Reliability versus Validity in Resting State and Task-based fMRI

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Acknowledgements:

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Functional Connectivity of Spontaneous Activity at Rest (i.e. "Resting State")

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- very popular (easy and fast to administer)
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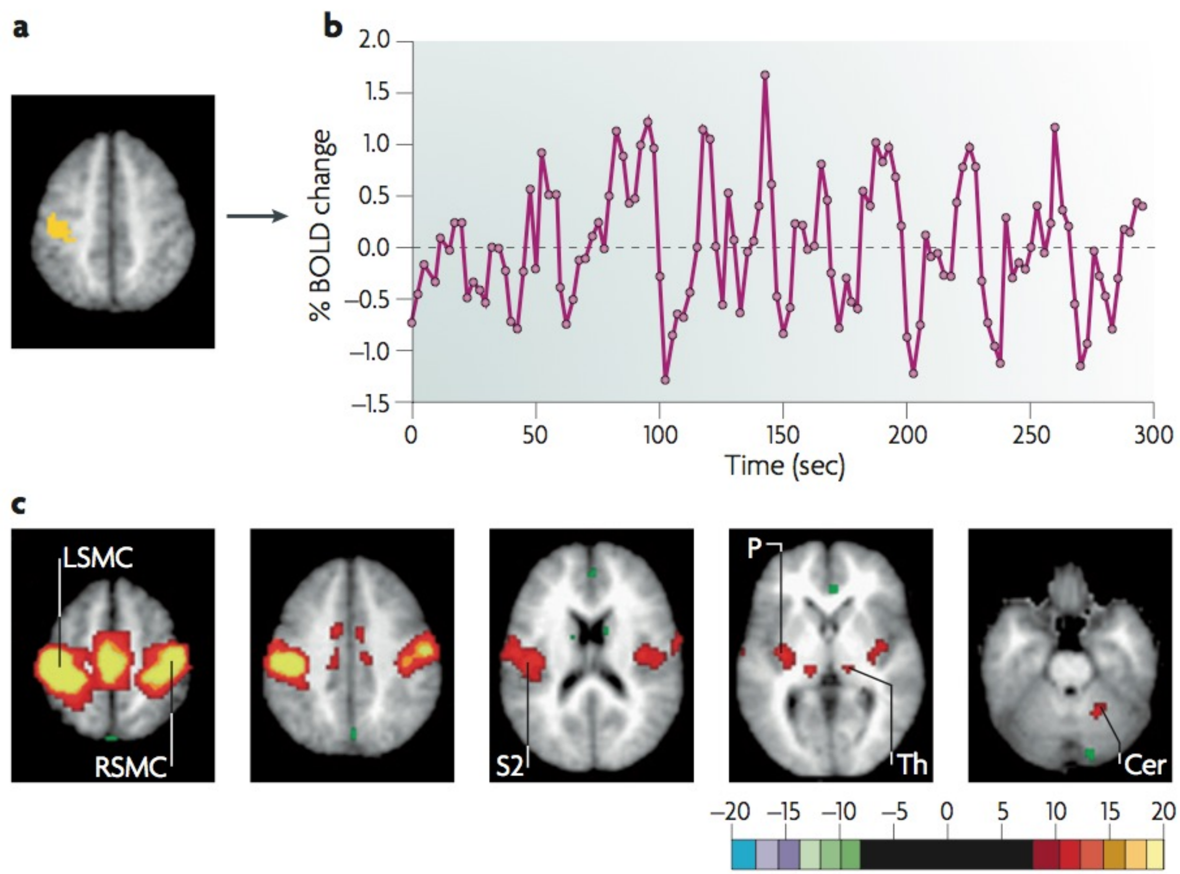
For review:

Fox & Raichle (2007). *Nat Rev Neurosci*

Fox & Greicius (2010). *Front Syst Neurosci*



Today's Talk

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- Test-retest reliability as a guide?
- Validity vs. test-retest reliability
    - our recent efforts to evaluate these issues experimentally

Why are artifacts so problematic ?

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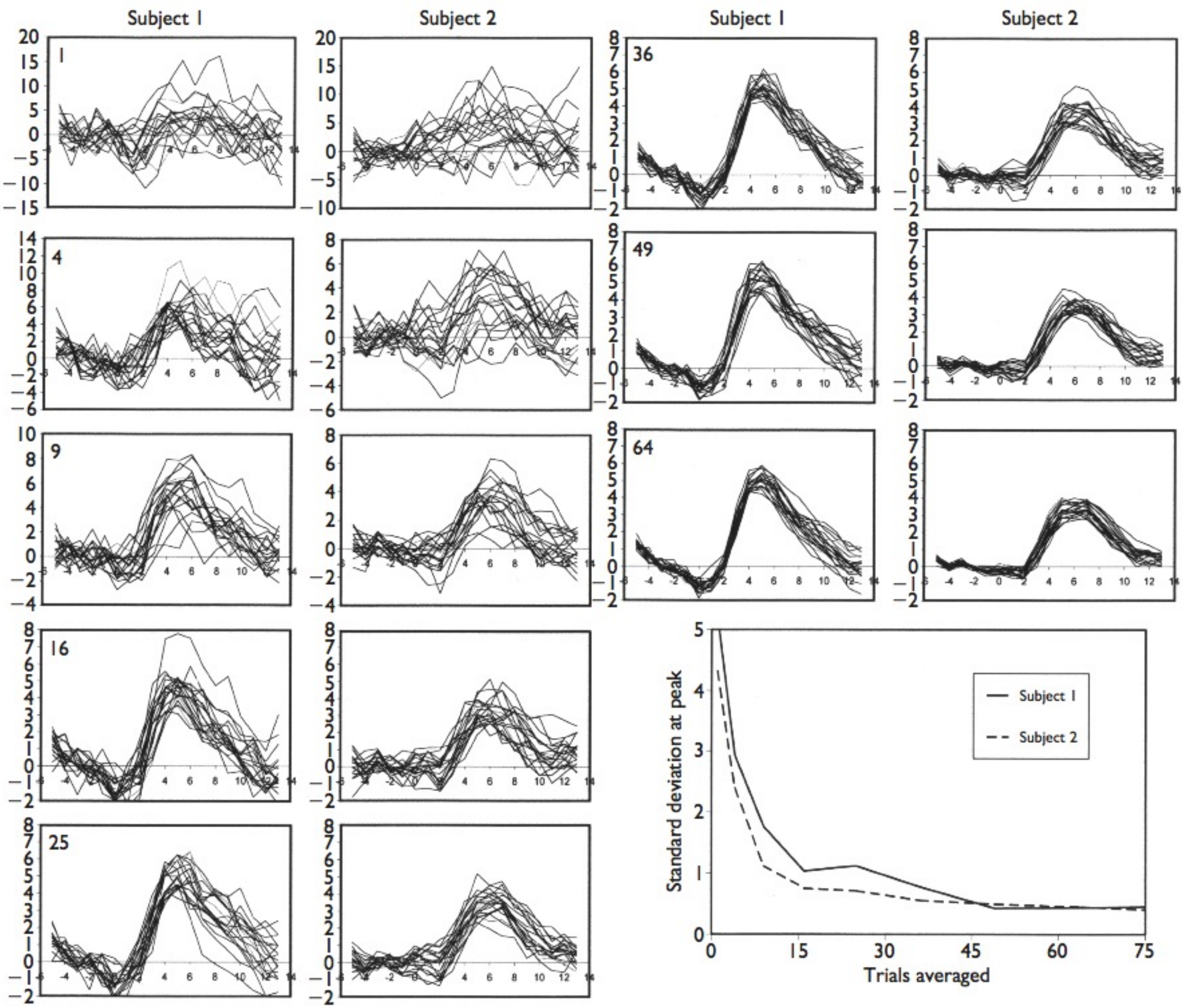
Task-based fMRI:

Improved Estimates of BOLD response with Trial Averaging

(e.g. Bandettini et al., 1993; Friston et al., 1995)

Huettel & McCarthy (2001). Neuroreport.



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No averaging!

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Resting-state fMRI:

No averaging!

Anything that causes temporal variation in the BOLD response can influence estimates of covariation

Common Noise Sources in fMRI

Time-varying artifacts affecting the BOLD signal:

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For good overview:

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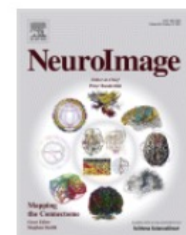
NeuroImage

Volume 80, 15 October 2013, Pages 349–359



Resting-state fMRI confounds and cleanup

Kevin Murphy[a], Rasmus M. Birn[b], Peter A. Bandettini[c, d]

Common Noise Removal Steps

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Goal: Remove noise variation in BOLD signal without removing or distorting neurally-derived variation

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- Decompose fMRI time series into statistically independent spatial components (e.g. Comon, 1994; McKeown et al., 1998; Kiviniemi et al., 2003; Beckmann et al., 2005; Perlbarg et al., 2007)

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- "Global Signal"

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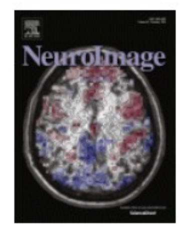
NeuroImage

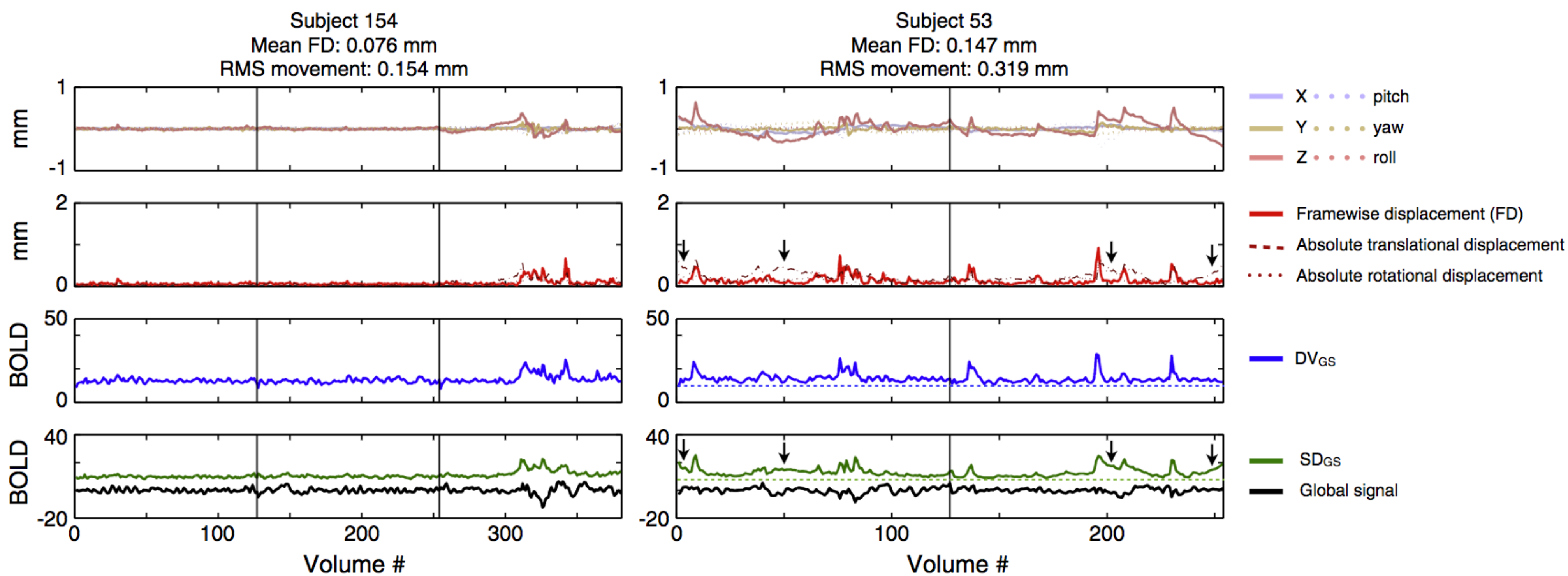
Volume 84, 1 January 2014, Pages 320-341



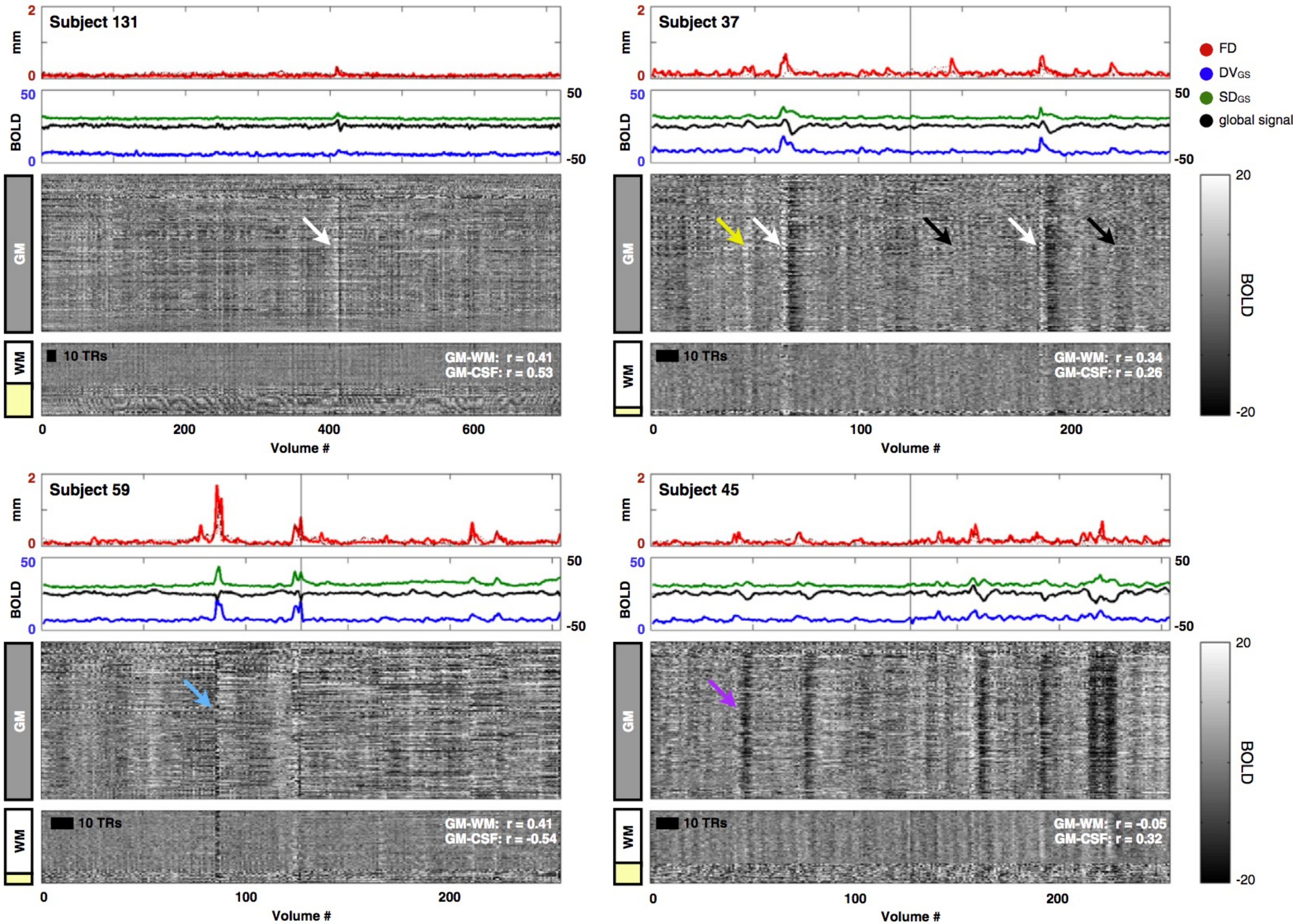
Methods to detect, characterize, and remove motion artifact in resting state fMRI

Jonathan D. Power [a], Anish Mitra [a], Timothy O. Laumann [a], Abraham Z. Snyder [a, b], Bradley L. Schlaggar [a, b, c, d], Steven E. Petersen [a, b, d, e, f, g]

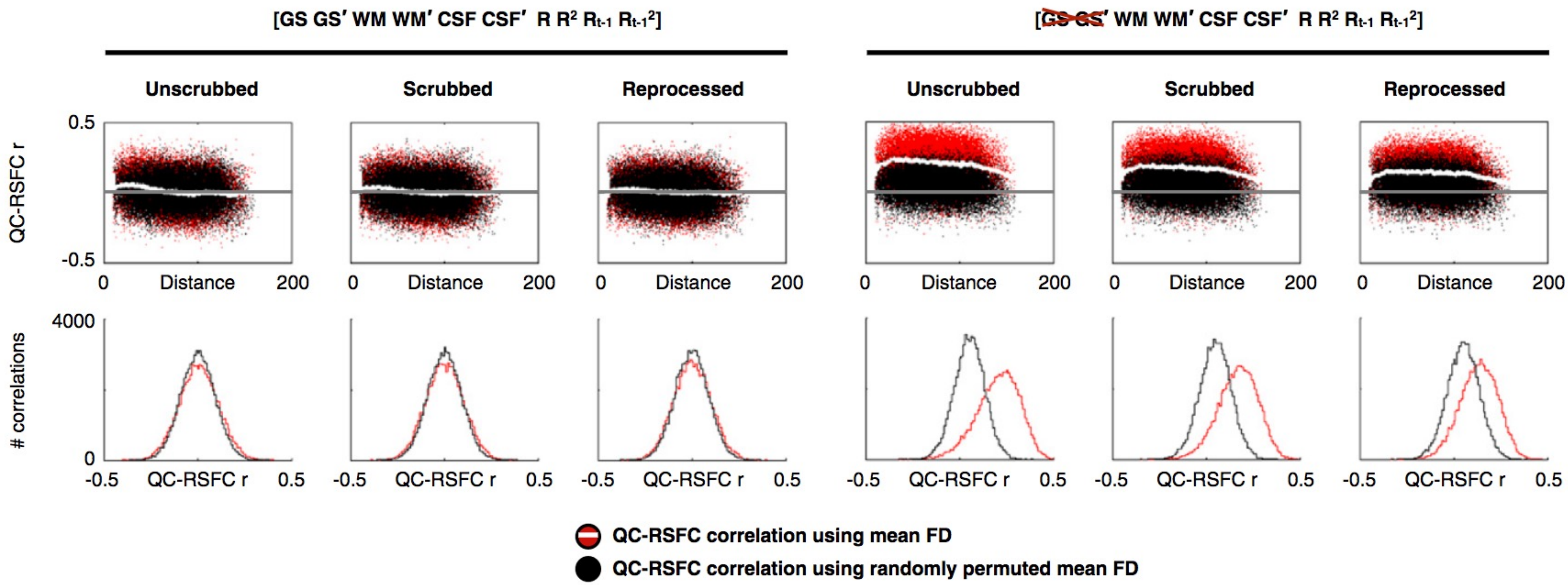
Transient head motions lead to corresponding changes in the BOLD signal

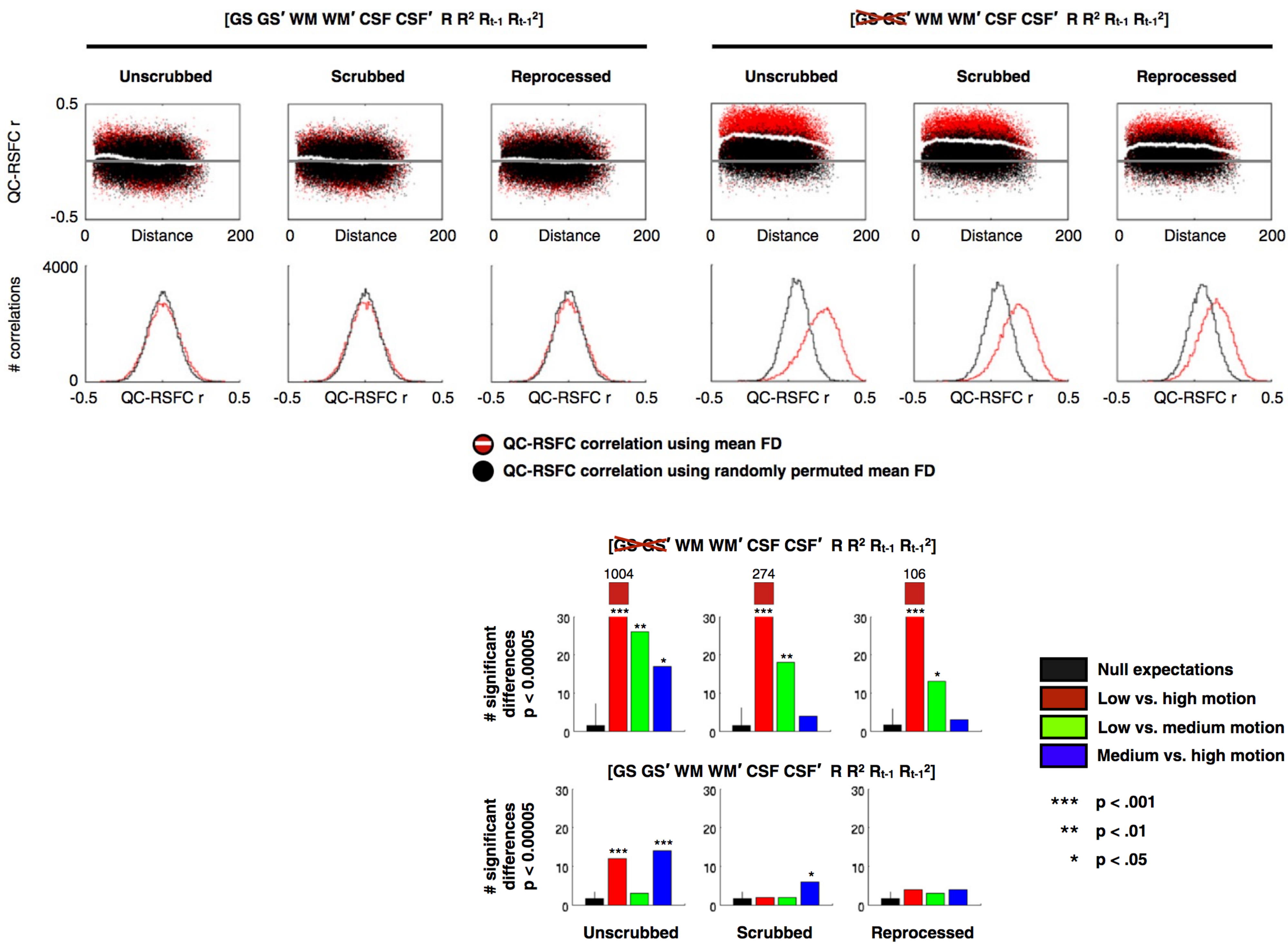


Power et al. (2014). Neuroimage



Subject 131
Subject 37
Subject 59
Subject 45
mm
BOLD
GM
WM
10 TRs
GM-WM: r = 0.41
GM-CSF: r = 0.53
GM-WM: r = 0.34
GM-CSF: r = 0.26
GM-WM: r = 0.41
GM-CSF: r = -0.54
GM-WM: r = -0.05
GM-CSF: r = 0.32
Volume #
FD
DVGS
SDGS
global signal


[GS GS′ WM WM′ CSF CSF′ R R² Rt-1 Rt-1²]
[GS GS′ WM WM′ CSF CSF′ R R² Rt-1 Rt-1²]
Unscrubbed
Scrubbed
Reprocessed
Unscrubbed
Scrubbed
Reprocessed
QC-RSFC r
0.5
-0.5
0
Distance
200
correlations
4000
0
-0.5
QC-RSFC r
0.5
QC-RSFC correlation using mean FD
QC-RSFC correlation using randomly permuted mean FD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Unscrubbed
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correlations
4000
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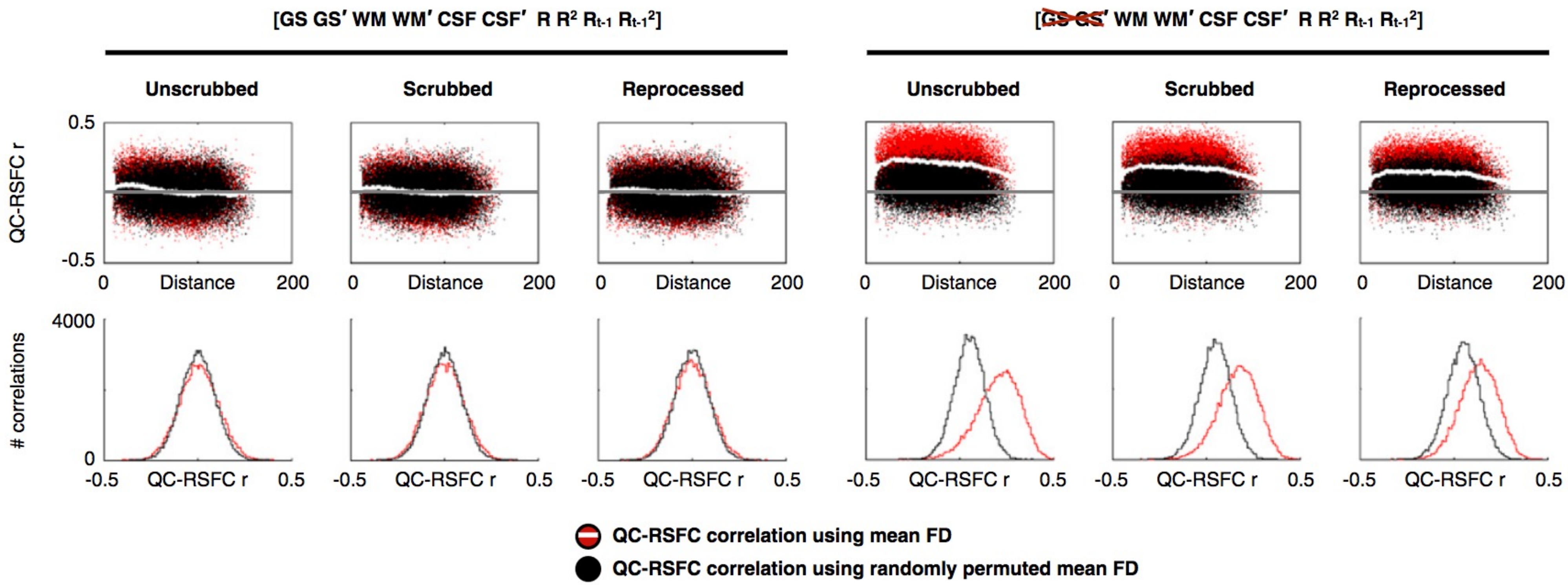
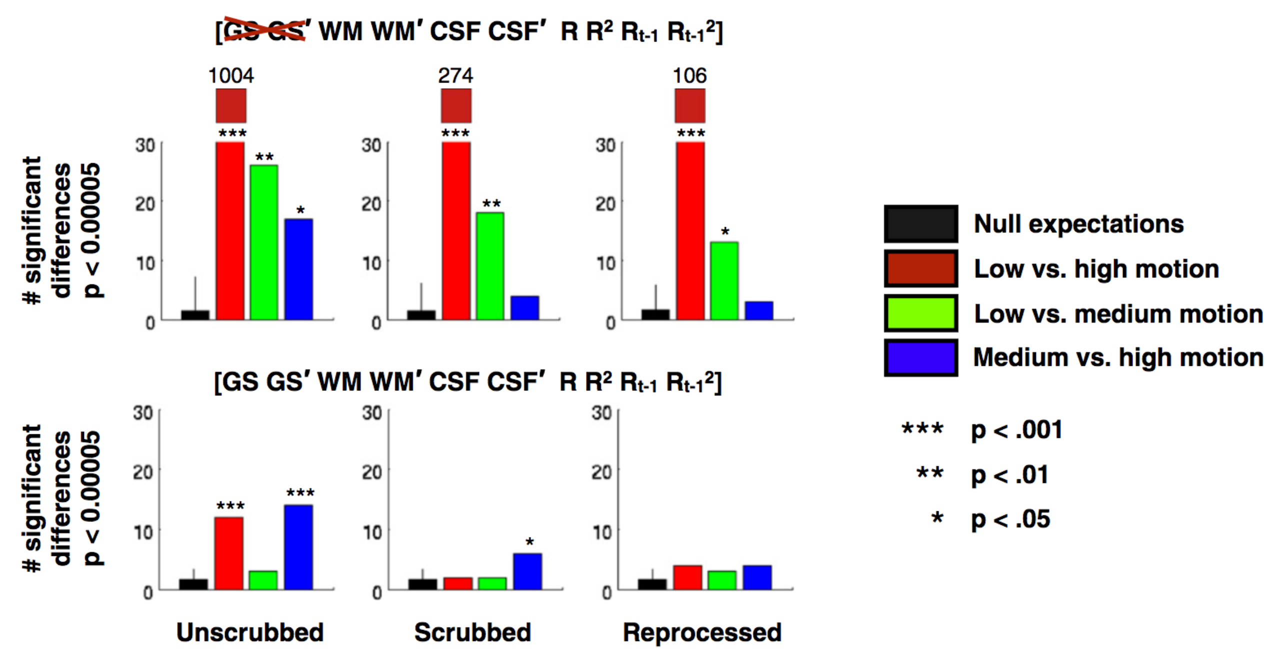
1004
274
106
significant differences p < 0.00005
Null expectations
Low vs. high motion
Low vs. medium motion
Medium vs. high motion
*** p < .001
** p < .01
* p < .05





Take Home:

Censor high-motion TRs,
Global Signal Regression

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We have some measures of certain artifacts (e.g.):

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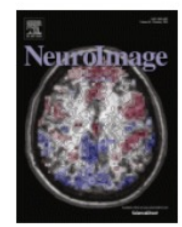

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Underlying assumption is that when noise is removed, "real" patterns should repeat

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Therefore, reliability of fMRI BOLD fluctuations and behavioral measures serves as an upper limit on our ability to measure any brain-behavior relationships.

Cerebral Cortex October 2009;19:2209-2229
doi:10.1093/cercor/bhn256
Advance Access publication February 16, 2009

The Resting Brain: Unconstrained yet Reliable

Zarrar Shehzad[1], A. M. Clare Kelly[1], Philip T. Reiss[2,3], Dylan G. Gee[1], Kristin Gotimer[1], Lucina Q. Uddin[4], Sang Han Lee[3], Daniel S. Margulies[5], Amy Krain Roy[1], Bharat B. Biswal[3,6], Eva Petkova[2,3], F. Xavier Castellanos[1,3] and Michael P. Milham[1]

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NeuroImage 76 (2013) 183–201

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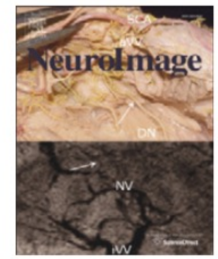

A comprehensive assessment of regional variation in the impact of head micromovements on functional connectomics

Chao-Gan Yan [a,b,c], Brian Cheung [b], Clare Kelly [c], Stan Colcombe [a], R. Cameron Craddock [b,d], Adriana Di Martino [c], Qingyang Li [b], Xi-Nian Zuo [e], F. Xavier Castellanos [a,c], Michael P. Milham [a,b,*]

[a] Nathan Kline Institute for Psychiatric Research, Orangeburg, NY, USA
[b] Center for the Developing Brain, Child Mind Institute, New York, NY, USA
[c] The Phyllis Green and Randolph Cowen Institute for Pediatric Neuroscience, New York University Child Study Center, New York, NY, USA
[d] Virginia Tech Carilion Research Institute, Roanoke, VA, USA
[e] Key Laboratory of Behavioral Science, Laboratory for Functional Connectome and Development, Magnetic Resonance Imaging Research Center, Institute of Psychology, Chinese Academy of Sciences, Beijing, China

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The Resting ... Reliable

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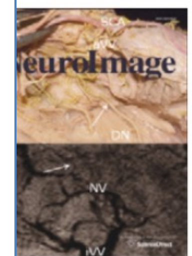

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Adriana Di Ma... ,*

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SCIENTIFIC DATA

OPEN

SUBJECT CATEGORIES
» Neuroinformatics
» Brain imaging
» Functional magnetic resonance imaging
» Cognitive neuroscience

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An open science resource for establishing reliability and reproducibility in functional connectomics

Xi-Nian Zuo[1,2,*], Jeffrey S. Anderson[3], Pierre Bellec[4], Rasmus M. Birn[5], Bharat B. Biswal[6], Janusch Blautzik[7], John C.S. Breitner[8], Randy L. Buckner[9], Vince D. Calhoun[10], F. Xavier Castellanos[11,12], Antao Chen[2], Bing Chen[13], Jiangtao Chen[2], Xu Chen[2], Stanley J. Colcombe[11], William Courtney[10], R. Cameron Craddock[11,14], Adriana Di Martino[12], Hao-Ming Dong[1,15], Xiaolan Fu[1,16], Qiyong Gong[17], Krzysztof J. Gorgolewski[18], Ying Han[19], Ye He[1,15], Yong He[20], Erica Ho[11,14], Avram Holmes[21], Xiao-Hui Hou[1,15], Jeremy Huckins[22], Tianzi Jiang[23], Yi Jiang[1], William Kelley[22], Clare Kelly[12], Margaret King[10], Stephen M. LaConte[24], Janet E. Lainhart[5], Xu Lei[2], Hui-Jie Li[1], Kaiming Li[17], Kuncheng Li[25], Qixiang Lin[20], Dongqiang Liu[13], Jia Liu[20], Xun Liu[1], Yijun Liu[2], Guangming Lu[26], Jie Lu[25], Beatriz Luna[27], Jing Luo[28], Daniel Lurie[11,14], Ying Mao[29], Daniel S. Margulies[18], Andrew R. Mayer[10], Thomas Meindl[7], Mary E. Meyerand[30], Weizhi Nan[1,15], Jared A. Nielsen[3], David O'Connor[11,14], David Paulsen[27], Vivek Prabhakaran[31], Zhigang Qi[25], Jiang Qiu[2], Chunhong Shao[32], Zarrar Shehzad[11,14], Weijun Tang[33], Arno Villringer[34], Huiling Wang[35], Kai Wang[1,15], Dongtao Wei[2], Gao-Xia Wei[1], Xu-Chu Weng[13], Xuehai Wu[29], Ting Xu[1,11,14], Ning Yang[1,15], Zhi Yang[1], Yu-Feng Zang[13], Lei Zhang[1,15], Qinglin Zhang[2], Zhe Zhang[1,15], Zhiqiang Zhang[26], Ke Zhao[1], Zonglei Zhen[20], Yuan Zhou[1], Xing-Ting Zhu[1,15] & Michael P. Milham[11,14]

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frontiers in
NEUROSCIENCE

ORIGINAL RESEARCH ARTICLE
published: 19 February 2015
doi: 10.3389/fnins.2015.00048

Evaluating the reliability of different preprocessing steps to estimate graph theoretical measures in resting state fMRI data

Nathassia K. Aurich[1], José O. Alves Filho[1], Ana M. Marques da Silva[1,2,3] and Alexandre R. Franco[1,2,4]*

[1] *Faculdade de Engenharia, PUCRS, Porto Alegre, Brazil*
[2] *Instituto do Cérebro do Rio Grande do Sul (InsCer-RS), PUCRS, Porto Alegre, Brazil*
[3] *Faculdade de Física, PUCRS, Porto Alegre, Brazil*
[4] *Faculdade de Medicina, PUCRS, Porto Alegre, Brazil*

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The Resting ... Reliable

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NeuroImage 117 (2015) 67–79

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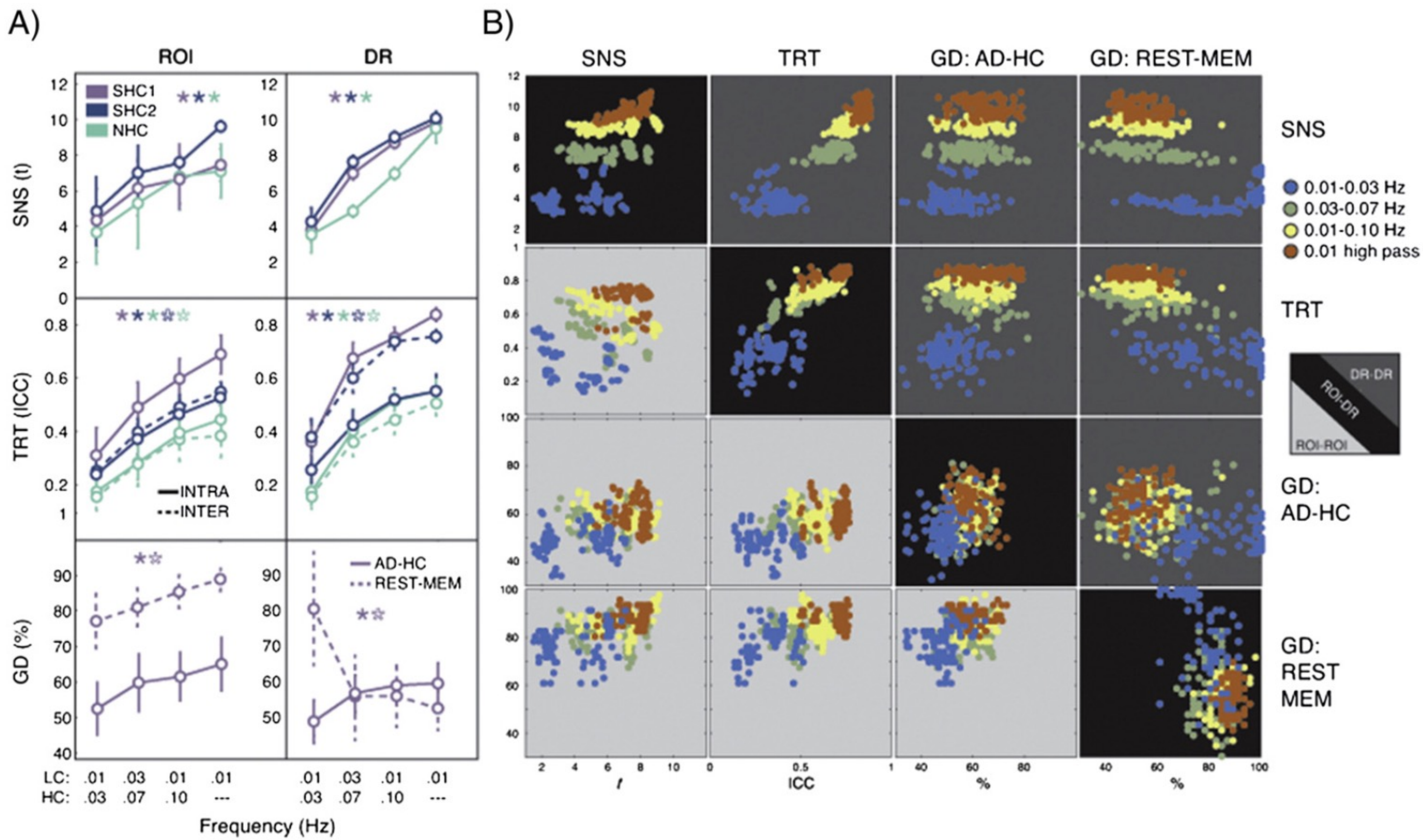
Optimization of rs-fMRI Pre-processing for Enhanced Signal-Noise Separation, Test-Retest Reliability, and Group Discrimination

CrossMark

William R. Shirer [a,*,1], Heidi Jiang [a,b,*,1], Collin M. Price [a], Bernard Ng [a,c], Michael D. Greicius [a]

[a] *Functional Imaging in Neuropsychiatric Disorders (FIND) Lab, Department of Neurology and Neurological Sciences, Stanford University School of Medicine, Stanford, USA*
[b] *Interdepartmental Program in Neuroscience, Northwestern University, Chicago, USA*
[c] *Parietal Team, Neurospin, INRIA Saclay, France*

Which procedures affect test-retest reliability (and other measures of data quality) ?



Shirer et al. (2015). Neuroimage

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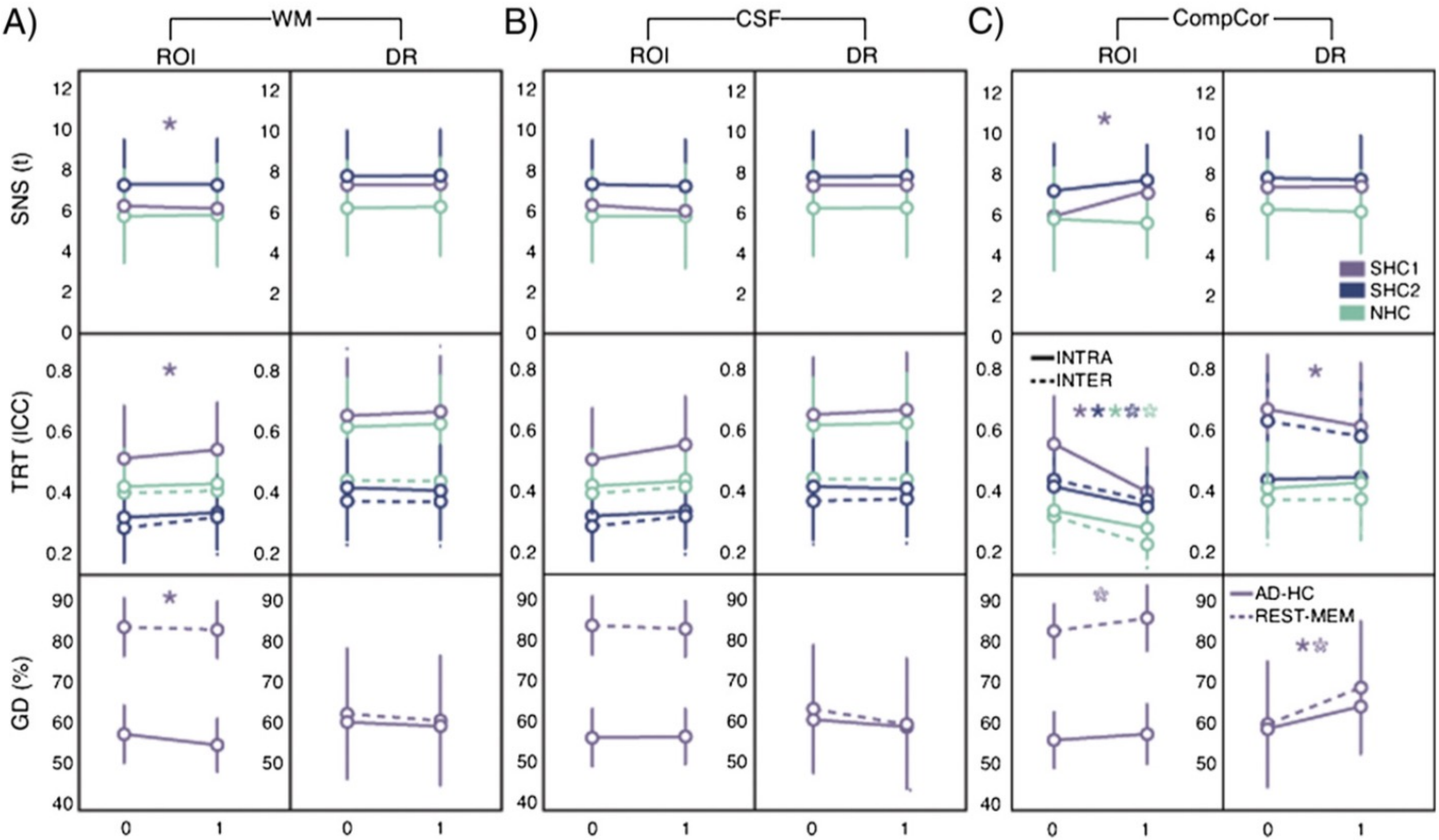

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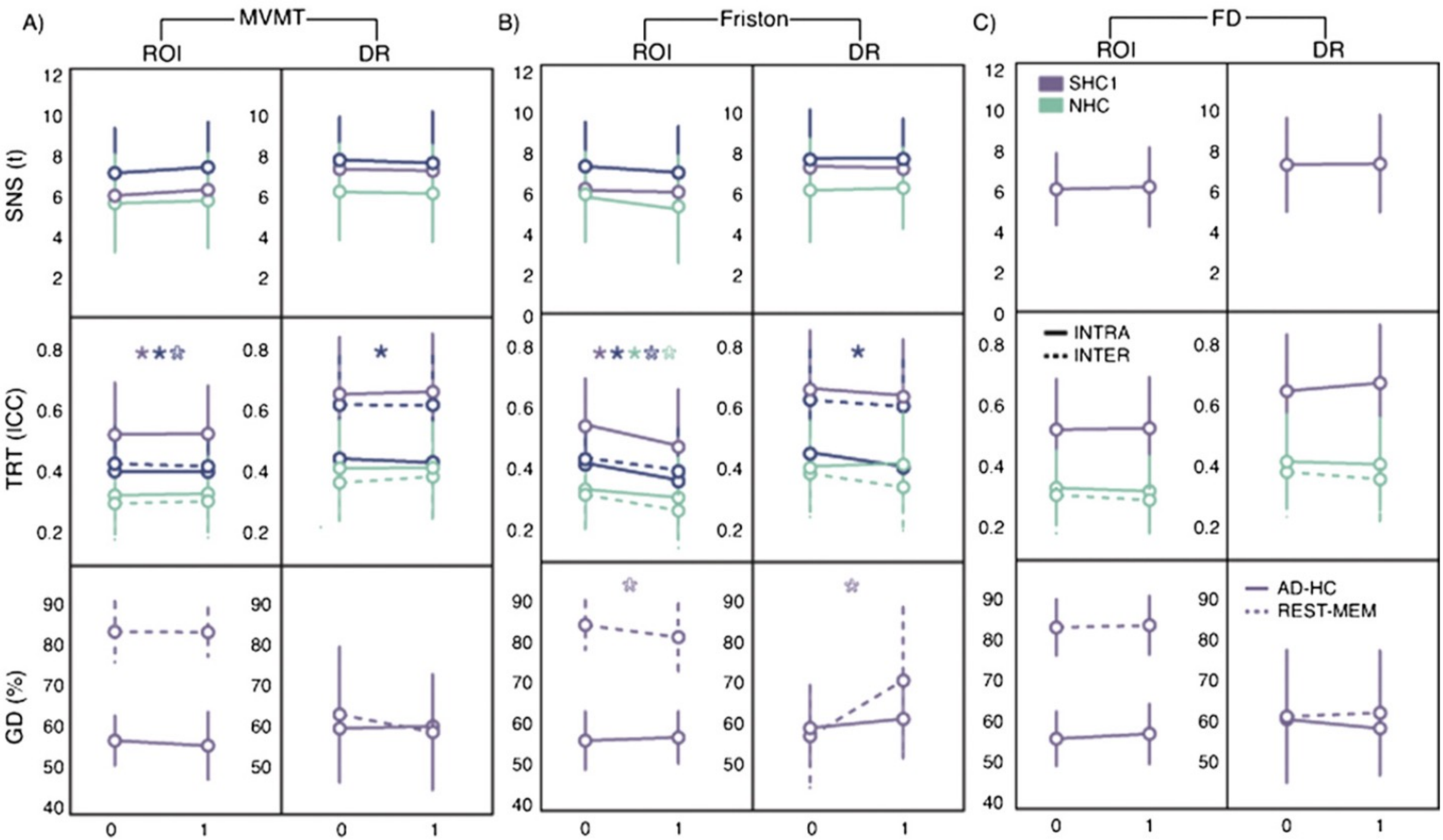

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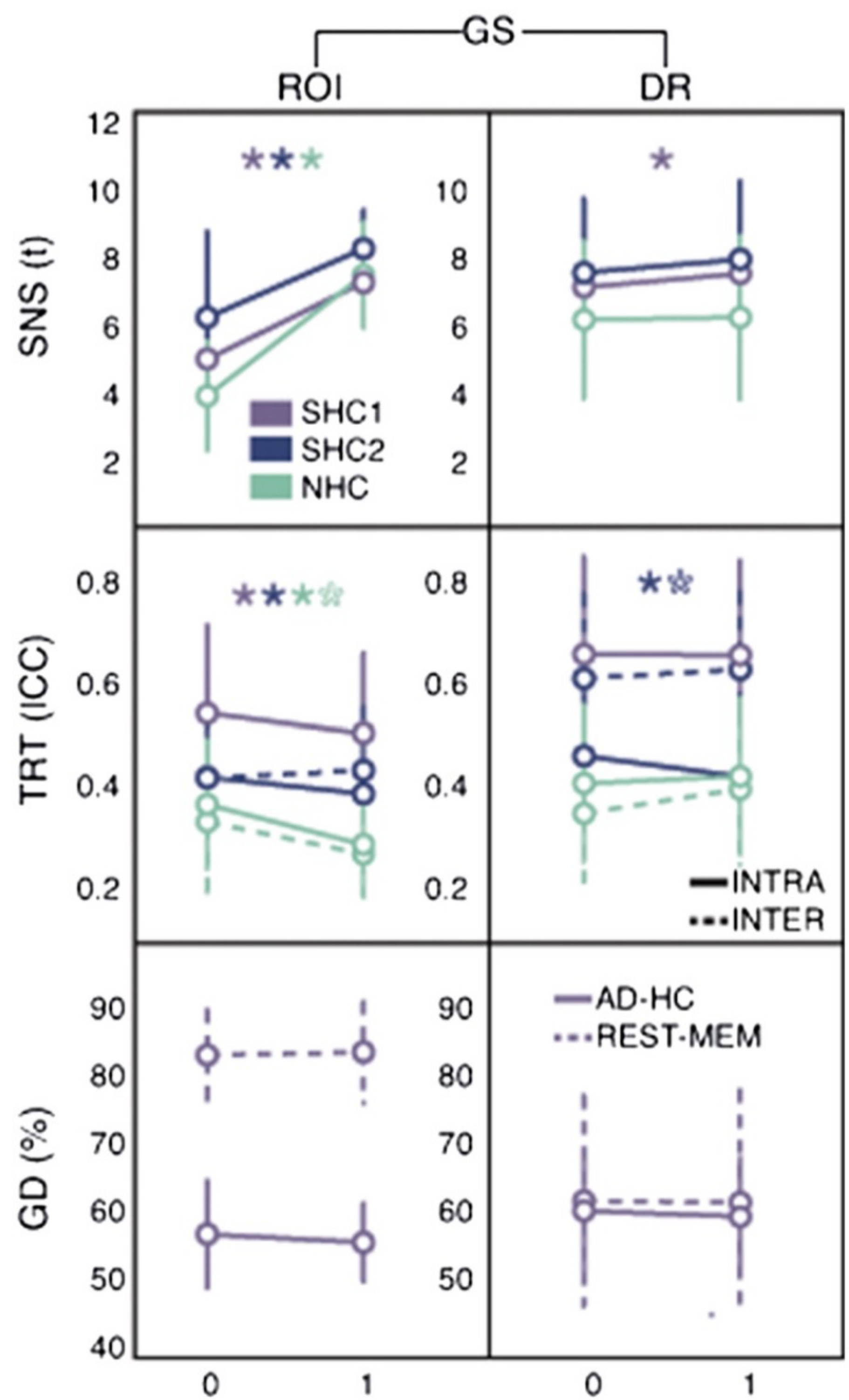

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Validity in this context refers to the extent to which we can use fMRI fluctuations/covariation to predict an independent behavioral measure that indexes the ability of interest

Previous Examples of Validity

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- Comparing clinical versus control group in resting-state correlations and predicting independent measures of clinical symptoms using the same regions (Gotts et al., 2012)

Resting-state Correlations Among Face-Selective Regions Predict Face Processing Ability Behaviorally

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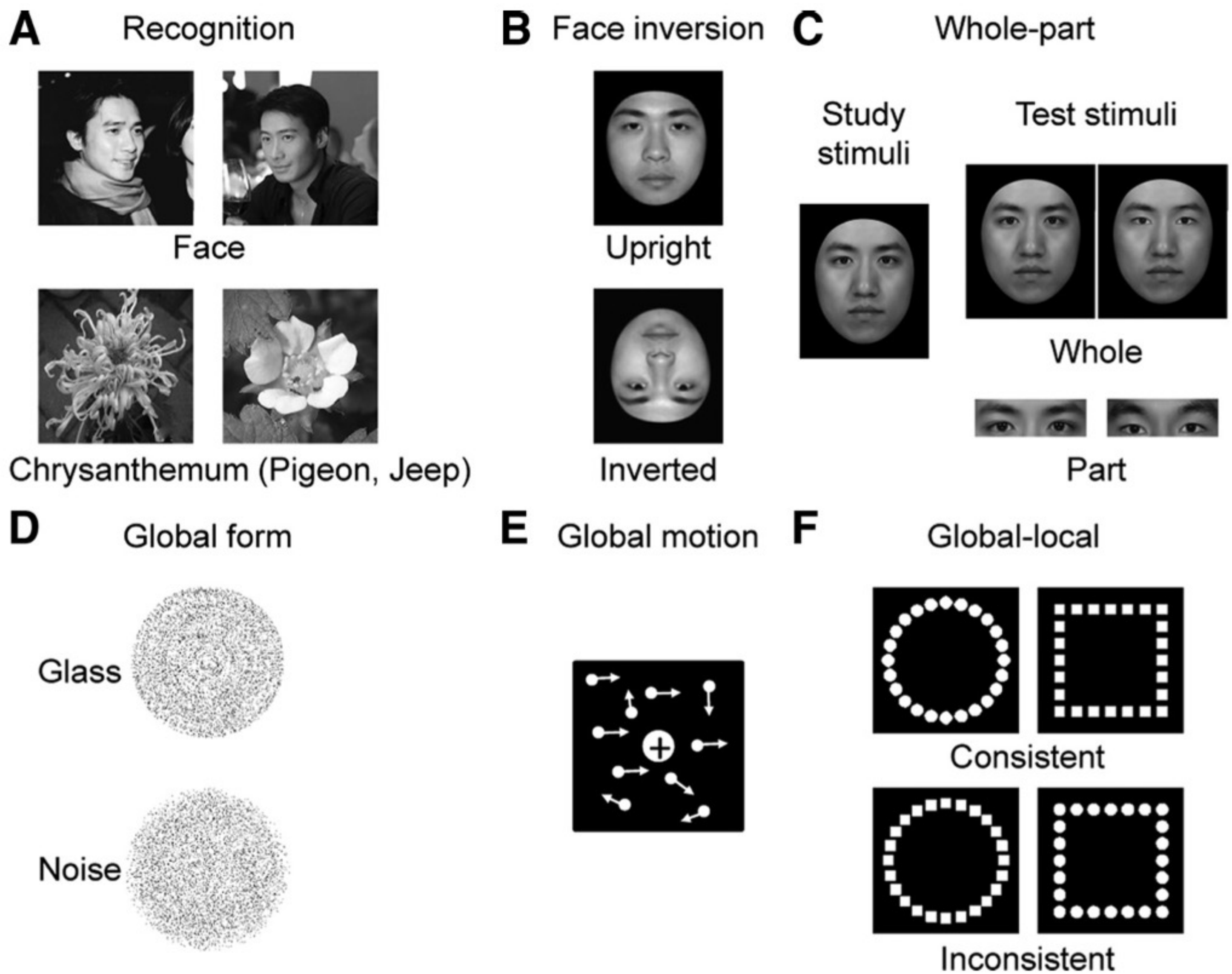
Zhu et al. (2011). J Neurosci



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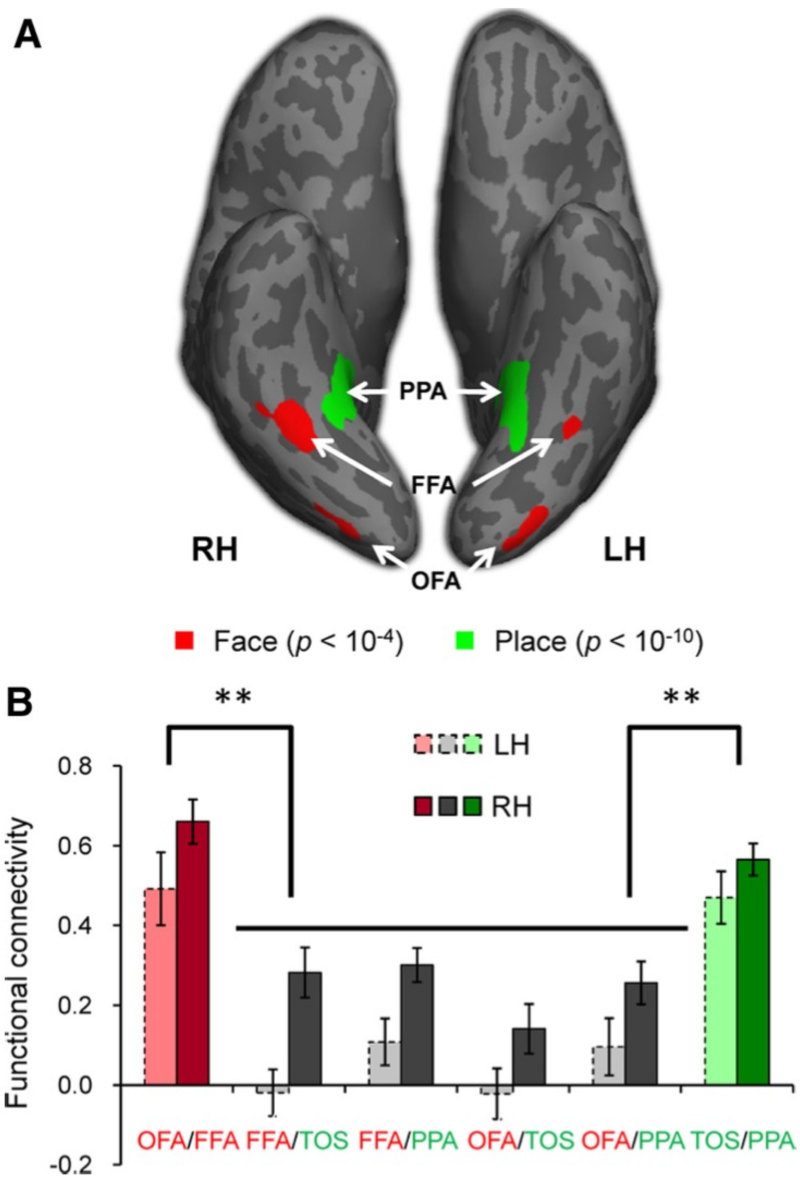
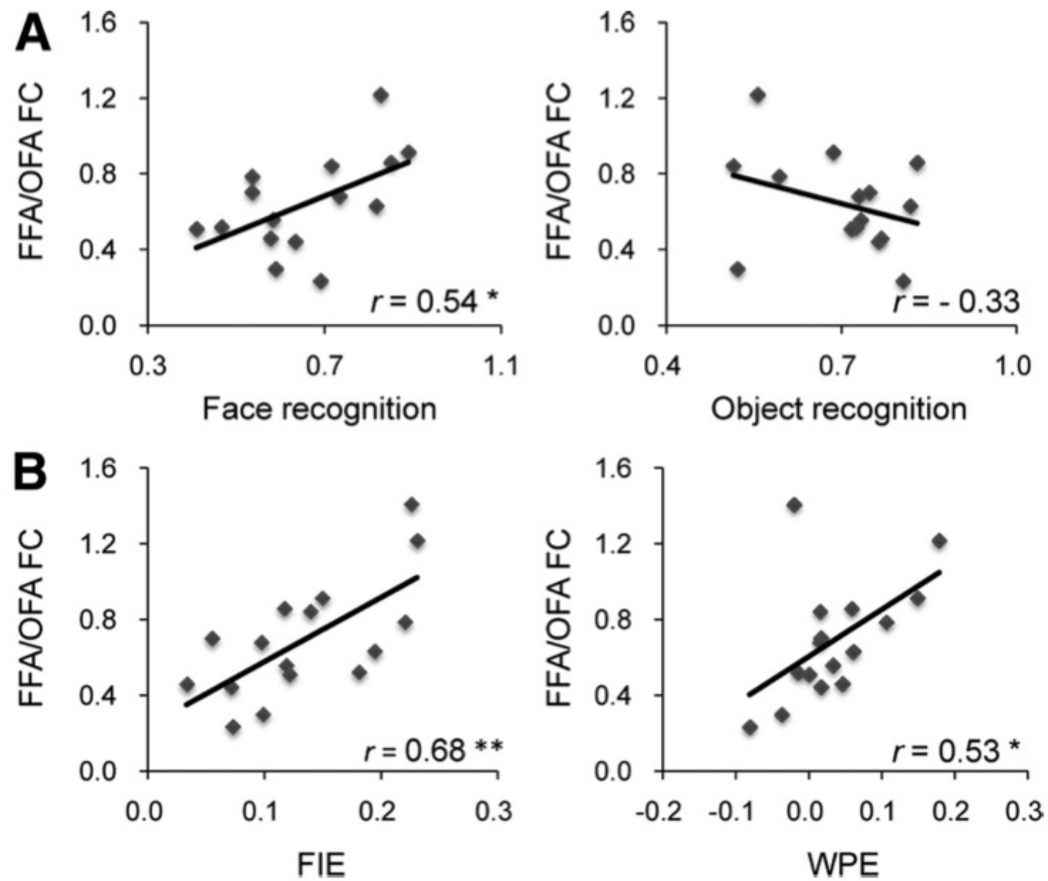




Inversion Effect

Whole-part Effect

Autism (ASD) vs. Typically Developing (TD)

Autism (ASD) vs. Typically Developing (TD)

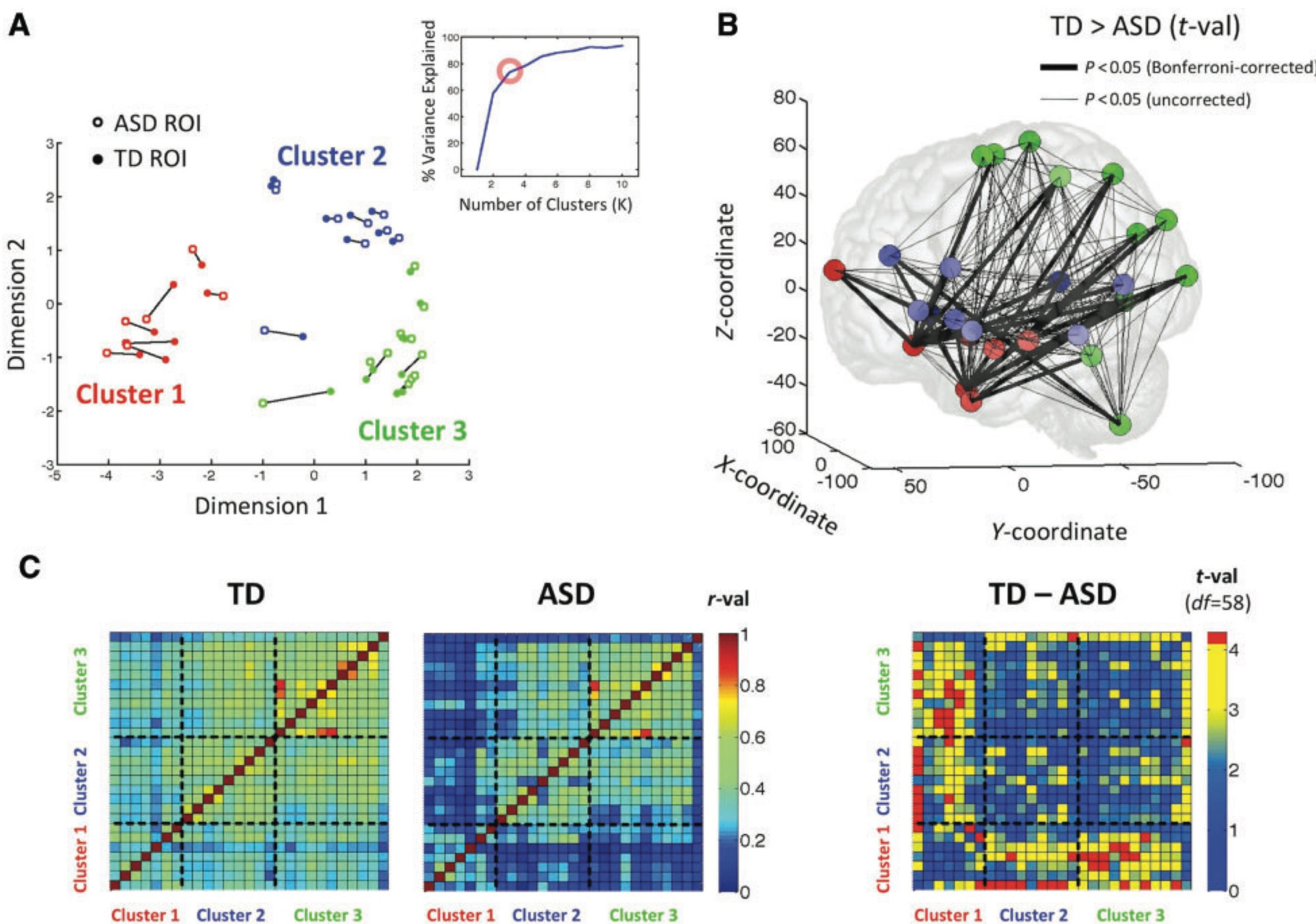
doi:10.1093/brain/aws160 Brain 2012: 135; 2711–2725 | 2711

BRAIN
A JOURNAL OF NEUROLOGY

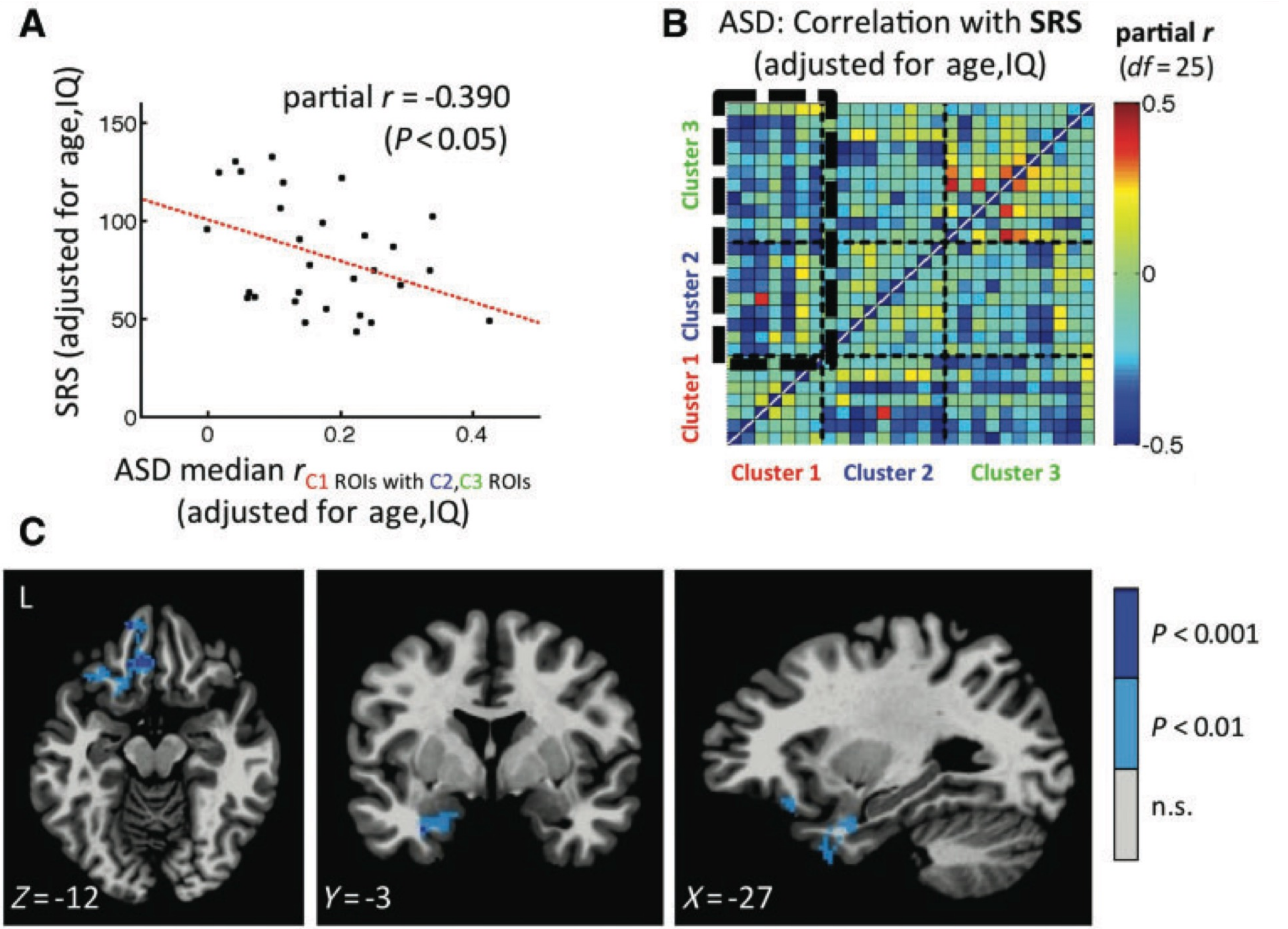
Fractionation of social brain circuits in autism spectrum disorders

Stephen J. Gotts,[1] W. Kyle Simmons,[2] Lydia A. Milbury,[1] Gregory L. Wallace,[1]
Robert W. Cox[3] and Alex Martin[1]

Whole-brain Differences in Functional Connectivity: TD > ASD



Agreement with Social Symptom Correlations (ASD only)



Does Preprocessing Affect Validity?

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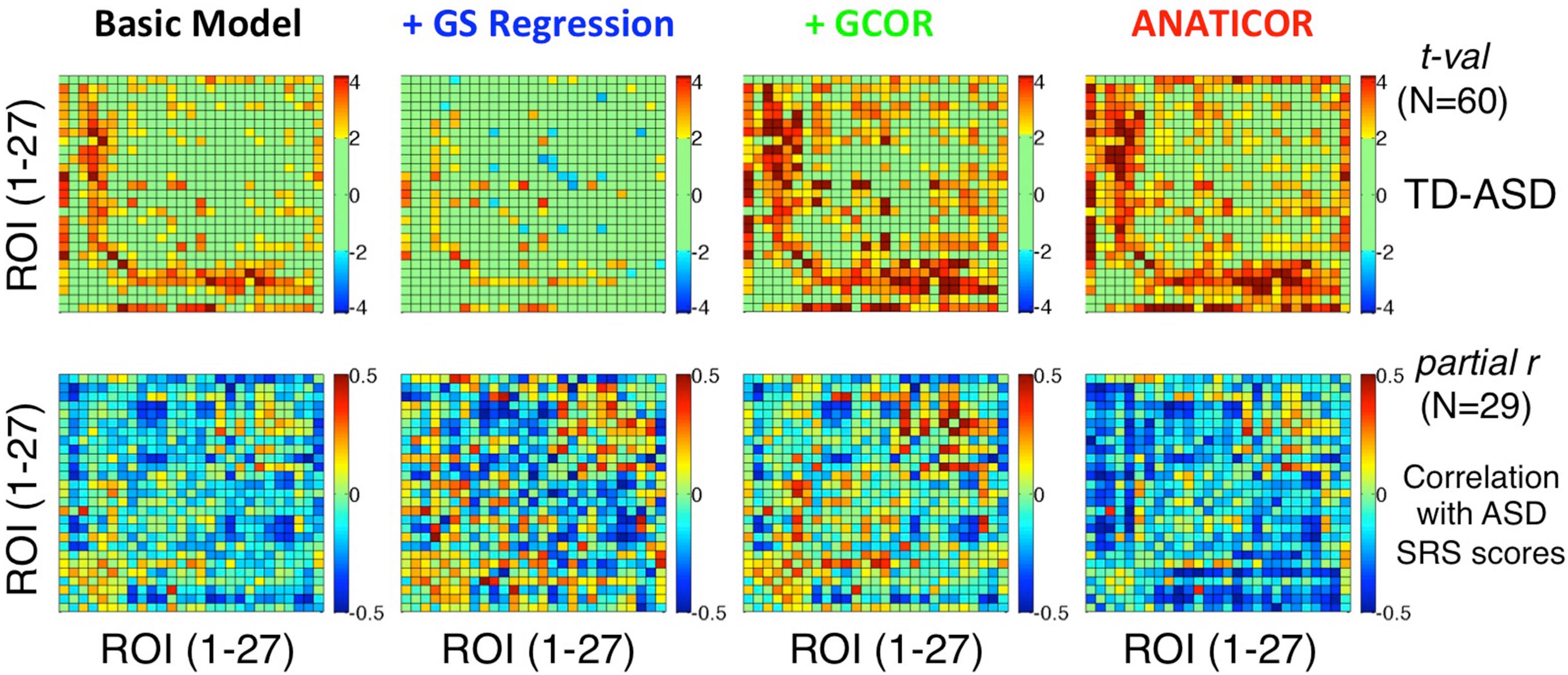
frontiers in
HUMAN NEUROSCIENCE

ORIGINAL RESEARCH ARTICLE
published: 12 July 2013
doi: 10.3389/fnhum.2013.00356

The perils of global signal regression for group comparisons: a case study of Autism Spectrum Disorders

Stephen J. Gotts[1]*, Ziad S. Saad[2], Hang Joon Jo[2], Gregory L. Wallace[1], Robert W. Cox[2] and Alex Martin[1]

[1] *Section on Cognitive Neuropsychology, Laboratory of Brain and Cognition, National Institute of Mental Health, National Institutes of Health, Bethesda, MD, USA*
[2] *Scientific and Statistical Computing Core, National Institute of Mental Health, National Institutes of Health, Bethesda, MD, USA*



Basic Model
+ GS Regression
+ GCOR
ANATICOR
t-val
(N=60)
TD-ASD
partial r
(N=29)
Correlation with ASD SRS scores
ROI (1-27)
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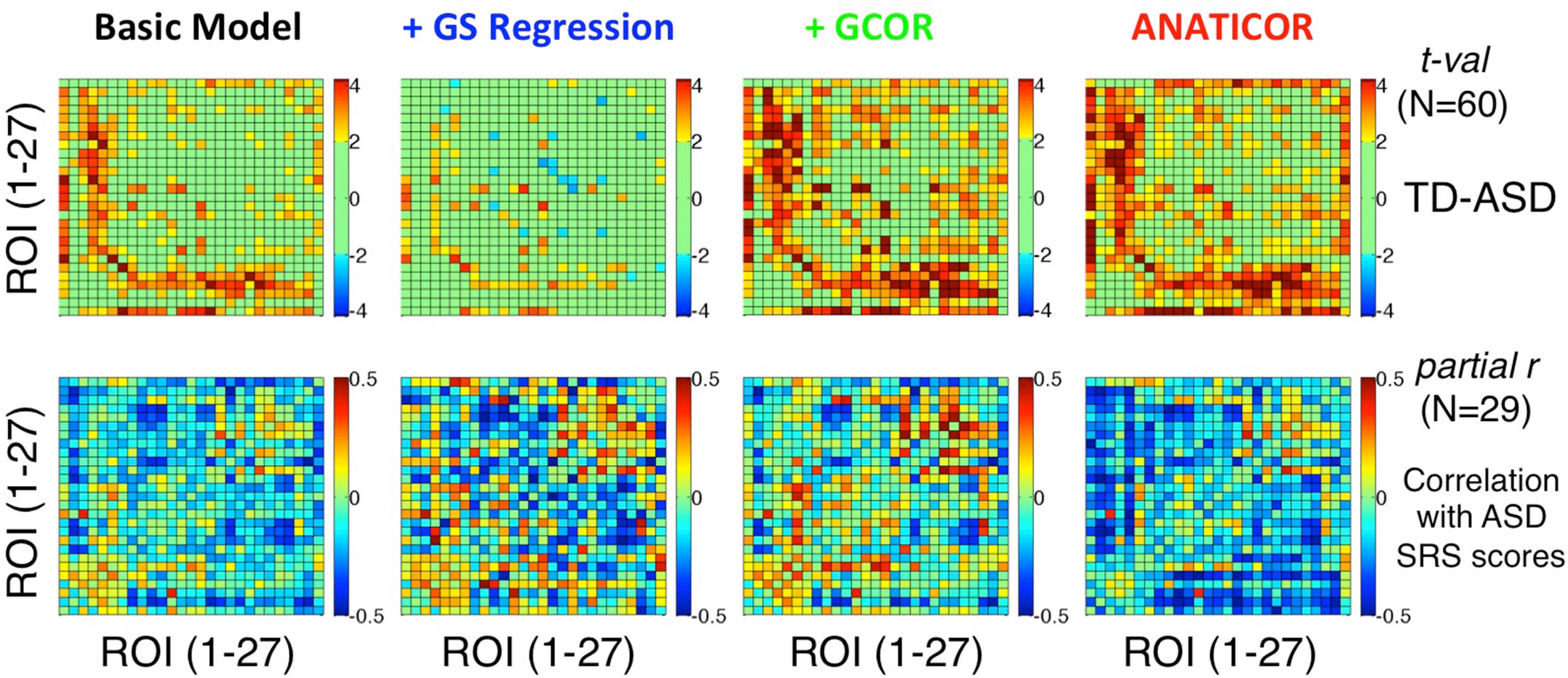
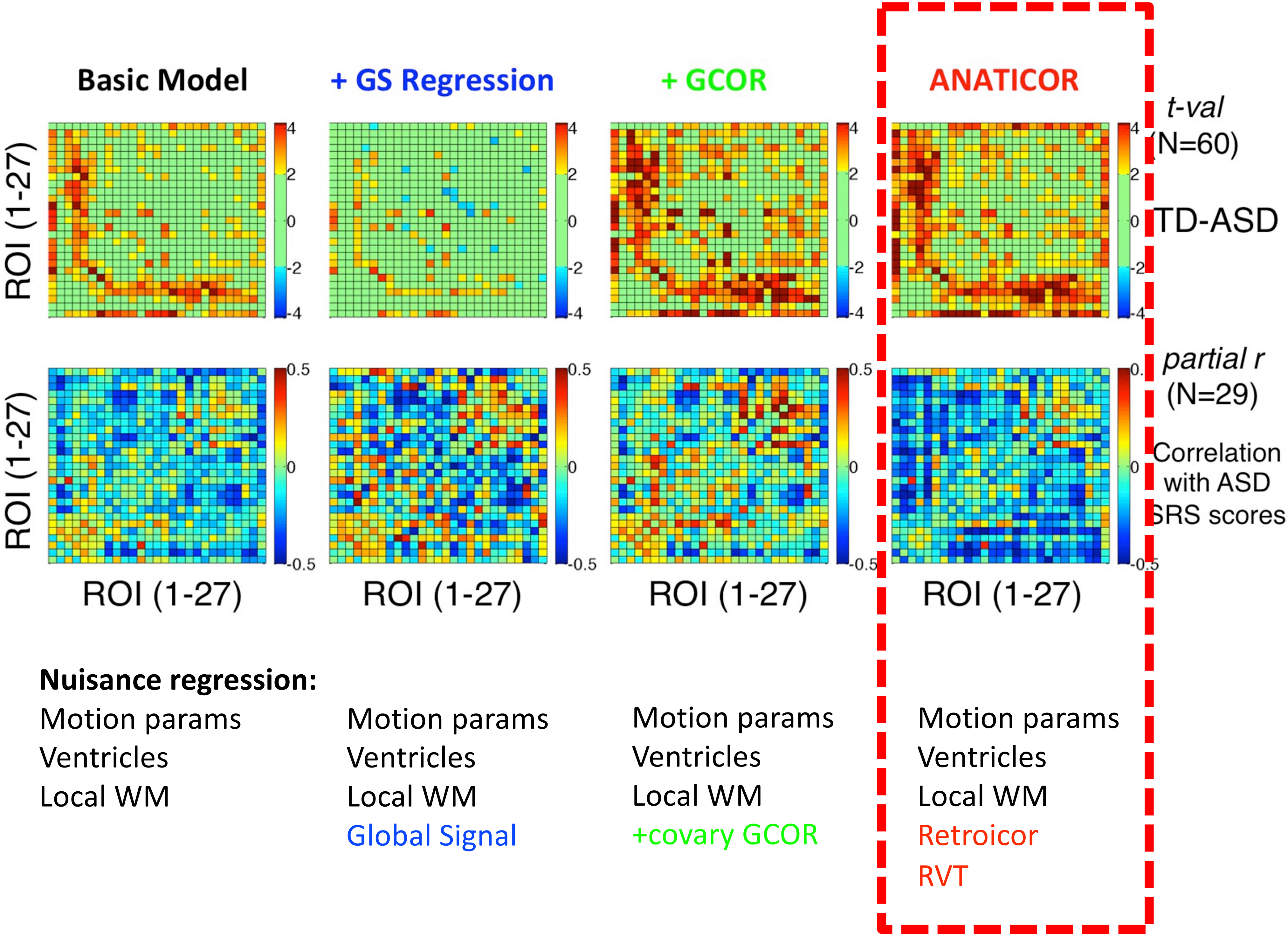


Nuisance regression:

Basic Model	+ GS Regression	+ GCOR	ANATICOR
Motion params	Motion params	Motion params	Motion params
Ventricles	Ventricles	Ventricles	Ventricles
Local WM	Local WM	Local WM	Local WM
	Global Signal	+covary GCOR	Retroicor
			RVT



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0
-2
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Examining Reliability and Validity Simultaneously: Current Study

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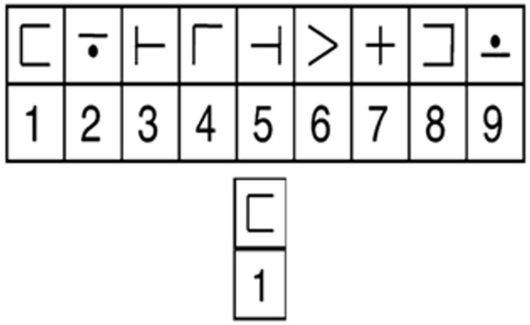
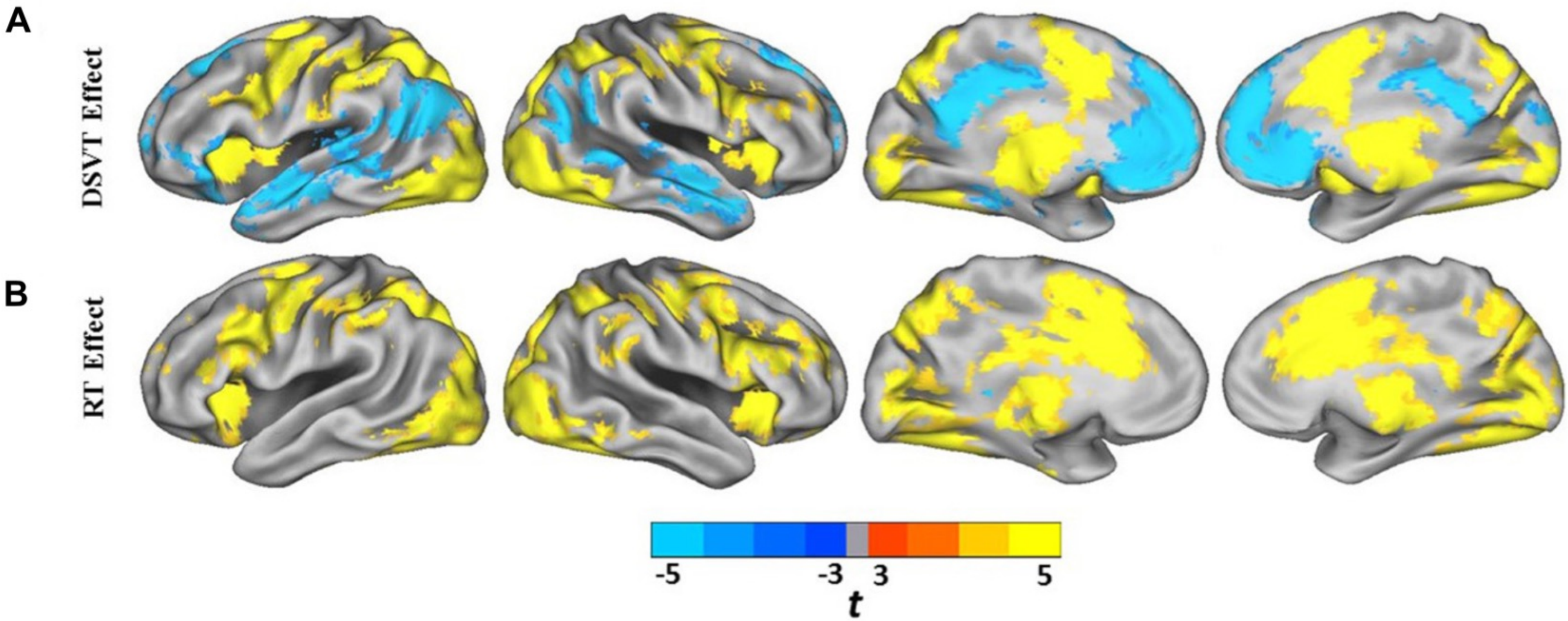


Digit Symbol Coding Task



Rao, Motes, & Rypma (2014). Frontiers Hum Neurosci

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"tiger"

”car"

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Does this agree with best test-retest reliability?

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2) optimally combined (OC) ME data (no nuisance regression)
3) OC + Motion params + Ventricles + local White Matter + GS
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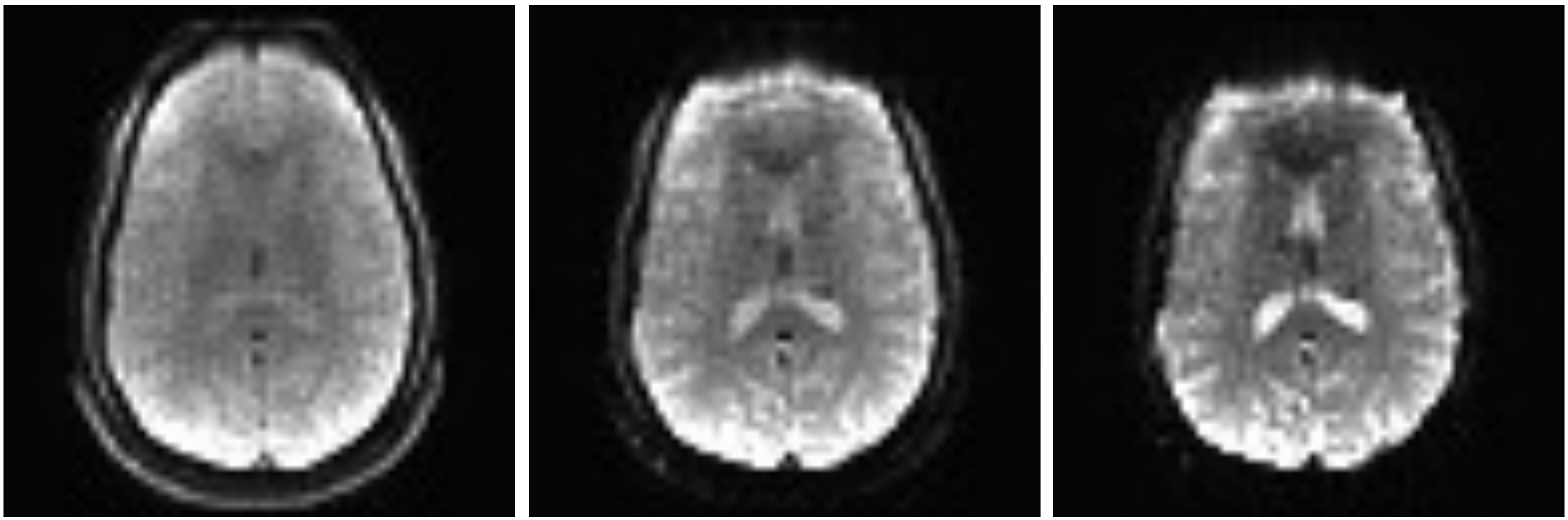
Single-echo pipelines (echo 2):
1) no blurring
2) blur 6mm FWHM
3) blur 6mm + Motion params + Ventricles + local White Matter + GS
4) blur 6mm + Motion params + Ventricles + local White Matter
5) blur 6mm + ANATICOR

Multi-echo EPI data

TE = 12.5 ms TE = 27.7 ms TE = 42.9 ms



Beta Weights vs. RT correlations

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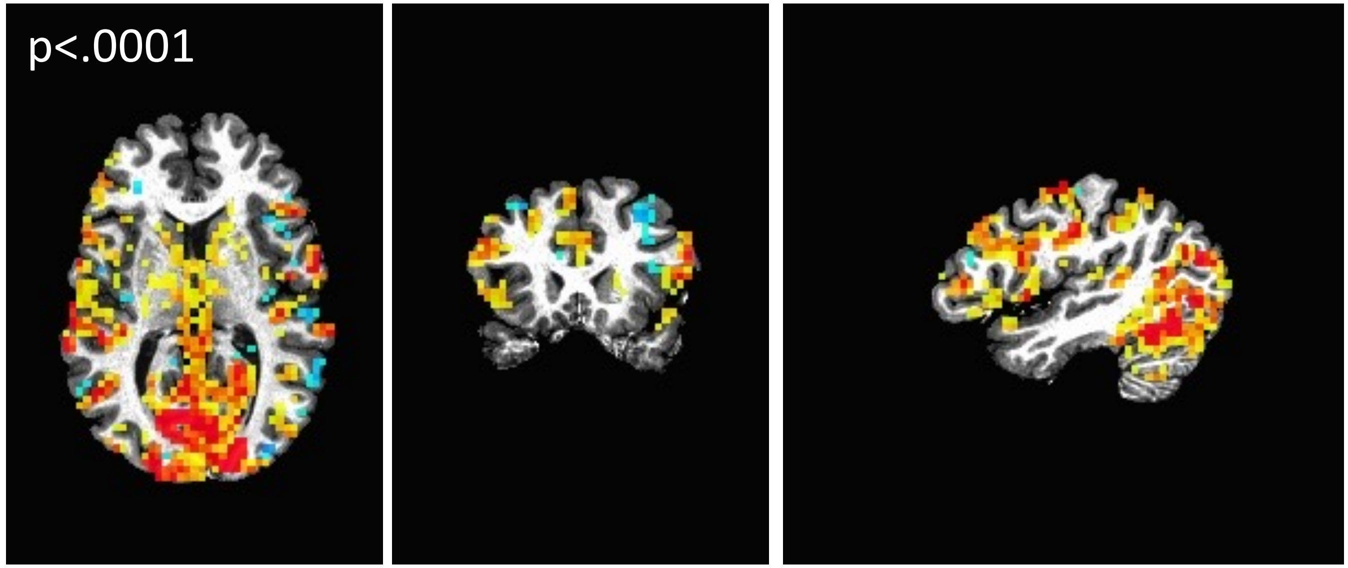
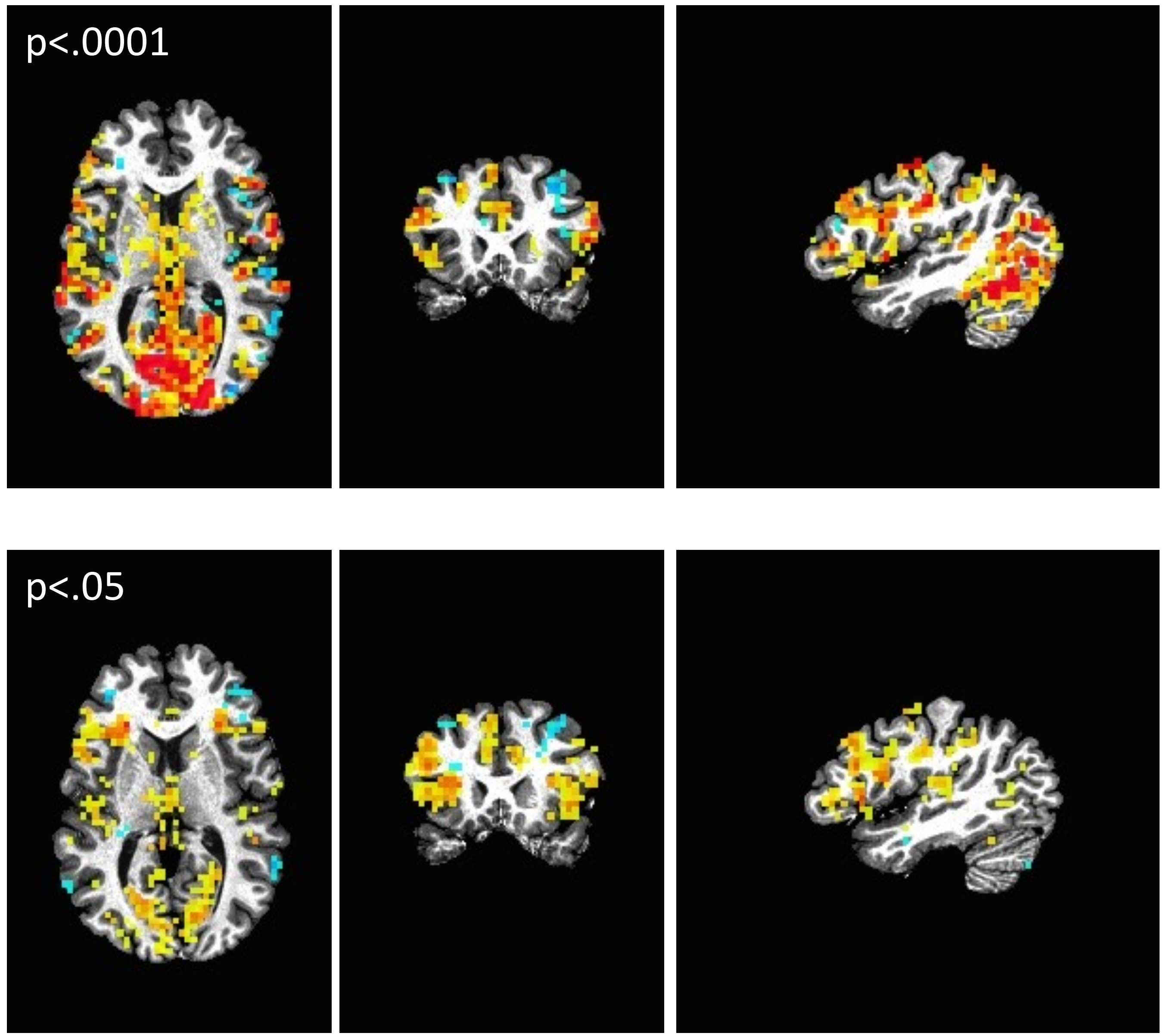
Stimulus vs 0



Beta Weights vs. RT correlations

Stimulus vs 0

Correlation of RT and BOLD



Results: Validity

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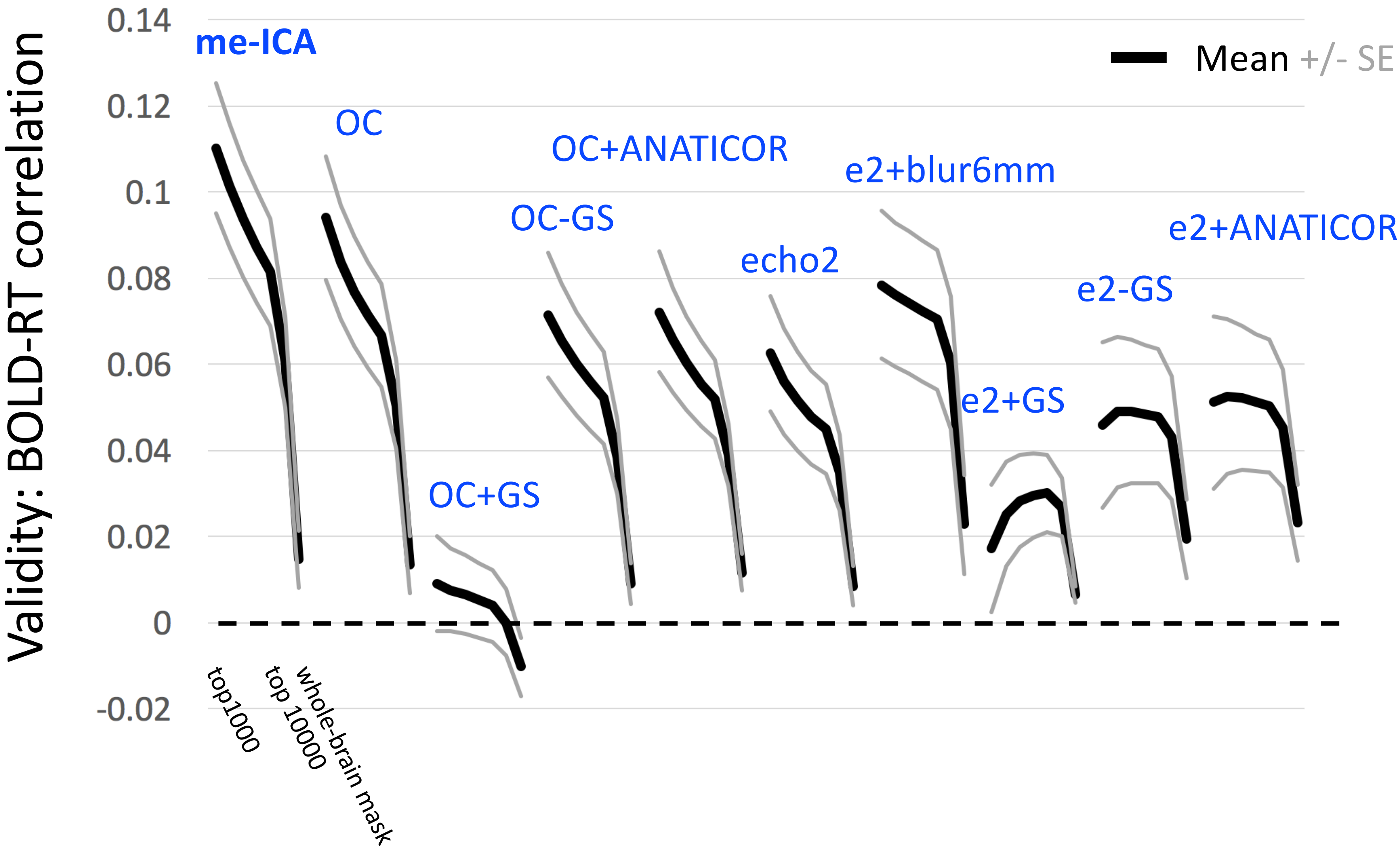

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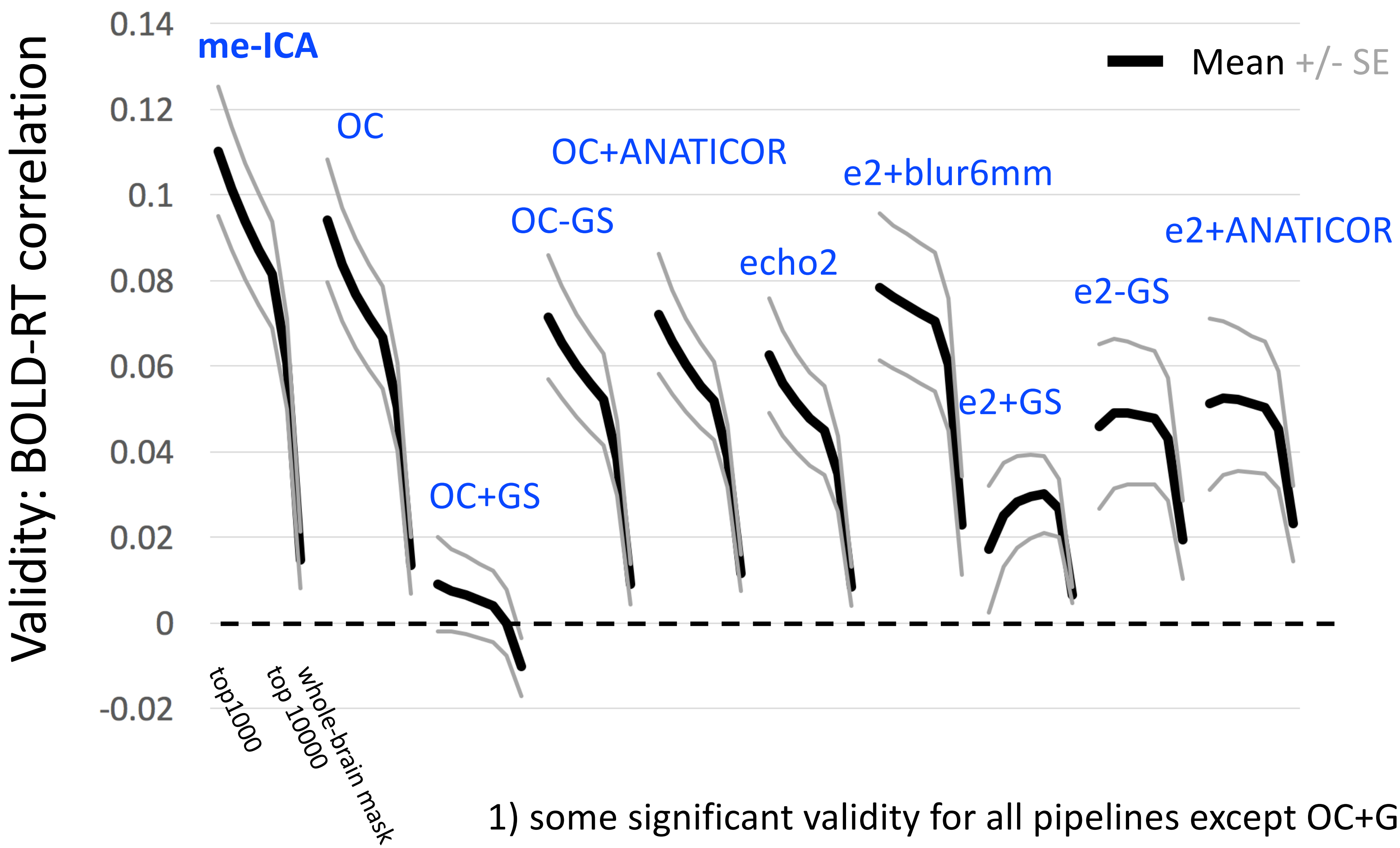

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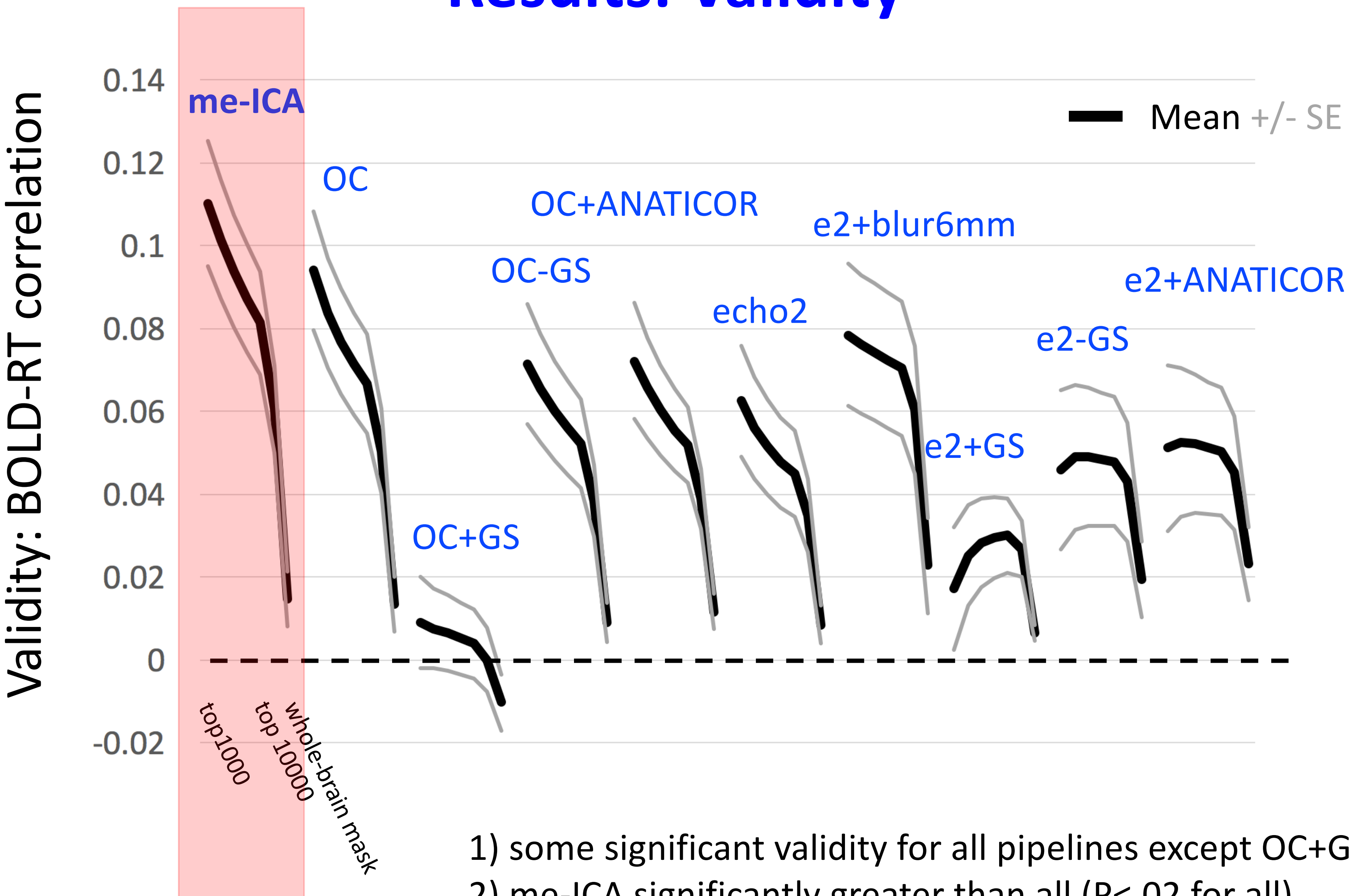

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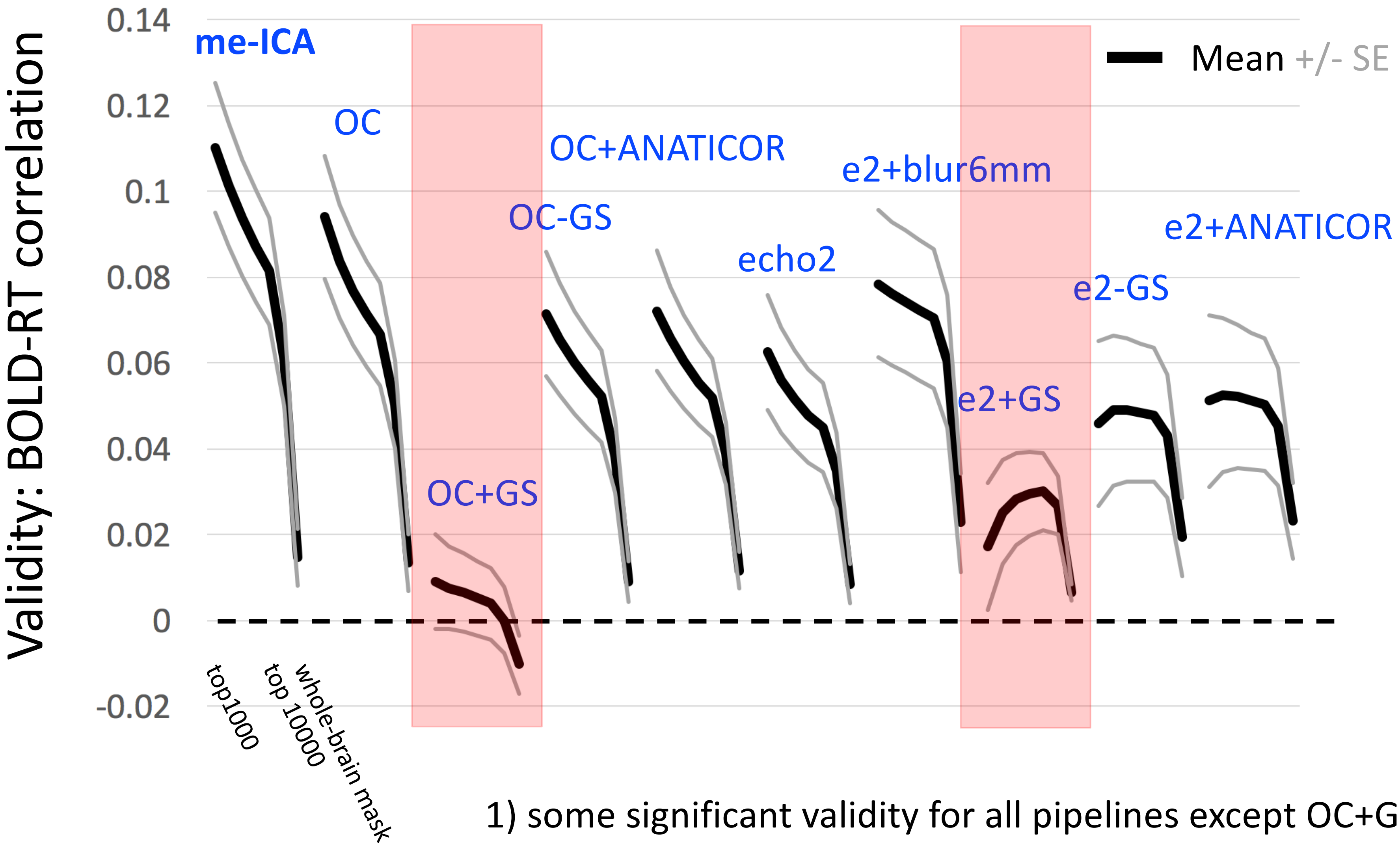

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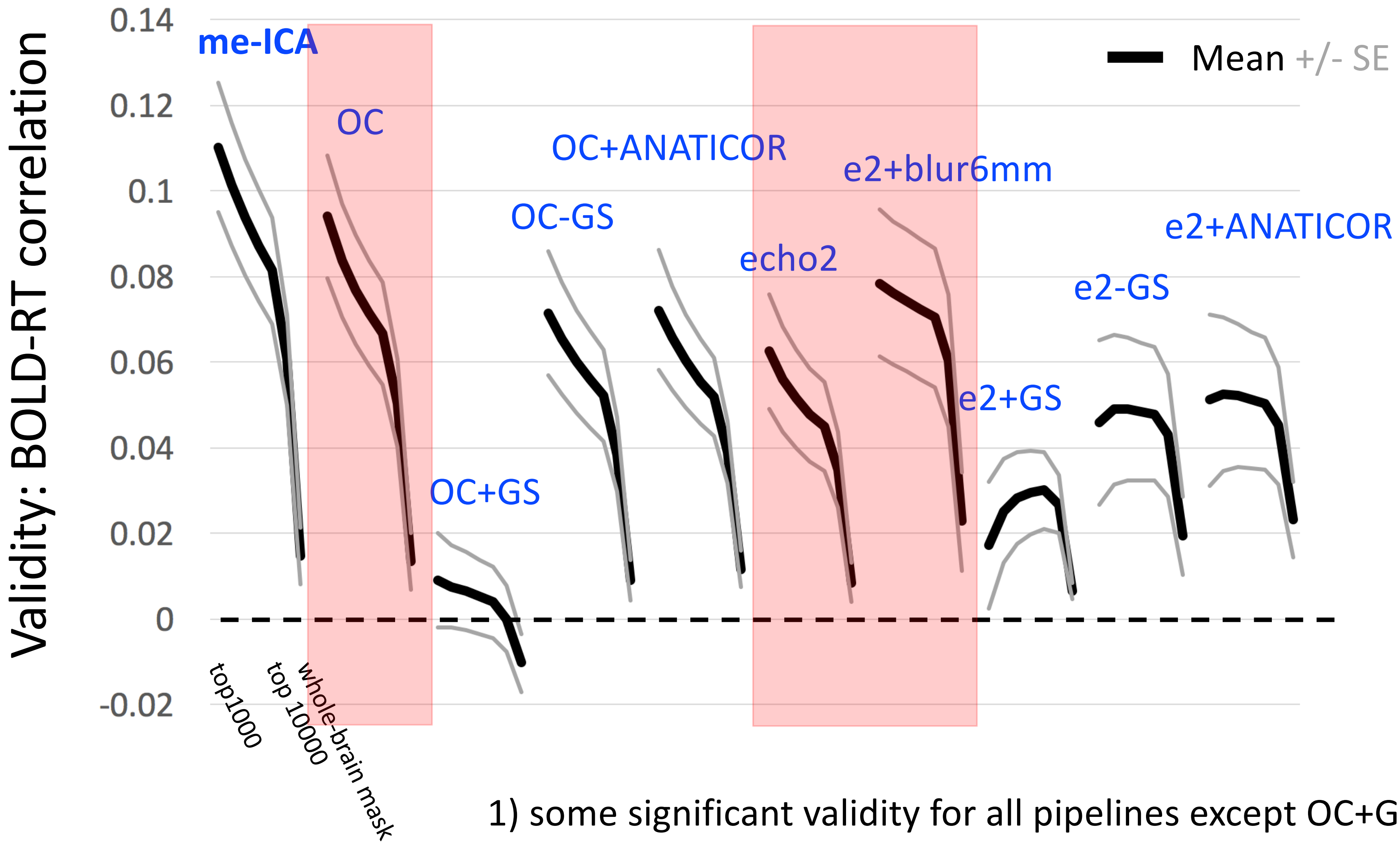

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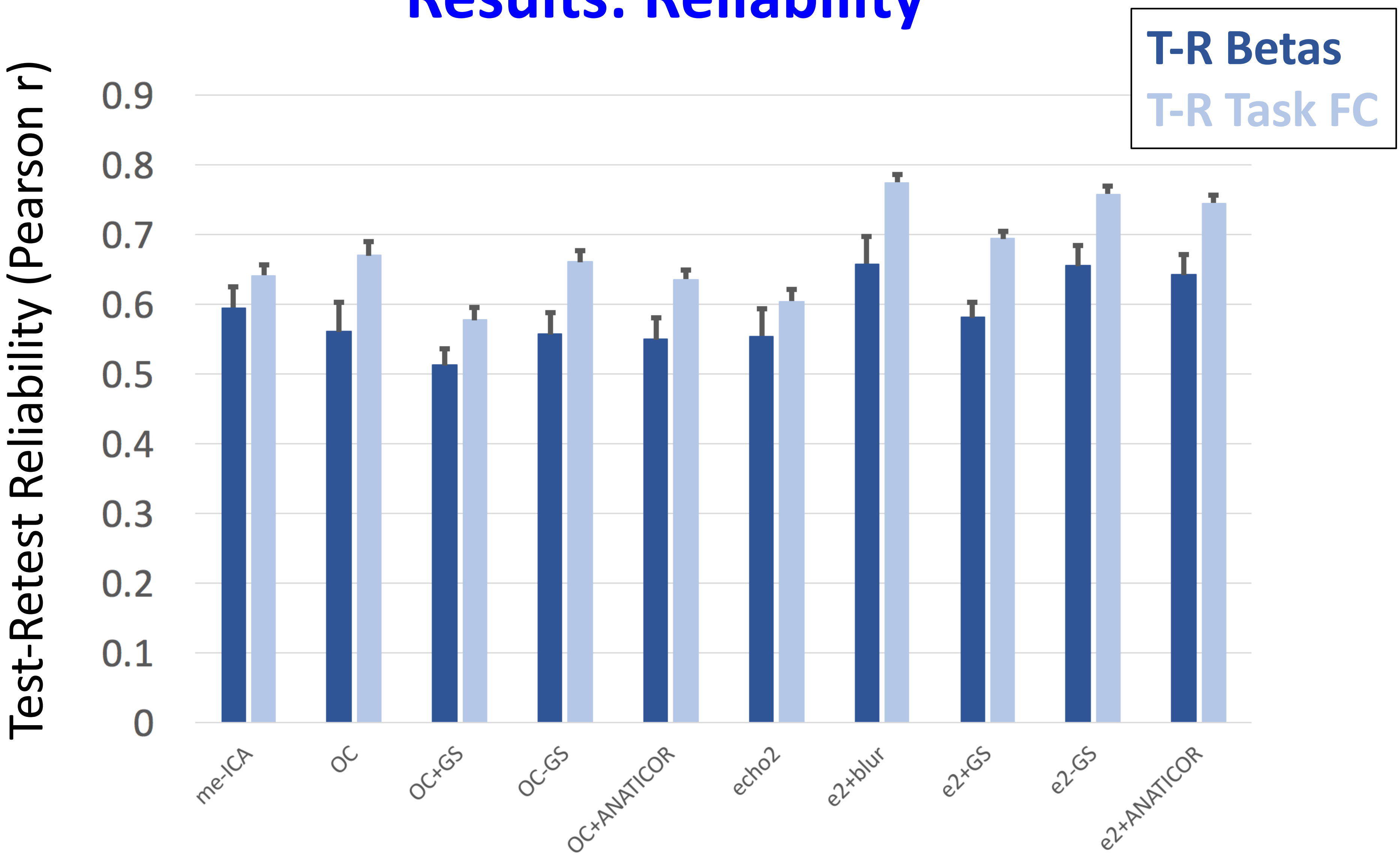

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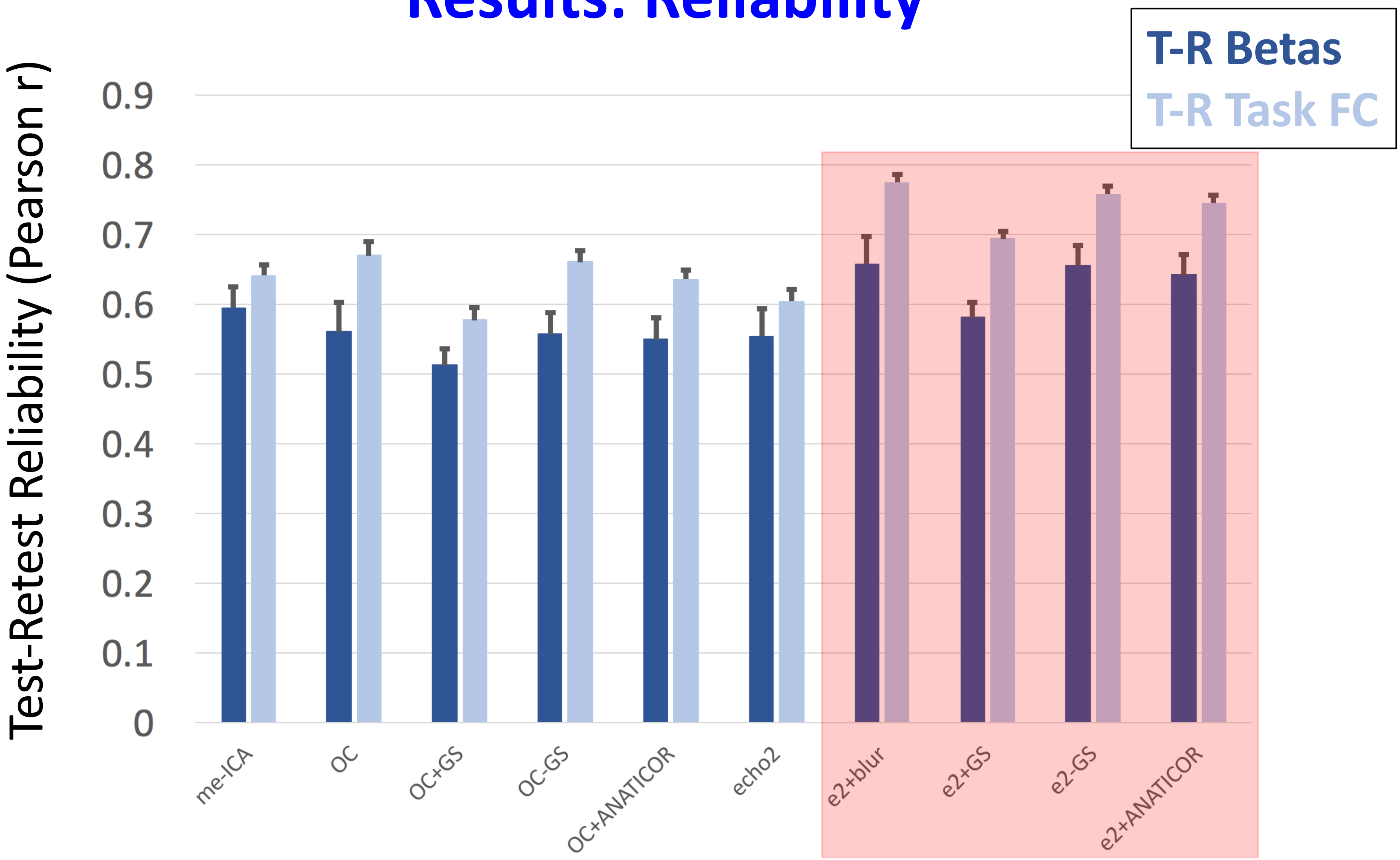

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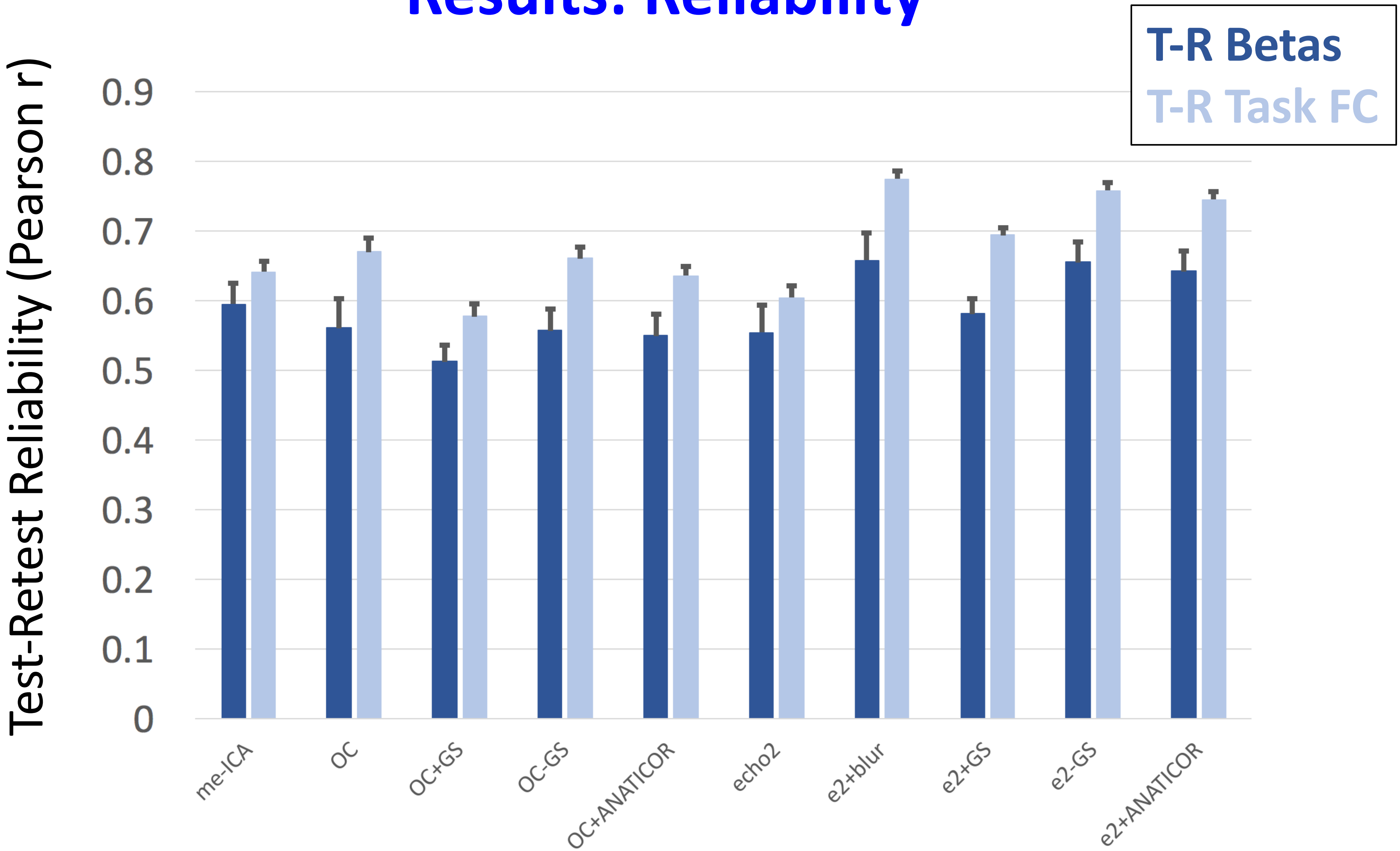

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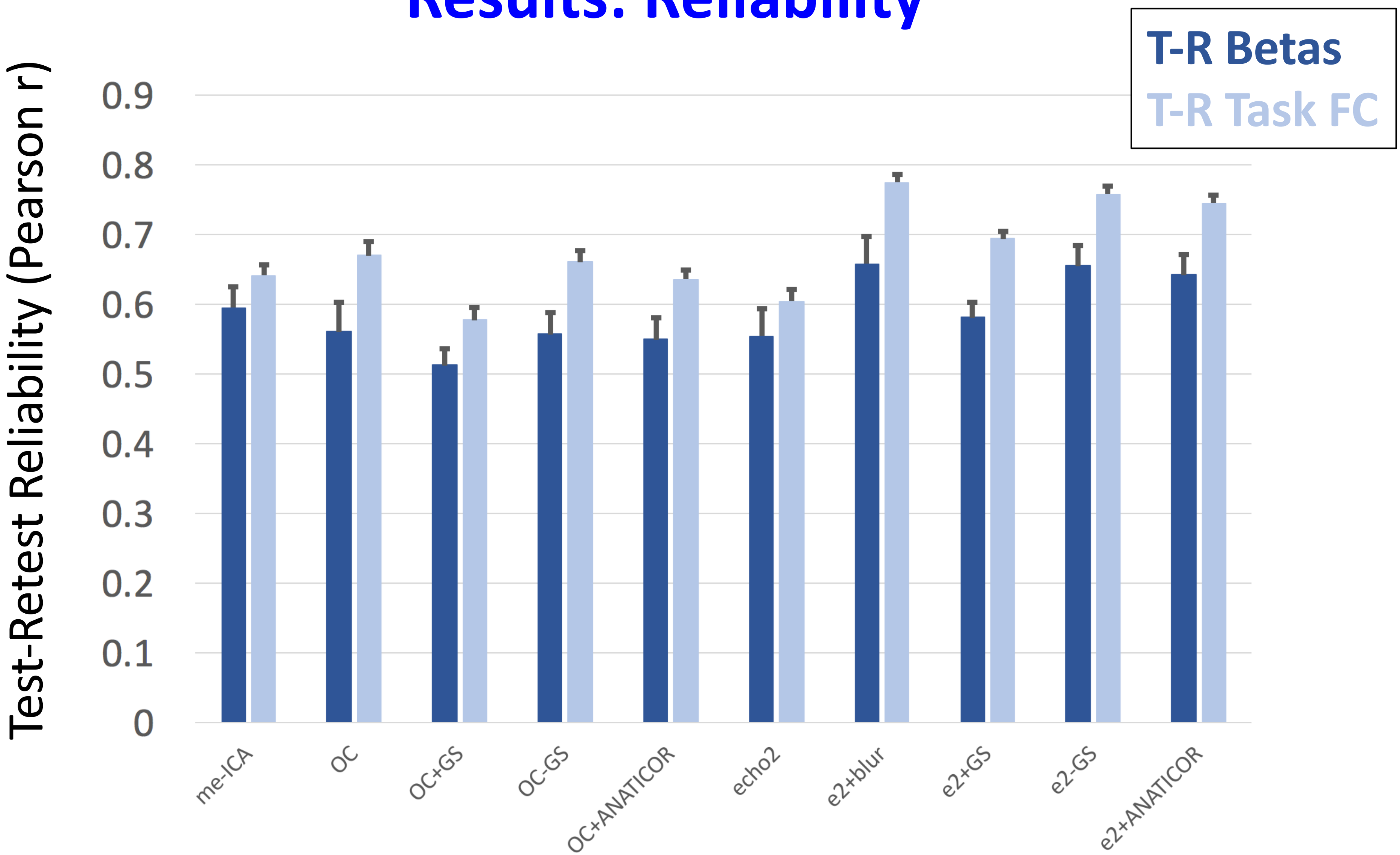

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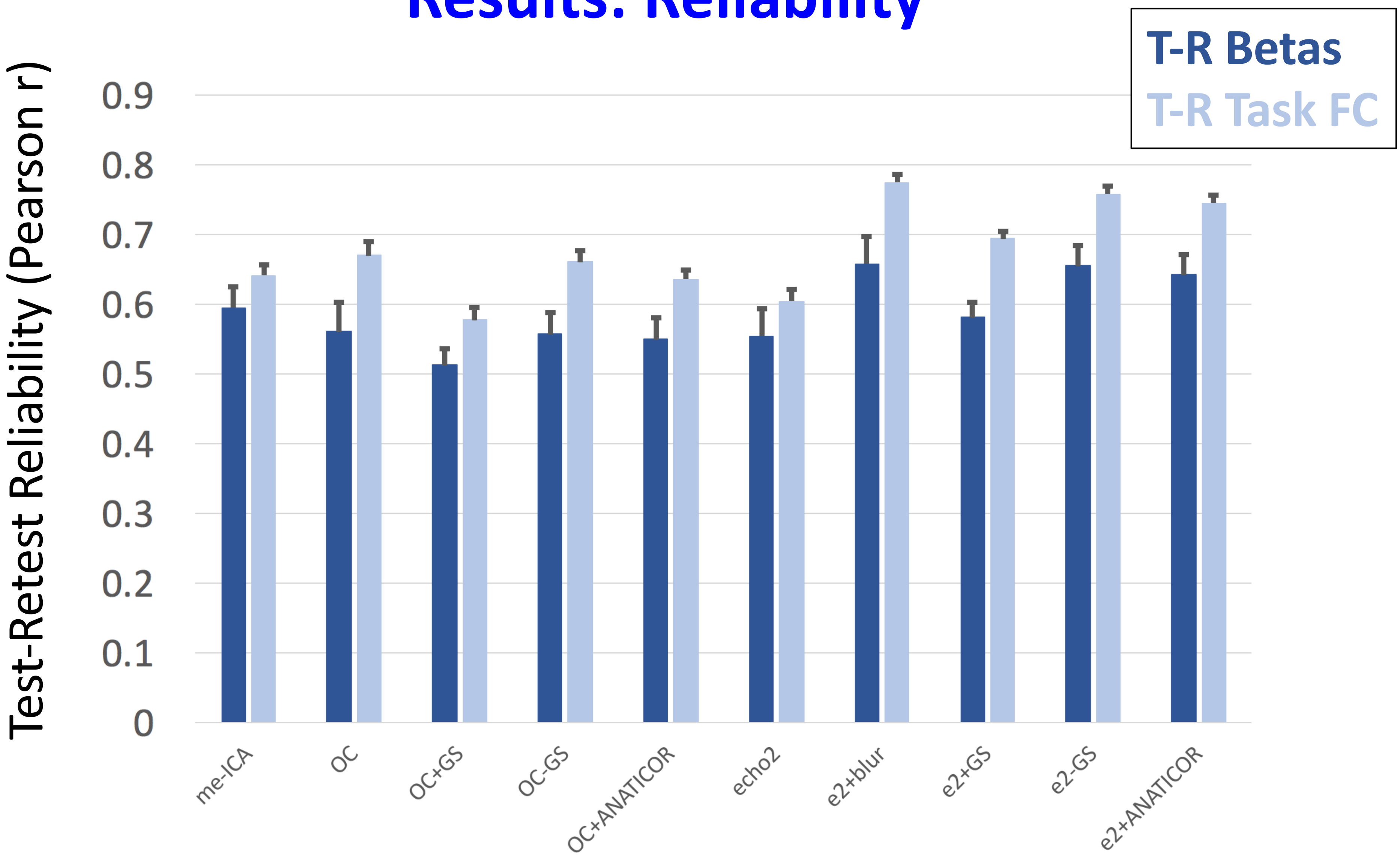

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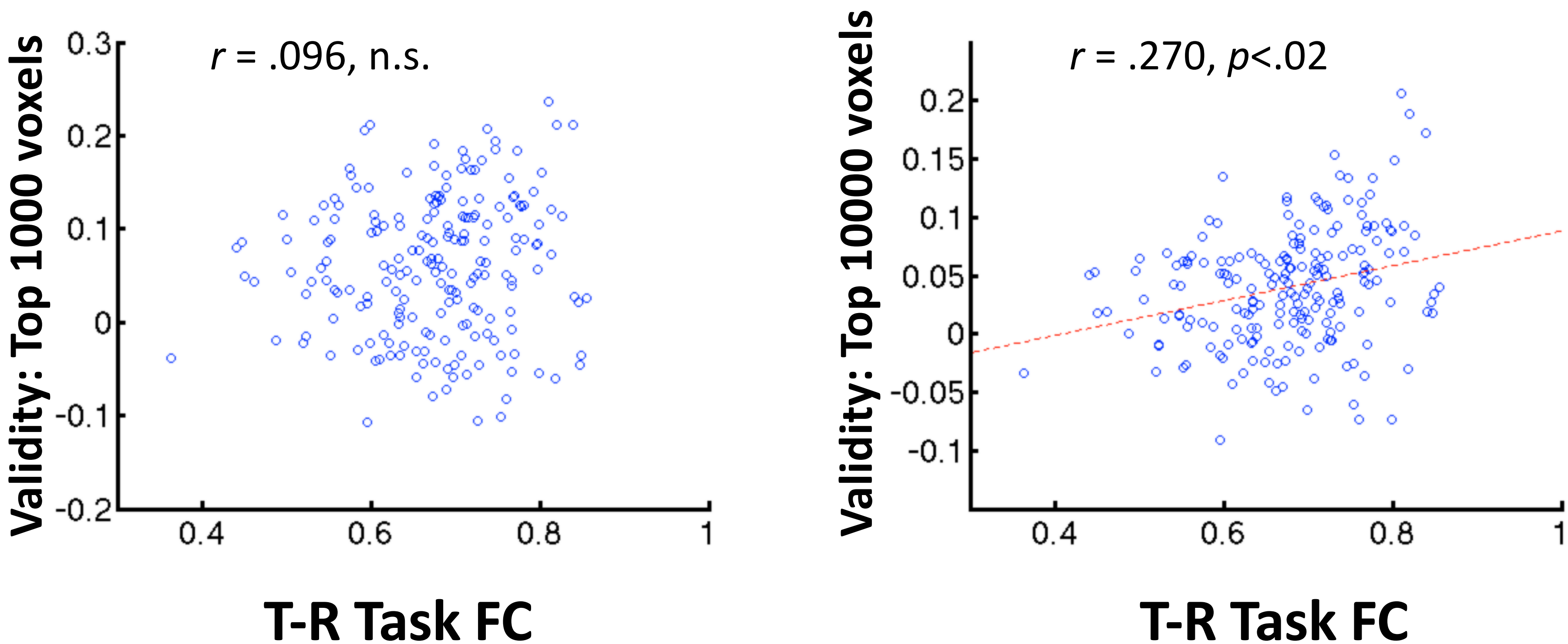
4) Only task-based FC reliability is related to validity at lower thresholds (r = 0.270, p<.02)

Reliability vs. Validity



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- These preliminary results indicate that most of the nuisance regression approaches are removing signal of interest in addition to noise, with a slightly detrimental effect overall
- We plan on repeating these analyses using rest data for the same participants, correlating average overall response time with resting-state FC (significant correlations exist in me-ICA cleaned data)

Example from Our Lab: Functional Lateralization of Verbal, Visuospatial, and Motor Abilities

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PNAS

PNAS PLUS

Two distinct forms of functional lateralization in the human brain

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[a]Section on Cognitive Neuropsychology, Laboratory of Brain and Cognition, and [b]Scientific and Statistical Computing Core, National Institute of Mental Health, National Institutes of Health, Bethesda, MD 20892

Edited by Geoffrey K. Aguirre, University of Pennsylvania, Philadelphia, PA, and accepted by the Editorial Board July 25, 2013 (received for review February 8, 2013)

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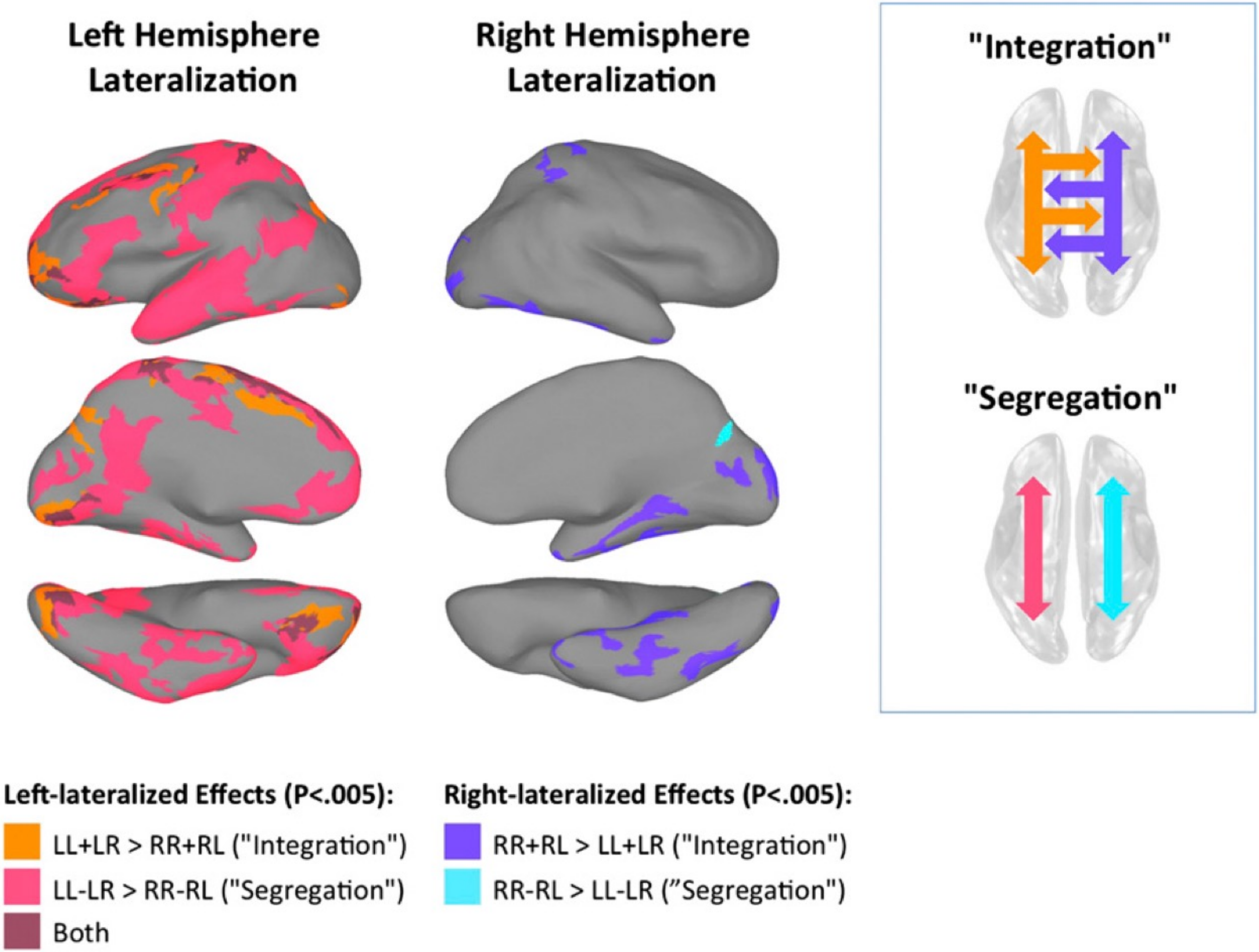
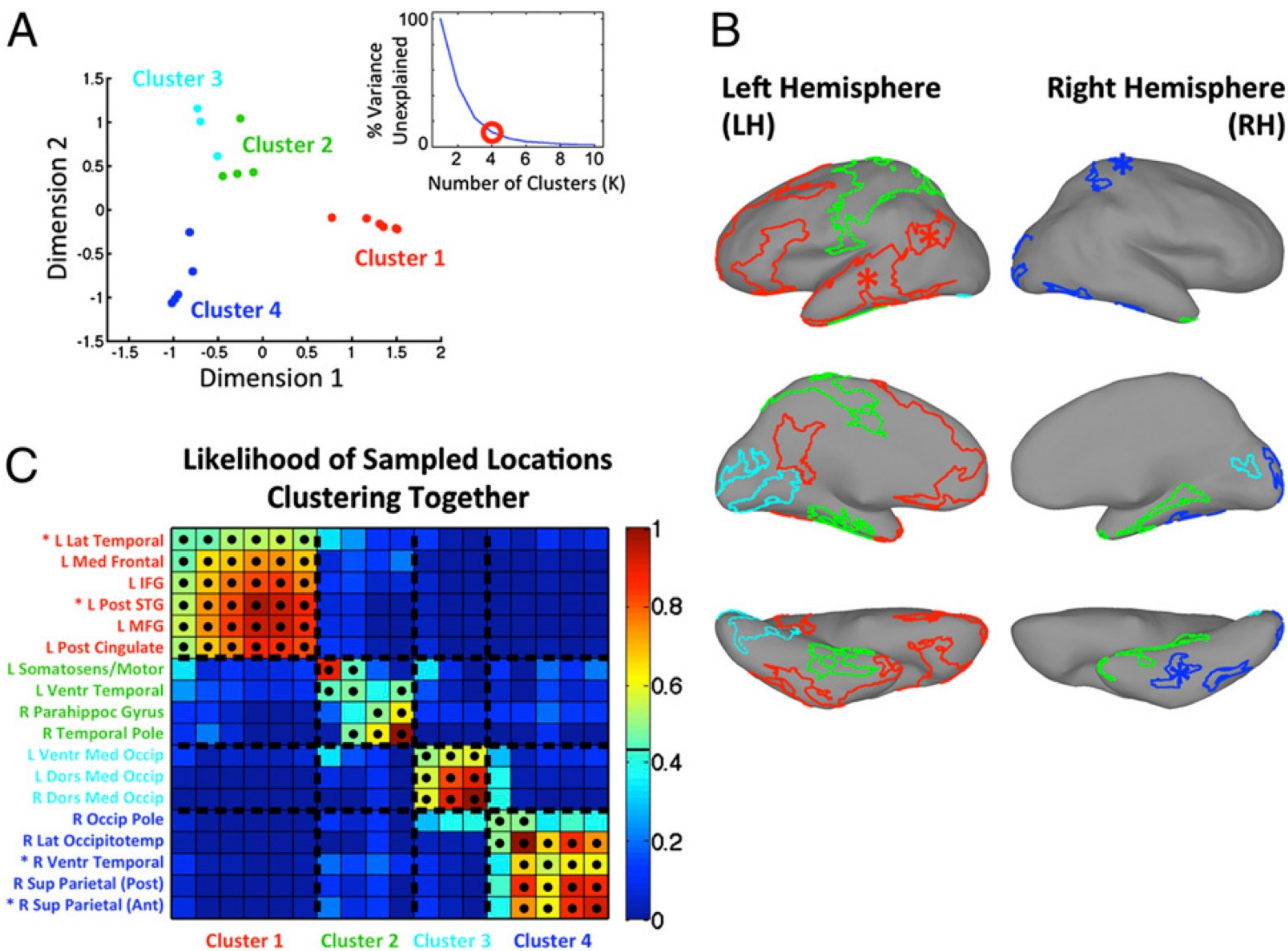
Do the hemispheres differ in their within- vs between-hemisphere interactions ?

Does lateralization magnitude predict goodness of function?

Qualitatively Different Forms of Lateralization on Left vs Right




A
B
C
Cluster 1
Cluster 2
Cluster 3
Cluster 4
Dimension 1
Dimension 2
% Variance Unexplained
Number of Clusters (K)
Left Hemisphere (LH)
Right Hemisphere (RH)
Likelihood of Sampled Locations Clustering Together
* L Lat Temporal
L Med Frontal
L IFG
* L Post STG
L MFG
L Post Cingulate
L Somatosens/Motor
L Ventr Temporal
R Parahippoc Gyrus
R Temporal Pole
L Ventr Med Occip
L Dors Med Occip
R Dors Med Occip
R Occip Pole
R Lat Occipitotemp
* R Ventr Temporal
R Sup Parietal (Post)
* R Sup Parietal (Ant)

Lateralization Magnitude Predicts Cognitive Ability