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RESEARCH ARTICLE

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Evaluation of denoising strategies for task-based functional connectivity: Equalizing residual motion artifacts between rest and cognitively demanding tasks

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Abstract

In-scanner head motion represents a major confounding factor in functional connectivity studies and it raises particular concerns when motion correlates with the effect of interest. One such instance regards research focused on functional connectivity modulations induced by sustained cognitively demanding tasks. Indeed, cognitive engagement is generally associated with substantially lower in-scanner movement compared with unconstrained, or minimally constrained, conditions. Consequently, the reliability of condition-dependent changes in functional connectivity relies on effective denoising strategies. In this study, we evaluated the ability of common denoising pipelines to minimize and balance residual motion-related artifacts between resting-state and task conditions. Denoising pipelines—including realignment/tissue-based regression, PCA/ICA-based methods (aCompCor and ICA-AROMA, respectively), global signal regression, and censoring of motion-contaminated volumes—were evaluated according to a set of benchmarks designed to assess either residual artifacts or network identifiability. We found a marked heterogeneity in pipeline performance, with many approaches showing a differential efficacy between rest and task conditions. The most effective approaches included aCompCor, optimized to increase the noise prediction power of the extracted confounding signals, and global signal regression, although both strategies performed poorly in mitigating the spurious distance-dependent association between motion and connectivity. Censoring was the only approach that substantially reduced distance-dependent artifacts, yet this came at the great cost of reduced network identifiability. The implications of these findings for best practice in denoising task-based functional connectivity data, and more generally for resting-state data, are discussed.

KEYWORDS
artifact, denoising, functional connectivity, motion, resting-state fMRI, task-concurrent connectivity

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1 | INTRODUCTION

In-scanner head motion is one of the major confounders in functional connectivity (FC) studies employing the blood oxygenation level dependent (BOLD) signal (Power, Barnes, Snyder, Schlaggar, & Petersen, 2012; Satterthwaite et al., 2012; Van Dijk, Sabuncu, & Buckner, 2012). Two critical issues make the technique highly susceptible to motion. The first is intrinsic to FC itself, which is defined as statistical dependencies among remote neurophysiological events (Friston, 2011), and is commonly estimated as temporal correlations between BOLD time series of different brain regions. Regrettably, any non-neuronal source of variance can introduce spurious correlations that may completely obscure neuronally-driven correlations. In addition, motion acts by adding both global and spatially-dependent variance (Power, Schlaggar, & Petersen, 2015), mimicking true functional connections. Second, investigators lack any a priori information regarding the exact temporal characteristics of neuronal-related variance, which makes the reliability of FC estimates dependent on the ability of researchers to detect, model and remove physiological noise, reducing its magnitude below the threshold that systematically affects results.

Consequently, a great effort has been made to develop (Behzadi, Restom, Liau, & Liu, 2007; Jo, Saad, Simmons, Milbury, & Cox, 2010; Patriat, Reynolds, & Birn, 2017; Power et al., 2014; Power et al., 2015; Pruim, Mennes, van Rooij, et al., 2015; Salimi-Khorshidi et al., 2014; Satterthwaite et al., 2013) and compare (Ciric et al., 2017; Muschelli et al., 2014; Parkes, Fulcher, Yucel, & Fornito, 2018; Pruim, Mennes, Buitelaar et al., 2015; Shirer, Jiang, Price, Ng, & Greicius, 2015; Siegel et al., 2017; Weissenbacher et al., 2009; Yan et al., 2013) numerous strategies for denoising BOLD data. There is substantial heterogeneity in the performance of these strategies, and even the most effective approaches were not able to fully account for motion-related artifacts in FC estimates (Parkes et al., 2018). While a relatively low residual motion-related variance may be considered acceptable when in-scanner motion is evenly distributed among factors of interest, it can still create concerns when it correlates with the investigated factors. Such situations are common in neuroscience research since they are often found in developmental, aging (Harms et al., 2018, and references therein) and clinical studies (Pardoe, Kucharsky Hiess, & Kuzniecky, 2016).

Another class of FC studies in which head motion is particularly serious is the one focused on network dynamics induced by cognitive engagement, which is generally assessed by comparing resting state to one or multiple task conditions. Indeed, it has been reported that subjects tend to move less when they are engaged in a cognitive task than when they are under unconstrained conditions (Huijbers, Van Dijk, Boenniger, Stirnberg, & Breteler, 2017). Even passive movie watching, which requires minimal attention, has been associated with lower head movement compared to rest (Vanderwal, Kelly, Eilbott, Mayes, & Castellanos, 2015), especially in young children (Greene et al., 2018). While such a behavioral trait may be exploited to reduce the detrimental effect of motion on image acquisitions, particularly on structural or diffusion images, it is prone to bias task-based FC studies. Therefore, whereas evidence from fMRI studies indicate that the brain accommodates task demands with specific and systematic network reconfigurations (reviewed in Gonzalez-Castillo & Bandettini, 2018), it is not clear to what extent such modulations are compounded by the different amount of motion between the functional conditions being compared. Moreover, denoising strategies have been specifically developed for study designs involving one condition per subject, and in particular for resting-state data. Their effectiveness has not been evaluated in the context of multiple steady-state conditions that are differently prone to motion, as during different prolonged cognitive engagements or physiological conditions.

In the current work, we sought to identify the appropriate procedures for mitigating and balancing residual motion-related effects across protracted functional conditions in task-based connectivity studies. Specifically, we employed a set of benchmark measures to investigate how popular denoising strategies perform in cleaning up BOLD data that span different steady-state functional conditions characterized by distinct amounts of head motion. To this aim, we analyzed data from our previous study (Tommasin et al., 2017; Tommasin et al., 2018) in which we collected BOLD fluctuations in a block-design fashion employing prolonged epochs of alternated resting-state and sustained working-memory task conditions. Leveraging on the peculiar acquisition protocol, both long and with multiple conditions within the same run, we evaluated the condition-specific performance of the pipelines according to benchmarks based either on minimizing motion-related artifacts or at maximizing network identifiability. In addition, in order to corroborate our findings, we evaluated the pipelines in a further, larger dataset, composed of two separate acquisitions of resting-state and stop-signal task scans (Poldrack et al., 2016). Finally, we examined the robustness of previously reported task-associated modulations in within-network FC (Tommasin et al., 2018) by exploring its variability under different denoising strategies and under stringent exclusion of motion-contaminated volumes.

2 | MATERIALS AND METHODS

2.1 | Subjects and datasets

Denoising strategies were evaluated in two fMRI datasets. The first, which we refer to as "Centro Fermi" (CF) dataset (40 runs from 20 healthy subjects), is composed of data collected at our laboratory for the evaluation of FC modulations following sustained task execution (Tommasin et al., 2017; Tommasin et al., 2018). Each CF run comprises multiple long-lasting epochs of either rest or working-memory task. Despite the limited sample size, the CF dataset was used as our primary dataset given its peculiar paradigm (detailed in the following section). For the second dataset, which serves for result corroboration and to counteract the sample-size limitation of the CF dataset, we used a subset of data from the Consortium for Neuropsychiatric Phenomics (CNP Poldrack et al., 2016). The CNP dataset comprises resting-state scans as well as six scans of BOLD acquisitions under