Basic Neuroscience
Short communication

On the importance of specialized radiofrequency filtering for concurrent TMS/MRI

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HIGHLIGHTS

► We discuss different methods for radiofrequency filtering for concurrent TMS/MRI.
► We quantified the efficacy of one approach of RF-filtering for concurrent TMS/MRI.
► We found that filtering external RF eliminates the main factor contributing to a loss in data quality in concurrent TMS/MRI.
► The RF-filter caused a reduction in the efficacy of TMS of ~7%.

ARTICLE INFO

Article history:
Received 18 April 2012
Received in revised form 7 July 2012
Accepted 26 July 2012

Keywords:
Transcranial magnetic stimulation
Magnetic resonance imaging
Concurrent TMS/MRI
Radio frequency noise
Echo planar imaging

ABSTRACT

The concurrent application of TMS and MRI is challenging due to the MR-image artifacts, which are produced by using the two techniques in combination. One such artifact arises from the introduction of radio frequency noise through the lead of the TMS-coil into the scanner. Here we describe four methods used in the literature to integrate TMS into the MR environment and quantify in detail the efficacy of one approach in filtering RF interference. We show that RF filtering has a dramatic effect on the overall signal-to-fluctuation-noise ratio (SNR) of the acquired echo-planar imaging data.

The reduction in SNR when integrating a TMS system into the MR scanner varies from 20% up to 80% (compared with MR scanner in the absence of TMS system), depending on the configuration used.

Using an RF-filter in-line with the TMS-coil eliminates much of this loss in SNR. However the RF filter also causes a ~7% decrease in the functional efficacy of TMS. Overall, this study highlights the importance of RF-filtering when designing and installing a concurrent TMS/MRI system.

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1. Introduction

The concurrent application of transcranial magnetic stimulation (TMS) and magnetic resonance imaging (MRI) allows the simultaneous manipulation and measurement of brain function. Although the feasibility of the combination was demonstrated in 1998 (Bohning et al., 1998), few groups have applied it successfully due to the significant technical challenges involved (Baudewig et al., 2001; Bestmann et al., 2008; Blankenburg et al., 2008; Bohning et al., 1999; Bungert et al., 2011; Moisa et al., 2010; Sack et al., 2007).

One problem, that has not been discussed specifically in the literature, arises from radiofrequency (RF) noise carried into the magnet room through the lead of the TMS-coil, which can lead to artifacts and significantly decrease the overall signal-to-fluctuation-noise ratio (SNR) (Friedman and Glover, 2006) of acquired data. To alleviate the general problem of RF interference, the MR magnet is placed within a screened room (Faraday cage) consisting of metal sheets in the walls, the ceiling and the floor that prevent RF from entering the room. Any electric connections made from inside the screened room to the outside need to be made through a penetration panel (a set of connectors with integrated filters), which prevents RF transmission. However, standard RF filters are not suitable for simultaneous TMS/MRI because of the high current (~5000 A) and the high voltage (~1500 V) delivered during each TMS pulse.

The presence of extraneous RF is readily identifiable for the majority of MR acquisitions as a vertical or horizontal interference line in the image (Haacke et al., 1999; Stadler et al., 2007). For echo planar imaging (EPI), however, RF artifacts affect only a few points in the image, making them very difficult to detect visually in functional MRI data.

In previous studies, RF interference was minimized either by shielding the stimulator from RF using a Faraday cage, or by using an in-line RF-filter to prevent RF from being transmitted through
the lead of the TMS into the screened scanner room. The application of all four resulting combinations (Fig. 1) has been previously reported.

Several groups have taken the simplest approach and connected the TMS-lead through a waveguide to the stimulator outside the screened scanner room (Bestmann et al., 2005, 2004, 2003; Sack et al., 2007) without RF filtering or screening of the stimulator (Fig. 1A). This effectively allows RF noise both from the environment and the stimulator into the system. The first method of RF filtering is achieved by feeding the TMS-coil through a waveguide (Moisa et al., 2009), with an in-line filter to block RF carried along TMS-lead (Fig. 1B). Here the authors noted that RF was not increased significantly when connecting the TMS-coil to the stimulator.

Second, rather than applying RF filtering of the stimulator itself (connected directly through waveguide), some early studies screened the stimulator, the lead of the TMS coil, and the legs of the subject in the scanner using sheets of aluminum foil (Bohning et al., 1999) (Fig. 1C). Finally, both methods have been combined by housing the stimulator in a shielded metal cabinet inside the magnet room, thus screening it from external RF. In addition, the stimulator has been connected to the TMS coil through an RF-filter box, with the cable further wound around ferrite sleeves to further attenuate the transmitted RF (Heinen et al., 2011; Ruff et al., 2007) (Fig. 1D). This approach provides good elimination of RF noise from outside and from the stimulator itself, but positioning the TMS-stimulator near the MR scanner is potentially dangerous due to attractive forces of the scanner field on the stimulator, This is particularly true as high field systems (3 T and above) become more popular than the moderate field strength 1.5 T systems used for these early studies.

The methods used for in-line RF filtering are well known in the research community and in recent years the leading manufacturers for solutions for concurrent TMS with fMRI (The Magstim Company, Whitland, Wales, UK and MagVenture, Farum, Denmark) provide such specialized RF filters.

Here we report the design and efficacy of such an in-line RF-filter for the TMS-coil with the stimulator located outside the magnet room (Fig. 1B). We quantify the magnitude of RF noise during concurrent TMS/fMRI by comparing this approach to a baseline without RF filtering (Fig. 1A). Additionally, we quantify the effect of the RF-filter on the physiological effectiveness of the TMS.

2. Materials

All experiments were conducted in a 3 T General Electric HDx whole-body scanner (GE Healthcare, Chalfont St. Giles, UK) using a quadrature head coil with an inner diameter of 28 cm for signal reception. The TMS-stimulator (Rapid2, The Magstim Company, Whitland, Wales, UK) was used with an MR-compatible 70 mm figure-of-eight TMS-coil with an 8 m long lead and a filter box, which incorporated an RF filter and a diode assembly for the suppression of leakage currents during recharge periods of the stimulator (Fig. 2A). The diode assembly consisted of a pair of diodes combined with a resistor, thus eliminating the need for a separate active relay element that was described previously (Weiskopf et al., 2009). For measurements without RF-filter, an adaptor was used for bypassing the filter box (Magstim). As outlined below, measurements of motor threshold were also obtained with a standard figure-of-eight coil with 2 m lead.

The RF filter is commercially available and was designed and constructed by Magstim, It is different to the one used previously (Heinen et al., 2011; Ruff et al., 2007). Internally it consists of four stages of Chebyshev low-pass filters, a commonly used method of filtering RF. The inductors inside the filter were purpose-built to allow transmission of higher current and voltages. The RF filter connects the TMS-coil inside the screened room with the stimulator outside of the screened room (Fig. 1B). To minimize RF interference, the casing of the filter itself forms an RF screen around the unit, and is directly attached to the magnet room’s RF screen via a waveguide. Measurements with a network analyzer showed a reduction in transmitted RF of >80 dB in a frequency range of 30–200 MHz.

3. Methods

3.1. RF noise measurements

Gradient-echo echo-planar (EP) images were acquired in vivo in a human volunteer (FOV 218 mm × 218 mm × 156 mm, resolution (3.4 mm)³, 30 slices, slice thickness 3.4 mm, TR 3000 ms, TE 35 ms, phase encode direction AP, 100 vol). Data preprocessing included movement correction, with all images registered to the volume at the mid-point of the timeseries (Jenkinson et al., 2002) and then high pass filtering (100 s). Signal-to-fluctuation-noise maps were calculated by dividing, voxel-by-voxel, the temporal mean by the temporal standard deviation. A similar protocol is an established method for fMRI quality assurance (Friedman and Glover, 2006).

SNR maps of EP-images from a human head were acquired each in four different configurations: (I) without the TMS-coil, to represent the ideal situation (baseline); (II) with the TMS-coil placed on the superior right of the head but disconnected from the stimulator, with the lead remaining within the screened room; (III) with the TMS-coil placed as in II but with the lead connected through the RF-filter, stimulator activated and charged to 100%, (IV) with the TMS-coil placed as in III but connected without the RF filter through the waveguide to the stimulator, and with the stimulator switched off, (V) same as IV but with the stimulator charged to 100%. Configuration III represents the method shown in Fig. 1B, while IV and V correspond to Fig. 1A.

Mean SNR values were calculated using the average over all voxels within a mask, using the same mask for all conditions. A threshold of 10% of the intensity of the brightest voxel in each condition was used. Only voxels with intensities above this threshold in all conditions were included in the mask. Loss in SNR was calculated relative to the unperturbed baseline (I).

The amount of RF interference present in the image is dependent on the level of background RF noise in the environment, which is subsequently transmitted into the screened room via the TMS equipment. As a result, the level of RF noise introduced will be site specific, and will potentially vary depending on the state of nearby equipment. Using the same procedure as outlined above, we performed four repeat measurements in a phantom, in
3.2. Motor threshold acquisition

Resting motor threshold (MT) was acquired in twelve participants (3 males, mean age 28) using the observation of movement method, as described previously (Varnava et al., 2011). For each participant, one MT was acquired for each of three Magstim coil configurations: a standard 70 mm figure-of-eight coil with short cable (2 m), an MR-compatible 70 mm figure-of-eight coil with longer 8 m connecting cable, and the same MR-compatible coil with the RF filter box installed (Fig. 2A). The order of acquisitions within each session was counterbalanced across participants using a Latin square design. Written consent was obtained from the participants and the study was approved by the local ethics committee at the School of Psychology.

4. Results and discussion

The results are shown in Fig. 2. Placing the TMS-coil close to the head without connecting it to the stimulator (II) slightly reduces the SNR of the EP-images relative to baseline (I). As visible in Fig. 2B in the coronal view, this reduction is greater in the superior regions, directly underneath the TMS-coil, which indicates that it is due to artifacts caused by the presence of the TMS-coil. As the filter box used in this work incorporates a diode assembly for eliminating leakage currents, these local effects are due to the magnetic susceptibility differences between the TMS coil and nearby tissue, rather than leakage currents (Weiskopf et al., 2009).

Significantly, if the TMS system is connected through the RF-filter to the stimulator (III), there is only a further 3% deterioration in the SNR, indicating that RF filtering is highly effective using this technique and additionally screening the stimulator would not result in significant improvements in image quality. If the TMS-coil is connected without RF filtering (V), the SNR is reduced by ~80% in all regions of the image. Thus, the effect of RF interference mediated by the TMS system is not purely local, but affects the whole image, and would grossly impair any data obtained using concurrent TMS/MRI.

Note that activating the stimulator (V) results in further loss in SNR relative to non-activation (IV), indicating that this is caused by RF noise originating from the stimulator.

Thus, any method that filters RF interference from the environment, but not from the stimulator itself, will result in incomplete RF cancelation. The extent of RF noise will vary between MR scanners at different locations, and at different field strengths. The variability in the efficacy of the RF filter is shown in Fig. 3. There is a significant
effect of filtering on the SFNR observed in all sessions, indicating that the filter box is successfully able to filter the (variable) amount of RF present in the environment.

At some sites, successful experiments using concurrent TMS/MRI have been carried out without RF-filtering, thus showing that it is possible. One publication states: ‘Pilot studies had revealed that the RF emission of the TMS stimulator did not interfere with MRI at 3 T, in contrast to previously reported RF interference at 1.5 T’ (Bestmann et al., 2004). It is possible that in their case there was a relatively low abundance of RF at the scanner frequency and that the methods for measuring RF-interference were not sensitive.

Our results suggest that specialized RF filtering is highly recommended when using concurrent TMS/MRI. Otherwise there is the risk of acquiring fMRI data that appears to be normal, but which is unusable due to excessive RF noise.

4.1. Analysis of MT

Individual estimates of cortical excitability were reliably related across coil conditions: MTs obtained using the standard coil correlated significantly with those measured using each of the MR-compatible configurations (both $R > 0.94$, both $p < 0.001$), which also correlated strongly with each other ($R = 0.98$, $p < 0.0001$). These results confirm the test/re-test reliability of MT.

A one-way repeated measures ANOVA of MT revealed a significant main effect of condition $F(2, 22) = 300.6$, $p < 0.0001$. As shown in Fig. 2C, Post hoc t-tests revealed that, relative to the standard coil ($M = 47.3\%$; $SE = 1.5\%$), MT was significantly elevated with the MR-compatible coil ($M = 58.9\%$; $SE = 1.8\%$; $t(11) = 18.2$, $p < 0.0001$) and the MR-compatible coil plus filter box ($M = 63.2\%$; $SE = 2.0\%$; $t(11) = 18.7$, $p < 0.0001$). Furthermore, the addition of the filter box significantly increased MT obtained with the MR-compatible coil ($t(11) = 9.2$, $p < 0.0001$).

These results indicate that, on average, the longer connecting lead of the MR-compatible coil attenuated the efficacy of TMS by 11.6% stimulator output (24.5% of baseline MT using a standard coil), while the filter box reduced TMS efficacy by a further 4.3% stimulator output (7.3% of MT using the MR-compatible coil without filter box). The changes can be related to an increase of the overall inductance and the overall resistance of the stimulator circuit, which leads to longer and stronger attenuation and therefore less efficient TMS-pulses. Using a thicker lead with lower resistance and a lower inductance per length unit could limit this reduction in efficacy.

5. Conclusions

This work has quantified, for the first time to our knowledge, the impact on image quality of RF interference introduced by a TMS system into the MR environment. We have summarized the approaches used in the literature to reduce the impact of RF noise on TMS–MRI experiments, and have demonstrated that a failure to provide adequate filtering can lead to a reduction in SFNR of 80%. However, this reduction depends on the level of RF noise in the environment so that the reduction may be significantly lower, depending on the site of the scanner. When RF is filtered from both the environment and the simulator itself, these losses in SFNR can be almost entirely recovered.

One disadvantage of the filtering mechanism we propose is a small but reliable increase in MT relative to MR-compatible TMS without filtering, which reflects a decrease in TMS efficacy of approximately 7%. This limitation could be reduced or eliminated by designing RF-filters specifically for Larmor frequencies of MR-scanners (e.g. 128 MHz for 3 T) rather than using a universal broadband approach. Such filters could be smaller and therefore have a decreased detrimental effect on the efficacy of the TMS system.

On balance, due to the potentially severe effects of RF interference on fMRI data, we strongly recommend the use specialized RF-filtering for concurrent TMS/MRI.

Financial disclosure

The project is collaboration between The Magstimg Company and Cardiff University as part of the Academia for Business (A4B) programme of the Welsh Assembly.

Acknowledgements

This work was supported by the Academia for Business (A4B) programme of the Welsh Assembly Government via grant HE 07 COL 3012 (CDC).

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