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基于对抗图自编码的阿尔兹海默症脑网络分析

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摘　要

阿尔兹海默症(Alzheimer's Disease, AD)的不同阶段会发生结构或功能连接的改变。这些基于连接的特征可以大大提高疾病诊断的准确性，并能给出疾病的成因解释。如何有效融合结构和功能影像来挖掘不同模态之间的互补信息仍然是一个挑战。本文提出了一种对抗图自编码器模型，来提取脑连接特征用于AD分析。具体地说，将扩散张量成像(Diffusion Tensor Imaging, DTI)和功能磁共振成像(functional Magnetic Resonance Imaging, fMRI)相结合，构建每个受试者的图结构数据。图编码器(生成器)将图数据转换为潜在表征。同时，利用fMRI数据估计潜在分布，对图编码器进行正则化约束，以保证良好的潜在表征。为了保证潜在表征的稳定性，图解码器从潜在表征中恢复图数据。最后，将潜在表征送给分类器，使其具有疾病类别信息。实验结果表明，该模型比其他相关模型具有更高的预测精度。总体而言，该方法可以重建AD早期的结构－功能连接，分析异常的脑连接并用于AD的早期诊疗研究。

关键词

图生成器，对抗学习，结构－功能脑连接

Adversarial Graph Autoencoder for Brain Network Analysis in Alzheimer's Disease

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Abstract

Alterations in the structural or functional connectivity take place at different stages of Alzheimer's

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Disease (AD). These connectivity-based features can greatly improve the disease diagnosis accuracy and explain the causes of the disease. How to effectively fuse structural and functional images for exploring complementary information remains challenging. This paper proposes an adversarial graph autoencoder model to extract connectivity-based features for AD analysis. Specifically, Diffusion Tensor Imaging (DTI) and functional Magnetic Resonance Imaging (fMRI) are combined to construct graph data for each subject. The graph encoder (generator) transforms the graph data into a latent representation. Meanwhile, the fMRI data is utilized to estimate the latent distribution, which can regularize the graph encoder to ensure good latent representation. To ensure the latent representation is stable, the graph decoder regains the graph data from the latent representation. Finally, the latent representation is sent to the classifier to make it class-discriminative. Experimental results demonstrate that the proposed model can achieve higher prediction accuracy than other related models. Generally, this method can reconstruct the structural-functional connectivity and analyze abnormal brain connections for early AD study.

Keywords

Graph Generator, Adversarial Learning, Structural-Functional Brain Connectivity

1. 引言

阿尔兹海默症(Alzheimer's Disease, AD)是老年人最常见的一种神经退行性疾病，其产生机理是大脑神经细胞的β淀粉样蛋白沉积[1]。这种疾病在病理改变上表现为记忆力下降、失语等脑功能下降[2]。目前尚无治疗 AD 的有效药物，但是 AD 的早期阶段即轻度认知障碍(Mild Cognition Impairment, MCI) [3]可以通过机器学习方法进行早期诊断，并通过适当的干预措施达到延缓或治愈疾病的目的。

近年来，早期 AD 患者脑部结构连接或者功能连接的异常变化在脑神经科学中被发现。例如，功能磁共振成像(functional Magnetic Resonance Imaging, fMRI) [4]揭示了在 MCI 阶段，脑部功能连接增强，弥散张量成像(Diffusion Tensor Imaging, DTI) [5]反映了在 AD 阶段，脑部解剖区域间结构连接减弱或消失。随着人工智能技术在医学图像分析中的广泛应用[6]-[13]，机器学习模型[14] [15]可以提高 AD 早期诊断的效率和精度，但是当前的研究无法有效利用结构和功能成像数据对复杂脑网路特征进行刻画，难以挖掘疾病相关的异常脑连接，不利于 AD 患者的早期诊疗。基于图网络分析的方法在许多领域获得了广泛的应用[16]-[21]，该方法有利于分析 AD 患者的脑网络特征，进而为疾病的早期诊断提供生物标志物。

基于上述观察启发，本文提出了一种对抗图自编码器学习网络模型用于 AD 早期预测和分析。它通过图生成器学习结构和功能连接的互补特征，并通过估算分布对隐层表征进行分布约束，挖掘潜在的异常脑连接特征，最后，通过图解码器重构图结构数据，使模型具有鲁棒性。本模型对 AD 进行早期诊断和异常脑连接分析，可以为该类认知疾病的临床早期治疗提供靶点。

2. 相关工作

2.1. AD 诊断与分析

当前的 AD 研究集中在单一模态和多模态的诊断和分析。针对单一模态的医学影像分析，Wang 等人[22]利用 DTI 数据构建脑网络结构并提取图拓扑系数特征，结果表明，AD 组比正常对照组在整体效率和

局部效率均有所下降。MRI 影像能直接反映脑部病变特征，Wang 等人[23] [24] [25]利用 3D 密集连接卷积网络对三维 MRI 影像进行特征提取，显著提升了早期阿尔兹海默症的诊断精度，类似地，Yu 等人[26] [27]基于 MRI 影像利用生成对抗网络模型不仅提升了 AD 的诊断精度，而且对疾病相关的脑区进行可视化成像，提高了模型的可解释性。fMRI 影像数据可以反映疾病相关的功能特征，Lei 等人[28]基于该模态的时序信息构建高阶功能连接特征，在 AD 分类方面取得了较好的效果，并预测了相关生物标志物。多模态融合相比于单模态可以显著提高 AD 诊断的精度，Yu 等人[29]基于 DTI 和 fMRI 构建图数据，并利用图卷积网络(Graph Convolutional Network, GCN)融合两种模态，在公开数据集上进一步提升了 MCI 的识别性能。Pan 等人[30]基于 DTI 和 fMRI 构建超图生成对抗网络模型，在脑连接的角度分析了疾病相关脑区特征，有助于认知疾病的靶点治疗。

2.2. 生成对抗网络

生成对抗网络(Generative Adversarial Network, GAN) [31]在学习表征分布方面具有很大的拟合能力，在医学图像分类[32]、脑网络分析[33] [34] [35]、跨模态合成[36] [37] [38] [39]、图像生成[40]、图像分割[41] [42]、超分辨率重构[43] [44] [45]和点云生成[46] [47] [48]等领域得到广泛的应用。其基本原理是利用变分推断使概率分布的熵最大化[49] [50] [51] [52]。该网络一般包含一个生成器和一个判别器，生成器的网络结构通常由多个卷积层和池化层交替连接，输出合成的数据(图片或者向量表征)，其目的是学习真实数据的分布；判别器通常设计成多个降采样的卷积核叠加，输入真实数据或者合成数据，输出判别真假的数值(1 或 0)，其目的是区分数据分布的真假。通过两个网络相互对抗学习，当达到纳什均衡时，生成器得到最大优化，从而学习到最优的隐层表征，并用于后续 AD 的预测和分析任务。

3. 数据与方法

3.1. 数据

本实验所使用的数据集是 ADNI 脑部影像数据集[53]，从该数据集下载并预处理 DTI 和 fMRI 两种模态数据，包含共 4 类疾病，分别是正常人(Normal Control, NC)、早期轻度认知障碍(Early Mild Cognition Impairment, EMCI)、晚期轻度认知障碍(Late Mild Cognition Impairment, LMCI)、阿尔兹海默症(AD)。为了平衡数据集，挑选四个疾病阶段(NC, EMCI, LMCI, AD)等量的被试共计 256 个样本，使用 10 折交叉验证对数据进行 3 个二分类实验，包括 NC vs. EMCI，NC vs. LMCI，NC vs. AD。其中，预处理过程使用的解剖学模板是 AAL90 [54]，预处理 DTI 数据后得到大小为 90 × 90 的脑部结构连接矩阵(A)，预处理 fMRI 数据后得到大小为 90 × 187 的时序数据 X。

3.2. 方法

3.2.1. 图自编码器

如图 1 所示，本模块编码结构连接矩阵(A)和功能时间序列(X)，使用三层 GCN 网络结构，激活层选用 Tanh 函数，第一层输出的特征维度为 128，第二层输出的特征维度为 96，第三层输出隐层节点特征 H，大小为 90 × 64。整个模块的表达式为：

$$H = GCN_3\left(GCN_2\left(GCN_1\left(A, X\right)\right)\right) \tag{1}$$

其中，$GCN_l = \tanh\left(\tilde{D}^{-0.5}\tilde{A}\tilde{D}^{-0.5}XW_l\right)$，$\tilde{A} = A + I_N$，$\tilde{D}_{ii} = \sum_j \tilde{A}_{ij}$，$\tilde{D}$ 为节点的度矩阵，$W_l\left(l = 1,2,3\right)$ 为模型的参数。图解码器的网络结构跟编码器类似，将 H 输入到解码器中，经过三层图卷积(特征维度分别为 96、128、187)，计算得到 128 维的解码特征 X'，其中第二层的输出经过矩阵内积和 sigmoid 函数激活，输出大小为 90 × 90 的重构结构连接矩阵 A'。重构损失函数为：

$$\mathscr{L}_{\text{Rec}}(A,X)=\mathbb{E}_{X\sim P_X}\left[\left\|X-X'\right\|_2\right]+\mathbb{E}_{A\sim P_A}\left[\left\|A-A'\right\|_2\right] \tag{2}$$

3.2.2. 判别器

本模块的目的是鉴别输入数据的真假。真样本是来自于分布 $p(H)$的采样 H'，大小为 90 × 64。这里分布 $p(H)$的估算方法为：将 X 进行 PCA 降维得到 Xp (大小为 90 × 64)，基于核密度方法估算 Xp 的分布，其计算公式为 $p(H)=\frac{1}{Nw}\sum_{i=1}^{N}K\left(\frac{H-x_i}{w}\right)$，其中，$w$ 为控制分布曲线宽度的参数，$K(.)$是高斯核，x_i 是 Xp 的行向量；假样本来自于图编码器的输出 H。超图判别器的网络结构为一个三层多层感知机(Multi-Layer Perceptron, MLP)，每层输出维度依次为：64、32、1。H 或 H' 经过判别器 D_H 后输出真或假。输出对抗损失函数为：

$$\mathscr{L}_D=\mathbb{E}_{H\sim q(H)}\left[\left(D_H(H)\right)^2\right]+\mathbb{E}_{H'\sim p(H)}\left[\left(D_H(H')-1\right)^2\right] \tag{3}$$

$$\mathscr{L}_G=\mathbb{E}_{H\sim p(H)}\left[\left(D_H(H)-1\right)^2\right] \tag{4}$$

3.2.3. 分类器

隐层特征 H 经过矩阵内积 $\sigma\left(HH^{\mathrm{T}}\right)$ 得到大小为 90 × 90 的多模态脑连接矩阵，再经过一个分类器，输出二分类的预测结果。该分类器由三层 MLP 构成，每层输出维度依次为 10、10 和 2。定义 y 为疾病标签，维度为 2 的向量，分类损失函数为：

$$\mathscr{L}_{\text{Cls}}(H)=\mathbb{E}_{H\sim q(H)}\left[y\log\left(C\left(\sigma\left(HH^{\mathrm{T}}\right)\right)\right)\right] \tag{5}$$

综合损失函数可以表示为：

$$\mathscr{L}_{\text{total}}=\mathscr{L}_G+0.1\mathscr{L}_D+\mathscr{L}_{\text{Rec}}+\mathscr{L}_{\text{Cls}} \tag{6}$$

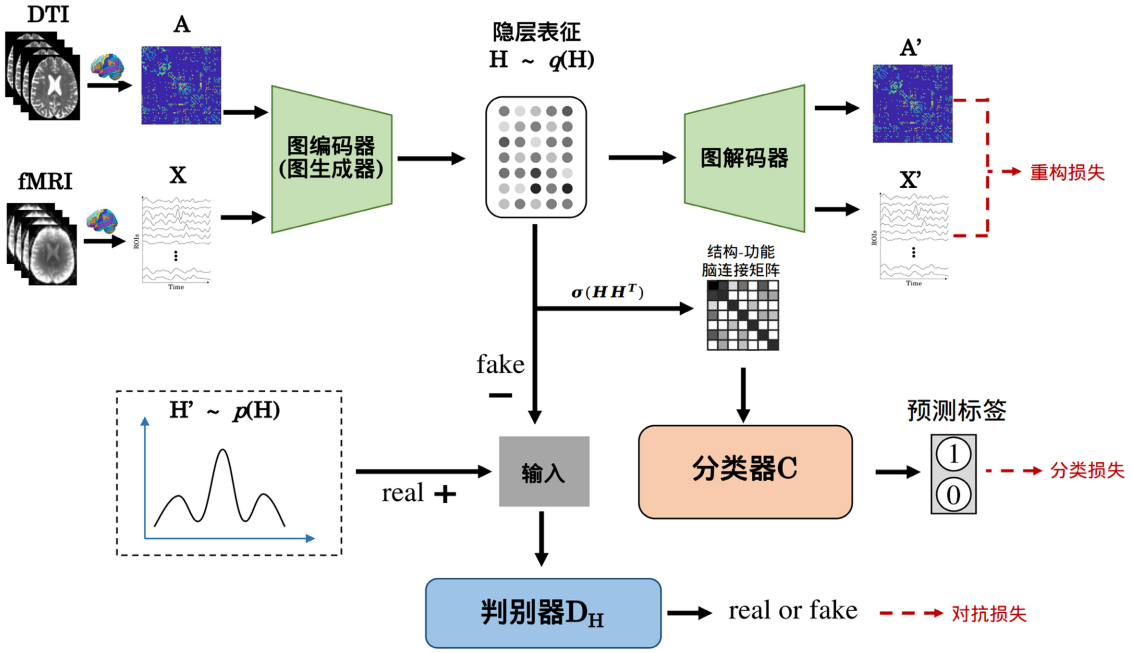

Figure 1. Overall framework of the proposed model
图 1. 本模型的整体框架图

4. 实验与结果

4.1. 实验设置

本模型训练和测试都是基于 TensorFlow 平台进行的，GPU 硬件为 Quadro P4000，显存 12 GB。图生成器和图解码器的初始学习速率为 0.0001，随着训练次数成指数衰减，判别器学习速率为 0.0004 固定不变，epoch 次数为 1000，batchsize 设置为 4，本次实验评估分类性能的指标分别为准确率(ACC)、灵敏度(SEN)、特异度(SPE)和 ROC 曲线面积(AUC)。

4.2. 实验结果

本次实验比较了不同方法的分类性能，分别为同一模态下(fMRI)和双模态下(fMRI 和 DTI)的实验对比结果。其中 MPCA 方法[55]是结构和功能连接矩阵进行多线性降维后利用 SVM 进行分类，DCNN 方法[56]是将结构连接矩阵和脑区时间序列在拓扑空间进行聚合，最后输出疾病类别。从表 1 可以看出，单模态比双模态的分类性能差很多，这是由于双模态可以提供疾病相关的互补信息；在多种算法中，本模型的分类性能最佳，在三个二分类任务(EMCI vs. NC, LMCI vs. NC, AD vs. NC)中最好的准确率分别为 86.72%、91.41%和 94.53%。

Table 1. Comparison of mean classification performance using different methods (%)
表 1. 不同方法的分类性能比较(%)

模态	方法	EMCI vs. NC				LMCI vs. NC				AD vs. NC			
		ACC	SEN	SPE	AUC	ACC	SEN	SPE	AUC	ACC	SEN	SPE	AUC
fMRI	SVM	72.66	78.12	67.19	79.32	75.00	68.75	81.25	80.21	79.69	79.69	79.69	83.78
	Ours	79.69	82.81	76.56	82.15	83.59	81.25	85.94	82.45	86.72	90.62	82.81	87.35
fMRI & DTI	MPCA	78.12	78.12	78.12	79.57	80.47	76.56	84.38	85.83	85.16	89.06	81.25	84.72
	DCNN	82.03	81.25	82.81	83.69	85.16	84.38	86.94	89.69	89.06	93.75	84.38	91.84
	Ours	86.72	90.62	82.81	88.50	91.41	87.50	95.31	92.60	94.53	96.88	92.19	96.26

图 2 定性展示了经验方法(Empirical)和模型重构方法(Reconstructed)计算 NC 阶段下的结构脑连接矩阵，其中，横纵和纵轴都是表示感兴趣脑区(Region of Interest, ROI)编号。通过比较这两种方法计算的结构连接矩阵在同一分类器(GCN)下的分类性能，如图 3 所示，本模型重构的结构连接矩阵要优于经验方法，说明本模型的图解码器能够很好的重构结构连接矩阵，确保了图编码器生成隐层表征的稳定性。通过 LOOCV 算法，对各个二分类任务下重要脑区进行了定性分析，如图 4 所示，在 EMCI vs. NC 中，10 个重要的脑区分别是：额中回(MFG.R)、眶部额下回(ORBinf.R)、嗅皮质(OLF.R)、内侧额上回(SFGmed.R)、海马旁回(PHG.L)、杏仁核(AMYG.L)、顶上回(SPG.L)、角回(ANG.R)、豆状苍白球(PAL.R)、颞极：颞上回(TPOsup.L)。在 LMCI vs. NC 中，眶部额下回(ORBinf.R)、嗅皮质(OLF.R)、海马(HIP.L)、杏仁核(AMYG.L)、中央后回(PoCG.L)、顶下缘角回(IPL.L)、楔前叶(PCUN.R)、丘脑(THA.R)、颞极颞上回(TPOsup.L)和颞下回(ITG.R)；在 AD vs. NC 中，10 个重要脑区分别是：眶部额下回(ORBinf.L)、内侧额上回(SFGmed.L)、脑岛(INS.R)、内侧和旁扣带脑回(DCG.R)、后扣带回(PCG.R)、海马旁回(PHG.R)、杏仁核(AMYG.L)、舌回(LING.R)、缘上回(SMG.R)和丘脑(THA.L)。其中海马体、海马旁回、杏仁核、嗅皮质、角回等脑区都已经被证实与阿尔兹海默症密切相关[57] [58]。

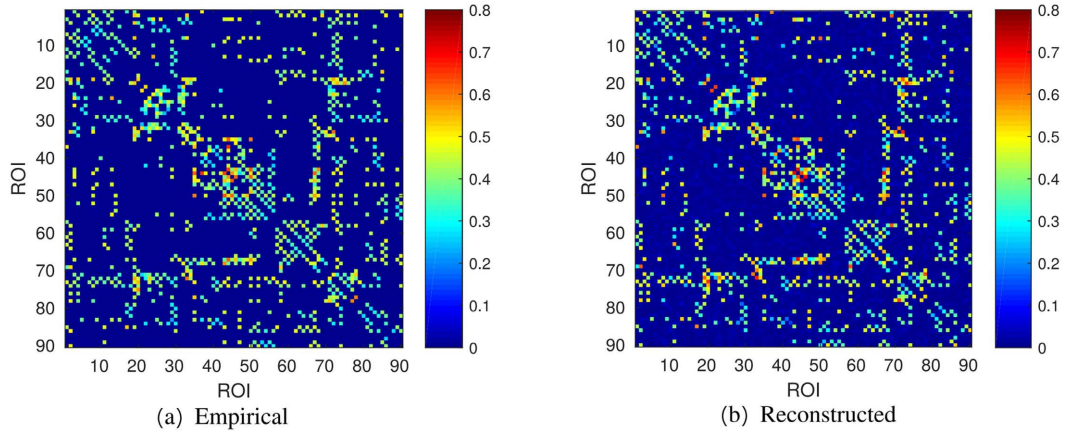

Figure 2. Schematic diagram of the brain connectivity matrices computed by different methods
图 2. 不同方法计算的脑连接矩阵示意图

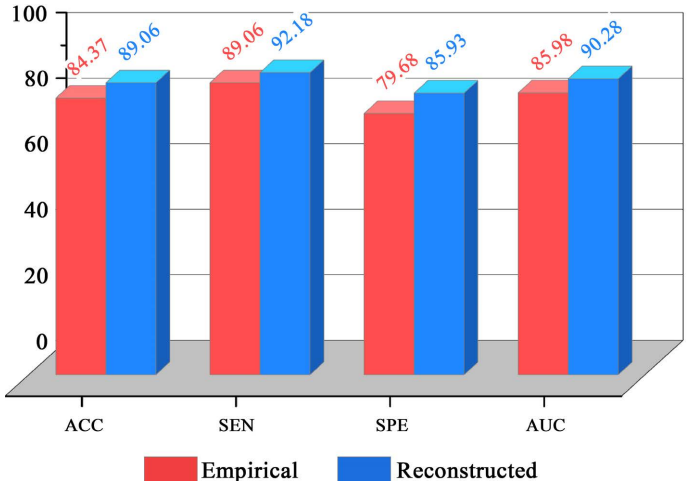

Figure 3. Comparison of classification performance of structural connectivities using different methods for AD vs. NC
图 3. 不同方法计算的结构连接矩阵在 AD vs. NC 下分类性能的比较

为了定量分析不同认知疾病阶段的脑连接变化特征，基于模型输出的结构－功能脑连接矩阵，使用 t 检验方法，并选取 p 值小于 0.001 的值作为异常重要脑连接。图 5 展示了阿尔兹海默症不同疾病阶段的重要脑连接可视化结果，其中品红色表示疾病阶段(EMCI、LMCI 或 AD)相对于 NC 阶段减少的脑连接，蓝色表示增加的脑连接。这些异常的脑连接可以反映阿尔兹海默症发展过程中脑部重要连接的受损情况，涉及到的脑区包括海马体、海马旁回、嗅皮质、后扣带回、角回，增加的异常脑连接包括：左侧海马(HIP.L)-左侧角回(ANG.L)、左侧海马(HIP.L)-右侧海马旁回(PHG.R)、左侧海马旁回(PHG.L)-左侧颞极颞上回(TPOmid.L)、右侧嗅皮质(OLF.R)-右侧脑岛(INS.R)，减少的异常脑连接包括：左侧海马(HIP.L)-左侧后扣带回(PCG.L)、左侧嗅皮质(OLF.L)-右内侧额上回(SFGmed.R)、右侧海马(HIP.R)-左侧枕上回(SOG.L)、左侧后扣带回(PCG.L)-右侧海马旁回(PHG.R)。

4.3. 消融实验

为了研究各个模块对实验结果影响，分别去掉判别器模块、图解码器模块，测试在 LMCI vs. NC 分类任务中的效果。去掉判别器模块，即该模型由图编码器、图解码器和分类器组成；去掉解码器模块，

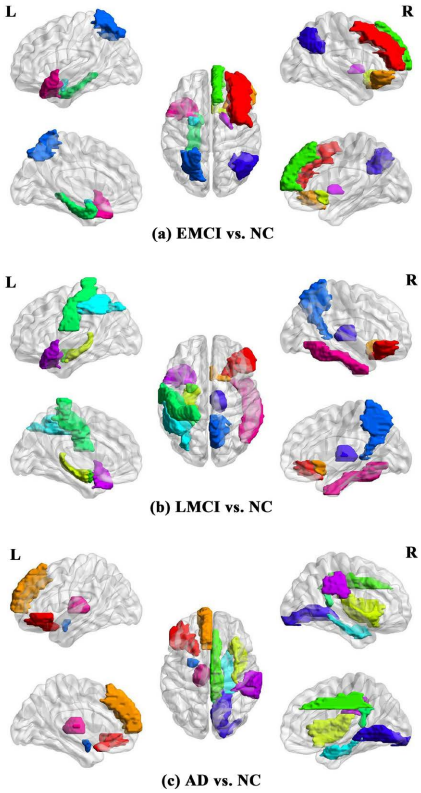

Figure 4. Visualization of 10 important ROIs for different classification tasks
图 4. 不同分类任务下 10 个重要脑区的可视化结果

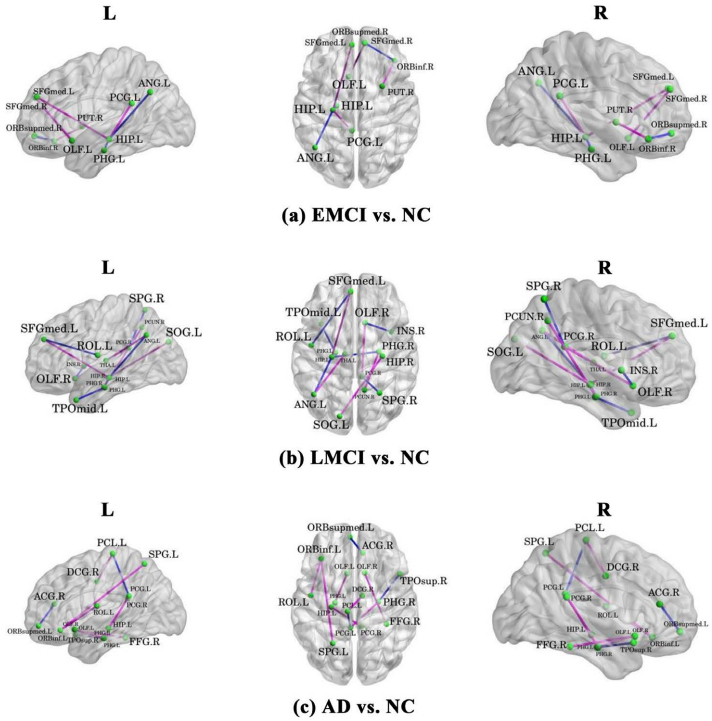

Figure 5. Important abnormal brain connections at different stages of AD (p-value < 0.001)
图 5. 不同认知疾病阶段重要的异常脑连接(p 值小于 0.001)

即该模型由图编码器、判别器和分类器组成。如图 6 所示，解码器模块在准确率(ACC)和灵敏度(SEN)指标上对模型影响很大，而判别器模块在特异度(SPE)和 ROC 曲线面积(AUC)指标上影响更大。总体来说，判别器和解码器模块都会影响实验结果的分类性能，它们在模型的隐层表征学习中起到很好的稳健性效果。

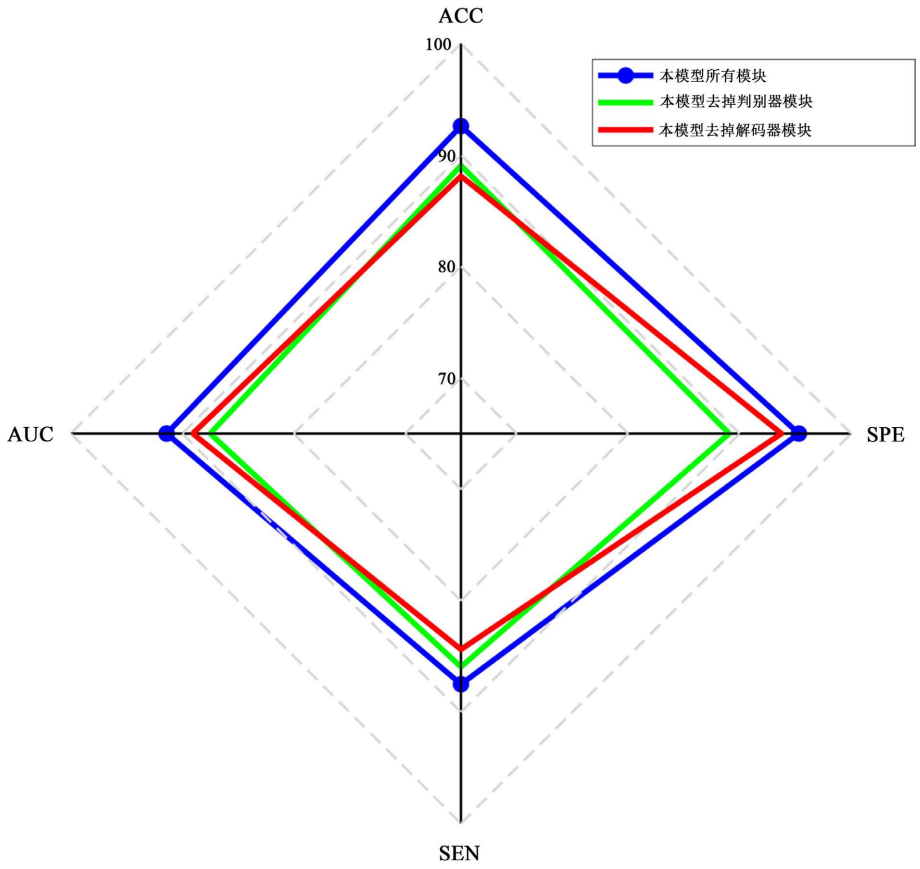

Figure 6. Influence of different modules on the classification performance of LMCI vs. NC
图 6. 不同模块对 LMCI vs. NC 分类性能的影响

5. 总结

本文提出了一种超图对抗性自编码器用于阿尔兹海默症的诊断和分析。利用估算分布对隐层表征进行约束，使得图生成器可以有效融合并学习到结构－功能的互补脑连接特征，图解码器使生成器网络结构更加稳定。实验结果表明，在同类模型比较中，该模型具有更高的预测精度。本模型可以重建脑部结构－功能连接特征，并进行异常脑连接分析，为认知疾病的早期筛查提供潜在的生物标志物。

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参考文献

[1] Cope, T.E., Rittman, T., Borchert, R.J., *et al*. (2018) Tau Burden and the Functional Connectome in Alzheimer's Disease and Progressive Supranuclear Palsy. *Brain*, **141**, 550-567. https://doi.org/10.1093/brain/awx347

[2] Alzheimer's Association (2019) 2019 Alzheimer's Disease Facts and Figures. *Alzheimer's & Dementia*, **15**, 321-387. https://doi.org/10.1016/j.jalz.2019.01.010

[3] Li, Y., Liu, J., Tang, Z. and Lei, B. (2020) Deep Spatial-Temporal Feature Fusion from Adaptive Dynamic Functional Connectivity for MCI Identification. *IEEE Transactions on Medical Imaging*, **39**, 2818-2830. https://doi.org/10.1109/TMI.2020.2976825

[4] Franzmeier, N. and Dyrba, M. (2017) Functional Brain Network Architecture May Route Progression of Alzheimer's Disease Pathology. *Brain*, **140**, 3077-3080. https://doi.org/10.1093/brain/awx304

[5] Pereira, J.B., Van Westen, D., Stomrud, E., *et al*. (2018) Abnormal Structural Brain Connectome in Individuals with Preclinical Alzheimer's Disease. *Cerebral Cortex*, **28**, 3638-3649. https://doi.org/10.1093/cercor/bhx236

[6] Wang, S.Q., Li, X., Cui, J.L., *et al*. (2015) Prediction of Myelopathic Level in Cervical Spondylotic Myelopathy Using Diffusion Tensor Imaging. *Journal of Magnetic Resonance Imaging*, **41**, 1682-1688. https://doi.org/10.1002/jmri.24709

[7] Wang, S., Shen, Y., Zeng, D., *et al*. (2018) Bone Age Assessment Using Convolutional Neural Networks. 2018 *International Conference on Artificial Intelligence and Big Data*, Chengdu, 26-28 May 2018, 175-178. https://doi.org/10.1109/ICAIBD.2018.8396189

[8] Hong, J., Feng, Z., Wang, S.H., *et al*. (2020) Brain Age Prediction of Children Using Routine Brain MR Images via Deep Learning. *Frontiers in Neurology*, **11**, Article ID: 584682. https://doi.org/10.3389/fneur.2020.584682

[9] Wang, S., Wang, X., Shen, Y., *et al*. (2020) An Ensemble-Based Densely-Connected Deep Learning System for Assessment of Skeletal Maturity. *IEEE Transactions on Systems, Man, and Cybernetics*: *Systems*, **52**, 426-437. https://doi.org/10.1109/TSMC.2020.2997852

[10] Wang, S., Shen, Y., Shi, C., *et al*. (2018) Skeletal Maturity Recognition Using a Fully Automated System with Convolutional Neural Networks. *IEEE Access*, **6**, 29979-29993. https://doi.org/10.1109/ACCESS.2018.2843392

[11] Zhang, Y., Wu, J., Liu, Y., *et al*. (2020) MI-UNet: Multi-Inputs UNet Incorporating Brain Parcellation for Stroke Lesion Segmentation from T1-Weighted Magnetic Resonance Images. *IEEE Journal of Biomedical and Health Informatics*, **25**, 526-535. https://doi.org/10.1109/JBHI.2020.2996783

[12] Wang, S., Hu, Y., Shen, Y., *et al*. (2018) Classification of Diffusion Tensor Metrics for the Diagnosis of a Myelopathic Cord Using Machine Learning. *International Journal of Neural Systems*, **28**, Article ID: 1750036. https://doi.org/10.1142/S0129065717500368

[13] Lei, B., Liang, E., Yang, M., *et al*. (2022) Predicting Clinical Scores for Alzheimer's Disease Based on Joint and Deep Learning. *Expert Systems with Applications*, **187**, Article ID: 115966. https://doi.org/10.1016/j.eswa.2021.115966

[14] Zeng, D., Wang, S., Shen, Y., *et al*. (2017) A GA-Based Feature Selection and Parameter Optimization for Support Tucker Machine. *Procedia Computer Science*, **111**, 17-23. https://doi.org/10.1016/j.procs.2017.06.004

[15] Wu, K., Shen, Y. and Wang, S. (2018) 3D Convolutional Neural Network for Regional Precipitation Nowcasting. *Image Signal Process*, **7**, 200-212. https://doi.org/10.12677/JISP.2018.74023

[16] Wang, S.Q. and Li, H.X. (2011) Quantitative Construction of Regulatory Networks Using Multiple Sources of Knowledge. 2011 *International Conference on Machine Learning and Cybernetics*, Vol. 1, 91-96. https://doi.org/10.1109/ICMLC.2011.6016667

[17] Wang, S.Q. and Li, H.X. (2012) Random Network Based Dynamic Analysis for Biochemical Reaction System. *Advanced Science Letters*, **10**, 554-558. https://doi.org/10.1166/asl.2012.3381

[18] Zhang, H., Sun, Y., Zhao, M., *et al*. (2019) Bridging User Interest to Item Content for Recommender Systems: An Optimization Model. *IEEE Transactions on Cybernetics*, **50**, 4268-4280. https://doi.org/10.1109/TCYB.2019.2900159

[19] Wang, S.Q. and Li, H.X. (2012) Defining Transcriptional Network by Combining Expression Data with Multiple Sources of Prior Knowledge. 2012 *International Conference on System Science and Engineering*, Dalian, 30 June-2 July 2012, 102-106. https://doi.org/10.1109/ICSSE.2012.6257157

[20] Wang, S., Hu, J., Shen, Y., *et al*. (2014) Modeling and Analysis of Gene Regulatory Networks with a Bayesian-Driven Approach. 2014 14*th International Symposium on Communications and Information Technologies*, Incheon, 24-26 September 2014, 289-293.

[21] Wang, S., Shen, Y., Hu, J., *et al*. (2015) Hadoop-Based Analysis for Large-Scale Click-Through Patterns in 4G Network. In: Xu, K. and Zhu, H.J., Eds., *International Conference on Wireless Algorithms, Systems, and Applications*, Springer, Cham, 829-835. https://doi.org/10.1007/978-3-319-21837-3_81

[22] Wang, T., Shi, F., Jin, Y., *et al*. (2016) Multilevel Deficiency of White Matter Connectivity Networks in Alzheimer's Disease: A Diffusion MRI Study with DTI and HARDI Models. *Neural Plasticity*, **2016**, Article ID: 2947136. https://doi.org/10.1155/2016/2947136

[23] Wang, S., Wang, H., Shen, Y., *et al*. (2018) Automatic Recognition of Mild Cognitive Impairment and Alzheimer's Disease Using Ensemble Based 3D Densely Connected Convolutional Networks. 2018 17*th IEEE International Conference on Machine Learning and Applications*, Orlando, 17-20 December 2018, 517-523. https://doi.org/10.1109/ICMLA.2018.00083

[24] Wang, H., Shen, Y., Wang, S., *et al*. (2019) Ensemble of 3D Densely Connected Convolutional Network for Diagnosis of Mild Cognitive Impairment and Alzheimer's Disease. *Neurocomputing*, **333**, 145-156. https://doi.org/10.1016/j.neucom.2018.12.018

[25] Wang, S., Wang, H., Cheung, A.C., *et al*. (2020) Ensemble of 3D Densely Connected Convolutional Network for Diagnosis of Mild Cognitive Impairment and Alzheimer's Disease. In: Wani, M.A., *et al*., Eds., *Deep Learning Applications*, Springer, Berlin, 53-73. https://doi.org/10.1007/978-981-15-1816-4_4

[26] Yu, W., Lei, B., Wang, S., *et al*. (2022) Morphological Feature Visualization of Alzheimer's Disease via Multidirectional Perception GAN. *IEEE Transactions on Neural Networks and Learning Systems*, 1-15. https://doi.org/10.1109/TNNLS.2021.3118369

[27] Yu, W., Lei, B., Ng, M.K., *et al*. (2021) Tensorizing GAN with High-Order Pooling for Alzheimer's Disease Assessment. *IEEE Transactions on Neural Networks and Learning Systems*, **33**, 4945-4959. https://doi.org/10.1109/TNNLS.2021.3063516

[28] Lei, B., Yu, S., Zhao, X., *et al*. (2021) Diagnosis of Early Alzheimer's Disease Based on Dynamic High Order Networks. *Brain Imaging and Behavior*, **15**, 276-287. https://doi.org/10.1007/s11682-019-00255-9

[29] Yu, S., Wang, S., Xiao, X., *et al*. (2020) Multi-Scale Enhanced Graph Convolutional Network for Early Mild Cognitive Impairment Detection. In: Martel, A.L., *et al*., Eds., *International Conference on Medical Image Computing and Computer-Assisted Intervention*, Springer, Cham, 228-237. https://doi.org/10.1007/978-3-030-59728-3_23

[30] Pan, J., Lei, B., Shen, Y., *et al*. (2021) Characterization Multimodal Connectivity of Brain Network by Hypergraph GAN for Alzheimer's Disease Analysis. In: Ma, H.M., *et al*., Eds., *Chinese Conference on Pattern Recognition and Computer Vision*, Springer, Cham, 467-478. https://doi.org/10.1007/978-3-030-88010-1_39

[31] Goodfellow, I., Pouget-Abadie, J., Mirza, M., *et al*. (2014) Generative Adversarial Nets. *Advances in Neural Information Processing Systems* 27: *Annual Conference on Neural Information Processing Systems* 2014, Montreal, 8-13 December 2014, 2672-2680.

[32] Wang, S., Wang, X., Hu, Y., *et al*. (2020) Diabetic Retinopathy Diagnosis Using Multichannel Generative Adversarial Network with Semisupervision. *IEEE Transactions on Automation Science and Engineering*, **18**, 574-585. https://doi.org/10.1109/TASE.2020.2981637

[33] Huang, J., Zhou, L., Wang, L. and Zhang, D. (2020) Attention-Diffusion-Bilinear Neural Network for Brain Network Analysis. *IEEE Transactions on Medical Imaging*, **39**, 2541-2552. https://doi.org/10.1109/TMI.2020.2973650

[34] Zuo, Q., Lei, B., Shen, Y., *et al*. (2021) Multimodal Representations Learning and Adversarial Hypergraph Fusion for Early Alzheimer's Disease Prediction. In: Ma, H.M., *et al*., Eds., *Chinese Conference on Pattern Recognition and Computer Vision*, Springer, Cham, 479-490. https://doi.org/10.1007/978-3-030-88010-1_40

[35] Pan, J., Lei, B., Wang, S., *et al*. (2021) DecGAN: Decoupling Generative Adversarial Network Detecting Abnormal Neural Circuits for Alzheimer's Disease.

[36] Hu, S., Yuan, J. and Wang, S. (2019) Cross-Modality Synthesis from MRI to PET Using Adversarial U-Net with Different Normalization. 2019 *International Conference on Medical Imaging Physics and Engineering*, Shenzhen, 22-24 November 2019, 1-5. https://doi.org/10.1109/ICMIPE47306.2019.9098219

[37] Hu, S., Shen, Y., Wang, S., *et al*. (2020) Brain MR to Pet Synthesis via Bidirectional Generative Adversarial Network. In: Martel, A.L., *et al*., Eds., *International Conference on Medical Image Computing and Computer-Assisted Intervention*, Springer, Cham, 698-707. https://doi.org/10.1007/978-3-030-59713-9_67

[38] Yu, B., Zhou, L., Wang, L., *et al*. (2020). Sample-Adaptive GANs: Linking Global and Local Mappings for Cross-Modality MR Image Synthesis. *IEEE Transactions on Medical Imaging*, **39**, 2339-2350. https://doi.org/10.1109/TMI.2020.2969630

[39] Hu, S., Lei, B., Wang, S., *et al* (2021) Bidirectional Mapping Generative Adversarial Networks for Brain MR to PET Synthesis. *IEEE Transactions on Medical Imaging*, **41**, 145-157. https://doi.org/10.1109/TMI.2021.3107013

[40] Hu, S., Yu, W., Chen, Z., *et al*. (2020) Medical Image Reconstruction Using Generative Adversarial Network for Alzheimer Disease Assessment with Class-Imbalance Problem. 2020 *IEEE* 6*th International Conference on Computer and Communications*, Chengdu, 11-14 December 2020, 1323-1327. https://doi.org/10.1109/ICCC51575.2020.9344912

[41] Wang, S., Chen, Z., You, S., *et al*. (2022) Brain Stroke Lesion Segmentation Using Consistent Perception Generative Adversarial Network. *Neural Computing and Applications*, **34**, 8657-8669. https://doi.org/10.1007/s00521-021-06816-8

[42] Hong, J., Yu, S.C.H. and Chen, W. (2022) Unsupervised Domain Adaptation for Cross-Modality Liver Segmentation via Joint Adversarial Learning and Self-Learning. *Applied Soft Computing*, **121**, Article ID: 108729. https://doi.org/10.1016/j.asoc.2022.108729

[43] You, S., Shen, Y., Wu, G., *et al*. (2022) Brain MR Images Super-Resolution with the Consistent Features. 2022 14*th International Conference on Machine Learning and Computing*, Guangzhou, 18-21 February 2022, 501-506.

https://doi.org/10.1145/3529836.3529939

[44] You, S., Lei, B., Wang, S., *et al*. (2022) Fine Perceptive GANs for Brain MR Image Super-Resolution in Wavelet Domain. *IEEE Transactions on Neural Networks and Learning Systems*, 1-13. https://doi.org/10.1109/TNNLS.2022.3153088

[45] Dharejo, F.A., Zawish, M., Deeba, F., *et al*. (2022) Multimodal-Boost: Multimodal Medical Image Super-Resolution Using Multi-Attention Network with Wavelet Transform. *IEEE/ACM Transactions on Computational Biology and Bioinformatics*, 1-14. https://doi.org/10.1109/TCBB.2022.3191387

[46] Hu, B., Lei, B., Shen, Y., *et al*. (2021) A Point Cloud Generative Model via Tree-Structured Graph Convolutions for 3D Brain Shape Reconstruction. In: Ma, H.M., *et al*., Eds., *Chinese Conference on Pattern Recognition and Computer Vision*, Springer, Cham, 263-274. https://doi.org/10.1007/978-3-030-88007-1_22

[47] Hu, B., Shen, Y., Wu, G., *et al*. (2022) SRT: Shape Reconstruction Transformer for 3D Reconstruction of Point Cloud from 2D MRI. 2022 14*th International Conference on Machine Learning and Computing*, Guangzhou, 18-21 February 2022, 507-511. https://doi.org/10.1145/3529836.3529902

[48] Kariyawasam, R.S., Song, M.K.K., Kodali, P., *et al*. (2022) Automated Medical Image Based Anatomical Point Cloud Generation for Collaborative Real-Time Augmented Reality Applications. *Medical Imaging* 2022: *Imaging Informatics for Healthcare, Research, and Applications*, Vol. 12037, 172-179. https://doi.org/10.1117/12.2612993

[49] Wang, S.Q. and He, J.H. (2007) Variational Iteration Method for Solving Integro-Differential Equations. *Physics Letters A*, **367**, 188-191. https://doi.org/10.1016/j.physleta.2007.02.049

[50] Wang, S.Q. and He, J.H. (2008) Variational Iteration Method for a Nonlinear Reaction-Diffusion Process. *International Journal of Chemical Reactor Engineering*, **6**, 1-8. https://doi.org/10.2202/1542-6580.1630

[51] Wang, S.Q. (2009) A Variational Approach to Nonlinear Two-Point Boundary Value Problems. *Computers & Mathematics with Applications*, **58**, 2452-2455. https://doi.org/10.1016/j.camwa.2009.03.050

[52] Mo, L.F. and Wang, S.Q. (2009) A Variational Approach to Nonlinear Two-Point Boundary Value Problems. *Nonlinear Analysis*: *Theory, Methods & Applications*, **71**, e834-e838. https://doi.org/10.1016/j.na.2008.12.006

[53] Weiner, M.W., Veitch, D.P., Aisen, P.S., *et al*. (2015) Impact of the Alzheimer's Disease Neuroimaging Initiative, 2004 to 2014. *Alzheimer's & Dementia*, **11**, 865-884. https://doi.org/10.1016/j.jalz.2015.04.005

[54] Tzourio-Mazoyer, N., Landeau, B., Papathanassiou, D., *et al*. (2002) Automated Anatomical Labeling of Activations in SPM Using a Macroscopic Anatomical Parcellation of the MNI MRI Single-Subject Brain. *Neuroimage*, **15**, 273-289. https://doi.org/10.1006/nimg.2001.0978

[55] Lu, H., Plataniotis, K.N. and Venetsanopoulos, A.N. (2006) Multilinear Principal Component Analysis of Tensor Objects for Recognition. 18*th International Conference on Pattern Recognition*, Vol. 2, 776-779.

[56] Atwood, J. and Towsley, D. (2016) Diffusion-Convolutional Neural Networks. 30*th Conference on Neural Information Processing Systems* (*NIPS* 2016), Barcelona, 5-10 December 2016, 1-9.

[57] Xu, L., Wu, X., Li, R., *et al*. (2016) Prediction of Progressive Mild Cognitive Impairment by Multi-Modal Neuroimaging Biomarkers. *Journal of Alzheimer's Disease*, **51**, 1045-1056. https://doi.org/10.3233/JAD-151010

[58] Berron, D., Van Westen, D., Ossenkoppele, R., *et al*. (2020) Medial Temporal Lobe Connectivity and Its Associations with Cognition in Early Alzheimer's Disease. *Brain*, **143**, 1233-1248. https://doi.org/10.1093/brain/awaa068