusion MRI in the Human Connectome Project. NeuroImage 80, 80-104

[11] Deichmann, R. et al. (2003) Optimized EPI for fMRI studies of the orbitofrontal cortex. NeuroImage 19, 430-441

[12] Tang H, Tabert MH, Albers M, Devanand DP, Wu EX, Brown TR. (2004) An optimized EPI pulse sequence using SENSE for fMRI studies of orbitofrontal and medial temporal brain areas. Proc. ISMRM

[13] Volz, S. et al. (2019) Maximising BOLD sensitivity through automated EPI protocol optimisation. NeuroImage 189, 159-170

[14] Brau A. New parallel imaging method enhances imaging speed and accuracy. GE Signa Pulse, 2007; 36-38.

[15] Blaimer, M. et al. (2004) SMASH, SENSE, PILS, GRAPPA: how to choose the optimal method. Top. Magn. Reson. Imaging TMRI 15, 223-236

[16] Schmidt, C.F. et al. (2005) Sensitivity-encoded (SENSE) echo planar fMRI at 3T in the medial temporal lobe. NeuroImage 25, 625-641

[17] Clare, S. et al. (2001) Single-shot T2(*) measurement to establish optimum echo time for fMRI: studies of the visual, motor, and auditory cortices at 3.0 T. Magn. Reson. Med. 45, 930-933

[18] Peters, A.M. et al. (2007) T2* measurements in human brain at 1.5, 3 and 7 T. Magn. Reson. Imaging 25, 748-753

[19] Goksan, S. et al. (2017) Optimal echo time for functional MRI of the infant brain identified in response to noxious stimulation: Optimal TE for fMRI of the Infant Brain. Magn. Reson. Med. 78, 625-631

[20] Haacke, E.M. et al. (2005) Imaging iron stores in the brain using magnetic resonance imaging. Magn. Reson. Imaging 23, 1-25

[21] Krause, F. et al. (2019) Active head motion reduction in magnetic resonance imaging using tactile feedback. Hum. Brain Mapp. DOI: 10.1002/hbm.24683

[22] Ekman, M. et al. (2017) Time-compressed preplay of anticipated events in human primary visual cortex. Nat. Commun. 8, 15276

[23] Schuck, N.W. and Niv, Y. (2019) Sequential replay of nonspatial task states in the human hippocampus. Science 364, eaaw5181

[24] Risk, B.B. et al. (2018) Impacts of simultaneous multislice acquisition on sensitivity and specificity in fMRI. NeuroImage 172, 538-553

[25] Moeller S, Xu J, Auerbach EJ, Yacoub E, Ugurbil K (2012) Signal Leakage(L-factor) as a measure for parallel imaging performance among simultaneously multi-Slice (SMS) excited and acquired signals. Proc Int Soc Magn Reson Med

[26] Xu, J. et al. (2013) Evaluation of slice accelerations using multiband echo planar imaging at 3 T. NeuroImage 83, 991-1001

[27] Todd, N. et al. (2016) Evaluation of 2D multiband EPI imaging for high-resolution, whole-brain, task-based fMRI studies at 3T: Sensitivity and slice leakage artifacts. NeuroImage 124, 32-42

[28] Cauley, S.F. et al. (2014) Interslice leakage artifact reduction technique for simultaneous mul-tislice acquisitions. Magn. Reson. Med. 72, 93-102

[29] Graessner J. (2013) Bandwidth in MRI? MAGNETOM Flash 22013

[30] Kaza, E. et al. (2011) Comparison of a 32-channel with a 12-channel head coil: Are there relevant improvements for functional imaging? J. Magn. Reson. Imaging 34, 173-183

[31] Triantafyllou, C. et al. (2011) Physiological noise and signal-to-noise ratio in fMRI with multi-channel array coils. NeuroImage 55, 597-606

[32] Murphy, K. et al. (2007) How long to scan? The relationship between fMRI temporal signal to noise ratio and necessary scan duration. NeuroImage 34, 565-574

[33] Andersson, J.L.R. et al. (2003) How to correct susceptibility distortions in spin-echo echo-planar images: application to diffusion tensor imaging. NeuroImage 20, 870-888

[34] Morgan, P.S. et al. (2004) Correction of spatial distortion in EPI due to inhomogeneous static magnetic fields using the reversed gradient method. J. Magn. Reson. Imaging 19, 499-507

[35] Holland, D. et al. (2010) Efficient correction of inhomogeneous static magnetic field-induced distortion in Echo Planar Imaging. NeuroImage 50, 175-183

[36] Bruder, H. et al. (1992) Image reconstruction for echo planar imaging with nonequidistantk-space sampling. Magn. Reson. Med. 23, 311-323

[37] Giannelli, M. et al. (2010) Characterization of Nyquist ghost in EPI-fMRI acquisition sequences implemented on two clinical 1.5 T MR scanner systems: effect of readout bandwidth and echo spacing. J. Appl. Clin. Med. Phys. 11, 170-180

[38] Ianni, J.D. et al. (2018) Ghost reduction in echo-planar imaging by joint reconstruction of images and line-to-line delays and phase errors: Joint Echo Planar Image, Delay and Phase Error Recon-struction. Magn. Reson. Med. 79, 3114-3121

[39] Clare S., Bowtell R., Morris P. (1998) Ghost artefact in fMRI: comparison of techniques for reducing the N/2 ghost. Proc. ISMRM

[40] Baldassano, C. et al. (2017) Discovering Event Structure in Continuous Narrative Perception and Memory. Neuron 95, 709-721.e5

[41] Bellmund, J.L.S. et al. (2018) Structuring Time in Human Lateral Entorhinal Cortex. bioRxiv. DOI: 10.1101/458133

[42] Brunec, I.K. et al. (2018) Multiple Scales of Representation along the Hippocampal Anteropos-terior Axis in Humans. Curr. Biol. 28, 2129-2135.e6

[43] Constantinescu, A.O. et al. (2016) Organizing conceptual knowledge in humans with a gridlike code. Science 352, 1464-1468

[44] Córdova, N.I. et al. (2019) Focusing on what matters: Modulation of the human hippocampus by relational attention. Hippocampus DOI: 10.1002/hipo.23082

[45] de Voogd, L.D. et al. (2018) Eye-Movement Intervention Enhances Extinction via Amygdala Deactivation. J. Neurosci. 38, 8694-8706

[46] Dimsdale-Zucker, H.R. et al. (2018) CA1 and CA3 differentially support spontaneous retrieval of episodic contexts within human hippocampal subfields. Nat. Commun. 9, 294.

[47] Garvert, M.M. et al. (2017) A map of abstract relational knowledge in the human hippocampal-entorhinal cortex. eLife 6, e17086

[48] Julian, J.B. et al. (2018) Human entorhinal cortex represents visual space using a boundary-anchored grid. Nat. Neurosci. 21, 191-194

[49] Kaplan, R. and Friston, K.J. (2019) Entorhinal transformations in abstract frames of reference. PLOS Biol. 17, e3000230

[50] Kim, M. and Maguire, E.A. (2018) Hippocampus, Retrosplenial and Parahippocampal Cortices Encode Multicompartment 3D Space in a Hierarchical Manner. Cereb. Cortex 28, 1898-1909

[51] Kok, P. and Turk-Browne, N.B. (2018) Associative Prediction of Visual Shape in the Hippocampus. J. Neurosci. 38, 6888-6899

[52] Montchal, M.E. et al. (2019) Precise temporal memories are supported by the lateral entorhinal cortex in humans. Nat. Neurosci. 22, 284-288

[53] Nau, M. et al. (2018) Hexadirectional coding of visual space in human entorhinal cortex. Nat. Neurosci. 21, 188-190

[54] Stangl, M. et al. (2018) Compromised Grid-Cell-like Representations in Old Age as a Key Mechanism to Explain Age-Related Navigational Deficits. Curr. Biol. 28, 1108-1115.e6

[55] Zeithamova, D. et al. (2018) Abstract Representation of Prospective Reward in the Hippocampus. J. Neurosci. 38, 10093-10101

[56] Marques, J.P. and Norris, D.G. (2018) How to choose the right MR sequence for your research question at 7 T and above? NeuroImage 168, 119-140

[57] Sclocco, R. et al. (2018) Challenges and opportunities for brainstem neuroimaging with ultrahigh field MRI. NeuroImage 168, 412-426

[58] Ladd, M.E., Bachert, P., Meyerspeer, M., Moser, E., Nagel, A.M., Norris, D.G., Schmitter, S., Speck, O., Straub, S., and Zaiss, M. (2018). Pros and cons of ultra-high-field MRI/MRS for human application. Prog. Nucl. Magn. Reson. Spectrosc. 109, 1-50.

[59] Torrisi, S. et al. (2018) Statistical power comparisons at 3T and 7T with a GO / NOGO task. NeuroImage 175, 100?110

[60] van der Zwaag, W. et al. (2009) fMRI at 1.5, 3 and 7 T: Characterising BOLD signal changes. NeuroImage 47, 1425-1434

[61] Han, S. et al. (2019) Gradient-echo and spin-echo blood oxygenation level-dependent functional MRI at ultrahigh fields of 9.4 and 15.2 Tesla. Magn. Reson. Med. 81, 1237-1246

[62] Yacoub, E. et al. (2001) Imaging brain function in humans at 7 Tesla. Magn. Reson. Med. 45, 588-594

[63] Carr, V.A. et al. (2010) Imaging the Human Medial Temporal Lobe with High-Resolution fMRI. Neuron 65, 298-308

[64] Berron, D. et al. (2017) A protocol for manual segmentation of medial temporal lobe subregions in 7 Tesla MRI. NeuroImage Clin. 15, 466-482

[65] Norris, D.G. and Polimeni, J.R. (2019) Laminar (f)MRI: A short history and future prospects. NeuroImage 197, 643-649

[66] Navarro Schröder, T. et al. (2015) Functional topography of the human entorhinal cortex. eLife 4, 1-17

[67] Poser, B.A. et al. (2010) Three dimensional echo-planar imaging at 7 Tesla. NeuroImage 51, 261-266

[68] Stockmann, J.P. and Wald, L.L. (2018) In vivo B0 field shimming methods for MRI at 7T. NeuroImage 168, 71-87

[69] Morris, L.S. et al. (2019) Ultra-high field MRI reveals mood-related circuit disturbances in depression: a comparison between 3-Tesla and 7-Tesla. Transl. Psychiatry 9

[70] Yoo, P.E. et al. (2018) 7T-fMRI: Faster temporal resolution yields optimal BOLD sensitivity for functional network imaging specifically at high spatial resolution. NeuroImage 164, 214-229

[71] Kasper, L. et al. (2017) The PhysIO Toolbox for Modeling Physiological Noise in fMRI Data. J. Neurosci. Methods 276, 56-72

[72] Hodgetts, C.J. et al. (2017) Ultra-High-Field fMRI Reveals a Role for the Subiculum in Scene Perceptual Discrimination. J. Neurosci. 37, 3150-3159

[73] Maass, A. et al. (2015) Functional subregions of the human entorhinal cortex. eLife 4, 1-20

[74] Shah, P. et al. (2018) Mapping the structural and functional network architecture of the medial temporal lobe using 7T MRI. Hum. Brain Mapp. 39, 851-865

[75] Sladky, R. et al. (2018) Unsmoothed functional MRI of the human amygdala and bed nucleus of the stria terminalis during processing of emotional faces. NeuroImage 168, 383-391

[76] Suthana, N.A. et al. (2015) High-resolution 7T fMRI of Human Hippocampal Subfields during Associative Learning. J. Neurosci. 27, 1194-1206

[77] Theysohn, N. et al. (2013) Memory-Related Hippocampal Activity Can Be Measured Robustly Using fMRI at 7 Tesla: Memory-Related Hippocampal fMRI At 7 Tesla. J. Neuroimaging 23, 445-451