Causal modeling of fMRI

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Causal analysis of fMRI data is often discussed in terms of ‘effective connectivity’: the influence one neuronal population exerts over another [1]. Much more than functional connectivity analysis, which groups brain regions with correlated time courses into semi-separated networks, effective connectivity analysis necessitates assumptions embedded in mathematical modeling. Recently, effective connectivity techniques that formulate causality in state-space models that make use of the temporal dynamics in the fMRI signal have become popular. Both Granger causality analysis [2-4] and Dynamic Causal Modeling [5] are conveniently viewed as state space models. Brain structures are represented by states or variables that describe time varying neural activity and the functional form of the model equations can embed assumptions on signal dynamics, temporal precedence or physiological processes from which signals originate. In addition to their dynamic signal model, which sets them apart from effective connectivity techniques such as structural equation modeling, state-space models can be distinguished from each other based on three important characteristics [6].

First, the development of state space models for causal analysis of fMRI data has moved from discrete to continuous models. Continuous models allow definition of causal coupling parameters independent of the (low) sampling rate of the fMRI data. However, there are problems with identifiability and aliasing in estimating continuous models from discrete data. Second, there is a distinction between deterministic to stochastic models. Stochastic models allow endogenous dynamics independent of designed exogenous inputs (e.g. stimulus sequences) and they allow interpretation of causality in the framework of Granger causality. However, dealing with continuous stochastic models leads to technical issues such as the properties and interpretation of Wiener processes and complex filtering algorithms.

Finally, causal models of brain connectivity are increasingly inspired by biophysical theories. For fMRI this is primarily applicable in a generative model of the complex chain of events separating neuronal population activity from the BOLD signal [5]. Inversion of such a model in a stochastic context can amount to a model-based deconvolution of the fMRI signal resulting in an estimate of latent neuronal population activity. If the biophysical model is appropriately formulated to be identifiable (possibly including priors on parameters), it can take variation in the hemodynamics between brain regions into account that can otherwise confound time series causality analyses of fMRI signals [7, 8].