Altered grey matter cortical and subcortical T1-weighted/T2-weighted ratio in premature-born adults

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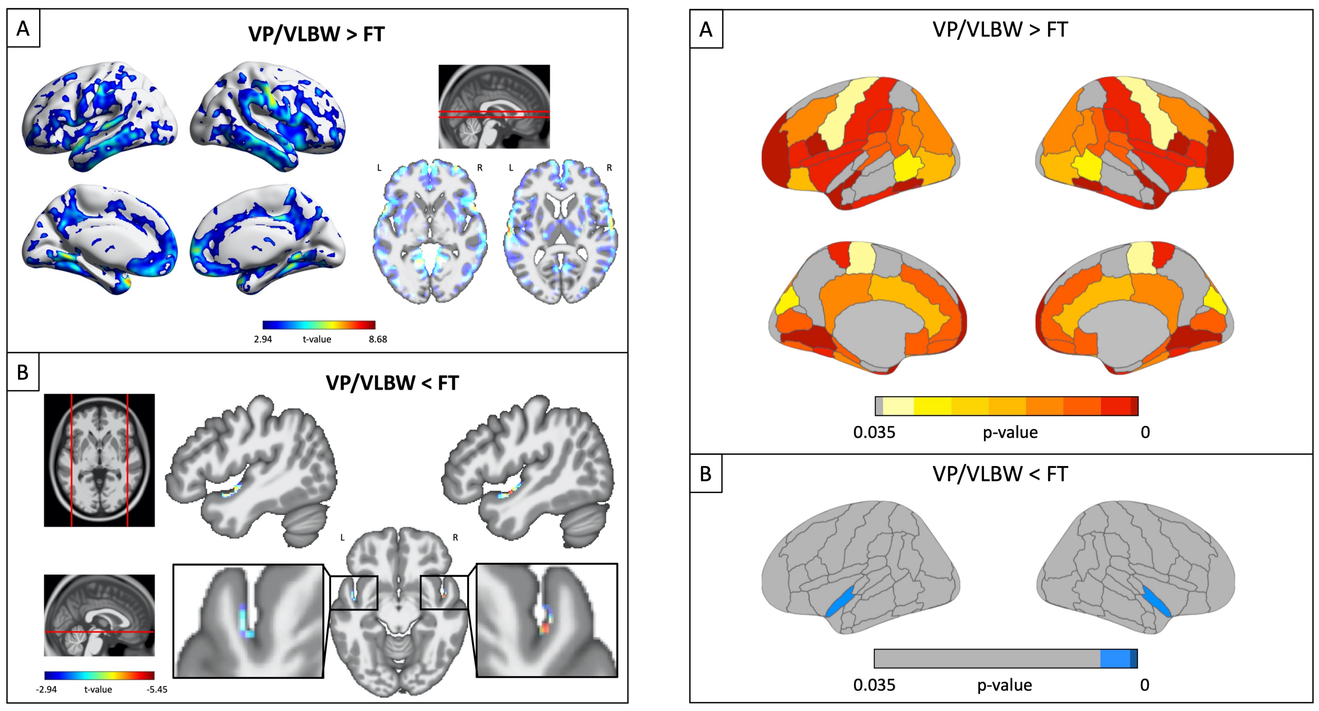
Background

- Preterm birth,(i.e., birth < 37 weeks of gestation (GA)) is associated with altered brain structure and an increased risk for cognitive impairments.
- Microscopic studies in newborns and animal models of prematurity reveal aberrant pre-oligodendrocytes maturation indicating impaired myelination, including cortical myelination (Volpe 2019).
- It has been suggested that the ratio of T1w and T2w MRI signal intensity (T1w/T2w ratio) is a proxy for myelin content (Glasser 2011). While alterations in GM T1w/T2w ratio have been reported in preterm born children (Vandewouw 2019), it remains unclear whether altered T1w/T2w ratio alterations last into adulthood and if so, are relevant for impaired cognitive performance.
- Other measures of GM structure such as thickness are lastingly altered after premature birth (Schmitz-Koep 2020), therefore, we hypothesized (i) altered grey matter (GM) T1w/T2w ratio in premature-born adults; (ii) these alterations are associated with lower cognitive performance.

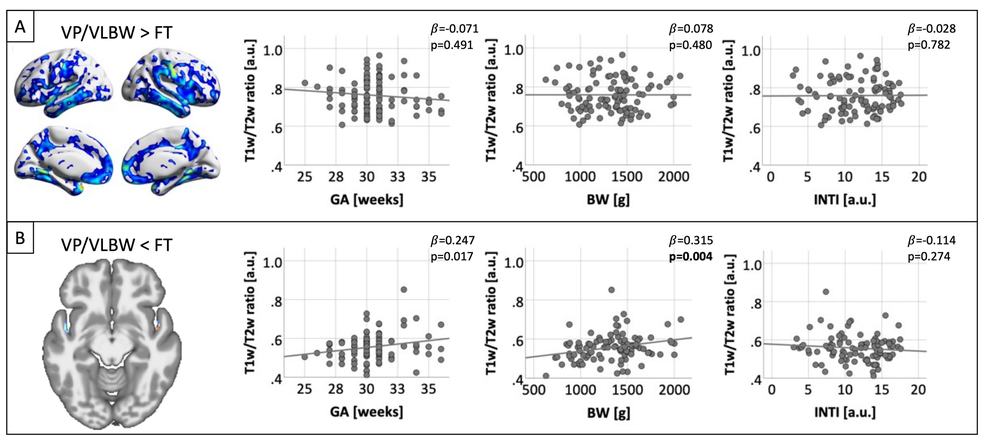
Results

1. Voxel-wise and ROI-based alterations in T1w/T2w ration in premature-born adults



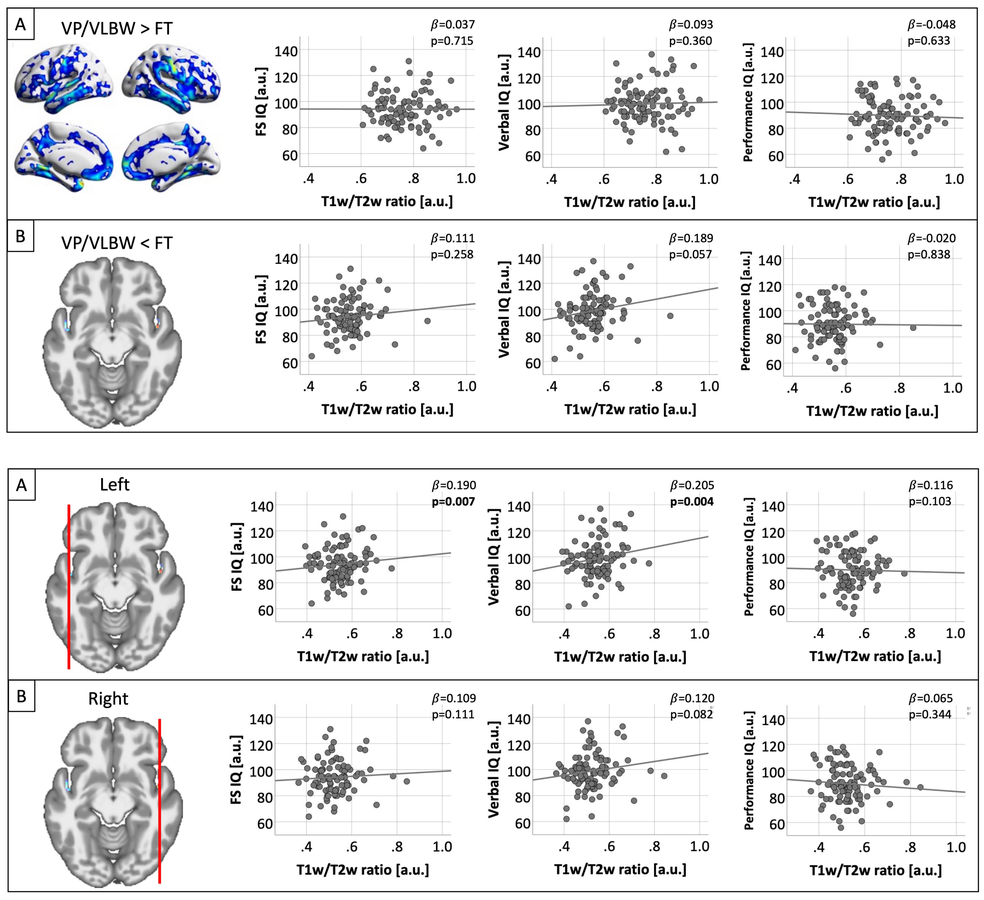
- Significantly higher T1w/T2w ratio was found in VP/VLBW subjects in widespread cortical areas, such as in frontal, parietal and temporal cortices, and in thalamus, putamen, pallidum, hippocampus & amygdala
- Significantly lower T1w/T2w ratio found in VP/VLBW subjects in small bilateral clusters in superior temporal gyri (STG)

2. Relationship between T1w/T2w ratio and variables of premature birth



- Lower T1w/T2w ratio in VP/VLBW subjects was significantly associated with lower BW. No significant associations were found between prematurity variables and regions with higher T1w/T2w ratio.

3. Relationship between T1w/T2w ratio and cognitive performance

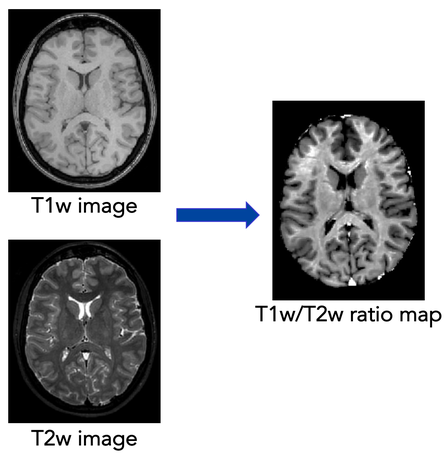


- No significant associations were found between IQ and regions with higher T1w/T2w. Lower T1w/T2w ratio in left STG was significantly associated with lower Verbal and FS-IQ in VP/VLBW adults.

Material and Methods

	VP/VLBW (n=101)			FT (n=109)			
	Mean	SD	Range	Mean	SD	Range	p-value
Sex (male/female)	58/43			64/45			0.850
Age (years)	26.7	± 0.6	25.7 – 28.3	26.9	± 0.7	25.5 – 28.9	0.147
GA (weeks)	30.5	± 2.1	25 – 36	39.7	± 1.1	37 – 42	<0.001
BW (g)	1325	± 313	630 – 2070	3391	± 447	2120 – 4670	<0.001
INTI (days)	11.6	± 3.8	3 – 18	n.a.	n.a.	n.a.	n.a.
GM (mm^3)	683	± 62	524 – 839	714	± 56	555 – 861	<0.001
Full-scale IQ[a]	94.1	± 12.7	64 – 131	102.4	± 11.9	77 – 130	<0.001
Verbal IQ[a]	98.8	± 14.0	62 – 137	105.7	± 14.2	77 – 143	0.001
Performance IQ[a]	89.8	± 13.5	56 – 118	98.5	± 10.4	69 – 125	<0.001

Table 1: Sample Characteristics (**VP**: very preterm (<32 weeks GA), **VLBW**: very low birth weight (<1500 g), **FT**: full term, **IQ**: intelligence quotient, **GM**: grey matter)



Images preprocessing using MRTool implemented in SPM 12[1] as previously described by Ganzetti et al., (2011) included:

- co-registration,
- bias correction
- generation of T1w/T2w ratio maps

- T1w images were normalized to a template space and segmented into GM, WM and CSF using CAT12[2]. GM T1w/T2w ratio was extracted using the GM mask. GM T1w/T2w ratio maps were then smoothed with a Gaussian kernel of 6 mm full-width at half maximum.
- Verbal, performance, and full-scale IQ were assessed using the Wechsler Adult Intelligence Scale.
- Voxel-wise group differences were conducted in SPM 12, controlled for voxel-wise volume alterations using the DPABI toolbox (Yan 2016) and corrected for multiple comparisons using the false discovery rate (FDR). Statistical significance was defined as $p<0.05$, FDR-corrected.
- To investigate whether group differences in GM T1w/T2w ratio were specifically related to prematurity or cognition, we extracted the T1w/T2w ratio in areas where T1w/T2w ratio differed significantly in VP/VLBW individuals compared to FT controls. In the VP/VLBW group, the T1w/T2w ratio values (for VP/VLBW<FT and VP/VLBW>FT, respectively) were then entered into a linear regression analysis in SPSS Version 26 (IBM Corp., Armonk, NY, USA) as dependent variable with GA and BW or IQ as independent variables. Finally, GM volume, gender and scanner were entered as covariates of no interest.

Conclusion

Our results demonstrate T1w/T2w ratio alterations in the GM of premature born adults and would suggest altered GM myelination development after premature birth with lasting and possibly functionally relevant effects into early adulthood.

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1. SPM (https://www.fil.ion.ucl.ac.uk/spm/software/spm12/)
2. CAT 12 Computational Anatomy Toolbox (http://www.neuro.uni-jena.de/cat/)

For more information, read our full publication!

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