White Matter Fiber Tracts & Deformational Plagiocephaly

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Introduction

- A substantial increase in positional plagiocephaly/brachycephaly (PPB) has been noted in healthy infants following the American Academy of Pediatrics back to sleep recommendations in an effort to prevent sudden infant death (Branch et al., 2015; Jung & Yun, 2020)
- Sick and premature infants are especially susceptible to PPB secondary to prolonged bed rest and or other movement restrictions (Marshall & Shahzad, 2020)
- Less severe forms of PPB may resolve spontaneously; however, studies demonstrate that some children without corrective intervention had positional head shape deformity later in childhood (Kunz et al., 2019; Wilbrand et al., 2016)
- There is concern and hypotheses that developmental problems associated with PPB may be the result of compression of the brain and deformation of the skull in the region of flattening, but these concerns/hypotheses have not been completely explored
- Many studies have linked PPB to gross and fine motor delays, communication deficits, vision and hearing problems, as well as delayed developmental milestones
- New opportunities using magnetic resonance imaging (MRI) with diffusion tensor imagining (DTI) and diffusion tension tractography (DTT) have allowed for the exploration of white matter fiber tracts (WMFT) microstructures of the brain
- Findings through DTT can serve as a link between brain characterizes and functional problems therefore making it a using tool to investigate relationships between PPB and infant development

Purpose and Aims

Purpose: To describe WMFT development for healthy infants with a range of plagiocephaly/brachycephaly severity.

Aims:

- 1. Describe the brain shapes by degree of PPB severity for well infants at 1-2 months and 3-4 months of age
- 2. Describe the brain WMFT microstructure for well infants at 1-2 months and 3-4 months of age
- 3. Determine if WMFT development correlates with PPB severity Cranial Vault Asymmetry Index (CVAI) and Cephalic Ratio (CR) measurement) and age

Methods

- An existing database of MRI images was utilized
  - Images were from a nutritional study of healthy infants: mothers had no known medical complications or conditions during pregnancy; infants were born at term gestation and had no known major health problems
- MRI data was collected using a 3 Tesla Siemens TrioTim system
- Infants were swaddled with a pediatric MedVac vacuum immobilization bag or blanket and their heads were stabilized inside the head coil with foam cushions
- All MRIs were assessed for quality and scans with poor quality and those with artifacts or missing diffusion sequences were excluded
- A standard approach for quantifying skull shapes from MRIs consisted of the following measurements:
  - Cranial length: glabella to the opisthocronion distance
  - Cranial width: eurion to the eurion distance
  - Right and left diagonal distances
- PPB type and severity were calculated as follows:
  - CVAI: diagonal distances, long-short divided by long
  - CR: ratio of width to depth and then multiplying by 100
- For both indexes, larger values indicated a more severe condition
- Two team members independently completed measurements of all MRIs and identified 30 scans with the most and least asymmetry
- A third team member independently verified the findings and removed MRIs where disagreements in measurements were detected
- 22 MRIs were recommended for data processing and analysis by a fourth member of the team
- A dMRI data quality check was performed, and an additional four MRIs were removed due to low quality
- 18 datasets were included for brain MRI diffusion data processing and tractography analysis
- WMFT were identified for the following 9 pathways:
  - Corpus callosum (CC), bilateral cingulum bundle (CB), corticospinal tract (CST), superior longitudinal fasciculus III (SLF-III), arcuate fasciculus (AF), inferior fronto-occipital fasciculus (IFOF), inferior longitudinal fasciculus (ILF), uncinate fasciculus (UF), and thalamo-frontal (TF).
  - For each WMFT, mean values of fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD) were exported for statistical analyses
- The sample was divided into two groups: 1-2 months and 3-4 months of age given the rapid growth of young infants' brains and increasing severity of plagiocephaly over time if left untreated
- Statistical analysis:
  - A comprehensive repeated-measures regression model was constructed for each of the four WMFT measures (FA, MD, AD, RD)
  - P <0.05 was used as the threshold for significance

Results

Table 1. Clinical Characteristics of Study Sample

		N (%) or Median [min — max]
Age group	1–2 mo	9 (50)
	3–4 mo	9 (50)
Sex	Male	11 (61)
	Female	7 (39)
Gestational age at birth, wk		39.5 [37.0 — 41.0]
Weight, kg: at birth		3.1 [2.2 — 4.3]
at study		5.3 [2.6 — 7.9]
Affected side	Left	4 (22)
	Right	14 (78)
CVAI (mean of 3 raters)		4.33 [0.77 — 10.56]
CR (mean of 3 raters)		81.8 [74.6 — 98.9]

- The sample was mostly white (39%), male (61%) infants with right-sided PPB (78%; Table 1)
- The severity of CVAI and CR in this study was mild overall
- As the severity of plagiocephaly/brachycephaly increased, a pattern of decreased FA and increased MD, AD, and RD were noted across 9 WMFT pathways
- FA (Table 2), MD, AD, and RD varied significantly among pathways (MD, AD, and RD not shown)
- FA, MD, AD, and RD was lower in the younger group (1-2 months) than the older group (3-4 months)
- Variation across the two age groups and 9 WMFT pathways was as follows:
  - For the most part FA had a negative association with CVAI, but this finding was not significant overall (p=0.32) or in either age group. FA had a positive association in CST and negative association in all other brain regions, but this was not significant. The association of FA with CR was negative overall (p=0.06) and in both age groups. A negative association of FA with CR varied among brain regions (p=0.004). The effect was strongest in CB (p=0.002) and TF (p=0.006)
  - MD had a positive association with CVAI overall (p=0.013) and in both age groups and all pathways. MD was not associated with CR overall (p=0.30) or in the two age groups and all pathways.
  - AD had a similar pattern to AD
  - RD had a positive association with CVAI overall (p=0.012) in both age groups and virtually every pathway, except CST which was weaker (p=0.20). The association of RD with CR was not significant overall (p=0.50), but it differed between the age groups, being stronger in the older infants (p=0.01)

Table 2. Fractional anisotropy (FA) in 18 infants with plagiocephaly. Variability by age cohort, brain pathway, and severity of plagiocephaly as measured by Cranial Vault Asymmetry Index (CVAI) and Cephalic Ratio (CR).

	Mean ± SE*	p**	%Difference /unit CVAI ± SE	p†	p‡	%Difference /unit CR ± SE	p†	p‡
All	0.245 ± 0.003	—	−0.53 ± 0.51	0.32	—	−0.57 ± 0.27	0.06	—
Age 1−2 mo	0.218 ± 0.005	<0.0001	−0.23 ± 0.70	0.75	0.41	−0.79 ± 0.41	0.07	0.28
Age 3−4 mo	0.275 ± 0.006		−0.82 ± 0.52	0.14		−0.34 ± 0.25	0.19	
AF	0.204 ± 0.006	<0.0001	−0.05 ± 0.98	0.96	<0.0001	−0.29 ± 0.49	0.56	0.004
CB	0.211 ± 0.005		−1.32 ± 0.87	0.13		−1.26 ± 0.40	0.002	
CC	0.312 ± 0.005		−0.40 ± 0.47	0.39		−0.57 ± 0.23	0.014	
CST	0.372 ± 0.006		0.50 ± 0.64	0.43		−0.19 ± 0.31	0.54	
IFOF	0.266 ±0.005		−0.70 ± 0.68	0.31		−0.71 ± 0.35	0.047	
ILF	0.254 ± 0.007		−0.12 ± 0.99	0.90		−0.58 ± 0.48	0.22	
SLF-III	0.192 ± 0.005		−0.82 ± 0.85	0.33		−0.10 ± 0.44	0.82	
TF	0.236 ± 0.004		−1.13 ± 0.68	0.10		−0.93 ± 0.34	0.006	
UF	0.211 ± 0.005		−0.68 ± 0.83	0.42		−0.47 ± 0.43	0.27	

*Adjusted by repeated-measures model for hemisphere, brain volume, and correlation among hemispheres and pathways; **Testing H0: equal means; †Testing H0: zero difference; ‡Testing H0: equal percentage differences.

Discussion

- Recognizing PPB can often affect the entire head shape, the investigators examined WMFT from a global perspective, rather than limiting the examination to specific regions of the brain
- A non-statistically significant but interesting pattern of decreased FA was noted across all pathways as the severity of PPB increased
- This study show that differences in WMFTs with the increasing severity of plagiocephaly and brachycephaly raise concerns for infant brain development in the context of PPB
- It is not known if these WMFT differences are associated with developmental problems or if they will improve with the resolution of head shape deformity
- There is a need for longitudinal studies of PPB that would include head shape assessments, brain WMFT microstructure images, and cognitive and behavioral assessments
- Limitations: this retrospective study is limited by a small sample size and non-traditional measurement techniques. The severity of CVAI and CR in this study was fairly mild overall. Findings may have differed, potentially in a more significant way, if the sample included children with more significant PPB

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