Take a deep breath: Multiecho fMRI denoising effectively removes head motion artifacts, obviating the need for global signal regression

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Power et al. (1) provide convincing evidence that multiecho independent components analysis (ME-ICA) effectively differentiates blood oxygen level-dependent (BOLD) from non-BOLD, or artifactual, signals in functional MRI (fMRI) data. Critically, ME-ICA removes spurious, distance-dependent effects caused by head motion in resting-state functional connectivity (RSFC) analyses, which have confounded many group studies. However, the authors also argue that ME-ICA unmasks persistent BOLD-related global signal correlates, attributed to "motion-associated" effects of respiration, and conclude that removal of this global signal by some means is necessary. Among other approaches, they recommend implementing global signal regression (GSR) following ME-ICA. To the contrary, we argue that there is no definitive evidence to date that respiration effects dominate, or even substantively contribute in any confounding way, to residual global signal following ME-ICA, and that GSR is ill-advised.

In their figure 2B, Power et al. report a correlation of 0.59 between variance in mean global signal and variance in respiration in ME-ICA–processed data from 12 participants, prior to GSR. However, the conclusion that respiratory effects are a primary source of the BOLD-related global signal is not empirically substantiated.

The methods reported by Power et al. describe only 12 participants with respiratory data, while their figure 2B depicts scatterplots with 19 data points: 2 scans were included from 8 of the participants, 1 scan was included from 3 of the participants, and data from 1 participant were excluded. Including repeated observations from a subset of participants is a statistically invalid calculation of a Pearson correlation coefficient (2). Moreover, this sample is underpowered for examining brain–behavior associations (3, 4). Even granting their reported correlation of 0.59 suggests that respiration accounts for about 35% of the variance in global signal, leaving a significant majority of variance unexplained. There is evidence that respiration can be significantly correlated with neural activity, although arising from different mechanisms (5). Thus, applying GSR post–ME-ICA potentially removes a substantial proportion of variance, not directly caused by respiration, that might carry signal dynamics of interest.

As the authors acknowledge, there is compelling evidence that GSR can distort correlation patterns in RSFC analyses (6–8), although this likely depends on multiple factors (9), including the unknown dimensionality of fMRI data (10). Despite these potentially detrimental effects of GSR, and the existence of arguably better, more targeted multivariate denoising approaches [e.g., Go Decomposition (GODEC) (1) or temporal ICA (5)], the authors recommend GSR implementation following ME-ICA as a viable method of denoising resting-state fMRI data.

The primary results from Power et al. are encouraging—ME-fMRI combined with ME-ICA processing effectively removes the confounding effects of head motion and other spurious sources of noise from fMRI signal. However, the conclusion that BOLD-related global signal is primarily caused by respiration is not substantiated. While some amount of respiration-related noise may remain in ME-ICA–processed data, the extent to which it contributes to the global signal, is correlated with neural signals of interest, and/or potentially confounds group analyses is unknown. Contrary to the authors' recommendation, we discourage implementation of GSR following ME-ICA.

Acknowledgments

This work was supported in part by the Natural Sciences and Engineering Research Council of Canada and Canadian Institutes of Health Research grants (to R.N.S.).

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The authors declare no conflict of interest.

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First published August 27, 2019.

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