2021 43rd Annual International Conference of the
IEEE Engineering in Medicine & Biology Society (EMBC)
Oct 31 - Nov 4, 2021. Virtual Conference

Associations between Cortical Asymmetry and Domain Specific Cognitive Functions in Healthy Children*

Rajikha Raja[1], Xiaoxu Na[1], Charles M. Glasier[1,2], Thomas M. Badger[2,3], Jayne Bellando[2], Xiawei Ou[1,2,3]

Abstract— **Cortical asymmetry and functional lateralization form intriguing and fundamental features of human brain organization, and is complicated by individual differences and evolvement with age. While many studies have investigated neuroanatomical differences between hemispheres as well as functional lateralization of the brain for different age groups, few have looked into the associations between cortical asymmetry and development of cognitive functions in children. In this study, we aimed to identify relationships between hemispheric asymmetry in brain cortex measured by MRI and cognitive development in healthy young children evaluated by a comprehensive battery of neuropsychological tests. Structural MRI data were obtained from 71 children in the age range of 7.5 to 8.5 years. Structural lateralization index (SLI), a reflection of the brain asymmetry, was computed for each of the 3 cortical morphometry measurements: cortical thickness, surface area and gray matter volume. A total of 34 bilateral regions were studied for the whole brain cortex as defined by the Desikan atlas. Region-wise SLI was correlated with domain specific cognitive scores using partial correlation analysis controlled for the potential confounding effects of age and sex. Significant correlations were identified between test scores of multiple cognitive domains and SLI of several cortical regions. Specifically, SLI of total surface area of precuneus and insula significantly correlated with measures of executive function behavior; significant relationships were also found between SLI of mean cortical thickness of superior parietal cortex and memory and language tests scores; in addition, SLI of parahippocampal gyrus also showed significant correlations with language test scores for all 3 morphometry features. These findings revealed regional hemispheric asymmetries that may be linked to specific cognitive abilities in children.**

Clinical relevance— **This study shows associations between structural lateralization in different brain cortical regions and variations in specific cognitive functions in healthy children.**

I. INTRODUCTION

Differences or asymmetries between left and right hemispheres of human brain are defined as structural or functional lateralization based on whether they are in structural anatomy or cognitive functions respectively [1]. Characterizing the associations between lateralization and cognitive abilities is important to fully understand brain asymmetry in the developing brain which may help identify developmental instability related to brain disorders [2]. These associations are complex to understand owing to the overlapping and mixed relations among them [3], [4]. Several studies have aimed at exploring the brain lateralization in structural and functional aspects in both children and adults [5], [6]. Varying results showing different or similar asymmetrical patterns between adults and children were reported previously, while majority of the studies focused on the adult population [7]. Moreover, most of the studies focused on the quantification of lateralization and its associations with biological variables such as age and gender [5], [8]. Only few studies reported on the relationships between structural lateralization and cognitive functions [9], [10], [11], [12], [13]. In this study, we aimed to identify the relationships between cortical structural asymmetry and different domains of cognitive development in 8-year-old children.

Multiple MRI modalities were utilized in previous studies of human brain lateralization [14], [15], [16], [17], [18]. For example, structural MRI can analyze the hemispheric differences related to morphometric measurements in cortical and sub-cortical regions. White matter microstructural and tract specific asymmetries can be studied using diffusion MRI and associated techniques. Language lateralization can be easily demonstrated using functional MRI. In this work, we utilized structural MRI to compute the brain asymmetry and structural lateralization in young children based on cortical morphometric measurements, and evaluated its relationships with a comprehensive set of neuropsychological test scores spanning various cognitive domains including intelligence, memory, language, academic skills and executive function.

II. MATERIALS AND METHODS

A. Participants

Seventy-one healthy children (31 boys and 40 girls) aged between 7.5 and 8.5 years were included in this study. Approval was obtained from the Institutional Review Board of the University of Arkansas for Medical Sciences for the study protocol, informed consents were obtained from the parent(s)/guardian(s) and assents were obtained from the children before all experimental procedures. All subjects were healthy full-term born and right-handed with a reported birth weight between 5th and 95th percentile for age and with no prior or current medical conditions known to impact brain development or neurodevelopmental outcomes. The study protocol mainly included a brain MRI scan and a battery of neuropsychological assessments.

B. MRI Acquisition

Structural MRI data were acquired from all subjects on a 1.5T Achieva scanner (Philips Healthcare, Best, the Nether-

*This project is supported by USDA-ARS 6026-51000-012-06S at the Arkansas Children's Nutrition Center and NIH 1R01HD099099

[1]Department of Radiology, University of Arkansas for Medical Sciences, Little Rock, AR 72205 USA
[2]Department of Pediatrics, University of Arkansas for Medical Sciences, Little Rock, AR 72205 USA
[3]Arkansas Children's Nutrition Center, Little Rock, AR 72205 USA
Corresponding Author: Xiawei Ou, PhD. E-mail: OuXiawei@uams.edu

lands). The transmitter and receiver were the built-in body coil and a standard 8-channel SENSE head coil respectively. 3D turbo field echo pulse sequence was used for acquiring T1 weighted images with the following imaging parameters: repetition time, TR=7.3 ms, echo time, TE=3.4ms, 8^o flip angle, isotropic voxel size 1x1x1 mm, matrix size of 256 x 232 x 150, and 2 averages, with a total scan time of 7 minutes. All subjects were scanned on the same scanner, and image quality control was performed on the scanner by trained MRI staff. Scans with apparent motion artifacts were repeated, and those not able to complete the scan were excluded from the study.

C. MRI Analysis

Cortical morphometry and volumetric measurements were derived from post-processing of T1 weighted images using the standard recon-all pipeline available in FreeSurfer software version 6. Initially the images were preprocessed which included motion correction, removing non-brain tissue and registration to the Talairach space. The subsequent processing involved 3 tissue segmentation into white matter, gray matter and cerebro-spinal fluid, intensity normalization, gray and white matter boundary tesselation, topology correction and surface deformation. The white and pial surface models finally created were inflated and registered to be used for cortical parcellation. We used the Desikan atlas [19] for cortical parcellation to extract 34 brain regions in each hemisphere. Total surface area, mean cortical thickness and total gray matter volume for each of the 34 bilaterally paired cortical regions were computed as part of FreeSurfer analysis.

D. Cortical Structural Lateralization Index

Structural lateralization index (SLI) was computed individually for the 3 cortical morphometry and volumetric measures (total surface area, mean cortical thickness, and total gray matter volume) for each of the 34 cortical regions to evaluate the asymmetry between brain hemispheres. The formula used for SLI calculation is:

$$SLI_m^r = \frac{LEFT_m^r}{LEFT_m^r + RIGHT_m^r}$$

where m denotes the MRI measure (total surface area, mean cortical thickness and total gray matter volume) and r denotes the brain region. The SLI values range between 0 and 1. SLI values greater than 0.5 indicate leftward laterality and less than 0.5 indicate rightward laterality. SLI value of 0.5 denotes symmetrical cortical feature for the brain region.

E. Neuropsychological Scores

Intelligence quotient (IQ), memory, executive function, academic skills and general language ability were the 5 different cognitive domains evaluated in this study. The cognitive measurements were obtained using the following neuropsychological tests: Reynolds Intellectual Assessment Scales (RIAS) for measuring IQ, Clinical Evaluation of Language Fundamentals, Fourth Edition (CELF-4) for measuring language abilities, Children's Memory Scale (CMS) for memory and learning measurements, Wide Range Achievement Test, Fourth Edition (WRAT-4) for academic skills, and Behavior Rating Inventory of Executive Function (BRIEF) for an assessment of executive function behaviors. RIAS tests provides a verbal and non-verbal IQ score which is consolidated to a composite IQ score. The verbal IQ score is based on 2 subtests, Guess What and Verbal Reasoning whereas non-verbal IQ score is based on 2 subtests, Odd Item Out and What's Missing. CELF-4 assessments include 3 different language scores: Core, Receptive and Expressive language scores. These scores are obtained from subtests including Concepts and Following Directions, Word Structure, Recalling Sentences, Formulated Sentences, Word Classes Receptive, and Sentence Structure. CMS tests measure the learning, memory and attention skills of children via different index scores including Visual Immediate, Visual Delayed, Verbal Immediate, Verbal Delayed, Attention/Concentration, Learning, Delayed Recognition, and provides a composite score of General Memory. WRAT-4 assessment evaluates the academic skills in individuals via 2 major subtests, Word Reading and Sentence Comprehension. The individual test scores are also combined to a composite score. All of these assessments have slightly varying reference ranges, though mostly falling in a range having a mean of 100 and standard deviation of 15. Higher scores indicate better cognitive functioning. BRIEF is a parental-reported questionnaire based assessment to evaluate the executive functioning and behaviors in children. It includes 8 subscales including Inhibit, Shift, Emotional Control, Initiate, Working Memory, Plan/Organize, Organization of Materials, and Monitor. A composite score named Global Executive Composite is derived based on two summary scores: Behavioral Regulation Index and Metacognition Index. BRIEF scores have a mean of 50 with standard deviation of 10, and higher BRIEF scores indicate more problems in executive function and behavior.

F. Statistical Analysis

Statistical analysis was conducted using Python Scipy v1.6.1 and statsmodels v0.12.2. Partial correlation analysis was performed to find correlations between SLI and cognitive scores controlled for age and sex as covariates. Spearman's correlation coefficients were calculated and the P values were adjusted for multiple comparison correction using FDR correction for the 34 cortical regions. $P < .05$ after FDR correction was defined as significant.

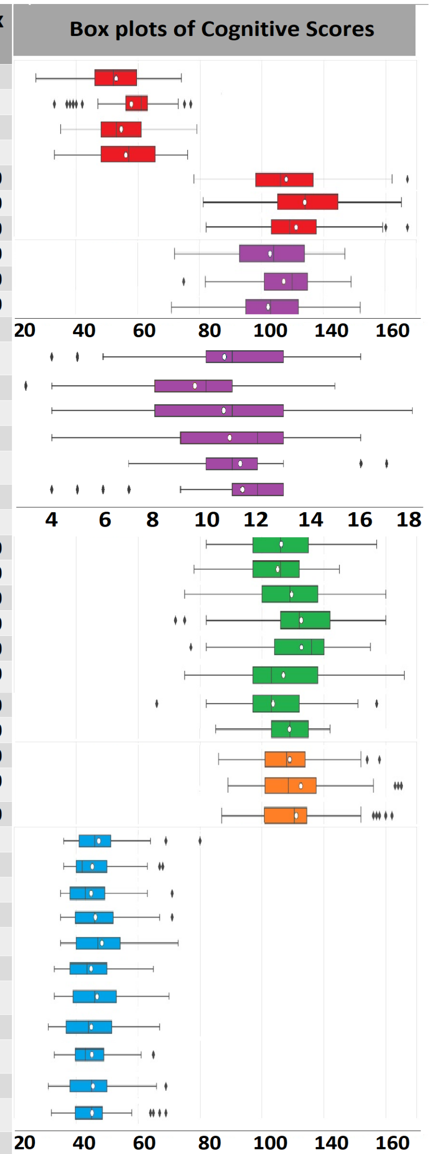
III. Results

A. Neuropsychological Scores

Seventy-one children (31 boys and 40 girls, at 7.9 ± 0.26 years of age) completed MRI and were included in this study. The detail information of the neuropsychological scores test are presented in Table.1, along with box plots showing the distribution for each of the scores. All scores were within the normal-for-the-age range.

TABLE I: Tabulated neuropsychological testing scores of various cognitive domains. Each row specifies the summary statistic of a cognitive score along with corresponding box plot in the rightmost column. Color coding is followed to differentiate between cognitive domains. RIAS, Reynolds Intellectual Assessment Scales; CELF, Clinical Evaluation of Language Fundamentals, Fourth Edition; CMS, Children's Memory Scale; WRAT-4, Wide Range Achievement Test, Fourth Edition; BRIEF, Behavior Rating Inventory of Executive Function; N, number of subjects included; SD, standard deviation; CI, confidence interval; Min, Minimum; Max, Maximum.

Cognitive Domains	Cognitive Scores	N	Mean ± SD	95% CI	Min-max
IQ (RIAS)	Guess What	71	52.96 ± 9.77	50.64-55.27	27.0-74.0
	Odd Item Out	71	57.83 ± 9.84	55.5-60.16	33.0-77.0
	Verbal Reasoning	71	54.55 ± 10.06	52.17-56.93	35.0-79.0
	What's Missing	71	56.03 ± 11.18	53.38-58.67	33.0-76.0
	Verbal IQ	71	107.8 ± 14.62	104.34-111.26	78.0-147.0
	Nonverbal IQ	71	113.82 ± 14.37	110.42-117.22	81.0-145.0
	Composite IQ	71	111.03 ± 12.77	108.01-114.05	82.0-147.0
Language (CELF-4)	Core Language	69	102.83 ± 13.13	99.67-105.98	72.0-127.0
	Receptive Language	67	107.28 ± 9.99	104.85-109.72	75.0-129.0
	Expressive Language	69	102.28 ± 13.54	99.02-105.53	71.0-132.0
	Concepts & Following Directions	69	10.71 ± 2.52	10.11-11.31	4.0-16.0
	Word Structure	69	9.55 ± 2.63	8.92-10.18	3.0-15.0
	Recalling Sentences	69	10.68 ± 2.84	10.0-11.36	4.0-18.0
	Formulated Sentences	69	10.91 ± 2.87	10.22-11.6	4.0-16.0
	Word Classes Receptive	67	11.31 ± 1.75	10.89-11.74	7.0-17.0
	Sentence Structure	69	11.41 ± 2.18	10.88-11.93	4.0-13.0
Memory (CMS)	Visual Immediate	69	106.2 ± 12.4	103.22-109.18	82.0-137.0
	Visual Delayed	69	105.0 ± 9.71	102.67-107.33	78.0-125.0
	Verbal Immediate	69	109.55 ± 13.5	106.31-112.79	75.0-140.0
	Verbal Delayed	69	112.64 ± 14.01	109.27-116.0	72.0-140.0
	General Memory	69	112.74 ± 12.71	109.69-115.79	77.0-135.0
	Attention/ Concentration	69	106.91 ± 15.89	103.09-110.73	75.0-146.0
	Learning	69	103.59 ± 12.55	100.58-106.61	66.0-137.0
	Delayed Recognition	69	108.84 ± 9.9	106.46-111.22	85.0-122.0
Academic Skills (WRAT-4)	Word reading	69	108.99 ± 11.56	106.21-111.76	86.0-138.0
	Sentence Comprehension	68	112.6 ± 15.06	108.96-116.25	89.0-145.0
	Reading Composite	68	111.1 ± 13.22	107.9-114.3	87.0-142.0
Executive (BRIEF)	Inhibit	68	47.32 ± 8.13	45.36-49.29	36.0-80.0
	Shift	68	45.22 ± 7.95	43.3-47.14	36.0-68.0
	Emotional Control	68	44.84 ± 8.03	42.89-46.78	35.0-71.0
	Initiate	68	46.28 ± 8.25	44.28-48.28	35.0-71.0
	Working Memory	68	48.37 ± 9.12	46.16-50.57	35.0-73.0
	Plan/Organize	68	44.84 ± 8.1	42.88-46.8	33.0-65.0
	Organization of Materials	68	46.78 ± 10.08	44.34-49.22	33.0-70.0
	Monitor	68	44.91 ± 9.19	42.69-47.14	31.0-67.0
	Behavioral Recognition	68	45.07 ± 7.48	43.26-46.88	33.0-65.0
	Metacognition	68	45.49 ± 8.86	43.34-47.63	31.0-69.0
	Global Executive Composite	68	45.19 ± 8.05	43.24-47.14	32.0-69.0



B. Structural Lateralization Indices

SLI of all 34 bilateral regions are shown in Fig.1 with 3 plots corresponding to the 3 morphometry measurements. Fig.1A shows the SLI range for total surface area in which 18 regions had SLI greater than 0.5, 14 regions had SLI lesser than 0.5, and 2 regions were close to symmetrical. Fig.1B shows the SLI range for mean cortical thickness in which 14 regions had SLI greater than 0.5, 18 regions had SLI lesser than 0.5, and 2 regions were close to symmetrical. Fig.1C shows the SLI range for total gray matter volume in which 18 regions had SLI greater than 0.5 and 14 regions had SLI lesser than 0.5, and 2 regions were close to symmetrical.

C. Correlation between SLI and Cognitive Scores

SLI of 4 cortical regions: superior parietal cortex, parahippocampul gyrus, insula, and precuneus showed significant correlation ($P < .05$ after FDR correction) with different cognitive domains including memory, language, and executive function (Fig. 2). Details regarding the significant correlations for the 4 regions with Spearman's correlation coefficient (R) and corresponding P values are elaborated in the following:

1) Insula: SLI of total cortical surface area of insula significantly and positively correlated with executive function measures including Working Memory score ($R = .44, P =$

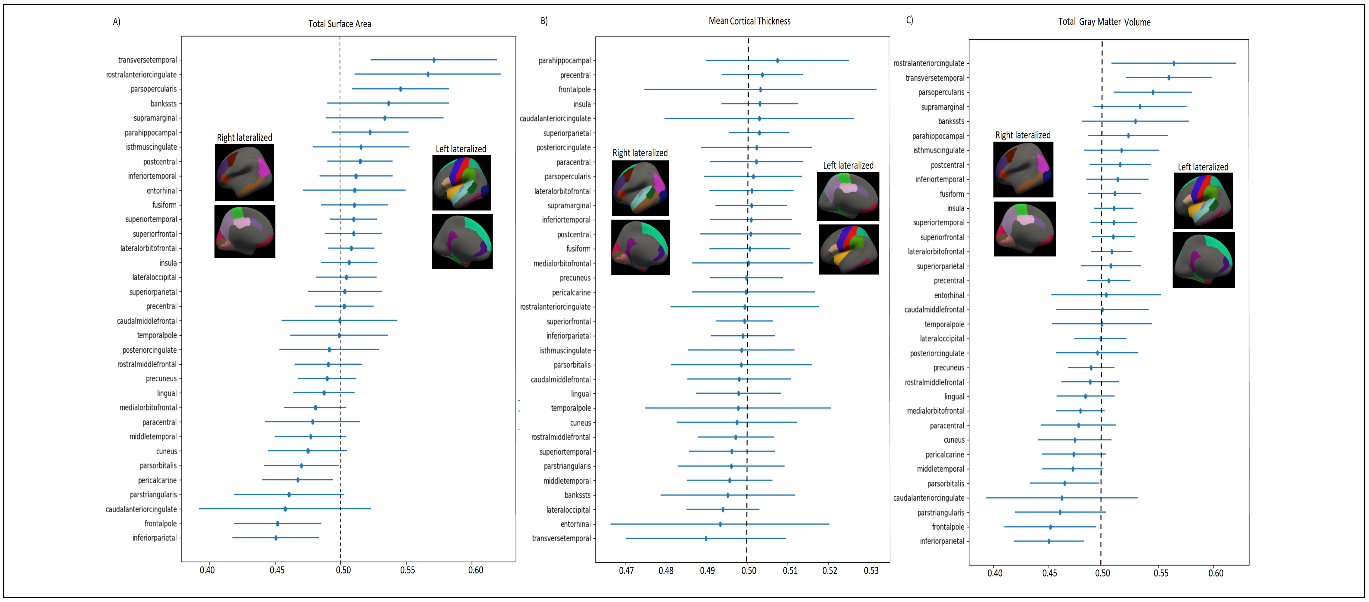


Fig. 1: Line Plots showing SLI information for the 34 brain regions, with mean value denoted in the center circle and the range of line showing the standard deviation. Dotted line indicates SLI of 0.5 (corresponding to symmetry). Lateralized regions were shown in the inflated brain template images. SLI values shown are for A) total cortical surface area B) mean cortical thickness and C) total cortical gray matter volume.

.02) and Metacognition score ($R = .42, P = .04$) (Fig. 2A).

2) Precuneus: SLI of total cortical surface area of precuneus significantly and negatively correlated with executive function measures including Global Executive Composite score ($R = -.44, P = .02$), Metacognition score ($R = -.40, P = .04$), and Plan-Organize score ($R = -.44, P = .02$) (Fig. 2B).

3) Superior Parietal Cortex: SLI of mean cortical thickness of superior parietal cortex significantly and positively correlated with memory and language measures including Delayed Recognition ($R = .44, P = .01$), Core Language ($R = .41, P = .04$), and Word Structure ($R = .46, P = .009$) (Fig. 2C).

4) Parahippocampal Gyrus: SLI of total cortical gray matter volume ($R = .42, P = .009$) and total cortical surface area ($R = .42, P = .009$) of parahippocampal gyrus significantly and positively correlated with language measures, specifically, Word Structure (Fig. 2D).

IV. Discussion

In this study, we investigated the associations between cortical gray matter asymmetries and cognitive functioning in healthy 8-year-old children. The results demonstrated significant relationships between cortical structural lateralization and differences in cognitive behavior in children. Insula and precuneus were the regions which showed lateralization-related associations with executive functions. SLI of surface area of insula showed positive correlation with executive functions, indicating that the surface area of insula tends to be more right lateralized for those with fewer problems in behavior related executive functions. This is interesting as previous studies of insula lateralization reported associations between asymmetry in insula and emotional behaviors and language for which leftward structural asymmetries were accompanied by larger left hemisphere dominance for gesture and language functions [20], [21]. The negative correlations between SLI of precuneus surface area and executive function and behavior issues indicate that this region tends to be more left lateralized in children with better executive functioning related to the ability to plan, organize, initiate and sustain working memory. This is somewhat consistent with a few studies that reported positive associations between left lateralized precuneus and language functions and arithmetic skills [21], [22]. Finally, left lateralization of superior parietal cortex and parahippocampal gyrus was related with increased language and memory scores. This is consistent with results reported in previous lateralization studies [14], [2]. Studies have also showed that various subtests assessing language functions correlated with left lateralization of parahippocampal gyrus [5], [23], consistent with findings in our current study.

While our study reported several novel relationships between cortical structural asymmetry and cognitive performance in children and may provide new information to help better understand brain structure-function relationships, there are a few limitations of our study. One is that the sample size is relatively small, which may have limited us to identify more relationships. In addition, the narrow age range of the cohort could be seen as both positive and negative. The positive side is establishing a specific relation pattern between SLI and cognitive performance at age 8 years which is a critical time that many of these cognitive functions start to develop drastically; whereas the limitation is that the findings of this study could not be

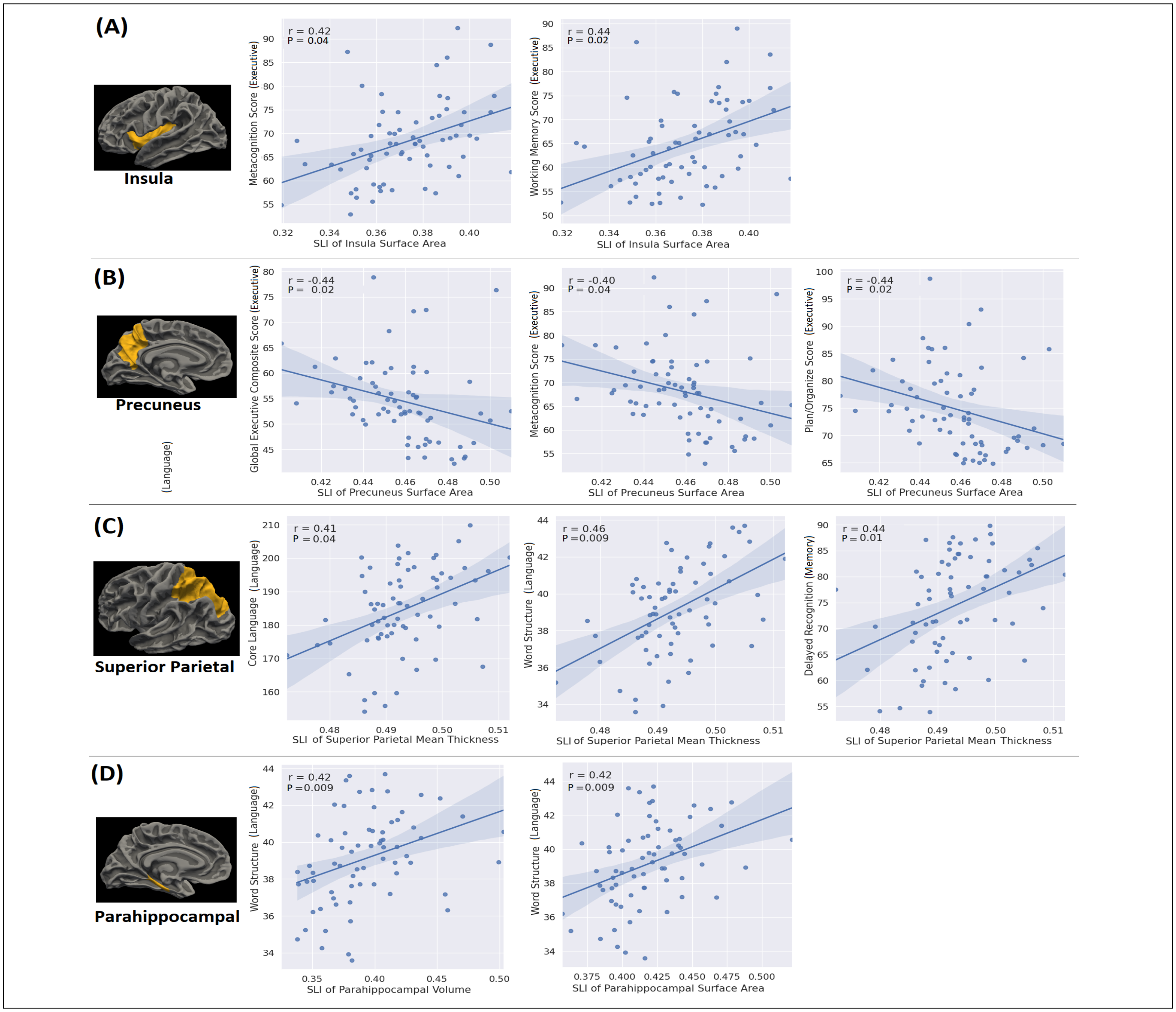


Fig. 2: Plots shown for FDR corrected significant correlations between SLI of morphometry measurements and cognitive scores. Brain regions are highlighted on the left, and correlations are illustrated by scatter plots on the right. A) SLI of total surface area of Insula positively correlated with executive function domain related BRIEF scores (Metacognition and Working Memory). B) SLI of total surface area of precuneus negatively correlated with executive function domain related BRIEF scores (Global Executive Composite, Metacognition and Plan/Organize). C) SLI of mean thickness of superior parietal cortex positively correlated with language domain related CELF scores (Core language and Word Structure) and with memory domain related CMS score (Delayed Recognition). D) SLI of total cortical gray matter volume and total surface area of parahippocampal gyrus positively correlated with language domain related CELF score (word structure).

generalized to children of all ages. Finally, we identified only the relationships between cortical gray matter asymmetries and cognitive scores whereas white matter and functional asymmetries were not evaluated in this study.

V. Conclusions

Our study of brain cortical asymmetry and cognitive functioning in healthy children indicated significant relationships between structural lateralization index in several brain regions and neuropsychological test performance in several measures. In general, more leftward lateralization tended to be associated with better language and memory functioning, while either more leftward or more rightward lateralization in different regions were associated with less executive functioning issues. Future studies including longitudinal analysis and additional modalities to understand white matter and functional lateralization can help to gain more insights in brain structure-function relationships.

Acknowledgment

This project was supported by USDA-ARS 6026-51000-012-06S at the Arkansas Children's Nutrition Center. The PI is also supported by NIH 1R01HD099099. None of the authors have any potential financial conflicts-of-interests related with this study.

References

[1] Norman Geschwind and Albert M. Galaburda. Cerebral Lateralization: Biological Mechanisms, Associations, and Pathology: III. A Hypothesis and a Program for Research. *Archives of Neurology*, 42(7):634–654, 1985.

[2] Arthur W. Toga Thompson and Paul M. Mapping brain asymmetry. *Nature Reviews Neuroscience*, 4:37–48, 2003.

[3] Sebastian Ocklenburg, Patrick Friedrich, Onur Güntürkün, and Erhan Genç. Intrahemispheric white matter asymmetries: the missing link between brain structure and functional lateralization? *Reviews in the Neurosciences*, 27(5):465–480, 2016.

[4] Esteves Madalena, Susana S Lopes, Armando Almeida, Nuno Sousa, and Hugo Leite-Almeida. Unmasking the relevance of hemispheric asymmetries–break on through (to the other side). *Progress in neurobiology*, page 101823, 2020.

[5] Xiang-Zhen Kong, Samuel R Mathias, Tulio Guadalupe, Laterality Working Group, David C Glahn, Barbara Franke, Fabrice Crivello, Nathalie Tzourio-Mazoyer, Simon E Fisher, Paul M Thompson, and Clyde Francks. Mapping cortical brain asymmetry in 17,141 healthy individuals worldwide via the ENIGMA Consortium. *PNAS*, 2017.

[6] Philip Shaw, Francois Lalonde, Claude Lepage, Cara Rabin, Kristen Eckstrand, Wendy Sharp, Deanna Greenstein, Alan Evans, ; J N Giedd, and Judith Rapoport. Development of Cortical Asymmetry in Typically Developing Children and Its Disruption in Attention-Deficit/Hyperactivity Disorder. *Arch Gen Psychiatry*, 66(8):888–896, 2009.

[7] L Jäncke and H Steinmetz. Anatomical brain asymmetries and their relevance for functional asymmetries. *The asymmetrical brain*, 187:229, 2003.

[8] Xiang-Zhen Kong, Merel C Postema, Tulio Guadalupe, Carolien de Kovel, Premika S W Boedhoe, Martine Hoogman, Samuel R Mathias, Daan van Rooij, Dick Schijven, David C Glahn, Sarah E Medland, Neda Jahanshad, Sophia I Thomopoulos, Jessica A Turner, Jan Buitelaar, Theo G M van Erp, Barbara Franke, Simon E Fisher, Odile A van den Heuvel, Lianne Schmaal, Paul M Thompson, Clyde Francks, Del Rey, and Correspondence Clyde Francks. Mapping brain asymmetry in health and disease through the ENIGMA consortium. *Human Brain Mapping*, 2020.

[9] Marco Catani, Matthew P.G. Allin, Masud Husain, Luca Pugliese, Marsel M. Mesulam, Robin M. Murray, and Derek K. Jones. Symmetries in human brain language pathways correlate with verbal recall. *Proceedings of the National Academy of Sciences of the United States of America*, 104(43):17163–17168, 2007.

[10] Ruma Madhu Sreedharan, Amitha C. Menon, Jija S. James, Chandrasekharan Kesavadas, and Sanjeev V. Thomas. Arcuate fasciculus laterality by diffusion tensor imaging correlates with language laterality by functional MRI in preadolescent children. *Neuroradiology*, 57(3):291–297, 2015.

[11] Ting Qi, Gesa Schaadt, and Angela D. Friederici. Cortical thickness lateralization and its relation to language abilities in children. *Developmental Cognitive Neuroscience*, 39(April):100704, 2019.

[12] Lateralization of the Arcuate Fasciculus from Childhood to Adulthood and its Relation to Cognitive Abilities in Children. *Human Brain Mapping*, 30:3563–3573, 2009.

[13] Ronald A Yeo, Sephira G Ryman, Jessica Pommy, Robert J Thoma, and Rex E Jung. General cognitive ability and fluctuating asymmetry of brain surface area. *Intelligence*, 2016.

[14] E Luders, K L Narr, P M Thompson, D E Rex, L Jancke, and A W Toga. Hemispheric Asymmetries in Cortical Thickness. *Cerebral Cortex*, 2005.

[15] F Lie Âgeois, A Connelly, J Helen Cross, S G Boyd, D G Gadian, F Vargha-Khadem, and T Baldeweg. Language reorganization in children with early-onset lesions of the left hemisphere: an fMRI study. *Brain*, 2004.

[16] Sacide E. Urger, Michael D. De Bellis, Stephen R. Hooper, Donald P. Woolley, Steven D. Chen, and James Provenzale. The superior longitudinal fasciculus in typically developing children and adolescents: Diffusion tensor imaging and neuropsychological correlates. *Journal of Child Neurology*, 30(1):9–20, 2015.

[17] Olumide A Olulade, Anna Seydell-Greenwald, Catherine E Chambers, Peter E Turkeltaub, Alexander W Dromerick, Madison M Berl B , William D Gaillard, Elissa L Newport, Rachel I Mayberry, and Nicholas B Turk-Browne. The neural basis of language development: Changes in lateralization over age. *PNAS*, 117(38):23477–23483, 2020.

[18] Vijay Narayan Tiwari, Jeong-Won Jeong, Eishi Asano, Robert Rothermel, Csaba Juhasz, and Harry T Chugani. A Sensitive Diffusion Tensor Imaging Quantification Method to Detect Language Laterality in Children: Correlation With the Wada Test. *Journal of Child Neurology*, 2011.

[19] Rahul S Desikan, Florent Ségonne, Bruce Fischl, Brian T Quinn, Bradford C Dickerson, Deborah Blacker, Randy L Buckner, Anders M Dale, R Paul Maguire, Bradley T Hyman, et al. An automated labeling system for subdividing the human cerebral cortex on mri scans into gyral based regions of interest. *Neuroimage*, 31(3):968–980, 2006.

[20] Szymon P Biduła and Gregory Kr. Structural asymmetry of the insula is linked to the lateralization of gesture and language. *European Journal of Neuroscience*, 41:1438–1447, 2015.

[21] Philippe Pinel and Stanislas Dehaene. Beyond hemispheric dominance: Brain regions underlying the joint lateralization of language and arithmetic to the left hemisphere. *Journal of Cognitive Neuroscience*, 22(1):48–66, 2010.

[22] Anna-Lisa Schuler, Lisa Bartha-Doering, · András Jakab, Ernst Schwartz, Rainer Seidl, Patric Kienast, Sonja Lackner, Georg Langs, Daniela Prayer, and · Gregor Kasprian. Tracing the structural origins of atypical language representation: consequences of prenatal mirror-imaged brain asymmetries in a dizygotic twin couple. *Brain Structure and Function*, 223:3757–3767, 2018.

[23] Lisa Bartha-Doering, Kathrin Kollndorfer, Gregor Kasprian, Astrid Novak, Anna Lisa Schuler, Florian Ph S. Fischmeister, Johanna Alexopoulos, William Davis Gaillard, Daniela Prayer, Rainer Seidl, and Madison M. Berl. Weaker semantic language lateralization associated with better semantic language performance in healthy right-handed children. *Brain and Behavior*, 2018.