COMBINING PHENOTYPIC AND RESTING-STATE FMRI DATA FOR AUTISM CLASSIFICATION WITH RECURRENT NEURAL NETWORKS

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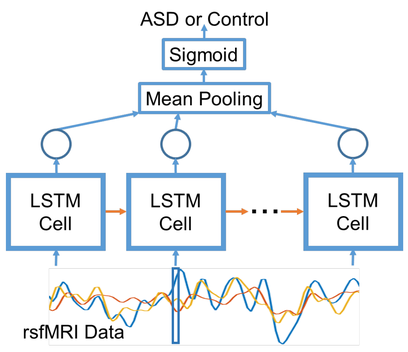
Background

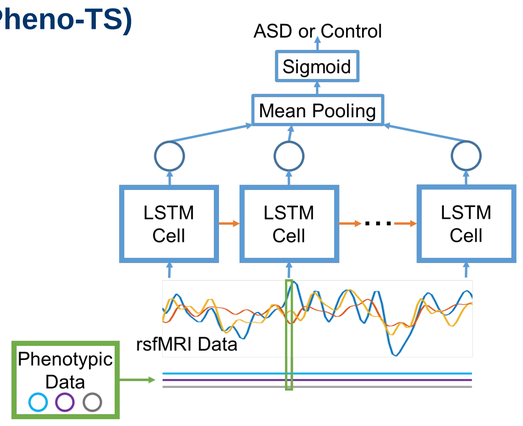
- Identification of autism spectrum disorder (ASD) from resting-state functional magnetic resonance imaging (rsfMRI) will help characterize causes of ASD
  → Improve diagnosis, treatment
- Recurrent neural network with long short-term memory (LSTM) showed improved classification from rsfMRI data[1]
- Challenges to accurately identifying ASD from rsfMRI:
  - Heterogeneity of ASD
  - Phenotypic information often available, but how to incorporate?
- Aims:
  1. Explore methods of combining phenotypic and rsfMRI data into a single LSTM-based neural network model
  2. Evaluate models using Autism Brain Imaging Data Exchange (ABIDE) I Dataset[2]

Methods: LSTM-Based Architectures

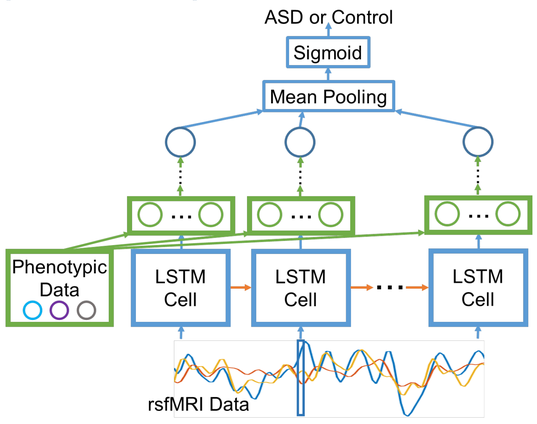
Base LSTM model[1] (rsfMRI-only)



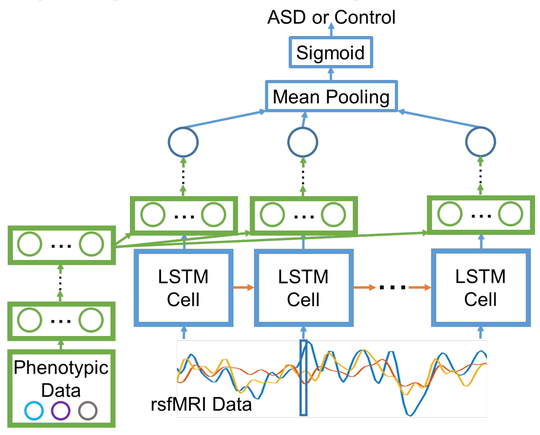
Input Phenotype + rsfMRI to LSTM (Pheno-TS)



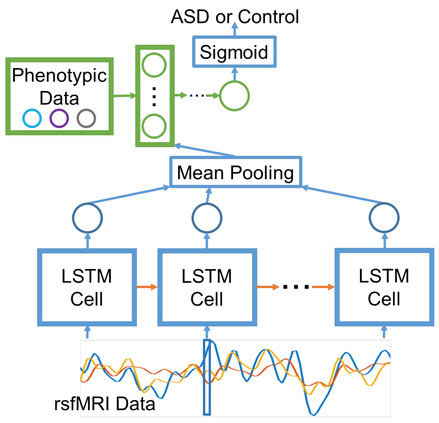
Combine Phenotype + LSTM outputs (Pheno-LSTM)



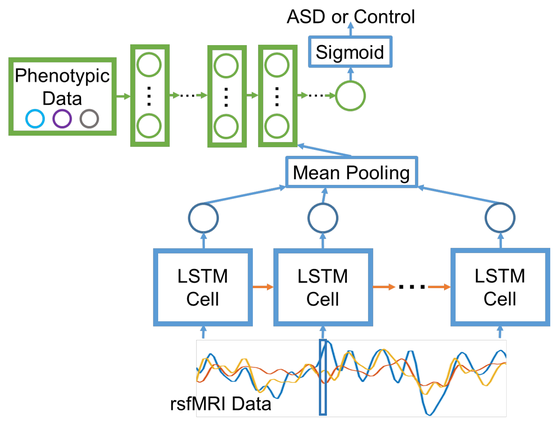
Combine Encoded Phenotype + LSTM outputs (PhenoEnc-LSTM)



Combine Phenotype + rsfMRI Score (Pheno-rsfScore)



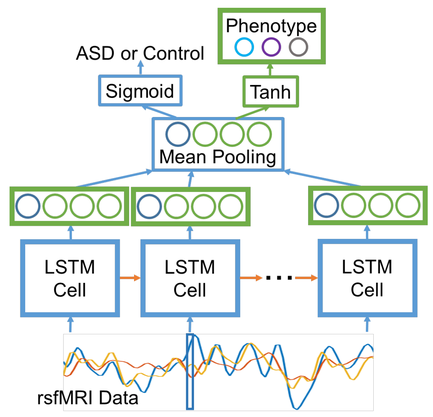
Combine Encoded Phenotype + rsfMRI Score (PhenoEnc-rsfScore)



Set Phenotype as Auxiliary Targets (Pheno-Target)

$$L(y,\hat{y}) = L_{ASD}(l,\hat{l}) + \lambda L_{pheno}(p,\hat{p})$$

L =Overall loss function
L_{ASD} = Loss for ASD classification label
L_{pheno} = Loss for phenotypic features
$y = [l,p]$
l = ASD classification label
p = Phenotypic data
$\hat{y}$ = Estimate for y
λ = Weight for phenotypic loss

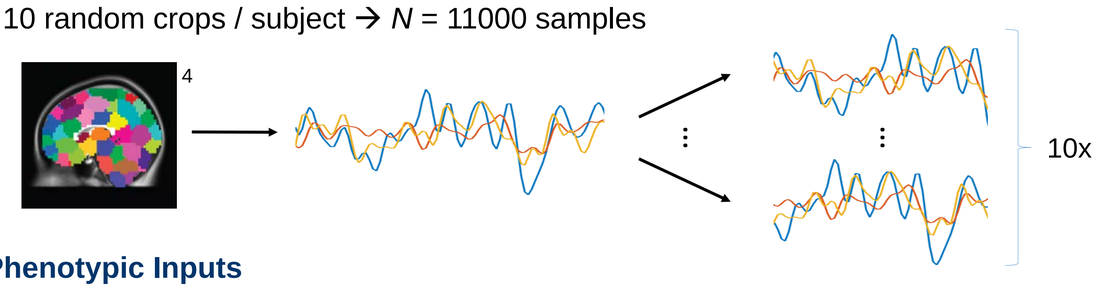


Experiments: ABIDE I Data

- rsfMRI, structural MRI, and phenotypic data for ASD/healthy subjects from 17 sites[2]
- Preprocessed data from Preprocessed Connectomes Project[3] using Connectome Computation System pipeline, no global signal regression, with band-pass filtering
  - 529 ASD + 571 typical controls = 1100 total subjects
  - Ages 6-64 years (median = 14.7 years), 5.8 male : 1 female

rsfMRI Inputs

- Mean rsfMRI time-series extracted from Craddock 200 atlas[4] regions
- Time-series normalized to percent signal change and resampled using 2 s interval
- Time-series cropped to fixed length (T = 90) from random starting points
- 10 random crops / subject → N = 11000 samples



Phenotypic Inputs

- Age, sex, handedness, full IQ, eye status during rsfMRI
- Each phenotype normalized to range [-1,1]

Experiments: Implementation and Evaluation

Neural Network Implementation

- Loss = binary cross-entropy (except Pheno-Target Loss = mean squared error), Optimizer = adadelta, LSTM dimension = 32, dropout = 0.5, λ = 0.1
- See paper for layers/number of nodes for each model

Classification Evaluation

- 10-fold cross-validation (CV), stratified across imaging sites
  - 85% training, 5% validation (for early stopping), 10% testing
  - All samples from each subject within training/validation/testing block
  - Subject label determined from mean of scores from all subject samples
- Evaluation measures:
  - Mean and standard deviation (SD) of classification accuracy
  - Difference from baseline accuracy (% more common class in dataset)

Experiments: Results

Classification Method	Phenotypic Data	Number of Subjects	Mean (SD) Classification Accuracy (%)	Difference from Baseline (%)
Parisot et al.[5]	Sex, Site	871	69.5	15.8
Nielsen et al.[6]	Age, Sex, Hand	964	60.0	6.4
Ghiassian et al.[7]	Age, Sex, Hand, Full IQ, PIQ, VIQ, Site, Eye	1111	65.0	13.4
rsfMRI-only[1]	None	1100	67.9 (4.3)	16.0
Pheno-only	Age, Sex, Hand, Full IQ, Eye		60.4 (3.6)	8.5
Pheno-TS			67.0 (3.5)	15.1
Pheno-LSTM			68.2 (4.1)	16.3
PhenoEnc-LSTM			68.1 (3.3)	16.2
Pheno-rsfScore			**70.1 (3.2)***	**18.2**
PhenoEnc-rsfScore			68.4 (4.7)	16.5
Pheno-Target			67.2 (4.0)	15.3

*Accuracy significantly better than rsfMRI-only model (one-tailed paired t-test, $p < 0.1$)

- Best model is 2.4% higher than best prior work[5], without using imaging site

Conclusions

- Incorporating phenotypic data is useful under the correct network architecture
- Classification accuracy of best model on ABIDE dataset outperforms recent work, without using imaging site → better generalizability
- Future directions
  - Incorporate structural MRI and behavioral measures
  - Investigate important brain regions/functional networks learned by the model

References

1. Dvornek et al., *MLMI*, 2017. 2. Di Martino et al., *Mol. Psychiatry*, 2014. 3. Craddock et al., *Neuroinformatics*, 2013. 4. Craddock et al., *Hum. Brain Mapp.*, 2012. 5. Parisot et al., *MICCAI*, 2017. 6. Nielsen et al., *Front. Hum. Neurosci.*, 2013. 7. Ghiassian et al., *PLoS ONE*, 2016.

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