

Automated fetal lateral ventricular width estimation from prenatal ultrasound based on deep learning algorithms

Ruizhi Liu¹, Bin Zou², Hongyang Zhang¹, Jingyu Ye², Cong Han¹, nianji zhan², Ying Yang², Hongguo Zhang¹, Fang Chen², Shucheng Hua¹, and Jian Guo²

¹Jilin University First Hospital

²BGI-Shenzhen

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Abstract

Ventriculomegaly (VM) is the medical term used to describe enlargement of the lateral ventricles to a level of 10 mm or more, which is the most frequent sign of possible CNS abnormality detected on prenatal ultrasound. In this paper, we aim to evaluate the feasibility of CNN-based DL algorithms predicting the fetal lateral ventricular width from prenatal ultrasound images. The data was collected from 626 pregnant women with gestational age between 22 to 26 weeks. 3456 brain images were picked out from all 49222 stored freeze-frame images. 2304 transventricular (TV) or transthalamic (TT) plane images were further picked out and the brain regions were detected and extracted. 1431 TV-TT planes had known lateral ventricular width. The mean absolute error (MAE) of the predicted lateral ventricular width was 1.01 mm. More than 65% test images had a MAE of less than 1 mm. If we used only the 610 cases with lateral ventricular width less than 15 mm to train and test the model, the MAE was 0.54 mm and more than 82% test images had a MAE of less than 1 mm. We also implemented heat maps to provide evidence that our regression model predicting the lateral ventricular width was based on the anatomical structure of lateral ventricular. The results shown that the regression model can locate the lateral ventricular region of images with large lateral ventricular width successfully and then predict its width based on this region.

Introduction

Fetal ultrasound has become one of the most important examinations during pregnancy in most countries around the world. The second-trimester, or mid-trimester, fetal ultrasound examination is done in the middle part of the pregnancy. This exam can evaluate several features of the pregnancy, which can be used to evaluate the fetal development and health status [1]. Another important goal of mid-trimester fetal ultrasound is to detect possible congenital anomalies. The Eurofetus study [2], a multicenter project aimed to examine the accuracy of routine mid-trimester ultrasonographic examination in unselected populations, found that over one half (56%) of fetal malformations were detected and 55% of major anomalies were identified before 24 weeks of gestation.

Convolutional neural network (CNN) is one of the main categories of deep learning algorithms and have been shown to achieve fruitful results in image analysis, including medical images like ultrasound [3-12]. In fetal ultrasound analysis, CNN have shown potential for multiple tasks, such as standard plane detection [13-18], fetal anatomy detection and classification [19-20], fetal body and amniotic fluid segmentation [21-24], fetal head detection and biometry evaluation [25-29], fetal abdominal circumference identification [30], fetal heart detection, standard viewing plane classification and fetal heart description [31-32], estimation of fetal gestational age [33] and fetal ultrasound image quality assessment [34]. Recently, Xie etc. [35] used

deep learning algorithms to classify fetal brain ultrasound images from standard axial planes as normal or abnormal.

Central nervous system (CNS) is the most complex system among the fetal system and one of the most frequent sites for prenatal diagnosed congenital abnormalities [36]. Ventriculomegaly (VM) is the medical term used to describe enlargement of the lateral ventricles to a level of 10 mm or more, which is the most frequent sign of possible CNS abnormality detected on prenatal ultrasound [37]. It is associated with an increased risk of CNS anomalies or congenital infections [38]. VM is typically seen during the second-trimester screening examination and the prevalence of it is much higher than specific CNS abnormalities like neural tube defects, etc. [39-40].

In this paper, we aim to evaluate the feasibility of CNN-based DL algorithms predicting the fetal lateral ventricular width from fetal brain ultrasound images. Experimental results show that CNN-based DL algorithms can predict the fetal lateral ventricular width with high precision.

Methods

Data resource

The data was collected from the First Hospital of Jilin University in China from January 2018 to June 2019. Patient identifiers were removed, and all data were anonymized. Every pregnant woman in this study gave written informed consent. All of the examinations were performed and diagnosed by a team of well-trained doctors from center for prenatal diagnosis of First Hospital of Jilin University. The GE Volution E8 ultrasound scanners were included for data acquisition. The study protocol was approved by Ethics Committee of the First Hospital of Jilin University (Changchun, China; permit No. 2018-429).

Deep learning algorithms for training

Picking out brain images

The first step of our scheme is to pick out brain images from all stored freeze-frame images (Figure 1). This can be done using a classification deep learning model. Several famous models have been proposed and shown good results in image classification related tasks, such as Oxford VGG model [41], Google Inception model [42] and Microsoft ResNet model [43]. Here we chose to apply transform learning using ResNet50, a 50-layer Residual Network, which showed good results for medical image classification [44].

Specifically, each image was first resized to 224×224 and then enter RetNet50 layer with the pretrained IMAGENET weights. GlobalAveragePooling2D is applied to the output of the last convolutional layer, following a classic fully connected dense layer with sigmoid activation. All layers are set as trainable, which means they can be updated with back propagation in each step.

The experiment was carried out with Jupyter Notebook, in an environment of Keras, using TensorFlow as backend. A workstation with four NVIDIA GeForce GTX 1080 Ti graphics cards, two Intel Xeon E5-2620 v4 CPUs and a Random Access Memory (RAM) of 64GB was used in this experiment. The labels were determined manually by one trained expert.

Picking out TV and TT planes and localization of brain region

After picking out all fetal brain images, we need to further pick out US images in the transventricular (TV) or transthalamic (TT) plane, in which the lateral ventricle can be measured. Moreover, we need to localize the brain region and remove the background around the fetal skull, which will influence the results hugely. Here we used Faster R-CNN [45], a state-of-the-art object detection algorithm, which combines the localization task and classification task together.

Specifically, we used the `fasterrcnn_resnet50_fpn` model in `torchvision` to perform the experiments, which uses `resnet50` as the backbone. The network parameters were initialized from a model pretrained on the COCO dataset. To make the algorithm more robust, we augmented the dataset by randomly cropping, flipping images and rotating images by angles of 90, 180 or 270 degrees, to simulate various fetal positions. The network would output zero, one or more detected objects and corresponding likelihood percentages. The first object, which has the largest percentage, was selected as the result.

The experiment was carried out with Jupyter Notebook, in an environment of `torch`. The system used in this experiment was the same with the first step. The bounding boxes of brains were manually labeled by one trained expert and reviewed by doctors. The US images in the TV and TT plane were selected by doctors.

Predicting the lateral ventricular width

A regression model was applied to do this task. Specifically, each brain region image will first resize to 224×224 and then enter RetNet50 layer with the pretrained IMAGENET weights. `GlobalAveragePooling2D` is applied to the output of the last convolutional layer, following a classic fully connected dense layer with linear activation. All layers were set as trainable, which means they can be updated with back propagation in each step. `mean_squared_error` was specified as the loss function when compiling the model. The experiment setting and the system used in this experiment was the same with the first step. The truth lateral ventricular width of each image was determined manually by doctors.

Interpretation of the results using heat maps

To provide evidence that our regression model predicting the lateral ventricular width of brain images was based on the anatomical structure of lateral ventricle, we implemented heat maps for visualization and interpretation. Here we used a technique called Class Activation Mapping (CAM) [46] to generate the heat maps. After superimposing the heat map to the grayscale image, we can see the key area, or the red color regions, that the algorithm activated most.

Experiments and Results

Data analysis

We started with 626 pregnant women with gestational age between 22 to 26 weeks, who underwent prenatal examinations at the First Hospital of Jilin University in China from January 2018 to June 2019. There are 90 cases with lateral ventricular width equal to or bigger than 10 mm and 16 cases with lateral ventricular width bigger than 15 mm. Actually, these 90 ventriculomegaly cases and the cases with lateral ventricular width near 10 mm were selected from 22616 pregnant women. The other normal cases were randomly selected from all normal cases. The average lateral ventricular (LV) width, which refers to the larger width of the left and right lateral ventricles, of the 626 cases was 7 mm (see Figure S1(a)). The average gestational age is 23.8 weeks. There were 49212 stored freeze-frame images (Figure S2) and the mean number of stored freeze-frame images is 78.6. Each frame had a size of 768x576 pixels.

Picking out brain images

70 cases were randomly selected as the validation set and 70 other cases were randomly selected as the test set. The other 486 cases were training set, which had 2731 brain images and 35687 other images. 2731 brain images and the same number of randomly selected other images were used for classification training. The training was terminated after 20 epochs and the model with the best overall validation accuracy was chose as the final model. 376 brain images and 4967 other images from the 70 test cases were successfully tested, and the overall test accuracy is 99.8%. The classification accuracy was 100% (376/376) and 99.8% (4955/4967)

for the brain images and other images, respectively. The sensitivity and specificity for brain images were 100% (376/376) and 96.9% (376/388), respectively.

Picking out TV and TT planes and localization of brain region

We randomly selected 60 cases as test set. The remaining 566 cases, which had 2094 TV-TT plane images and 1044 other images, were training set. 1044 other images and the same number of randomly selected TV-TT plane images were used for training. The training was terminated after 20 epochs and the last model was chose as the final model. 210 TV-TT plane images and 108 other images were successfully tested. The AP@0.5 and AP@0.75 were all 0.992 and the mAP@[.5,.95] was 0.92. The mAR@[.5,.95] was 0.945. Then we chose the first object detected, which has the largest percentage, as the result. The overall test accuracy is 98.1% (312/318). The detection accuracy for the TV-TT plane images and other images was 97.6% (205/210) and 99.1% (107/108), respectively. The sensitivity and specificity for TV-TT plane images were 97.6% (205/210) and 99.5% (205/206), respectively.

Predicting the lateral ventricular width

The lateral ventricular width shown in each brain region image was determined by doctors. From all the 2304 TV-TT planes, 1431 planes had confirmed lateral ventricular width. Other planes either did not show clear lateral ventricle or the lateral ventricular width cannot be determined.

We performed two experiment. The first one was to use all the 626 cases, corresponding to 1431 images with known lateral ventricular width, to train and test the regression model. The second one was to use the 610 cases with lateral ventricular width less than 15 mm, corresponding to 1351 images, to train and test the model.

For the first experiment, 60 cases were randomly selected as the test set, which had 141 images. Other 60 case were randomly selected as the validation set, which had 132 images. The remaining 506 cases, which had 1158 images, were training set. The training was terminated after 100 epochs and the model with the least mean square error (MSE) was chose as the final model. The mean absolute error (MAE) of the test set was 1.01 mm. More than 65% test images had a MAE of less than 1 mm (Figure 2(a), Figure S3(a) and Table S1).

For the second experiment, 58 cases were randomly selected as the test set, which had 107 images. Other 58 case were randomly selected as the validation set, which had 118 images. The remaining 495 cases, which had 1124 images, were training set. The training was terminated after 100 epochs and the model with the least MSE was chose as the final model. The MAE of the test set was 0.54 mm. More than 82% test images had a MAE of less than 1 mm (Figure 2(b), Figure S3(b) and Table S2).

We also evaluated the possibility of the two models to predict lateral ventricular width in the case level. For each test case, we set the predicted LV width as the largest predicted LV width of all its TV and TT planes. For the first model, 235 TV and TT planes from the 60 test cases were tested. The MAS was 1.47 mm (Figure 2(c), Figure S3(c) and Table S3). For the second model, 203 TV and TT planes from the 58 test cases were tested. The MAE was 0.73 mm (Figure 2(d), Figure S3(d) and Table S4). If we set the threshold for the two models as 10 mm, the sensitivity was 100% (8/8) and 75% (6/8), and the precision was 57% (8/14) and 86% (6/7), respectively (Figure 2(c-d)).

From Figure 2(c) and Figure S3(c) we can see that there was a case with large prediction error of 9.2 mm. The truth LV width was 4.4 mm and the predicted width was 13.6 mm. We analyzed the prediction result of this case. This case had three TV or TT planes and the predicted LV width was 4.94 mm, 5.60 mm and 13.6 mm, respectively (Figure S4). Based on the rule we used, the predicted LV width of this case was set as 13.6 mm. We found that the last image (Figure S4(c)) was not a regular TV or TT plane, hence the large prediction error, 9.2 mm, was not a normal result.

Interpretation of the results using heat maps

We generated heat maps and their corresponding overlay images for all test images (Figure 3 and Figure 4). The results were all reviewed by an expert. For the first experiment, 97 out of 141 heat maps were activated in/around the lateral ventricular regions. Moreover, all the 141 heat maps were activated at the left-upper corner. Figure 3 shows some examples. For the second experiment, 74 out of 107 heat maps were activated on/around the lateral ventricular regions. 28 of them were also activated on other regions. Other 34 heat maps were not activated on/around the lateral ventricular regions. Figure 4 shows some examples.

We can see that for images with large lateral ventricular width, the heat maps were activated on/around the lateral ventricular regions, as we expected. We performed further analysis to investigate this phenomenon. Figure S5(a) and Figure S5(c) shows distribution of lateral ventricular width of images whose heat maps did not activate the lateral ventricular regions for the first and second experiment, respectively. Compared with Figure S5(b) and Figure S5(d), which refer to distribution of lateral ventricular width of images whose heat maps activate the lateral ventricular regions for the first and second experiment, the mean LV width was much smaller ($p < 0.001$ for both experiments).

These results indicate that the regression models can locate the lateral ventricular regions of images with large lateral ventricular width successfully and then predict their width based on these regions with small error.

Discussion

Main Findings

This study is the first to predict the fetal lateral ventricular width using CNN-based DL algorithms. Our study shows that the scheme can automatically pick out brain images from all stored freeze-frame images. The sensitivity and specificity for brain images were 100% (376/376) and 96.9% (376/388), respectively. The scheme can recognize TV and TT planes and extract the brain regions. The sensitivity and specificity for TV-TT planes were 97.6% (205/210) and 99.5% (205/206), respectively. For the regression model, the MAE of the predicted lateral ventricular width was 1.01 mm. More than 65% test images had a MAE of less than 1 mm. If we used the 610 cases with lateral ventricular width less than 15 mm to train and test the model, the MAE was 0.54 mm and more than 82% test images had a MAE of less than 1 mm. The heat maps provide evidence that our regression model predicting the lateral ventricular width was based on the anatomical structure of lateral ventricular.

Strengths and Limitations

Many psychiatric and neurodevelopmental disorders are associated with enlargement of the lateral ventricles thought to have origins in prenatal brain development [47]. Moreover, VM is one of the most commonly detected fetal anomalies at the mid-trimester ultrasound (US) and occurs in up to 2 per 1000 births [39-40]. Therefore, recognizing this anomaly precisely and as early as possible is very important.

A previous study [35] used deep learning algorithms to classify fetal brain ultrasound images from standard axial planes as normal or abnormal. However, it is not suitable to combine together the ventriculomegaly cases and other CNS anomaly cases to train the classification model. One reason is that the number of VM cases is much higher than other CNS anomaly cases. In our dataset, from all the 22616 pregnant women, there are 90 VM cases (including 16 hydrocephalus cases) and only 24 other CNS anomaly. Another reason is that, predicting VM will focus only on the lateral ventricular region, while different other regions may be evaluated for other CNS anomaly prediction.

Moreover, the study [35] limited the ultrasound images as standard axial planes, while our study used all TV and TT planes. This is a real problem that many cases have no standard axial planes stored and inexperienced

scanner may not be able to find out the desired standard planes. The authors claimed that 70690 out of 92748 cases contained no eligible standard axial neurosonographic planes and only about 16000 images can be used. In our study, the lateral ventricular width can be measured in more than half of the TV and TT planes and we have 1431 available images from 626 cases.

In this study, we did not have any scale reference in the images and the resolution of images were different. The ratio of the brain regions to the whole images were also not the same. To solve this problem, we detected and extracted the brain regions first and then resize the brain regions into a same size. Experiment results shown that this was a feasible way to mitigate the influence of these kinds of difference.

This study used only 626 pregnant women with gestational age between 22 to 26 weeks to train and test the models. We got a MAE of 1.01 mm for the first experiment, which use all the 626 cases to train and test the regression model, and a MAE of 0.54 mm for the second experiment, which use the 610 cases with lateral ventricular width less than 15 mm to train and test the model. If we use more data, such as the data from the third trimester of pregnancy, to train the models, the MAE would potentially be reduced.

The lateral ventricular width is a continuous value. For ventriculomegaly the threshold is 10 mm. For our models, we recommend a smaller threshold like 9 mm or 8 mm. If the predicted lateral ventricular width is bigger than this value, doctors should pay attention to this fetal. A relatively small threshold can reduce false negative prediction, which may lead to serious consequence. However, false positive prediction is inevitable. In the first experiment, 53 images were predicted with lateral ventricular width bigger than 9 mm. Among them, 30 were actually bigger than 10 mm and the ground truth of other 23 images ranging from 8.3 mm to 0.99 mm. On the other hand, only a small fraction of fetuses has large lateral ventricular width, if our models can filter out most cases with small lateral ventricular width, the workload of doctors can be reduced hugely.

Interpretation

Although the lateral ventricular width is usually measured in TV planes, some doctors may measure this value in the TT plane or a transitionary plane between TV and TT planes. In our dataset, a considerable portion of TT planes were stored and used to measure the lateral ventricular width. Furthermore, if the lateral ventricular width is very large, it is usually hard to distinguish between TV and TT planes. For these reasons, we used TV and TT planes for lateral ventricular width estimation.

We built two models to predict the lateral ventricular width. The second one was to use the 610 cases with lateral ventricular width less than 15 mm, to train and test the model. The reason is that, severe fetal ventriculomegaly with lateral ventricular diameter >15 mm (also sometimes classified as fetal hydrocephalus) is unusual and their ultrasound images are much different from those of normal or mild fetal ventriculomegaly cases. This kind of cases can be detected using algorithms classifying fetal brain as normal or abnormal, such as study [35] did. Furthermore, after ignored these cases, the performance of the model improved remarkably.

After training the regression model to predict the lateral ventricular width, we generated heat maps and their corresponding overlay images for all test images. We found that, for the first experiment, all the heat maps were activated at the left-upper corner. We guess the model used the left-upper corner of each image to train something like a base value to lower the overall MSE. The final predicted lateral ventricular width combined the so-called base value with the value related to the lateral ventricular region. If the lateral ventricular width was small, the model might not detect the lateral ventricular region, and the final predicted lateral ventricular width would be only determined by the left-upper corner of the image. This was not very precision, but it was safe for images with small lateral ventricular width. It was similar for the second experiment that, the predicted lateral ventricular width of most images with small lateral ventricular width were based on other areas rather than the lateral ventricles.

It was worth noting that some images had markers on the lateral ventricles. Was it possible that the models localized the lateral ventricles and predicting lateral ventricular width using these markers? From the heat

maps we can see that, some images with large lateral ventricular width and without markers were activated on the lateral ventricles, while some images with small lateral ventricular width and with markers were not activated on the lateral ventricles. We can conclude that the regression model predicting lateral ventricular width did not depend on the markers.

Conclusion

In this paper, we developed deep learning algorithms that automatically picked out brain images from all stored freeze-frame images, recognized TV and TT planes and extract the brain regions, and predicted the fetal lateral ventricular width with high precision. It could potentially be applied as assistive tool in prenatal sonographic diagnosis to help reduce the number of false negatives, making possible for automated US diagnosis and/or assessment.

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Disclosure of Interests

The authors declare that they have no competing interests

Contribution to Authorship

J.G., S.H. and F.C. initiated this project. R.L., H.Y.Z., C.H., H.G.Z. and S.H. made the diagnosis, acquired the data, labeled the data. B.Z., J.Y. and N.Z. performed the experiments. B.Z., Y.Y. and R.L. analyzed the data and the results. R.L., B.Z., J.G. and S.H. wrote the paper. All authors reviewed the manuscript.

Details of Ethics Approval

The procedures of the study received ethics approval on May 8th 2018 from the Medical Ethics Committee of First Hospital of Jilin University (No. 2018-429).

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