



# Longitudinal reliability of functional connectivity in depressed adolescents

Christopher Camp, Dylan Nielson, Hanna Keren, Georgia O'Callaghan, Sarah Jackson, Lisa Gorham and Argyris Stringaris

Mood, Brain, and Development Unit, National Institute of Mental Health, Bethesda, MD



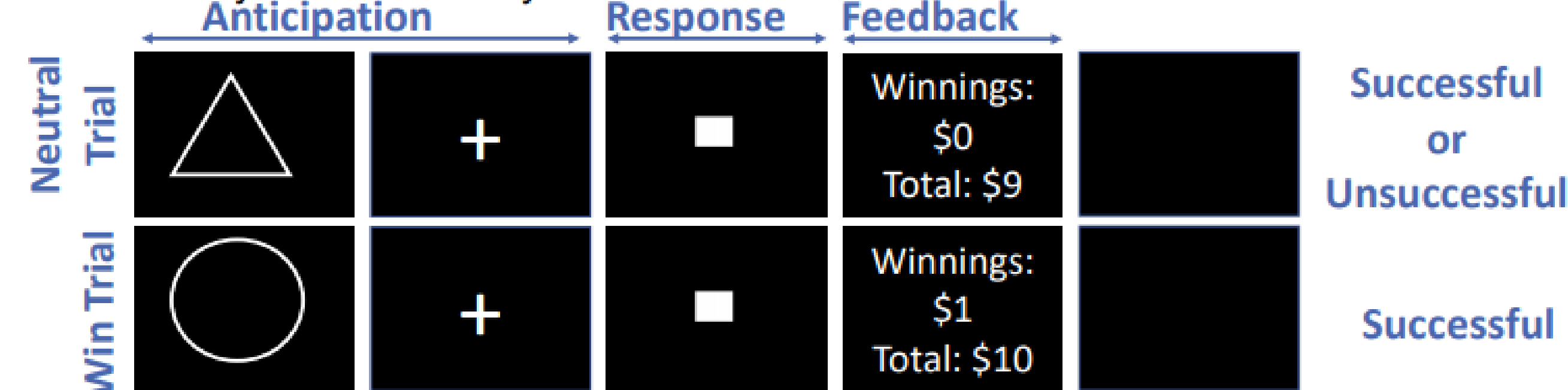
## Introduction

- Reliability is essential for interpretation of fMRI results, but is often underreported or insufficient
- Reliability is especially important for longitudinal investigations and clinical predictions
- We adhere to the reporting recommendations of Koo and Li<sup>1</sup>

## Methods

- Longitudinal sample of 32 adolescents (median age = 16.25, 24 females) with Major Depressive Disorder (MDD) from cohort of 133
- Scanned in one of two 3T GE Discovery MR 750 scanners between three and four times over the course of one year at four month intervals for 105 scans
- Scans consisted of one 8 minute block of rest (TR = 2.5 s) and 15 minutes of the Monetary Incentive Delay

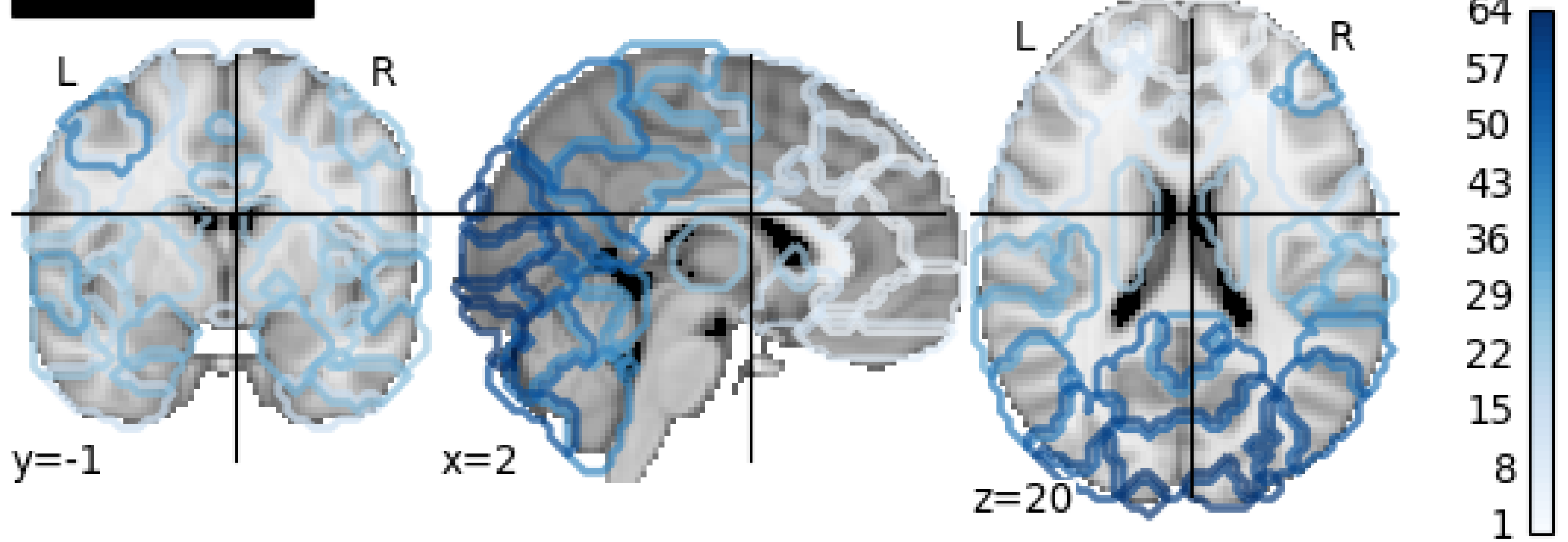
Monetary Incentive Delay task



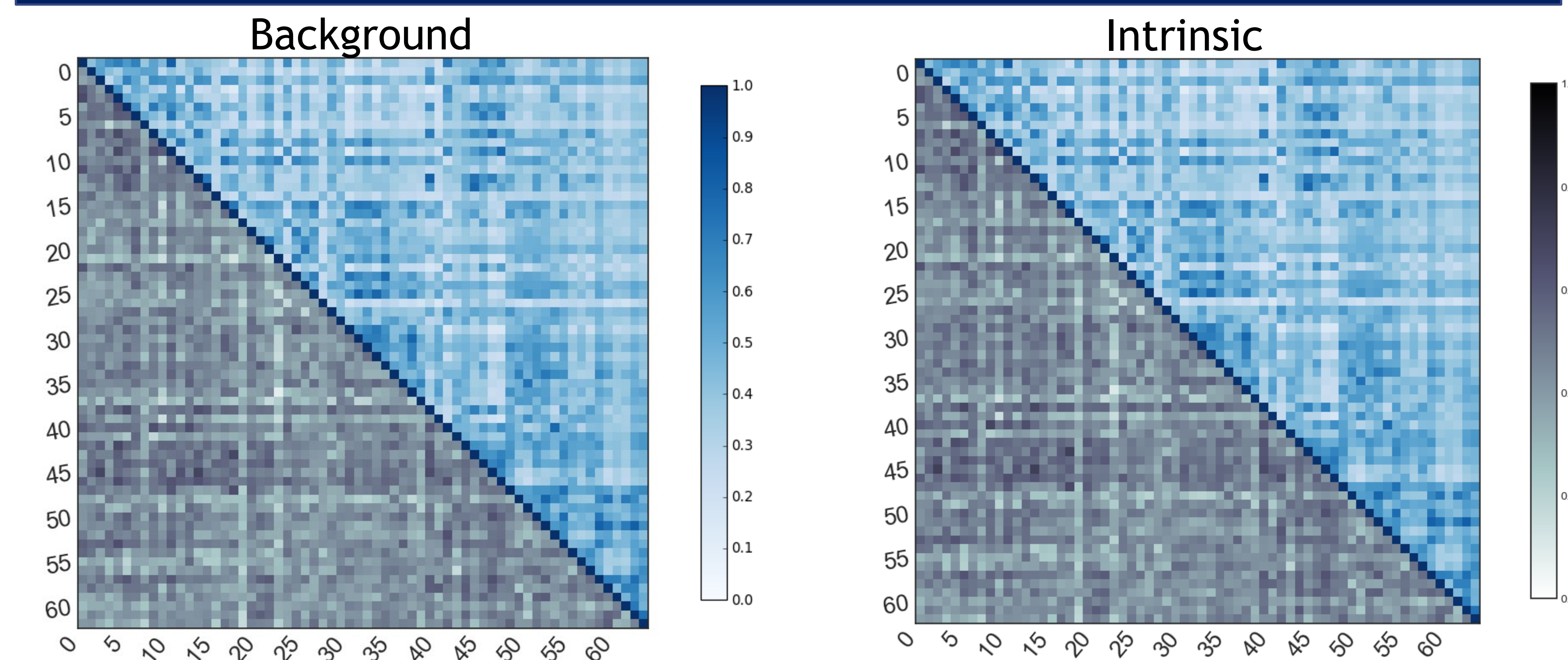
## ICC

- Generated intrinsic functional connectivity and task background connectivity bootstrap analysis of stable cluster parcellation (BASC) in Nilearn<sup>2</sup>
- Regressed metrics with five confound groups
- Reliability within subjects quantified with single measurement, absolute agreement, two-way random mixed effects model intra-class correlation (ICC (2,1))
- Bootstrapped 1000 samples with replacement

BASC Atlas

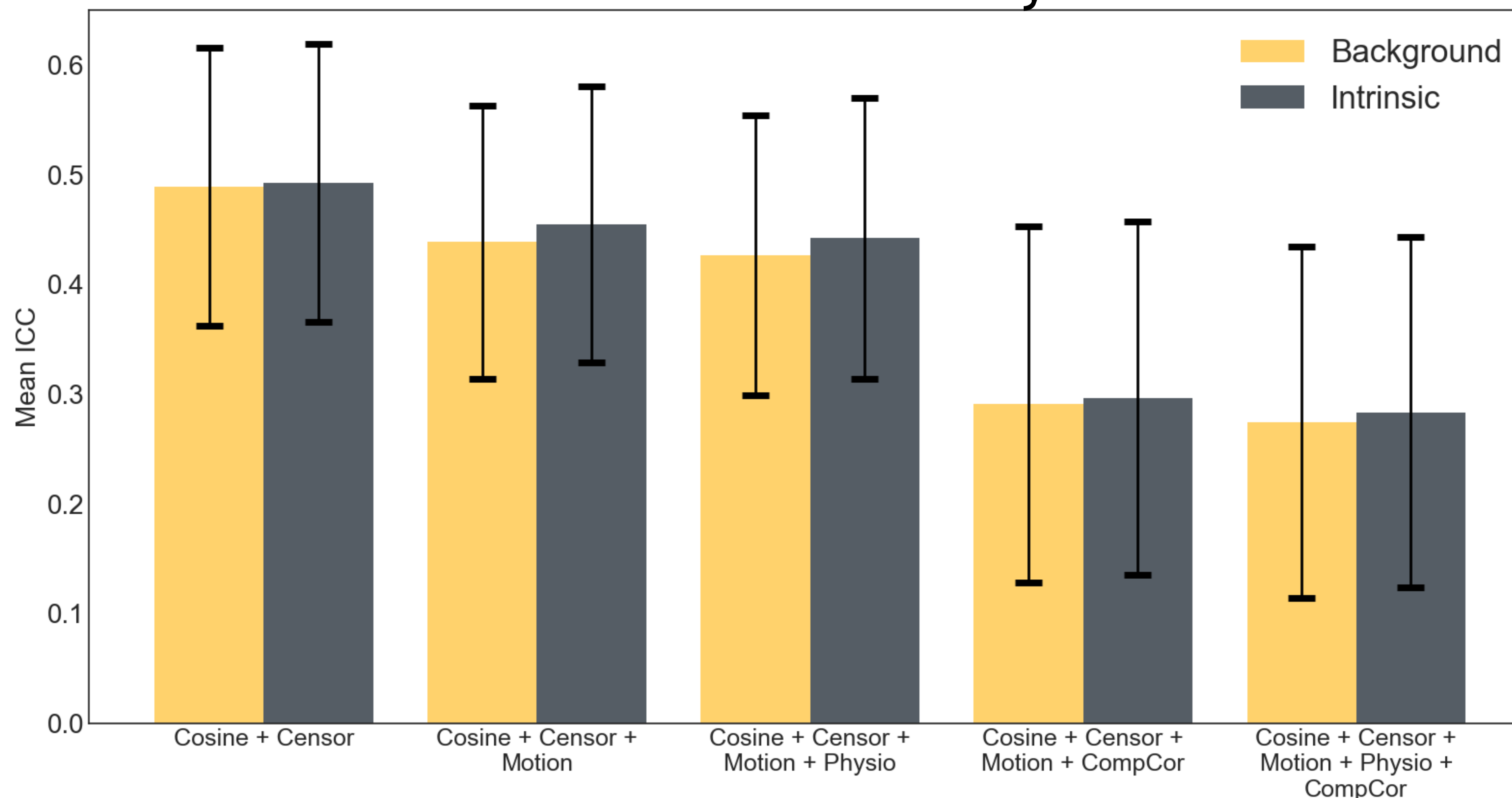


## Results



Average correlation matrix (upper triangle) and ICC matrix (lower triangle) for background and intrinsic connectivity with cosine, censor, motion, and physiological confound regression, on left and right, respectively. Axes correspond to BASC regions.

## Mean ICCs of Connectivity Metrics



Confound groups with CompCor regression were significantly less reliable than all other groups (corrected  $p < .05$ ). Background and intrinsic reliability did not significantly differ. Error bars represent standard deviation of bootstrapped ICCs.

## Results Summary

- Connectivities with the Component Based Noise Reduction Method<sup>3</sup>, or CompCor, were significantly less reliable (corrected  $p < .05$ ) than other regressions
- Connectivities with motion and physiological regressors were less reliable than those with only cosine and censor regression, but this difference did not survive correction for multiple comparisons (uncorrected  $p < .05$ )
- Reliabilities were below the 'fair' threshold of 0.5 as set by Koo and Li<sup>1</sup>

## Discussion

- We find regression of cosine, censor, motion, and physiological confounds to be the most effective strategy for reducing noise while preserving reliability
- We find reliabilities within the functional connectivity of a difficult and valuable subject cohort that are comparable with other fMRI studies and even some structural MRI studies<sup>4,5</sup>
- The longitudinal nature of this study and the high rate of observations for each subject combined with bootstrapping gives us a significantly improved estimation of fMRI reliability

## References

- Abraham, A., Pedregosa, F., Eickenberg, M., Gervais, P., Mueller, A., Kossaifi, J., Gramfort, A., Thirion, B., & Varoquaux, G. (2014). Machine learning for neuroimaging with scikit-learn. *Frontiers in Neuroinformatics*, 8. <https://doi.org/10.3389/fninf.2014.00014>
- Behzadi, Y., Restom, K., Liu, J., & Liu, T. T. (2007). A Component Based Noise Correction Method (CompCor) for BOLD and Perfusion Based fMRI. *NeuroImage*, 37(1), 90-101. <https://doi.org/10.1016/j.neuroimage.2007.04.042>
- Bennett, C. M., & Miller, M. B. (2010). How reliable are the results from functional magnetic resonance imaging? *Annals of the New York Academy of Sciences*, 1191(1), 133-155. <https://doi.org/10.1111/j.1749-6632.2010.05446.x>
- Koo, T. K., & Li, M. Y. (2016). A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. *Journal of Chiropractic Medicine*, 15(2), 155-163. <https://doi.org/10.1016/j.jcm.2016.02.012>
- Nikolaïdis, A., Solon Heinsfeld, A., Xu, T., Bellec, P., Vogelstein, J., & Milham, M. (2020). Bagging improves reproducibility of functional parcellation of the human brain. *NeuroImage*, 214, 116678. <https://doi.org/10.1016/j.neuroimage.2020.116678>