Effects of Preprocessing on Local Homogeneity of fMRI data

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Introduction:

Local functional connectivity - or the degree of homogeneity in brain function - is fast gaining popularity within the neuroscience research community. In particular, certain diseases and psychological conditions have been associated with disruptions in brain activity at the local level [1-5]. Algorithms that provide a measure of small-scale connectivity in fMRI data do so by gauging the degree of affinity between time series of neighbouring voxels, and thus rely on the assumption that preprocessing does not affect any intrinsic correlations. However, many of the preprocessing routines employ interpolation, and by its very nature, interpolation introduces artificial correlations. To our knowledge, none of the works published on the subject have taken the issue into account.

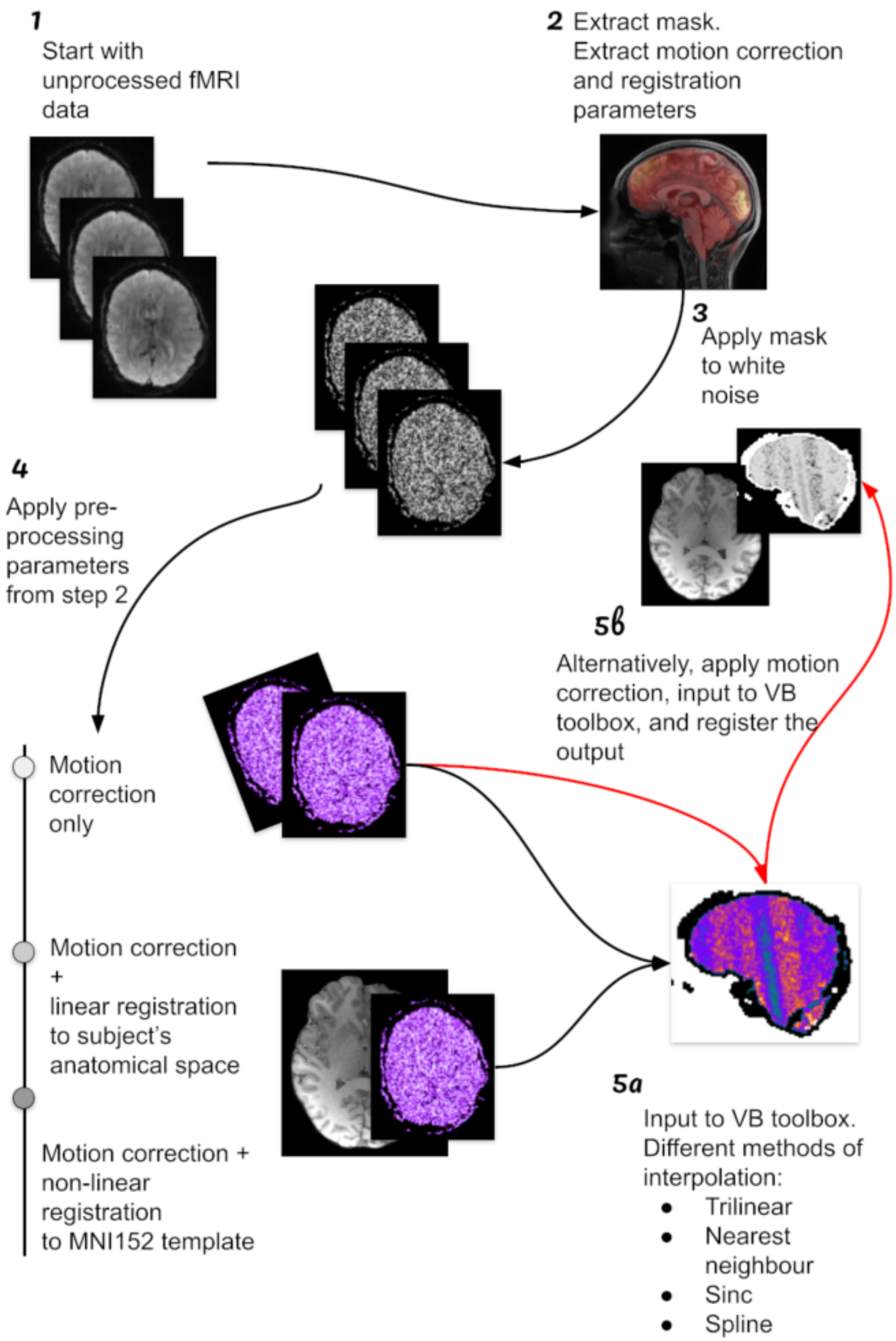
Methods:

We study the effect that two important aspects of preprocessing which involve interpolation -

namely, motion correction and registration - have on functional connectivity at the voxel level. To this end, we apply them to stochastic data (white noise), as this is known to be uncorrelated and thus free of any genuine local homogeneity.

A binary 4D mask was produced using unprocessed HCP functional data [6], and was then applied to a 4D data array representing white noise. The degree of local homogeneity was determined with a modified version of the Vogt-Bailey (VB) toolbox [7], which makes use of spectral graph theory principles to calculate the VB index at every voxel. The value of the VB index indicates the strength of the connections within the immediate neighbourhood of the voxel (it factors in pairwise correlations in said neighbourhood). Areas where the fMRI data is strongly correlated therefore have a high VB index.

A brain map of VB indices was generated prior to preprocessing, and then again after employing FSL tools [8,9] to implement motion correction and/or registration - either linear registration to the subject-specific anatomical space or nonlinear registration to a standard template (Fig. 1). Different types of interpolation methods were used. In cases where both motion correction and registration were carried out, the individual transformations were combined and applied in a single interpolation step.



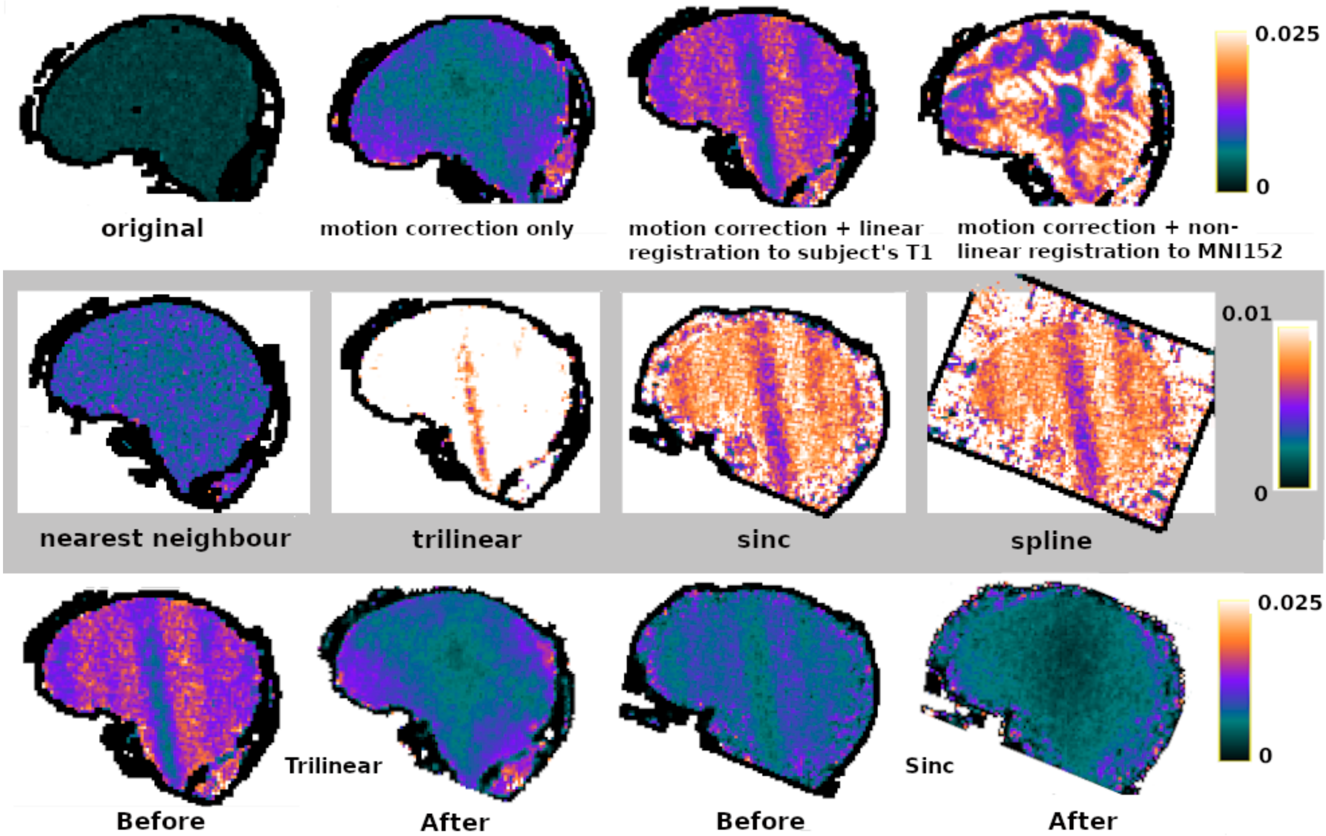
·Methodology flowchart.

Results:

Interpolation carries the risk that adjacent voxels in the preprocessed image have drawn data from one or more common voxels in the original image, and consequently that their time series have become artificially correlated.

Indeed, our results indicate that the preprocessing introduced local connectivity in the noise distribution independently of the interpolation method used, although to varying degrees (Fig. 2). The trilinear technique fared the worst, probably due to its linear nature (given that correlation is a measure of linear interdependence). Sinc and, especially, spline interpolation smeared out the data, giving rise to VB maps in which the brain-background boundary is displaced. Nearest neighbour interpolation, however, generated very little correlation, highlighting the fact that interpolation is the source of the problem.

Interestingly, in the case of data that underwent non-linear registration, it was noted that some areas with high VB values traced out anatomical structures in the brain, suggesting that the warp field encodes more and/or stronger local deformations in the vicinity of said structures.



VB index maps showing the effects of interpolation. The *top panel* features the map for the original white noise distribution, as well as for noise that had undergone motion correction only, or motion correction followed by linear / non-linear registration. Trilinear interpolation was employed throughout. The *middle panel* illustrates the outcome of applying both motion correction and linear registration with different methods of interpolation. The images in the *bottom panel* were obtained by first doing motion correction using trilinear or sinc interpolation, generating a VB map and then (linearly) registering this to the data subject's structural space (without changing the interpolation technique).

Conclusions:

Our results imply that standard preprocessing steps can have an adverse effect on local connectivity measures. This appears to result from the use of interpolation, and may have significantly impacted numerous studies investigating brain function at the local level. In such studies, therefore, any preprocessing that involves interpolation should be applied with care and ideally kept to a minimum. Additionally, feeding the data to the local homogeneity algorithm after motion correction and then registering the output to a template space might help to mitigate the problem (Fig. 2).

Modeling and Analysis Methods:

Connectivity (eg. functional, effective, structural)
fMRI Connectivity and Network Modeling [2]
Motion Correction and Preprocessing [1]
Segmentation and Parcellation

Keywords:

FUNCTIONAL MRI
Other - Preprocessing; fMRI connectivity

[1|2]Indicates the priority used for review

Abstract Information

My abstract is being submitted as a Software Demonstration.

No

Please indicate below if your study was a "resting state" or "task-activation” study.

Other

Healthy subjects only or patients (note that patient studies may also involve healthy subjects):

Healthy subjects

Was any human subjects research approved by the relevant Institutional Review Board or ethics panel? NOTE: Any human subjects studies without IRB approval will be automatically rejected.

Yes

Was any animal research approved by the relevant IACUC or other animal research panel? NOTE: Any animal studies without IACUC approval will be automatically rejected.

Not applicable

Please indicate which methods were used in your research:

Functional MRI

For human MRI, what field strength scanner do you use?

3.0T

Which processing packages did you use for your study?

FSL
Other, Please list - VB Toolbox, MRtrix

Provide references using author date format

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