

Perturbation-Enabled Data Augmentation Improves the Generalizability of Classifiers in Network Neuroscience

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Abstract

Machine learning models are commonly applied to human brain imaging datasets in an effort to associate function or structure with behaviour, health, or other individual attributes. Such models often rely on low-dimensional maps relating brain regions, generated by complex processing pipelines. However, the numerical instabilities inherent to pipelines limits the fidelity of these estimates, and results in bias-rich derivatives serving as inputs to these machine learning models. This work seeks to take advantage of numerical instabilities in pipelines towards reducing the bias in networks used by machine learning models. We found that resampling brain networks across a series of numerically perturbed outcomes led to more consistently generalizable performance in all tested classifiers, preprocessing strategies, and dimensionality reduction techniques when tasked with an age classification task. Importantly, this finding does not hinge on a large number of perturbed networks in order to exhibit improved performance, suggesting that even minimally perturbing a dataset reduces bias in the resulting models.

Keywords

Stability — Network Neuroscience — Neuroimaging — Machine Learning — Generalizability

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Introduction

- machine learning has become commonplace for the identification and characterization of individual biomarkers.
- in neuroimaging, models accept processed imaging data and seek to relate structure or function to phenotypes.
- the development of biomarkers through this approach has been widely applied, such as linking sex, age, bmi, etc., to brain structure.
- however, these models are sensitive the data used for training, and performance out-of-sample often degrades significantly.
- this truth of machine learning is not helped by the fact that bias-rich estimates are used as inputs to the machine learning models, as scientific pipelines at best provide “estimates” of structure or function, rather than capturing true and unobstructed signal.
- the impact that numerical instabilities play in determining the results of pipelines have been clearly demonstrated across operating systems, data perturbations, and pipeline perturbations through MCA
- a benefit of characterizing instabilities through perturbation approaches is that they result in a series of estimates

of derivatives for each sample in a dataset.

- here, we take advantage of a range of possible – and equally plausible – outputs from a MCA experiment on structural connectomes estimation pipeline to augment out dataset.
- we classify brain networks based on participant age, and resample the samples used for this task based on the augmented dataset.
- we evaluate the impact of data augmentation through MCA, explore the relationship between the change in performance and baseline performance for the classification task, and identify any relationship between these potential benefits and the number of MCA simulations performed per sample.

Materials & Methods

The objective of this study was to evaluate the impact of aggregating collections of unstable brain networks towards learning robust brain-phenotype relationships. We sampled and aggregated simulated networks within individuals to learn relationships between brain connectivity and individual an trait, in this case age, and compared this to traditional baseline performance on this tasks. We compared aggregation strategies with respect to baseline validation performance, performance out-of-sample, and generalizability.

All developed software and analysis resources for this project have been made available through GitHub at <https://github.com/gkpapers/2020AggregateMCA>.

Dataset

An existing dataset containing Monte Carlo Arithmetic (MCA) perturbed structural human brain networks was used for these experiments¹. The perturbations introduced for the generation of brain networks in this dataset were at the level of machine-error, simulating expected error over a typical pipeline execution. This dataset contains a single session of data from 100

individuals ($100 \times 1 \times 1$). The derived brain networks were generated with a probabilistic structural connectome estimation pipeline² using a fixed random seed, and Monte Carlo Arithmetic (MCA) perturbations were added to all Python-implemented operations throughout the pipeline^{3,4}. Each sample was simulated 20 times, resulting in 2,000 unique graphs. Further information on the processing and curation of this dataset can be found here⁵.

This collection enabled the exploration of subsampling and aggregation methods in a typical learning context for neuroimaging^{6,7}. Exploring the relationship between the number of simulations and performance further allows for MCA-enabled resampling to be evaluated as a method of dataset augmentation.

As the target for classification, individual-level phenotypic data strongly implicated in brain connectivity was desired. Participant age, which has consistently been shown to have a considerable impact on brain connectivity^{8–11}, was selected and turned into a binary target by dividing participants into adult (> 18) and non-adult groups (68% adult).

Preprocessing

Prior to being used for this task, the brain networks being were represented as symmetric 83×83 adjacency matrices, sampled upon the Desikan-Killiany-Tourville¹² anatomical parcellation. To reduce redundancy in the data, all edges belonging to the upper-triangle of these matrices were preserved and vectorized, resulting in a feature vector of 3,486 edges per sample. All samples were preprocessed using one of four standard techniques:

Raw The raw streamline count edge-weight intensities were used as originally calculated.

Log Transform The \log_{10} of edge weights were taken, and edges with 0 weight prior to the transform were reset to 0.

Rank Transform The edges were ranked based on their intensity, with the largest edge having the maximum value. Ties

were settled by averaging the rank, and all ranks were finally min-max scaled between 0 and 1.

Z-Score The edge weights were z-scored to have a mean intensity of 0 and unit variance.

Machine Learning Pipelines

The preprocessed connectomes were fed into pipelines consisting of two steps: dimensionality reduction and classification. Dimensionality reduction was applied using one of two methods:

Principal Component Analysis The connectomes were projected into the 20 dimensions of highest variance. The number of components was chosen to capture approximately 90% of the variance present within the dataset.

Feature Agglomeration The number of features in each connectome were reduced by combining edges according to maximum similarity/minimum variance using agglomerative clustering¹³. The number of resulting features was 20, to be consistent with the number of dimensions present after PCA, above.

After dimensionality reduction, samples were fed into one of five distinct classifiers as implemented through scikit learn¹⁴:

Support Vector Machine The model was fit using a radial basis function (RBF) kernel, L2 penalty, and a balanced regularization parameter to account for uneven class membership.

Logistic Regression A linear solver was used due to the relatively small dataset size. L2 regularization and balanced class weights were used, as above.

K-Nearest Neighbour Class membership was determined using an L2 distance and the nearest 10% of samples, scaling with the number of samples used for training.

Random Forest 100 decision trees were fit using balanced class weights, each splitting the dataset according to a maximum of 4 features per node (corresponding to the rounded

square root of 20 total features).

AdaBoost A maximum of 50 decision trees were fit sequentially such that sample weights were iteratively adjusted to prioritize performance on previously incorrectly-classified samples, consistent with¹⁵.

The hyperparameters for all models were refined from their default values to be appropriate for a small and imbalanced dataset. The performance for all pipeline combinations of preprocessing methods, dimensionality reduction techniques, and models using the reference (i.e. unperturbed) executions in the dataset ranged from an F1 score of 0.64–0.875 with a mean of 0.806; this evaluation was performed on a consistent held-out test set which was used for all experiments, as described in a following section. This set of models was chosen as it includes i) well understood standard techniques, ii) both parametric and non-parametric methods, iii) both ensemble and non-ensemble methods, and iv) models which have been commonly deployed for the classification neuroimaging datasets^{8,16–22}.

Dataset Sampling

A chief purpose of this manuscript involves the comparison of various forms of aggregation across equivalently-simulated pipeline outputs. Accordingly, the dataset was resampled prior to dimensionality reduction and classifiers were trained, evaluated, and combined according to the following procedures:

Reference Networks generated without any MCA perturbations were selected for input to the models, serving as a benchmark.

Jackknife The datasets were repeatedly sampled such that a single randomly chosen observation of each unique network was selected (i.e. derived from the same input datum). This resampling was performed 100 times, resulting in the total number of resamplings being $5 \times$ larger than the number of unique observations per network, ensuring a broad and overlapping sampling of the datasets.

Median The edgewise median of all observations of the same network were used as the samples for training and evaluation.

Mean Similar to the above, the edgewise mean of all observations for each network were computed and used as input data to the classifiers in both collections.

Consensus A distance-dependent average network²³ was computed across all observations of each network. This data-aware aggregation method, developed for structural brain network analysis, preserves network properties often distorted when computing mean or median networks.

Mega-analysis All observations of each network were used simultaneously for classification, increasing the effective sample size. Samples were organized such that all observations of the same network only appeared within a single fold for training and evaluation, ensuring double-dipping was avoided.

Meta-analysis Individual classifiers trained across jackknife dataset resamplings, above, were treated as independent models and aggregated into an ensemble classifier. The ensemble was fit using a logistic regression classifier across the outputs of the jackknifed classifiers to learn a relationship between the predicted and true class labels.

The robustness and possible benefit of each subsampling approach was measured by evaluation on a subset of all MCA simulations, including 9 distinct numbers of simulations, ranging from 20 to 2 simulations per sample. Combining the dataset sampling methods, the set of simulations, preprocessing strategies, dimensionality reduction techniques, and classifier models, there were 2,200 models trained and evaluated.

Training & Evaluation

Prior to training models on the brain networks, 20% of subjects were excluded from each dataset for use as an out-of-sample test dataset for all experiments. With the remaining 80% of subjects, cross validation was performed following a

stratified grouped k -fold approach ($k = 5$). In this approach, samples were divided into training and validation sets such that the target variable was proportionally represented on each side of the fold (stratified), conditional upon all observations from the same individual, relevant for the mega-analysis dataset sampling method, falling upon the same side of the fold (grouped). This resulted in 5 fold-trained classifiers per configuration, each trained on 64% of the samples and validated on 16%, prior to each being tested on the remaining 20% of held-out samples. All random processes used in determining the splits used the same seed to remove the effect of random sampling.

Classifiers were primarily evaluated on both the validation and test (out-of-sample) sets using F1 score, a standard measure for evaluating classification performance. The generalizability of predictions was defined as:

$$G = 1 - |F1_{test} - F1_{validation}| \quad (1)$$

where a score of 1 (maximum) indicates the equivalent performance across both the validation and test sets, and a lower score (minimum of 0) indicates inconsistent performance. The absolute change in performance was used in Eq. 1, resulting in a score which penalizes spurious over-performance similarly to under-performance, as all inconsistency is undesirable when applying a classifier out-of-sample.

Differences in F1 score and Generalizability were used to measure the change in performance between the reference and other dataset sampling techniques, and statistical comparisons were made through Wilcoxon Signed-Rank Tests.

Results

The figures and findings presented in this section represent a summary of the complete experiment table which consists of performance measures and metadata for all 2,200 models tested. The complete performance table alongside the table of significant differences, are made available through the GitHub repository.

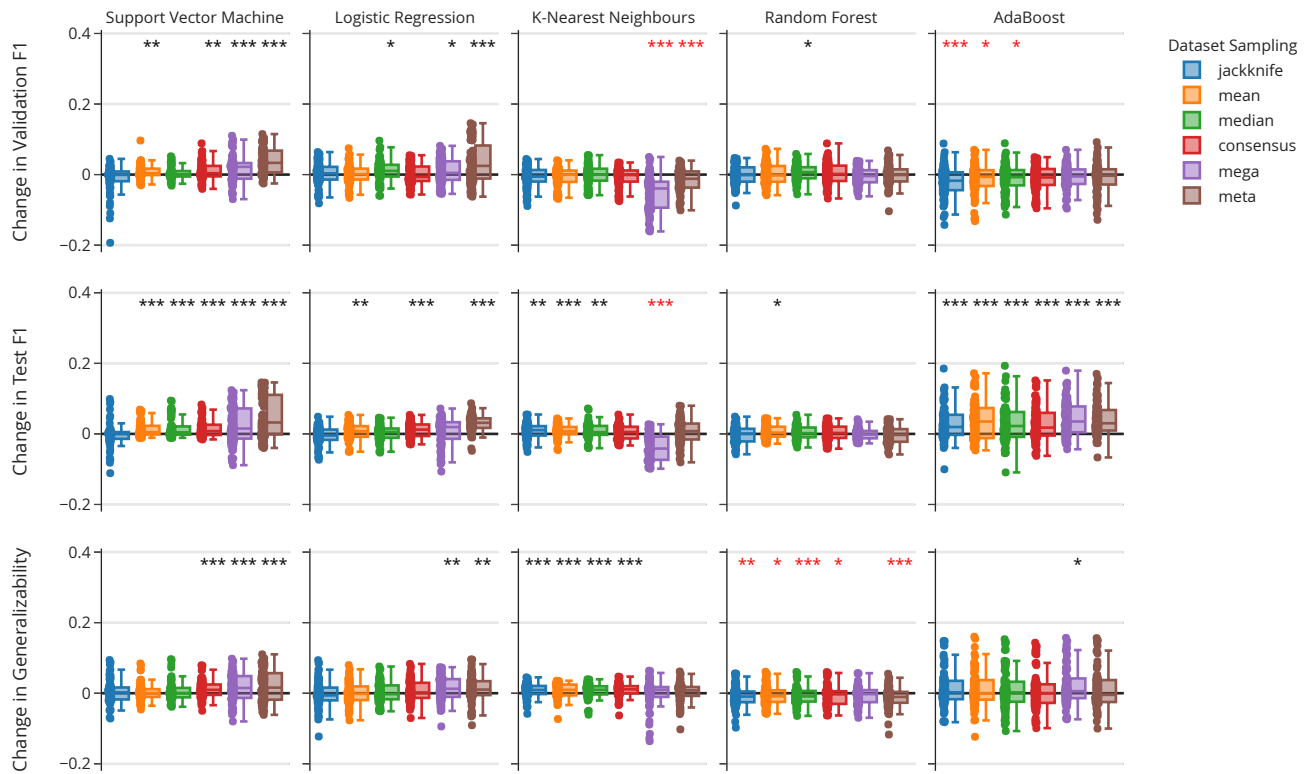


Figure 1. Relative change in classifier performance with respect to classifier type and dataset sampling strategies as measured by change in F1 score on the validation set (top) or test set (middle), as well as the generalizability of performance (bottom). Each star annotation indicates an order of magnitude of statistically significant change, beginning at 0.05 for one star and decreasing from there, with those in black or red indicating an increase or decrease due to resampling, respectively.

Data Resampling Improves Classification

The change in performance for each model and dataset sampling technique is shown in Figure 1. The change in performance was measured as a change in F1 score on the validation set, the change in F1 score on the test set, and the change in overall generalizability, a measure which summarizes the similarity between validation and test performance for a given model.

The support vector machine and logistic regression models improve across each of these three measures for a variety of dataset sampling techniques, meaning that the addition of the MCA-perturbed samples improves the training, testing, and

overall generalizability of the classifiers.

Distinctly, k-nearest neighbours (KNN) and AdaBoost classifiers experience minimal change in validation and often see their performance decline. However, the improvement of these classifiers on the test set suggests that resampling reduced overfitting in these classifiers. In the case of KNN, this translates to improved generalizability, while in the case of AdaBoost generalizability was largely unchanged, suggesting that the model went from underperforming to overperforming after dataset resampling. The unique decline in performance when using the mega-analytic resampling technique on KNN classifier is suggestive of poor hyperparameterization, as there

is a strong relationship between the number of samples in the dataset and the k parameter of the model. At present this parameter was scaled linearly with the number of MCA simulations used, however, it is both possible that an improved scaling function exists or that the model performance degrades with large sample sizes making it a poor model choice given this resampling technique.

The random forest classifiers uniquely did not see a significant change in validation or testing performance across the majority of resampling techniques. However, these classifiers did experience a significant decrease in the generalizability of their performance, meaning that there was a larger discrepancy between training and testing performance in many cases. This distinction from the other models is likely due to the fact that random forest is a simple ensemble technique which takes advantage of training many independent classifiers and samples them to assign final class predictions. It is likely that this approach forms more generalizable predictions generally, and thus the addition of more data does not improve performance further. While AdaBoost is also an ensemble method, the iterative training of models based on sample difficulty allows for the added variance in those samples to play an increasingly central role in the construction of class relationships.

Across all classifier types, it was found that both mega- and meta-analytic approaches outperformed other methods slightly, though this was not statistically significant. Additionally, while certain combinations of preprocessing, dimensionality reduction, and classifiers performed more harmoniously than others, there was no significant relationship between the performance of any single resampling method and preprocessing or dimensionality reduction technique. The above results show that dataset augmentation through MCA-perturbed pipeline outputs may be an effective way to improve the performance and generalizability of non-ensemble classifiers tasked with modeling brain-phenotype relationships, both within and out of sample.

Resampling Leads to Consistent Performance

To better characterize the benefit of resampling, the relationship between the magnitude of improvement and the baseline performance of the classifier were further explored (Figure 2). We found that the increase in the generalizability of a classifier was inversely related to the baseline generalizability (Figure 2; top). In other words, the less generalizable a classifier was originally, the more its generalizability improved (significant at $p < 0.05$ for all dataset sampling strategies and classifier other than KNN). There were several situations in which the generalizability of models were noted to decrease, however, though this only occurred for models with high generalizability scores (all > 0.935). Importantly, the relative change in generalizability shifts scores towards a single “mode”, suggesting a less biased estimate of the true generalizability of performance on the task, and mitigating both under- and over-performance due to chance.

When exploring the relationship between F1 and generalizability (Figure 2; bottom), it becomes apparent that even for the majority of models which may not have improved performance along both axes, either their generalizability or F1 score is improved. While an ideal classifier would reside in the top-right of the shown plots, the dataset resampling techniques consistently shift the distributions in this direction and improve classifiers along one if not both of these axes. Importantly, the variance in performance across both of these axes is significantly decreased, suggesting that resampling lead to the development of more reliable and reproducible classifiers.

Number of Simulations is Largely Unimpactful

While we previously note an increase in classifier performance due to perturbation-enabled dataset resampling, it was important to explore the relationship between the number of simulated samples and the performance (Figure 3). There was no relationship between the number of independent simulations and performance, as measured by either F1 or generalizability,

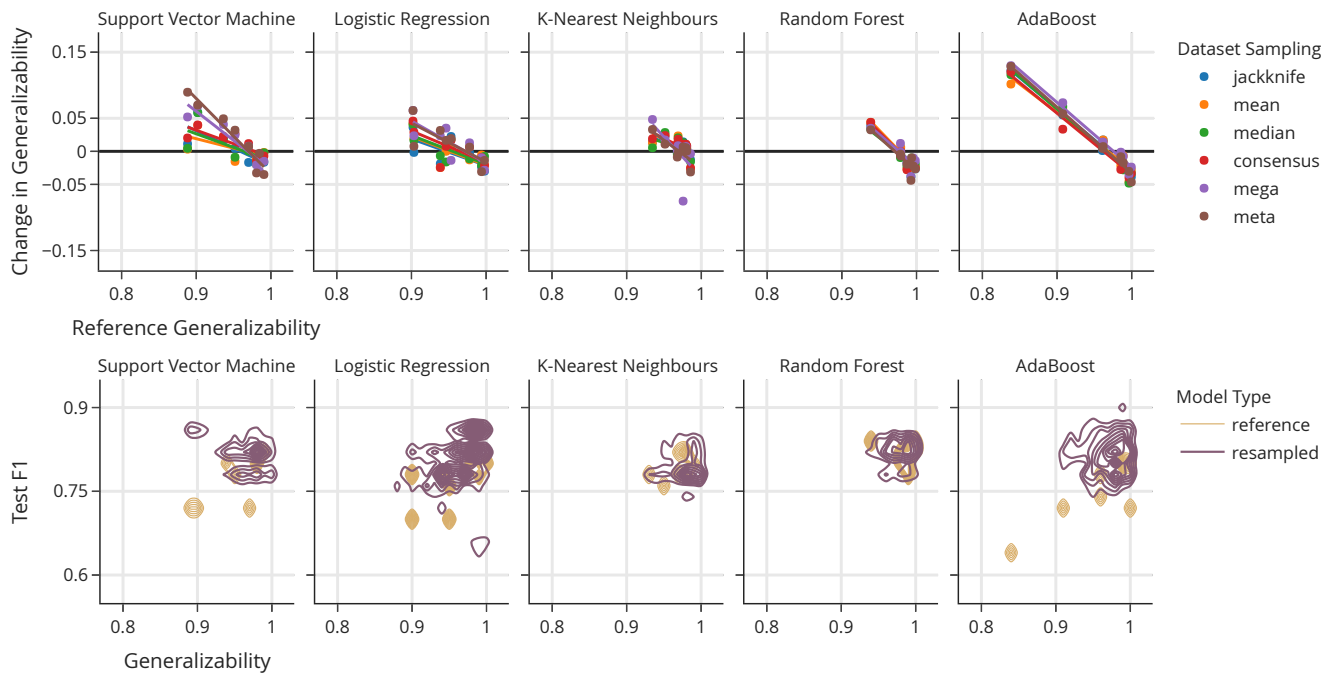


Figure 2. Relationship between generalizability and resampling. Top: change in the generalizability of classifiers with respect to the reference generalizability. Each data point represents the mean change in generalizability for all models using the same preprocessing and dimensionality reduction techniques for a given classifier and dataset sampling strategy. Bottom: contour density distributions of generalizability and F1 scores across all models for both reference and resampled training.

for all dataset resampling techniques other than mega-analysis.

In the case of the mega-analytic approach, however, there was a significant positive relationship between the number of samples used and the generalizability of performance, though there remained no increase in F1 score. The mega-analysis approach is the only approach which changes the number of samples being provided directly to the classifiers, thus mimics an increase in sample size for traditional experiments. While outlying samples may play a small role in many of the proposed forms of resampling, or non-existent in the median case, the mega analytic approach treats all simulations with equal importance as unique samples in the dataset. It is for this reason that the observed relationship here is consistent to what one would expect when increasing the number of samples in their experiment.

Discussion

The numerical perturbation of analytic pipelines provides a unique, data-agnostic, and computationally unintrusive method for dataset augmentation. A technique such as MCA, samples can be simulated across an array of controlled executions and used to enrich collections. We demonstrate that such a collection can be used to improve the training, testing, and generalizability of classifiers.

Through the training and evaluation of 2,200 combinations of preprocessing method, dimensionality reduction technique, classifier type, and resampling strategy, we found consistent improvement across all measured axes. Interestingly, while there was a statistically significant improvement in many classifiers, there was no significant difference between the improvement provided by each resampling strategy. This result importantly demonstrates that the added variability in results obtained through MCA is meaningful itself and the most im-

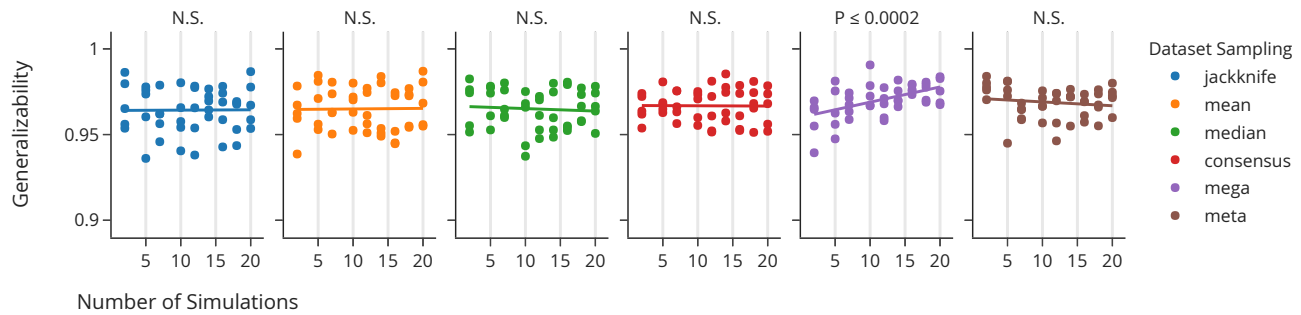


Figure 3. The generalizability of classifiers using each dataset sampling technique with respect to the number of MCA simulations. Each number of simulations was sampled a single time, to avoid artificial skewing of the dataset due to the inclusion of “higher” or “lower” quality samples; a single drawing of each split mimics a true perturbation experiment context.

portant determination of performance is the inclusion of this variability.

While the non-ensemble methods benefited the most from the dataset resampling strategies, the results presented in Figure 2 demonstrate that variability in performance across classifier configuration is reduced in all cases, and often improved along one or both of the F1 and generalizability axes.

Although performance was improved by the integration of MCA simulated samples, performance was not significantly related to the number of simulations used in any case other than the mega-analytic resampling strategy. The independence of performance and number of simulations is encouraging, as a key limitation for using Monte Carlo methods is the often extreme computational overhead. The ability to use a small number of simulations and achieve equivalent performance through the majority of resampling techniques allows for significantly better performance without either added data collection and a theoretical doubling the sample processing time.

An important limitation of our claim that classifiers with poorer baseline performance benefit more from augmentation is the limit to which that claim remains true. For example, it is unlikely that the trend observed here, with a mean baseline performance of 0.81, would hold across models operating

with baseline performance near chance. Characterizing the behaviour of this technique across a range of classification contexts and performances would shed light on whether this technique could be applied globally or if it is limited to making “good” models better.

While the results presented here provide strong evidence in favour of dataset augmentation through numerical perturbations, the improvement from these methods could not be situated relative to further data acquisition or data subsampling due to the limited size of the available repeated-measures dataset¹. It is likely, however, that the methods demonstrated here will work harmoniously with traditional methods of dataset augmentation, and that is an exciting avenue for future work.

A common issue in many machine learning contexts is the unbalanced nature of datasets. When using a nearest-neighbour classifier, for instance, a dramatic difference the membership of each group could have significant impact on model hyper-parameters and performance. In contexts where improved sampling is not possible, such as when considering a clinical population, perturbation-augmented datasets could be applied for realistic upsampling of data. In this case, a mega-analytic aggregation strategy could be used in which more simulations would be performed for members of

the under-represented class. This application is particularly important, as upsampling is often challenging in biological contexts where realistic simulation models are sparse.

Conclusion

This work demonstrates the benefit of augmenting datasets through numerical perturbations. We present an approach which leverages the numerical instability inherent to pipelines for creating more accurate and generalizable classifiers and representations of brain-phenotype relationships. While the approach and results demonstrated here were specifically relevant in the context of brain imaging, the data-agnostic method for inducing perturbations and off-the-shelf machine learning techniques used suggest that this approach may be widely applicable across domains. This work uniquely shows that numerical uncertainty is an asset which can be harnessed to increase the robustness of learned relationships among data.

Data & Code Availability

The perturbed connectomes were publicly available data resource previously produced and made available by the authors¹. They can be found persistently at <https://doi.org/10.5281/zenodo.4041549>, and are made available through The Canadian Open Neuroscience Platform (<https://portal.conp.ca/search>, search term "Kiar"). All software developed for processing or evaluation is publicly available on GitHub at <https://github.com/gkpapers/2020AggregateMCA>. Experiments were launched on Compute Canada's HPC cluster environment.

Author Contributions

GK was responsible for the experimental design, data processing, analysis, interpretation, and the majority of writing. All authors contributed to the revision of the manuscript. TG and ACE contributed to experimental design, analysis, interpretation. The authors declare no competing interests for this work. Correspondence and requests for materials should be addressed to Gregory Kiar at gregory.kiar@mail.mcgill.ca.

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