Longitudinal changes of MRI intensity contrast in autism: direct observations and predictions from cross-sectional data

Gleb Bezgin, John D. Lewis, Alan C. Evans

Montreal Neurological Institute, McGill University, Montreal, Canada

Dataset: ABIDE1+2 (360 subjects in the cross-sectional sample, 21 subjects x2 time points in the longitudinal [1])
MRI data processing: done with CIVET-2.1 pipeline ([2], version released November 2016)
Measure: contrast between white and gray matter intensity values (the ratio henceforth abbreviated as WGR [3])

We *explored* how WGR changes with age in ASD and typical development (TD). This change was assessed by the "angle" metric in the longitudinal sample [4]

PLS analysis [5] identified clusters characteristic for diagnostic group differences (bootstrap ratio, *BSR*)

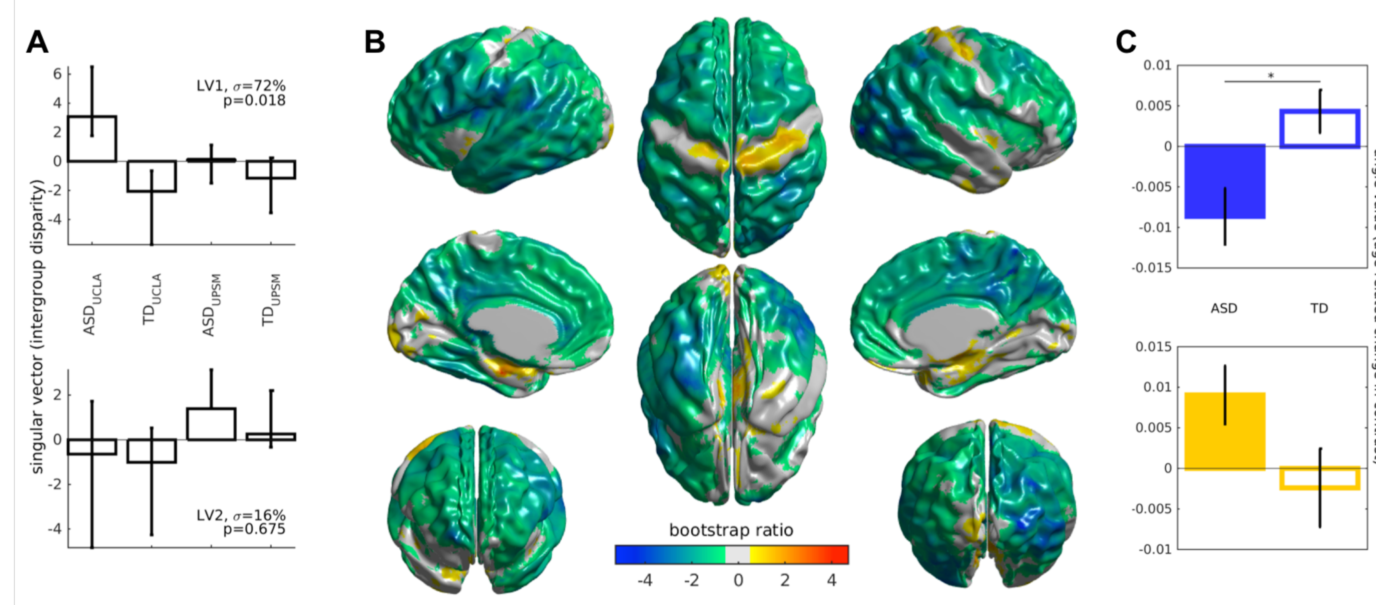


Figure 1.
PLS analysis on the longitudinal WGR sample

$$\alpha_i^{lngt} = \arctan\left(\frac{WGR_i^{flp} - WGR_i^{bsl}}{age_i^{flp} - age_i^{bsl}}\right)$$

longitudinal

PLS

cross-sectional

...and an analogous metric for the cross-sectional sample

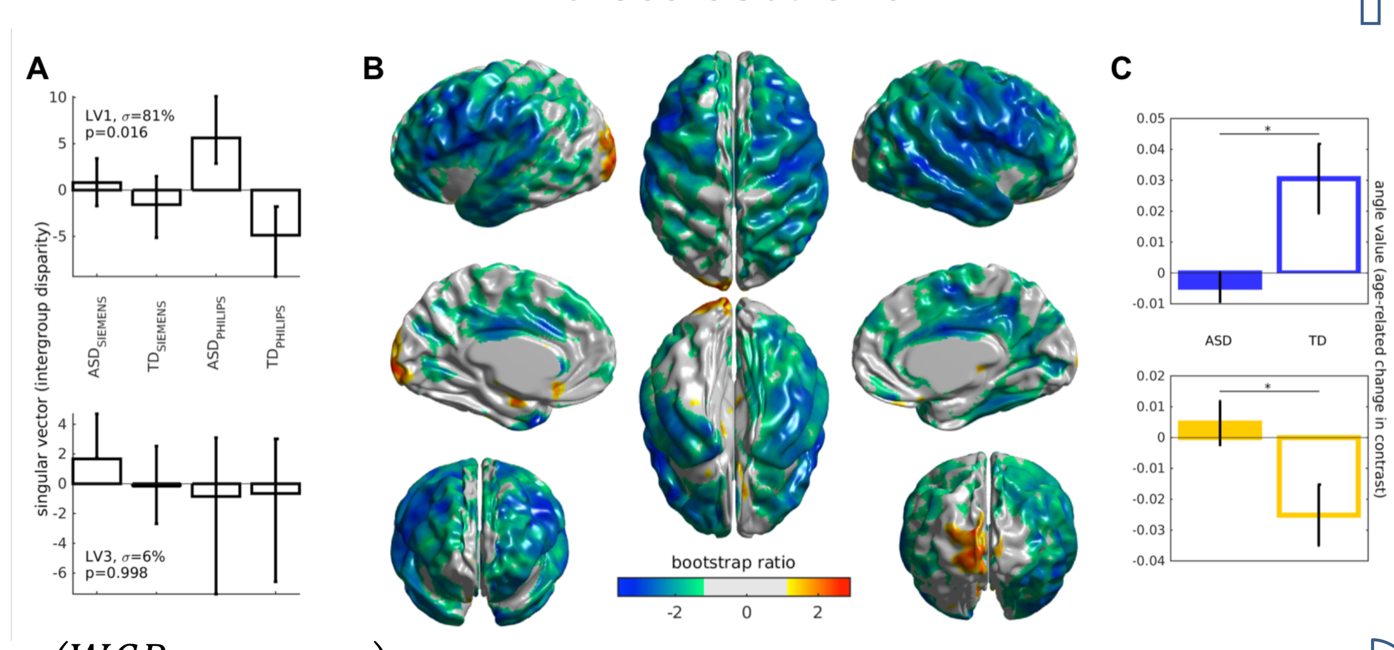


Figure 2.
PLS analysis on the cross-sectional WGR sample

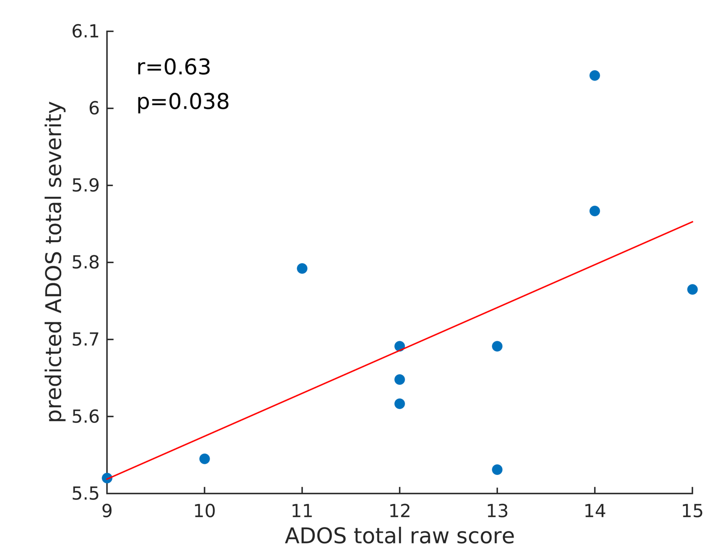
$$\alpha_i^{crsc} = \arctan\left(\frac{WGR_i - \mu_{WGR_{\neg i}}}{age_i - \mu_{age_{\neg i}}}\right)$$

data

predictions

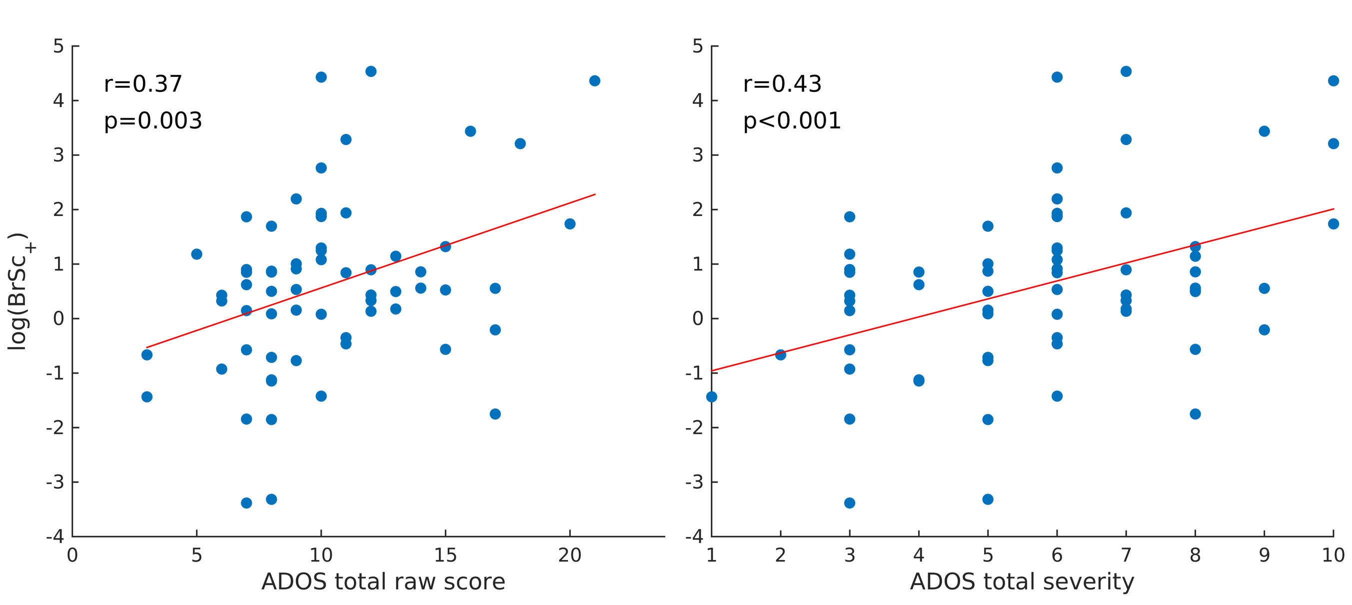
data

singular values indicative of inter-subject differences in the cross-sectional sample, were predictive of severity scores in the *longitudinal* sample (Figure 5)...



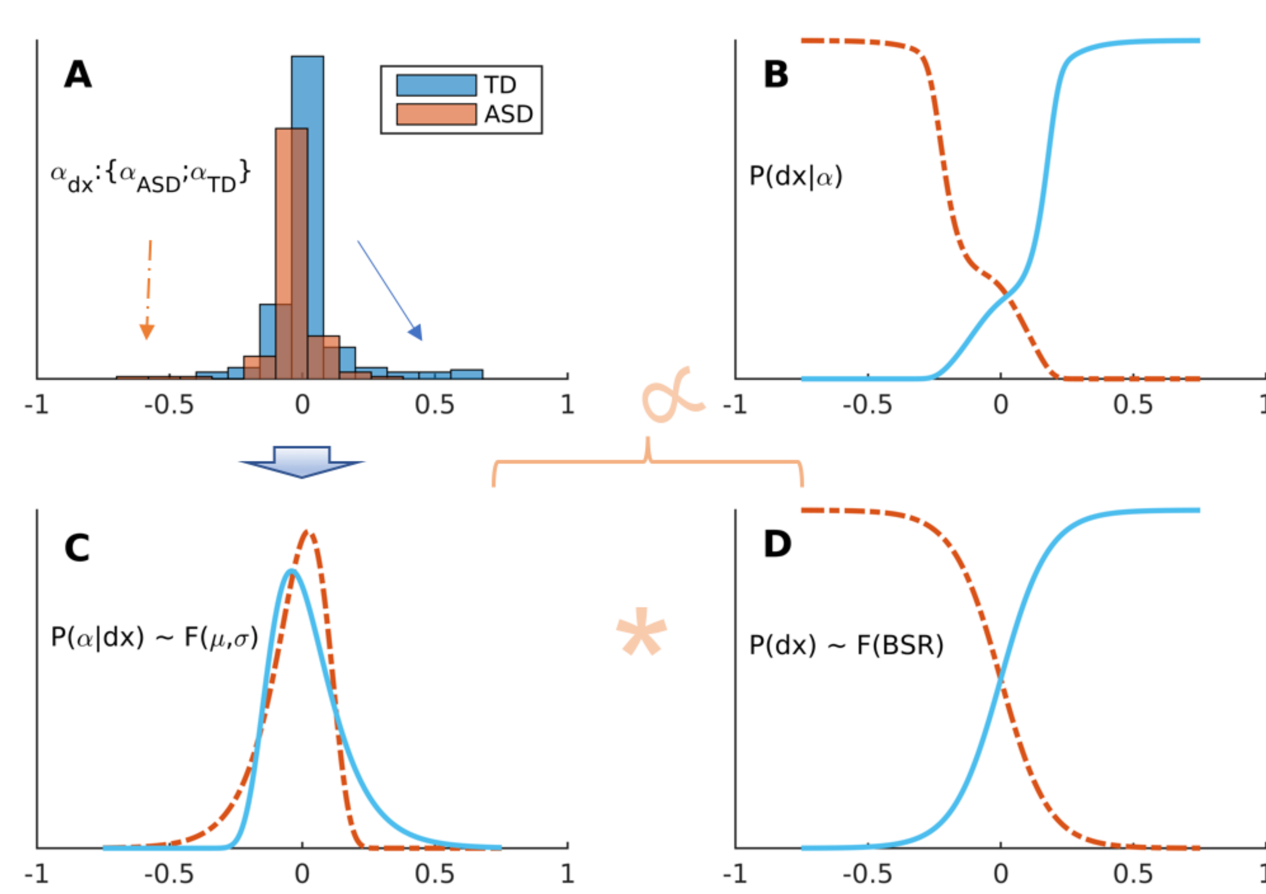
$$S_i^{lngt} = \beta_0^{crsc} + \beta_1^{crsc} * BrSc_i^{crsc} + \frac{\sum_{i-w<k<i+w} \varepsilon_k}{K}$$

...following correlation with raw ADOS scores and total severity within the cross-sectional sample (Figure 6):



Cross-sectional angle data were input to the model, Figure 3:

$$P(dx|\alpha) \propto P(\alpha|dx) * P(dx)$$



the prior parameter was informed by PLS BSR

Distribution tails were representative of group differences, thus were well fitted with extreme value distributions:

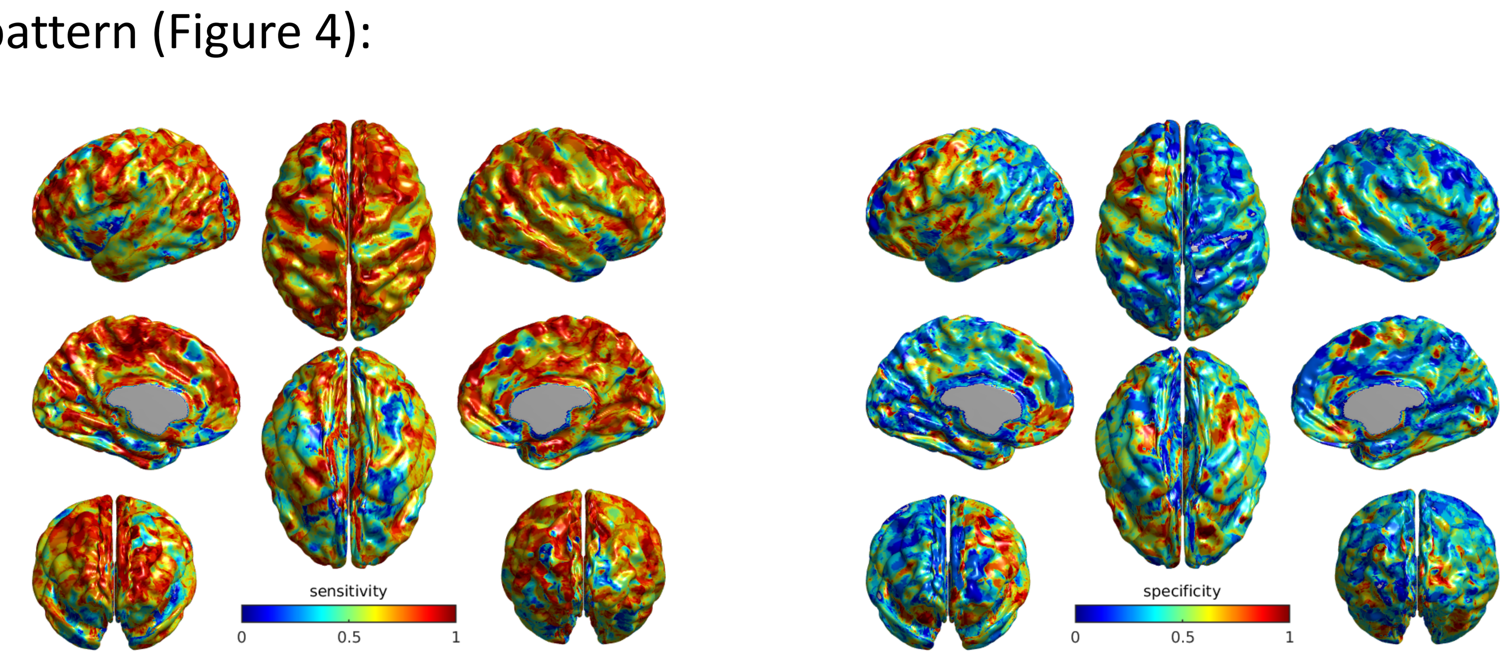
$$P(\alpha|dx) = \sigma^{-1} \exp\left(\frac{\pm\alpha - \mu}{\sigma}\right) * \exp\left[-\exp\left(\frac{\pm\alpha - \mu}{\sigma}\right)\right]$$

$$P(dx) = \left[1 + \exp\left(\pm\frac{x * BSR}{BSR_{max}}\right)\right]^{-1}$$

Conclusions

1) Exploration of data distributions gives hint on inter-study variability
2) General age-related cortical contrast decrease in autism spectrum disorder is consistent across investigated longitudinal and cross-sectional samples
3) A Bayesian modelling approach predicts diagnostic outcomes in the longitudinal sample from independent data in the cross-sectional sample
4) Symptom severity scores in autism correlate with brain patterns related to the diagnostic group difference

The whole-cortex model predicted 10 out of 12 ASD outcomes correctly (83% sensitivity) and 6 out of 9 TD outcomes correctly (67% specificity). Predictions by individual vertices resulted in the following pattern (Figure 4):



References

1. Di Martino A et al. (2014) Mol Psychiatry 19(6):659-67.
2. Kim JS et al. (2005) Neuroimage 27:210-21.
3. Salat DH et al. (2009) Neuroimage 48(1):21-8.
4. http://fcon_1000.projects.nitrc.org/indi/abide/abide_II.html
5. McIntosh AR et al. (2004) Neuroimage 23:764-75.

Acknowledgements

This research was supported by Azrieli Foundation BC_Azrieli_MIRI_3388, Brain Canada, Compute Canada, JS McDonnell Collaborative Research Grant 220020255. We would like to thank Yuval Yakubov, Kevin Tian, Vasily Vakorin, Andrii Trifonov.

For further information

Please contact Dr. Gleb Bezgin at: *gleb.bezgin@mcgill.ca*