The Bavarian Longitudinal Study: Altered cortical macro- und microstructure in very preterm born adults

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Background

- Very preterm birth is associated with altered brain development and an increased risk for cognitive deficits (Wolke, Johnson, and Mendonça 2019)
- Individuals born very preterm show structural brain alterations that remain detectable into adulthood (Meng et al. 2016)
- This work combines insights from two studies to shed light on the long-term consequences of very preterm birth on macro- and microstructural properties of the cortex

Methods

- ≈100 very preterm-born (<32 weeks of gestation and/or birth weight <1500g, VP/VLBW) adults and ≈100 full-term (FT) controls
- 26 years of age
- Structural MRI (T1w, 3T), full-scale intelligence quotient (IQ) using the Wechsler Adult Intelligence Scale
- Cortical macrostructure -> Cortical thickness (CTh; see Figure 1)
- Cortical microstructure -> Percent contrast of gray-to-white matter signal intensities (GWPC; Figure 1; Andrews et al. 2017): Grey matter intensities (GMI) sampled at different percentile fractions of the distance from the white matter surface to the pial surface (0%, 10%, 20%, 30%, 40%, 50%, and 60%), white matter intensity (WMI) sampled at 1 mm into the white matter
- ROI-based (Desikan-Killiany atlas)
- Group comparison: General linear models with sex and scanner as factors of no interest, false discovery rate (FDR) corrected
- Relationship with IQ: Two-tailed partial correlation analyses; mediation analysis

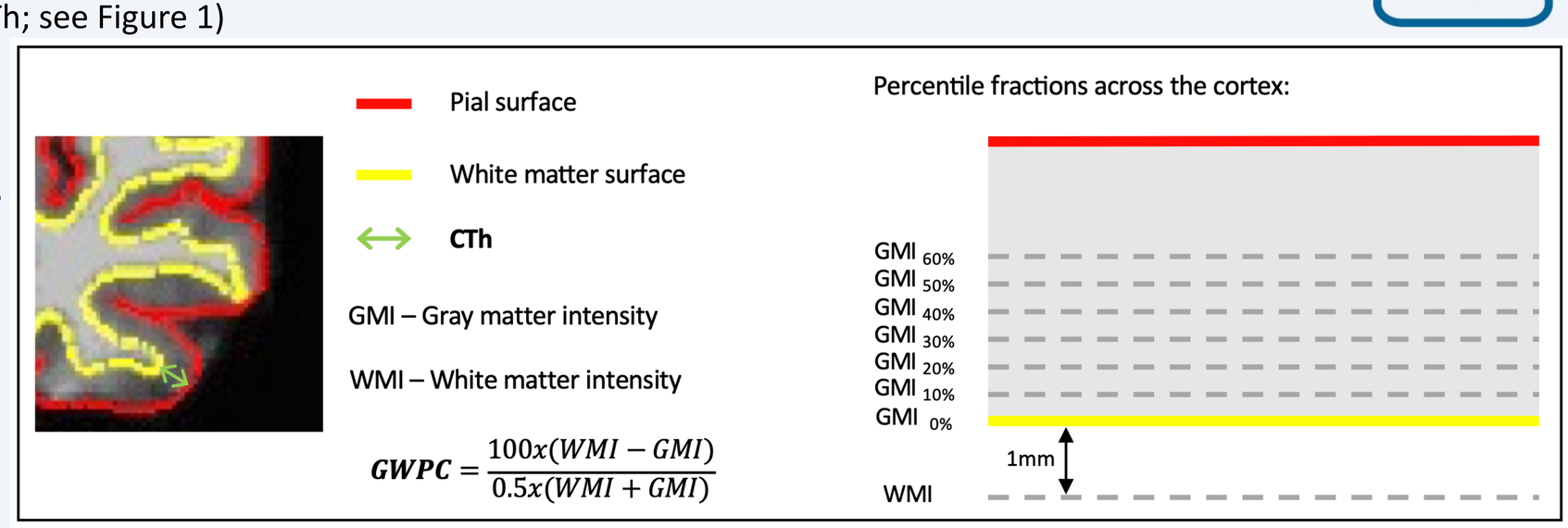

Figure 1: CTh and calculation of GWPC across the cortex.

Results

	VP/VLBW (n=101)			FT (n=111)			
	Mean/n	SD	Range	Mean/n	SD	Range	p-value
Sex (male/female)	58/43			66/45			0.765
Age (years)	26.7	± 0.6	25.7 – 28.3	26.8	± 0.7	25.5 – 28.9	0.182
GA (weeks)	30.5	± 2.1	25 – 36	39.7	± 1.1	37 – 42	**<0.001**
BW (g)	1325	± 313	630 – 2070	3398	± 444	2120 – 4670	**<0.001**
Full-scale IQ (a.u.)	94.1	± 12.7	64 – 131	102.5	± 11.9	77 – 130	**<0.001**

- CTh was lower in very preterm-born adults compared to controls in frontal, parietal, and temporal associative cortices, predominantly in the left hemisphere (Figure 2)
- CTh was positively correlated with GA and BW, particularly in the left hemisphere, and negatively correlated with intensity of neonatal treatment within limited regions bilaterally
- CTh in the left hemisphere was positively correlated with IQ, and mediated the relationship between preterm birth and IQ
- GWPC was lower in frontal, parietal, and temporal associative cortices after very preterm birth, predominantly in the right hemisphere, differences were pronounced in middle cortical layers (20%-40%)
- GWPC was higher in right paracentral lobule in VP/VLBW adults
- GWPC in frontal and temporal cortices was positively correlated with BW, and negatively with duration of ventilation ($p<0.05$)
- GWPC in right paracentral lobule was negatively correlated with IQ ($p<0.05$)

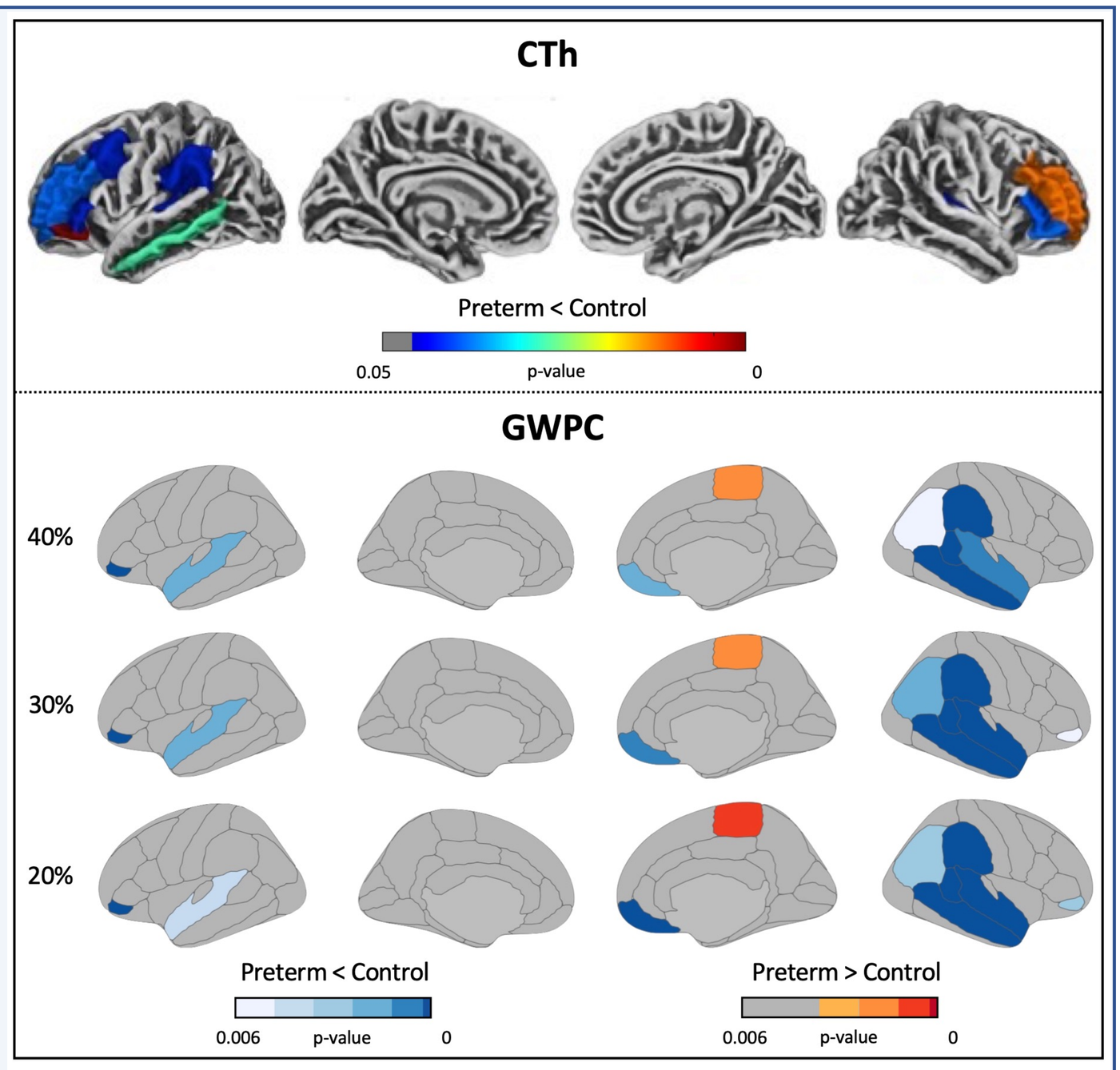

Figure 2: Group comparisons of CTh and GWPC between preterm-born adults and controls. P-values are color-coded. Statistical significance was defined as $p < 0.05$, FDR-corrected.

Conclusion

1) Very preterm birth is associated with long-term alterations in cortical structure, affecting both macro- and microstructure.
2) Prematurity has differential effects on associative and primary cortices.
3) Altered cortical macro- and microstructure contribute to cognitive deficits that persist into adulthood following preterm birth.

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CTh: GWPC:

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