A Framework for Causal Inference for fMRI Time Series Data Measured with Systematic Error

Abstract:
Functional magnetic resonance imaging (fMRI) has facilitated major advances in understanding human brain function. Neuroscientists are interested in using fMRI to study the effects of external stimuli on brain activity and causal relationships among brain regions, but have not stated what is meant by causation or defined the effects they purport to estimate. We construct a framework for causal inference using blood oxygenation level dependent (BOLD) fMRI time series data. In the usual literature on causal inference, potential outcomes, assumed to be measured without systematic error, are used to define unit and average causal effects. However, the potential BOLD responses are measured with stimulus dependent systematic error. Thus we define unit and average causal effects that are free of systematic error, using a linear mixed model to estimate these effects. In contrast to the usual case in a randomized experiment, where adjustment for intermediate outcomes leads to biased estimates of treatment effects, here the failure to adjust for systematic error leads to biased estimates. These results are important for neuroscientists, who typically do not adjust for systematic error. They should also prove useful to researchers in other areas where responses are measured with error and in fields where large amounts of data are collected on relatively few subjects. To illustrate the approach, data from a social evaluative threat task are analyzed and results that adjust for systematic error compared with results that do not do so. Extensions of the basic framework and model are also discussed.