Linking Adolescent Brain MRI to Obesity via Deep Multi-cue Regression Network

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Abstract. Adolescent obesity has become a significant public health problem for the potential risk of various diseases in later life. Recent biomedical studies have revealed that obesity is associated with structural changes in the brain. Thus the computer-aided analysis of adolescent obesity based on brain MRI is of great clinical value. While previous methods typically rely on hand-crafted MRI features for obesity prediction, we propose to link adolescent obesity and brain MRI through a deep learning framework. The newly released brain MRI data from the large-scale Adolescent Brain Cognitive Development (ABCD) study has paved the way for such an exploration. In this paper, we propose a deep multi-cue regression network (DMRN) for MRI-based analysis of adolescent obesity. Specially, in DMRN, we first design a feature encoding network to automatically extract high-dimensional features from brain MR images, followed by a regression network to predict Body Mass Index (BMI) scores for obesity analysis. To take advantage of other prior knowledge of studied subjects, our DMRN framework further explicitly incorporates the demographic information (e.g., waist circumference) of subjects into the learning process. Experiments have been conducted on 3,779 subjects with T1-weighted MRIs from the ABCD dataset. The results have provided some useful findings: (1) we consolidate the relationship between adolescent obesity and brain MRI as well as demographic information through a deep learning model; (2) we use visualization method to explain the prediction results by highlighting potential biomarkers in the brain MR images that are associated with adolescent obesity.

1 Introduction

Adolescent obesity has become a significant public health problem, which is estimated to affect millions of young people worldwide [1,2]. Adolescents who are obese have a potential risk of poor diseases in later life, such as heart diseases, diabetes and various cancers [3,4]. While obesity is primarily characterized by weight gain, a recent study suggests that it is related to structural changes of the brain which may trigger impairments in the nerve system [5]. However, a

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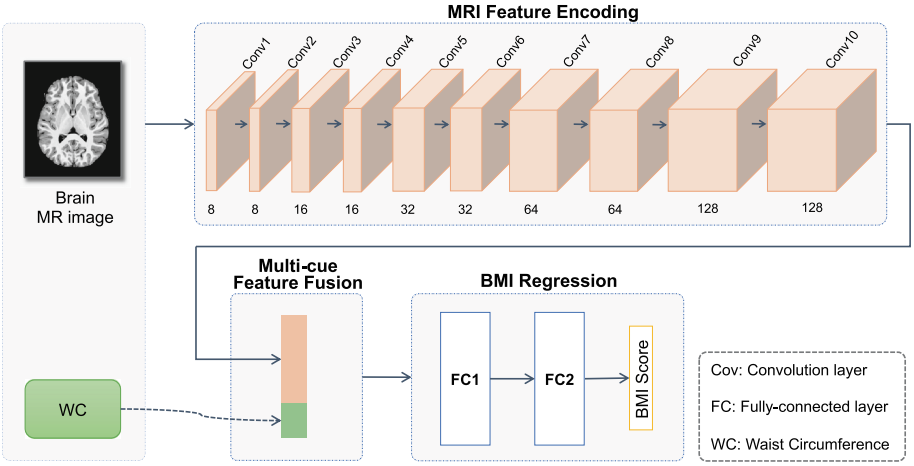

Fig. 1. Overview of the proposed deep multi-cue regression network (DMRN) for adolescent obesity prediction based on structural MR images, including (1) MRI feature encoding, (2) multi-cue feature fusion, and (3) BMI regression. The input data include the brain MR image and the demographic information (i.e., waist circumference, WC) of each subject, while the output is the BMI score.

clear association between adolescent brain structure and obesity still remains an open problem currently. Therefore, it is of great clinical value to conduct more in-depth research on such correlation to bridge the gap.

Structural magnetic resonance imaging (MRI) has been widely used in brain morphology analysis due to its sensitivity and high spatial resolution [6–10]. In this work, we investigate the association between brain structural changes and adolescent obesity, based on a recently released large-scale MRI dataset, i.e., the NIH Adolescent Brain and Cognitive Development (ABCD) [11]. The ABCD dataset is currently the largest longitudinal study of over 11,000 young people aged 9–10 from 21 research sites across the United States. As the newly released and largest dataset of adolescent brain MRIs, the ABCD dataset has paved the way for further pushing forward the research on exploring the relationship between adolescent obesity and the corresponding brain structural changes. Among the various indicators of obesity, the Body Mass Index (BMI) is the most widely-used measurement which has been used by the World Health Organization (WHO) for clinical diagnosis of obesity [12]. Since BMI is easily calculated and reliable for indicating obesity, BMI is used as the clinical indicator of obesity in our analysis.

In the literature, several machine learning methods have been proposed to analyze obesity [13,14]. However, these methods only used facial or body images to train the model, which could not essentially reflect the relationship between obesity and its biological causes (e.g., structural changes of the brain). In addition, existing studies generally rely on small-scale datasets, which greatly limits

the scope and depth of the analysis. Based on the large-scale ABCD dataset, some research has been conducted to study the relationship between adolescent obesity and brain structure [15]. However, they merely rely on demographic information of subjects, and do not investigate the association between obesity with brain MR images.

In this paper, we intend to link brain structural MRI to adolescent obesity through a deep learning framework. To this end, we propose a deep multi-clue regression network (DMRN) to predict BMI scores of subjects, as illustrated in Fig. 1. As can be seen from this figure, the proposed DMRN consists of three key components: (1) a *MRI feature encoding* module that extracts feature representations of the input MR images, (2) a *multi-cue feature fusion* module that fuses MRI features and demographic information, and (3) a *BMI regression* module that predicts BMI scores for measuring obesity. Different from previous studies, our DMRN can automatically extract informative MRI features which are associated with obesity, without requiring any hand-crafted representations or expert knowledge. Especially, DMRN is able to explicitly incorporate the demographic information (e.g., waist circumference) of subjects into the learning process, which is expected to further improve the prediction performance by introducing more prior knowledge of studied subjects.

The major contributions of this work is two-fold. *First*, we introduce a simple but effective deep model to a novel application, i.e., studying structural changes in adolescent brains that are linked to obesity. To the best of our knowledge, this is among the first attempt to link adolescent obesity to brain MRI on such a large-scale (i.e., 3,779 subjects) adolescent brain MRI dataset. *Besides*, we employ a visualization method to analyze the network outputs by highlighting potential obesity-related biomarkers in MRIs. The results can offer valuable information for related research and encourage the development of AI models for adolescent obesity analysis.

2 Method

2.1 Materials and Image-Processing

A total of 3,779 T1-weighted brain MR images of adolescents aged 9–10 and their corresponding raw adolescent anthropometrics scores (i.e., weight, height, waist circumference, and age) from the ABCD dataset were downloaded and included in our study. As the obesity indicator, BMI is calculated based on the ratio of weight and height (all the original weight and height scores are measured and offered by the ABCD study) as follows:

$$\mathrm{BMI} = 703 \times \frac{\mathrm{weight}}{\mathrm{height}^2} \tag{1}$$

where weight and height are measured by pound (lb) and inch (in), respectively.

All T1-weighted MR images were pre-processed through a standard pipeline, including (1) anterior commissure-posterior commissure alignment, (2) skull

stripping, (3) intensity correction, (4) linear alignment with the Colin27 template, (5) image normalization and background removal, and (6) intensity inhomogeneity correction using N3 algorithm. Finally, all the pre-processed MR images had the same size of $181 \times 217 \times 181\,\mathrm{mm}^3$ with the spatial resolution of $1 \times 1 \times 1\,\mathrm{mm}^3$.

2.2 Proposed Method

As shown in Fig. 1, the proposed deep multi-cue regression network (DMRN) consists of three modules: (1) MRI feature encoding, (2) multi-cue feature fusion, and (3) BMI regression. In the following, we first present the detail of each module, and then introduce the visualization method and implementation of DMRN.

MR Feature Encoding. As illustrated in the top panel of Fig. 1, we exploit a 3D convolutional neural network as the backbone to extract feature representations of each input MRI (with the whole image as the input). Specifically, the MRI feature encoding backbone contains ten convolutional (Conv) layers (size: $3 \times 3 \times 3$) to extract local-to-global representations of brain MRIs. The filter numbers of these sequential Conv layers are 8, 8, 16, 16, 32, 32, 64, 64, 128, and 128, respectively. The stride for each Conv layer is set to 1, and each Conv layer is followed by batch normalization and rectified linear unit (ReLU). To reduce over-fitting and increase receptive field, down-sampling operations (with the stride of $2 \times 2 \times 2$) are plugged into four Conv layers (i.e., Conv2, Conv4, Conv6, Conv8 and Conv10), respectively. As a plug-in module, the MRI feature encoding backbone can be replaced with any other network architectures, e.g., residual blocks.

Multi-cue Feature Fusion. To take advantage of other prior knowledge (e.g., demographic information) of studied subjects, we incorporate the demographic factor, i.e., waist circumference (WC), into the learning process. As shown in the bottom left panel of Fig. 1, we concatenate the waist circumference with the learned MR feature vector of the convolution layers. Here, the WC value is encoded as a vector (ranging from 0 to 1). Then, the concatenated feature vector is further fed into a regression module for BMI prediction.

Regression Module for BMI Prediction. With the multi-cue representations (i.e., concatenation of MRI features and WC) as input, two successive fully-connected layers are employed for BMI score estimation. Let $\mathcal{X} = \{X_i\}_{i=1}^N$ and $\mathbf{y} = \{y_i\}_{i=1}^N$ represent the feature representations and ground-truth BMI scores of N training subjects, respectively. For the i-th subject X_i ($i = 1, \cdots, N$), we denote its BMI score as y_i. The proposed model aims to link the input and the obesity measurement scores via a non-linear mapping ϕ: $\mathcal{X} \rightarrow \mathbf{y}$, with the objective function defined as follows:

$$\min_{\mathbf{W}} \frac{1}{N} \sum_{X_i \in \mathcal{X}} (y_i - \phi(X_i, \mathbf{W}))^2 \tag{2}$$

where $\mathbf{W}$ denotes the parameters of the DMRN model.

Visualization of Discriminative Regions. We use a visualization method [16] to show potential biomarkers in brain MR images that are associated with obesity. The results can be used as a useful complement to MRI analysis by experts and help to interpret the prediction results of DMRN. To this end, we calculate the gradient of the output feature maps of DMRN (w.r.t. each input brain MR image). The gradient can describe how the output varies when a specific voxel value changes, thus indicating the contributions of different brain regions for predicting BMI scores. In the training process, the gradient can be easily calculated by the back-propagation algorithm.

Implementation. The proposed DMRN model was implemented using Python based on PyTorch. The input of the network was linearly-aligned brain MR image (size: $181 \times 217 \times 181$) and a demographic factor (i.e., waist circumference), while the output was the estimated BMI score. At the training phase, the Adam optimizer was adopted with a mini-batch size of 2 and a learning rate of 1×10^{-3}. A dropout rate of 0.5 was used to prevent over-fitting. The network was trained in an end-to-end manner for 30 epochs.

3 Experiment and Discussion

Experimental Setup. A total of $3,779$ subjects with T1-weighted MRIs from ABCD are included in the experiments. All these subjects are partitioned into three subsets, including a training set (60%), a validation set (20%), and a test set (20%), and such data partition is fixed[1]. Based on the training set, we construct a specific model and save the trained model that achieves the smallest validation loss on the validation set. The model is then applied to the independent test set. To evaluate the performance of BMI prediction, two metrics are used in the experiments, including (1) mean square error (MSE), and (2) mean absolute error (MAE). For these two metrics, lower values indicate better performance.

The proposed DMRN is first compared with two conventional machine learning method using different hand-crafted features, including (1) support vector regressor (SVR) using ROI features (gray matter volume in 90 ROIs defined in AAL template) [17], and (2) SVR using WC as features. We further compare DMRN with two deep learning models, including (1) AlexNet [18] and (2) VoxCNN [19]. Specifically, the AlexNet consists of five $3 \times 3 \times 3$ Conv layers (with the channel numbers of 64, 64, 128, 128, and 256, respectively), followed by three fully-connected layers for regression. The VoxCNN contains ten $3 \times 3 \times 3$ Conv

[1] https://sibis.sri.com/abcd-np-challenge/.

Table 1. Results of BMI prediction achieved by the proposed method and several other methods on the ABCD dataset.

Method	Validation Result		Testing Result	
	MSE	MAE	MSE	MAE
ROI+SVR	19.26	5.05	19.50	5.12
WC+SVR	22.57	6.01	22.32	5.95
AlexNet	18.61	4.95	18.05	4.88
VoxCNN	17.33	4.25	16.98	4.01
DMRN-MRI	15.16	3.06	15.06	3.09
DMRN (Ours)	**14.80**	**3.01**	**14.01**	**2.87**

layers (with the channel numbers of 8, 8, 16, 16, 32, 32, 32, 64, 64, and 64, respectively), followed by two fully-connected layers for regression. We also compare our DMRN with its variant (called DMRN-MRI) that uses only MRIs as input. For the fair comparison, all deep learning methods share the same input MR images and ground-truth BMI scores, while our DMRN also uses a demographic factor (i.e., WC) as input.

Results of BMI Prediction. The experimental results achieved by six different methods on the ABCD dataset for BMI prediction are listed in Table 1. From Table 1, one can observe that the proposed DMRN achieves relatively higher precision, with consistently better performance than the other methods.

Based on the results, we can draw the following conclusions. *First*, a deep learning model (e.g., our DMRN) for BMI prediction could be trained from brain MR images, by automatically learning MRI features. This also implies that the adolescent obesity and brain structure have some correlation. Without hand-crafted analysis with prior expert knowledge, deep learning for MRI-based BMI prediction has offered a new perspective to mine the relationship between obesity and brain structure. *Second*, these results indicate that our deep network is relatively suitable for the task of BMI prediction compared to the other two CNN models. This implies that the task-oriented feature encoding and multi-cue feature fusion strategy are helpful to learn informative feature representations to boost the prediction performance of BMI.

Obesity-Related Brain Regions in MRI. Previous studies have revealed that obesity is associated with certain regions of the brain. Note that our method is totally based on automated learning from brain MR images (without any neuroscience knowledge). To understanding the output of the proposed deep network, we aggregate saliency maps learned by our method on the whole cohort (grouped by high BMI > 40 and low BMI < 10 [12]) to visualize obesity-related patterns in MRIs. The result is shown in Fig. 2.

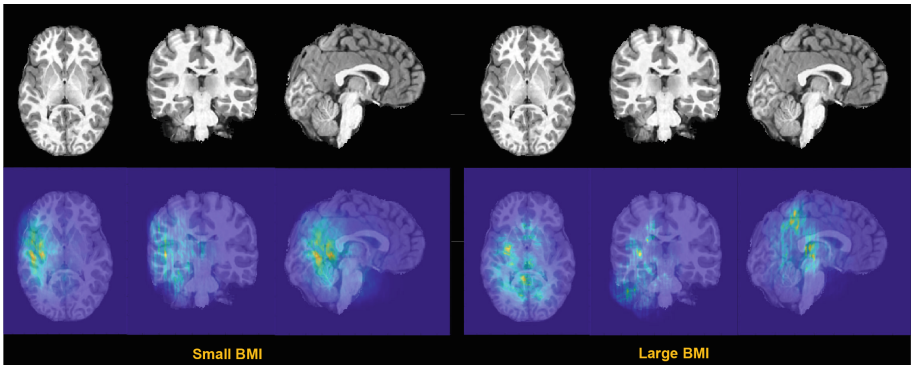

Fig. 2. Relevance heatmaps generated by our deep multi-cue regression network (DMRN) for BMI score prediction. The highlighted parts (in yellow color) indicate the ares that are more closely related to obesity. (Color figure online)

From Fig. 2, it can be observed that different brain regions have different contributions to obesity in terms of BMI prediction. In addition, Fig. 2 shows that brain regions that are closely associated with obesity may have some differences between the cohorts with different BMI scores.

Ablation Study. To investigate the impact of demographic information and the role of our multi-cue fusion strategy for BMI prediction, we conduct several ablation experiments based on two variants of DMRN. Note that height and weight information are highly correlated with ground-truth BMI (see Eq. 1), and BMI is the output, thus they are not used in the ablation study.

First, we analyze the impact of multi-cue fusion strategy, by removing waist circumference (WC) from DMRN. That is, we train the network solely based on MR images and denote this variant as "DMRN-MRI", with results shown in Table 1. From Table 1, we can see that DMRN with WC information performs better than DMRN-MRI that uses only MR images. This implies that the proposed multi-cue fusion strategy (for fusing MRI and WC) helps to improve the performance of BMI prediction, and WC is positively correlated with obesity. This is consistent with the findings of some related research studies [20].

We further investigate whether the age information is helpful in BMI prediction. Specifically, we replace the WC value with age (in months) as demographic information in DMRN, and denote this variant with "DMRN-Age". We encode the age (normalized into the range of $[0, 1]$) with MR features in the multi-cue fusion module, with experimental results reported in Table 2. Table 2 shows that the age information does not impact the prediction significantly, suggesting that there is no obvious correlation between obesity and age. This is different from the cases in some other type of diseases caused by brain impairment, such as Alzheimer's disease and autism spectrum disorder.

Table 2. Results of BMI prediction achieved by two variants of the proposed DMRN on the ABCD dataset.

Method	Validation Result		Testing Result	
	MSE	MAE	MSE	MAE
DMRN-MRI	15.16	3.06	15.06	3.09
DMRN-Age	**15.13**	**3.05**	**15.03**	**3.02**

Limitations and Future Work. Even though our DMRN is effective in predicting adolescent obesity, there are still several limitations that need to be addressed in the future. *First*, only T1-weighted structural brain MR images are used in this paper. As the largest collaborative study for adolescent development, the ABCD dataset consists of multi-modal neuroimaging data, such as T2-weighted structural MRI, Diffusion tensor imaging (DTI), and functional MRI (fMRI). It is interesting to extend our DMRN to a multi-modal version to take advantage of those multi-modal neuroimages, which will be our future work. *Second*, we equally treat subjects from 21 research centers in the ABCD database, ignoring the differences in data distribution among multiple imaging centers. Considering that such data heterogeneity may have a negative impact on the robustness of the learned model, we plan to develop advanced data adaptation techniques [21,22] to handle this challenging problem. *Third*, to improve the prediction precision, more complex CNN architectures (e.g., residual or dense networks) could be used as backbones to more efficiently encode MR images, which will also be studied in future.

4 Conclusion

In this paper, we developed a deep multi-cue regression network (DMRN) for MRI-based analysis of adolescent obesity in terms of BMI. The proposed DMRN consists of a MRI feature encoding module, a multi-cue feature fusion module, and a BMI regression module. Besides the input MRI, DMRN can also explicitly incorporate two demographic factors (i.e., waist circumference and age) into the learning process. Experiments were performed on the newly released ABCD dataset which offers a relatively large number of adolescent brain MRIs. Experimental result suggest that the BMI can be reliably predicted based on brain MR images via DMRN, thus demonstrating the association between adolescent obesity and brain structure. Besides, we also visualize the learned heatmaps in the brain MR images to indicate important imaging biomarker that may be associated with obesity.

References

1. Abarca-Gómez, L., et al.: Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128.9 million children, adolescents, and adults. Lancet **390**(10113), 2627–2642 (2017)

2. Ogden, C.L., Carroll, M.D., Kit, B.K., Flegal, K.M.: Prevalence of childhood and adult obesity in the United States, 2011–2012. Jama **311**(8), 806–814 (2014)
3. Biro, F.M., Wien, M.: Childhood obesity and adult morbidities. Am. J. Clin. Nutr. **91**(5), 1499–1505 (2010)
4. Arnold, M., et al.: Obesity and cancer: an update of the global impact. Cancer Epidemiol. **41**, 8–15 (2016)
5. Li, N., Yolton, K., Lanphear, B.P., Chen, A., et al.: Impact of early-life weight status on cognitive abilities in children. Obesity **26**(6), 1088–1095 (2018)
6. Giedd, J.N., et al.: Brain development during childhood and adolescence: a longitudinal MRI study. Nat. Neurosci. **2**(10), 861–863 (1999)
7. Liu, M., Zhang, D., Shen, D.: Relationship induced multi-template learning for diagnosis of Alzheimer's disease and mild cognitive impairment. IEEE Trans. Med. Imaging **35**(6), 1463–1474 (2016)
8. Liu, M., Zhang, J., Adeli, E., Shen, D.: Landmark-based deep multi-instance learning for brain disease diagnosis. Med. Image Anal. **43**, 157–168 (2018)
9. Pan, Y., Liu, M., Wang, L., Xia, Y., Shen, D.: Discriminative-region-aware residual network for adolescent brain structure and cognitive development analysis. In: Zhang, D., Zhou, L., Jie, B., Liu, Mingxia (eds.) GLMI 2019. LNCS, vol. 11849, pp. 138–146. Springer, Cham (2019). https://doi.org/10.1007/978-3-030-35817-4_17
10. Liu, M., Zhang, J., Lian, C., Shen, D.: Weakly supervised deep learning for brain disease prognosis using MRI and incomplete clinical scores. IEEE Trans. Cybern. **50**(7), 3381–3392 (2019)
11. Volkow, N.D., et al.: The conception of the abcd study: from substance use to a broad NIH collaboration. Dev. Cogn. Neurosci. **32**, 4–7 (2018)
12. Garvey, W.T.: The diagnosis and evaluation of patients with obesity. Curr. Opin. Endocr. Metab. Res. **4**, 50–57 (2019)
13. Jiang, M., Shang, Y., Guo, G.: On visual BMI analysis from facial images. Image Vis. Comput. **89**, 183–196 (2019)
14. Dantcheva, A., Bremond, F., Bilinski, P.: Show me your face and i will tell you your height, weight and body mass index. In: ICPR, pp. 3555–3560 (2018)
15. Ronan, L., Alexander-Bloch, A., Fletcher, P.C.: Childhood obesity, cortical structure, and executive function in healthy children. Cereb. Cortex **30**(4), 2519–2528 (2019)
16. Simonyan, K., Vedaldi, A., Zisserman, A.: Deep inside convolutional networks: visualising image classification models and saliency maps. In: ICLR (2014)
17. Drucker, H., et al.: Support vector regression machines. In: NIPS, pp. 155–161 (1997)
18. Krizhevsky, A., Sutskever, I., Hinton, G.E.: Imagenet classification with deep convolutional neural networks. In: NIPS, pp. 1097–1105 (2012)
19. Korolev, S., Safiullin, A., Belyaev, M., Dodonova, Y.: Residual and plain convolutional neural networks for 3D brain MRI classification. In: ISBI (2017)
20. Walls, H.L., et al.: Comparing trends in BMI and waist circumference. Obesity **19**(1), 216–219 (2011)
21. Cheng, B., Liu, M., Shen, D., Li, Z., Zhang, D.: Multi-domain transfer learning for early diagnosis of Alzheimer's disease. Neuroinformatics **15**(2), 115–132 (2017)
22. Wang, M., Zhang, D., Huang, J., Yap, P.T., Shen, D., Liu, M.: Identifying autism spectrum disorder with multi-site fMRI via low-rank domain adaptation. IEEE Trans. Med. Imaging **39**(3), 644–655 (2019)