The Origins of fMRI Contrast in SPEN Imaging at Ultra High Magnetic Fields

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Introduction: Spatiotemporal encoding (SPEN) is a novel spin manipulation technique capable of delivering arbitrary multidimensional NMR spectra or MRI images in a single scan [1]. At the core of SPEN lies replacing the conventional time- or phase-encoding increments used in nD NMR/MRI, by frequency-swept (chirped) pulses executed under the action of field gradients. When considered in a real-time or fMRI setting, SPEN provides significantly higher immunity to B_0-inhomogeneities and chemical-shift offsets than EPI counterparts [2]. The sequence can also deliver images that are fully refocused vis-à-vis T2* and/or T2 effects [2, 3]; all these features make SPEN a promising option for ultra-high magnetic field studies. Recent studies have reported fMRI SPEN experiments of the visual human cortex at 3T [4]. This presentation examines the origin of the function-derived activation detected by SPEN fMRI, with a series of preclinical high (7T) and ultra-high (17.2T) magnetic field studies. Artifact-free images of a rat's head with good resolution in all areas and localized activation maps upon forepaw stimulation were obtained in a single scan using a variety of SPEN sequences. These included T2*-weighted acquisitions and a fully T2*-refocused variant where each readout event coincides with its own TE –and thereby all T2* contributions are absent [2]. Our data shows that, besides the normal T2*-weighted BOLD contribution which arises in non-refocused sequences, fMRI SPEN signals contains a strong component caused by apparent T1-related inflow effects. This contribution can be modulated by varying the scanning repetition rate; measurements obtained at 7T support this finding.

Methods: Experiments were conducted on Bruker Avance III 17.2T and 7T scanners using custom-written sequences. Ten male SD rats (250~300 g) were anesthetized using medetomidine with an initial dose of 110 µg/kg followed, after 20 minutes, by administration of a continuous injection. This continuous injection was gradually increased within a 2-hour period, from 100 µg/kg/h to 300 µg/kg/h, in order to avoid down-regulation of the receptors. Electric stimuli were delivered to rat forepaw using a Phymep isolated pulse stimulator (pulse duration 0.3 ms, frequency 7 Hz, current intensity of 2.3mA). We used a block-design paradigm consisting of 5 blocks (30s rest, 30s activation), with 10 minutes rest between sessions to prevent habituation and ensure a return to baseline. Studies lasted up to 3 hours. Common acquisition parameters: FOV: 2 cm x 2 cm, matrix size 100 x 100, slice thickness 1.2 mm, BW 400 kHz at 17.2T, 357 kHz at 7T. GE EPI parameters: TE=11 ms, TR=1500 ms. SPEN parameters: T_{acq}= 25ms, $T_{exc,full\text{-}refocusing}$ = 25msec, $T_{exc,non\text{-}refocused}$ = 5msec. For GE-EPI three coronal slices were acquired, which included the primary and secondary somatosensory cortex. One of the activated slices was choosen as focus of the 2D SPEN acquisitions. All SPEN data were post-processed with in-house Matlab image-reconstruction algorithms based on super-resolution (SR) principles [5]. Statistical analyses were performed using SPM 8, including slice-timing, motion correction and spatial smoothing. Clusters were considered significant when the associated p value were smaller then $p<0.005$.

Results: Figure 1 compares typical GE EPI and SPEN activation maps, overlaid on the average single-scan images acquired during the functional tasks. Surprisingly, even in the absence of all T2* contributions, the fully refocused SPEN image observed for TR=1.5s yields strong, localized activation maps with good t-score levels (Fig. 1b). Increasing TR from 1.5s to 3s substantially lowers these t-score levels and activates much fewer pixels (Fig. 1c). This TR dependence strongly suggests that T1-related effects contribute to the fMRI SPEN signal at these high fields. Further evidence of this contribution is found by performing similar experiments at 7T. Such experiments (data not shown) showed that as the field decreases and T1s get progressively shorter, the fMRI contrast in the fully refocused SPEN acquisitions also decreases: For TR=1.5s the t-scores for SPEN were approximately three times smaller than for GE EPI. An additional set of experiments, shown in Figure 2, evidences that switching from a fully T2*-refocused SPEN sequence where $T_{exc} = T_{acq}$, to a non-refocused condition, brings out a classical T2*-driven BOLD contrast with very similar activation maps (in terms of t-score and size of the activated region) as GE EPI.

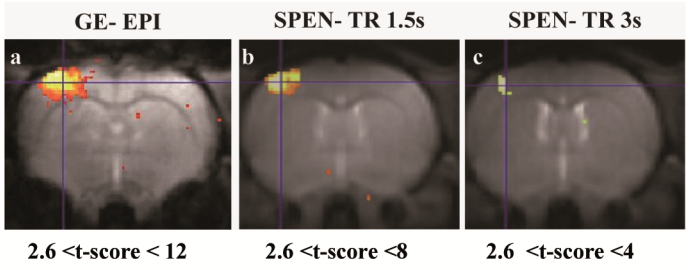

Figure 1. Comparison between GE EPI and SPEN fMRI maps recorded at 17.2 T. (a) GE- EPI, (b) fully T2*-refocused SPEN; TR 1.5s (c) fully T2*-refocused SPEN; TR 3s.

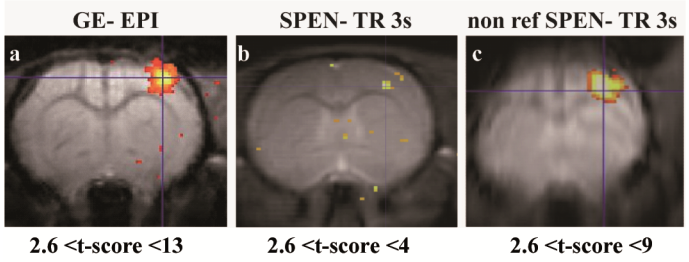

Figure 2. Comparison between GE-EPI, fully refocused and non –refocused SPEN fMRI maps recorded at 17.2 T. (a) GE- EPI, (b) fully refocused SPEN; TR 3s (c) non refocused SPEN ; TR 3s.

Discussion: This study shows that single-scan SPEN can be used as method of choice for ultra-high magnetic field fMRI, delivering a strong activation related to T1 based in-flow and/or to T2* effects –depending on the chosen sequence parameters. This finding, coupled with the good image quality and the absence of susceptibility or chemical shift artifacts, make SPEN imaging at ultra-high magnetic field a very attractive and interesting tool to explore functional activation.

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