Comparison of pre-normalization methods on the accuracy and reliability of group ICA results

Abstract No:

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Introduction:

Spatial independent component analysis (ICA) has emerged as a robust technique to identify functionally connected networks in resting-state and task-modulated fMRI data. Despite its broad application, there is little consensus on how data should be processed prior to ICA.
Here, we compare three methods in common use: 1) No Normalization (NN), where data is left in its raw intensity units (Calhoun, 2004), 2) Intensity Normalization (IN), which involves voxel-wise division of the time series mean, and 3) Variance Normalization (VN), voxel-wise z-scoring of the time series (Beckmann, 2004). The effects of these preprocessing methods are evaluated by comparing the components identified by ICA, assessing the test-retest reliability of component parameters (Zuo, 2010), and through complementary use of simulated data.

Methods:

Twenty-three healthy participants completed 2 separate resting-state fMRI scans (3T Siemens Trio, TR=2s, TE=29ms, 3.4×3.4×5mm) on visits separated by roughly 3 months. Subjects were instructed to passively stare at a fixation cross throughout a 5-minute (150-volume) scan. Canonical preprocessing involved slice-timing correction, motion correction, de-spiking, spatial smoothing and normalization to MNI space. Variable preprocessing then involved the appropriate NN, IN, or VN transformation. For all datasets, we applied group ICA using GIFT (Calhoun, 2004) and ICASSO (Himberg, 2004), with a model order of 30 (the mean of the MDL estimates). Subject-specific (and visit-specific) spatial maps (SMs) and time courses (TCs) were back-reconstructed using GICA3 in GIFT, a recently developed improvement of GICA1 (Calhoun, 2001b).

To assess reliability, subject-specific TCs and SMs for components of interest were described with a set of parameters, including 1) amplitude (a) estimated as the TC standard deviation, 2) band-limited amplitude (A) of the TC spectrum in the range [0.01 Hz, 0.125 Hz], 3) temporal correlations (tc) between component pairs, 4) mean (μ) voxel amplitude over the SM, 5) coefficient (β) from the regression of the group map onto the subject-specific map, and 6) loading parameter of the first principle eigenvector (PC1) of the subject-specific maps, described in (Glahn et al., 2010). Intra-class correlation coefficients (ICCs) were then calculated for each of the parameters to quantify test-retest reliability (Shrout, 1979).

Simulated data were an extension of those described previously (Correa, 2005), and contained 8 true sources, 3 of which had distinct time series and variable magnitude over 32 subjects. ICA was applied to the simulated NN, IN, and VN datasets with model orders ranging from 4 to 12.

Results:

From the resting-state data, ICA identified 12 components considered to be resting-state networks, 3 of which are displayed in Figure 1A (left: primary visual cortex; middle: somato-motor cortex; right: posterior default mode network). Though the group SMs are largely comparable across preprocessing methods, NN and IN were more similar to each other than to VN (Rsq between NN and IN: mean±std, 0.88±0.07; Rsq(NN,VN): 0.72±0.16; paired t-test: $t(11)=3.68$, $P<0.005$). In addition, the z-scored values of VN were lower for some components. Scatter-plots of the voxel intensities reveal a roughly linear relationship between NN and IN, but a sub-linear relationship between NN and VN (Fig. 1B), suggesting that VN may be degrading the estimation of component shape.

Preprocessing also impacted the test-retest reliability of component parameters. As shown by the average ICC statistics for component parameters in Figure 1C, reliability was always highest for IN (asterisks denote significant differences, $P < 0.01$), suggesting that component amplitudes across subjects are best captured with IN preprocessing.

Simulations concurred that the SMs of NN and IN were more similar to each other than to VN (see Fig. 2; for model order = 8, Rsq(NN,IN): 0.998 ± 0.003; Rsq(NN,VN): 0.953 ± 0.055; $t(7)=2.31$, $P=0.054$). Simulations also verified that VN degrades the estimation of component shape, as evidenced by the scatter plots of true values versus estimated voxel values (Fig. 3A) and the difference maps in Figure 2 ($\hat{S}$-S). For the majority of model orders and components, the Rsq between true and estimated SMs was lowest for VN, assessed by group (Fig. 3B, left, circles) and single-subject maps (Fig. 3B, left, squares). Rsq values between true and estimated TCs were roughly equivalent across NN, IN, and VN (see Fig. 3B, right). Finally, simulations confirmed that relative component magnitudes are best estimated by IN preprocessing, regardless of model order (Fig. 4).

Conclusions:

Based on our analyses of real and simulated data, we find that VN preprocessing compromises not only the shapes of the components (the relative voxel amplitudes within a component), but also the estimation of component amplitudes between subjects. ICA decompositions of NN and IN datasets yielded very similar results, however the IN datasets showed greater test-retest reliability of component parameters and superior estimation of component amplitude in simulations. Thus, we recommend the use of IN preprocessing prior to applying ICA, particularly in studies involving comparisons between subject groups (e.g., healthy controls and clinical populations) where accurate estimation of relative component magnitude is of primary concern.

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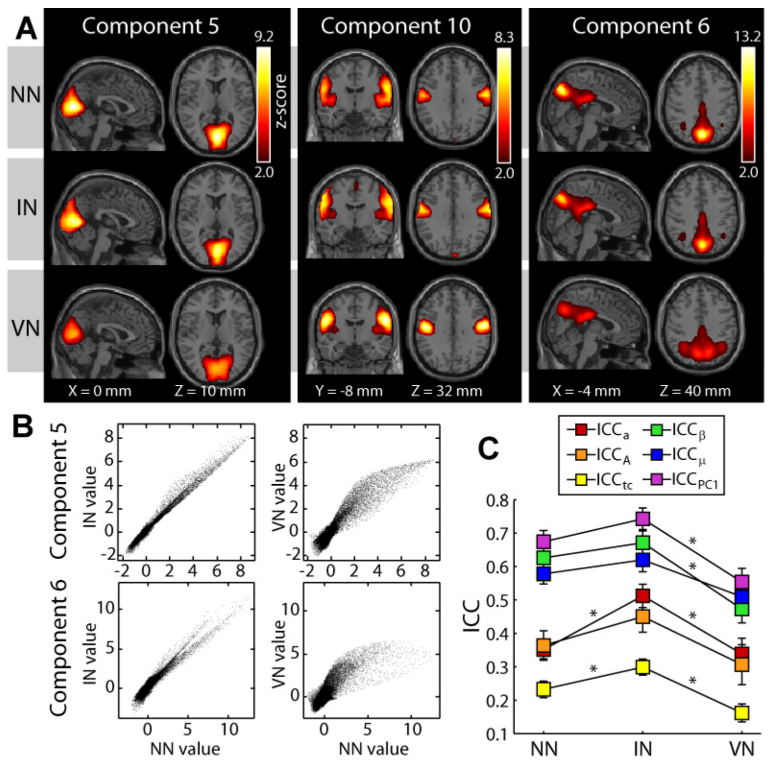
Categories

- Multivariate Modeling, PCA and ICA (Modeling and Analysis)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Component 10
Component 6
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IN
VN
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2.0
13.2
2.0
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Z = 10 mm
Y = -8 mm
Z = 32 mm
X = -4 mm
Z = 40 mm
B
Component 5
Component 6
IN value
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IN
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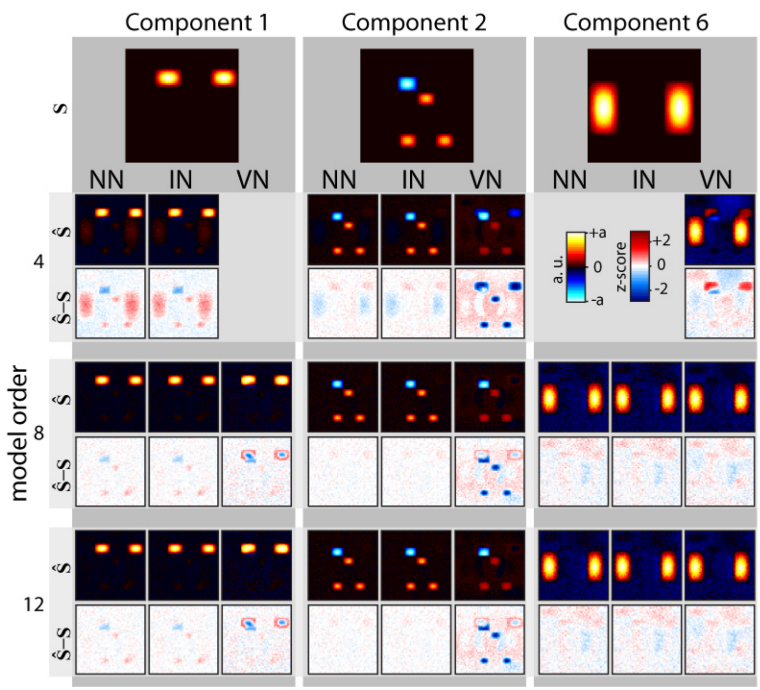

Component 1
Component 2
Component 6
S
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IN
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4
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model order
a. u.
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+2
0
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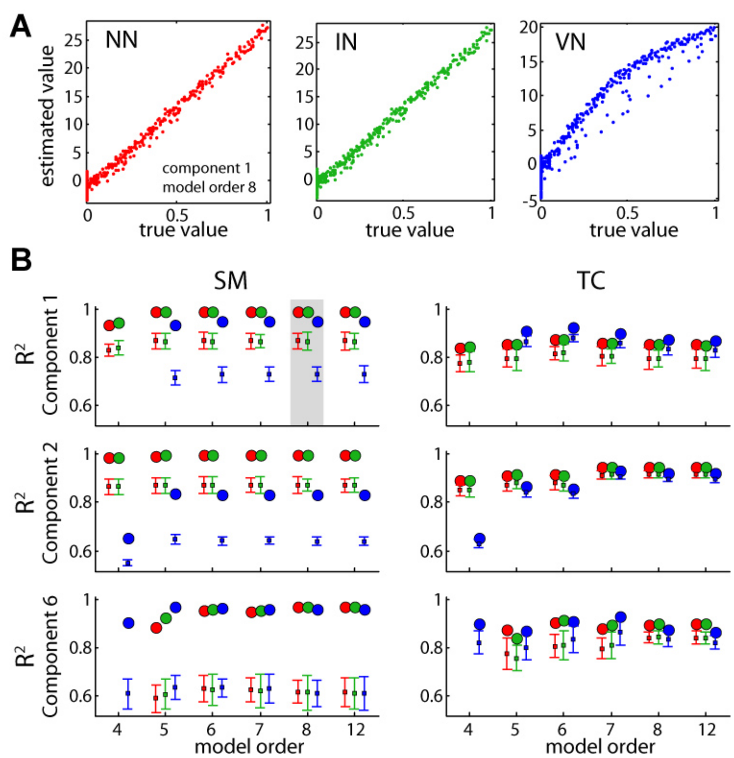

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TC
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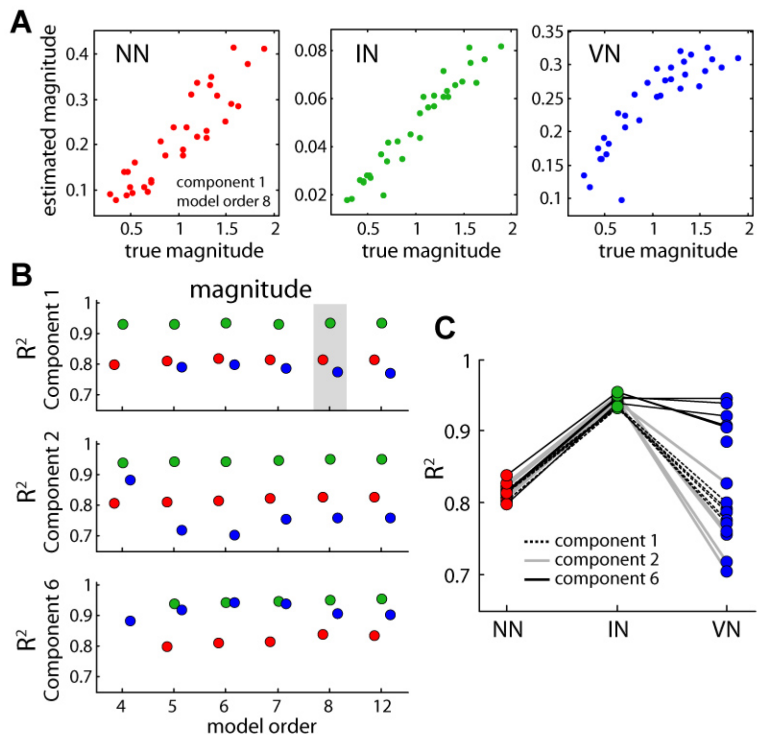
Component 1
Component 2
Component 6
model order



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IN
VN
estimated magnitude
true magnitude
component 1
model order 8
B
magnitude
R^2
Component 1
Component 2
Component 6
model order
C
component 1
component 2
component 6
NN
IN
VN