Anatomical Details of the Brainstem and Cranial Nerves Visualized by High Resolution Readout-segmented Multi-shot Echo-planar Diffusion-weighted Images using Unidirectional MPG at 3T

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We compared diffusion-weighted imaging (DWI) with readout-segmented multi-shot echo-planar imaging (rs-EPI) and single-shot EPI, both using unidirectional motion-probing gradient, in 10 patients for visualization of the anatomical structures in the brainstem. DWI by rs-EPI was significantly better than DWI by single-shot EPI for visualizing the medial longitudinal fasciculus, lateral lemniscus, corticospinal tract, and seventh/eighth cranial nerves and offered significantly less distortion of the brainstem.

Keywords: brainstem, diffusion-weighted imaging, magnetic resonance, medial longitudinal fasciculus, readout-segmented

Introduction

Diffusion-weighted imaging (DWI) to visualize the detailed anatomy of the brainstem and cranial nerves has been tried using multi-shot diffusion sequences, such as propeller-type acquisition1, line scan diffusion imaging,2 multi-shot spiral echo-planar imaging (EPI) with reduced field of view (FOV),3 cardiac-gated multi-shot EPI,4 or readout-segmented multi-shot EPI (rs-EPI).5 Usually performed as diffusion tensor imaging (DTI) with numerous motion-probing gradient (MPG) directions, these sequences often require long scan times, and misregistration from distortion difference or motion between the scans with different MPG directions obscures small structures. Diffusion-weighted neurography using unidirectional MPG and single-shot EPI has been proposed as a robust technique for visualizing the brachial or sacral plexus because there is no misregistration between images with different MPG directions.6 Single-shot EPI provides excellent time efficiency in terms of signal-to-noise ratio (SNR) but suffers severely from susceptibility-based distortion near bone and air. Cardiac-gated multi-shot EPI with unidirectional MPG to visualize brainstem structures has been reported at 1.5 tesla.7 The rs-EPI technique does not require cardiac gating and is based on the readout-segmented EPI method,8 which has been modified to incorporate 2-dimensional (2D) navigator phase correction9 and navigator-based reacquisition.5 Detailed elsewhere, this technique uses the same diffusion preparation as single-shot EPI DWI, but the k-space trajectory is divided into multiple segments in the readout direction. The k-space trajectory for each shot is similar to that of single-shot EPI, but instead of traversing all kx points, only a subset of points segmented in readout direction is sampled. The short kx range enables reduced echo spacing and susceptibility artifact. The navigator signal acquired using the second spin-echo samples the central kx segment for every shot, and this navigator data is used to apply a 2D phase correction in the image domain. The 2D correction allows correction of the nonlinear phase errors characteristic of non-rigid-body brain motion caused by pulsation of cerebrospinal fluid (CSF).9 Images acquired using this scheme of DWI with rs-EPI have higher spatial resolution and less susceptibility artifact than those obtained with single-shot EPI DWI, especially when the technique is combined with parallel imaging.5

In this study, we set up a protocol for acquisition
of DWI with rs-EPI using unidirectional MPG within a clinically acceptable scan time to visualize the detailed anatomy of the brainstem and cranial nerves, and we compared the degree of geometrical distortion and visibility of small structures in the brainstem and cisterns between images obtained by DWI with rs-EPI and DWI with single-shot EPI using unidirectional MPG at 3T.

Materials and Methods

All scans were performed on a 3T unit using a 32-channel phased array head coil (Verio, Siemens, Erlangen Germany). Initially, to establish pulse sequence parameters, we scanned 2 healthy male volunteers aged 28 and 60 years using an axial rs-EPI sequence with b-factors of 500, 700 and 1000 s/mm² and obtained images with MPG in 3 orthogonal directions. Scan parameters for rs-EPI were: axial slice parallel to the bilateral cisternal segment of the trigeminal nerves; repetition time (TR), 3800 ms; echo times (TE), 76 ms for b-factor of 500 s/mm², 81 ms for b-factor of 700 s/mm², and 88 ms for b-factor of 1000 s/mm²; 4 times of averaging; 12 slices of 4-mm thickness with 0.4-mm gap; 320 × 256 matrix; unidirectional MPG in slice-selective direction (superior-inferior, S-I), phase-encoding direction (anterior-posterior, A-P), or readout direction (right-left, R-L); GRAPPA (auto-calibrating partially parallel acquisitions) parallel imaging technique with acceleration factor of 2; number of k-space segmentation, 21; square field of view (FOV), 163 mm; and scan time of 6 to 7 min for each MPG direction depending on the frequency of navigator-based reacquisition. For example, rs-EPI with b-factor of 700 s/mm² in the S-I direction takes 6 to 7 min. Voxel size was 0.5 mm × 0.6 mm × 4 mm. Two radiologists, with 12 and 22 years’ experience in the field of MR imaging of the brain, subjectively evaluated images for positive or negative visualization of the brainstem and cranial nerve anatomy, discussing differing assessments to reach consensus. Referring to the anatomical literature, they assessed whether the brainstem anatomy was depicted: the medial and lateral lemniscus (ML, LL), medial longitudinal fasciculus (MLF), superior cerebellar peduncle in the pons (SCP), scattered fibers of the corticospinal tract in the pons (CST), trigeminal (Vth) nerve, and facial/vestibulocochlear (VII/VIIIth) nerve complex. Fibers of the ML, LL, CST, and MLF are anatomically aligned nearly parallel to the S-I direction; the cranial nerves stated above are oriented nearly perpendicular to the S-I direction; and the SCP is aligned oblique to the S-I direction. For example, the ML, LL, CST, and MLF are expected to show lower signal than surrounding tissues on DWI with MPG in the S-I direction. The individual structures merited positive scores for visualization if: the CST was scattered in 4 or more band-like structures in the pons; the SCP was observed as a boomerang-shaped structure in the posterior part of the pons lateral to the aqueduct; the fifth cranial nerve was visualized continuously from the root exit zone to Meckel’s cave; nerves of the seventh/eighth nerve complex could be followed continuously from the brainstem to the fundus of the internal auditory canal and the geniculate ganglion could be recognized, even if nerve shapes were distorted; and the ML, LL and MLF structures could be recognized in the positions indicated in the anatomical literature.

In the volunteer study, delineation of the enumerated structures was better with DWI with MPG in the S-I direction than either the A-P or R-L direction (Fig. 1). Delineation of the brainstem structures was better in images acquired with a b-factor of 700 s/mm² than 500 or 1000 s/mm². In both volunteers, all of the ML, LL, and MLF could be identified bilaterally only on rs-EPI images obtained with MPG of b = 700 s/mm² in the S-I direction (Table 1, Fig. 2). Based on these findings, we employed DWI with MPG in the S-I direction and b = 700 s/mm² for further evaluation in patients.

Ten consecutive patients with vertigo and/or hearing loss (6 men, 4 women, aged 27 to 74 years) underwent MR examination for inner ear pathol-ogy. The protocol also included DWI of the brainstem using rs-EPI and single-shot EPI. No patient showed any abnormality in the brainstem and cranial nerves in the cisterns on conventional MR images, including T₂-weighted and 3-dimensional (3D) fluid-attenuated inversion recovery (FLAIR) images. Scan parameters of axial DWI with rs-EPI were the same as applied for volunteers. MPG was applied only in the S-I direction with b-factor of 700 s/mm², and scan time was 6 to 7 min. Scan parameters of single-shot EPI were: the same axial slices as for rs-EPI; TR, 3800 ms; TE, 102 ms; number of averaging, 32, the maximum value of the scanner; 12 slices of 4-mm thickness with 0.4-mm gap; 192 × 192 matrix; b, 700 s/mm² only in slice direction (S-I); GRAPPA acceleration factor of 2; square FOV, 220 mm; and scan time, 2 min 15 s. Voxel size was 1.1 mm × 1.1 mm × 4 mm. Parameters of single-shot EPI were determined similarly as for our clinical protocol except for b-factor, number of excitations, and MPG direction. Normally, we apply a b-factor of 1000 s/mm² in 3 orthogonal directions and one to 2 as the number of averaging. We could not obtain the same spatial
Readout-segmented multi-shot echo-planar imaging (rs-EPI) of a 28-year-old male volunteer. a) Image with no motion-probing gradient (MPG), b = 0; b) image with MPG in superior-inferior (S-I) direction; c) image with MPG in right-left (R-L) direction; d) image with MPG in anteroposterior (A-P) direction. All diffusion-weighted images were acquired with b-factor of 700 s/mm². Fibers of the bilateral medial longitudinal fasciculus (MLF) are visualized only on the image with MPG in the S-I direction (b). The MLF is visualized as a spot with low signal on the image with MPG in the S-I direction (b).

Table 1. Visibility of each structure on diffusion-weighted images with readout-segmented echo-planar imaging (rs-EPI) in 2 volunteers (4 sides)

| MPG direction | Anterior-posterior (A-P) | Right-left (R-L) | Superior-inferior (S-I) |
|---------------|--------------------------|------------------|------------------------|
| b-factor (s/mm²) | 500 700 1000 | 500 700 1000 | 500 700 1000 |
| superior cerebellar peduncle (SCP) in the pons | 2/4 3/4 3/4 | 0/4 1/4 0/4 | 2/4 4/4 3/4 |
| medial lemniscus (ML) | 1/4 2/4 1/4 | 2/4 4/4 2/4 | 2/4 4/4 2/4 |
| lateral lemniscus (LL) | 1/4 2/4 1/4 | 0/4 2/4 0/4 | 0/4 4/4 1/4 |
| scattered corticospinal tract (CST) fibers in the pons | 1/4 2/4 2/4 | 3/4 3/4 3/4 | 3/4 4/4 4/4 |
| medial longitudinal fasciculus (MLF) | 0/4 1/4 0/4 | 0/4 2/4 0/4 | 1/4 4/4 0/4 |
| fifth cranial nerve (Vth) | 0/4 0/4 0/4 | 4/4 4/4 4/4 | 4/4 4/4 4/4 |
| seventh and eighth nerve complex (VII/VIIIth) | 4/4 4/4 3/4 | 0/4 0/4 0/4 | 4/4 4/4 4/4 |

MPG, motion-probing gradient

resolution by single-shot EPI as with rs-EPI because of scanner limitations.

Two radiologists evaluated images in the same fashion as for volunteers for positive or negative delineation of structures stated above for DWI with rs-EPI and single-shot EPI DWI of 20 sides in 10 patients. We then compared results of rs-EPI and single-shot EPI using Fisher’s exact probability test.

To compare the degree of susceptibility-based distortion, we measured the anterior-posterior length of the pons at the level of the root exit zone of the trigeminal nerve for rs-EPI, single-shot EPI, and 3D FLAIR by turbo spin echo (TSE) sequence, measuring the length at the midline of the pons. We obtained 3D FLAIR using the same axial orientation as for rs-EPI and single-shot EPI, with spatial resolution of 0.7 mm × 0.7 mm × 0.8 mm and scan time of 5.5 min. We defined length as the linear distance from the anterior surface of the pons to the anterior edge of the fourth ventricle and used the length measured on 3D FLAIR by TSE as the
Fig. 2. Readout-segmented multi-shot echo-planar imaging (rs-EPI) of a 60-year-old male volunteer. All 3 images are obtained with motion-probing gradient (MPG) in the superior-inferior (S-I) direction. Images with a) b-factor of 500 s/mm², echo time (TE) of 76 ms; b) b-factor of 700 s/mm², TE of 81 ms; c) b-factor of 1000 s/mm², TE of 88 ms. Delineation of the superior cerebellar peduncle (SCP), medial lemniscus (ML), medial longitudinal fasciculus (MLF), and lateral lemniscus (LL) is best on the image with b-factor of 700 s/mm² (b). On the image with b-factor of 500 s/mm², signal decrease of the fibers aligned parallel to the S-I direction, such as the corticospinal tract (CST), ML, LL, and MLF is not enough for clear differentiation from surrounding tissue (a). On the image with b-factor of 1000 s/mm², signal decrease of the fibers aligned parallel to the S-I direction is prominent, especially in the CST; however, in the posterior part of the pons, surrounding tissues of the ML, LL and MFL also become dark, probably as a result of longer echo time (c). A balance of the degree of diffusion weighting and T₂-weighting seems important for delineating small structures in the brainstem.

Results

Table 2 delineates the visibility of anatomical structures. Visibility was significantly better on rs-EPI for the LL, MLF, CST, and seventh/eighth nerve complex (P < 0.05) (Fig. 3). The average ratio of anterior-posterior length of the pons on single-shot EPI (1.188 ± 0.193) was significantly larger than that on rs-EPI (1.017 ± 0.046), which objectively suggests more prominent elongation due to distortion on single-shot EPI than on rs-EPI. Although visualization of the seventh/eighth nerve complex was better on rs-EPI, residual susceptibility-based distortion of the nerves remained, even
Table 2. Visibility of each structure on diffusion-weighted images with readout-segmented echo-planar imaging (rs-EPI) and single-shot EPI in 10 patients (20 sides)

| Structure                              | rs-EPI | Single-shot EPI |
|----------------------------------------|--------|-----------------|
| superior cerebellar peduncle (SCP) in the pons | 20/20  | 18/20 n.s.      |
| medial lemniscus (ML)                  | 20/20  | 20/20 n.s.      |
| lateral lemniscus (LL)                 | 15/20  | 8/20 P<0.05     |
| scattered corticospinal tract (CST) fibers in the pons | 20/20  | 7/20 P<0.05     |
| medial longitudinal fasciculus (MLF)   | 20/20  | 4/20 P<0.05     |
| fifth cranial nerve (Vth)              | 20/20  | 18/20 n.s.      |
| seventh and eighth nerve complex (VII/VIIIth) | 20/20  | 8/20 P<0.05     |

Fig. 3. A 74-year-old man complaining of vertigo with no abnormal findings on conventional magnetic resonance imaging. Enlarged images of the pons are presented: (a, c) Readout-segmented multi-shot echo-planar images (rs-EPI); (b, d) single-shot EPI diffusion-weighted images. The lateral lemniscus (LL) is visualized on rs-EPI (a) but not single-shot EPI (b). The corticospinal tract (CST) is divided into multiple low signal bands on the rs-EPI image (a) but not the single-shot EPI image (b). The medial lemniscus (ML) is visualized on both rs-EPI and single-shot EPI images (a, b). The superior cerebellar peduncle (SCP) is visualized as a boomerang-shaped area of hyperintensity on both rs-EPI (c) and single-shot EPI images (d). However, the medial longitudinal fasciculus (MLF) can be recognized only on rs-EPI (e) in this patient.

Discussion

Our results showed that rs-EPI could provide higher spatial resolution DWI with less distortion than single-shot EPI. Better delineation of small structures in the brainstem and cranial nerves by rs-EPI might be valuable for a variety of clinical studies. However, the scan time of rs-EPI in the present study was longer than that of single-shot EPI. Unlike the previously reported high resolution DWI of the brainstem using multi-shot EPI without navigator echo,7 rs-EPI in the present study did not require cardiac gating. Cardiac gating sometimes fails because of incomplete triggering signal in the magnet room, arrhythmia, and the patient’s muscle contraction. Previously reported cardiac-gated DWI by multi-shot EPI without navigator echo could not compensate for phase errors induced by other causes, such as respiration or gross motion. The rs-EPI in the present study rejected data with significant phase error and is thought, therefore, to be more robust than gated DWI by multi-shot EPI. The spatial resolution of previously reported cardiac-gated DWI by multi-shot EPI was 0.8 mm × 1.1 mm × 5 mm, which is 3.6 times larger than the 0.5 mm × 0.6 mm × 4 mm of rs-EPI in the present study.

The intensive computer memory requirement of rs-EPI for navigator echo-based reacquisition limited the number of slices to fewer than expected in a given repetition time on the current scanner hardware. Although distortion was less than with single-shot EPI, susceptibility-related distortion was still significant in the vicinity of bone and air, as seen for the seventh/eighth nerve complex.

The results of the initial volunteer scans showed better delineation of the MLF, ML, and LL on rs-EPI with b-factor of 700 s/mm² than those with b-factor of 500 and 1000 s/mm². With b-factor of 500 s/mm², the decrease in signal of white matter fibers aligned in the S-I direction was insufficient to be delineated from surrounding tissue. On images with b-factor of 1000 s/mm², signal decrease of surrounding tissue probably due to longer echo time of the images with b-factor of 1000 s/mm² might have obscured white matter fibers aligned in the S-I direction. The moderate degree of T₂ and diffusion weighting on the rs-EPI images with b-factor of 700 s/mm² might have synergistically contributed to the excellent visualization of fine anatomical structures shown.

Line scan DTI using 0.9 mm × 0.9 mm resolution was previously employed to visualize the MLF.2
Other studies used DTI by single-shot EPI to evaluate the sensory white matter tract of the ML, but they employed in-plane spatial resolution of 1 mm × 1 mm or 1.7 mm × 1.7 mm. In the brainstem, the LL is the smaller auditory pathway than the ML, and decreased fractional anisotropy of the bilateral LL has been reported in patients with unilateral congenital cochlear nerve deficiency using single-shot EPI DTI with in-plane resolution of 1.5 mm × 1.5 mm. Compared to these previous DTI studies, we applied higher in-plane spatial resolution (0.5 mm × 0.6 mm) in our rs-EPI protocol, so it is quite reasonable that we could visualize small structures, such as the LL, ML, and MLF. Furthermore, we used DWI with unidirectional MPG and thereby obtained images free of misregistration among data with different MPG directions. The present method might be applied clinically to evaluate MLF syndrome, multiple system atrophy, Parkinson disease, long-term sensorineural hearing loss, and other conditions.

Our study has some limitations. Though we referred to anatomical literature, there is no histological proof for the visualized anatomy. Therefore, it is not perfectly proved that the small structures visualized, such as the MLF and LL, exactly reflect the true anatomy. In addition, limitations of the scanner did not permit the same scan time and spatial resolution for rs-EPI and single-shot EPI. The maximum value of the scanner for averaging number for single-shot EPI was 32, so the scan time of single-shot EPI was only one-third that of rs-EPI. The lower spatial resolution of single-shot EPI likely affected our results because the distortion of single-shot EPI would have been more prominent if the resolution of single-shot EPI was the same as that of rs-EPI. Echo time could not be same, and the longer echo time for single-shot EPI might have caused the heavier contamination of T2 contrast with that method. Quantitative analysis is difficult based only on DWI by unilateral MPG with a single b-value. Unlike pixel value on fractional anisotropy or apparent diffusion coefficient maps, that on DWI itself is susceptible to receiver coil inhomogeneity, tilt angle of the head, and T2 shine-through effect. Despite these limitations, the robustness of our present study results encourages the further detailed optimization and clinical study using rs-EPI to visualize small structures in the brainstem.
Conclusions

High spatial resolution DWI with rs-EPI using a unidirectional MPG can be obtained in a clinically acceptable scan time and might be a robust method to visualize fine structures in the brainstem and cisterns. Moderate T2-weighted contrast and signal suppression of tracts parallel to the S-I direction achieved using the proposed method might have synergistically contributed to the excellent visualization of fine anatomical structures shown in this study.

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