Introduction

Numerous functions of the central nervous system such as processing of sensory signals from the periphery and from the viscera, motor execution, reflexes or autonomic functions, involve the spinal cord. To investigate its functional role in vivo, functional magnetic resonance imaging (fMRI) experiments based on the blood-oxygenation-level-dependent (BOLD) contrast (Ogawa et al., 1990, 1993) represent a valuable non-invasive approach (e.g. Brooks et al., 2012; Eippert et al., 2009; Maieron et al., 2007; Sprenger et al., 2012). fMRI of the spinal cord is technically more challenging than in the brain due to the small size of the gray matter structure and the inhomogeneity of the magnetic flux density in the spinal canal, which is caused by differences of the magnetic susceptibilities, in particular of the vertebrae and the vertebral disks (e.g., Cooke et al., 2004; Maieron et al., 2007). Nevertheless, fMRI of the human spinal cord has provided important insights into the human spinal cord physiology (Eippert et al., 2009; Mainero et al., 2007; Sprenger et al., 2012). For instance, it could be shown that the modulation of pain perception by higher cognitive functions, e.g. attention or in the context of placebo analgesia, can already be detected at the spinal level (Eippert et al., 2009; Sprenger et al., 2012).

With the recent progress in spinal cord fMRI interest has risen to also target its functional interaction with the brain. Studies investigating functional connectivity between the brain and the spinal cord systems would be informative with regard to many pertinent research questions such as top-down and bottom-up modulation of neuronal activity during physiological signaling in health and its alteration in pathological conditions including its interference with therapeutic approaches.

Performing separate fMRI experiments of the brain and the spinal cord successively is straightforward because individual fMRI protocols are well established for each region. However, such measurements are not suitable for a reliable estimation of the functional or effective connectivity between the brain and the spinal cord which requires to sample the response to each, individual stimulus in all regions considered (Friston et al., 1997, 2003), i.e. the brain and the spinal cord must be covered within the same measurement.

Combined T2*-weighted measurements of the human brain and cervical spinal cord with a dynamic shim update

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Abstract

Important functions of the central nervous system such as sensory processing and motor execution, involve the spinal cord. Recent advances in human functional MRI have allowed to investigate spinal cord neuronal processes using the blood-oxygenation-level-dependent (BOLD) contrast. However, to assess the functional connectivity between the brain and the spinal cord, functional MRI measurements covering both regions in the same experiment are required. Unfortunately, the ideal MRI setup differs considerably for the brain and the spinal cord with respect to resolution, field-of-view, relevant receive coils, and, in particular, shim adjustments required to minimize distortion artifacts. Here, these issues are addressed for combined T2*-weighted MRI measurements of the human brain and the cervical spinal cord by using adapted parameter settings (field-of-view, in-plane resolution, slice thickness, and receiver bandwidth) for each region, a dynamic receive coil element selection where for each slice only the elements with significant signal contributions are considered, and, most importantly, the implementation of a dynamic update of the frequency and field-of-view, relevant receive coils, and, in particular, shim settings individually adapted to the brain and spinal cord subvolume. The feasibility of this setup for combined measurements is demonstrated in healthy volunteers at 3 T. Although geometric distortions are slightly more pronounced and the temporal signal-to-noise ratio is lower as compared to measurements focusing to the brain or spinal cord only, the overall image quality can be expected to be sufficient for combined functional MRI experiments. Thus, the presented approach could help to unravel the functional coupling between the brain and the spinal cord.

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Such combined fMRI measurements are challenging because the desired setups differ considerably between brain and spinal cord measurements. First, typical acquisition parameters like resolution, slice thickness, and field-of-view, differ by a factor of two or more. For instance, most brain fMRI acquisitions employ isotropic voxel sizes between $2.0 \times 2.0 \times 2.0 \text{ mm}^3$ and $4.0 \times 4.0 \times 4.0 \text{ mm}^3$, protocols for the spinal cord usually have an in-plane resolution of $1.0 \times 1.0 \text{ mm}^2$ or even below and a slice thickness of $4 \text{ mm}$ or more (see, e.g., Giove et al., 2004). However, standard MRI sequences can only handle a single parameter set for all slices yielding a non-optimal or insufficient image quality in at least one of the regions, which could hamper the reliable detection or localization of activations. Second, different receive coils are relevant for the brain and the spinal cord. Acquiring data for the brain and the spinal cord with all available coil elements rather than those optimal for each part, leads to a reduced signal-to-noise ratio. Third, and most importantly, the optimum shim adjustment usually differs considerably between the brain and the spinal cord. BOLD fMRI experiments are based on $T^2$*-weighted acquisitions that in the presence of a non-optimal shim setup suffer from signal dropouts. Furthermore, echo-planar imaging (Mansfield, 1977) which is commonly used in $T^2$*-weighted fMRI, can exhibit geometric distortions that can degrade the image quality significantly.

In this work, we provide a practical approach for combined $T^2$*-weighted measurements of the human brain and the cervical spinal cord with an accordingly extended echo-planar imaging pulse sequence. First, specific parameters (e.g., in-plane resolution, slice thickness, field-of-view) with an individually optimized timing (i.e., receiver bandwidth, echo spacing, echo time) were used for the brain and the spinal cord subvolumes. Second, the receive coil elements were dynamically selected such that for each slice only elements with significant signal contributions are included. Third, the frequency and the linear shims were dynamically updated during the measurement (Blamire et al., 1996; Morrell and Spielman, 1997) to use different values for the brain and the spinal cord subvolume. The feasibility of this approach to perform combined $T^2$*-weighted measurements of the human brain and cervical spinal cord is demonstrated in healthy volunteers at 3 T.

Material and methods

Measurements were performed on a 3 T whole-body MR system (TIM Trio, Siemens Healthcare, Erlangen, Germany) using a 12-element head and a 4-element neck coil (both receive-only). The MR system is (TIM Trio, Siemens Healthcare, Erlangen, Germany) using a 12-element brain and cervical spinal cord is demonstrated in healthy volunteers at 3T.

In the present study are shown in Fig. 1a. 40 slices in total divided into two subvolumes with parallel slices were measured in descending order. The upper subvolume covered 32 slices in the brain with an orientation along the anterior and posterior commissures. The lower subvolume covered eight slices in the cervical spinal cord and its slices were oriented approximately perpendicular to the spinal cord. It was centered between the vertebral bodies C5 and C6 (Fig. 1a). The slices in the brain had a field-of-view of $224 \times 256 \text{ mm}^2$, a voxel size of $2.0 \times 2.0 \times 2.0 \text{ mm}^3$ and a gap between the slices of 1 mm, i.e. typical parameters for standard brain fMRI experiments. For the slices in the spinal cord, the field-of-view was set to $112 \times 128 \text{ mm}^2$, the resolution was $1.0 \times 1.0 \times 5.0 \text{ mm}^3$ and no gap between the slices was used. These parameters are very similar to previous human spinal cord fMRI experiments (see, e.g., Eippert et al., 2009; Giove et al., 2004; Sprenger et al., 2012; Summers et al., 2010b). The isocenter was positioned about 15–30 mm above the uppermost spinal cord slice which was at vertebral level C2. Slice distances from the isocenter for the spinal cord were between 70 mm and 20 mm and for the brain between 40 mm and 160 mm for the lowermost and uppermost slices, respectively.

Two spatial saturation pulses were applied posterior and anterior to the spinal cord, in particular to avoid aliasing artifacts for the field-of-view chosen. Compared to recent studies (Eippert et al., 2009; Sprenger et al., 2012), their orientation was tilted such that they did not affect the brain volume covered (Fig. 1a). Although the effect of the posterior saturation pulse in such a setup can be marginal for a slim neck (cf. Fig. 1a), it can help to avoid artifacts in volunteers with a more muscular neck.

Shim setups were determined with the shim procedure and algorithm provided by the manufacturer. It involved a 3D gradient-echo acquisition with two echoes and analyzed the phase difference between the two echoes to estimate the actual field distribution (see, e.g., Schneider and Glover, 1991; Webb and Macovski, 1991) and to calculate the currents that were required for the different shim coils to realize a more homogeneous field in a cuboidal adjustment volume. To find a reasonable shim setup for the combined measurements, different adjustment volumes were considered (Fig. 1b) that contained (i) both the brain and the spinal cord target volume (“full” volume, dashed in Fig. 1b), (ii) only the volume covered by the brain slices, or (iii) only a small region surrounding the targeted spinal cord volume.

Echo-planar imaging (Mansfield, 1977) was used with different timings for the two subvolumes in order to provide optimal parameters for the chosen resolutions and slice thicknesses (Fig. 1c). For both subvolumes, ramp sampling was applied during the readout gradient pulses to minimize the echo spacing. The bandwidths per pixel were 1502 Hz and 1086 Hz yielding echo spacings of 0.75 ms and 1.05 ms for the brain and spinal cord slices, respectively (see Fig. 1c). Compared to a measurement with a fixed timing for all slices, a shorter echo spacing and echo time could be realized for the slices in the brain that have a lower in-plane resolution. Thus, geometric distortions were slightly reduced and signal dropouts related to susceptibility differences were less pronounced (Fig. 1d). As sketched in Fig. 1c, only the signals acquired with the head coil elements were considered for the brain slices and only those received with the neck coil elements for the spinal cord slices. Thus, coil elements that do not provide a significant signal contribution to the particular subvolume, but only noise, were ignored which increases the SNR accordingly.

Flow rephasing was applied in the slice direction (see Fig. 1c) to minimize signal variations related to pulsatile flow of the cerebrospinal fluid (e.g., Finsterbusch et al., 2012). For the spinal cord slices, a slice-specific gradient moment was applied in the slice direction (“z-shim”, see Fig. 1c) (Constable, 1995; Frahm et al., 1988) in order to minimize intensity modulations along the spinal cord (Finsterbusch et al., 2012) that are caused by the field inhomogeneities related to the different magnetic susceptibilities of vertebral bodies and vertebral disks (e.g., Cooke et al., 2004; Maieron et al., 2007). The optimum moment for each slice in each volunteer was determined from a reference acquisition (Finsterbusch et al., 2012) that stepped through a predefined moment range (21 equidistant steps between $\pm 7.6 \text{ mT m}^{-1}$). It covered only the lower, i.e. spinal cord, subvolume to shorten the acquisition time (repetition time 2.0 s, total acquisition time 48 s). The moment that provided the highest signal intensity in the spinal cord was determined for each slice and used in subsequent acquisitions (cf. Finsterbusch et al., 2012). Note that the z-shim gradient moments were also applied with flow rephasing (see Fig. 1c).

Parallel imaging using GRAPPA (Griswold et al., 2002) with an acceleration factor of two and 48 reference lines was applied to shorten the echo train, i.e. to minimize the echo times and geometric distortions. Thus, echo train lengths of 41 ms and 58 ms and echo times of 30 ms and 38 ms could be achieved for brain and spinal cord slices, respectively. In addition to the two spatial saturation pulses (see above), chemical shift saturation pulses were applied with a frequency offset of 407 Hz to suppress fat signals yielding acquisition times of 78 ms and 95 ms per
slice for the brain and the spinal cord slices, respectively. Thus, a repetition time of 3.27 s was obtained for the combined measurement, i.e. for the total volume. The resonance frequency and the linear shims were determined for both subvolumes independently (see below). For the combined measurements, the frequency and linear shims were set to the values determined for the adjustment volume in the brain shown in (b) but for the slices in the brain, a frequency offset and gradient offsets (blue) were applied to match the settings determined for the adjustment volume in the brain shown in (b). (d) Comparison of echo-planar images acquired in the brain with a fixed sequence timing (bandwidth per pixel 1086 Hz, echo spacing 1.05 ms) that is determined by the higher resolution of the spinal cord slices (left), and with a timing that is adapted to the lower in-plane resolution (1502 Hz, 0.75 ms) of the brain slices (right). With the latter, geometric distortions and signal dropouts (arrows) are reduced. See text for details.

Fig. 1. (a, b) Geometric setup for the combined measurements performed in the present study showing (a) the two subvolumes in the brain and the cervical spinal cord (yellow), respectively, the locations of the head (red) and neck coil (green) relative to the volunteer, and the two saturation pulses (cyan) and (b) the adjustment volumes considered. The full (dashed) adjustment volume in (b) was used for the second order shims, the others (solid) for the frequency and the linear shims. (c) Basic echo-planar imaging pulse sequence used with optimized timings for the two slice groups, flow rephasing in the slice direction, and a slice-specific z-shim gradient moment (magenta) applied for the spinal cord slices to minimize signal losses related to field inhomogeneities. The system’s frequency and linear shim values were set to values determined for the spinal cord adjustment volume shown in (b) but for the slices in the brain, a frequency offset and gradient offsets (blue) were applied to match the settings determined for the adjustment volume in the brain shown in (b). (d) Comparison of echo-planar images acquired in the brain with a fixed sequence timing (bandwidth per pixel 1086 Hz, echo spacing 1.05 ms) that is determined by the higher resolution of the spinal cord slices (left), and with a timing that is adapted to the lower in-plane resolution (1502 Hz, 0.75 ms) of the brain slices (right). With the latter, geometric distortions and signal dropouts (arrows) are reduced. See text for details.
obtained for the spinal cord. However, during the measurement, a frequency offset and gradient offsets were applied for the brain slices in order to provide a dynamical update of the zero- (frequency-) and first-order shims (see Fig. 1c) (Blamire et al., 1996; Morrell and Spielman, 1997). The second-order shims could not be modified dynamically on this MR system and remained fixed during each measurement.

To assess the temporal signal-to-noise ratio (SNR) in vivo, 50 measurements (total acquisition time 2.7 min) were performed. The mean signal intensity of these measurements was divided by their standard deviation on a pixel-by-pixel basis to obtain maps of the temporal SNR.

The image reconstruction algorithm provided by the manufacturer includes several steps like regridding and the correction of frequency drifts and concomitant gradient effects that depend on the echo spacing and the timing and amplitude of the readout gradient pulse. In particular, the influence of concomitant gradient fields on echo-planar images is significant for the large off-center positions that are required, and must be corrected to avoid an apparent shearing of the subvolumes (e.g. Zhou et al., 1998). Because only one value for each of these parameters could be defined for the reconstruction, two reconstructions were performed successively, one with the parameters for the spinal cord subvolume, the other with the parameters used for the brain subvolume, to obtain optimal reconstruction results for both regions.

Furthermore, the reconstruction was extended to discard non-relevant coil elements for the different slices. Only the data of the head coil were used for the slices in the brain, and only the data of the neck coil for the spinal cord slices (see above).

As anatomical references, T1-weighted measurements were performed using a 3D MPRAGE sequence (Mugler and Brookeman, 1990) with an isotropic resolution of 1.0 mm (240 coronal slices, field-of-view 240 × 320 mm², echo time 3.5 ms, echo spacing 7 ms, flip angle 9°, inversion time 1100 ms, repetition time 2300 ms).

The geometric distortions of the echo-planar images and their variation between measurements targeting the brain only and the combined measurements were analyzed for a group of seven volunteers using SPM8 (Wellcome Department of Imaging Neuroscience, London, UK). Echo-planar images of each volunteer were co-registered to the individual’s T1-weighted anatomical data. Subsequently, two different processing approaches were considered that aimed to visualize and quantify the additional geometric distortions of the combined measurements compared to brain-only measurements on a group level. In the first approach, echo planar images were spatially normalized to the SPM EPI template using the standard SPM algorithm (Friston et al., 1995). As this step fits the acquired echo-planar images to the SPM EPI template, it compensates individual distortions. The affine and non-linear parameters required for it allow for a comparison of distortions between combined and brain-only measurements.

Results

The dynamic coil selection applied improved the SNR, in particular for the spinal cord. For the slices in the brain, the signal amplitude was slightly reduced (by about 3%) but the noise level was decreased by more than 10% which yielded an overall SNR increase (data not shown). In the spinal cord, the signal amplitude was about 2% lower when using only the neck coil elements but the noise level was reduced by more than 45%, i.e. the SNR gain was about 80% (data not shown). The noise reduction was more pronounced in this case because more elements (twelve) were discarded that provide mostly noise.

Results for the different shim approaches considered are summarized in Fig. 2. When performing the shim adjustment for the full volume (see Fig. 1b), the image quality for the brain slices was acceptable while the spinal cord suffered from very low signal amplitudes (Fig. 2a). Optimizing the adjustment for the spinal cord volume (see Fig. 1b), yielded a reasonable result for the spinal cord but degraded the brain images considerably (Fig. 2b). Modifying the second-order shim values to those determined for the full volume, did not significantly affect the spinal cord and improved the brain images but their quality was still not acceptable (Fig. 2c). On the other hand, a shim optimization for the brain volume (see Fig. 1b) did not provide reasonable images of the spinal cord (Fig 2d). Using the second-order shim values of the full volume instead, retained a good image quality in the brain with a slight compression in the phase-encoding, i.e. posterior–anterior, direction but did not improve the spinal cord data significantly (Fig. 2e). The best results (Fig. 2f) were obtained (i) using the second-order shim values of the full volume for both regions and (ii) adjusting the frequency and first-order (linear) shim values on-the-fly to the values determined for the brain and the spinal cord, respectively, i.e. performing a dynamic update of these values during the measurement (see Fig. 1c).

Example images of three volunteers are presented in Fig. 3. The image quality achievable with the combined measurement in the brain and the spinal cord is comparable to that of previous studies focusing on either the brain or the spinal cord (see Fig. 3a) but geometric distortions were slightly more pronounced. This can be seen in Figs. 3b and c where images acquired with a shim optimized either for the brain or the spinal cord are shown for comparison. Most obvious is an apparent compression of the brain in the phase-encoding direction for the combined measurements. It is related to the fact that only the frequency and linear shims were optimized for each subvolume while the second-order shims were non-optimal for both subvolumes. This is expected to introduce additional distortions compared to measurements focusing on one of the subvolumes alone. The improvement achievable in the spinal cord with a slice-specific z-shim is also visible in some slices of Figs. 3b and c.

Results of a comparison of the brain images obtained with a brain-optimized shim (see Fig. 2d) and the shim for the combined measurement (see Fig. 2f) in a group of seven volunteers are summarized in Fig. 4. For the combined measurements, the images clearly show a more pronounced compression in the posterior–anterior (y) direction (Fig. 4b) compared to the measurement with the shim being optimized for brain (Fig. 4a) which is most obvious in the corresponding difference images (Fig. 4c). This is also reflected in the scaling parameters required to normalize the data to the EPI template (Figs. 4d and e). While the data with the brain-optimized shim required a zoom factor of 1.096 ± 0.04 (mean ± standard deviation) in the y direction, those of the combined measurement needed a factor of 1.139 ± 0.05 which is significantly higher (t6 = 3.04, p = 0.02). Other zoom and shearing parameters were similar for the two measurements. However, both measurements showed a consistent but unusual large scaling factor in the head–feet (z) direction (1.255 ± 0.05). It seems to be related to the pronounced offcenter position of the brain slices (more than 100 mm) where gradient non-linearities could become relevant and effectively shift slices closer together than intended. For the data normalized to the EPI template (Figs. 4d and e), only a marginal difference was observed (Fig. 4f). This means that despite the more pronounced compression in the posterior–anterior direction, a reliable normalization result could be obtained for the combined measurements, i.e. it can be expected that the analysis of EPI data on the group level is only marginally affected by the additional distortions present in the combined measurement.

Aside from distortions, other image artifacts such as ghosting were observed occasionally. Typically, these artifacts could be reduced with
a re-adjustment of the system frequency or the frequency offset applied for the brain slices, respectively (data not shown). However, it was not always possible to find values for which ghosting could be avoided completely in all slices. In particular, the lowermost slices of both subvolumes were more likely affected and sometimes could only be improved significantly at the expense of ghosting artifacts in upper or central slices. A reason for this could be their vicinity to regions with susceptibility differences and their position at the border of the adjustment volume which may yield a non-optimal shim setup for these slices.

Another problem may arise from the fat saturation that is applied with a frequency offset compared to water (about 400 Hz at 3 T). If the resonance frequencies of the brain and spinal cord water differ similarly, the fat saturation applied for one subvolume, e.g. the brain, may saturate the water in the other subvolume, i.e. the spinal cord, which results in a considerably reduced signal amplitude. This problem can be circumvented by using a fixed frequency for fat saturation, which, however, means that it is effective only for one of the regions.

Fig. 5 shows results of the measurements performed to estimate the temporal SNR obtained either with a setup optimized for the brain and the spinal cord only or with combined measurements (Fig. 5a). The averaged temporal SNR in brain gray matter and the spinal cord was decreased by about 10% for the combined measurements (35.1 ± 8.5 vs. 31.4 ± 8.6 in the brain and 9.7 ± 3.0 vs. 8.6 ± 2.1 in the spinal cord) which could be related to the reduced field homogeneity and a correspondingly shortened T2* relaxation time. But in the spinal cord (Fig. 5b) a reduction of up to 20% could be observed in individual slices when ghosting artifacts were pronounced. They vary in time and, thus, increase the signal intensity variation within the spinal cord. Cerebrospinal fluid also yielded a pronounced temporal standard deviation, in particular around the spinal cord. This is related to the pulsatile flow over the cardiac cycle (e.g., Quencer et al., 1990) that cannot be accounted for sufficiently with the (first-order) flow compensation applied in the slice direction. However, this also affects measurements that cover the cervical spinal cord only.

Discussion

In the present work, we have presented an implementation of combined T2*-weighted measurements of the human brain and cervical spinal cord in vivo. The chosen setup involved voxel sizes and fields-of-view that were adapted to each region. The timing was optimized accordingly to provide a shorter echo time and echo train length for the slices in the brain that were acquired with a
Fig. 3. Example images obtained in three different volunteers showing (a) all 40 slices acquired with a combined measurement and (b, c) four brain and four spinal cord slices acquired with the shim optimized for the corresponding subvolume (upper) and the combined measurement with a slice-specific z-shim for the spinal cord slices (lower). See text for details.
lower spatial resolution, which reduced geometric distortions and signal dropouts. To achieve the best reconstruction results, a separate image reconstruction was used in the present study to consider the corresponding readout gradient moment, e.g. for regridding and correction of concomitant gradient fields (e.g., Du et al., 2002; Zhou et al., 1998). Furthermore, the relevant coil elements were dynamically selected with only the signal from the head coil being used for the slices in the brain and only the signal of the neck coil elements contributing to the slices covering the spinal cord. This approach improves the signal-to-noise ratio in the spinal cord considerably.

Finally, a dynamic update of the frequency and the linear shim values (Blamire et al., 1996; Morrell and Spielman, 1997) was performed during the measurement to provide the optimum values determined for each of the two regions. These settings are crucial to obtain image quality suitable for combined fMRI studies in both regions. Nevertheless, the combined acquisitions showed (i) slightly increased geometric distortions, in particular in the brain, (ii) an increased sensitivity to ghosting artifacts, and (iii) a slightly reduced temporal signal-to-noise ratio. However, it should be emphasized that these issues are solely related to the compromises that are required to cover the brain in the same acquisition as well, and includes the second-order shim settings, the dynamic coil selection, and the position of the isocenter relative to the subvolumes.

So far, only a few studies aimed to perform combined fMRI measurements of the human brain and the spinal cord during the same experiment (Cahill and Stroman, 2011; Ghazni et al., 2010; Komisaruk et al., 2002; Mainiero et al., 2007). They either considered only a very limited brain volume, up to the thalamus and usually with only a minor extend in left-right and/or posterior–anterior direction (Cahill and Stroman, 2011; Ghazni et al., 2010; Mainiero et al., 2007), or included only the uppermost section of the spinal cord, i.e. C1 (Komisaruk et al., 2002). The spatial resolution (3 × 3 mm² or 4 × 4 mm² in-plane) in the studies based on T2*-weighted BOLD fMRI (Komisaruk et al., 2002; Mainiero et al., 2007) was not optimal for the anatomical features of the spinal cord. To overcome this problem, other studies (Cahill and Stroman, 2011; Ghazni et al., 2010) employed RF refocused fast-spin-echo acquisitions with a high nominal in-plane resolution (typically 1 × 1 mm²). However, the T2-related signal decay during the long echo train may blur the image significantly in the phase-encoding direction. Furthermore, these approaches suffer from a low temporal resolution (typically 1 s per slice) and are, thus, not ideal for fMRI experiments.

Recently, BOLD signal responses to a hypercapnia paradigm were investigated in the human brain and spinal cord using a single stack of 30 slices with a fixed voxel size of 1.5 × 1.5 × 4.0 mm² (Cohen-Adad et al., 2010). BOLD effects could be observed reliably in both target regions in all participants but for fMRI applications the in-plane resolution could be considered to be too coarse in the spinal cord and the slice thickness to be not optimal in the brain. Furthermore rather large slice gaps between 4.4 mm and 5.2 mm had to be used that increase the risk of missing focal activation in fMRI.

In contrast, the approach presented here aimed to retain a well-established setup for brain fMRI and combine it with state-of-the-art spinal cord acquisitions without significant compromises regarding the volume coverage, the spatial resolution, the field-of-view, echo spacing, and slice thickness and orientation for both subvolumes. The brain and spinal cord subvolumes were covered with different slices, which not only allowed for specific geometry parameters but also for a dynamic selection of the relevant receive coil elements and a dynamic shim update for each region. Thus, the signal-to-noise ratio and the field homogeneity can be expected to be improved compared to sagittal and coronal orientations where brain and spinal cord regions are covered in the same slice. Regarding BOLD fMRI based on T2*-weighted echo-planar imaging this also implies that geometric distortions and signal dropouts are less pronounced.

A further improvement could be achieved if a dynamic update of higher-order shims could be performed (Koch et al., 2006) which was not possible in the current study due to limitations of hardware control. Even with the dynamic update of linear shims, residual distortions were observed as compared to the brain-only acquisition. Most likely, this difference is related to the second-order shim settings that were not optimized for the brain but for a much larger adjustment volume in order to retain a sufficient image quality in the spinal cord. The main effect of these distortions was a slight compression in the anterior–posterior direction. Although it can easily be corrected for with standard fMRI preprocessing algorithms (cf. Fig. 4), a reduction of these distortions with an adapted second-order shim
setup for each region would be desirable. In addition, such a dynamic update could help to reduce the ghosting artifacts and increase the temporal SNR.

In the present study, 32 brain slices were used (covering 95 mm) to be able to estimate the achievable image quality in a large brain volume. When targeting functional or effective connectivity between specific brain regions and the spinal cord, e.g. with dynamic causal modeling (Friston et al., 2003) or psychophysiological interaction analyses (Friston et al., 1997) a shorter repetition time than that used in the present study (3.27 s), is desirable which means that the number of slices must be reduced accordingly. Compared to conventional brain fMRI, the acquisition time per slice was prolonged from 63.8 ms to 78.5 ms in the brain and to 94.8 ms in the spinal cord. While the additional time required for the spinal cord slices is caused by the increased spatial resolution, a general time penalty is related to the spatial saturation pulses (see Fig. 1a). They are required to avoid aliasing in the spinal cord but were applied with each slice, i.e. also for the brain slices, to retain steady-state conditions.

To shorten the acquisition time per slice and to increase the volume coverage for a given repetition time, the saturation pulses could be skipped which could require to increase the field-of-view to avoid artifacts for volunteers with large necks. Alternatively, the saturation pulses could be applied for the spinal cord slices only. However, it may be necessary to perform the saturation twice or even more often prior to the first spinal cord slice to ensure a sufficient saturation effect.

Unlike for conventional measurements that cover either the brain or the spinal cord, the slice offcenter positions for combined measurement were as large as 160 mm for the brain where gradient non-linearities can become relevant. On the scanner used, the effective gradient amplitude is reduced by up to 10% for such an offset which not only degrades the effective in-plane resolution and slice thickness but also can yield an apparent scaling of the object in the image plane and an unwanted slice shift. Because these effects increase with the distance from the isocenter, non-rigid-body transformations may be required for a proper normalization between volunteers or with brain-only measurements.

The temporal SNR values that were obtained in the spinal cord in the present study (9.7 for the shim optimized for the spinal cord and 8.6 for the combined acquisition), are very similar to the value of 9.2 that can be calculated from data acquired for a previous study (Finsterbusch et al., 2012). The latter protocol, with minor modifications, has been
successfully applied for spinal cord fMRI (Sprenger et al., 2012), i.e. it can be expected that the image quality of the combined acquisitions is sufficient for fMRI of the spinal cord. In a previous study investigating the BOLD response to hypercapnia with EPI on an identical MR system (Cohen-Adad et al., 2010) a much higher value of 14 is reported for the spinal cord. Most likely, this difference is due to the much smaller voxel volume that was used in the current study (5 mm³ vs. 9 mm³). This is consistent with the value of 35 that is reported for the brain and is practically the same as in the present study (35.1) because the voxel sizes in the brain were also very similar (8 mm³ vs. 9 mm³).

Conclusion

The feasibility of combined T2*-weighted measurements of the human brain and cervical spinal cord has been demonstrated in vivo. Using (i) geometry parameters including voxel size and field-of-view adapted to each region and a correspondingly optimized sequence timing, (ii) a dynamic coil element selection, and (iii) a dynamic update of the frequency and linear shim values, an image quality that can be adapted to each region and a correspondingly optimized sequence using (i) geometry parameters including voxel size and the functional interplay between the brain and the spinal cord.

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Conflict of interest statement

The authors have no actual or potential conflict of interest including any financial, personal or other relationships with other people or organizations within three (3) years of beginning the work submitted that could inappropriately influence (bias) their work.

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