A formal set of criteria for the quality control of network analysis in mice.

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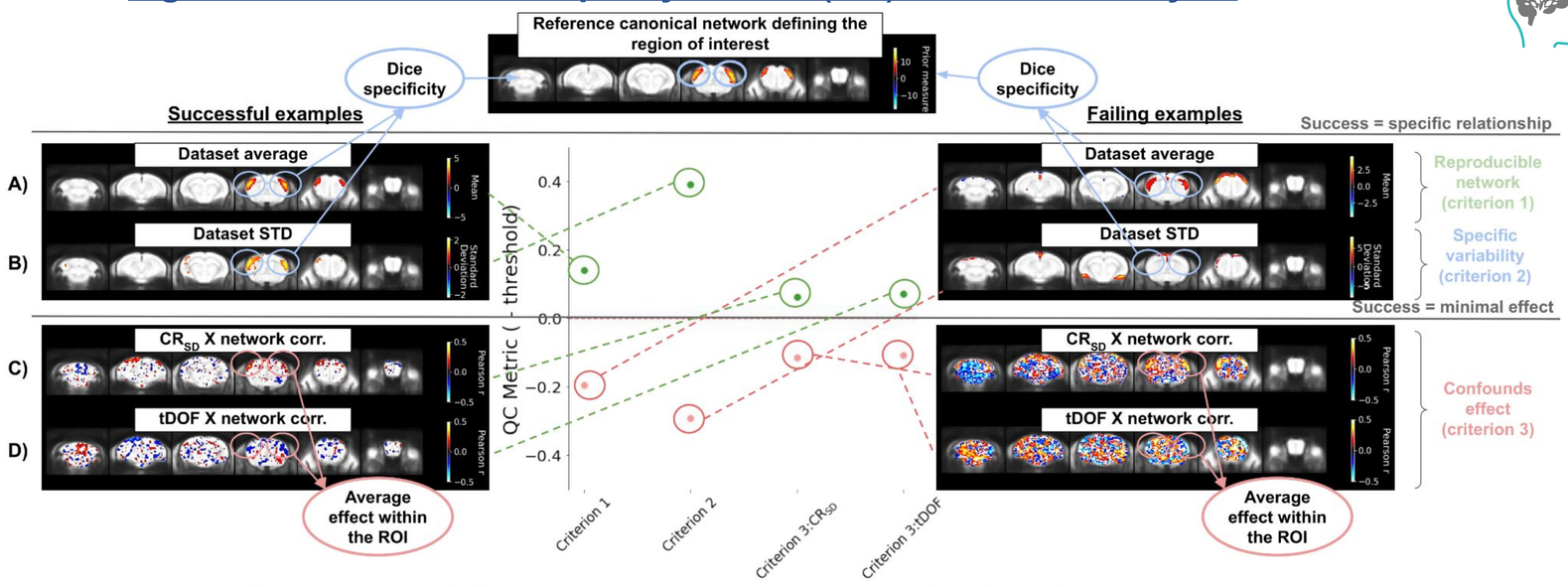
Background

- Recent work revealed important inconsistency in the mapping of resting-state networks across sites of mouse fMRI acquisition (Grandjean et al. (2020) Neuroimage.)
- Multiple factors can confound network analysis (Ciric et al. (2018) Nature Protocols.), and the non-standardized analysis poses reproducibility challenges (Botvinik-Nezer et al. (2020) Nature.)
- There are no formal guidelines for evaluating the integrity of network analysis prior to interpretation.
- **Goal:** explore data quality issues in mouse fMRI datasets to define criteria evaluating analysis integrity.

Datasets and processing software

- Datasets: 17 different mouse fMRI acquisitions from a multi-site study (https://openneuro.org/datasets/ds001720/versions/1.0.2) and a anesthetized and awake acquisitions from (https://openneuro.org/datasets/ds001653/versions/1.0.2)
- Image processing and analysis automated with RABIES (https://github.com/CoBrALab/RABIES), confound correction consists of motion frame censoring and the regression of 6 motion parameters (except for **figure 2B**).

Figure 1: 3 criteria for the quality control (QC) of network analysis



QC metric	Thresholds			
	DR:S1N	SBC:S1N	DR:DMN	SBC:DMN
A) Criterion 1 - Dice overlap between dataset mean and canonical network ROI	**Failure:** Dice<0.75	**Failure:** Dice<0.65	**Failure:** Dice<0.6	**Failure:** Dice<0.55
B) Criterion 2 - Dice overlap between dataset STD and canonical network ROI	**Uncertain:** Dice<0.3 **Failure:** Dice<0.2			
C) Criterion 3:CR_{SD} - average correlation for CR_{SD} within canonical network ROI	**Uncertain:** Avg.Corr.>0.15 **Failure:** Avg.Corr.>0.25			
D) Criterion 3:tDOF - average correlation for tDOF within canonical network ROI	**Uncertain:** Avg.Corr.>0.15 **Failure:** Avg.Corr.>0.25			

Figure 1: 3 criteria are evaluated to determine the integrity of network analysis at the dataset level: 1) reproducibility of the network, 2) specificity of individual variability and 3) minimal confound effects. Network connectivity is computed on each scan in a dataset (e.g using dual regression (Beckmann et al. (2009). Neuroimage.) in this example), and voxelwise statistical maps are compared to the canonical network brain map to evaluate the criteria (see table above). The canonical network map (we show above the somatomotor network obtained using group-ICA)) is thresholded to include 4% of the voxels with the highest values and define the main region of interest (ROI). The dataset mean (**A)**) and STD (**B)**) maps are similarly thresholded to evaluate Dice specificity. The two confounds included are the variance modelled by confound regression (CR_{sd}) during the confound correction preprocessing step (**C)**) and the temporal degrees of freedom (tDOF) (**D)**).

Figure 2: analysis QC outcomes across mouse fMRI datasets

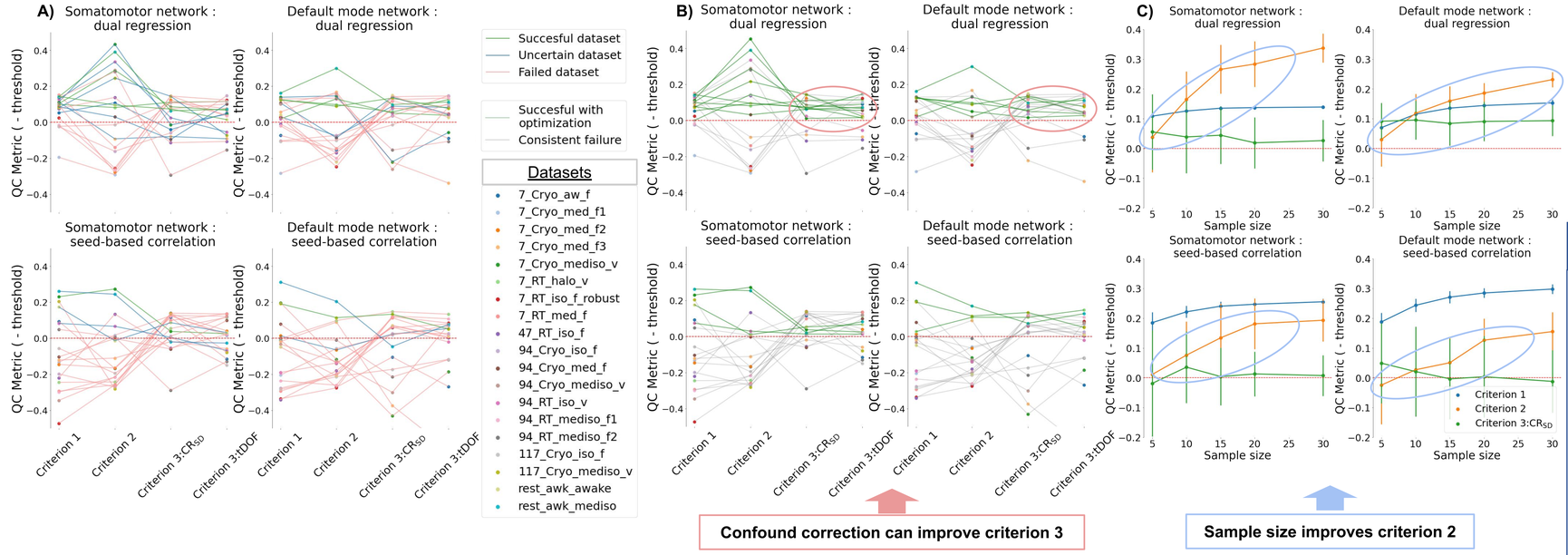


Figure 2: Evaluation of analysis QC across 19 mouse fMRI datasets, and 4 different connectivity analyses. **A)** Results of the analysis QC across datasets/analyses. The QC metrics from the same dataset are linked by a line, and the line is color-coded according to the classified outcome (successful in green, uncertain in blue and failed in red). **B)** Same as in A), but showing in green which dataset could reach success by varying confound correction (9 different models). **C)** The rest_awk_mediso dataset was subsampled to test the effect of sample size on QC metrics. Results are showing the average across 50 random subsampling iterations and its associated error bars (standard deviation).

Implications

- We report a high failure rate in meeting basic expectations from network analysis in mouse fMRI datasets.
- Increasing statistical power and applying more stringent confound correction are associated with improvements over criterion 2 and 3 respectively.
- The RABIES software generates the entire analysis QC report automatically, allowing its sharing along with publications to improve transparency and comparison between studies.