

### Titre de l'étude

**Etude méthodologique de l'imagerie de la plasticité synaptique par IRM de diffusion**

### Auteurs/PI/Institution/Labo

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### Contexte/Objectif de l'étude

Mettre au point une méthodologie et une base de données en IRM de diffusion multimodale permettant d'évaluer la plasticité synaptique par IRM de diffusion chez des sujets sains jeunes et âgés.

### Prestation du Plateau Technique

#### Séquences :

3D T1 : 1\*1\*1 mm, 4mn23

DWI\_IVIM : 2\*2\*2,1 mm, 11b (0 à 1500) 9mn54

DfMRI : 3\*3\*4mm, 5b (1500, 1000, 500, 250, 0)

EPI : 3\*3\*4mm, TR/TE= 2000/35ms

#### Matériel :

- Antenne 8 CX
- NNL googles

Période : juillet 2010 – octobre 2012

### Publication (2017)



Original contribution

Comparison of BOLD, diffusion-weighted fMRI and ADC-fMRI for stimulation of the primary visual system with a block paradigm

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#### ARTICLE INFO

Article history:  
Received 4 July 2016  
Received in revised form 30 January 2017  
Accepted 31 January 2017  
Available online xxx

Keywords:  
Diffusion-weighted functional MRI  
BOLD  
ADC  
Primary visual system V1  
fMRI stimulation paradigm  
IVIM  
Cytarchitectur  
Cytarchitectonic  
Grey matter

#### ABSTRACT

The blood oxygen level-dependent (BOLD) effect is extensively used for functional MRI (fMRI) but presents some limitations. Diffusion-weighted fMRI (dfMRI) has been proposed as a method more tightly linked to neuronal activity. This work proposes a protocol of dfMRI acquired for several b-values and diffusion directions that is compared to gradient-echo BOLD (GE-BOLD) and to repeated spin-echo BOLD (SE-BOLD) acquisitions performed with  $b = 0 \text{ s/mm}^2$ , which was also used to ensure the reproducibility of the response. A block stimulation paradigm of the primary visual system (V1) was performed in 12 healthy subjects with checkerboard alternations (2 Hz frequency). dfMRI was performed at 3 T with 5 b-values ( $b = 1500, 1000, 500, 250, 0 \text{ s/mm}^2$ ) with TR/TE = 1004.93 ms,  $\Delta b = 45.4 \text{ ms/50 ms}$ , and 6 spatial directions for diffusion measures. GE-BOLD was performed with a similar block stimulation design timing. Apparent Diffusion Coefficient (ADC)-fMRI was computed with all b-values used. An identical Z-score level was used for all fMRI modalities for the comparison of volumes of activation. ADC-fMRI and SE-BOLD fMRI activation locations were compared in a voxel-based analysis to a cytoarchitectural probability map of V1. SE-BOLD activation volumes represented only 55% of the GE-BOLD activation volumes ( $P < 0.0001$ ). dfMRI activation volumes averaged for all b-values acquired represented only 12% of GE-BOLD ( $P < 0.0001$ ) and only 22% of SE-BOLD activation volumes ( $P < 0.005$ ). Compared to SE-BOLD-fMRI, ADC-fMRI activations showed fewer pixels outside of V1 and a higher average probability of belonging to V1. dfMRI and ADC-fMRI acquisition at 3 T could be easily post-processed with common neuro-imaging software. dfMRI and ADC-fMRI activation volumes were significantly smaller than those obtained with SE-BOLD. ADC-fMRI activations were more precisely localized in V1 than those of SE-BOLD-fMRI. This validated the increased capability of ADC-fMRI compared to BOLD to enhance the precision of localizing an fMRI activation in the cytoarchitectural zone V1, thereby justifying the use of ADC-fMRI for neuro-scientific studies.

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#### 1. Introduction

The blood oxygen level-dependent (BOLD) signal [1] is extensively used in research and clinical practice to perform functional MRI

Abbreviations: ADC, apparent diffusion coefficient; BOLD, blood oxygen level-dependent; CPMG, Carr-Purcell-Meiboom-Gill; dfMRI, diffusion-weighted fMRI; DW, diffusion-weighted; EDO, extra-vascular dynamic dephasing; ESO, extra-vascular static dephasing; FEAT, fMRI Expert Analysis Tool; FLAME, fMRI local analysis of mixed effects; fMRI, functional MRI; FWHM, full width at half maximum; GE, gradient-echo; GRE, Gaussian random field; ICA, independent component analysis; IVA, intra-vascular dynamic averaging; IFS, intra-vascular frequency shift; IVIM, intra-vascular incoherent motion; MFG, magnetic field gradients; MNI, Montreal Neurological Institute; MRI, Magnetic Resonance Imaging; SE, spin-echo; SPM, Statistical Parametric Mapping; VBA, voxel-based analysis; VOI, volume of interest.  
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<http://dx.doi.org/10.1016/j.mri.2017.01.022>  
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(fMRI). BOLD is dependent on vascular processes presumably reflecting "brain activation" toward a hypothesized coupling process between neuronal activity, blood oxygenation and dynamics [2].

The BOLD effect is caused by a local decrease in magnetic susceptibility in tissue when paramagnetic deoxyhemoglobin is converted to diamagnetic oxyhemoglobin in brain vessels near activation. This is due to an increase in blood oxygen consumption and blood flow in brain vessels [1]. To ensure maximal sensitivity, BOLD is generally measured with gradient echo (GE) MRI pulse sequences, very sensitive to magnetic susceptibility [3]. Using spin echo (SE) pulse sequences instead of GE pulse sequences makes the BOLD signal insensitive to local T<sub>2</sub>-based relaxation [3] and therefore less intense.

As BOLD is a method sensitive to blood dynamics and oxygenation in large and small vessels [4–7] and not directly to neuronal activity, BOLD currently has some limitations [2]. However, two different types of novel fMRI imaging methods overcoming the limitations of BOLD and

### Publication 2 (2015)

#### Accuracies and Contrasts of Models of the Diffusion-Weighted-Dependent Attenuation of the MRI Signal at Intermediate $b$ -values



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**ABSTRACT:** The diffusion-weighted-dependent attenuation of the MRI signal  $E(b)$  is extremely sensitive to microstructural features. The aim of this study was to determine which mathematical model of the  $E(b)$  signal most accurately describes it in the brain. The models compared were the monoexponential model, the stretched exponential model, the truncated cumulant expansion (TCE) model, the biexponential model, and the triexponential model. Acquisition was performed with nine  $b$ -values up to 2500 s/mm<sup>2</sup> in 12 healthy volunteers. The goodness-of-fit was studied with  $F$ -tests and with the Akaike information criterion. Tissue contrasts were differentiated with a multiple comparison corrected nonparametric analysis of variance.  $F$ -test showed that the TCE model was better than the biexponential model in gray and white matter. Corrected Akaike information criterion showed that the TCE model has the best accuracy and produced the most reliable contrasts in white matter among all models studied. In conclusion, the TCE model was found to be the best model to infer the microstructural properties of brain tissue.

**KEYWORDS:** diffusion MRI, model accuracy, kurtosis, cumulant expansion, Akaike information criterion, brain, IVIM

**CITATION:** Nicolas et al. Accuracies and Contrasts of Models of the Diffusion-Weighted-Dependent Attenuation of the MRI Signal at Intermediate  $b$ -values. *Magnetic Resonance Insights* 2015;8:11–21 doi:10.4137/MRI.S25301.

**RECEIVED:** February 25, 2015. **RESUBMITTED:** April 23, 2015. **ACCEPTED FOR PUBLICATION:** April 25, 2015.

**ACADEMIC EDITOR:** Seshini Vejan, Editor in Chief

**TYPE:** Original Research

**FUNDING:** This work was supported by the LECMA (Ligue Européenne Centre la Maladie d'Alzheimer), the EPHE (Ecole Pratique des Hautes Etudes), and by the 2013 joint fellowship of the CNRS (Coopérative Française de Neurovasculaires) and France AIC, dedicated to fundamental stroke research. The authors confirm that the funder had no influence over the study design, content of the article, or selection of this journal.

**COMPETING INTERESTS:** Authors disclose no potential conflict of interest.

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#### Introduction

Diffusion MRI (dMRI) is a powerful *in vivo* method for exploring biological microstructures.<sup>1</sup> The contrast of diffusion-weighted (DW) images is dependent on the magnitude of the diffusion-weighting factor ( $b$ -value). In clinical practice, especially for fast and early detection of ischemic stroke, DW images are generally acquired with a unique  $b$ -value ( $b = 1000$  s/mm<sup>2</sup>). The geometric mean of DW images over three spatial directions is then used to calculate apparent diffusion coefficient (ADC) maps<sup>2</sup> with the help of a monoexponential model (MEM) formalism. As it uses the same limited range of  $b$ -values but is acquired for 6–60 spatial directions,<sup>3</sup> diffusion tensor imaging is also an MEM that includes the effect of water diffusion anisotropy<sup>3</sup> and leads to the calculation of a rotationally invariant form of the ADC, the mean diffusivity.

On the other hand, the higher the  $b$ -value, the more sensitive the DW images are to smaller absolute random displacements of water molecules, and therefore to the microscopic structures of brain tissue.<sup>1</sup> Therefore, high  $b$ -value dMRI consists of recording series of DW images with successively increasing  $b$ -values up to relatively high values ( $b = 2500$  to  $\sim 12,000$  s/mm<sup>2</sup>). The number of spatial direction measures acquired is adapted depending on the time constraints. The

DW-dependent attenuation of the MRI signal obtained in each image pixel is related by Fourier transformation to the water displacement probability distribution ( $g$ -space method). In brain tissue, the standard deviation of this distribution has a characteristic length scale of tenths of  $\mu\text{m}$ ,<sup>4,5</sup> making it possible to investigate some microstructural changes related to cerebral insults.<sup>2</sup> However, Fourier transformation of the DW-dependent attenuation of the MRI signal ( $g$ -space) requires experimentally challenging conditions, whereas signal modeling is more flexible. Indeed, the DW-dependent attenuation of the MRI signal (designated as  $E(b)$ ) acquired with intermediate or high  $b$ -values needs to be modeled numerically with a mathematical function describing its non-exponential decay, which is relevant to the postulated properties of the microscopic structures present in brain tissues.<sup>4,6–8</sup> High  $b$ -value dMRI modeling and  $g$ -space are very sensitive to microscopic water displacements, highlighting white matter (WM) structures<sup>7,8</sup> or cerebral insults in animals<sup>9–12</sup> and in human brains,<sup>5,13</sup> and thus having a potential clinical interest.

Two types of models are needed for the study of diffusion imaging. The first (signal models) describes empirically how the  $E(b)$  signal decays, whereas the second (tissue models) describes how the signal relates to the underlying tissue

### Publication 3