University of Iowa Carver College of Medicine
University of Iowa Health Care

Department of Neurology

Tranel Lab | Boes Lab

Uncovering the Latent Structure of Visuospatial Ability and Predicting Visuospatial Dysfunction

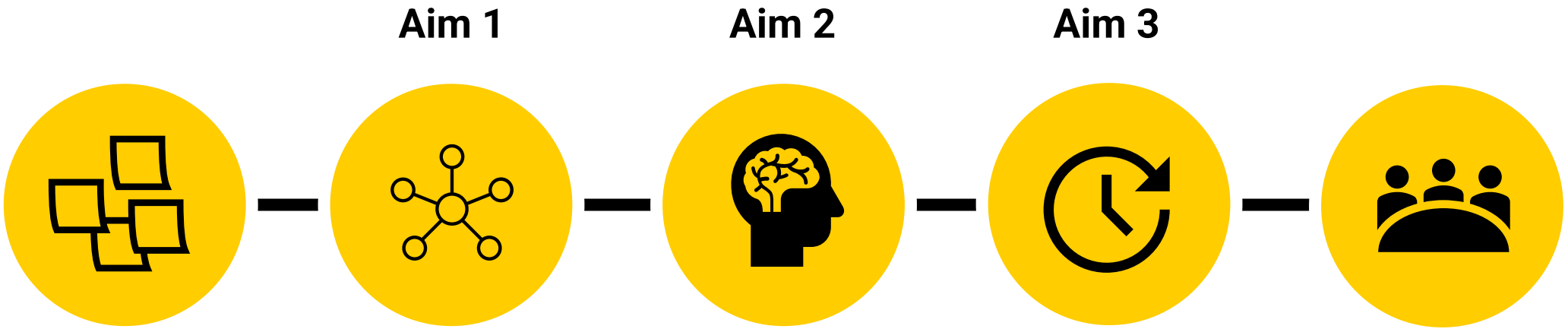
Doctoral Dissertation Defense

May 16, 2023

CHANGING MEDICINE.
CHANGING LIVES.®

Jax Skye, BS

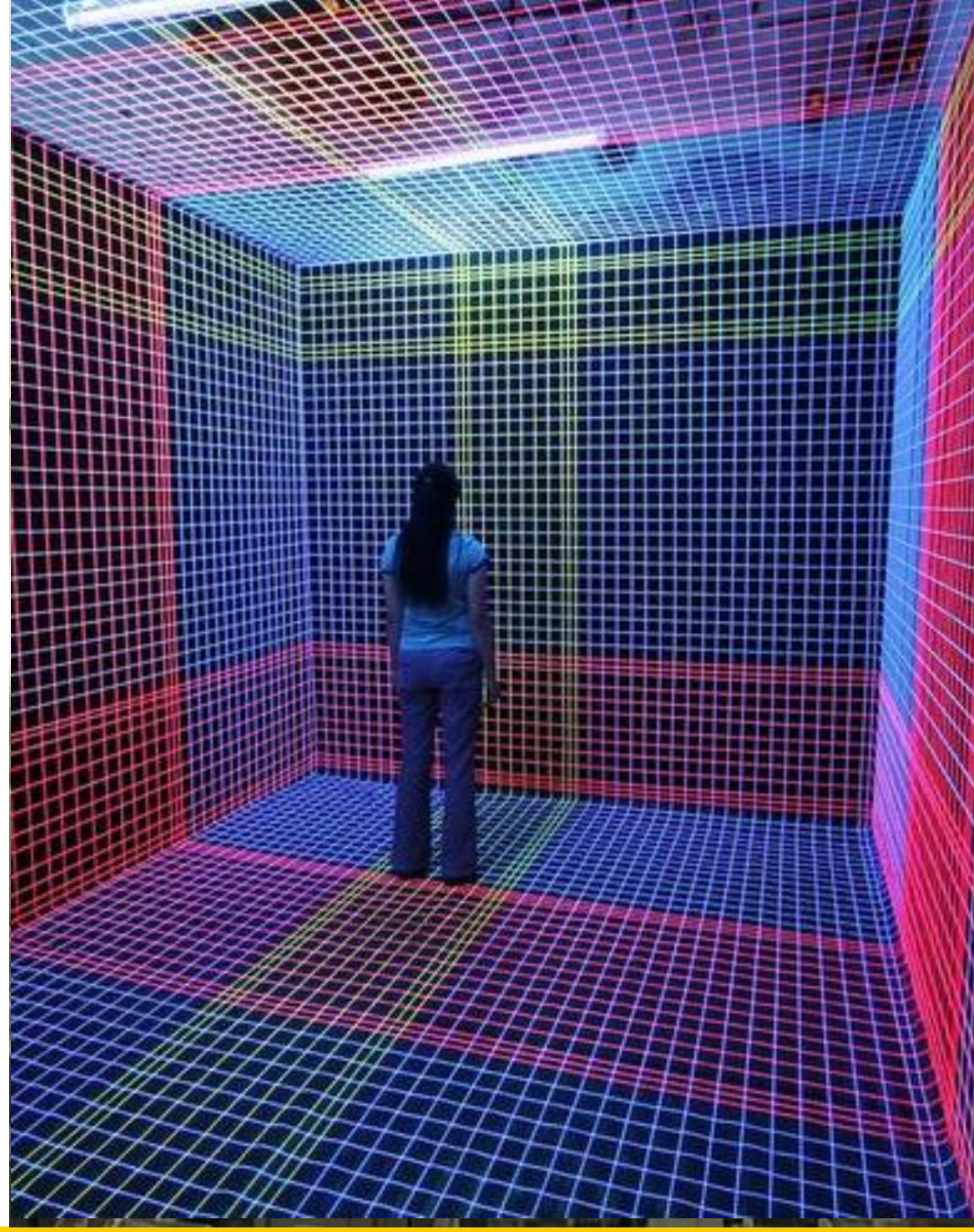
Where are we going?



Background

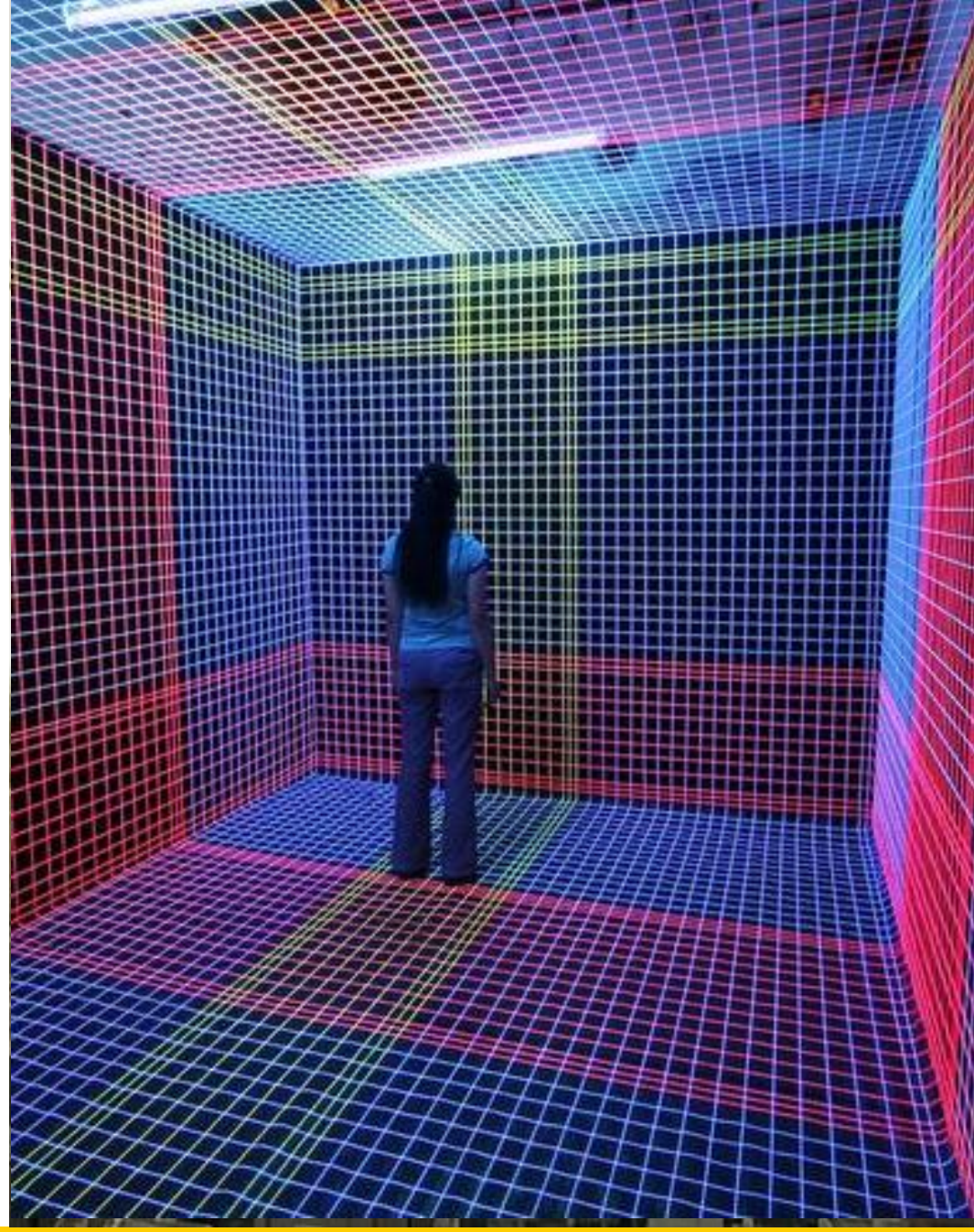
Visuospatial Ability

The ability to perceive, understand, and utilize visual information to create a map of one's spatial environment



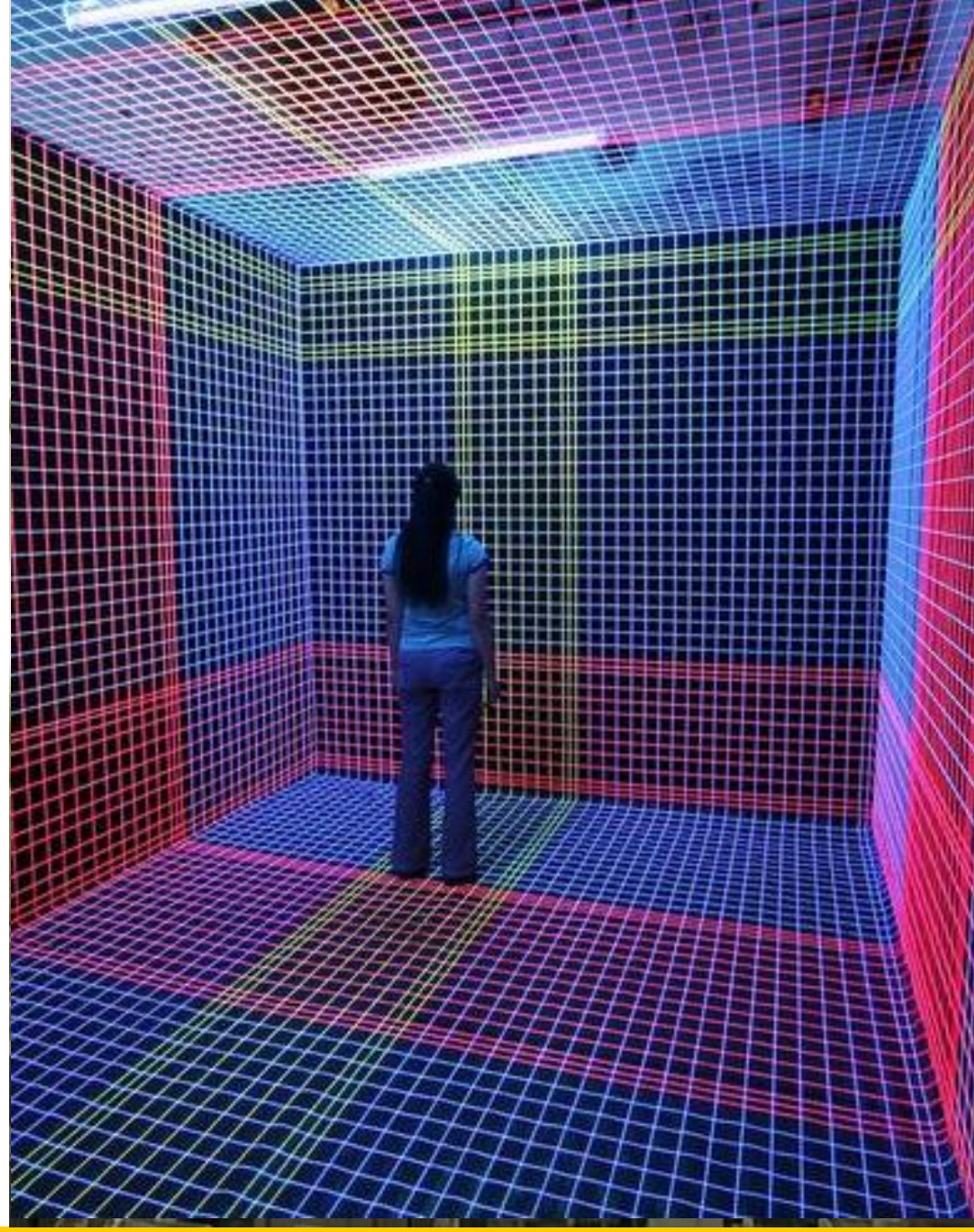
Visuospatial Ability

The ability to **perceive**, understand, and utilize visual information to create a map of one's spatial environment



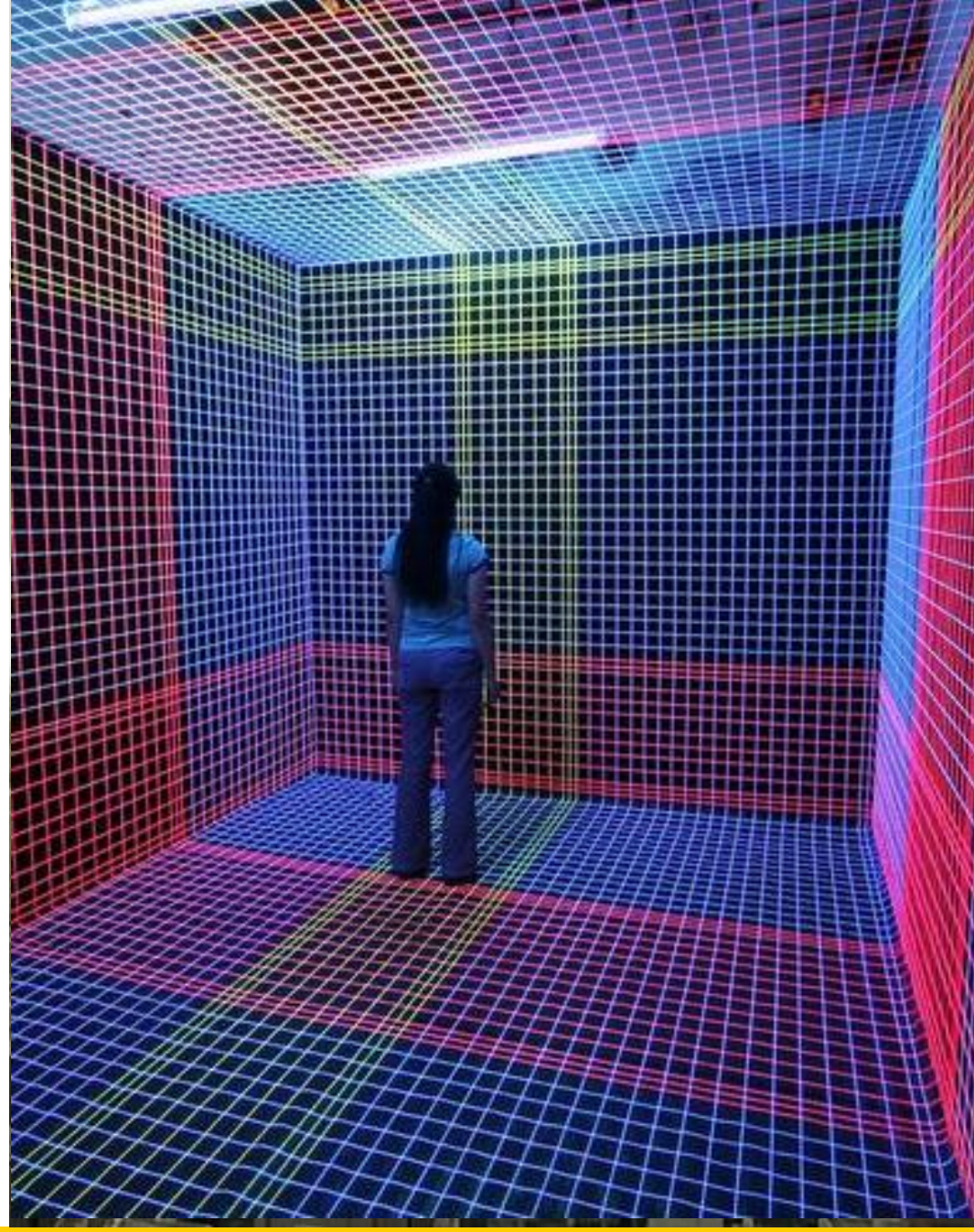
Visuospatial Ability

The ability to perceive, **understand**, and utilize visual information to create a map of one's spatial environment



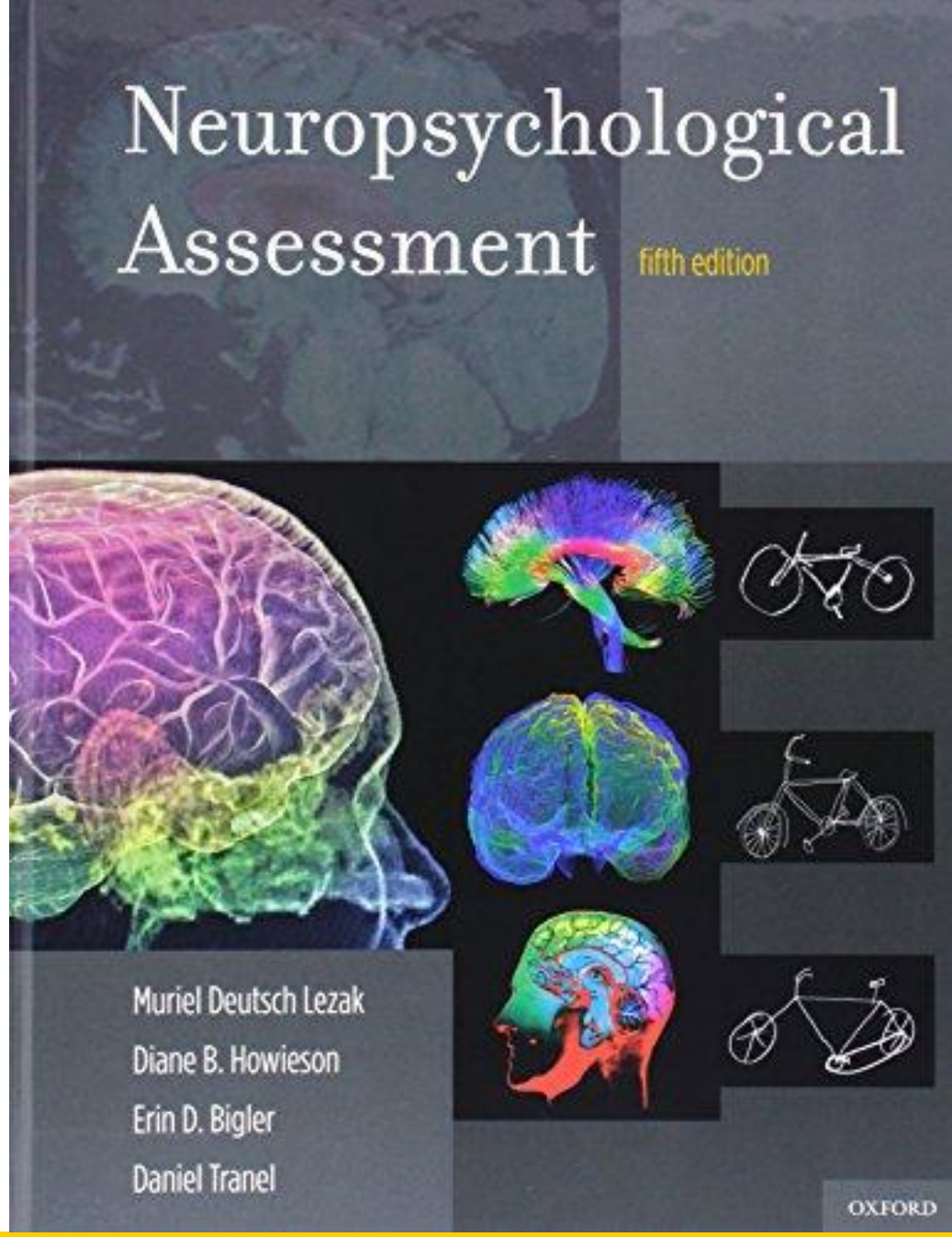
Visuospatial Ability

The ability to perceive, understand, and **utilize** visual information to create a map of one's spatial environment



Neuropsychological Assessment

- Clinical neuropsychology
- Identifies specific behavioral and cognitive impairments
- Standardized assessment
- Informs diagnoses and treatment recommendations

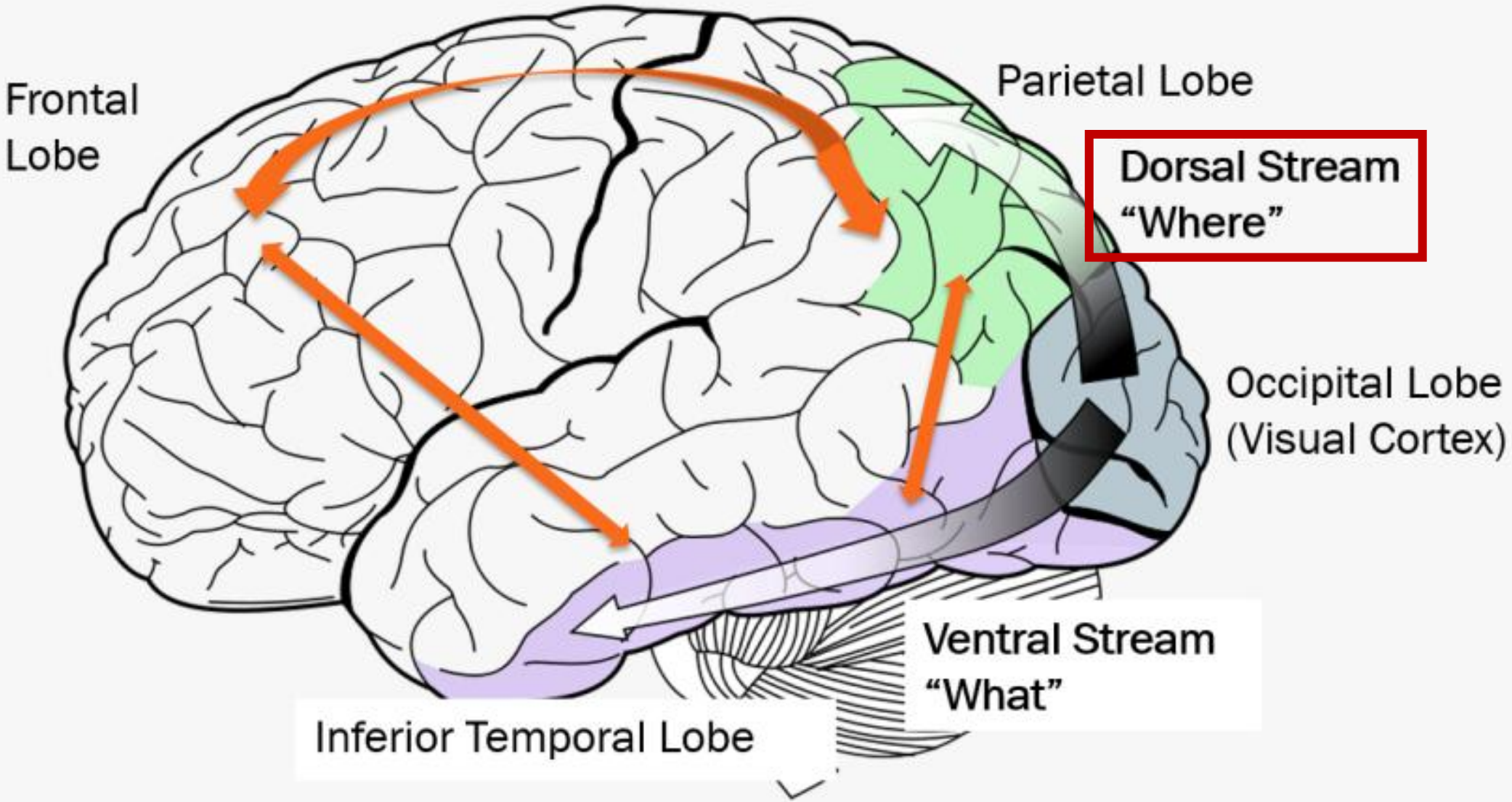


Neuropsychological Tests of Visuospatial Ability

WAIS subtests

- Digit-Symbol Coding
- Matrix Reasoning
- Block Design
- Picture Completion
- Symbol Search

- Benton Facial Recognition Test
- Judgment of Line Orientation
- Hooper Visual Organization Test
- Rey-Osterrieth Complex Figure copy
- Clock Drawing
- Benton Visual Retention Test
- Spatial Span


Frontal Lobe
Parietal Lobe
Dorsal Stream
"Where"
Occipital Lobe
(Visual Cortex)
Ventral Stream
"What"
Inferior Temporal Lobe

Why do we need to predict visuospatial dysfunction?

Inform recommendations

Set realistic recovery expectations

Guide cognitive rehabilitation

Aim 1

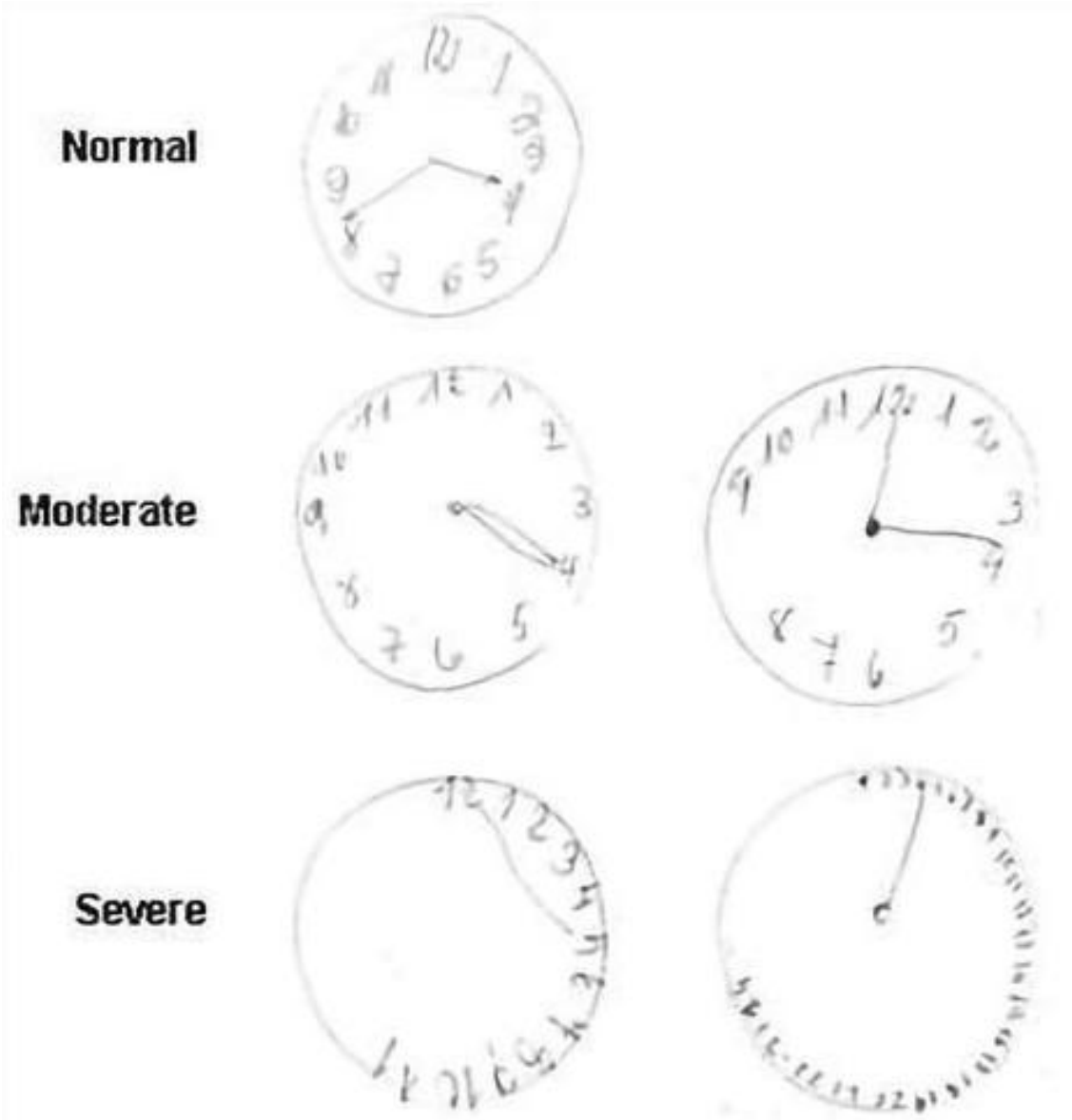
Identify and describe relationships between constituent processes that comprise visuospatial ability

Exploratory Factor Analysis

A data reduction technique

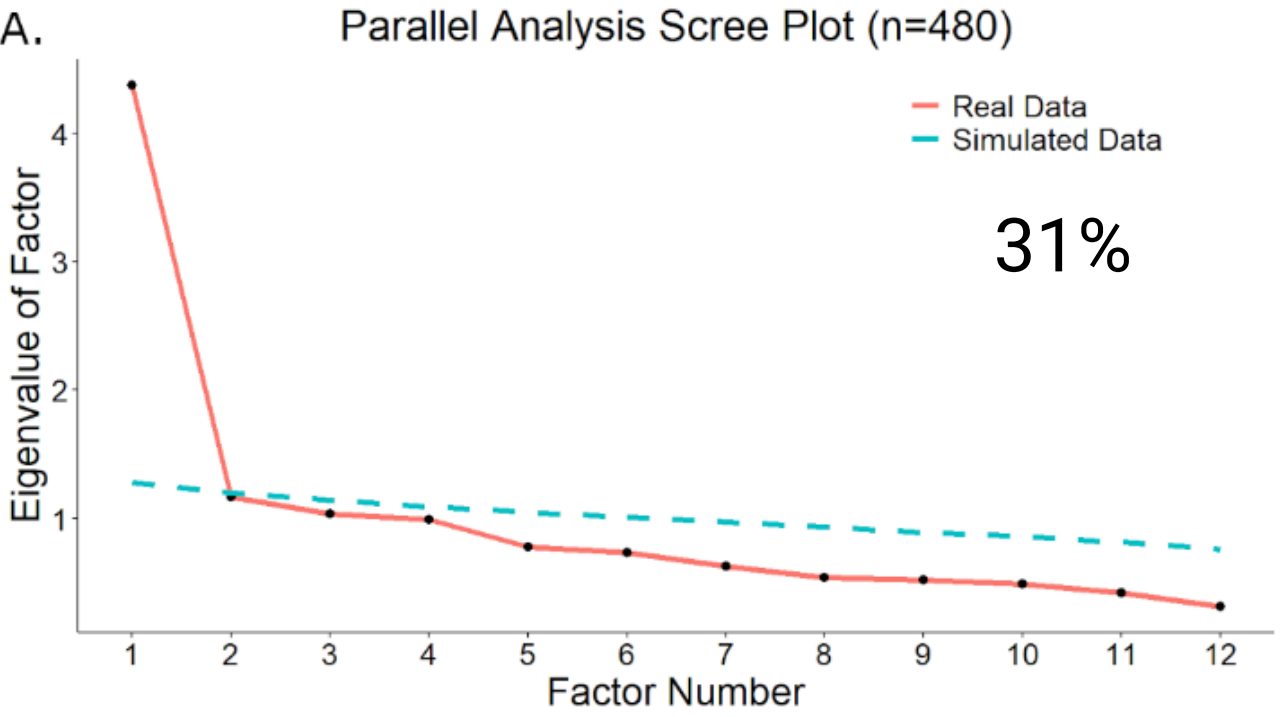
Neuropsychological Assessments of Visuospatial Function

- Processing speed
- Visuoconstruction
- Facial recognition
- Visual memory
- Working memory



		Iowa Registry Cohort (n=480)	Benton Clinic Cohort (n=117)	Washington University Cohort (n=104)
Age (in years)	mean (sd)	52.5 (15.0)	54.8 (14.9)	53.6 (10.4)
Education (in years)	mean (sd)	13.6 (2.67)	13.1 (2.12)	13.1 (2.36)
Gender	Men	258	60	55
	Women	222	59	49
Handedness	Right	437	107	95
	Left	34	10	9
	Both	9	2	0
Race	African American	6	1	69
	American Indian	2	0	0
	Caucasian	470	118	35
	Other/Unknown	2	0	0
Ethnicity	Hispanic	2	2	2
	Non-Hispanic	477	117	102
	Unknown	1	0	0
Lesion volume (in mm^3)	mean (sd)	46,066 (66,880)	47,329 (70,246)	29,814 (42,511)

		Iowa Registry Cohort (n=480)	Benton Clinic Cohort (n=117)	Washington University Cohort (n=104)
Lesion laterality	Right	183	44	54
	Left	196	58	50
	Bilateral	101	15	0
Etiology	Ischemic stroke	260	79	104
	Hemorrhage	104	7	0
	Tumor resection	87	19	0
	Focal contusion	16	0	0
	Herpes simplex or limbic encephalitis	12	0	0
	Epilepsy resection	0	14	0
	Multiple etiologies	1	0	0


A.
Parallel Analysis Scree Plot (n=480)
Real Data
Simulated Data
31%
Eigenvalue of Factor
Factor Number
1
2
3
4
5
6
7
8
9
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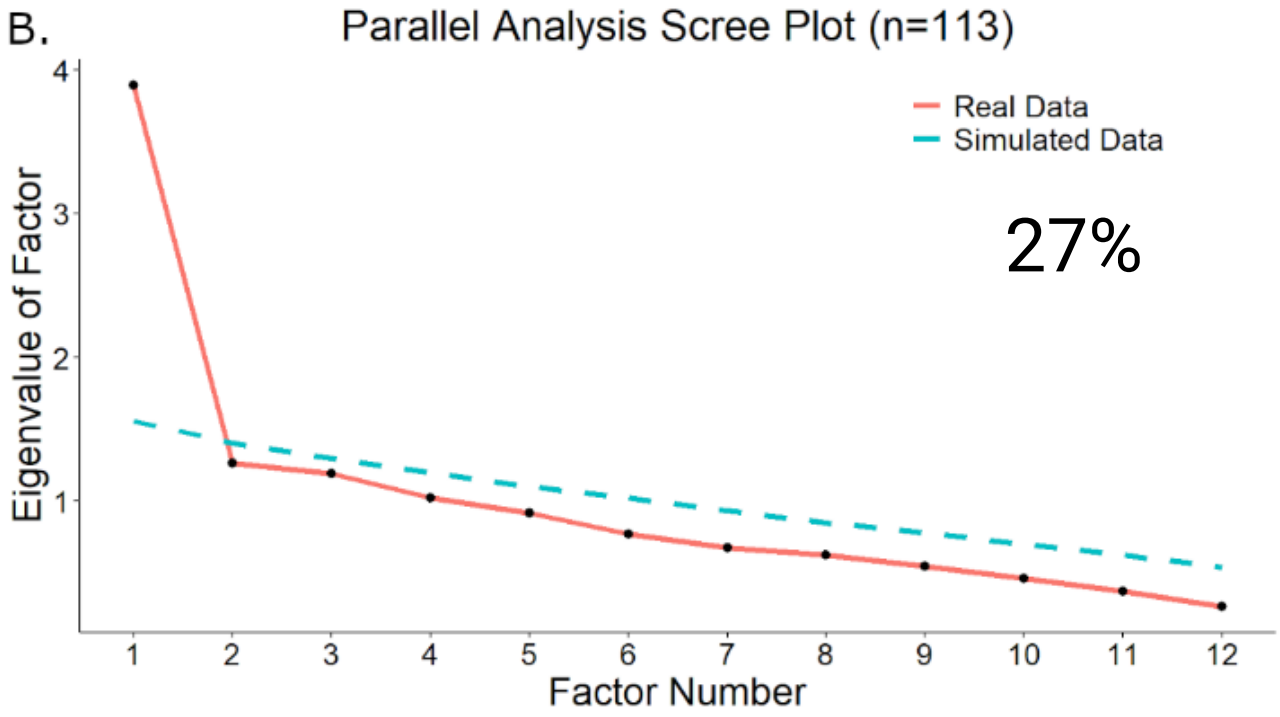
B.
Parallel Analysis Scree Plot (n=113)
Real Data
Simulated Data
27%
Eigenvalue of Factor
Factor Number
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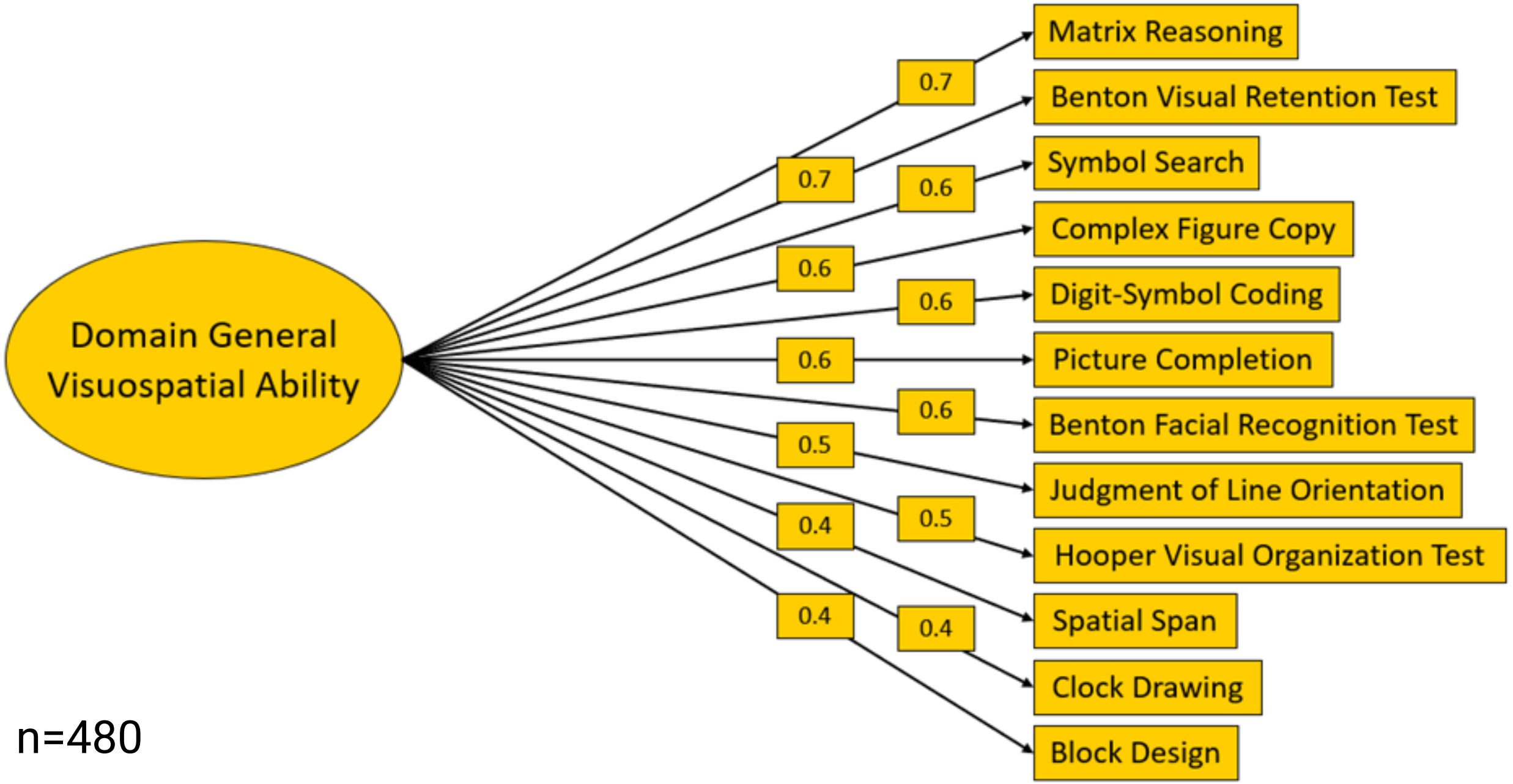
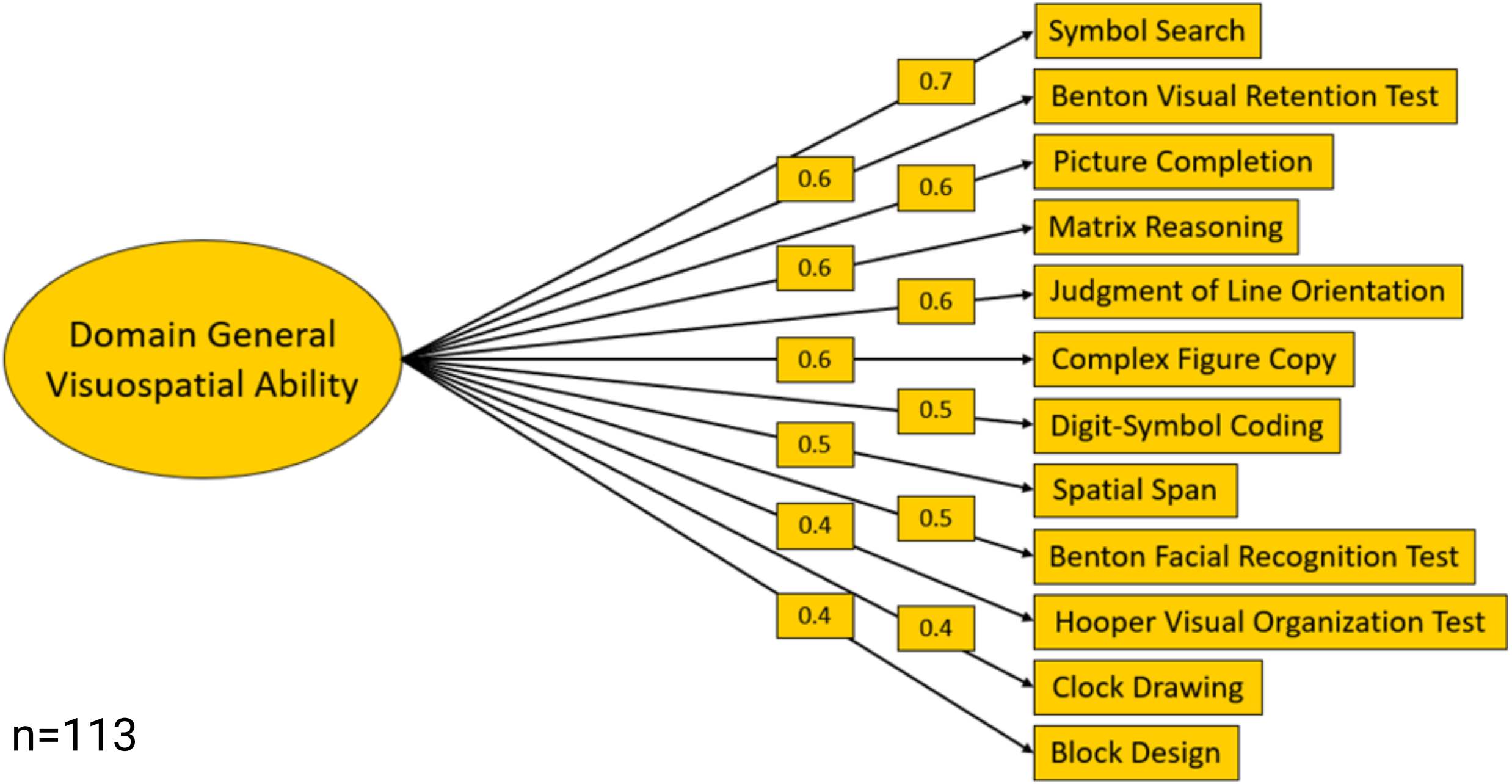
11
12


Domain General Visuospatial Ability
0.7
0.7
0.6
0.6
0.6
0.6
0.5
0.4
0.5
0.4
0.4
Matrix Reasoning
Benton Visual Retention Test
Symbol Search
Complex Figure Copy
Digit-Symbol Coding
Picture Completion
Benton Facial Recognition Test
Judgment of Line Orientation
Hooper Visual Organization Test
Spatial Span
Clock Drawing
Block Design

n=480


Domain General Visuospatial Ability
0.7
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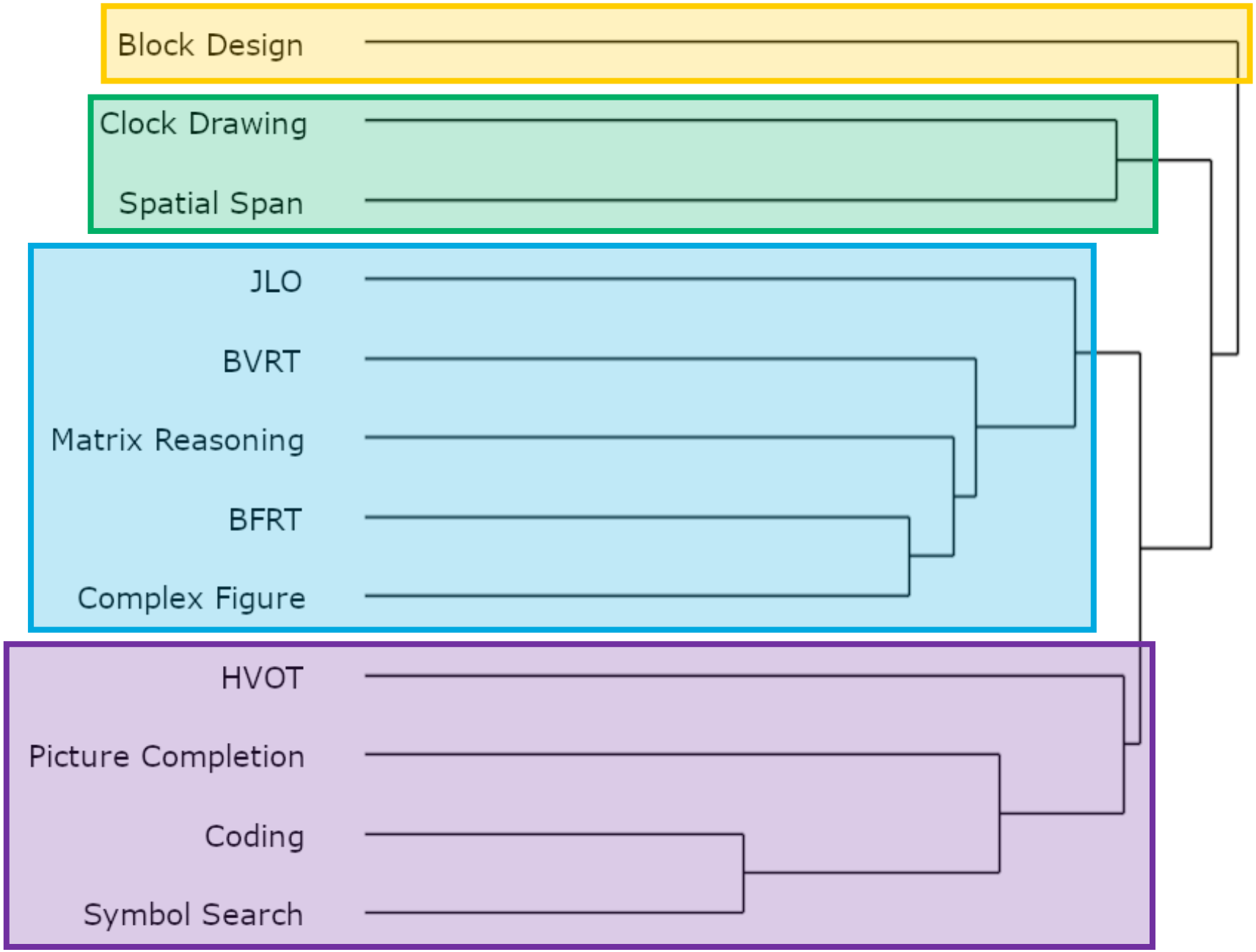
n=113


Block Design
Clock Drawing
Spatial Span
JLO
BVRT
Matrix Reasoning
BFRT
Complex Figure
HVOT
Picture Completion
Coding
Symbol Search

Aim 1 Conclusion

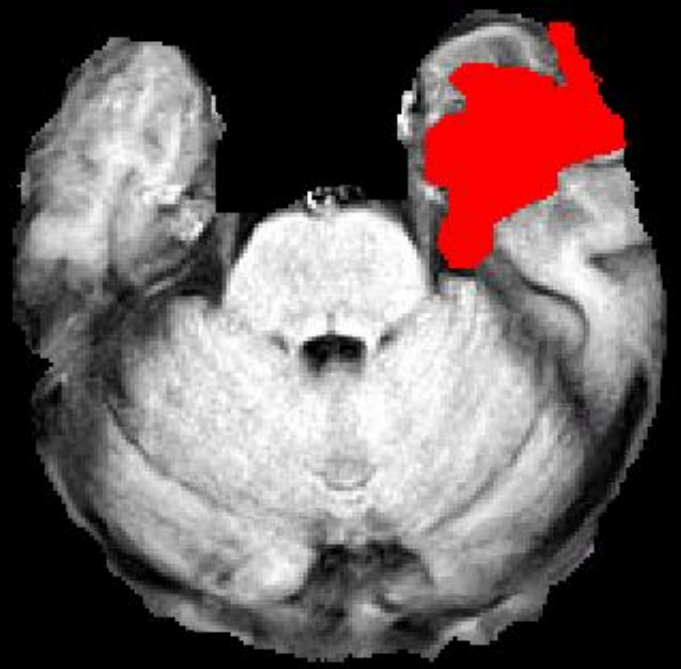
The covariance among twelve tests sensitive to visuospatial dysfunction was best captured by one factor, domain general visuospatial ability.

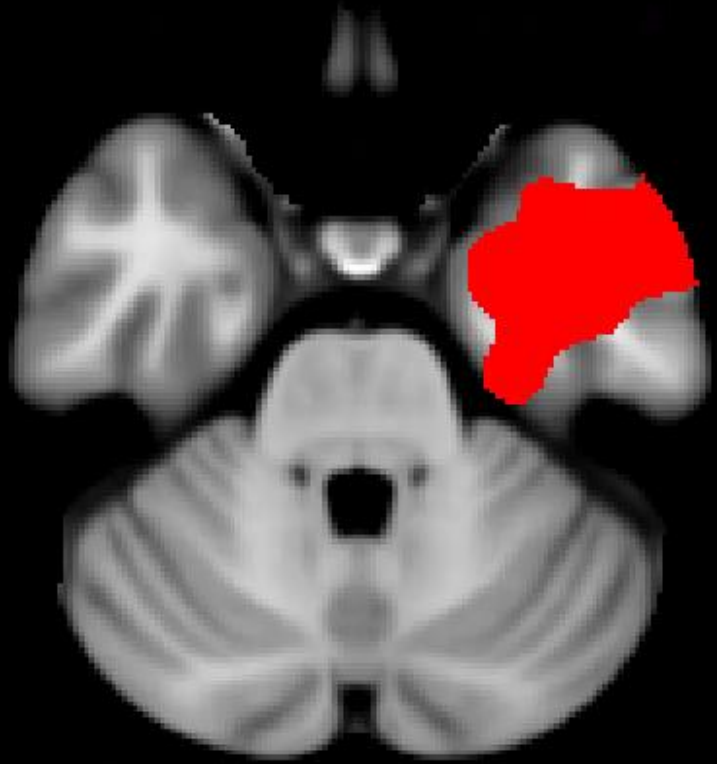
Aim 2

Identify neural correlates of the latent variable identified in Aim 1 using multivariate lesion-symptom mapping and lesion network mapping

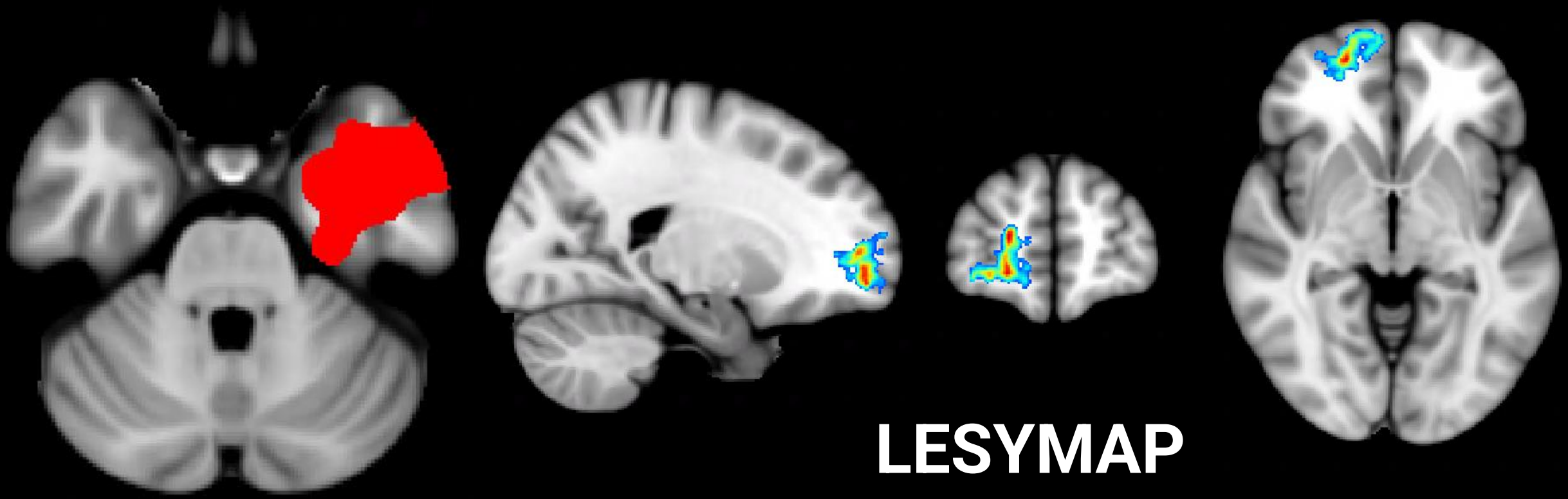
Functional Neuroanatomy of Visuospatial Ability

Lesion-Symptom Mapping

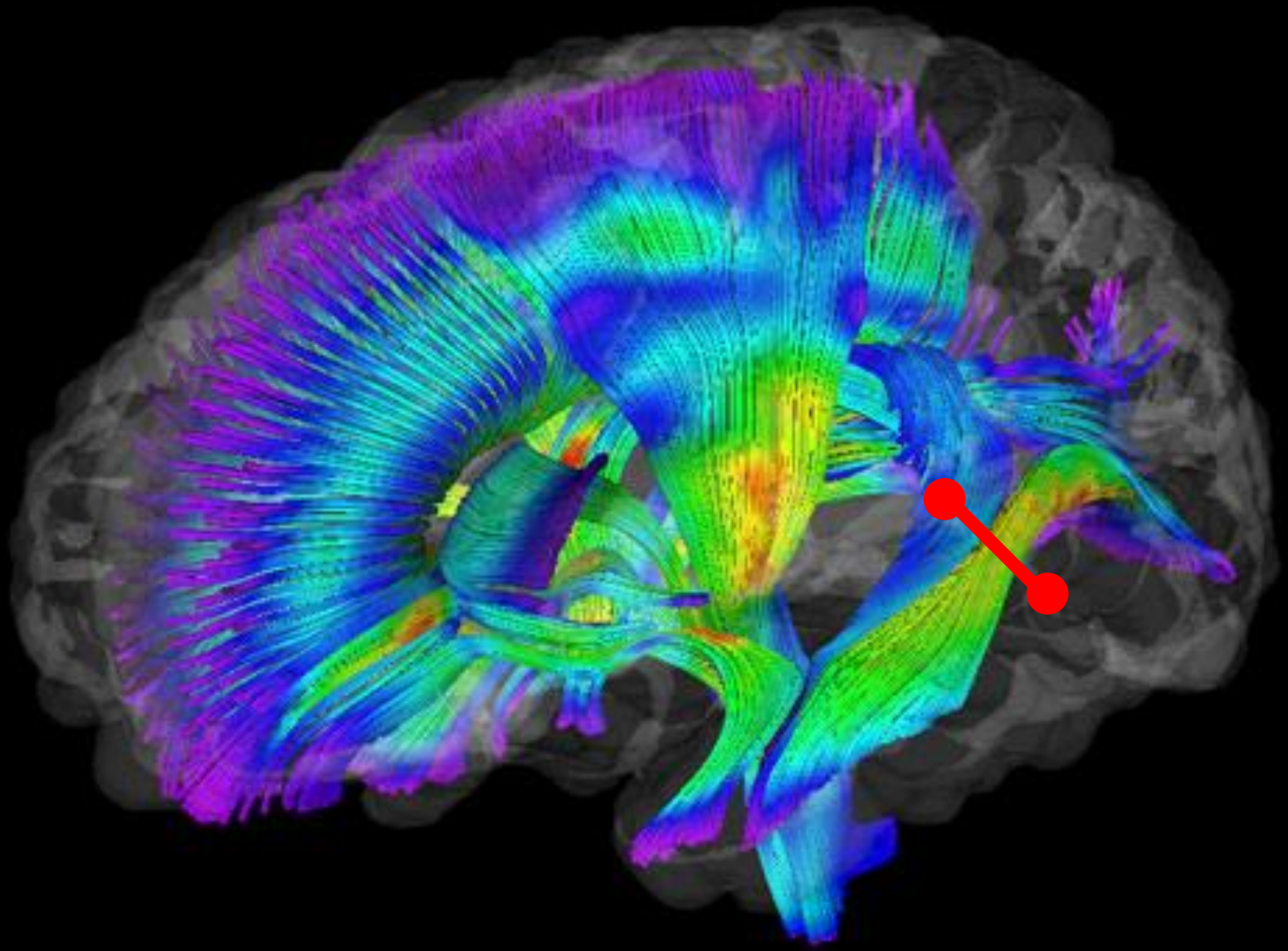




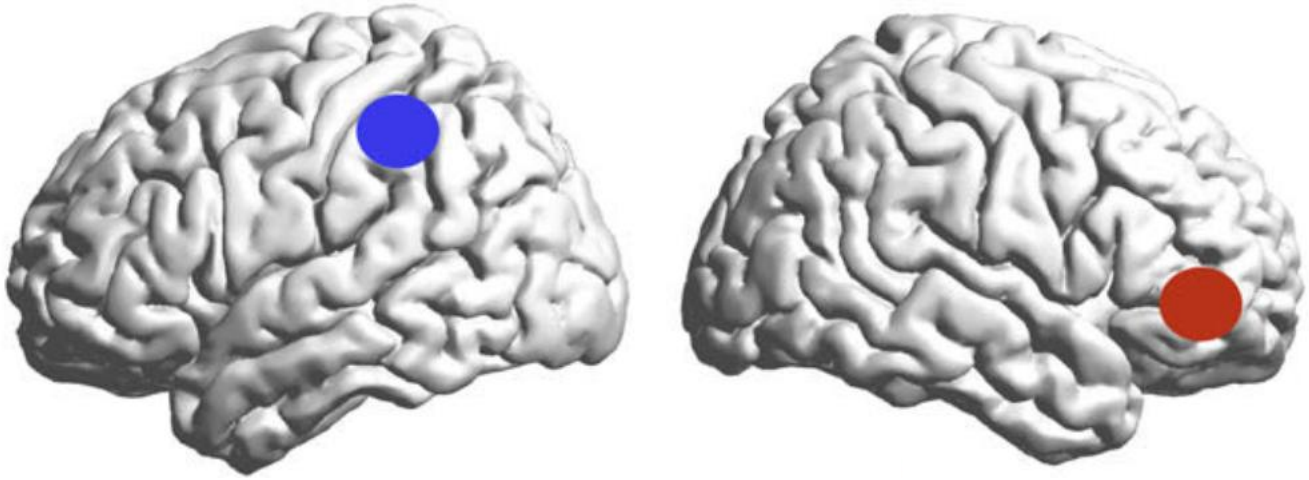
Lesion-Symptom Mapping

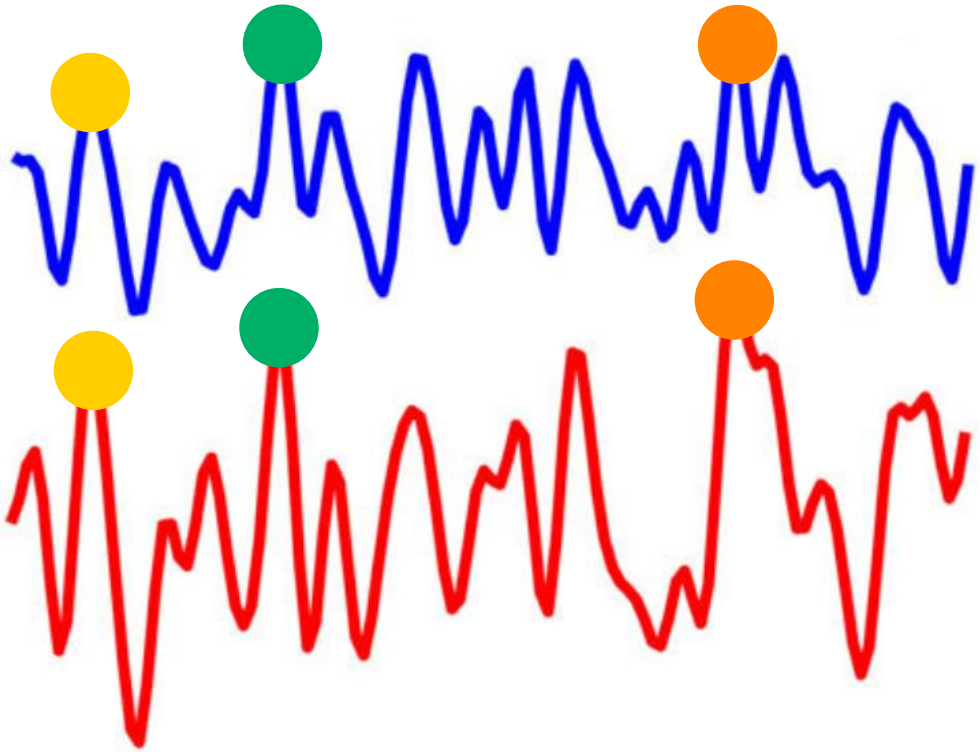


Structural Lesion Network Mapping



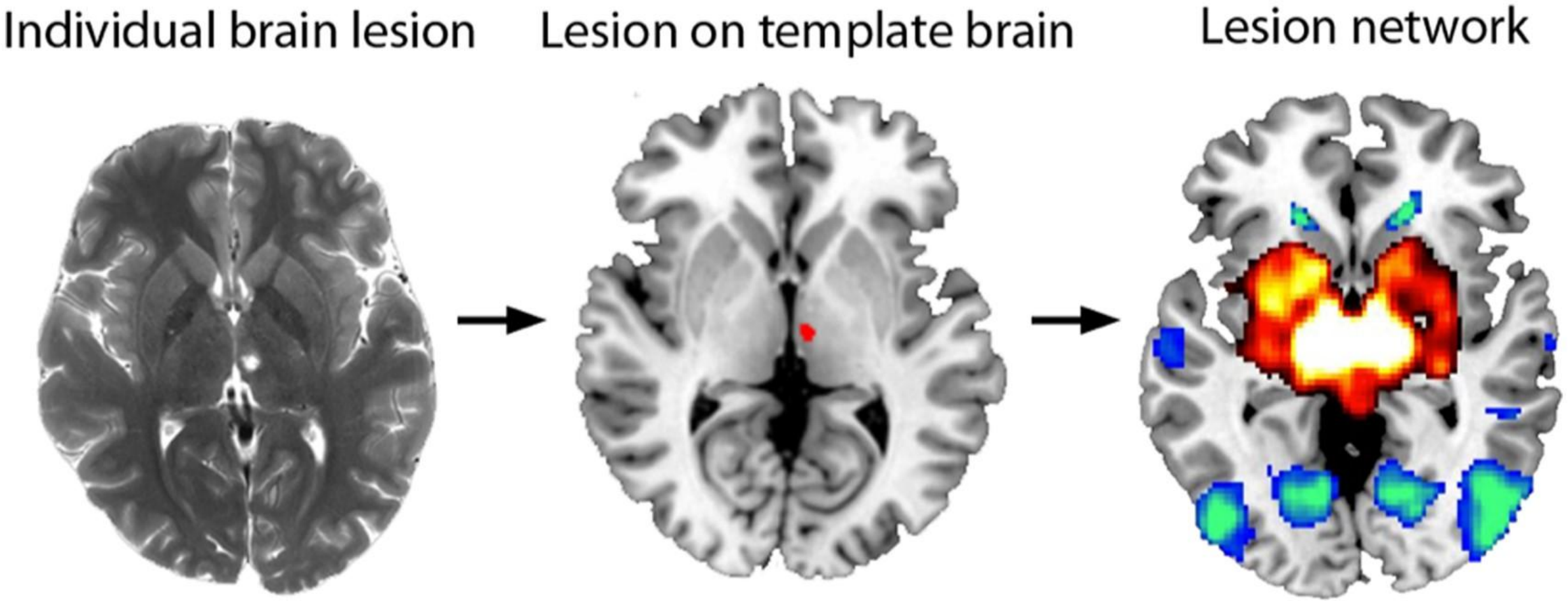
Functional Connectivity





(adapted from King, J. & Anderson, J., 2018)

Functional Lesion Network Mapping



(Boes, 2021; Boes et al., 2015)

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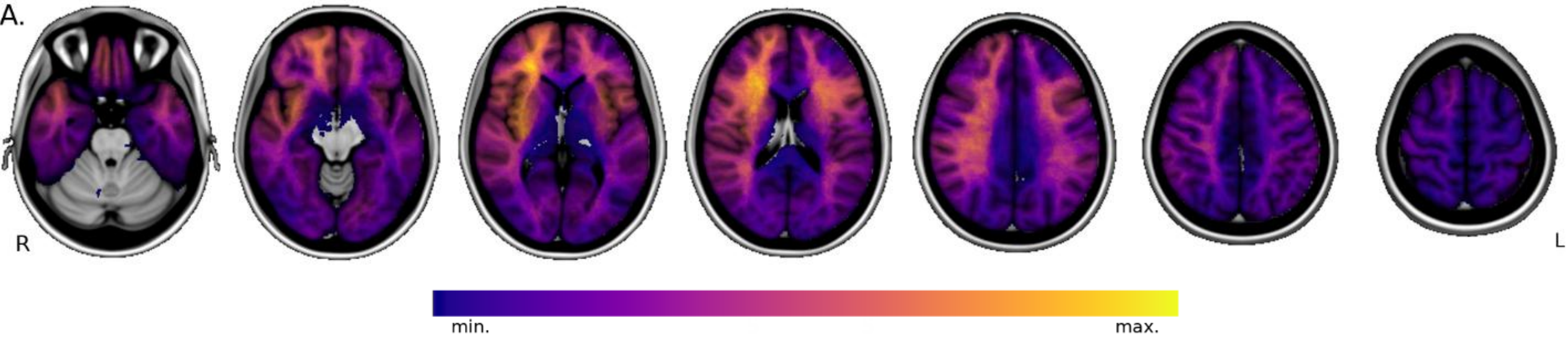
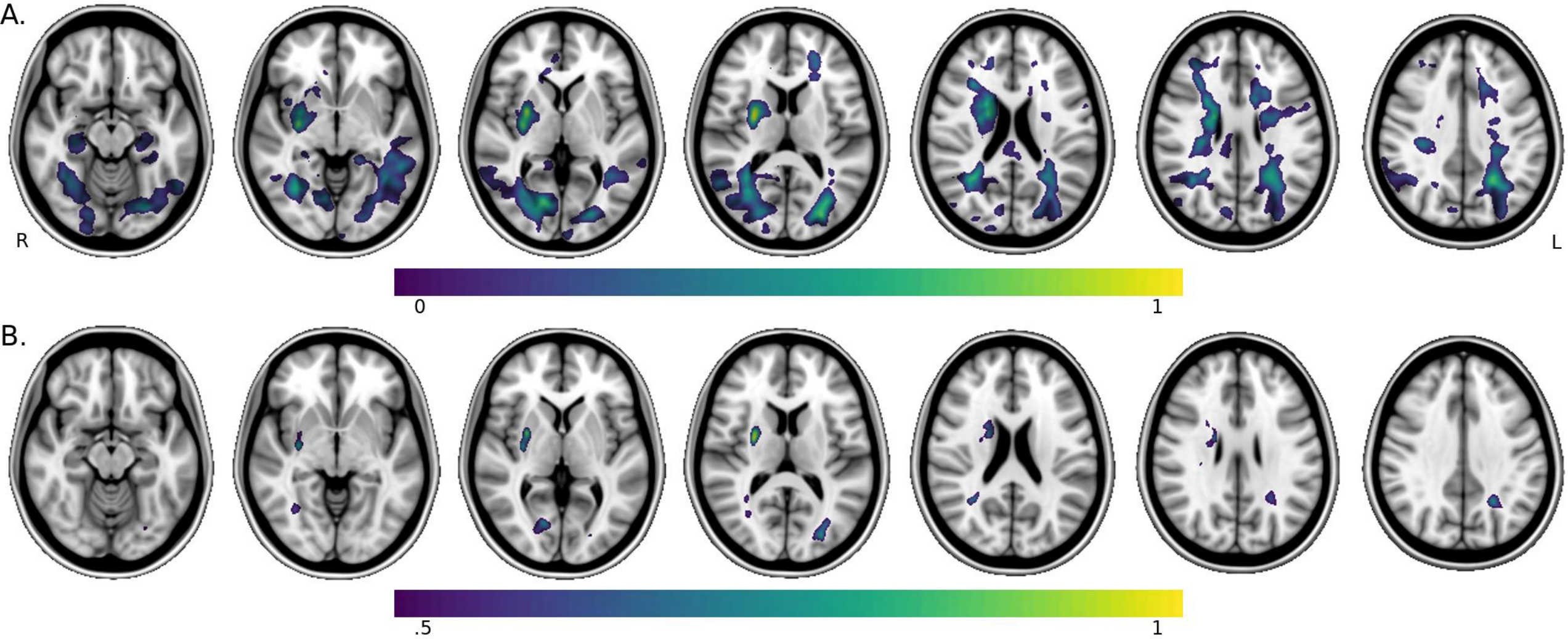
Lesion Overlap Map: Iowa Registry Cohort



LESYMAP: Domain General Visuospatial Ability

n=480, r=.237, p=1.52x10^{-7}



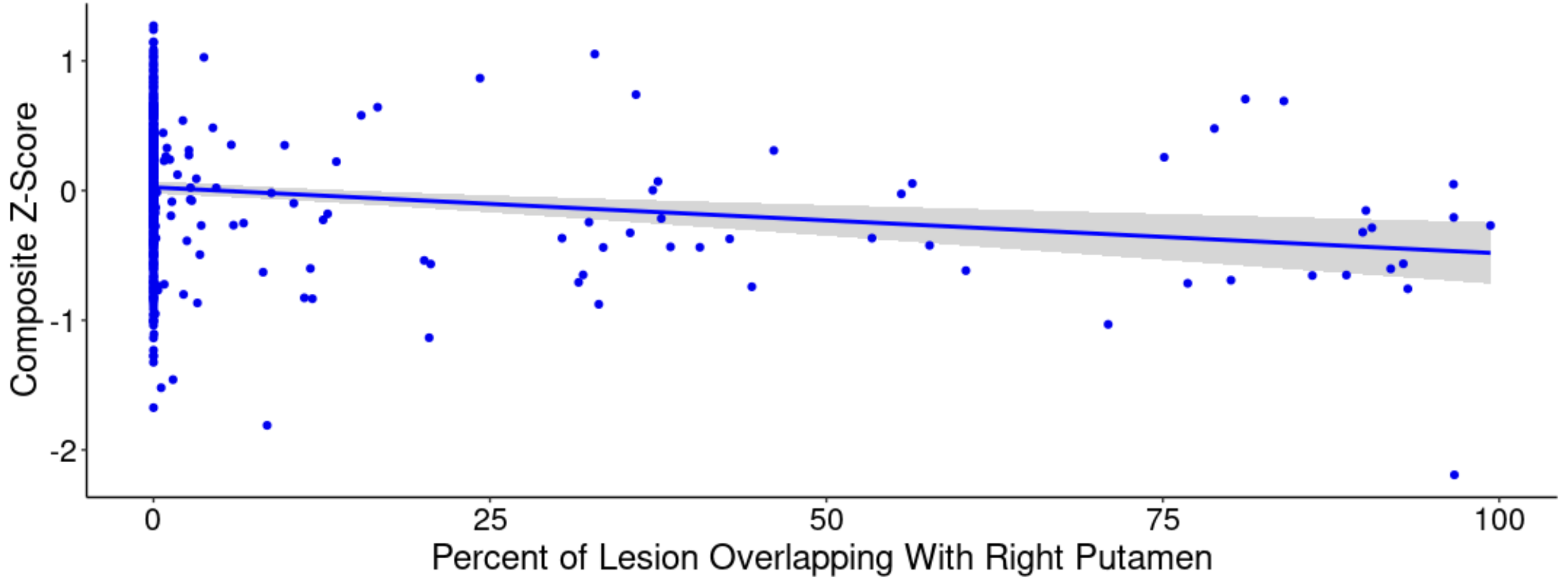
What's going on in the right putamen?

After covarying for lesion volume, domain general visuospatial ability is worse in patients when more of their lesion intersects with the right putamen.

$$F_{2,\,477} = 25.4, \qquad p = 3.3 * 10^{-11}$$

$$\frac{number\ of\ lesioned\ voxels\ in\ the\ right\ putamen}{number\ of\ voxels\ in\ whole\ lesion}$$

LESYMAP: Domain General Visuospatial Ability



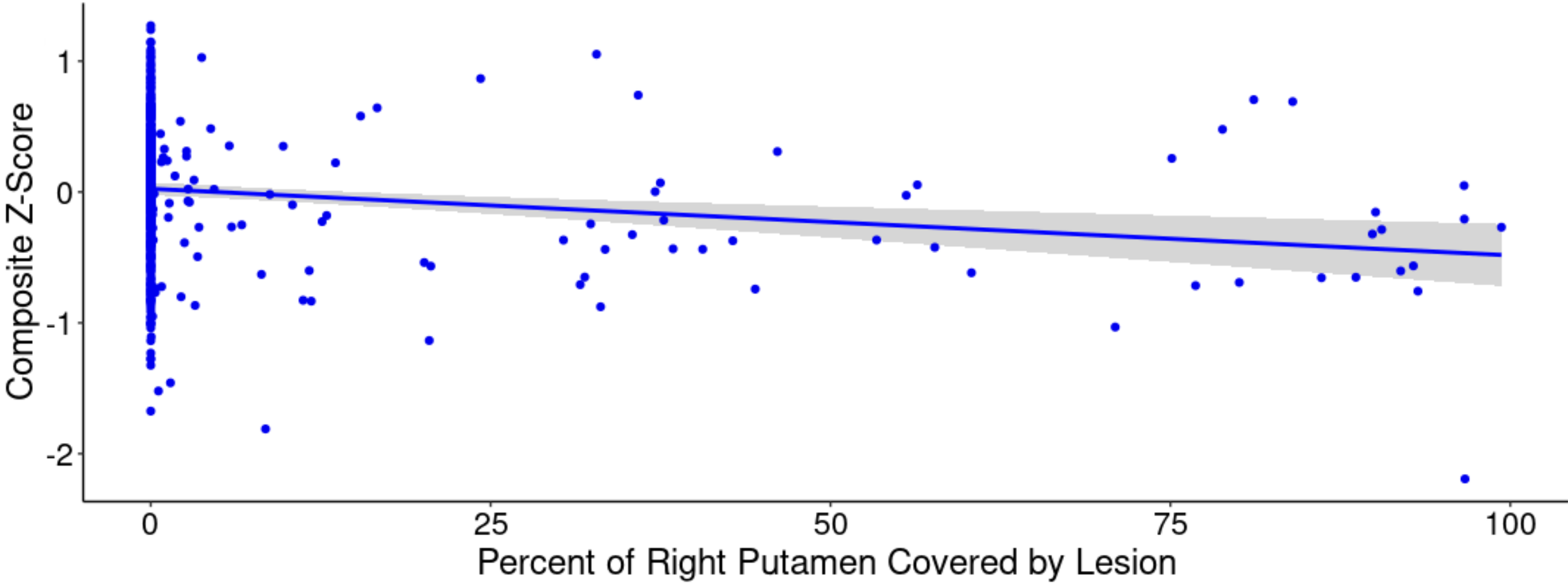
What's going on in the right putamen?

After covarying for lesion volume, domain general visuospatial ability is worse in patients who have more of their right putamen lesioned.

$$F_{2,\,477} = 27.1, \qquad p = 7.0 * 10^{-12}$$

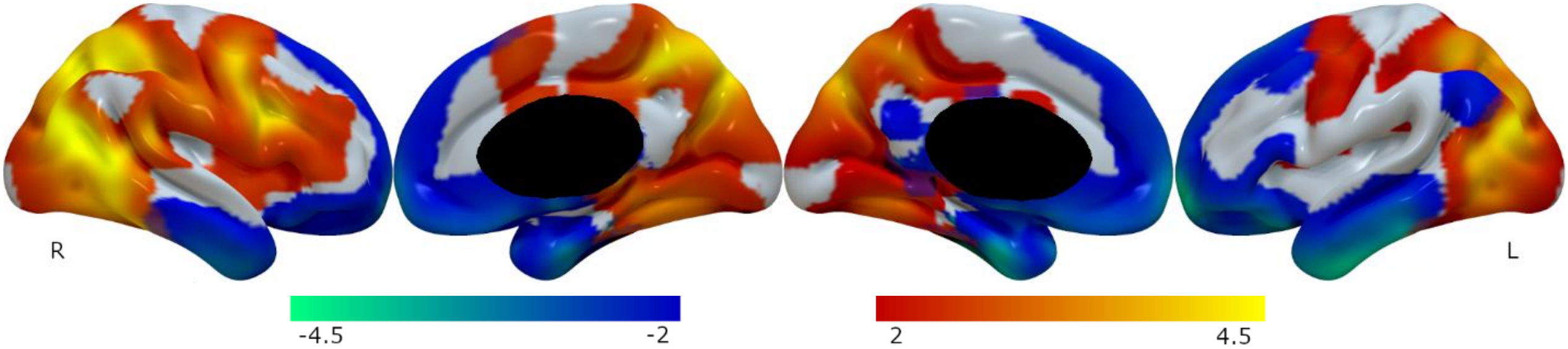
$$\frac{number\ of\ lesioned\ voxels\ in\ the\ right\ putamen}{total\ number\ of\ voxels\ in\ the\ right\ putamen}$$

LESYMAP: Domain General Visuospatial Ability



Functional Connectivity Mapping Ability

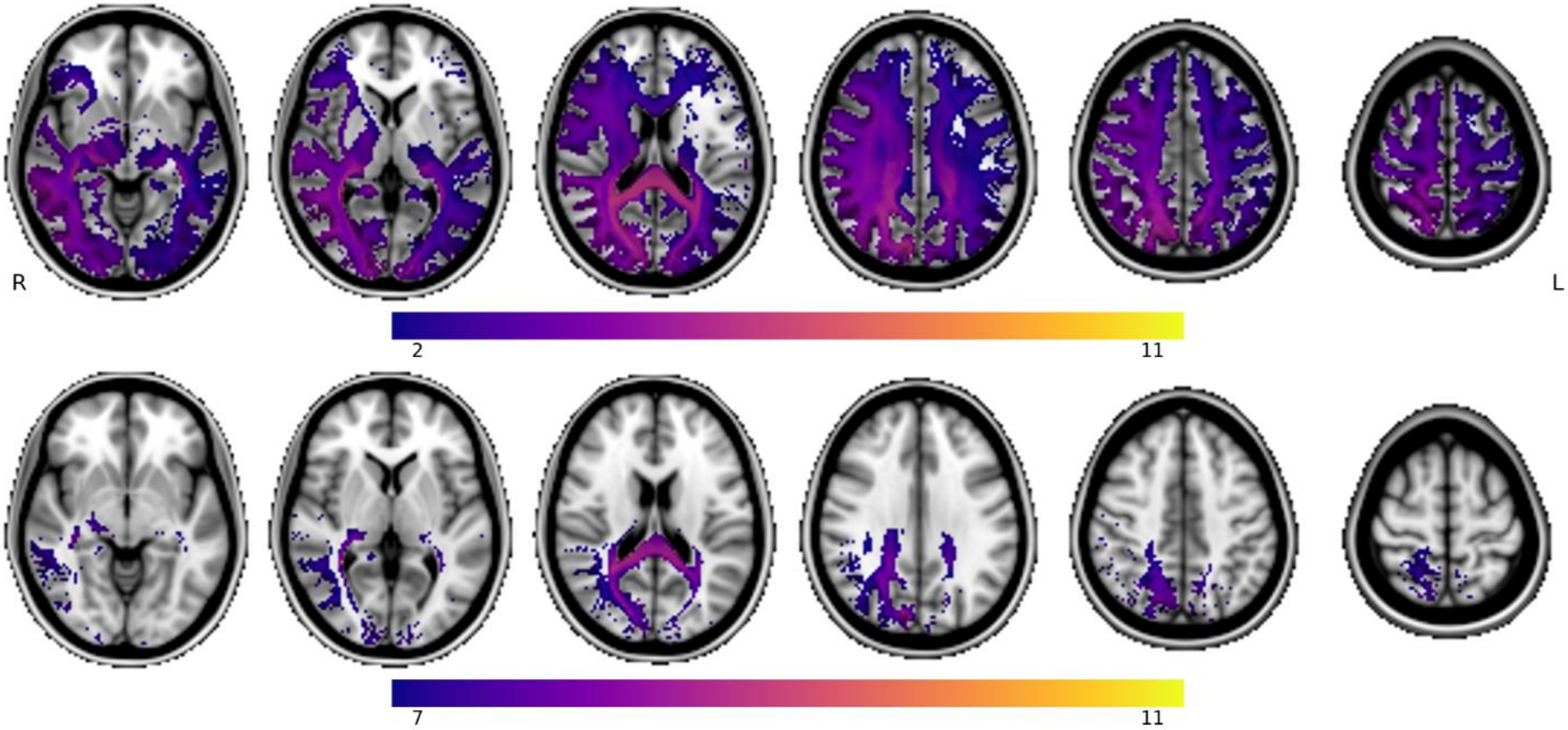
n=480, t=5.10, p=2.59x10^{-3}



Dorsal Attention Network: r=.440
Visual Network: r=.387

Structural Covariance Network Mapping Spatial Ability

n=480, t=10.3, p=3.98x10^{-4}



General Intelligence (*g*)

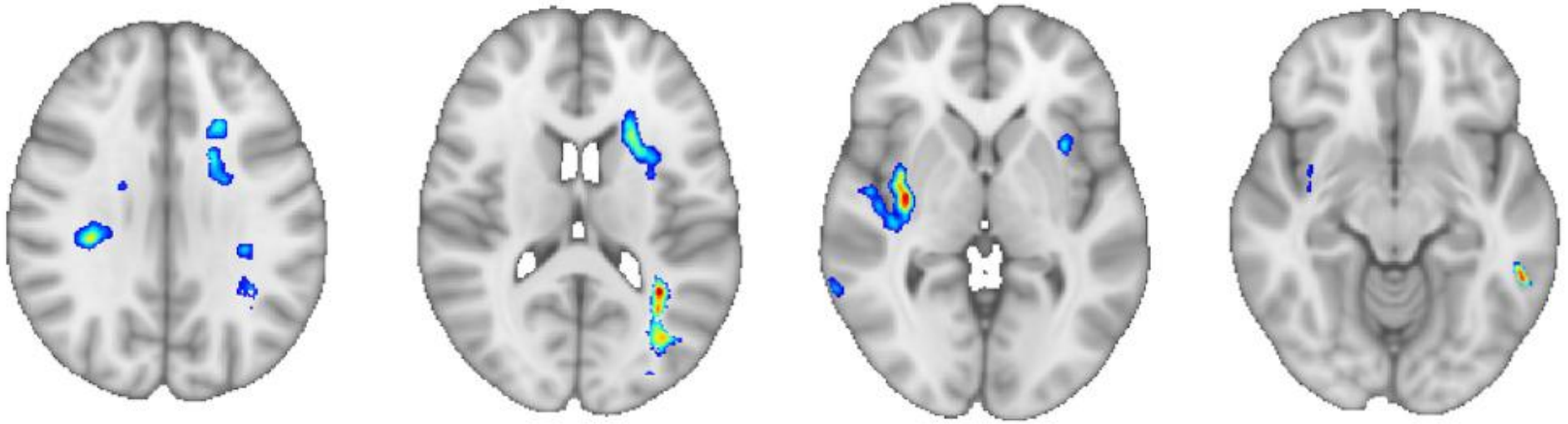
General intelligence (*g*) is a psychometric construct that captures general cognitive ability as a summation of positive correlations across multiple cognitive tests.

Domain General Visuospatial Ability is highly correlated with *g* ($r=.569$, $p=1.36 \times 10^{-42}$).

Role of *g* in Domain General Visuospatial Ability

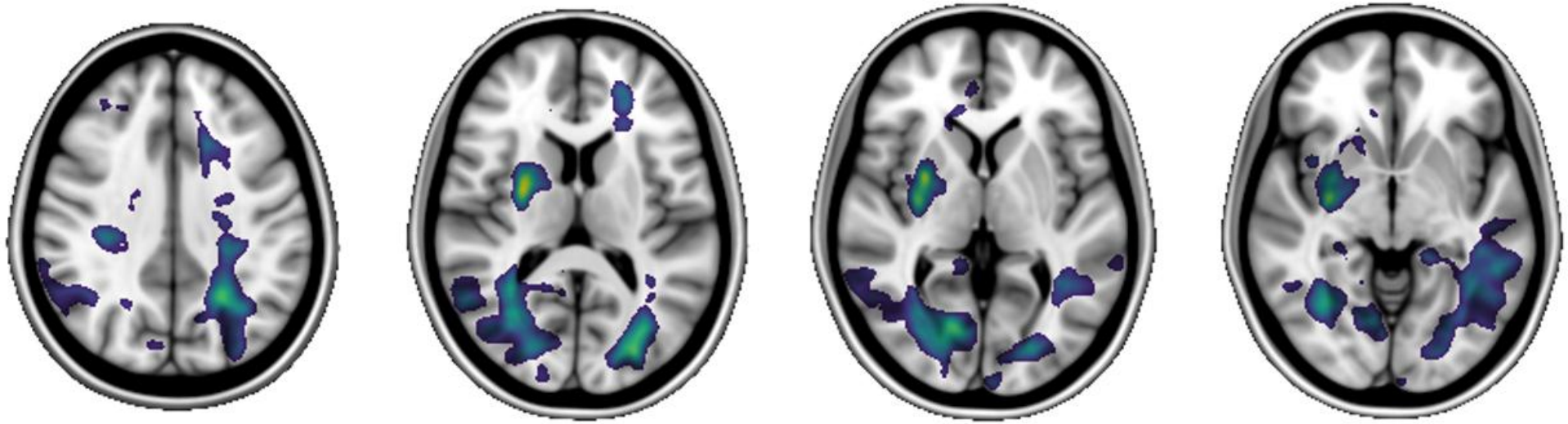
Bowren's *g*

(Bowren et al, 2020)

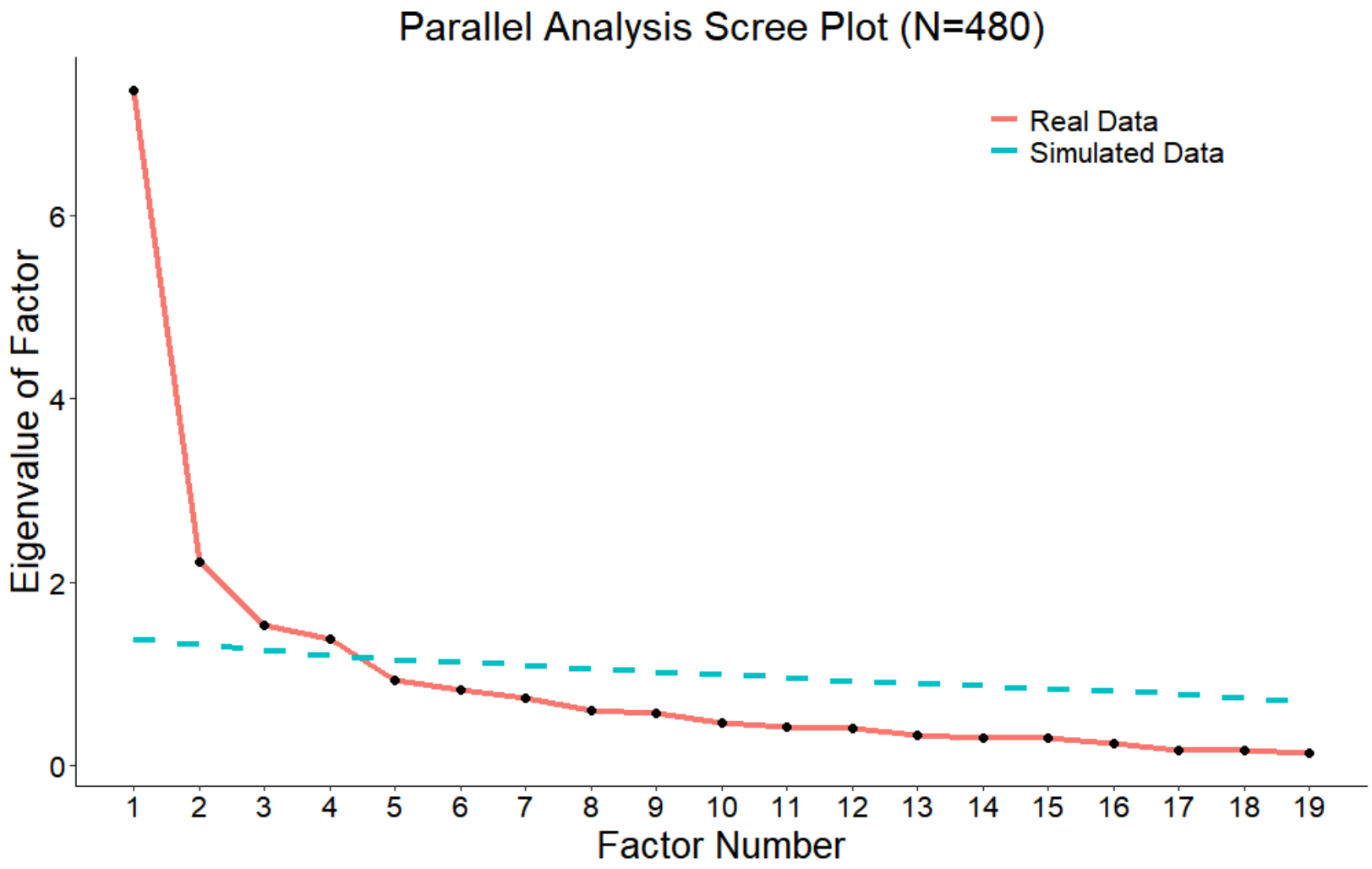


Domain General Visuospatial Ability

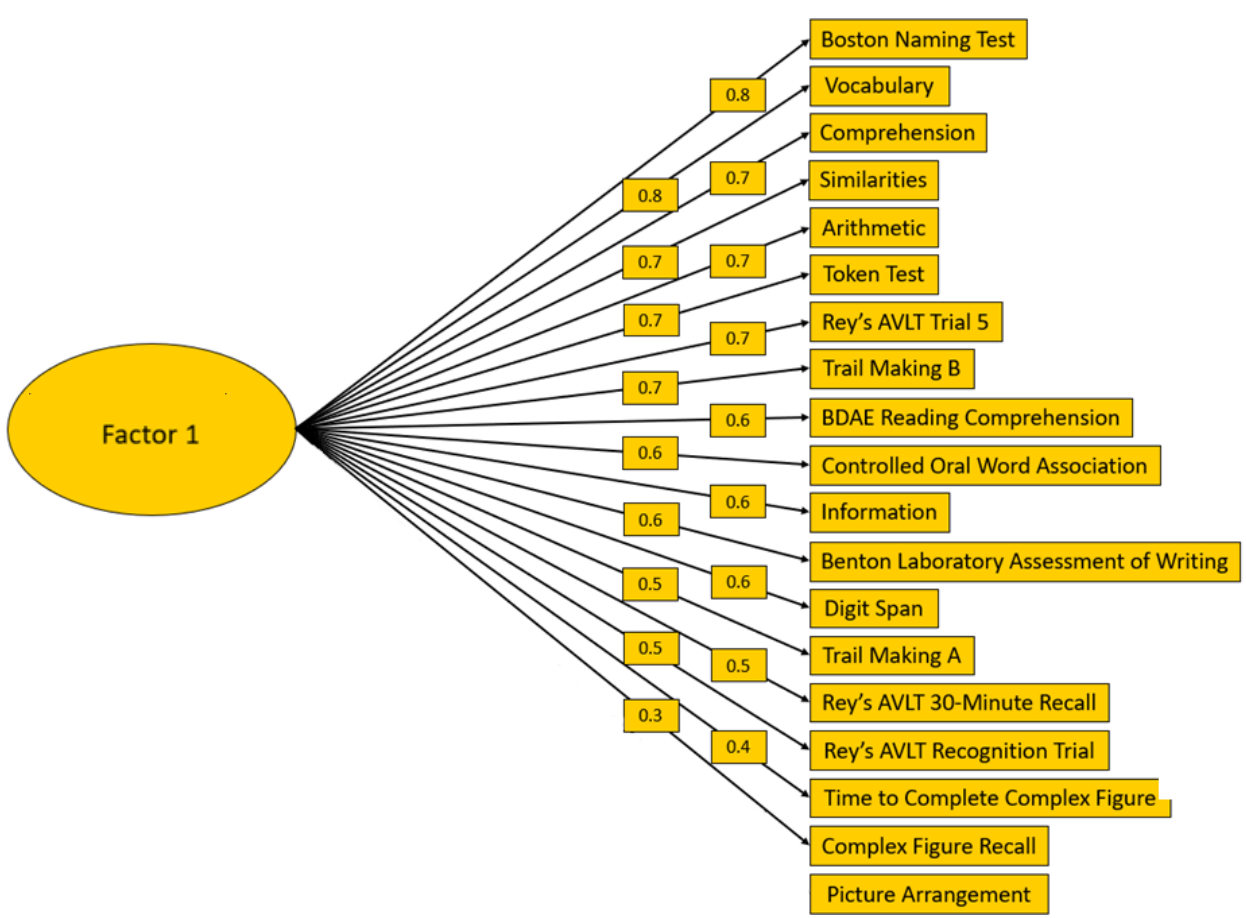
(Skye et al, 2023)

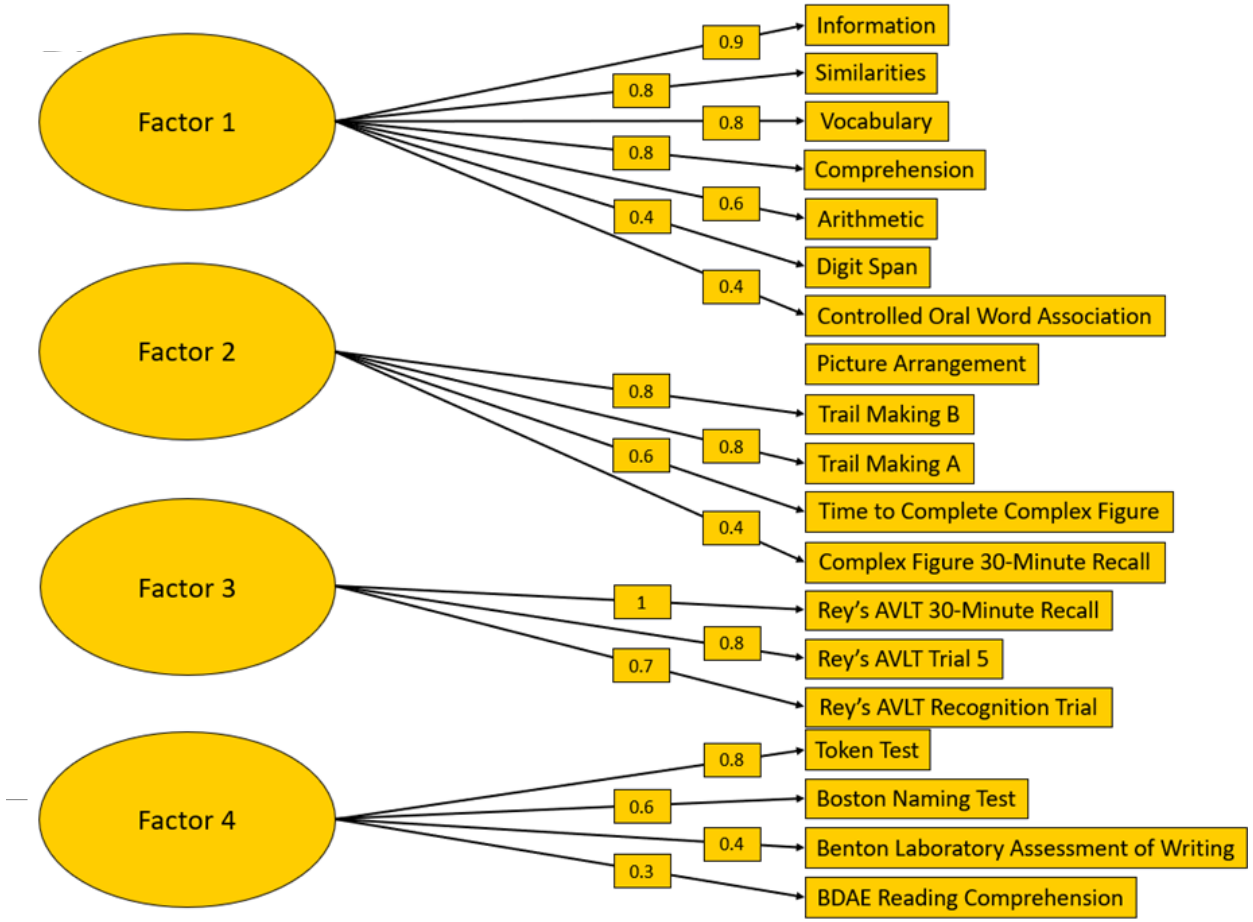


Role of *g* in Domain General Visuospatial Ability

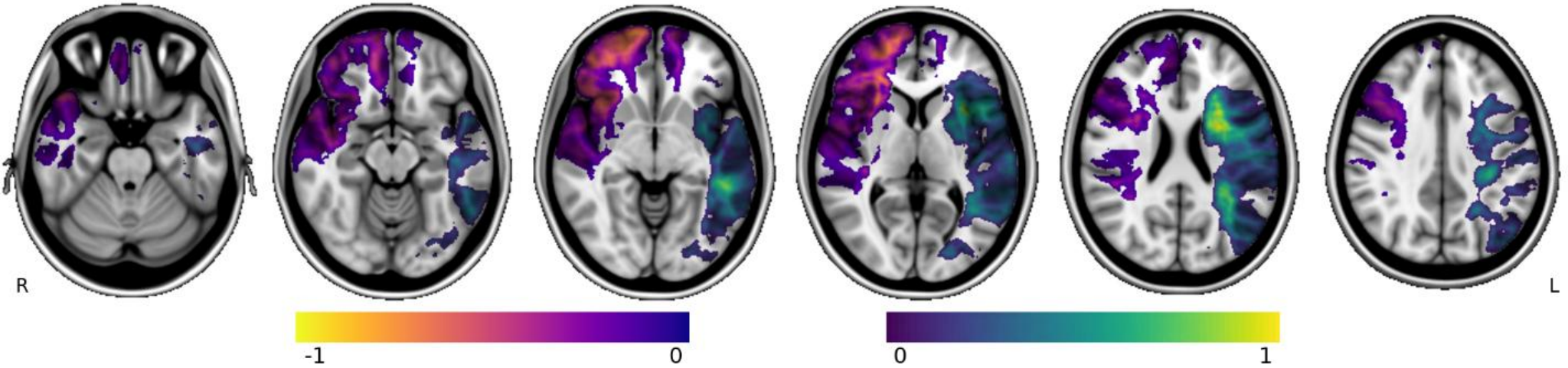


Role of *g* in Domain General Visuospatial Ability

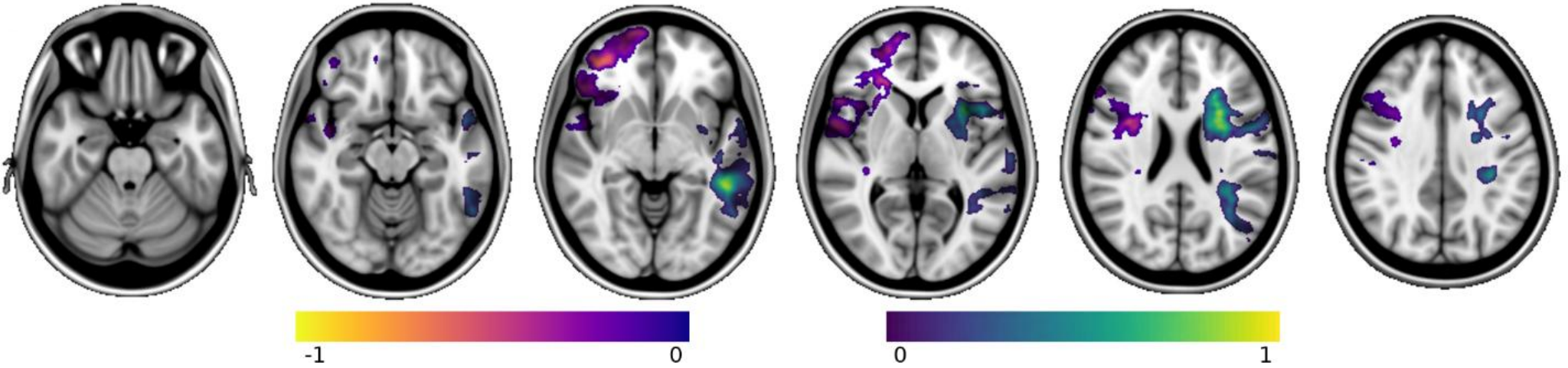




LESYMAP: *g*



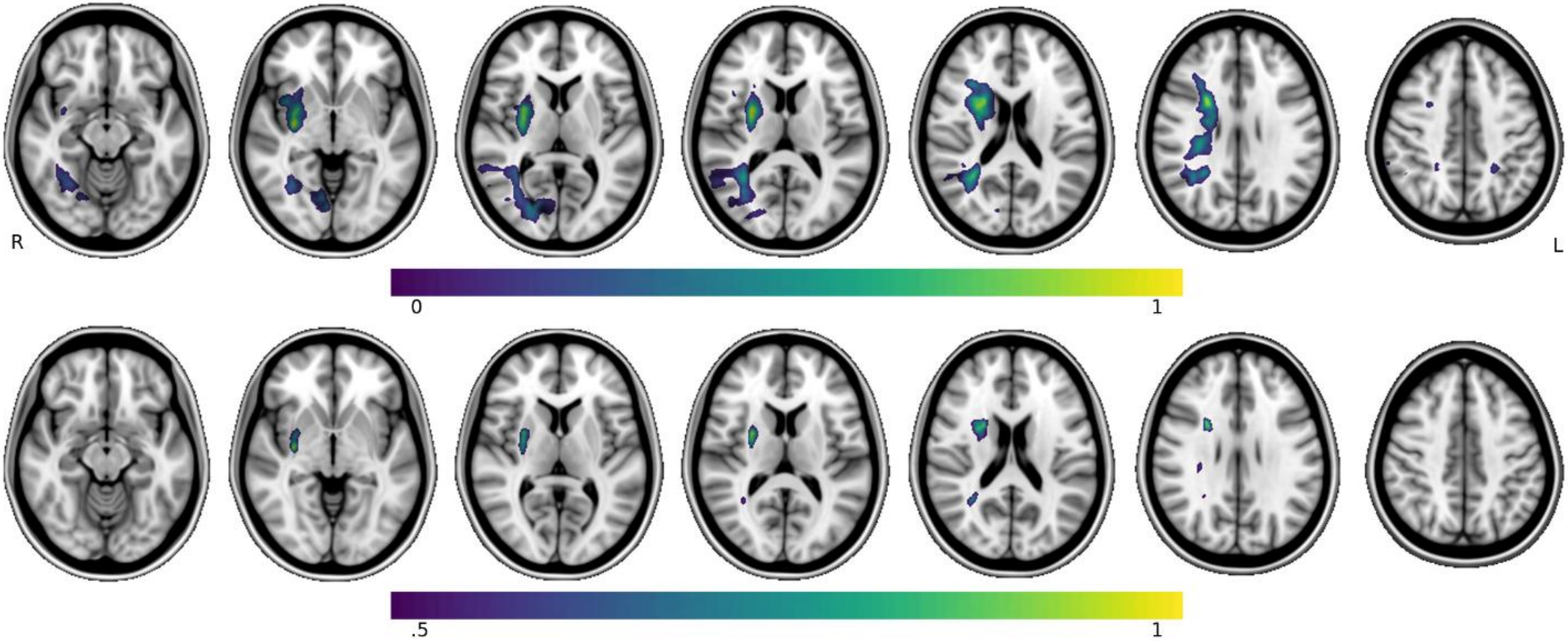
1-factor solution



1st factor of 4-factor solution

LESYMAP: Domain General Visuospatial Ability Covarying for *g*

n=480, r=.425, p=1.75x10^{-22}



Aim 2 Conclusion

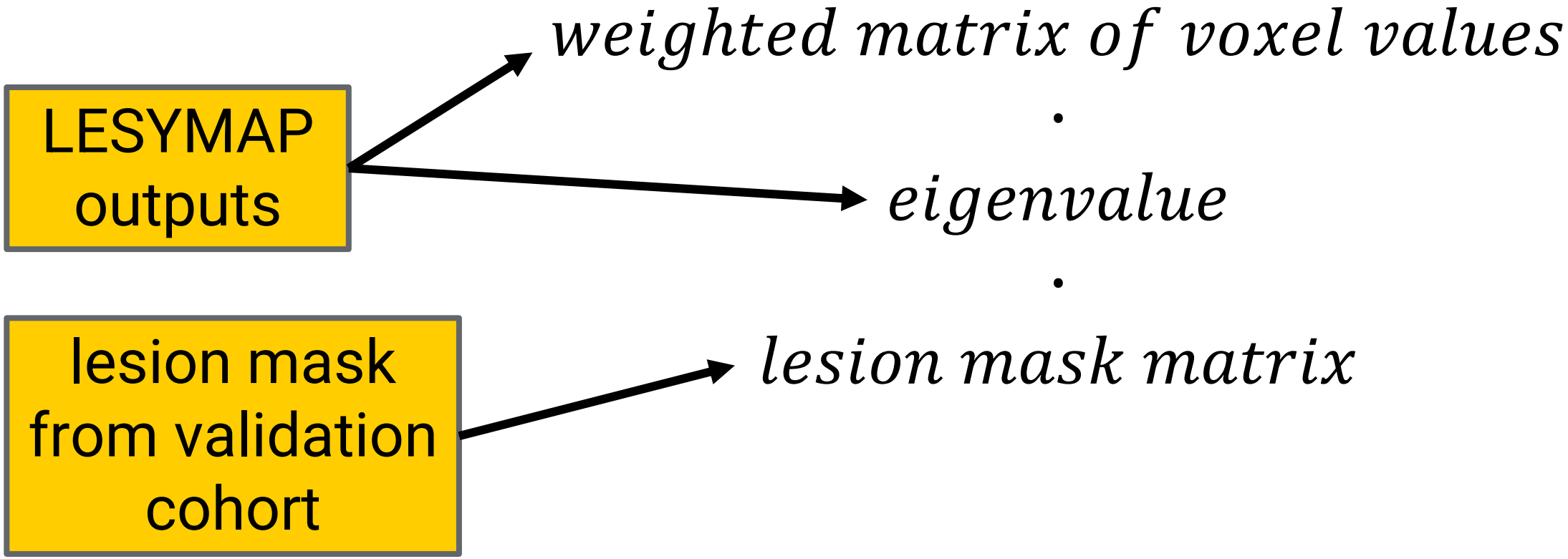
Chronic visuospatial dysfunction is associated with damage to the right putamen, distributed white matter including the dorsal visual stream, dorsal attention network, and visual network.

Aim 3

Evaluate the predictive ability of factor-derived lesion-symptom maps and lesion network maps in two validation datasets.

Predicting Visuospatial Dysfunction

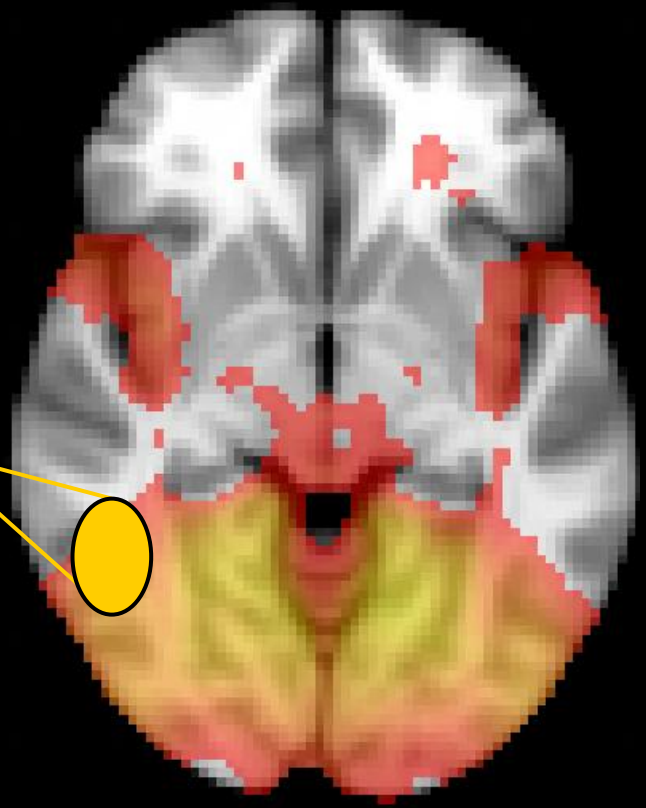
How to predict visuospatial dysfunction in other patient cohorts



How to predict visuospatial dysfunction in other patient cohorts

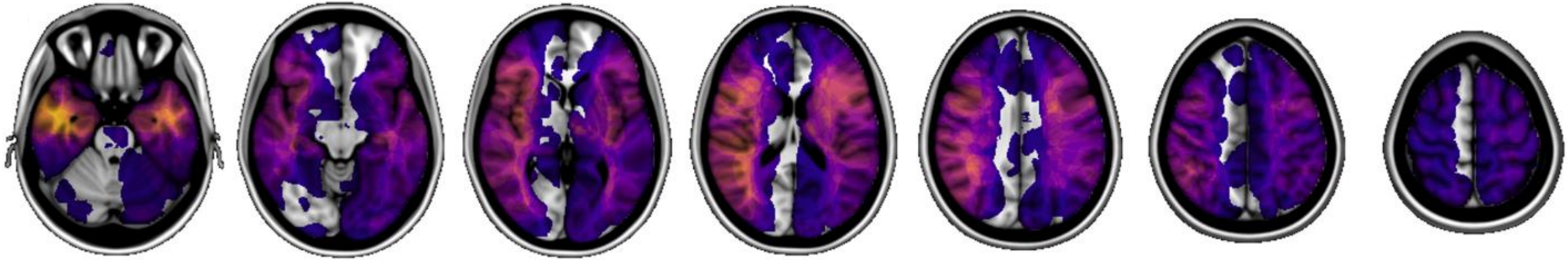
$$LL = \sum_{n=1}^{n_{max}} [voxel\ intensities \cdot voxel\ volume]$$

0	0	2	0
4	6	6	10
7	9	13	13
8	10	11	14



Benton Clinic Cohort

LESYMAP: n=117, r=.0964, p=.301



Amount of patient's lesion covering right putamen

adj. R^2=.0380, F(2,114)=3.29, p=.0409

Lesioned : total voxels in right putamen

adj. R^2=.0360, F(2,114)=3.16, p=.0460

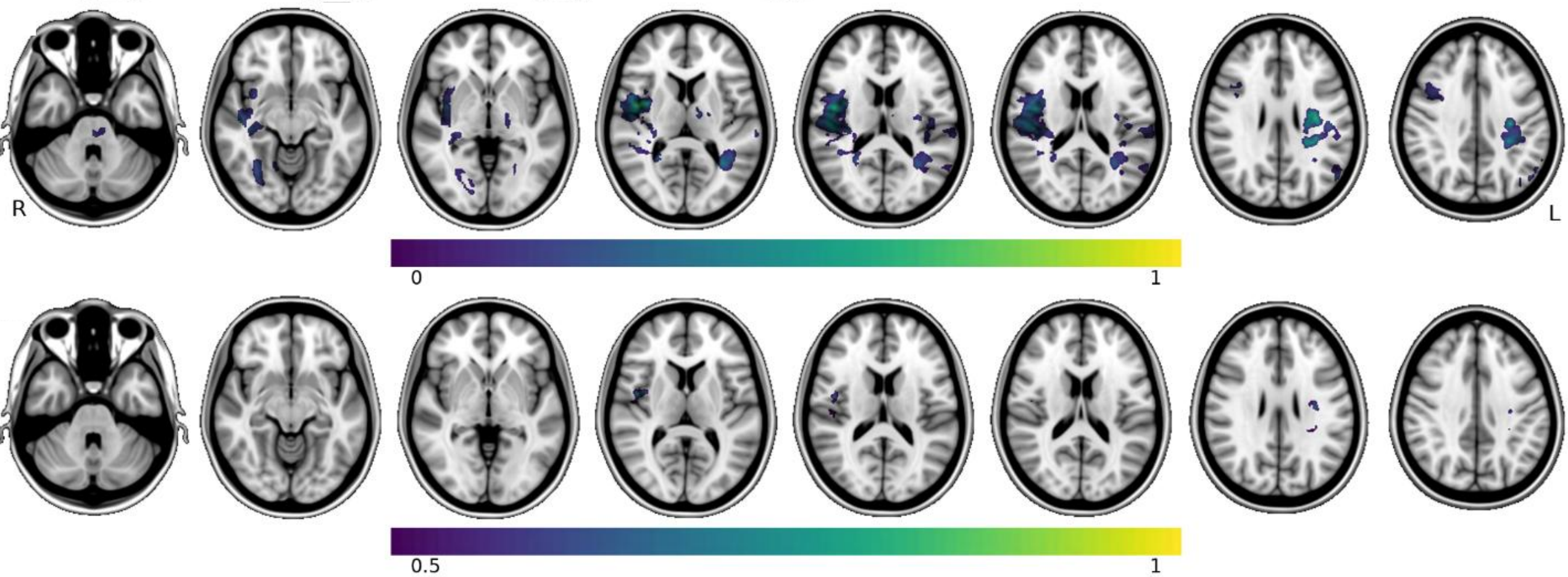
Benton Clinic Cohort

A linear model with fLNM, sLNM, and lesion volume as predictors best predicts outcomes in the Benton Clinic cohort.

RMSE=.628, R^2=.0998, AIC=220.7, BIC=234.5
adj. R^2=.0664, F(3,113)=3.75, p=.0130

Washington University Cohort

LESYMAP: n=104, r=.193, p=.0493



Washington University Cohort

A linear model with fLNM, sLNM, and lesion volume as predictors best predicts outcomes in the Washington University cohort.

$RMSE=.584$, $R^2=.115$, $AIC=175.1$, $BIC=188.3$

adj. $R^2=.144$, $F(3,100)=6.76$, $p=3.39\times10^{-4}$

Aim 3 Conclusion

A linear model with functional lesion network mapping, structural lesion network mapping, and lesion volume as predictors best predicts outcomes in two validation cohorts.

Conclusions and Future Directions

Conclusion

One factor best represents visuospatial ability.

Conclusion

Damage to the right putamen is most associated with domain general visuospatial dysfunction.

Conclusion

Functional lesion network mapping, structural lesion network mapping, and lesion volume predict domain general visuospatial dysfunction.

Future Directions

- Mix Iowa Registry and Benton Clinic cohorts
- Network correlates of right putamen
- Control for **nonverbal *g*** on individual tests
- Use ridge regression to test models

THANK YOU TO OUR AWESOME REGISTRY PATIENTS!!!

Thank you!

Tranel Lab

Boes Lab

Jeff Long, PhD

Justin Sipla, PhD

James Traer, PhD

IOWA

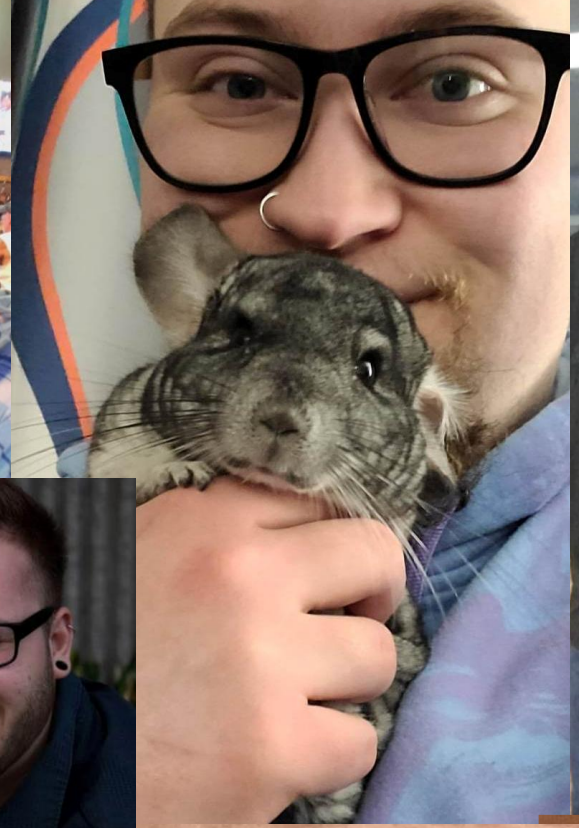
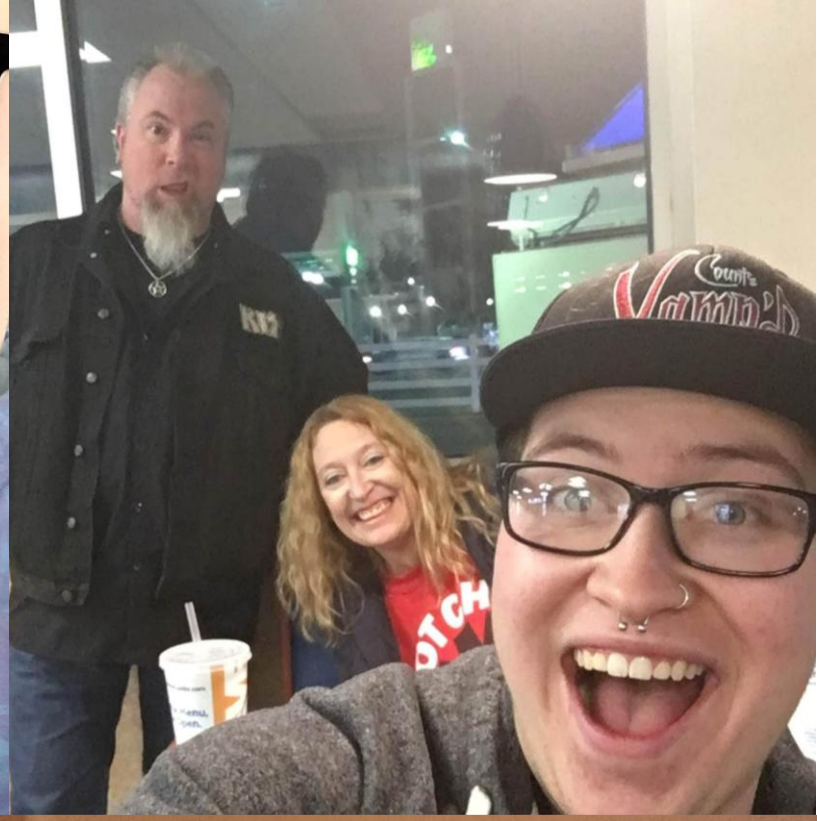
Interdisciplinary Graduate Program in Neuroscience

UNIVERSITY OF IOWA HOSPITALS & CLINICS

University of Iowa Health Care

Funding:
NIH Diversity Supplement 3R01NS114405-01S2



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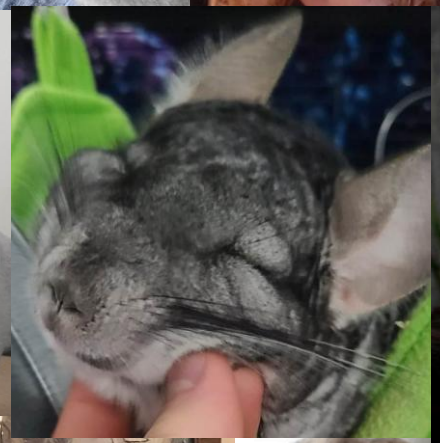




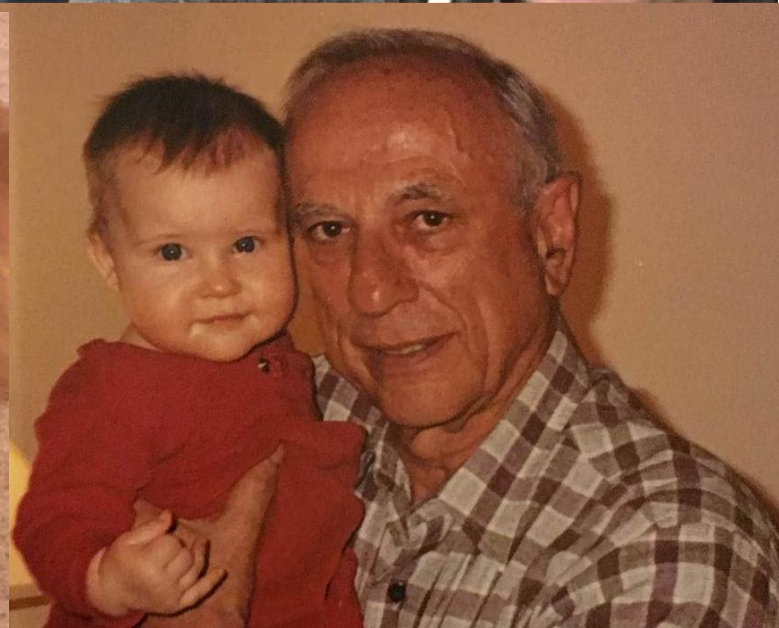

Celebrating 150 years of advancing medical research, education, and patient care to help people live longer, healthier lives

University of Iowa Carver College of Medicine
University of Iowa Health Care

Questions?

Jax Skye
Departments of Neurology and Pediatrics

→ **jax-skye@uiowa.edu**

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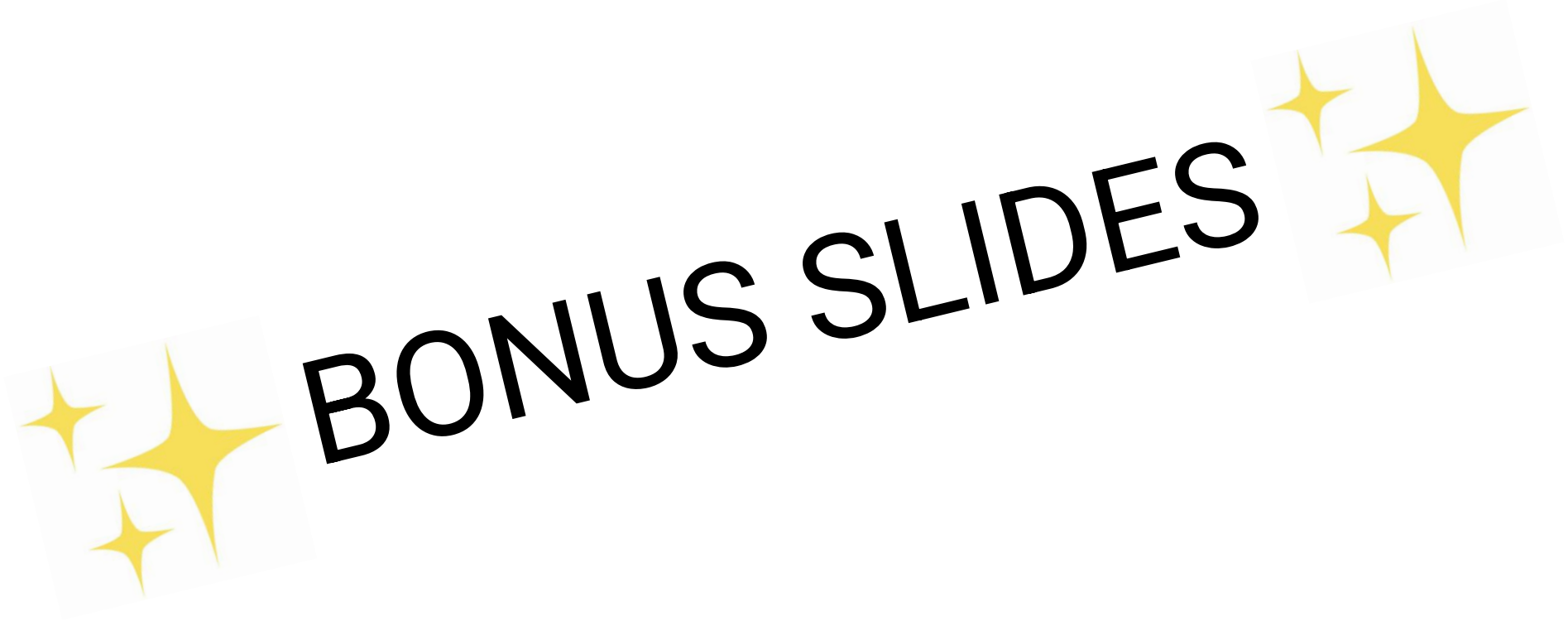
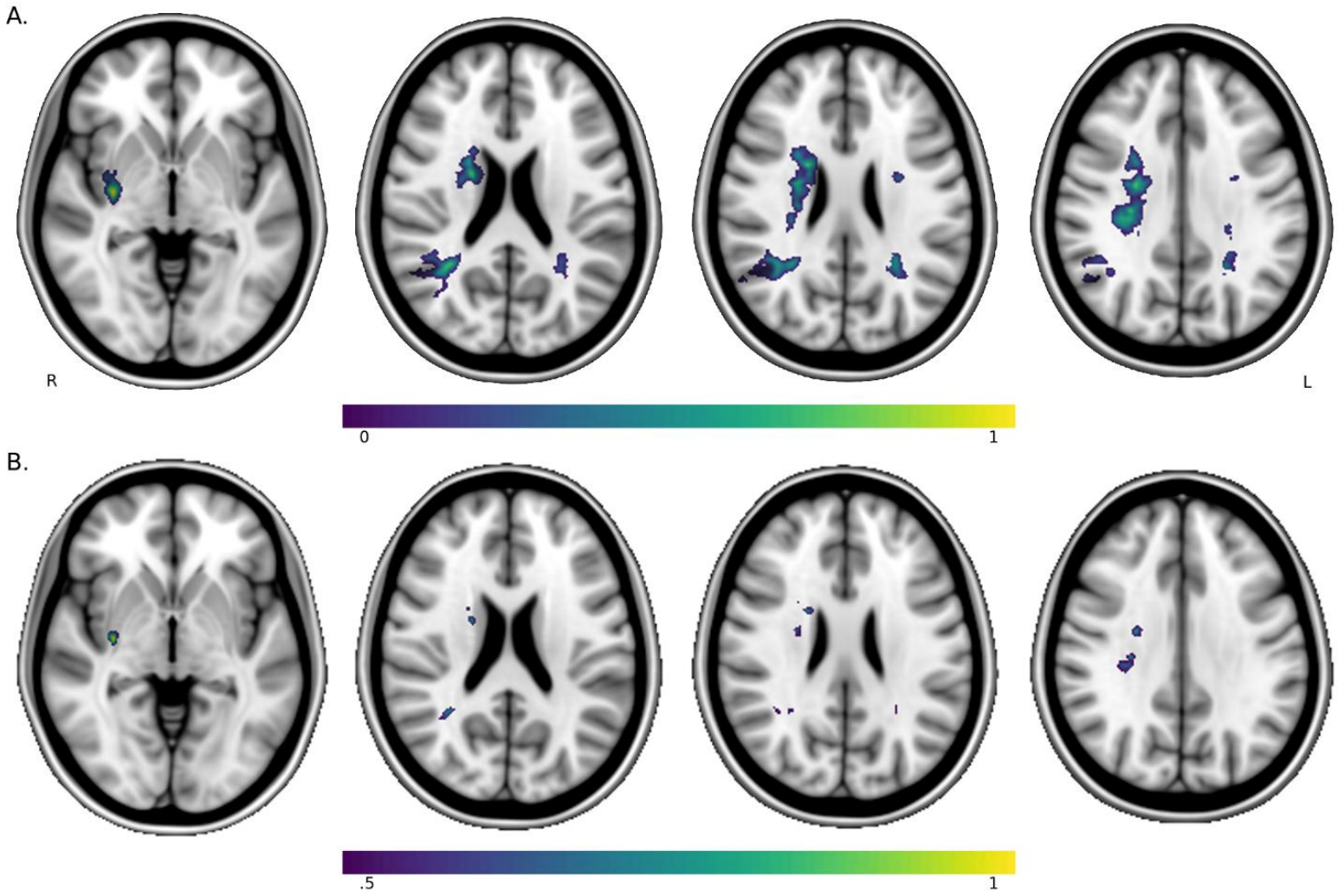
Supplementary Material



Block Design



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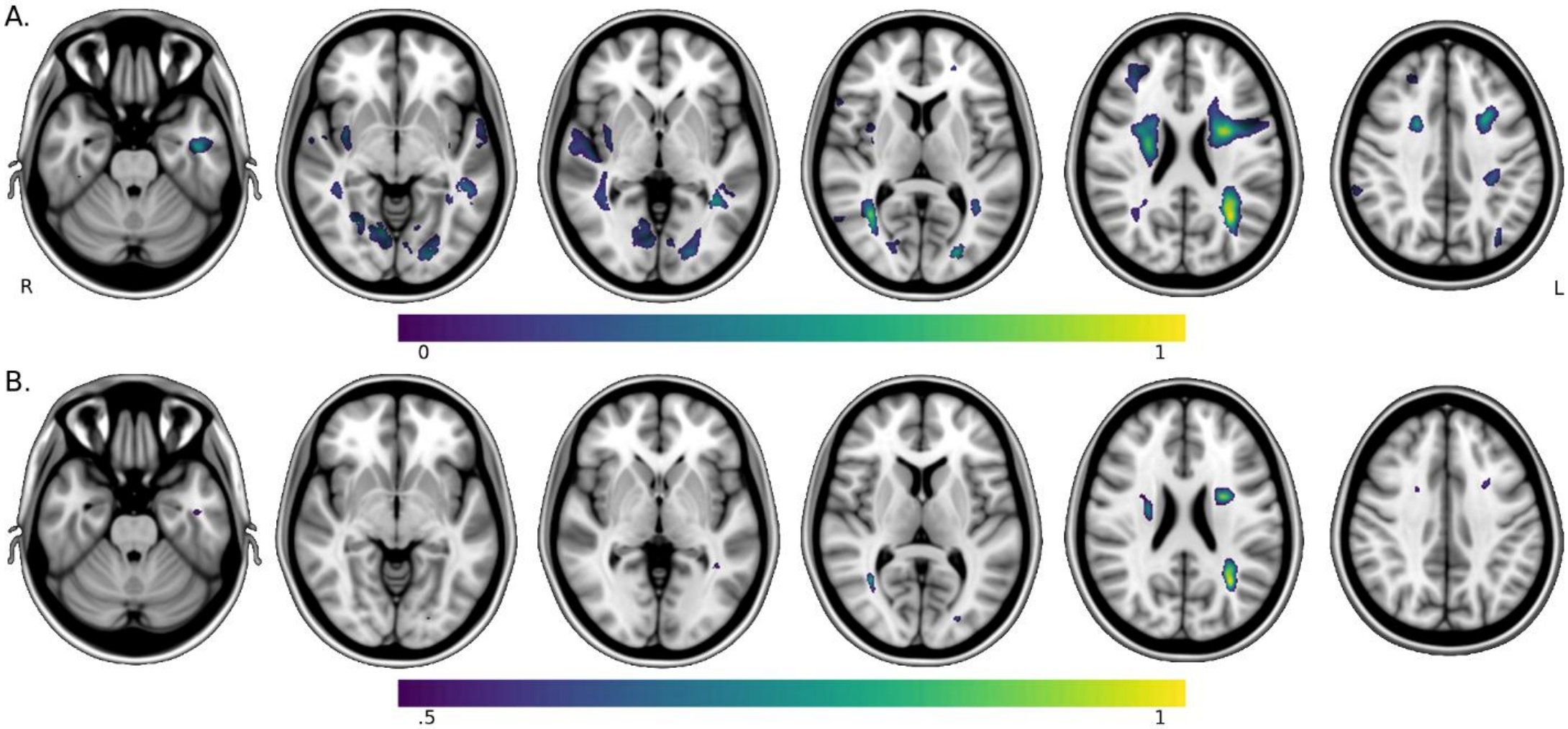
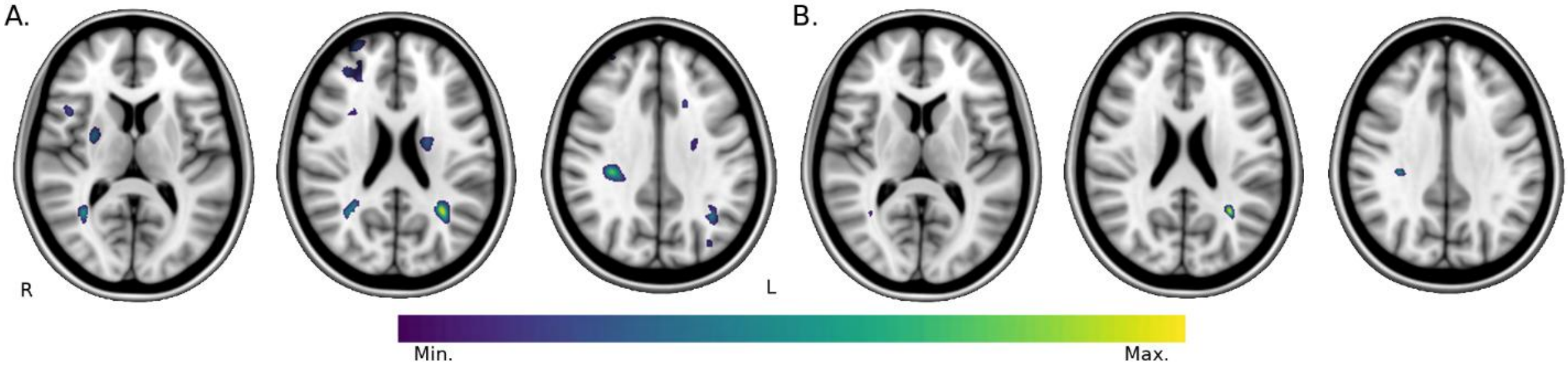
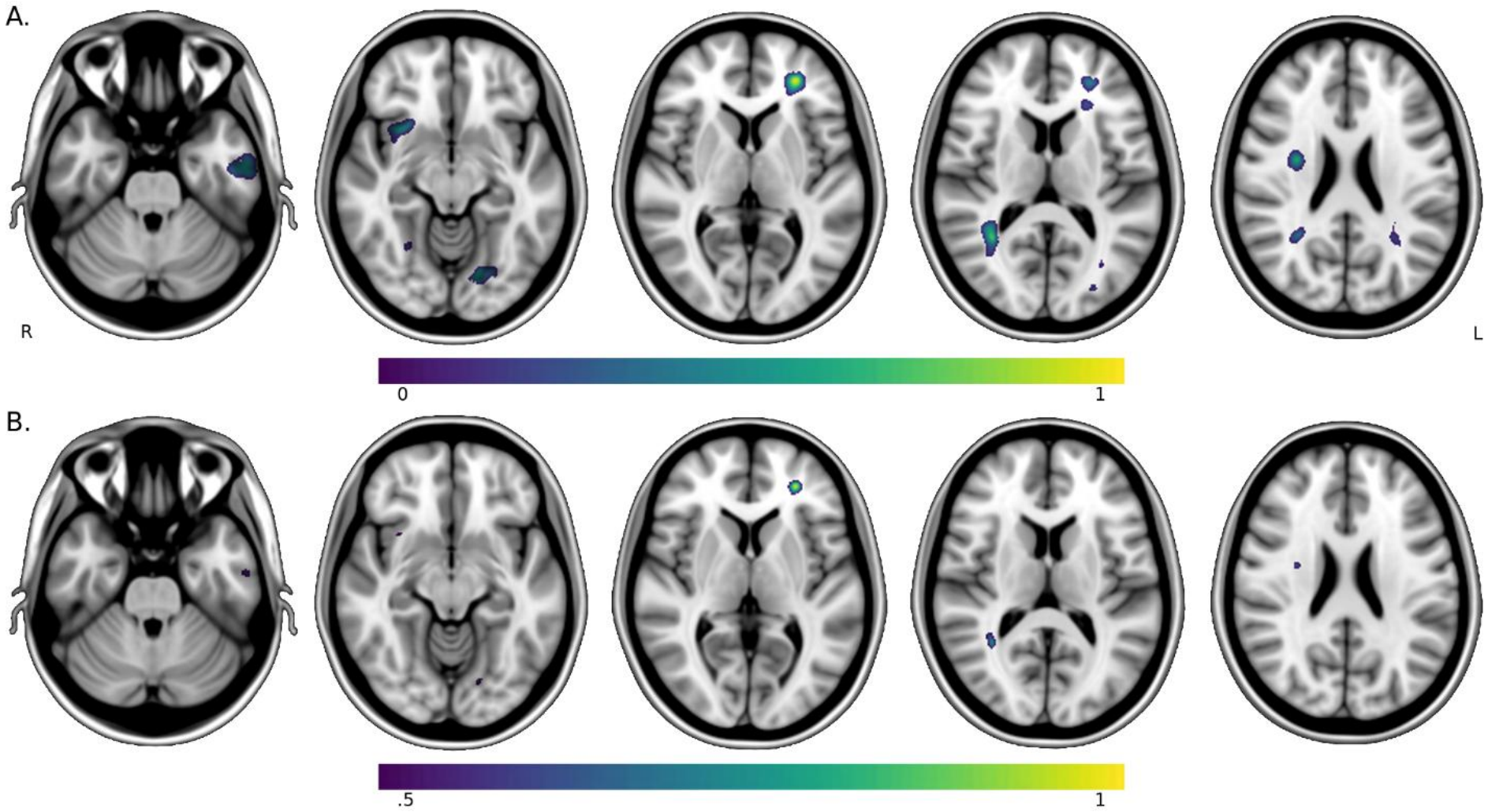


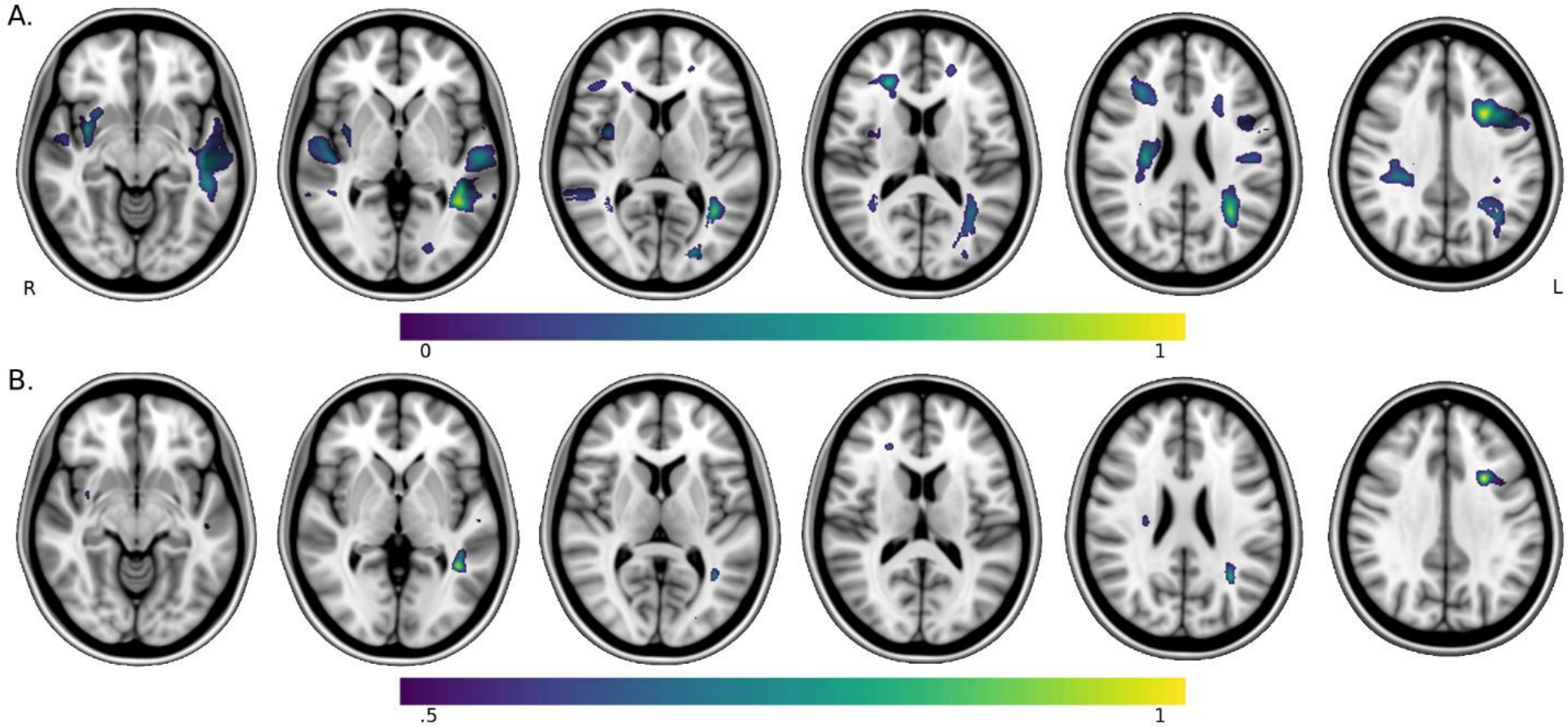
Matrix Reasoning



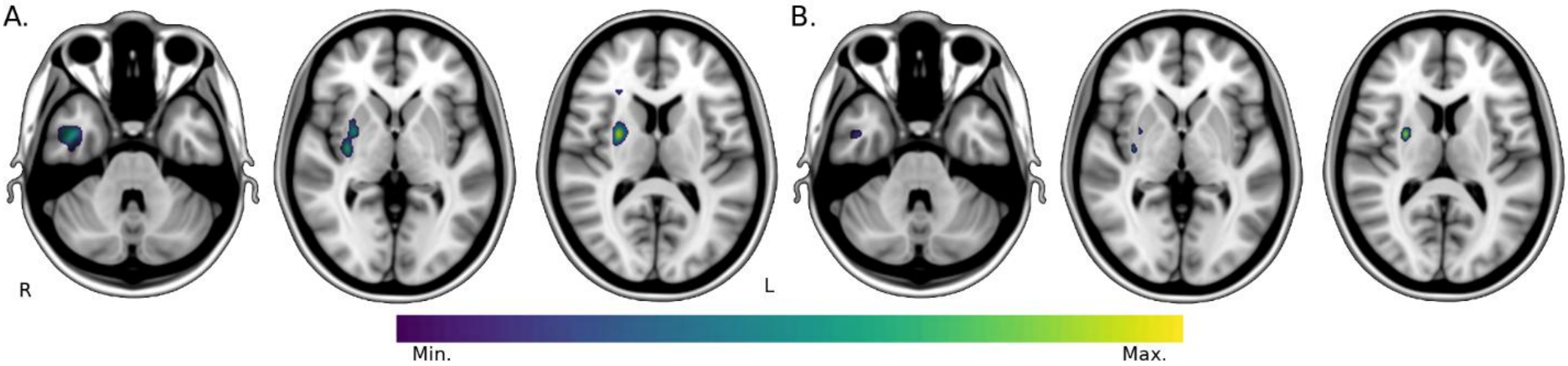
Picture Completion



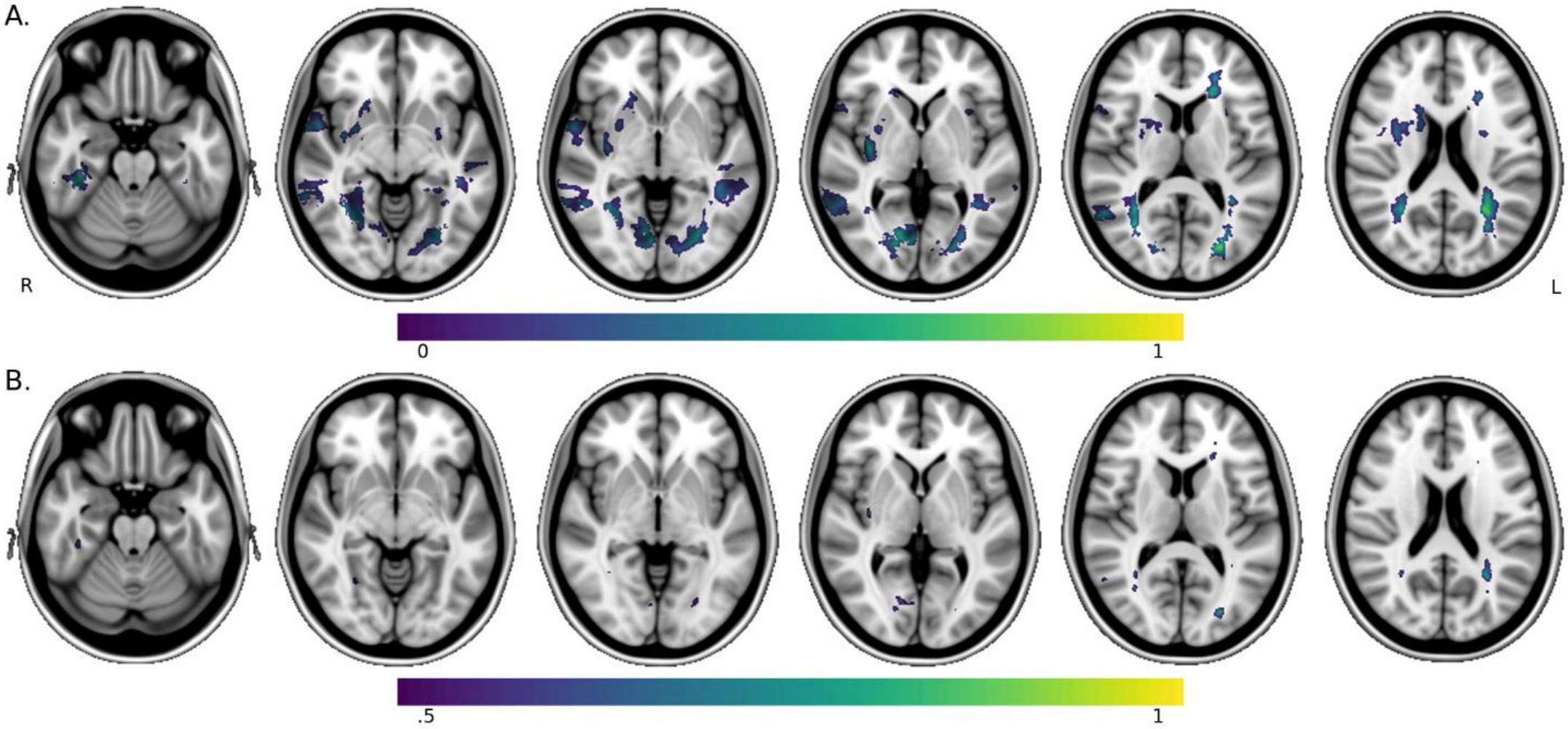
Symbol Search



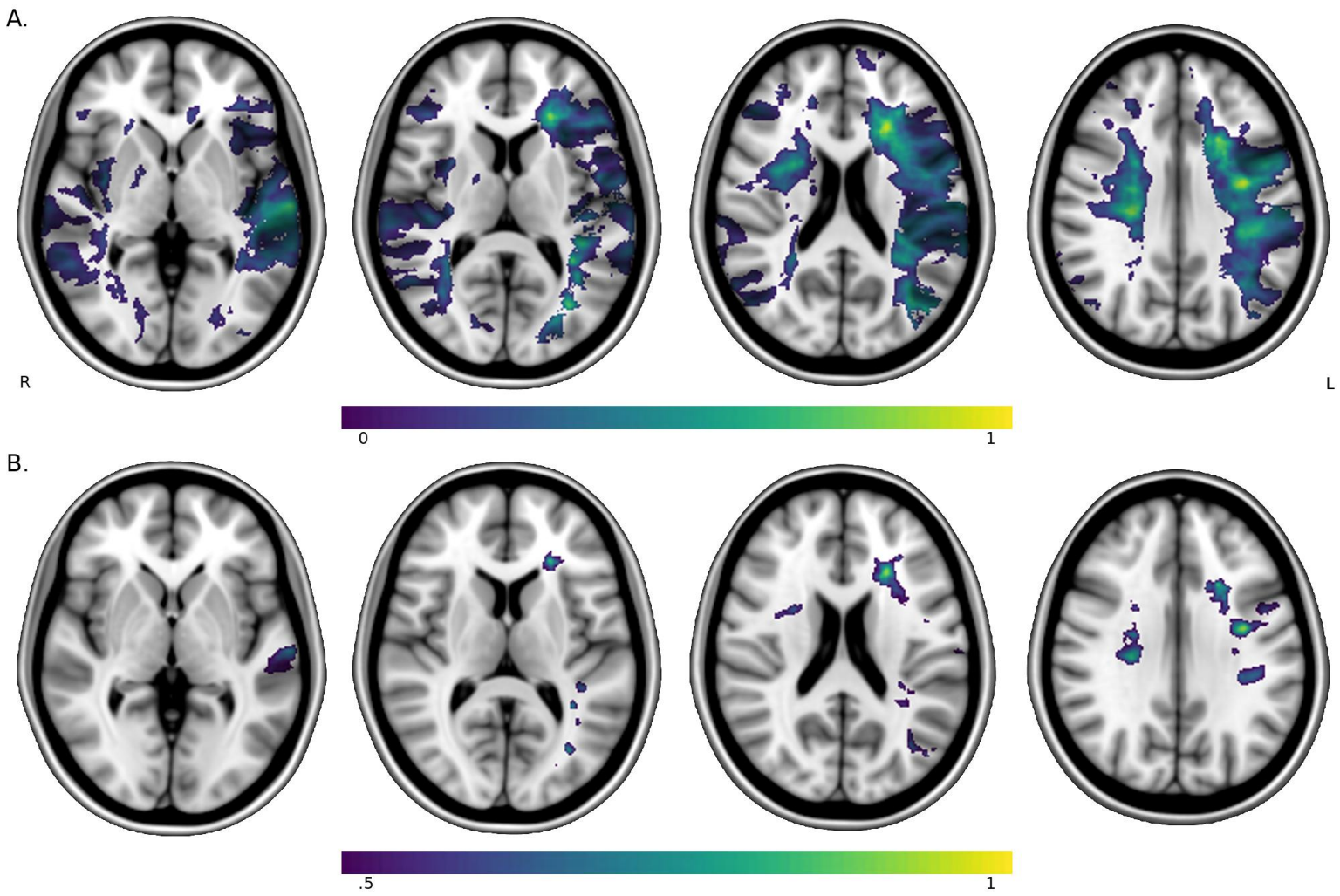
Benton’s Facial Recognition Test



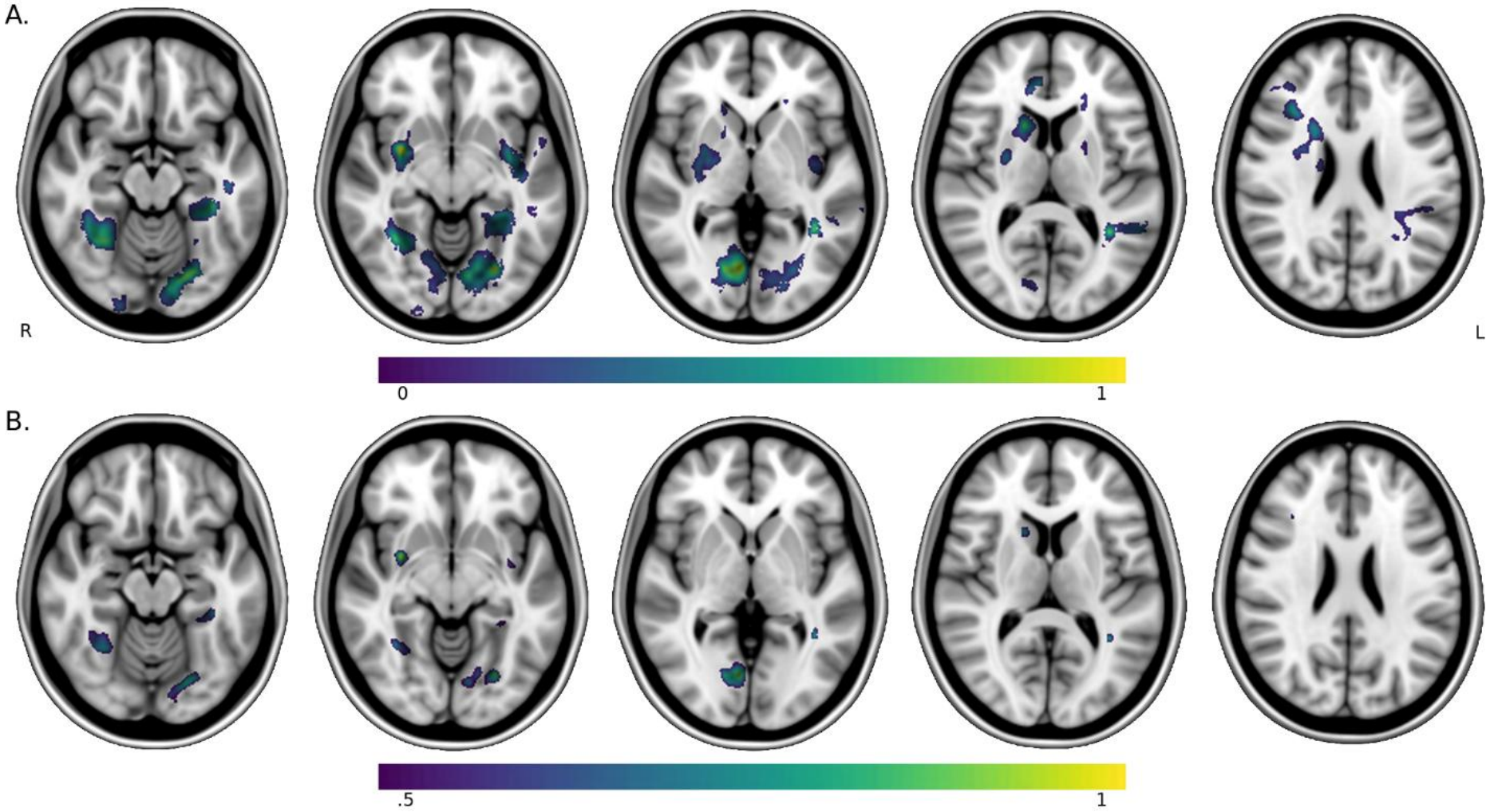
Benton's Visual Retention Test



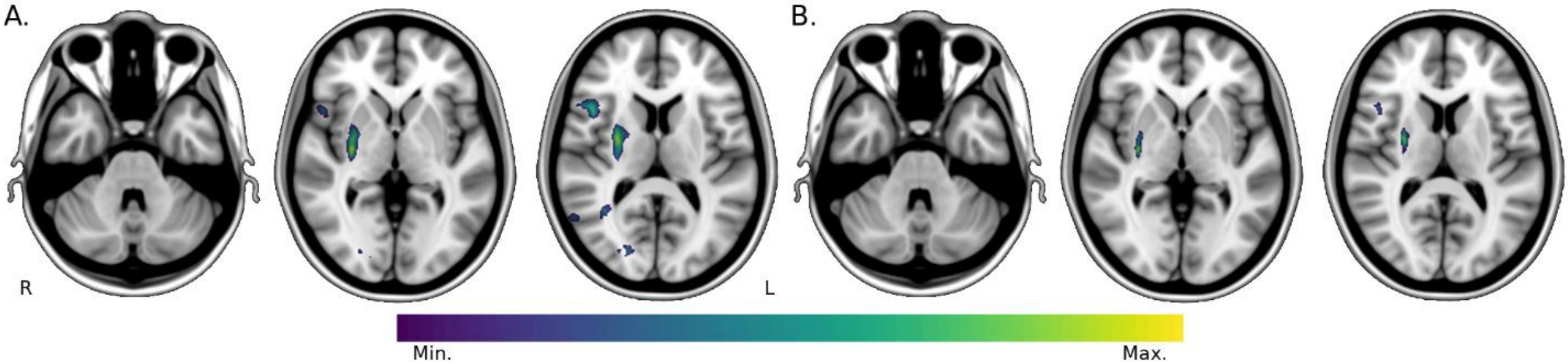
Clock Drawing



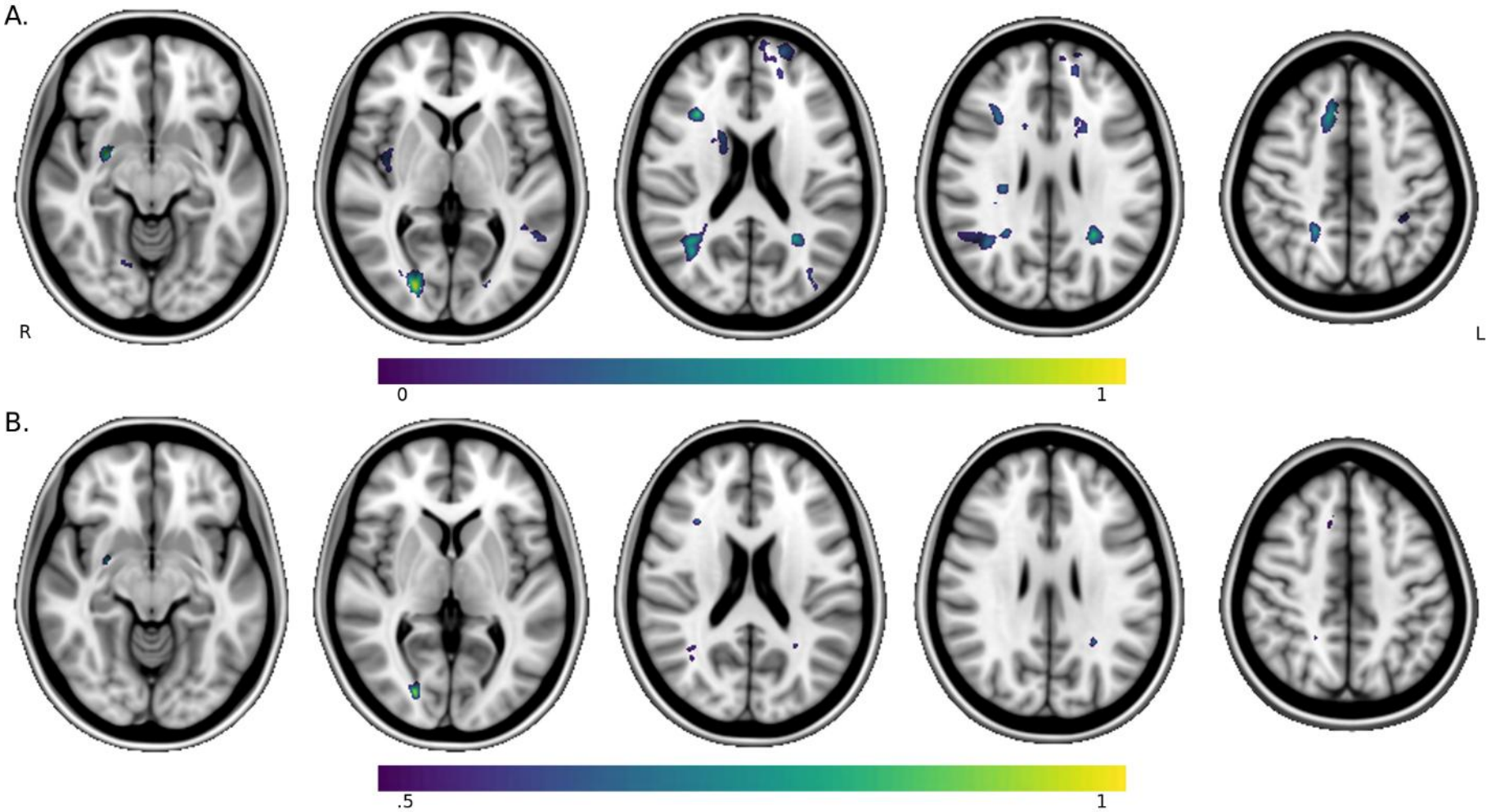
Hooper's Visual Organization Test



Judgment of Line Orientation



Rey-Osterrieth Complex Figure Copy

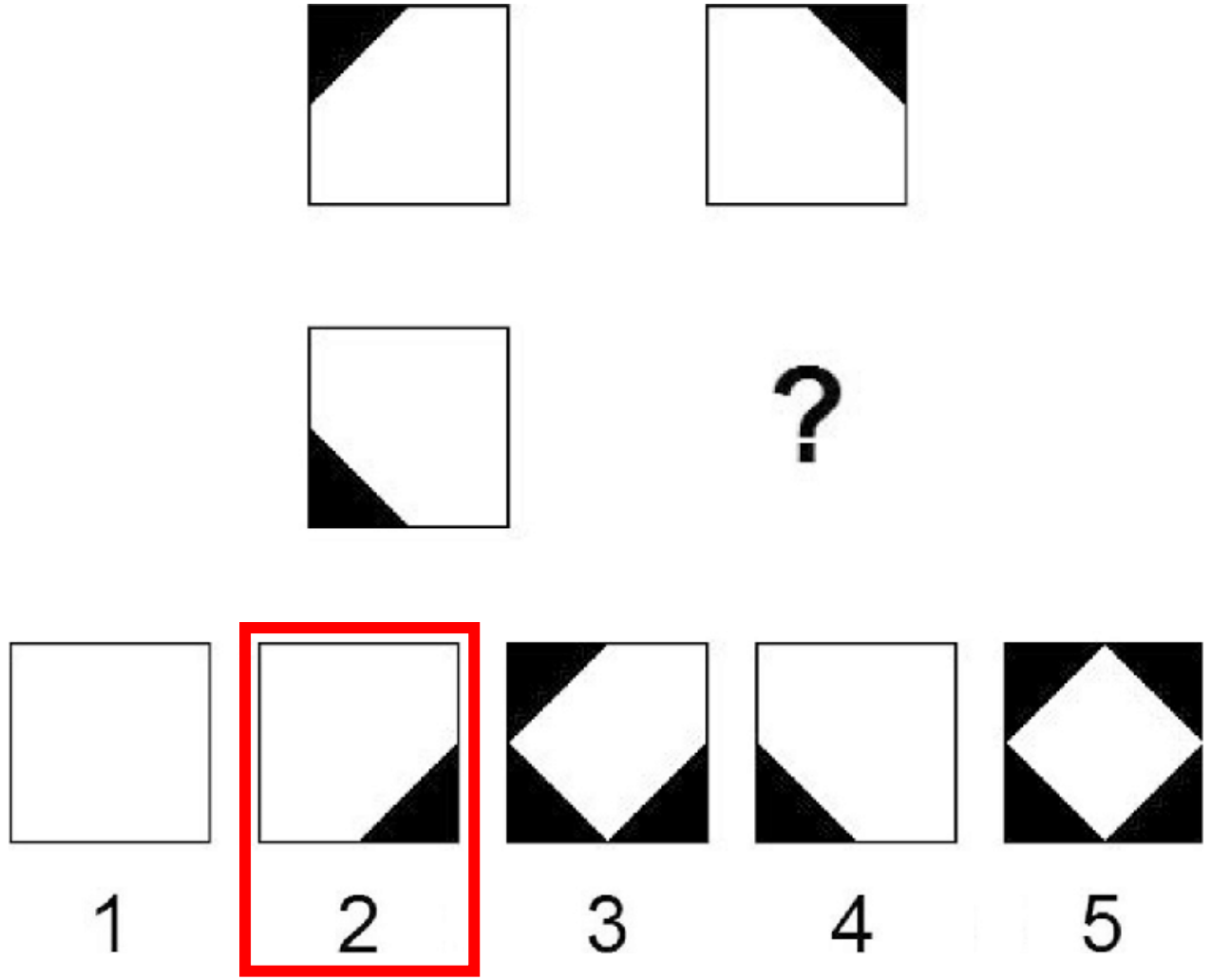


Spatial Span

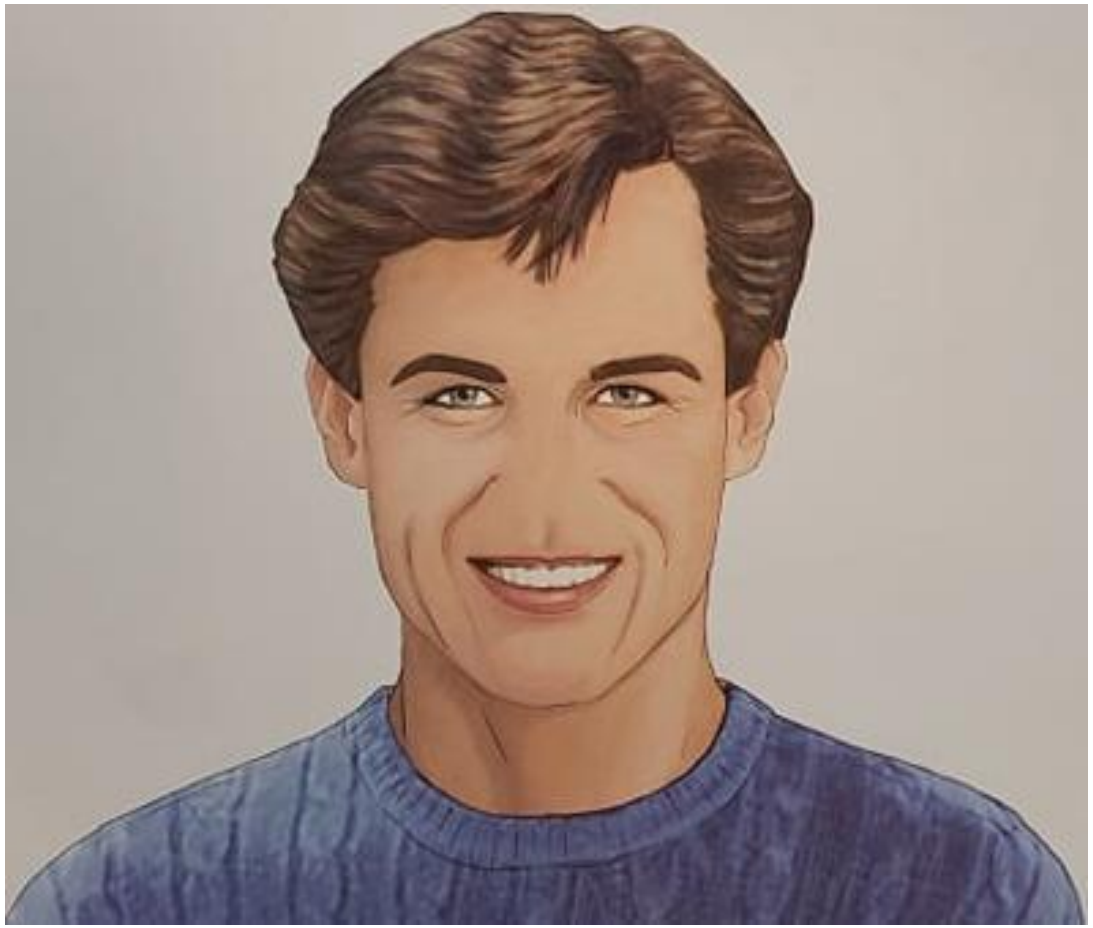
Block Design (BD)

Digit Symbol Coding (CD)

Matrix Reasoning (MR)



Picture Completion (PC)



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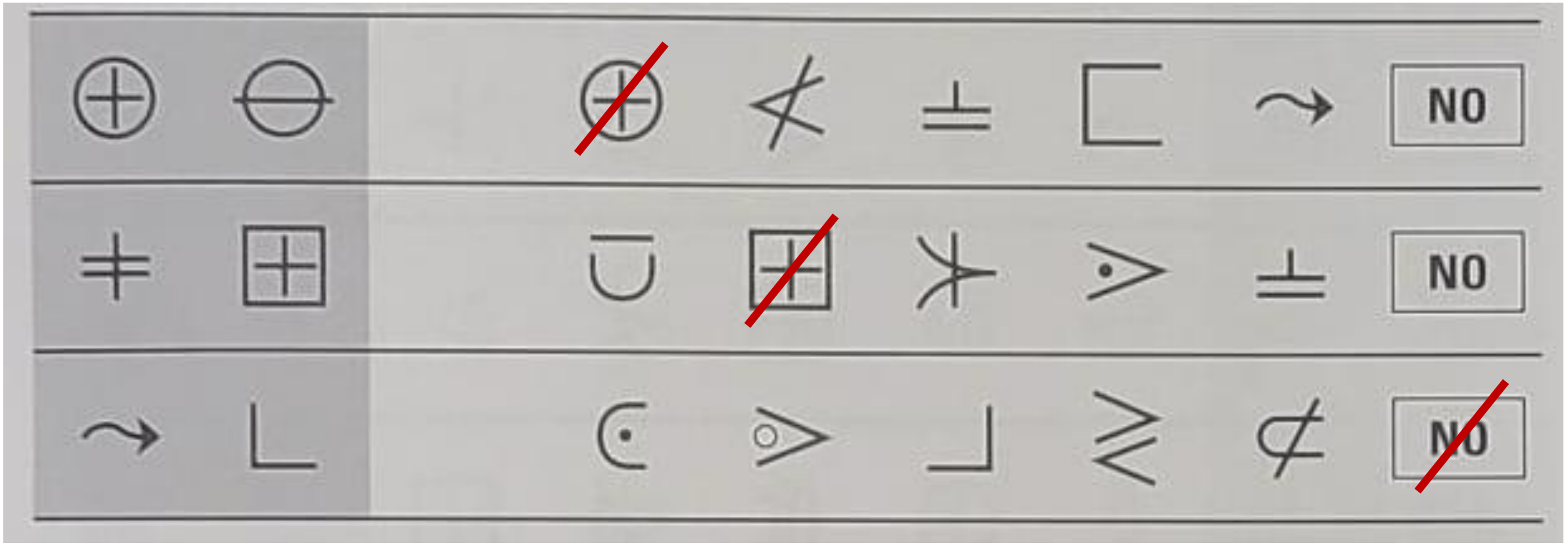
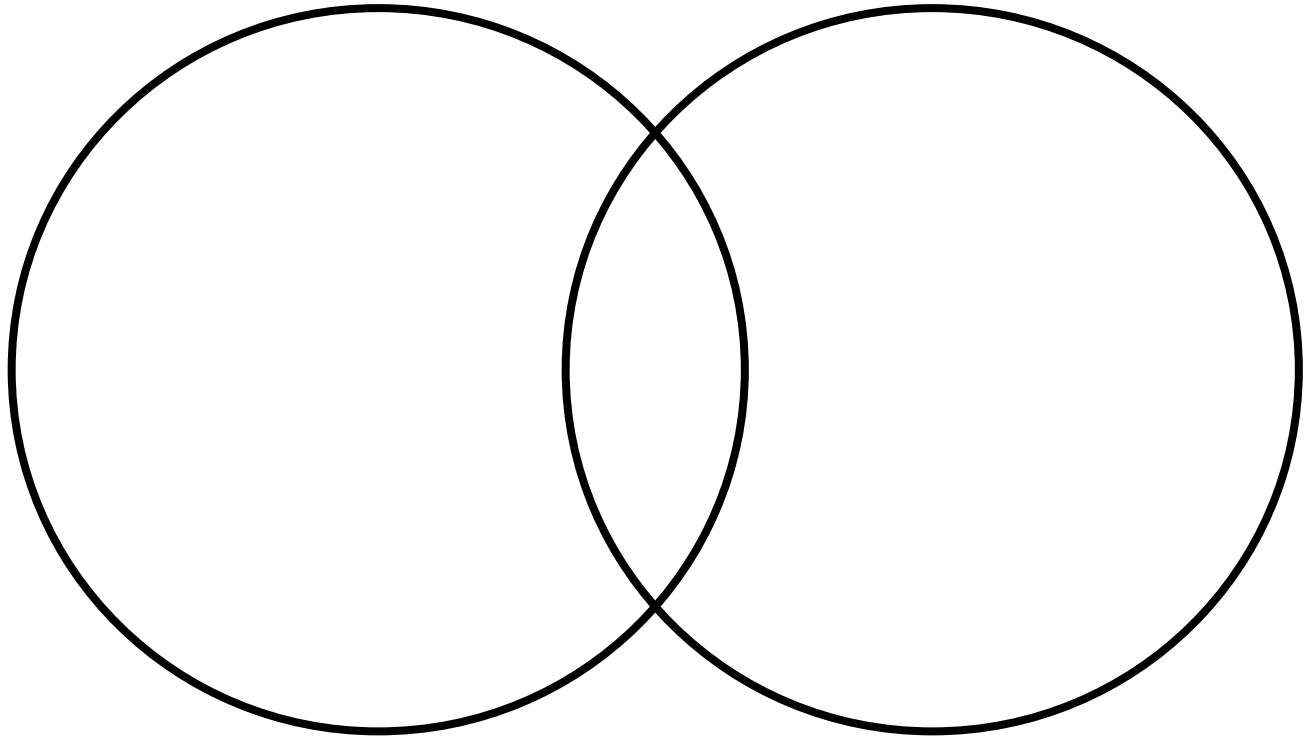
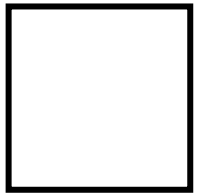


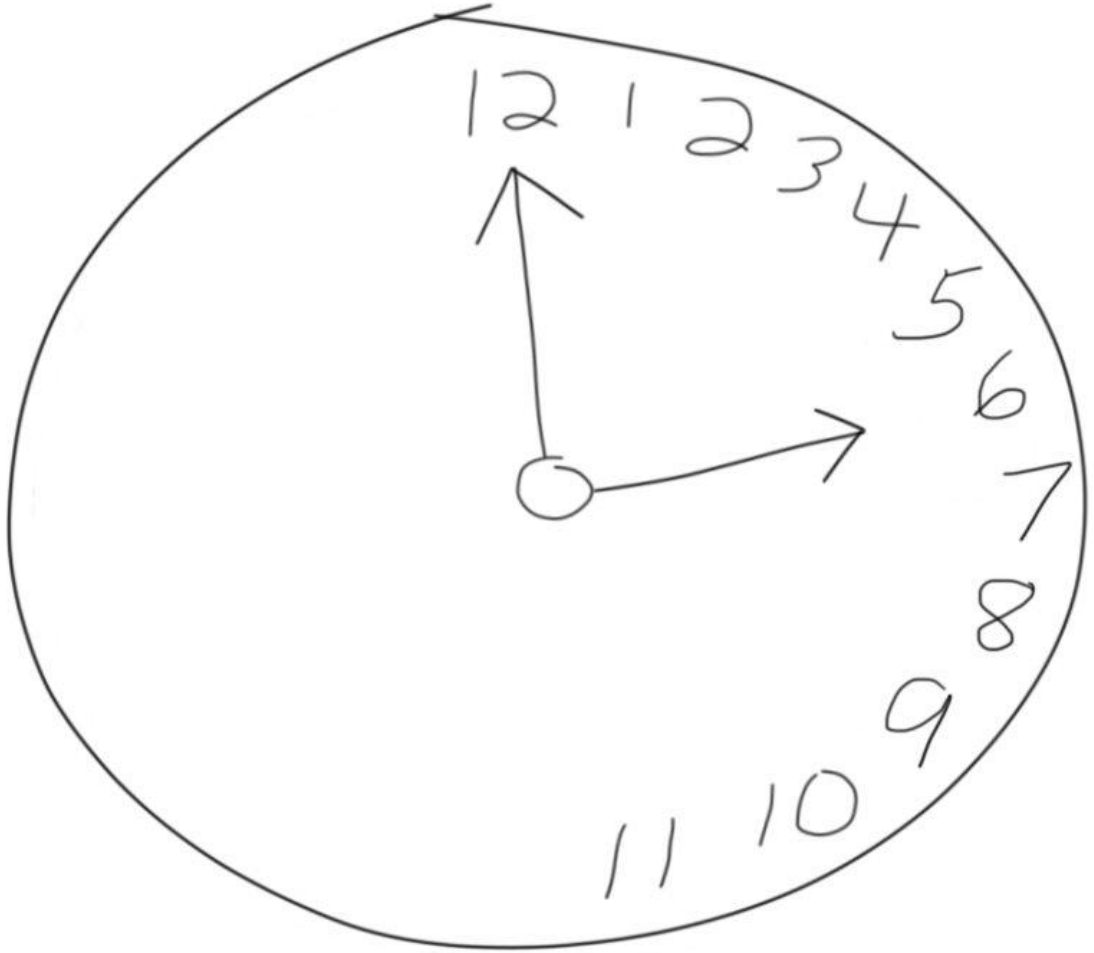
Benton Facial Recognition Test (BFRT)

Benton Visual Retention Test (BVRT)

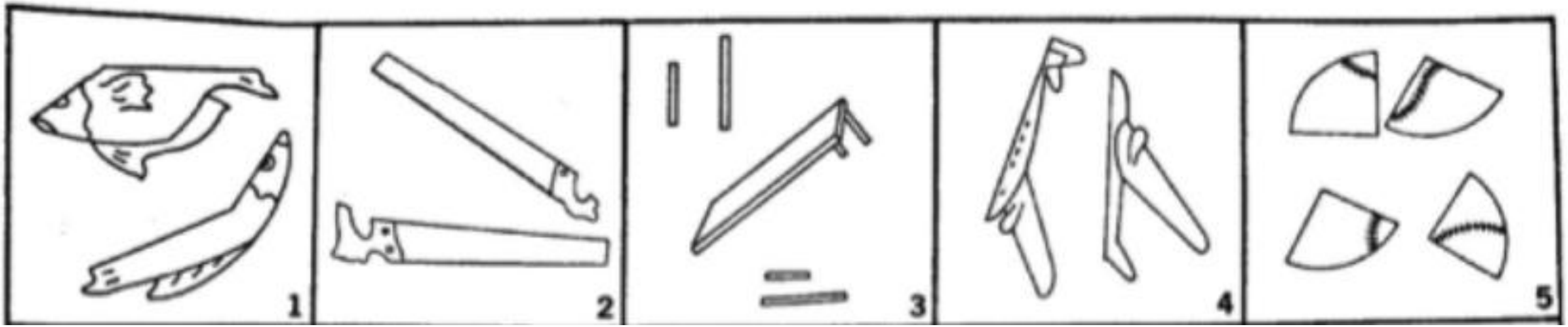




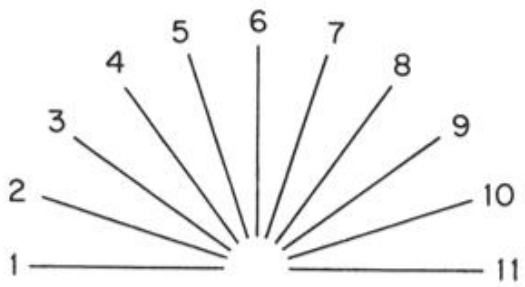
Clock Drawing



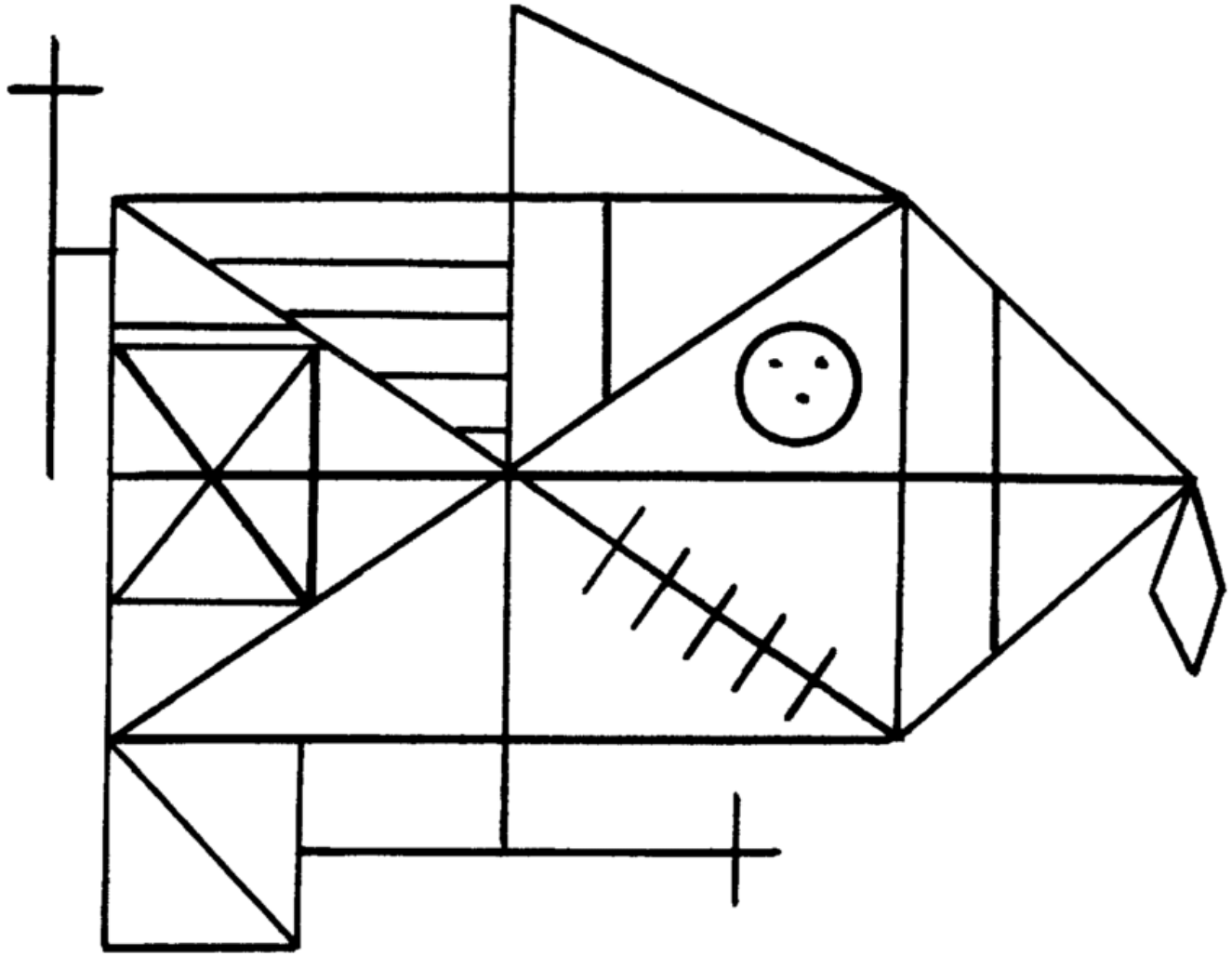
Hooper Visual Organization Test (HVOT)



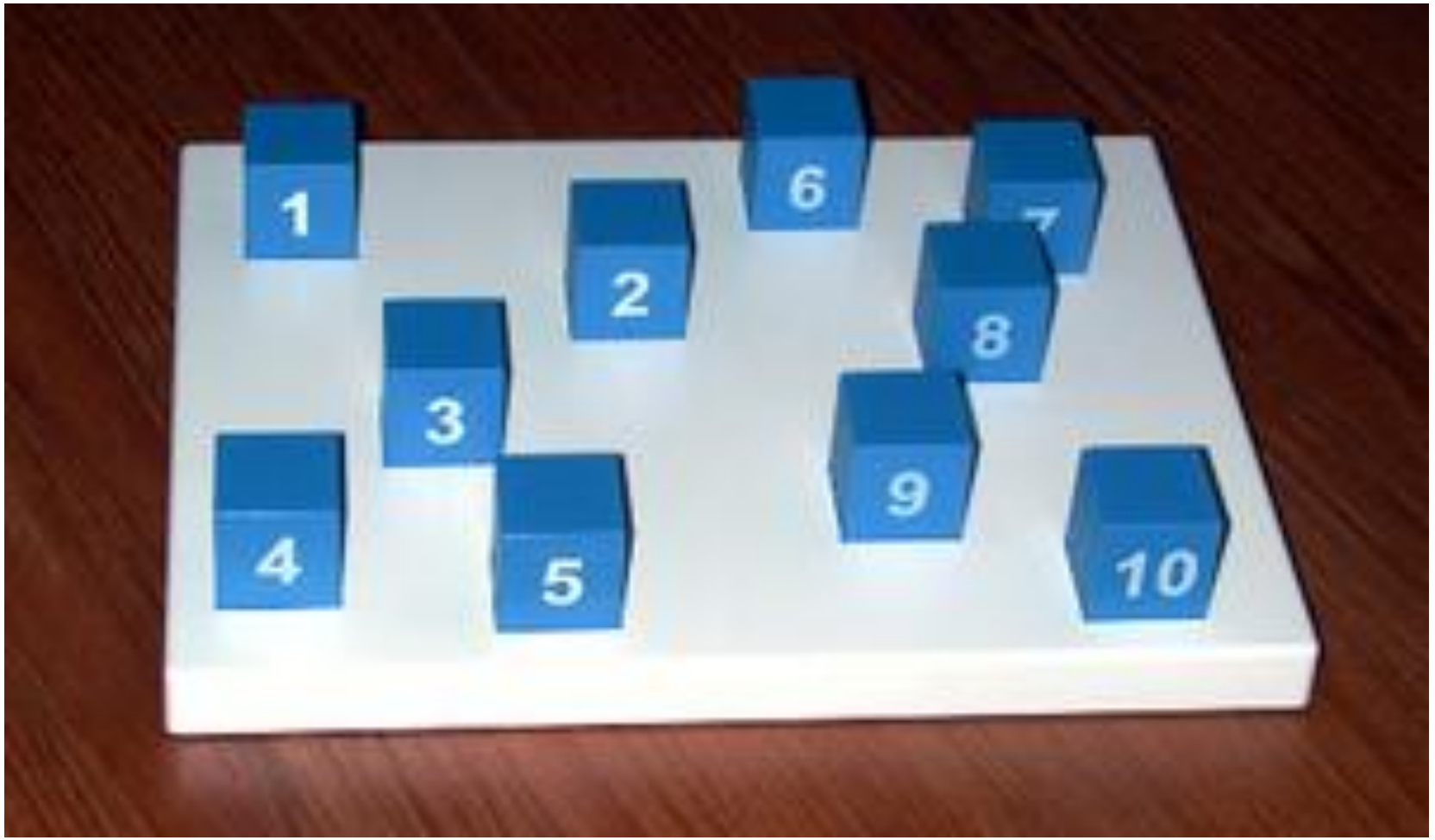
Judgment of Line Orientation (JLO)



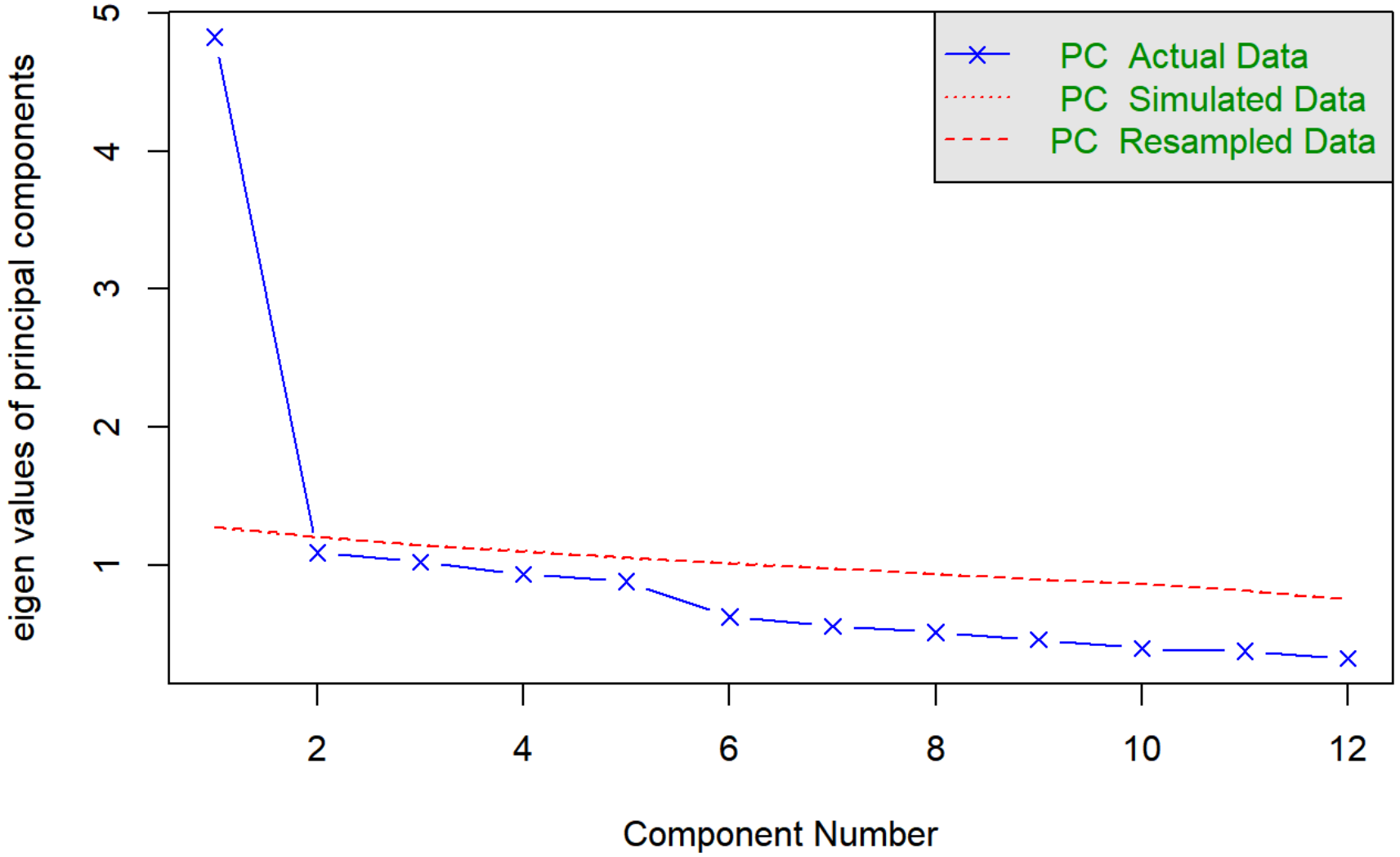
Rey-Osterrieth Complex Figure Test (CFT)



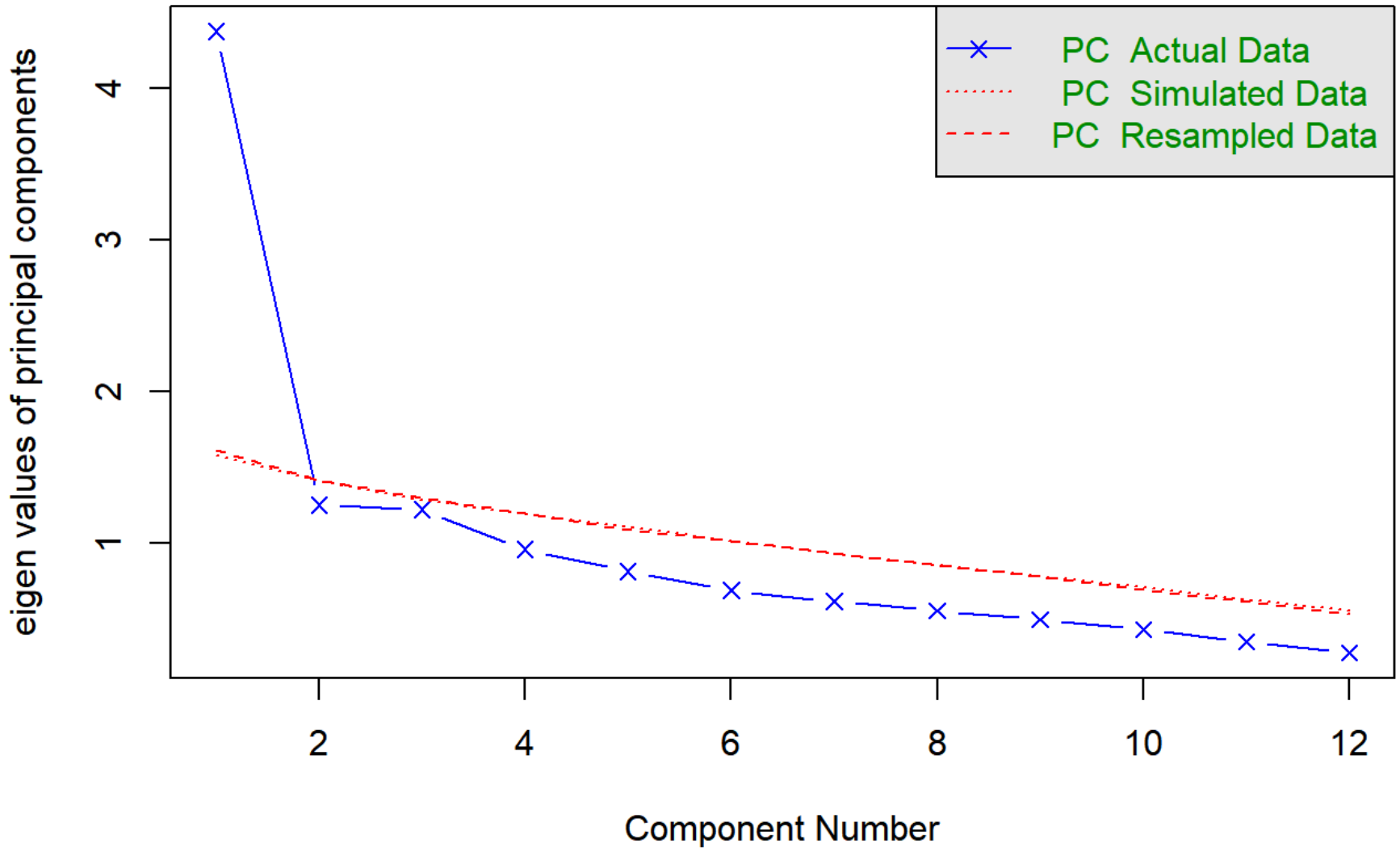
Spatial Span (SpaS)



PA Scree Plot For Patients with 8+ Tests



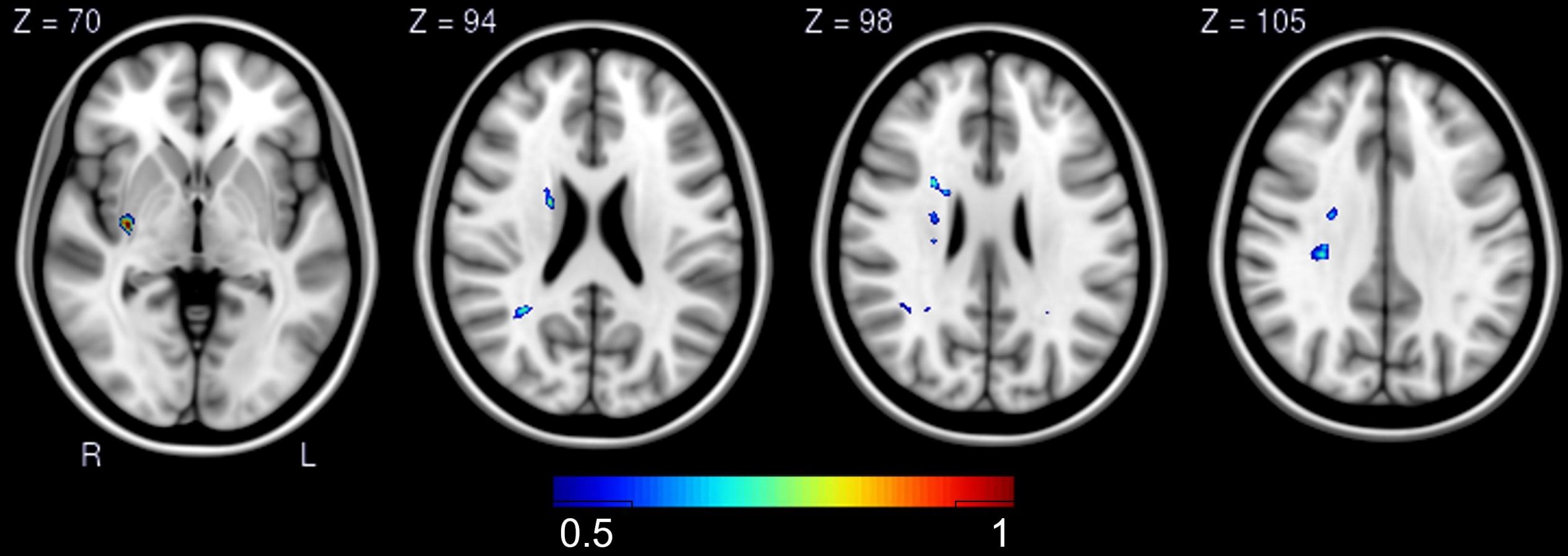
PA Scree Plot For Patients with All Tests



Bonus Slides

Individual Test LESYMAPs

Block Design



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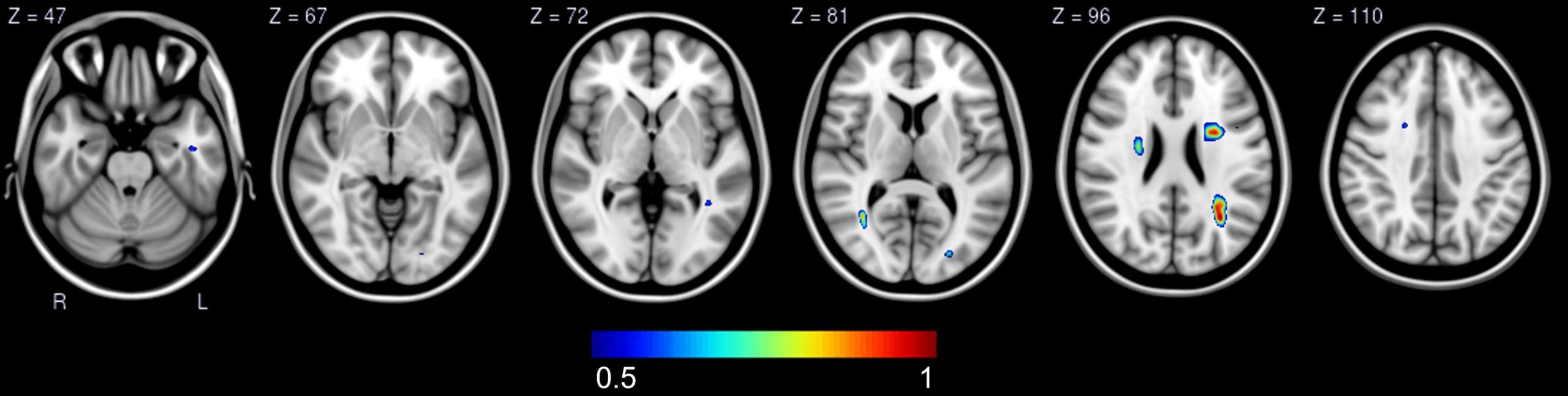
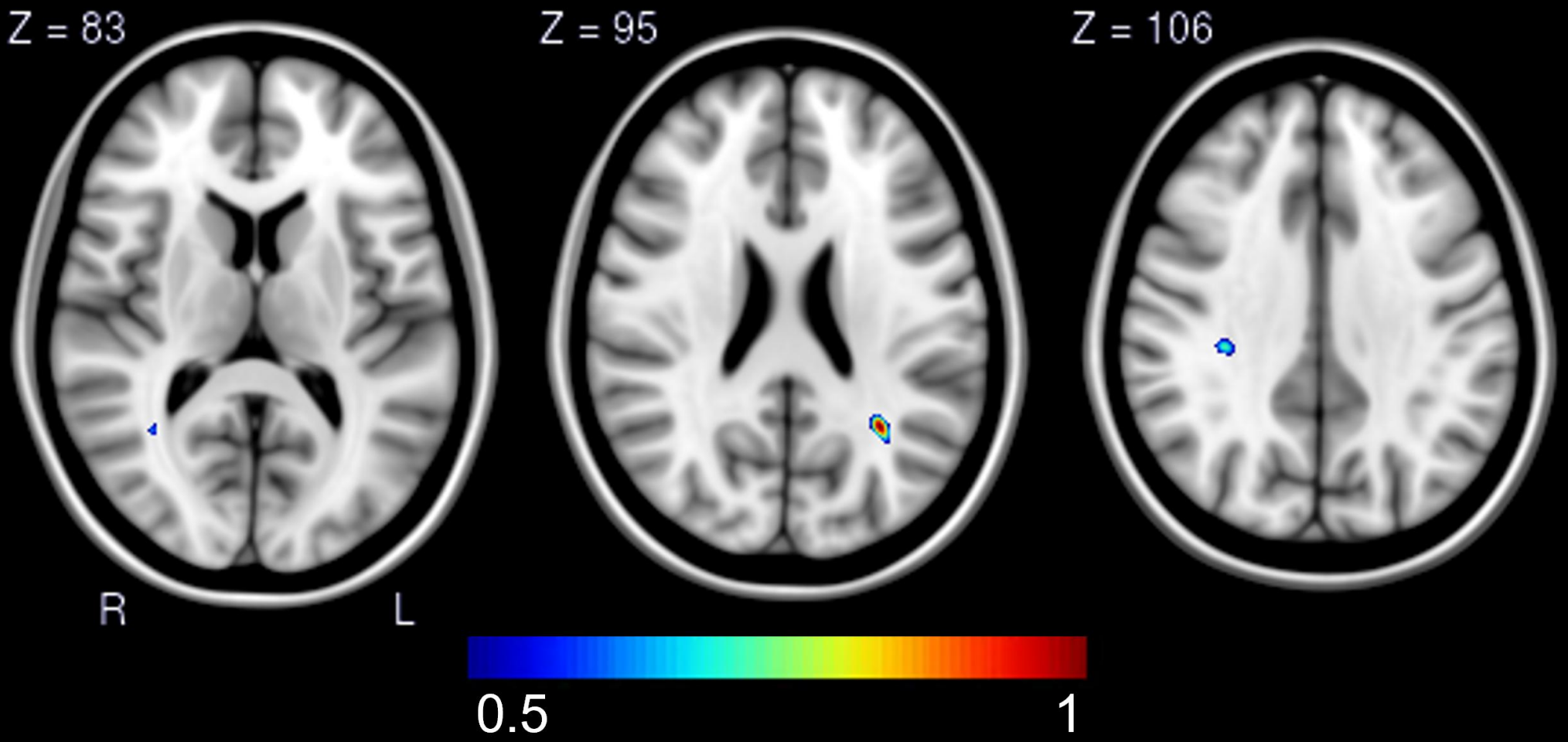
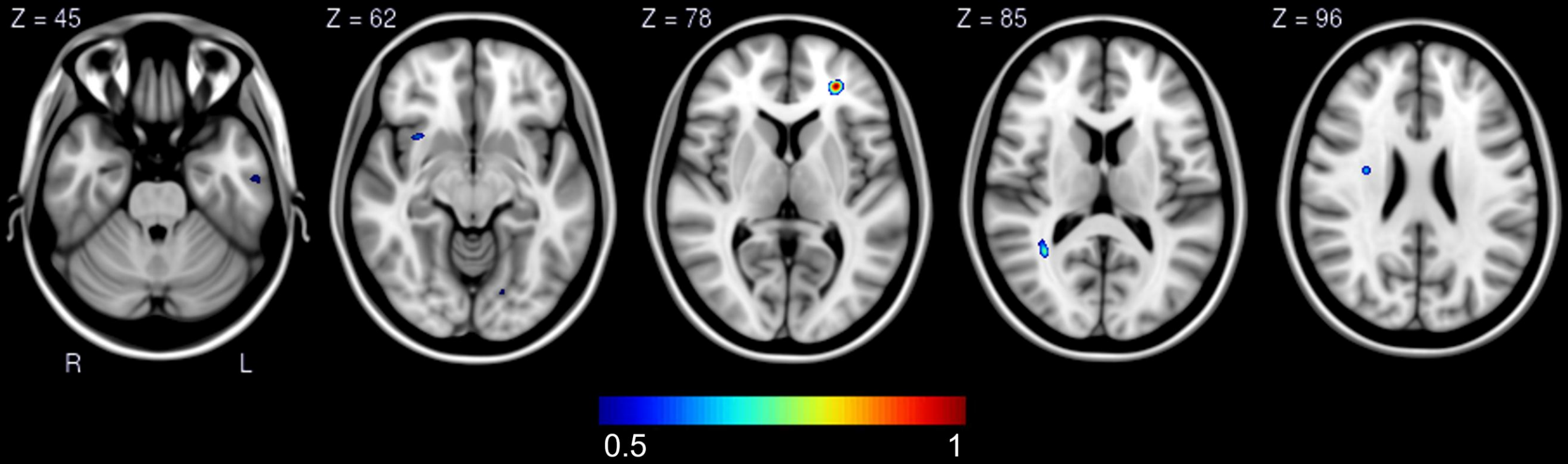


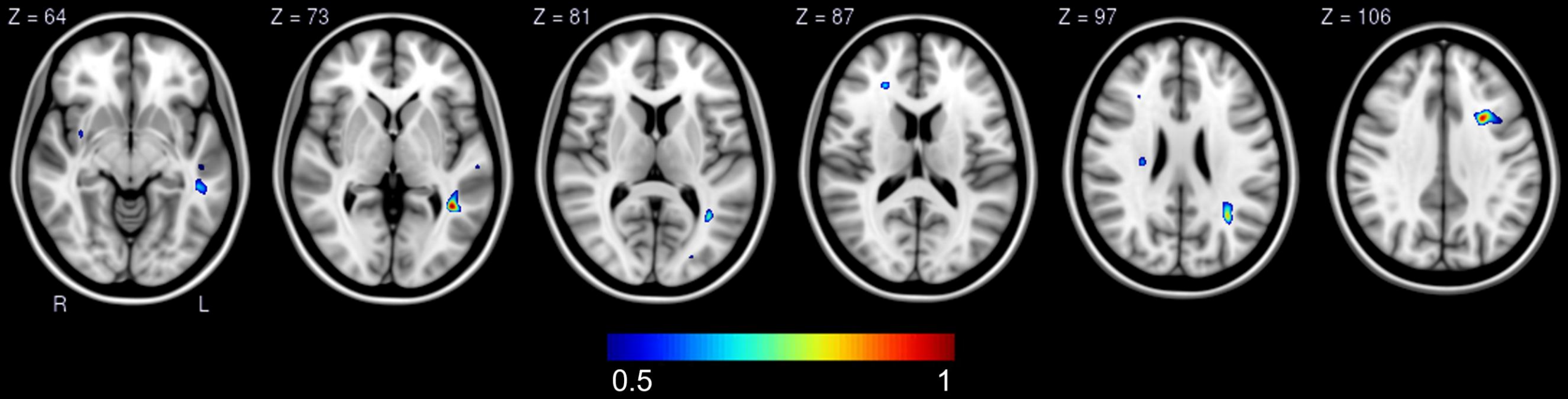
Matrix Reasoning



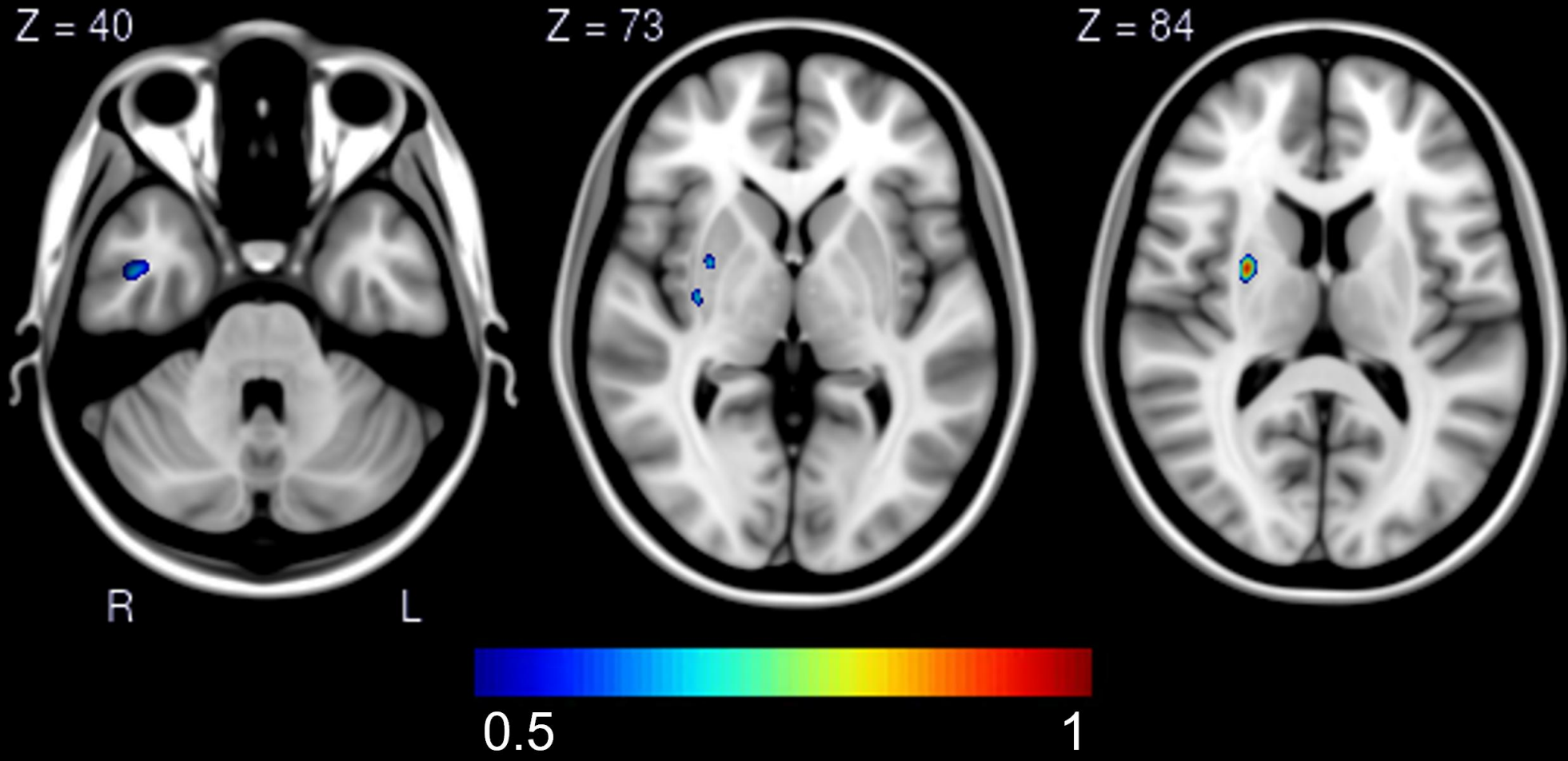
Picture Completion



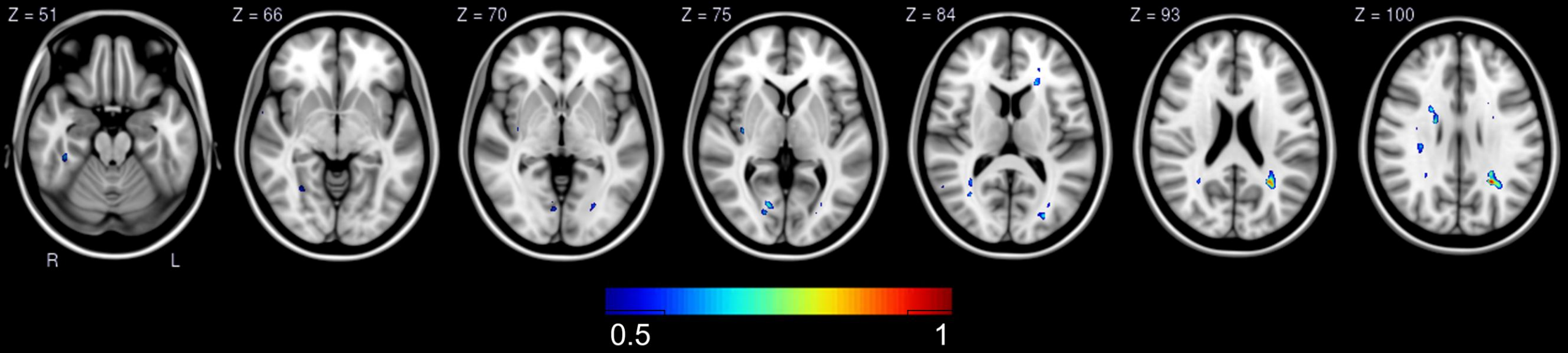
Symbol Search



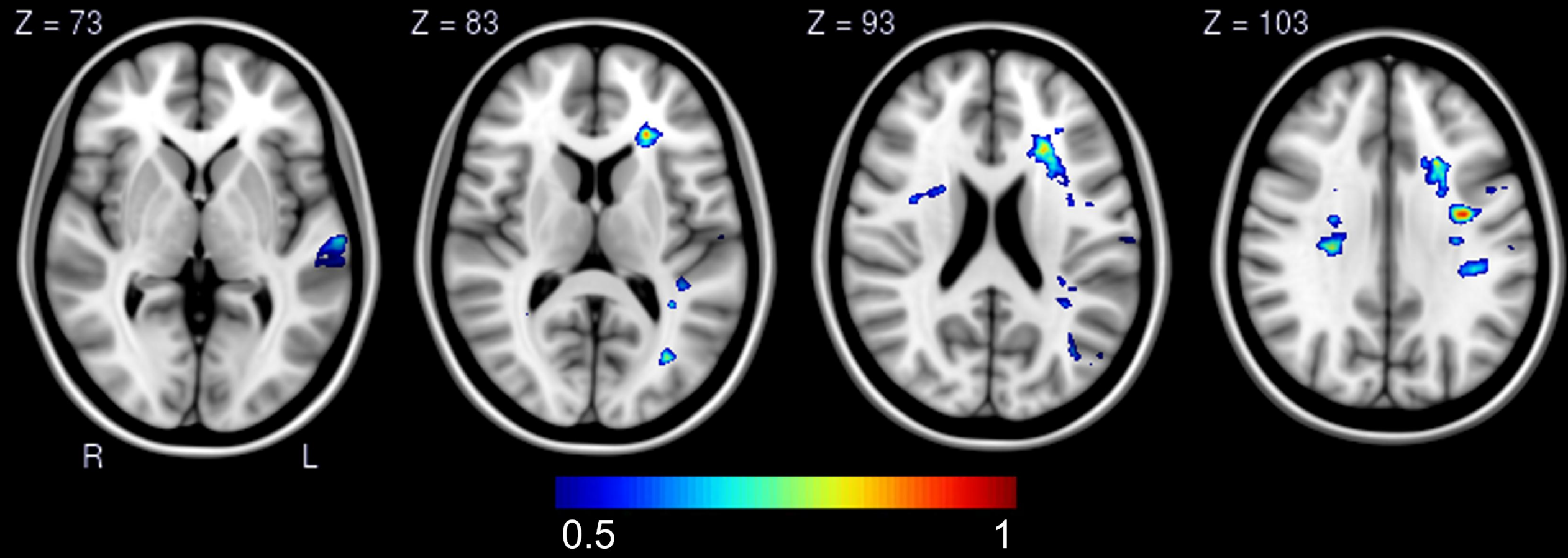
Benton Facial Recognition Test



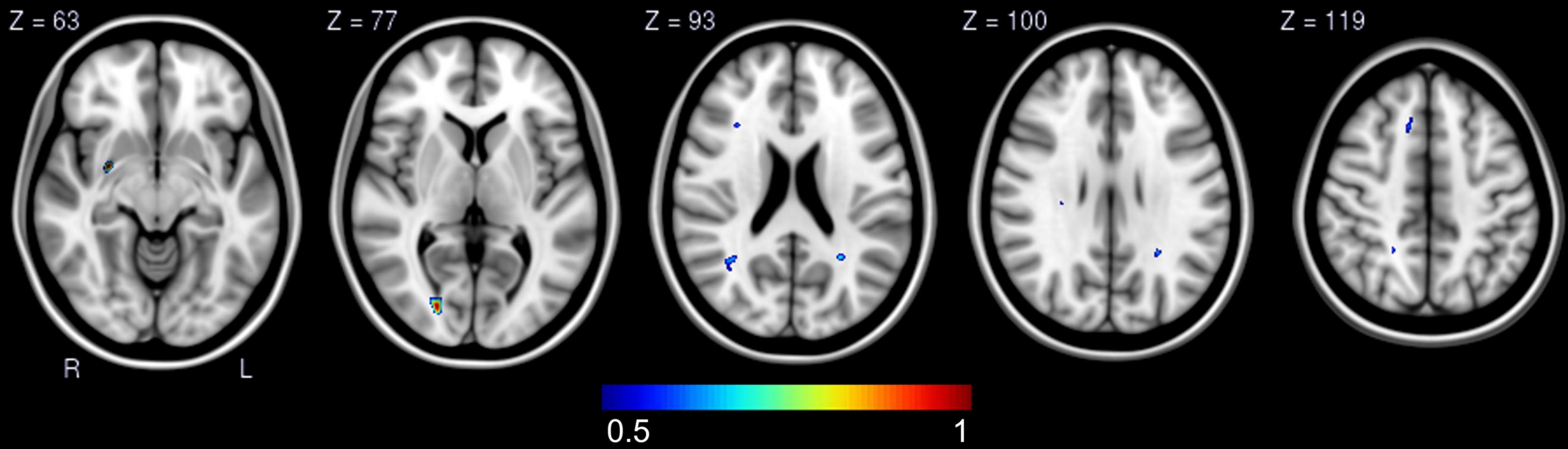
Benton Visual Retention Test



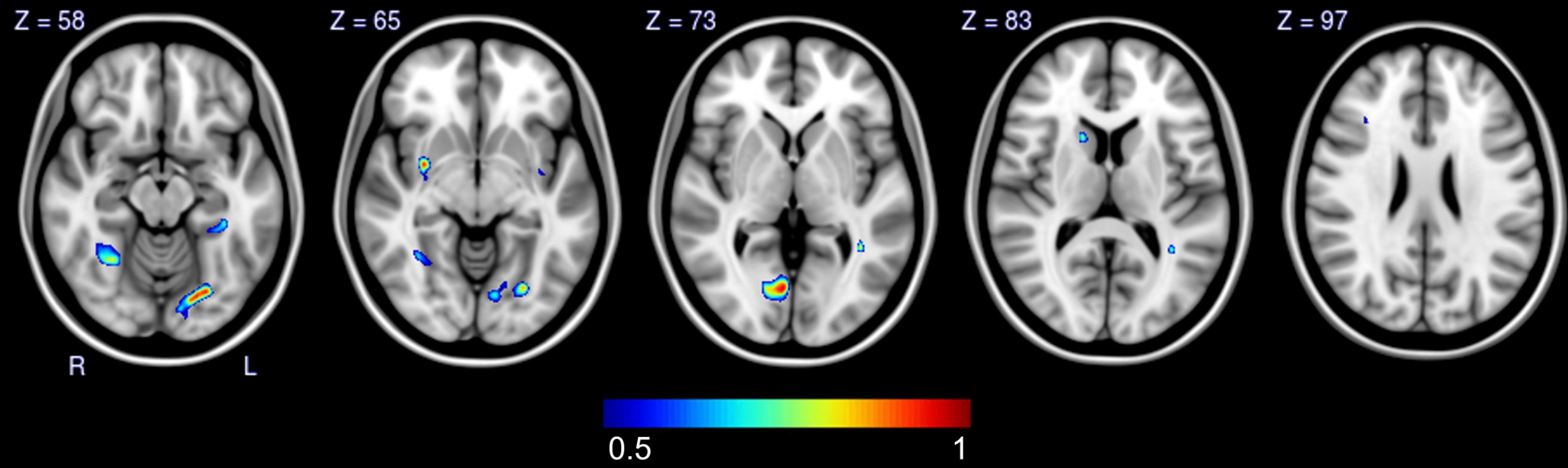
Clock Drawing



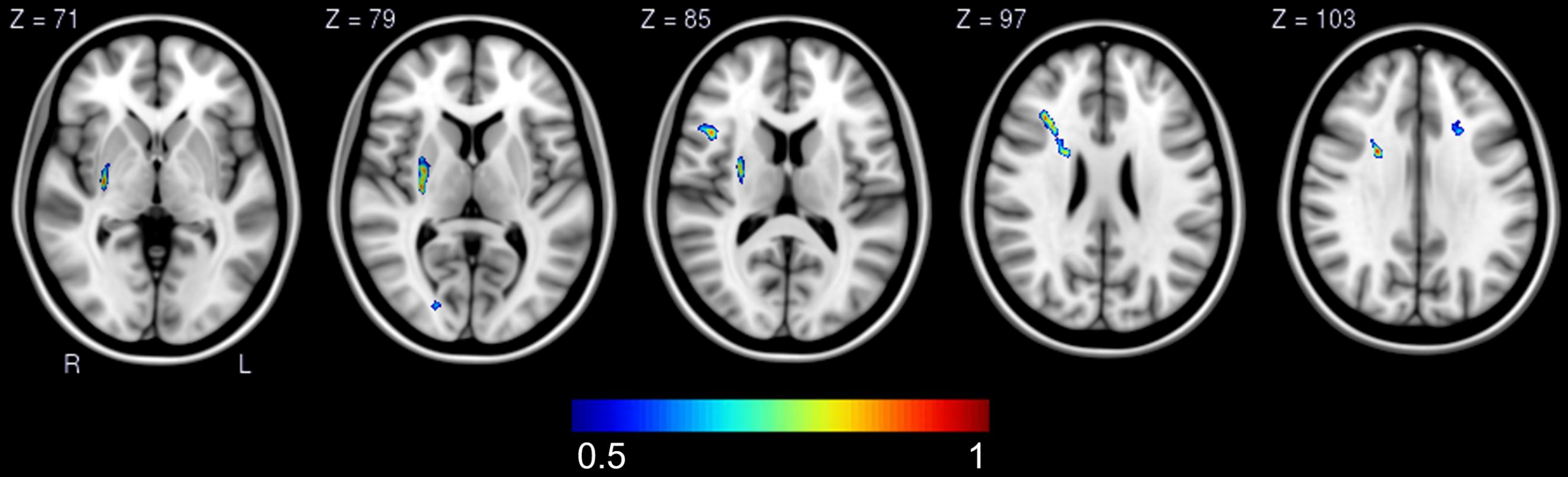
Complex Figure Copy



Hooper Visual Organization Test



Judgment of Line Orientation



Bonus Slides

Neuropsychological tests to be used