

Investigating the field-dependence of the Davis model: Calibrated fMRI at 1.5, 3 and 7 tesla

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Purpose Calibrated functional magnetic resonance imaging (fMRI) has emerged as a promising tool to non-invasively measure stimulus evoked changes in the cerebral metabolic rate of oxygen consumption (CMRO₂).¹ Such experiments are most often performed at 3T, but with the emergence of 7T research systems and the clinical dominance of 1.5T there is interest in translating this method to other field strengths. It is clear that as a physiological parameter CMRO₂ should not be affected by the field strength at which it is measured. However, calibrated fMRI relies on a simple model of the Blood Oxygenation Level Dependent (BOLD) signal known as the Davis model¹ and it is unclear how translation to different field strengths affects its accuracy. Previously the accuracy of the assumed values of α and β in the Davis model equation across field strengths has been examined.² Here we implemented a standard calibrated fMRI protocol at 1.5, 3 and 7T to test the level of agreement in the measured estimates of CMRO₂ across field strengths.

Methods In this pilot study, 4 consenting subjects (1 female, mean age 26±3 years) were scanned on 1.5T Avanto, 3T Verio and 7T systems (Siemens Healthcare, Erlangen, Germany). Because specific absorption rate (SAR) was anticipated to be the limiting factor on sequence design at 7T, a pulsed arterial spin labeling sequence (FAIR with QUIPSS II saturation³) was implemented to measure cerebral blood flow (CBF), and only 6 slices were acquired. A single TE at 17ms provided sufficient SNR for both CBF and BOLD analysis at 3 and 7T; a dual echo version of the same sequence was implemented at 1.5T (TE1/TE2=17/50ms) to ensure sufficient BOLD signal. Other imaging parameters were TR=3s, T11=700ms, T12=1800ms, BW=3004 Hz/Px, FOV=265x265mm, resulting in 4.1x4.1x5.0mm³ voxels.

A bilateral finger tapping motor task was chosen to easily allow a consistent implementation across scanner suites. Subjects were given audio cues over the intercom systems and were instructed to perform 4 blocks of fast finger tapping (48s ON, 48s OFF), and were then exposed to 2 blocks of hypercapnia (3 min duration, each followed by 2 mins of air). Gas delivery and sampling was achieved through a nasal cannula (dual Nare, Flexicare, Mountain Ash, UK) in conjunction with a CO₂ gas analyzer (CO2 100C, Biopac Systems, Goleta, CA, USA). A 10% CO₂ gas mixture was delivered, which mixed with room air at a ratio of approximately 1:1, resulting in a ~5% CO₂ stimulus.

Data were analyzed using FSL,⁴ with a highpass filter of 300s and a spatial smoothing kernel of 6mm (for ROI definition only). To avoid circular analysis, data from motor tasks 1+2 were used to create a region of interest (ROI), and only data acquired during motor tasks 3+4 were analyzed to quantify response to motor stimuli. ROIs were defined for each scanning session based on the intersection of BOLD and CBF responses to motor tasks 1+2 (responses were deemed significant if p<0.01 for BOLD, or p<0.10 for ASL). Voxels with a BOLD response to either stimulus <0 or >15%, or a CBF response <0 or >200% relative to baseline, were assumed to be noise or to contain significant fractions of white matter or CSF, and were excluded from further analysis. Mean values within the resulting ROI for BOLD and CBF responses to motor tasks (3+4) and to hypercapnia were used to calculate M and CMRO₂ using Eq. 1, with $\alpha=0.2$ and $\beta=1.5/1.3/1$ at 1.5/3/7T respectively.⁵⁻⁸

Results All subjects completed all scans successfully. Examples of fractional BOLD and CBF responses to motor tasks are shown in Fig. 1 (taken from the same subject; data have been smoothed), along with initial motor ROIs defined by the intersection of statistically significant BOLD and flow responses. Group average responses within motor ROIs are shown in the table below (4 subjects at each field strength; CBF and CMRO₂ are quoted relative to baseline values, with 1 indicating no change). The calibration parameter M is equal to $TE \times A \times CBV_0 \times [dHb]_{v0}^\beta$, where A is a proportionality constant, CBV₀ is the baseline cerebral blood volume and [dHb]_{v0} is the baseline venous deoxyhemoglobin concentration of the blood. As the optimal BOLD-weighted echo time varies with field strength, it is instructive to scale M to this optimal echo time for each field strength (50/35/25ms at 1.5/3/7T).¹⁰ To do this we assume that A has no dependence on TE, and multiply the calculated M by the ratio (optimal TE/actual TE). Fig. 2 shows variation in M with field strength, where each subject is represented by a different color.

Discussion As expected, BOLD responses to both motor and hypercapnic stimuli were strongly dependent on field strength. BOLD echo times were close to optimal at 1.5 and 7T, hence the BOLD response appears smallest at 3T (see Fig. 1). After adjusting M to the optimal BOLD echo time, M increases monotonically with field strength (Fig. 2). This relationship has previously been predicted by simulations to be linear.² The relationship between M and field strength is a complex one, due to the opposing effects of reduced echo time and increase magnetic field on the BOLD response. As stated above, CMRO₂ should not be affected by field strength. It is difficult to verify this hypothesis based on the 4 subjects scanned so far, but it is encouraging that CMRO₂ measured at 1.5 and 7T is equivalent (to within experimental error/noise).

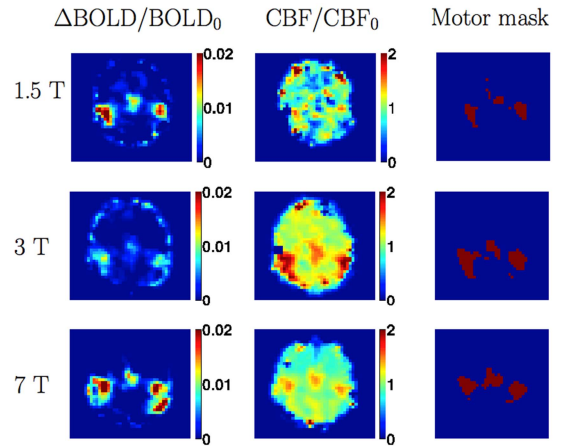
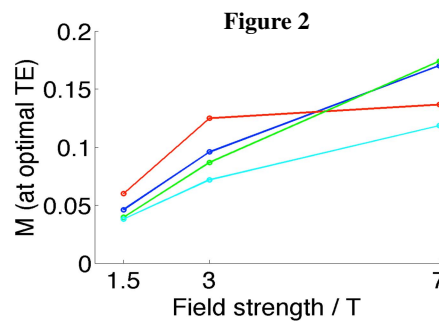


Figure 1

$$\frac{\Delta BOLD}{BOLD_0} = M \left\{ 1 - \left(\frac{CMRO_2}{CMRO_{2|0}} \right)^\beta \left(\frac{CBF}{CBF_0} \right)^{\alpha-\beta} \right\} \quad \text{Eq. 1}$$

	1.5 T	3 T	7 T
	Mean ± SD	Mean ± SD	Mean ± SD
BOLD to CO2	1.61% ± 0.34%	1.06% ± 0.37%	1.45% ± 0.22%
BOLD to motor	1.75% ± 0.14%	0.80% ± 0.11%	2.09% ± 0.19%
CBF to CO2	1.40 ± 0.03	1.26 ± 0.05	1.21 ± 0.01
CBF to motor	1.71 ± 0.06	1.61 ± 0.07	1.53 ± 0.09
M	4.59% ± 1.00%	4.61% ± 1.09%	10.20% ± 1.83%
M at optimal TE	4.59% ± 1.00%	9.49% ± 2.24%	14.99% ± 2.69%
CMRO ₂ to motor	1.14 ± 0.12	1.29 ± 0.07	1.10 ± 0.04



References 1. Davis TL *et al.* PNAS 1998; 95: 1834-9. 2. Blockley N *et al.*, Proc. ISMRM 2013 #2347. 3. Wong EC *et al.* MRM 1998; 39: 702-8. 4. Jenkinson M *et al.* NeuroImage 2012; 62: 782-90. 5. Chen J and Pike G. NMR Biomed 2009; 22: 1054-62. 6. Davis T, *et al.* PNAS 1998; 95:1834-9. 7. Mark C *et al.* NeuroImage 2009; 54:1102-11. 8. Uludag K *et al.* NeuroImage 2009; 48: 150-65. 9. Hoge RD *et al.* MRM 1999; 42: 849-63. 10. van der Zwaag W *et al.* NeuroImage 2009; 47: 1425-34.