Personalized Federated Multi-Center Medical Data Analysis with Local and Global Uncertainty

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Abstract. Multi-center brain disease diagnosis is essential for developing effective treatments and improving patient outcomes. However, concerns about data leakage have hindered its development, and data heterogeneity caused by differences in data collection devices and regional population characteristics is a significant challenge. In this paper, we propose a personalized federated multi-center brain disease diagnosis framework based on local and global uncertainty (PFLGU) and evaluate its performance in diagnosing autism and schizophrenia across multiple centers. First, we design two parallel classifiers for each center to generate uncertainty of samples. Second, based on the uncertainty, we utilize the min-max optimization approach for local training. Then, we use the average uncertainty of samples at each center as its weight for federated aggregation. Finally, we obtain a personalized model at each center that effectively incorporates information from other centers. Experimental results demonstrate that the proposed PFLGU framework improves multi-center diagnostic performance for autism and schizophrenia.

Keywords: Multi-center brain disease diagnosis · Personalized federated learning · Local and global uncertainty · Medical image analysis.

1 Introduction

In recent years, multi-center based brain disease diagnosis has attracted more and more attention because it can improve accuracy, identify new patterns, and provide diverse and representative data [17, 15, 5]. However, the existence of stringent privacy regulations in many countries renders it increasingly unfeasible to share medical data [16]. For instance, the Health Insurance Portability and Accountability Act (HIPAA) mandates healthcare providers and organizations to uphold patients' health information privacy and security, with failure to comply attracting financial penalties and reputational damage [3].

To tackle these privacy concerns about medical data, federated learning has become increasingly prevalent in various medical scenarios. For example, Bai

et al. developed a federated learning framework for COVID-19 diagnosis using chest CT scans from multiple hospitals, achieving comparable performance with radiologists and addressing privacy concerns in data sharing [1]. Guo et al. proposed a solution for MR image reconstruction based on federated learning that ensures patient privacy,and developed a cross-site modeling approach to align learned intermediate features from different sources with the target site's feature distribution [7]. Liu et al. proposed two domain adaptation methods in the federated learning formulation to boost neuroimage analysis performance and find reliable disease-related biomarkers [10]. However, due to the complexity of multi-center medical data, the application of federated learning in brain disease diagnosis faces some challenges.

On the one hand, different acquisition devices and regional demographic characteristics lead to differences in data distribution, which makes the existing federated learning methods limited by the heterogeneity of multi-center data. On the other hand, most of the current methods only generate a global model that is shared to all participating centers, which fails to protect the privacy of the model. In practice, to encourage more healthcare providers and organizations to participate in multi-center diagnostics, it is essential not only to address the limitations of data heterogeneity but also to train a personalized private model for each center. Therefore, some personalized federated learning methods have been proposed. For example, Per-FedAvg sended an initial shared model that centers can easily adapt to their local dataset and generate a personalized model [6]. FedRep used a deep neural network with shared lower layers and center-specific higher layers to exploit shared representations among centers to enhance personalization [4]. Although these methods devise a personalized model for each center, they can not effectively facilitate the exchange of valuable information among the centers.

In this paper, we develop a personalized federated multi-center brain disease diagnosis method that incorporates both local and global uncertainty (PFLGU). We apply this method to multi-center datasets for autism and schizophrenia, achieving promising results. The main innovations of our proposed PFLGU model can be summarized as follows: (1) We design a local classifier and a global classifier for each center, and mitigate the heterogeneity of multi-center data by continuously reducing the disagreement between the two classifiers. (2) We capture the uncertainty of samples using both local and global classifiers, and introduce a min-max uncertainty step to capture the information interaction among different centers, thereby enhancing the model's generalization ability. (3) Numerous experiments demonstrate that the proposed method outperforms current federated learning methods and can provide reliable biomarkers for brain disease diagnosis.

2 Method

Fig. 1 illustrates the framework of our method, which consists of a private mapper, a local classifier and a global classifier in each center, as well as a federated

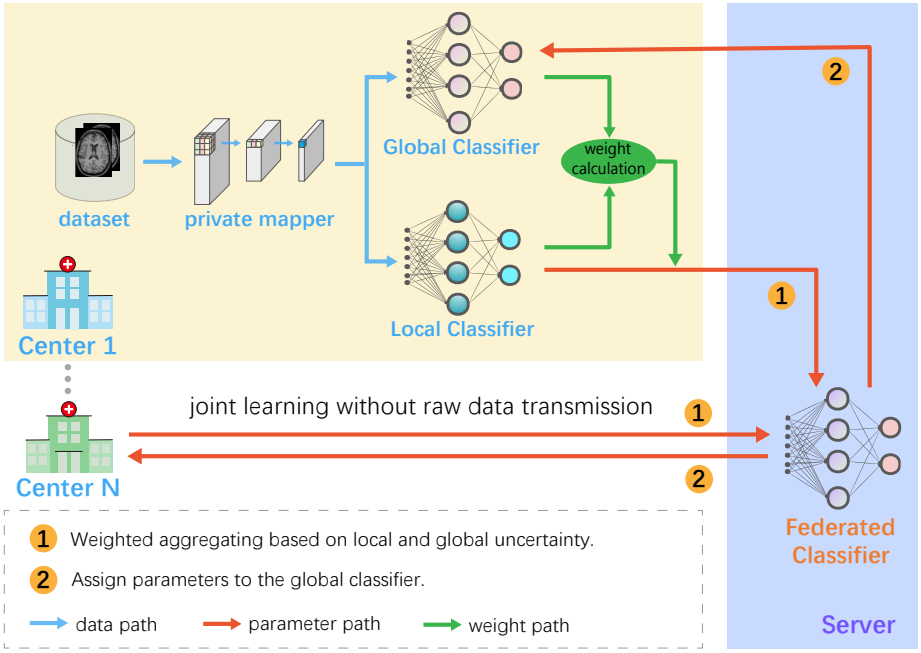

Fig. 1. The framework of the proposed method.

classifier on the federated server. The private mapper uses multiple convolutional neural networks to automatically extract features from the data, and a local classifier consisting of fully connected layers performs the classification [12]. The parameters of the federated classifier are aggregated from the local classifiers of each center. In addition, we design a global classifier in each center, whose parameters are assigned by the federated classifier. The difference in classification generated by the two classifiers is considered as the sample's uncertainty. Our method involves several steps. Firstly, we select high uncertainty samples by maximizing the uncertainty. Secondly, we train the private mapper using the selected high-uncertainty samples to minimize the uncertainty. Next, we train the local classifier for each center on its entire dataset, with the objective of enhancing the accuracy of diagnosis. Finally, we employ the uncertainty of each center as weighting coefficients for federated aggregation, assigning larger weighting coefficients to centers with higher uncertainty. After multiple iterations of the aforementioned steps, we can obtain a personalized model for each center that integrates information from other centers. This approach effectively alleviates the heterogeneity of multi-center data while preserving privacy.

2.1 Local training

Drawing inspiration from shared representation learning, our model is carefully structured with two core elements: a private mapper and a local classifier. We

utilize advanced min-max optimization techniques to significantly enhance the training of the private mapper, allowing it to accurately process and clarify the certainty hidden within the inherent uncertainty of the sample data. This involves a detailed quantification of the differences in output between the local classifier F_l and the global classifier F_g, which effectively guides the private mapper towards robust generalization. Furthermore, the local classifier preserves the unique characteristics of each center, ensuring a careful balance between customization and generalization of diagnostic models across diverse centers. This dual approach not only enhances the model's accuracy in a local context but also improves its generalization across a larger scale. Furthermore, the proposed method fosters information exchange and collaboration among different diagnostic centers. The essence of our methodology is encapsulated by the following generalized optimization objective:

$$\min_{M}\max D\left(P_{F_l}(M(x)), P_{F_g}(M(x))\right) \tag{1}$$

where M denotes the private mapper, and D represents a generic measure of the distributional difference between the outputs produced by the two classifiers. It is important to note that this formulation is not a literal equation but rather a conceptual representation of our strategy to harness uncertainty in model training. Fig. 2 illustrates our local training steps.

Before starting the federated learning procedure, we initialize the parameters of the global classifier. After completing data preprocessing and feature mapping, we input the features into the local classifier. We then aggregate the local classifier parameters from each center and assign them to the global classifier in each center.

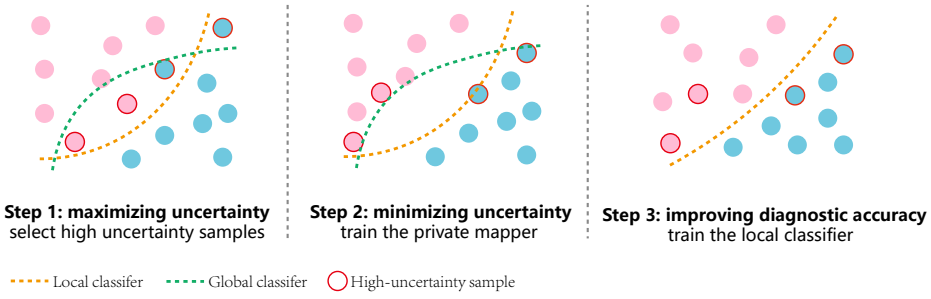

Fig. 2. The process of local training in the proposed method.

Step 1: maximizing uncertainty In this step, our objective is to maximize uncertainty. We indirectly achieve this by selecting highly uncertain samples. Specifically, we input preprocessed data from each center into their respective

private mappers, then pass the outputs to two classifiers to obtain two classification results. At last, we identify samples misclassified by both classifiers or that cause disagreement between them as high uncertainty samples for screening.

Step 2: minimizing uncertainty This step aims to minimize the uncertainty with selected high uncertainty samples, thus improving the generalizability of the private mapper. After screening for high uncertainty samples, our main concern is that these samples may cause overfitting of the local classifiers. To address this issue, we freeze the parameters of both classifiers and only update the parameters of the private mapper. In this step, we hope the private mapper to extract features that minimize the samples' uncertainty generated by the parallel classifier. w_M denotes parameters of private mapper M and the function for step 2 is as follows:

$$w_M^* = \underset{w_M}{\operatorname{argmin}} \frac{1}{s} \sum_{k=1}^{s} |F_l(M(x_k)) - F_g(M(x_k))| \tag{2}$$

where F_l and F_g denote local classifier and global classifier respectively, and the data $x_k, k \in (1, ..., s)$ is from the set S, while y_k is the corresponding label of x_k.

Step 3: improving diagnostic accuracy In this step, we aim to train the local classifier for each center with their whole dataset, thus improving the accuracy of diagnosis. To avoid compromising the generalizability of the private mapper, we freeze its parameters during this step. Additionally, we also freeze the parameters of the global classifier since they will be overwritten by the federated classifier. The functions for Step 3 are as follows:

$$w_{F_l}^* = \underset{w_{F_l}}{\operatorname{argmin}} - \sum_{k=1}^{n} y_k \cdot log F_l(G\,(x_k)) \tag{3}$$

where $x_k, k \in (1, ..., n)$ is from each entire dataset, n denotes the capacity of the dataset, and y_k is the corresponding label of x_k. The parameters of local classifier F_l denoted by w_{F_l}. After training the local classifier, we measure the samples' average uncertainty of each center and record it for use in the subsequent federated aggregation process. For each center $i \in (1, ..., N)$, the uncertainty u_i can be calculated by:

$$u_i = \frac{1}{n} \sum_{k=1}^{n} |F_l(G(x_k)) - F_g(G(x_k))| \tag{4}$$

2.2 Federated aggregation

In PFLGU, we utilize uncertainty u_i recorded during step 3 of local training as the weight of center i. Different with traditional federated learning whose objective is to obtain a robust global model, we aim to amplifying the uncertainty across multiple centers so that we could comprehensively extract the certainty

during local training. Therefore, we assign larger weighting coefficients to centers with higher uncertainty. The formula for calculating the weight α_i of each center i is provided below:

$$\alpha_i = \frac{e^{u_i}}{\sum_{i=1}^{N} e^{u_i}} \tag{5}$$

The formula for federated weighted averaging is as follows:

$$\theta_{fed} = \sum_{i=1}^{N} \alpha_i \cdot \theta_i \tag{6}$$

where θ_i denotes the parameters of local classifier in each center, and θ_{fed} denotes the parameters of federated classifier, which will be assigned to global classifiers in each center. After several rounds of local training and federated aggregation, the private mapper and the local classifier on each center form the personalized diagnostic model of that center.

3 Experiment and Results

3.1 Experimental Settings

All the methods are implemented using PyTorch and trained on a single GPU (NVIDIA GeForce RTX3080). We optimize the proposed method via Adam algorithm [8, 11]. To evaluate the effectiveness of the model, we use 5-fold cross-validation in all subsequent experiments. Two evaluation metrics are utilized to assess the classification performance: classification accuracy (ACC) and the F1 score ($F1$). Higher values of these metrics indicate better performance. In addition to these indicators, we also recorded the standard deviation (std) among each center to evaluate the stability of various methods in each center.

3.2 Datasets and Data Pre-processing

The Autism Brain Imaging Data Exchange (ABIDE) dataset comprises resting-state fMRI and clinical data from 1,112 subjects across 17 different sites. In this study, we have selected five sites, namely Leuven, USM, UCLA, UM, and NYU, where the number of subjects is more than 50. This subset of the dataset includes 468 subjects, out of which 218 are diagnosed with Autism Spectrum Disorder (ASD), and 250 are age-matched typical control individuals. For the schizophrenia fMRI datasets, we utilize data from the Nanjing Brain Hospital (NBH), The Center for Biomedical Research Excellence (COBRE), Nottingham, Taiwan, and Xiangya datasets. The five centers contains a total of 655 subjects, out of which 258 are patients with schizophrenia and 397 are age-matched typical control individuals. Besides, to ensure consistency and accuracy, we only selected subjects who met the following criteria: (1) absence of other DSM-IV diseases; (2) no history of drug abuse; (3) no clinically significant head trauma.

During the data preprocessing, we performed several steps on the resting-state fMRI data [18]. First, we conducted slice-timing correction, image realignment, and nuisance regression. Next, we used the anatomical automatic labeling (AAL) atlas to extract the mean time series for a set of 90 pre-defined regions-of-interest (ROIs) in both the ABIDE and schizophrenia datasets. Finally, we calculated the correlation matrix as functional connectivity, represented by a symmetrical 90×90 matrix for each dataset, using the mean time sequences of ROIs. Each element of the correlation matrix represents the Pearson correlation coefficient between a pair of ROIs.

3.3 Results and Discussion

We compare our method with baseline, FedAvg [13], FedProx [9], Per-FedAvg [6] and FedRep [4]. In the baseline method, each center trains their model without any communication with other centers. FedAvg is a widely used federated learning approach that optimizes deep networks from decentralized data while minimizing communication overhead. It averages model updates from each center to produce a global model. FedProx is an enhanced approach of FedAvg that incorporates a proximal term into the optimization problem to address the issue of straggling centers. FedAvg and FedProx are traditional federated learning algorithms that generate a multi-center global model, while FedRep and Per-FedAvg are personalized federated learning algorithms that generate a personalized model at each center.

Table 1. Performance comparison of different methods on ABIDE and Schizophrenia datasets. The values (%) are denoted as mean±std.

Method	ABIDE		Schizophrenia	
	ACC	F1	ACC	F1
baseline	67.02±09.88	66.74±14.84	78.97±10.50	79.21±10.29
FedAvg	67.89±09.89	65.30±17.55	77.46±10.61	77.41±10.35
FedProx	71.17±09.70	69.12±13.40	78.73±09.10	77.56±11.46
Per-FedAvg	71.84±08.73	70.12±12.83	80.01±08.57	80.26±09.53
FedRep	71.38±10.01	72.28±13.12	78.94±10.25	78.37±10.50
Ours	**74.73±09.23**	**75.13±11.33**	**81.30±08.76**	**81.75±09.34**

The results presented in Tab. 1 indicate that PFLGU achieves the best average accuracy and F1 score for both multi-center autism and schizophrenia diagnoses. Specifically, our proposed method exhibits a lower standard deviation when compared to traditional federated learning methods, namely FedAvg and FedProx. This finding suggests that our approach provides better stability across multiple centers, which is a crucial factor in the context of multi-center brain disease diagnosis. Furthermore, compared to personalized federated learning methods, such as FedRep and Per-FedAvg, our approach demonstrates higher accuracy and F1 score, indicating its superior performance. Specifically,

Table 2. Ablation study of our proposed method on ABIDE and Schizophrenia datasets. The values (%) are denoted as mean±std.

Method	ABIDE		Schizophrenia	
	ACC	F1	ACC	F1
Ours-1	66.68±07.22	65.75±17.48	78.09±09.94	78.55±09.05
Ours-2	70.64±08.51	72.15±08.71	78.61±11.70	78.38±13.12
Ours	**74.73±09.23**	**75.13±11.33**	**81.30±08.76**	**81.75±09.34**

our method facilitates each center to effectively absorb information from other centers, contributing to the improvement of model accuracy.

There are two main modules in the proposed framework: min-max uncertainty and uncertain-weighted aggregation mechanism. To explore the contribution of each module, we conduct ablation experiments on ABIDE and Schizophrenia datasets, and the experimental results are shown in Tab. 2. The simplified models we use in ablation experiments include: (1) Ours-1: We remove the max-min uncertainty. (2) Ours-2: The federated aggregation eschews the use of each center's uncertainty as a variable weight, instead opting for an equal weighting across all centers. As can be seen from Tab. 2, no matter which module is removed, the experimental performance will be degraded, which indicates that the proposed method can effectively aggregate the disease characteristics of different centers under privacy protection. In addition, the model performance is optimal when the two modules are used in combination, which indicates that the proposed two modules are closely connected and promote each other.

Overall, our proposed method improves the accuracy of multi-center brain disease diagnosis. It ensures effective treatment for a wider range of individuals, offering significant benefits to the field.

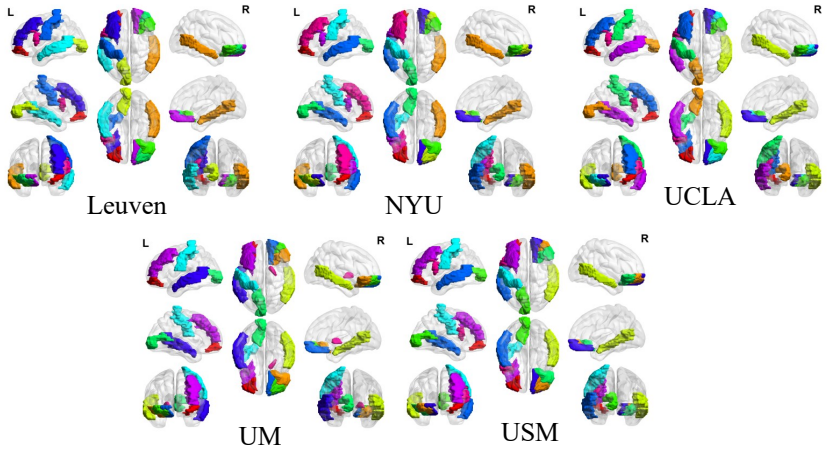

Fig. 3. Distribution of the 10 most important brain regions on the ABIDE dataset.

3.4 Biomarker Detection

In addition, to measure the ability of the proposed method in identifying clinical biomarkers, we use the sophisticated guided back-propagation technique to find the 10 most important brain regions for brain disease diagnosis, and the experimental results are shown in Fig. 3. It can be found from Fig. 3 that the important brain regions in different centers all include Middle frontal gyrus, Middle temporal gyrus, Hippocampus and other regions. These brain regions control higher cognition, emotion regulation and memory functions and are closely related to the development of autism [14, 2]. Therefore, the proposed method can provide effective biomarkers for brain disease diagnosis.

4 Conclusion

In this paper, we propose a novel personalized federated multi-center brain disease diagnosis framework that effectively captures communication information across different centers, and alleviates the heterogeneity of multi-center data distribution. Specifically, we design separate local and global classifiers for each center to reduce the discrepancy between them, thereby alleviating the heterogeneity of multi-center data. Secondly, we capture sample uncertainty using both local and global classifiers, and introduce a min-max optimization approach to capture the information interaction between different centers, thus enhancing the model's generalization ability. Extensive experiments demonstrate the effectiveness and stability of the proposed method, which can provide effective biomarkers for brain disease diagnosis.

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