On the relationship between gray matter and behavioral data: lessons learned

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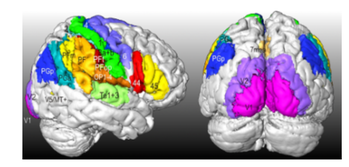
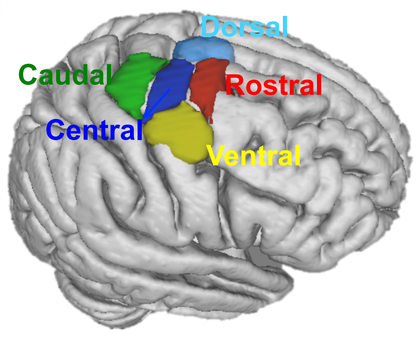


Introduction

Co-activation based parcellation of the right premotor cortex (PMd)[1]:



Quantitative functional decoding of the five subregions:[1]

Brainmap database:

hundreds of fMRI and PET studies

"Behavioral domain" and "paradigm class" metadata

Combination of forward P(Activation|Task) and backward inferences P(Activation|Task)

Significance: *P* <.05 corrected for multiple tests.

	Rostral	Caudal	Central	Ventral	Dorsal
Flexion/Extension					
Isometric force					
Drawing					
Finger tapping					
Sequence recall/learning					
Visual pursuit/tracking					
Visual attention/distractor					
Saccades					
Anti-saccades					
Mental rotation					
Imagined movement					
N-back					
WCST					

➔ **Aim of this study: Confirmation/completion of behavioral profiles of the 5 PMd subregion with cognitive-morphologic correlations.**

Methods

Big datasets of healthy population:

Forschungszentrum Jülich (FZJ):
n = 87, age range: 21-71, 54% female

NKI:
n = 126, age range: 18-81, 65% female

Cohorts matched for age, gender, education, depression and handedness scores

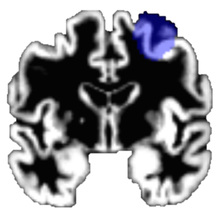
Behavioral data:

Standard neuropsychological tests (attention, executive functioning, working memory, verbal fluency)
+ basic upper limbs motor assessment in FZJ

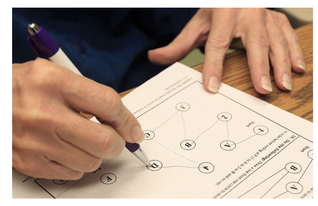
Brain structural data:

T1-image (1mmx1mmx1mm)
Voxel-based morphometry (VBM8[2], unified segmentation approach)
Grey matter volume (GMV) within the five subregions (ROIs):
sum adjusted for tissues (GM and white matter) total volume

Cognitive-morphologic correlations:



GMV ROI



Behavioral performance
E.g. Trail Making Test (TMT)

Full correlation + Partial correlation
Significance set at *P* < .05 uncorrected for multiple tests

Random sampling:

Partial correlation in 1000 subsamples (n = 30)

Results

	Full correlation					Partial correlation				
	Rostral	Caudal	Central	Ventral	Dorsal	Rostral	Caudal	Central	Ventral	Dorsal
FZJ sample										
10s-R			.10		-.17	-.09	-.20		-.10	-.10
10s-L	-.08		.13	.13	-.14	-.11	-.14			
10s-Median			.16	.12	-.17	-.11	-.20			-.10
10x30-R	-.18	**-.26**		.12		**-.23**	**-.34**	-.13		
10x30-L	-.11	-.10		.18		-.14	-.16		.13	
10x30-Median	-.12	-.13		.17		-.17	-.20	-.10	.11	
TMT-A		.10	.13	.14		-.12				
TMT-B		-.14				-.14	**-.24**	-.10	-.11	
DST		.09			-.09				-.09	
DS-F Span			.12	.13			-.08			
DS-B Span	-.11	-.15	-.17		-.16	-.20	**-.25**	**-.24**		-.12
Benton f	.10	-.12			.09	.17		.11	.14	
Benton w	-.09	.16			-.08	-.15	.08	-.08	-.11	
Stroop Read	.15	.11	.13	.14		.09		.11		
Stroop Name						-.10				
Stroop CW		.14	.16	**.23**	-.12		.11	.15	.18	-.09
Block Tap-F	.16	.14	.17	.15	-.08	.08		.15		
Block Tap-B	.12		.09	.15	-.11				.11	-.09
COWAT	.09	.07		0,10	-.12					-0,10
NKI sample										
TMT_A	.11			-.09		.12			-.10	-.07
TMT_B	.14		.15	**.22**	.08	.16	-.09	.07	**.22**	.10
CardSort._F		-.22			-.15		-.21			-.14
CardSort._R	.11	-.14	.11			.12	-.14			
VF_Letters	-.17	-.11	-.15	-.10	-.11	-.16	-.11	-.15	-.09	-.10
VF_Categ.							-.10			
VF_Switching		.10	.07				.09			
DF_Fill.Dots	-.07	-.08	**-.20**		-.10	-.07	-.09	**-.22**		-.11
DF_Emp.Dots	-.09	-.12	**-.20**		**-.18**	-.09	-.14	**-.23**		-.18
DF_Switching		-.13	-.12	-.15	-.08		-.12	-.12	-.15	-.07
Stroop Read	.08		.10	.09	-.08	.09		.07	.07	-.08
Stroop Name					-.11					-.12
Stroop CW				.10	-.17			-.09	.08	-.16
20 Questions	-.16			-.15	**-.19**	-.17	-.09	-.10	-.19	**-.22**
WordContext	-.17	-.19	-.22	-.13	-.20	-.17	-.17	-.24	-.14	-.19
Tower Test	**.26**	**.22**	**.19**	.10	.16	**.26**	**.21**	**.24**	.11	.14
ANT_Alert		-.14					-0,13			
ANT_Orient			.10							
ANT_Conflict	-.07	**-.24**		-.15		-.07	**-.24**	-.10	**-.19**	

Notes: Bold font indicates significant correlations. Color code: red = positive; blue = negative. DST, digit symbol test, DS; digit span; COWAT, Controlled Oral Word Association Test; VF/DF, verbal fluency/design fluency; ANT, Attentional Network Task.

General findings:

Low correlation coefficients (<.35)

Small proportion of significant correlations (6.6 %)

High proportion of significant negative correlation (> 50%)

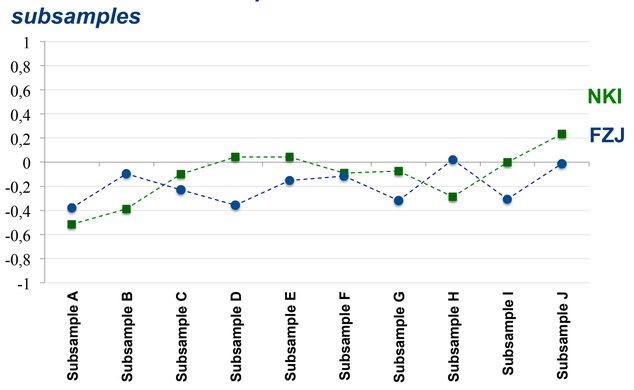
Inconsistency across samples: Magnitude, significance and direction of correlations vary across samples

Random sampling:

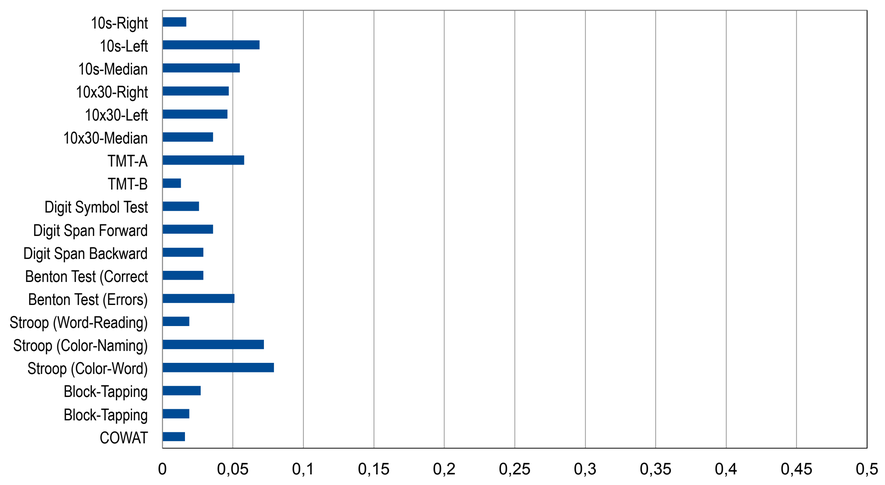
Proportion of significant correlation below or around .05 (/1000 sampling)

Random variations of correlation in direction and magnitude

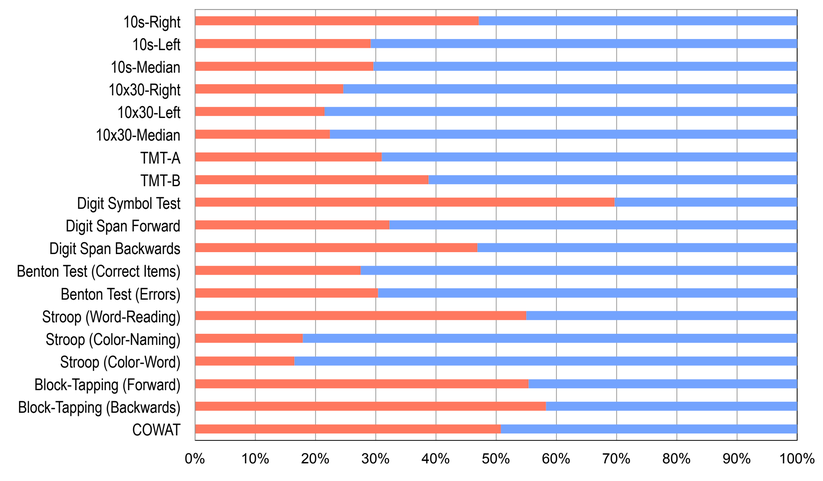
Variations of coefficient correlation between GMV of caudal ROI and TMT-B performance across 10 random subsamples



Proportion of significant correlations for rostral ROI out of 1000 random subsamples of FZJ:



Percentage ratio of positive (red) and negative (blue) correlation coefficient in rostral PMd ROI across 1000 subsamples of FZJ cohort:



Conclusions

No confirmation or completion of the profiles revealed by functional decoding based on fMRI-activations.

Mostly correlations whose directions were opposite to those expected (i.e., we expected more GMV to be related to better test performance).

Unstable correlations across samples and subsamples

➔ Limitation of such correlations in healthy population: The results may not be replicable across similar distinct samples.

From a more conceptual point of view: functional specialization of some cortical regions, as highlighted by fMRI studies, does not necessarily imply a significant covariance of their actual structure with related standard task performance in the healthy population.

References:

[1] Genon, S., Müller, V.I., Cieslik, E., Hoffstaedter, F., Langner, R., Fox P.T., Eickhoff S.B. (2014). 'Examining the right dorsal premotor mosaic: a connectivity-based parcellation approach'. OHBM Annual Meeting.

[2] Friston, K.J., Ashburner, J. (2000). 'Voxel-Based Morphometry-The methods'. NeuroImage, vol. 11, pp. 805-821.

Acknowledgment: This study was supported by the Deutsche Forschungsgemeinschaft (DFG, EI 816/4-1; S.B.E. and LA 3071/3-1; R.L. and S.B.E.), the National Institute of Mental Health (R01-MH074457; S.B.E.) and the Helmholtz Initiative on systems biology (The Human Brain Model; S.B.E.) and the Universitätsklinikum Düsseldorf.

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