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Response from Martin McKeown, Makeig, Brown, Jung, Kindermann, Bell and Sejnowski

As Professor Friston eloquently describes in his commentary[1], current techniques for analysing fMRI data can be dichotomized into either data-driven methods, like independent component analysis (ICA), or hypothesis-driven methods, like the General Linear Model[2]. These two approaches are complementary and mirror the exploratory and confirmatory aspects of scientific investigation. Imaging studies driven by hypotheses derived from cognitive psychology and related disciplines can at best support or refute currently formulated psychological models. Counterintuitive or unanticipated time courses of activation of localized brain areas are less likely to be discovered with such analysis methods. For example, in our paper, we demonstrated transiently task-related (TTR) ICA components whose time courses could not be anticipated before the experiment[3].

The ICA implementation described in our paper fully characterizes the data by separating them into sparse maps, or spatial modes, and associated time courses. Employing an ICA algorithm capable of looking for non-sparse as well as sparse maps found maps that were all sparse[4]. Many of these maps can be identified with known artifacts, such as blood vessel pulsations, head movements and slow drifts. These highly spatially structured signals are not easily modeled by *a priori* estimates as required by hypothesis-driven methods. The other key ICA assumption, that the maps are spatially independent, does not preclude the possibility of spatial overlap, because maximal independence can be achieved with overlap in high-dimensional spaces, especially as positive and negative regions of those maps can cancel.

Friston also rightly points out some of the inherent weaknesses of ICA. In an attempt to find maps that are maximally independent, ICA might tend to fragment broad areas of activation into multiple maps, all having highly correlated time courses. Like all linear models, ICA will be less sensitive to finding non-linear activation relationships between voxels, if these exist. More recent work takes advantage of an important by-product of ICA analysis; that the probability of observing the data conditioned on the ICA model is relatively easy to calculate, in order to estimate how well a linear model fits the data[5]. This report found that some brain regions (e.g. around blood vessels) might fit less well than say, subcortical white matter using an ICA model. Also, purely data-driven techniques like ICA, as Friston says, do not lend themselves to straightforward statistical analyses, potentially limiting their use for functional neuroimaging studies specifically designed to test certain hypotheses, rather than for exploratory analysis.

As the field continues to mature, we foresee the development of hybrid methods that will attempt to take advantage of these two complementary approaches: first employing powerful data-driven techniques to characterize the underlying nature of the signals and noise, then testing hypotheses of interest in the context of this accurate characterization. 'Data-driven' or 'hypothesis-driven' analysis methods will then refer to the extremes of a continuum, to be altered to fit the particular needs of the experimenter.

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