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A validation of dynamic causal modelling for 7T fMRI

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ABSTRACT

Background: There is growing interest in ultra-high field magnetic resonance imaging (MRI) in cognitive and clinical neuroscience studies. However, the benefits offered by higher field strength have not been evaluated in terms of effective connectivity and dynamic causal modelling (DCM).

New method: In this study, we address the validity of DCM for 7T functional MRI data at two levels. First, we evaluate the predictive validity of DCM estimates based upon 3T and 7T in terms of reproducibility. Second, we assess improvements in the efficiency of DCM estimates at 7T, in terms of the entropy of the posterior distribution over model parameters (i.e., information gain).

Results: Using empirical data recorded during fist-closing movements with 3T and 7T fMRI, we found a high reproducibility of average connectivity and condition-specific changes in connectivity – as quantified by the intra-class correlation coefficient (ICC = 0.862 and 0.936, respectively). Furthermore, we found that the posterior entropy of 7T parameter estimates was substantially less than that of 3T parameter estimates; suggesting the 7T data are more informative – and furnish more efficient estimates.

Compared with existing methods: In the framework of DCM, we treated field-dependent parameters for the BOLD signal model as free parameters, to accommodate fMRI data at 3T and 7T. In addition, we made the resting blood volume fraction a free parameter, because different brain regions can differ in their vascularization.

Conclusions: In this paper, we showed DCM enables one to infer changes in effective connectivity from 7T data reliably and efficiently.

1. Introduction

Functional magnetic resonance imaging (fMRI) measures the blood oxygenation level dependent (BOLD) signal as a reflection of neuronal activity. The signal arises from magnetic susceptibility differences between deoxygenated blood in venous vessels and the surrounding tissue (Ogawa et al., 1990). Intrinsic signal-to-noise ratio (SNR) and BOLD signal contrast increase with field strength, which can be exploited to improve spatial resolution (Yacoub et al., 2001). These and related reasons have motivated an interest in using ultra-high field (7T and above) MRI in cognitive and clinical neuroscience studies (Martino et al., 2018).

Several studies have investigated the potential benefits of 7T MRI for detecting and characterizing functional connectivity (Hale et al., 2010; Newton et al., 2012; Vu et al., 2017). Specifically, Hale et al. (2010) assessed the effects of increased contrast-to-noise ratio (CNR) – at higher field strength – on estimates of functional connectivity. They showed increased temporal correlation within the sensory motor and default mode networks at 7T, compared to 3T. In addition, Newton et al. (2012) and Vu et al. (2017) showed that improved spatial resolution reduced partial volume effects; allowing for more efficient estimates of functional connectivity throughout the brain at 7T. However, to our knowledge, there have been no studies exploring how the benefits offered by higher field strength influence estimates of effective connectivity, defined as the (model-based) influence of one (neuronal) system on another.

In this paper, we address the efficiency of dynamic causal modelling (DCM) for 7T fMRI data. DCM is a method for inferring directed effective connectivity from brain imaging data, using Bayesian inference. Specifically, DCM has been developed for estimating effective connectivity from task-based and resting-state fMRI time series (Friston et al., 2003, 2014, 2017). Validity and test-retest reliability of DCM

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estimates at 3T have been investigated by numerous studies (Schuyler et al., 2010; Razi et al., 2015; Frassle et al., 2015; Rowe et al., 2010). However, we do not know whether estimates of connectivity parameters are affected by the field strength, and how different field strengths affect the accuracy of those estimates. This paper addresses these issues by comparing neurodynamic parameters estimated from DCM-3T and DCM-7T. We hypothesized that estimates of connectivity and neural responses (induced and modulated by experimental input) do not differ when the BOLD signal is acquired at higher field strengths, since the underlying interactions between neuronal populations do not change. However, the efficiency of these estimates should increase with field strength; i.e., the posterior uncertainty should decrease with field strength.

In brief, we address the effect of 7T data on DCM at two levels. First, we establish the predictive validity of DCM estimates based upon 3T and 7T in terms of reproducibility. DCM was applied to experimental data acquired during fist-closing movements at 3T and 7T fMRI (Grefkes et al., 2008; Frassle et al., 2015). Bayesian model averages (Penny et al., 2010) of effective connectivity parameters were then compared using the intra-class correlation coefficient (ICC) (Shrout and Fleiss, 1979). To illustrate the consistency of the results under both field strengths, we compared the neuronal and haemodynamic responses (under 3T and 7T) based on the respective Bayesian model averages. Second, given the higher intrinsic SNR at 7T over 3T, we ask whether the 7T affords more efficient parameter estimates. To quantify the reduction in posterior uncertainty, we assess the negative entropy of the (marginal) posterior distribution of DCM parameters from 7T and 3T fMRI. We predicted that the posterior entropy of 7T parameters estimates would be smaller, due to its improved spatial resolution and SNR.

This paper is structured as follows. In the Methods section, we first review the generative model of fMRI data used in DCM, with a special focus on the field strength-dependent components. We then illustrate the basic procedures by applying the DCM to 3T and 7T data which were acquired from the same subjects, under the same paradigm. In the Results section, we present the results of our comparative analysis, in terms of parameter estimates and the posterior confidence in these estimates at different field strengths. We conclude with a short discussion of future extensions of the current work.

2. Methods

The generative model of fMRI data in DCM comprises three components: (i) a neurodynamic model based on a network or graph of connected regions or nodes, (ii) a haemodynamic model mapping neuronal activity to haemodynamics at each node, and (iii) a BOLD signal model mapping haemodynamics to the measured BOLD signal (Buxton et al., 1998; Friston et al., 2000, 2003; Stephan et al., 2007). The following subsections describe each of these components. In particular, we focus on priors for the field strength-dependent parameters in the BOLD signal model; because physiological parameters in the neurodynamic and haemodynamic models are not affected by the field strength. This is followed by a description of image preprocessing, standard general linear model (GLM) and DCM analyses of the empirical data used in this study.

2.1. Neurodynamic model

In DCM, neurodynamics are described by the following differential equation (Friston et al., 2003)

$$\begin{aligned} \dot{z}_t &= \mathfrak{J}_t z_t + C u_t \\ \mathfrak{J}_t &= \mathrm{A} + \sum_{i=1}^{M} u_t(i) B^i, \end{aligned} \tag{1}$$

where t indexes continuous time and the dot notation denotes a time derivative. The entries in z correspond to neuronal activity in $j = 1, \ldots,$ J regions, and $u(i)$ is the i of M experimental inputs. An [J × J] matrix, $\mathfrak{J}$, denotes the effective connectivity between and within regions, and an $[J \times M]$ matrix, C, denotes the extrinsic influence of inputs on regional activity. The effective connectivity $\mathfrak{J}$ is further characterized by an $[J \times J]$ matrix, A, that specifies which regions are connected in the absence of experimental input, and an $[J \times J]$ matrix, B^i, that specifies which of these average connections changes a result of input i. Usually, the B^i parameters are of greatest interest – as these describe how connections among brain regions respond to experimental manipulations. A strong connectivity means the directed influence of one region on another is manifest quickly or with a small time constant (Friston et al., 2003). This means that effective connectivity is measured in rate constants for hertz. Neuronal activity fluctuations in each region lead to changes in haemodynamic responses that cause the observed BOLD response (see below).

2.2. The haemodynamic model

The haemodynamic model involves a set of differential equations modelling changes in four haemodynamic variables; including vasodilatory signal s, inflow f_{in}, volume of the venous balloon v, and total deoxyhemoglobin within the venous balloon q, normalized to their values at rest (Buxton et al., 1998; Friston et al., 2000). Based on empirical evidence DCM generally assumes a linear mapping between neuronal activity and blood flow (Miller et al., 2001): neuronal activity z causes an increase in an inducing signal s that drives the inflow change f_{in} (Friston et al., 2000):

$$\begin{aligned} \dot{s} &= z - \kappa s - \gamma(f_{in} - 1) \\ \dot{f}_{in} &= \mathrm{s}, \end{aligned} \tag{2}$$

where κ is the rate of signal decay, and γ is the rate of autoregulatory feedback by blood flow. This model includes negative feedback from the blood flow f_{in} on the inducing signal s.

This inflow change then drives changes in blood volume v, and deoxyhemoglobin q (Buxton et al., 1998):

$$\begin{aligned} \tau\dot{v} &= f_{in} - f_{out} \\ \tau\dot{q} &= f_{in}\frac{E(f_{in},\rho)}{\rho} - f_{out}\frac{q}{v}, \end{aligned} \tag{3}$$

with

$$\begin{aligned} f_{out} &= v^{\frac{1}{\alpha}} \\ E(f_{in},\rho) &= 1 - (1-\rho)^{\frac{1}{f_{in}}}, \end{aligned} \tag{4}$$

where τ is the mean transit time that represents the average time it takes to traverse the venous compartment, outflow f_{out} is modeled as a power of blood volume, α is Grubb's exponent (Grubb et al., 1974), E is oxygen extraction fraction, and ρ is the resting oxygen extraction fraction. In Eq. (3), the rate of blood volume changes $\dot{v}$ is modeled as the difference between inflow and outflow from the venous compartment with a time constant τ. The rate of deoxyhemoglobin changes $\dot{q}$ is modeled as the delivery of deoxyhemoglobin into the venous compartment, minus that expelled.

2.3. BOLD Signal Model

The BOLD signal is modeled as (Buxton et al., 1998; Stephan et al., 2007):

$$y = \frac{\Delta S}{S_0} \approx V_0\left[k_1(1-q) + k_2\left(1 - \frac{q}{v}\right) + k_3(1-v)\right], \tag{5}$$

where V_0 is the resting blood volume fraction, q and v are normalized deoxyhemoglobin and blood volume content, respectively. The first and second terms describe the extravascular and intravascular signal, and the third describes the effect of changing the balance. The field-