

Evaluating Shortcut Utilization in Deep Learning Disease Classification through Counterfactual Analysis

Vibujithan Vigneshwaran^{1,2}

VIBUJITHAN.VIGNESHWAN@UCALGARY.CA

Emma A.M. Stanley^{1,2}

EMMA.STANLEY@UCALGARY.CA

Raissa Souza^{1,2}

RAISSA.SOUZADEANDRAD@UCALGARY.CA

Erik Ohara^{1,2}

ERIK.OHARA@UCALGARY.CA

Matthias Wilms^{1,2,3,4,5}

MATTHIAS.WILMS@UCALGARY.CA

Nils D. Forkert^{1,2,5}

NILS.FORKERT@UCALGARY.CA

¹ Department of Radiology, University of Calgary, Calgary, AB, Canada

² Hotchkiss Brain Institute, University of Calgary, Calgary, AB, Canada

³ Department of Pediatrics, University of Calgary, Calgary, AB, Canada

⁴ Department of Community Health Sciences, University of Calgary, Calgary, AB, Canada

⁵ Alberta Children’s Hospital Research Institute, University of Calgary, Calgary, AB, Canada

Editors: Under Review for MIDL 2025

Abstract

Although deep learning models can surpass human performance in many medical image analysis tasks, they remain vulnerable to algorithmic shortcuts, where spurious correlations in the data are exploited, which may lead to reduced trust in their predictions/classifications. This issue is especially concerning when models rely on protected attributes (*e.g.*, sex, race, or site) as shortcuts. Such shortcut reliance not only impairs their ability to generalize to unseen datasets but also raises fairness concerns, ultimately undermining their purpose for computer-aided diagnosis. Previous techniques for analyzing protected attributes, such as supervised prediction layer information tests, only highlight the presence of protected attributes in the feature space but do not confirm their role in solving the primary task. Determining the impact of protected attributes as shortcuts is particularly challenging, as it requires knowing how a model would perform without those attributes — a counterfactual scenario typically unattainable in real-world data. As a workaround, researchers have addressed the absence of counterfactuals by generating *synthetic* datasets with and without protected attributes. In this study, we propose a novel approach to evaluate *real-world* datasets and determine the extent to which each protected attribute is used as a shortcut in a classification task. Therefore, we define and train a causal generative model to produce causally-grounded counterfactuals, removing protected attributes from activations and allowing us to measure their impact on model performance. Employing T1-weighted MRI data from 9 sites (835 subjects: 426 with Parkinson’s disease (PD) and 409 healthy), we demonstrate that counterfactually removing the ‘site’ attribute from the penultimate layer of a trained classification model reduced the AUROC for PD classification from 0.74 to 0.65, indicating a 9% performance improvement achieved by using ‘site’ as a shortcut. In contrast, counterfactually removing the ‘sex’ attribute had minimal impact on performance, with only a slight change of 0.004, indicating that ‘sex’ was not utilized as a shortcut by the classification model. The proposed method offers a robust framework for assessing shortcut utilization in medical image classification, paving the way for improved bias detection and mitigation in medical imaging tasks. The code for this work is available on [GitHub](#).

Keywords: shortcuts, causality, counterfactual, Parkinson’s disease, bias mitigation

1. Introduction

While deep learning models have surpassed human capabilities in many medical image analysis tasks, a significant concern are algorithmic shortcuts, where models learn spurious correlations in the training data, potentially resulting in biased predictions/classifications (Geirhos et al., 2020; Brown et al., 2023). This issue becomes particularly problematic when models rely on protected attributes (*e.g.*, sex, race, or site) as shortcuts to make predictions. Such reliance hinders the ability of models to generalize to unseen datasets, ultimately undermining their intended purpose of computer-aided diagnosis and, thereby, reducing trust in model predictions. Thus, shortcuts — along with their causes, evaluation, and mitigation — have been studied across various subfields of medical image analysis, including aspects such as fairness, bias mitigation, and harmonization (Stanley et al., 2024; Souza et al., 2023; Vigneshwaran et al., 2024b). However, in any case, the crucial initial step is to identify the extent to which a model relies on shortcuts, a challenge that remains mostly unresolved.

Disparities in performance across protected attribute subgroups may indicate that the model is relying on shortcuts. However, it is not possible to conclude that a model is using these attributes as shortcuts solely based on performance disparities, as these differences may result from a combination of distribution shifts and shortcut learning (Castro et al., 2020). Researchers have explored the presence of protected attributes within disease classification models using methods like the supervised prediction layer information test (SPLIT) and multitask learning (Glocker et al., 2023). SPLIT involves training the model for a primary task (*e.g.*, disease classification) and then retraining only the final layer for a secondary task (*e.g.*, race classification). For example, Souza et al. (2024b) demonstrated that even when attributes, such as site, scanner type, and sex, are not explicitly included, they can still be inferred from the penultimate layer of a deep learning disease classification model. However, the presence of protected attributes in the penultimate layer alone does not necessarily mean that these attributes are actually being used for the primary task. A good example of this is provided by Glocker et al. (2023), who demonstrated that even when a disease classification model’s backbone is randomly initialized (*i.e.*, not trained), it can still infer information about racial identity in the penultimate layer. This is because current deep learning models have such high capacities that even random transformations can find some information about protected attributes in the model.

In order to determine if protected attributes are not only present in the model but are actually influencing the primary task, researchers have used visual feature space exploration techniques like principal component analysis (PCA) and t-SNE. These methods aim to explore the information encoded within a model, how it is distributed, and how it aligns with the primary task (Glocker et al., 2023). However, quantifying the extent to which protected attributes contribute as actual shortcuts may be challenging because it requires knowledge of how well the model *would* perform if it did not have access to those attributes. Such a *counterfactual* dataset is typically unattainable in real-world scenarios. As a preliminary step, Stanley et al. (2025) addressed this challenge by using a synthetic dataset to measure the degree of shortcut utilization in a classification model. Therefore, they generated *counterfactual* synthetic datasets, both with and without the presence of a protected attribute,

which enabled the quantification of the degree to which a shortcut was utilized in a deep learning classification task.

In this work, rather than relying on synthetic data that has limited usefulness in clinical applications, we propose using causally-grounded counterfactuals on *real-world* data. Specifically, we counterfactually remove latent representations of protected attributes to quantify shortcut utilization in classification models. In this context, counterfactuals represent hypothetical scenarios produced by querying causal generative models with questions such as “What would the latent representations look like if they did not contain any protected attributes?” and have recently been utilized in the field of algorithmic fairness (Kusner et al., 2018; Cornacchia et al., 2023). However, to the best of our knowledge, our work is the first to utilize counterfactuals to quantify the extent to which a deep learning image-based disease classification model relies on and makes use of shortcuts. It is important to note that our goal is not to develop a fair prediction model or to mitigate bias in the data. Instead, we aim to first determine whether certain protected attributes are used in deep learning disease prediction/classification models as shortcuts and then assess the extent of their contribution to the final prediction.

2. Methodology

As a representative case example, we first train a multi-site Parkinson’s disease (PD) classification model and identify performance disparities across sex and site subgroups. First, using SPLIT and PCA, we demonstrate the presence of sex and site attributes in the penultimate layer. Next, we apply our proposed causal analysis-based technique to counterfactually remove these attributes and validate their removal through updated SPLIT and PCA analyses. Finally, we evaluate the impact of these attributes on classification performance by computing differences in the model’s accuracy.

2.1. Classification model

For PD classification, we used a modified SFCN model (Peng et al., 2021). In this modification, we replaced the original model’s final $1 \times 1 \times 1$ convolution layer with a fully connected layer to map all channels to a single output neuron, which served as the logit. The model was trained until convergence, and the model with the best validation loss was selected. We utilized brain imaging data from nine sites, including 835 subjects (426 with PD and 409 healthy) to develop and evaluate our method. The following hyperparameters were used to achieve the best validation loss: number of channels = [28, 58, 128, 256, 256, 64], learning rate = 1×10^{-4} , and weight decay = 1×10^{-5} . PyTorch was used for the implementation of the model, which was trained on an NVIDIA RTX 3090 GPU. We refer to all layers except the final layer as the “backbone” and the final layer as the “prediction layer” throughout the remainder of this work.

2.2. Counterfactually removing protected attributes

Our approach to removing protected attributes from a trained classification model is based on asking the hypothetical question: “What would the activations in the penultimate layer

look like if they did not contain any protected attributes?” This involves extracting activations from the penultimate layer and generating all possible counterfactual activations for a specific protected attribute. These counterfactual activations are then averaged to remove any information related to the protected attribute. For example, for the ‘site’ attribute, the extracted 64-dimensional activations from the penultimate layer for each image are referred to as $\mathbf{x}_i^{site}$, and the corresponding counterfactual activations are denoted as $\mathbf{x}_{i \rightarrow j}^{site}$, where the subscript i represents the original site and the variable $j \in [1, n]$ indicates the counterfactual site, and n is the number of sites. The activation with the site attribute removed for each image is denoted as $\mathbf{x}^{-site}$ and is calculated as follows:

$$\mathbf{x}^{-site} = \frac{1}{n} \sum_{j=1}^n \mathbf{x}_{i \rightarrow j}^{site} \quad (1)$$

The causal analysis used in the background of the proposed method to remove potential shortcuts starts with a directed acyclic graph (DAG), which represents causal relationships between variables. In a DAG, each node corresponds to a variable, and each directed edge indicates a causal influence. In this work, the MACAW framework (Vigneshwaran et al., 2024a) was used as the backbone causal generative model as it directly encodes a DAG within a normalizing flow (Kobyzev et al., 2021). This encoding is achieved using causally masked autoencoders, which incorporate causal domain knowledge by masking connections to preserve the causal dependencies between parent and child nodes. Once the normalizing flow is masked, the model is trained to learn a joint probability distribution through maximum likelihood estimation. After model training, counterfactuals can be generated to investigate hypothesized alternate scenarios. In our setup, this allows us to explore how changes in a specific protected attribute (*e.g.*, site) affect the activations. The model’s inherent invertibility ensures deterministic behavior, enabling the precise generation of counterfactuals.

We first predefined a DAG to incorporate domain knowledge into the MACAW model. The causal graph used in this work is shown in Figure 3(a), where sex, site, scanner, and PD status are set as causal variables influencing the activations. The prior distributions for each causal variable were estimated from the training data. For sex and PD, a Bernoulli distribution was used, while site values were one-hot encoded and modeled with a One-Hot categorical distribution as the prior. The model was trained until convergence, and the version with the best validation loss was selected. The following hyperparameters were used to achieve the best validation loss: hidden layer multipliers = [4,6,4], learning rate = 1×10^{-4} , weight decay = 1×10^{-5} , and number of MACAW layers = 6.

2.3. The supervised prediction layer information test (SPLIT)

SPLIT was proposed by Glocker et al. (2023) to confirm the presence of protected attributes in the penultimate layer. Therefore, the SFCN model described above was trained until convergence to classify PD and healthy subjects. Then, all backbone parameters were frozen, and the prediction layer was replaced with a new one. This new prediction layer was trained specifically to classify protected attributes, including site and sex in this work, learning a new set of weights assigned to the features in the penultimate layer. A model (prediction layer) was trained for sex classification, while separate models were trained for

each site using a one-vs-rest approach. Each model was trained until convergence, and the model parameters with the best validation loss were selected. The performance of the new prediction layer was then evaluated on test data.

2.4. Unsupervised feature space exploration with PCA

This test projects the model’s activation space onto a lower-dimensional PCA space and qualitatively evaluates whether the PCA modes for PD classification and those for the protected attributes form visible groupings in scatter plots. If such groupings are observed, it suggests that the protected attributes are being used as shortcuts to some extent. Therefore, features (activations) from the penultimate layer were first extracted by passing the test data through the backbone of the SFCN model, resulting in a 64-dimensional feature vector for each test image. Next, the feature space was decomposed into principal components using PCA. The first and second principal components were marginalized and visualized for PD, site, and sex to qualitatively identify patterns.

3. Experiments

3.1. Data

We utilized brain imaging data from nine sites, including 835 subjects (426 with PD and 409 healthy) to develop and evaluate our shortcut utilization evaluation method. The studies included were the BioCog (Clinical, Magnetic Resonance, and Genetic Biomarkers of Cognitive Decline and Dementia in Parkinson’s Disease) (Acharya et al., 2007), C-BIG (Montreal Neurological Institute’s Open Science Clinical Biological Imaging and Genetic Repository) (Das et al., 2022), Neurocon (Badea et al., 2017), Tao Wu (Badea et al., 2017), OpenNeuro Japan (Yoneyama et al., 2018), PD MCI Calgary (Lang et al., 2019), and Hamburg (Talai et al., 2021). For this work, we included subjects with T1-weighted magnetic resonance imaging (MRI) datasets and known ground truth labels. All studies received ethics approval from their respective local ethics boards, and written informed consent was obtained from all participants in compliance with the Declaration of Helsinki. In the preprocessing step (Camacho et al., 2023), the T1-weighted images underwent skull-stripping using HD-BET (Isensee et al., 2019), resampling to 1 mm isotropic resolution with linear interpolation, and bias field correction (Tustison et al., 2010). Each T1-weighted MRI data was then affinely registered to the PD25-T1-MPRAGE- 1 mm atlas (Xiao et al., 2017) and center-cropped to $160 \times 192 \times 160$ voxels. The data was stratified by site and sex and split into training (50%), validation (10%), and testing (40%) sets. The following integer identifiers were assigned to the sites for reference: ‘PD MCI Calgary: 0, UKBB: 1, Hamburg: 2, C-BIG: 3, Neurocon: 4, OpenNeuro Japan: 5, PD MCI PLS: 6, Taowu: 7, BioCog: 8’ (Figure 4).

3.2. PD classification

After training, the model was evaluated on the test set, achieving an overall area under the receiver operating characteristics (AUROC) of 0.74. This performance is comparable to other multisite PD classification studies (Camacho et al., 2023). Subsequently, we analyzed the performance of the model across individual sites and sexes. As illustrated in Figure 1(a), different sites exhibited varying performance, with site 2 achieving an AUROC of

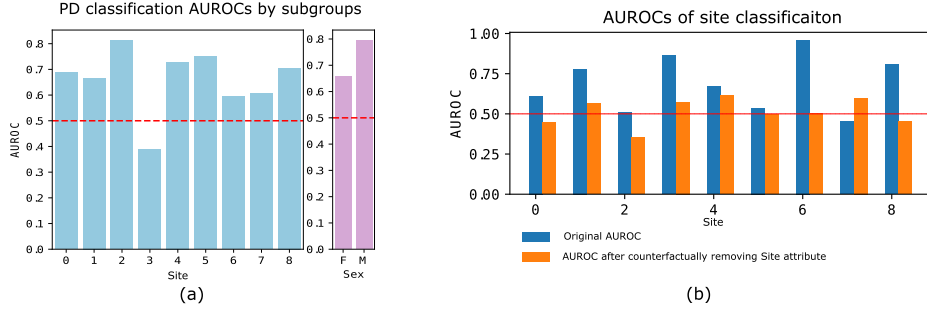


Figure 1: (a) The model’s performance for Parkinson’s disease (PD) classification was analyzed across different subgroups, revealing significant variations in AUROC scores. (b) The AUROC for site classification was compared before and after the counterfactual removal of the site attribute.

0.81, while site 3 had an AUROC of 0.38. Additionally, a disparity in performance between male (0.65) and female (0.79) participants was observed. These discrepancies might be related to algorithmic shortcutting or underlying distribution shifts.

3.3. Presence of protected attributes

When performing SPLIT on the data for each site to determine the presence of site-specific information in the penultimate layer, certain sites (sites 6, and 8) were easily distinguishable from others, achieving AUROC values close to 0.9. However, some sites (sites 2, 5, and 7) had AUROC values close to chance level (Figure 1(b)). Additionally, sex classification using SPLIT on the penultimate layer achieved an AUROC of 0.62, suggesting the presence of protected attributes to some extent.

Next, we analyzed the activation space of the penultimate layer using PCA. The results revealed visible groupings of sites in the scatter plots, and the distributions of certain sites aligned more closely with healthy subjects, while others aligned with PD subjects (Figure 2). However, no distinct alignment patterns were observed when comparing sex distributions (Figure 5). These findings suggest that site information may serve as a shortcut to some extent in the trained PD deep-learning classification model.

3.4. Removing protected attributes counterfactually

We applied the proposed technique to counterfactually remove site and sex information from the activation layers in separate experiments (*i.e.*, one for site removal and another for sex removal). After counterfactually removing these attributes from the penultimate layer, we evaluated their presence using SPLIT. The AUROCs for all sites dropped to approximately 0.5 (to chance level), while the sex classification AUROC decreased from 0.62 to 0.47. These results confirm that the counterfactual method successfully removed site and sex information from the penultimate layer.

Furthermore, we analyzed the PCA modes after the removal of the site and sex attributes. As shown in Figure 2, the site distributions became more homogenous, with no

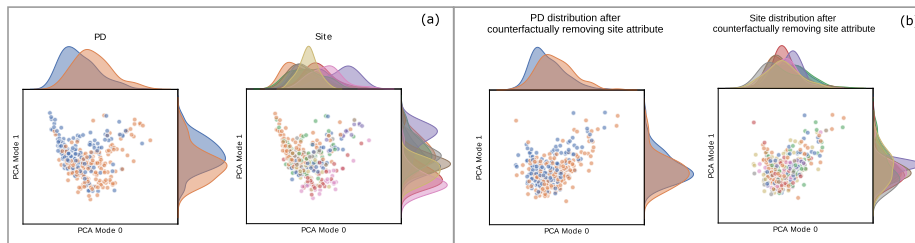


Figure 2: (a) PCA modes 1 and 2 of the activation space were visualized based on PD labels and site labels, (b) the visualization was then repeated after counterfactually removing site attribute from the activations.

groupings or alignment observed between specific sites and PD classes. Similarly, after the removal of the sex attribute, the male and female distributions overlapped more strongly, indicating the successful removal of the sex attribute. However, there was minimal change in the PD distributions after removing the sex attribute, suggesting that sex was not utilized as a shortcut in the classification task. (Figure 5).

3.5. Classification performance after removing protected attributes

We hypothesized that if the model utilized protected attributes as shortcuts, removing these attributes would result in a change in model performance, indicating that performance disparities were caused by shortcuts. After removing the site attribute, the PD classification AUROC decreased from 0.74 to 0.65, demonstrating a 0.09 performance drop that may be attributable to the use of the site as a shortcut. In contrast, removing the sex attribute resulted in a negligible performance change (0.004), indicating that sex information was minimally present in the penultimate layer and not or only to a very small extent used as a shortcut for PD classification. Consequently, the removal of sex information had little impact on the model’s performance.

We further analyzed site- and sex-wise shortcut utilization within subgroups. Figure 3 illustrates the AUROC differences observed after removing protected attributes. Notably, removing the site attribute led to significant performance reductions for the data from certain sites (*e.g.*, sites 7 and 8), while removing the sex attribute caused minimal changes. Interestingly, the data from some sites and the female population showed slight AUROC improvements after attribute removal, which may suggest that the model is shifting toward better generalization. However, a more comprehensive analysis, including comparisons of sample sizes and PD distribution across subgroups, is required to validate this hypothesis.

4. Conclusion

We demonstrated in this work that causally-grounded counterfactuals can be used for a quantification of the extent to which protected attributes are used as shortcuts in classification tasks. Our findings revealed that counterfactually removing the site attribute from the penultimate layer resulted in a 0.09 AUROC reduction in PD classification, indicating that site-related information was used as a shortcut in the initial classification model.

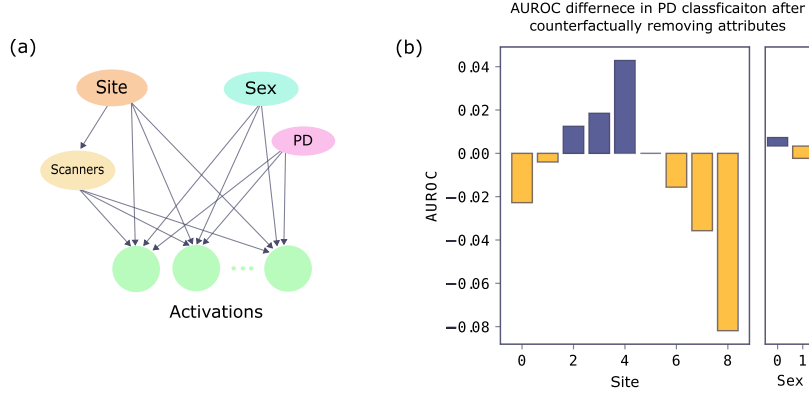


Figure 3: (a) Causal directed acyclic graph (DAG) used for counterfactual generation. (b) Site- and sex-wise AUROC changes after removing the corresponding protected attributes.

Conversely, removing the sex attribute had minimal impact on classification performance, suggesting that sex was not utilized as a shortcut.

To accurately measure the impact of protected attributes, it is crucial to modify only the protected attributes without altering disease-related information in the feature space. Additionally, when multiple protected attributes are present, it is essential to adjust them in accordance with their causal relationships. Traditional harmonization techniques, such as ComBat (Orlhaç et al., 2022), cannot be used for this purpose because they harmonize feature distributions across subgroups without first disentangling disease effects and protected attributes. Researchers (Brown et al., 2023; Souza et al., 2024a) have previously used adversarial multitask learning for disentangling. However, such adversarial techniques fail to address the underlying causal structure in the data and may inadvertently modify other attributes. This is because they are designed as an iterative re-learning process for the primary task, making it difficult to observe the direct impact of removing only the protected attribute information.

The primary limitation of this work lies in the predefined causal graph used. We selected a graph where the PD variable is not influenced by other factors, enabling straightforward disentanglement of PD from protected attributes. However, alternative causal graph structures are also plausible. Additionally, the proposed method focuses solely on detecting shortcuts and does not address or propose any direct method for bias mitigation. This limitation arises from the inclusion of the PD attribute in the causal graph, which is necessary to disentangle protected attributes from the feature space. However, incorporating the PD attribute in the graph prevents the direct application of this method for new predictions. If a workaround is developed to exclude the PD attribute while maintaining the disentanglement, this method could be extended as a shortcut-mitigation technique in the future. In the meantime, this method can still be used as a tool for technical research to explore biases and strategies for reducing them. Given the MACAW model’s capability to handle complex causal structures, this technique is highly adaptable to other datasets/diseases, and deep learning models.

Acknowledgments

This work was supported by the Canadian Neuroanalytics scholar (CNS) program, the Canada Research Chairs program, the River Fund at Calgary Foundation, and the NSERC Discovery Grant program.

References

- Hernish J Acharya, Thomas P Bouchard, Derek J Emery, and Richard M Camicioli. Axial signs and magnetic resonance imaging correlates in parkinson’s disease. *Canadian journal of neurological sciences*, 34(1):56–61, 2007.
- Liviu Badea, Mihaela Onu, Tao Wu, Adina Roceanu, and Ovidiu Bajenaru. Exploring the reproducibility of functional connectivity alterations in parkinson’s disease. *PLoS One*, 12(11):e0188196, 2017.
- Alexander Brown, Nenad Tomasev, Jan Freyberg, Yuan Liu, Alan Karthikesalingam, and Jessica Schrouff. Detecting shortcut learning for fair medical ai using shortcut testing. *Nature communications*, 14(1):4314, 2023.
- Milton Camacho, Matthias Wilms, Pauline Mouches, Hannes Almgren, Raissa Souza, Richard Camicioli, Zahinoor Ismail, Oury Monchi, and Nils D Forkert. Explainable classification of parkinson’s disease using deep learning trained on a large multi-center database of t1-weighted mri datasets. *NeuroImage: Clinical*, 38:103405, 2023.
- Daniel C Castro, Ian Walker, and Ben Glocker. Causality matters in medical imaging. *Nature Communications*, 11(1):3673, 2020.
- Giandomenico Cornacchia, Vito Walter Anelli, Fedelucio Narducci, Azzurra Ragone, and Eugenio Di Sciascio. Counterfactual reasoning for bias evaluation and detection in a fairness under unawareness setting, 2023. URL <https://arxiv.org/abs/2302.08204>.
- Samir Das, Rida Abou-Haidar, Henri Rabalais, Sonia Denise Lai Wing Sun, Zaliqa Rosli, Krishna Chatpar, Marie-Noëlle Boivin, Mahdiah Tabatabaei, Christine Rogers, Melanie Legault, et al. The c-big repository: an institution-level open science platform. *Neuroinformatics*, 20(1):139–153, 2022.
- Robert Geirhos, Jörn-Henrik Jacobsen, Claudio Michaelis, Richard Zemel, Wieland Brendel, Matthias Bethge, and Felix A. Wichmann. Shortcut learning in deep neural networks. *Nature Machine Intelligence*, 2(11):665–673, November 2020. ISSN 2522-5839. doi: 10.1038/s42256-020-00257-z. URL <https://doi.org/10.1038/s42256-020-00257-z>.
- Ben Glocker, Charles Jones, Mélanie Bernhardt, and Stefan Winzeck. Algorithmic encoding of protected characteristics in chest x-ray disease detection models. *EBioMedicine*, 89, 2023.
- Fabian Isensee, Marianne Schell, Irada Pflueger, Gianluca Brugnara, David Bonekamp, Ulf Neuberger, Antje Wick, Heinz-Peter Schlemmer, Sabine Heiland, Wolfgang

- Wick, Martin Bendszus, Klaus H. Maier-Hein, and Philipp Kickingeder. Automated brain extraction of multisequence MRI using artificial neural networks. *Human Brain Mapping*, 40(17):4952–4964, 2019. ISSN 1097-0193. doi: 10.1002/hbm.24750. URL <https://onlinelibrary.wiley.com/doi/abs/10.1002/hbm.24750>. eprint: <https://onlinelibrary.wiley.com/doi/pdf/10.1002/hbm.24750>.
- Ivan Kobyzev, Simon J.D. Prince, and Marcus A. Brubaker. Normalizing Flows: An Introduction and Review of Current Methods. *IEEE Transactions on Pattern Analysis and Machine Intelligence*, 43(11):3964–3979, November 2021. ISSN 1939-3539. doi: 10.1109/TPAMI.2020.2992934. Conference Name: IEEE Transactions on Pattern Analysis and Machine Intelligence.
- Matt J. Kusner, Joshua R. Loftus, Chris Russell, and Ricardo Silva. Counterfactual fairness, 2018. URL <https://arxiv.org/abs/1703.06856>.
- Stefan Lang, Alexandru Hanganu, Liu Shi Gan, Mekale Kibreab, Noémie Auclair-Ouellet, Tazrina Alrazi, Mehrafarin Ramezani, Jenelle Cheetham, Tracy Hammer, Iris Kathol, et al. Network basis of the dysexecutive and posterior cortical cognitive profiles in parkinson’s disease. *Movement Disorders*, 34(6):893–902, 2019.
- Fanny Orlhac, Jakoba J Eertink, Anne-Ségolène Cottureau, Josée M Zijlstra, Catherine Thieblemont, Michel Meignan, Ronald Boellaard, and Irène Buvat. A guide to combat harmonization of imaging biomarkers in multicenter studies. *Journal of Nuclear Medicine*, 63(2):172–179, 2022.
- Han Peng, Weikang Gong, Christian F. Beckmann, Andrea Vedaldi, and Stephen M. Smith. Accurate brain age prediction with lightweight deep neural networks. *Medical Image Analysis*, 68:101871, 2021. ISSN 1361-8415. doi: <https://doi.org/10.1016/j.media.2020.101871>. URL <https://www.sciencedirect.com/science/article/pii/S1361841520302358>.
- Raissa Souza, Matthias Wilms, Milton Camacho, G Bruce Pike, Richard Camicioli, Oury Monchi, and Nils D Forkert. Image-encoded biological and non-biological variables may be used as shortcuts in deep learning models trained on multisite neuroimaging data. *Journal of the American Medical Informatics Association*, 30(12):1925–1933, 2023.
- Raissa Souza, Emma AM Stanley, Vedant Gulve, Jasmine Moore, Chris Kang, Richard Camicioli, Oury Monchi, Zahinoor Ismail, Matthias Wilms, and Nils D Forkert. Harmonytm: multi-center data harmonization applied to distributed learning for parkinson’s disease classification. *Journal of Medical Imaging*, 11(5):054502–054502, 2024a.
- Raissa Souza, Anthony Winder, Emma A. M. Stanley, Vibujithan Vigneshwaran, Milton Camacho, Richard Camicioli, Oury Monchi, Matthias Wilms, and Nils D. Forkert. Identifying biases in a multicenter mri database for parkinson’s disease classification: Is the disease classifier a secret site classifier? *IEEE Journal of Biomedical and Health Informatics*, 28(4):2047–2054, 2024b. doi: 10.1109/JBHI.2024.3352513.
- Emma A M Stanley, Raissa Souza, Anthony J Winder, Vedant Gulve, Kimberly Amador, Matthias Wilms, and Nils D Forkert. Towards objective and systematic evaluation of bias

- in artificial intelligence for medical imaging. *Journal of the American Medical Informatics Association*, 31(11):2613–2621, 06 2024. ISSN 1527-974X. doi: 10.1093/jamia/ocae165. URL <https://doi.org/10.1093/jamia/ocae165>.
- Emma A. M. Stanley, Raissa Souza, Matthias Wilms, and Nils D. Forkert. Where, why, and how is bias learned in medical image analysis models? *eBioMedicine*, 111, January 2025. ISSN 2352-3964. doi: 10.1016/j.ebiom.2024.105501. URL [https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964\(24\)00537-1/fulltext](https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(24)00537-1/fulltext). Publisher: Elsevier.
- Aron S Talai, Jan Sedlacik, Kai Boelmans, and Nils D Forkert. Utility of multi-modal mri for differentiating of parkinson’s disease and progressive supranuclear palsy using machine learning. *Frontiers in Neurology*, 12:648548, 2021.
- Nicholas J. Tustison, Brian B. Avants, Philip A. Cook, Yuanjie Zheng, Alexander Egan, Paul A. Yushkevich, and James C. Gee. N4ITK: Improved N3 Bias Correction. *IEEE transactions on medical imaging*, 29(6):1310–1320, June 2010. ISSN 0278-0062. doi: 10.1109/TMI.2010.2046908. URL <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3071855/>.
- Vibujithan Vigneshwaran, Erik Ohara, Matthias Wilms, and Nils Forkert. Macaw: A causal generative model for medical imaging, 2024a. URL <https://arxiv.org/abs/2412.02900>.
- Vibujithan Vigneshwaran, Matthias Wilms, Milton Ivan Camacho Camacho, Raissa Souza, and Nils Forkert. Improved multi-site parkinson’s disease classification using neuroimaging data with counterfactual inference. In *Medical Imaging with Deep Learning*, pages 1304–1317. PMLR, 2024b.
- Yiming Xiao, Vladimir Fonov, M Mallar Chakravarty, Silvain Beriault, Fahd Al Subaie, Abbas Sadikot, G Bruce Pike, Gilles Bertrand, and D Louis Collins. A dataset of multi-contrast population-averaged brain mri atlases of a parkinson s disease cohort. *Data in brief*, 12:370–379, 2017.
- Noritaka Yoneyama, Hirohisa Watanabe, Kazuya Kawabata, Epifanio Bagarinao, Kazuhiro Hara, Takashi Tsuboi, Yasuhiro Tanaka, Reiko Ohdake, Kazunori Imai, Rei Ogura, Yasutaka Kato, Michihito Masuda, Tatsuya Hattori, Mizuki Ito, Satoshi Maesawa, Daisuke Mori, Masahisa Katsuno, and Gen Sobue. Openneuro japan dataset. <https://openneuro.org/datasets/ds000245/versions/00001>, 2018.

Appendix A. Data distribution

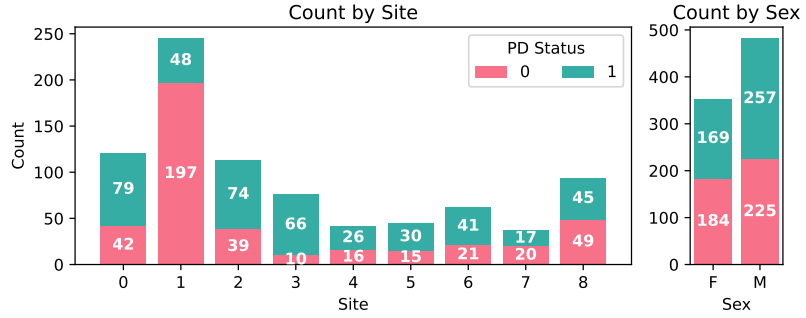


Figure 4: Total data distribution by protected attributes - site and sex.

Site	0			1			2			3			4			5			6			7			8			
Source	Tr	V	Te	Tr	V	Te	Tr	V	Te	Tr	V	Te	Tr	V	Te	Tr	Va	Te	Tr	V	Te	Tr	V	Te	Tr	V	Te	
Category	Value																											
PD	0	21	4	17	98	20	79	20	3	16	4	1	4	8	1	7	7	2	6	11	2	8	10	2	8	25	5	19
	1	40	8	31	24	5	19	37	7	30	32	7	27	13	3	10	15	3	12	21	4	16	8	2	7	22	5	18
Sex	0	24	5	19	49	10	39	19	3	15	19	4	16	11	2	9	12	3	10	14	2	10	8	2	7	21	4	16
	1	37	7	29	73	15	59	38	7	31	17	4	15	10	2	8	10	2	8	18	4	14	10	2	8	26	6	21

Appendix B. Sex PCA distribution after counterfactuals

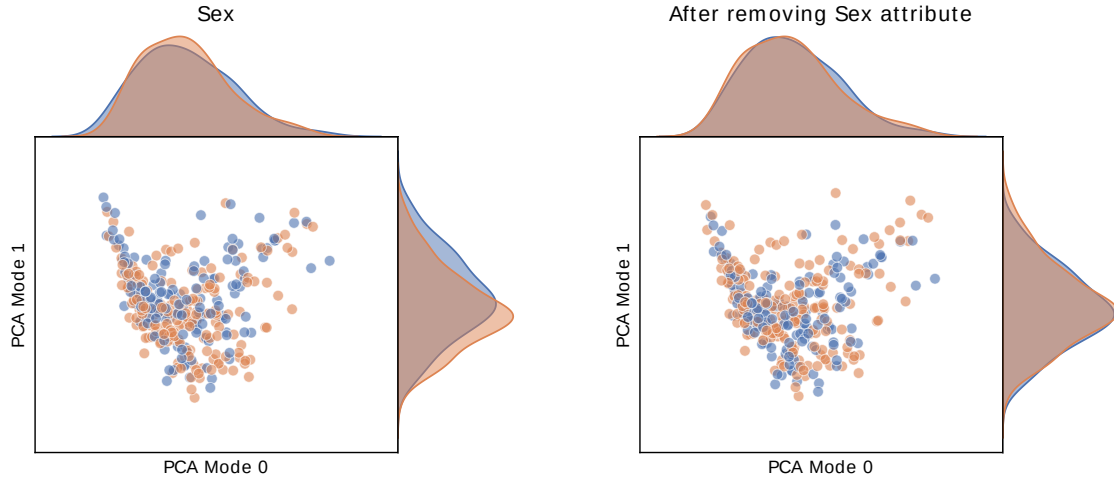


Figure 5: PCA modes 1 and 2 of the activation space were visualized based on sex, and after counterfactually removing sex attribute from the activations.