Conditional generative adversarial networks support the detection of focal cortical dysplasias



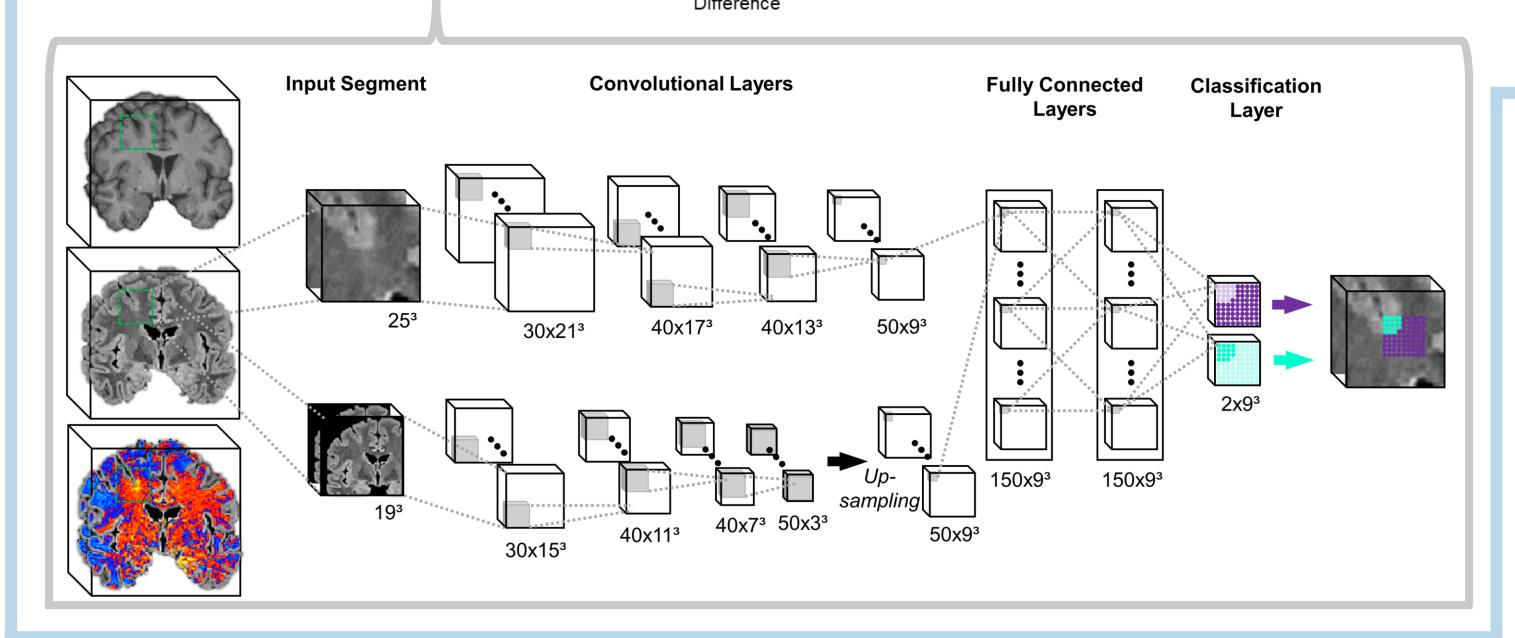
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INTRODUCTION

Focal cortical dysplasias (FCDs) are congenital disruptions of neuronal migration and constitute a major cause of therapy-refractory focal epilepsy. If amenable to epilepsy surgery, more than 80% of patients reach seizure-freedom after a complete resection of the lesion [1]. However, FCDs may be easily overlooked in conventional visual assessment of MRI. Morphometric postprocessing routines have been proven useful for the detection of FCDs and their use may enhance the postoperative outcome.[2,3] However, as even most elaborate approaches do not yield satisfactory sensitivity, the development of novel approaches is warranted on clinical grounds. MRI features of FCD type IIb include cortical T2-signal hyperintensities but they have sparse correlates in T1-weighted MR-volumes. We here describe for the first time an approach leveraging on this apparent difference in MR-modalities and the power of conditional generative adversarial networks (cGAN) in modality synthesis,[4] to create a difference image between the real FLAIR, showing hyperintensities, and a T1-based synthetic FLAIR, not showing hyperintensities. We show that the integration of this information in a 3D convolutional neural network (CNN) [5] supports the detection of FCDs.

METHODS Modality synthesis Difference image Preprocessing Synthetic FLAIR Brain extraction **cGAN** Bias field correction trained on 80 Masking healthy controls Co-registration Slicewise input (coronal) Classification Intensity normalization Resampling **Multiscale 3D CNN** FOV crop trained using 5-fold cross-validation Thresholding



RESULTS

cGAN performance

- Robust generation of synthetic FLAIR images on non-lesional brains $(MSE\pm\sigma = 22.57\pm12.00; SSIM \pm\sigma = 0.92\pm0.04)$
- Regions near the lesion showed high difference between synthetic and real FLAIR in the FCD-cohort

CNN performance

of extralesional clusters

	Input	Sensitivity (TP/P)	Specificity (TN/N)	1	2	≥3
Classifier #1	T1+FLAIR	80.95% (34/42)	71.43% (40/56)	^^^	^	Ť
Classifier #2	T1+FLAIR +GANdiff	92.86% (39/42)	96.43% (54/56)	††††† †	Ť	-

Training and evaluation of cGAN

- 80 datasets of healthy controls (37 females; age=44.8±10.6 y)
- Coronal slices of T1w as input and corresponding FLAIR slices as groundtruth modality
- Mean squared error (MSE) and structural similarity index (SSIM) calculated on separate sample of 15 healthy controls (7 $age=42.6\pm12.3 y$

FCD patient cohort

- 42 patients (18 females; age=38.8±11.4 y) with histologically proven FCD type IIb
- Manually labelled ground-truth lesion masks

Lesion segmentation and validation

- T1w, FLAIR and cGAN difference images passed as input to a multiscale 3D CNN
- 5-fold cross-validation scheme used to estimate sensitivity
- Additional out-of-sample specificity was estimated on a separate cohort of 56 mesial temporal lobe epilepsy patients (35 females; age=39.2±11.5 y)

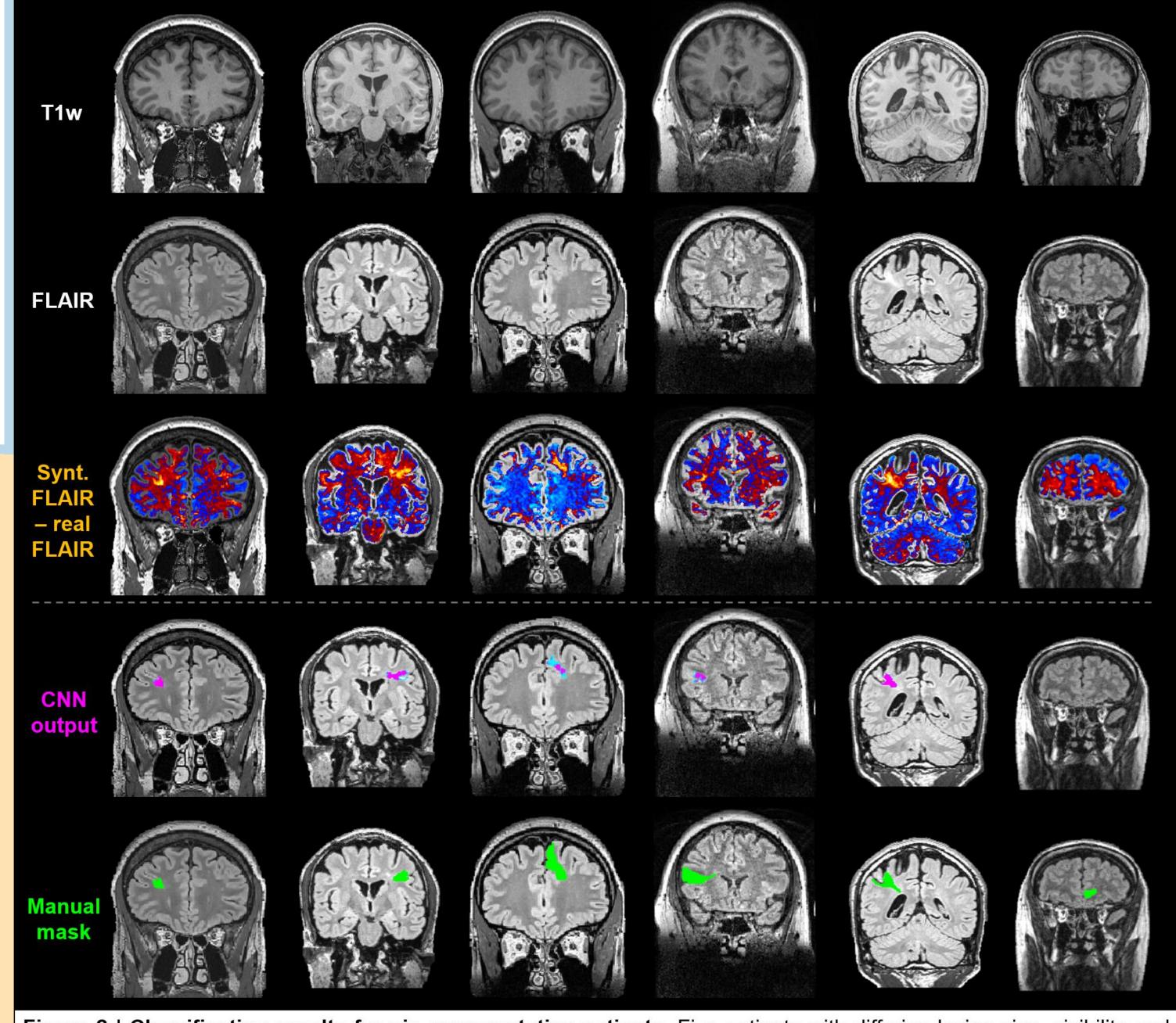


Figure 2 | Classification results for six representative patients. Five patients with differing lesion size, visibility and data quality in which the CNN classifier correctly detected the FCD lesion, as well as one patient (rightmost) in which the classifier failed to detect the lesion. The first three rows indicate the input to the CNN.

DISCUSSION

Our combined approach using a cGAN for modality synthesis followed by a multiscale 3D CNN outperforms current state-of-the-art methods on a comparably large FCD dataset. Notably, our classifier shows only few false positive clusters in our FCD and two false positive clusters in an additional TLE patient cohort. However, our approach needs to be further tested on larger FCD datasets, possibly including multi-centric data from different scanners, head coils and MR-sequence parameters. Furthermore, a generalization of our approach to any pathology imaged with complementary modalities is conceivable.



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