Cerebral blood flow alterations in preterm-born adults

Klinikum rechts der Isar
Technische Universität München

Technische Universität München

A. Menegaux [1,2], M. Mora[1,2], R. Berg,[1,2] J. Wendt[1,2], C. Zimmer[1,2], C. Preibisch[1,2], E. Rieger-Fackeldey,[3] P. Bartmann[4], C. Sorg[1,2,5]

[1]TUM-Neuroimaging Center and departments of [2]Diagnostic and Interventional Neuroradiology, [3]Neonatology and [5]Psychiatry of Klinikum Rechts der Isar, Technische Universität München TUM
[4]Department of Neonatology, University Hospital Bonn

Contact: aurore.menegaux@tum.de

Background

- Preterm birth (i.e., birth before 37 weeks of gestation) is associated with altered brain structure and an increased risk for cognitive and motor impairments (Volpe 2019).
- Arterial development in humans is completed between 20 and 24 weeks of gestation (GA) in the brainstem and cerebellum followed by the basal ganglia and diencephalon between 24 to 28 weeks GA and lastly in the cortex and germinal matrix (Brew et al., 2014). Preterm birth is thus a critical period for vascular development.
- Altered brain perfusion and its association to cognitive and motor impairments has previously been reported in preterm-born infants (Tortora et al., 2017; Dubois et al., 2021).

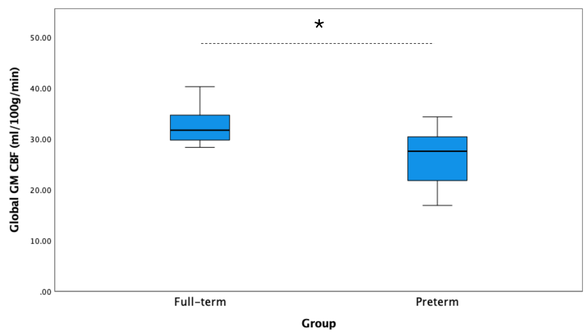
- However, whether such alterations persist in adulthood remains unclear.

- We aimed at investigating this question in a preliminary study of 12 preterm-born adults and 12 term-born controls aged 22 to 47 years.

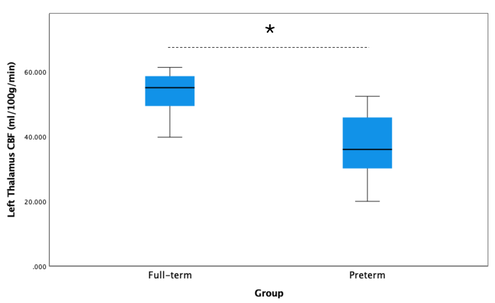
Results

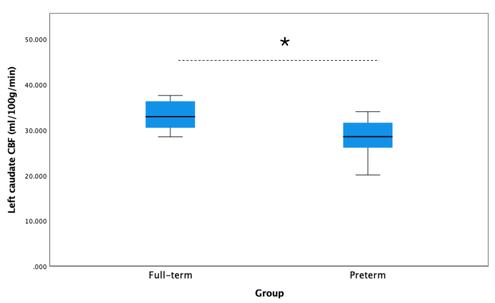
Between groups: Sample characteristics

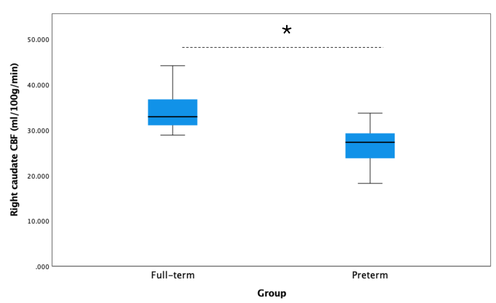
	Preterm (n=12)			Full Term (n=12)			
	Mean	SD	Range	Mean	SD	Range	p-value
Sex (male/female)	4/8			3/9			0.65
Age (years)	29.5	± 8.4	20 – 44	30.0	± 6.7	23 – 47	0.15
GA (weeks)	29.7	± 2.9	25 – 35	37 <			
TMT-A	23.6	± 4.9	12 – 32	23.3	± 7.7	16 – 41	0.92
TMT-B	54.9	± 12.9	30 – 78	47.2	± 9.7	35 – 60	0.17
Digit Span	14.8	± 2.8	9 – 19	17.0	± 3.3	13-22	0.06



- Significantly lower global grey matter CBF in very preterm compared to term-born adults (p = 0.005).
- Significantly lower CBF in widespread cortical regions such as temporal pole (p < 0.001) as well as in subcortical regions such as left (p = 0.041) and right caudate (p = 0.005) or left thalamus (p < 0.001) were observed.







In the preterm group:

- Significant positive correlation between left caudate CBF and GA (r = 0.67, p = 0.047) and trend towards significance for right caudate (r = 0.71, p = 0.076)
- Close to significant positive correlation between GA and Digit Span score (r = 0.89, p = 0.070)
- Significant positive correlation between left thalamus CBF and Digit Span score (r = 0.58, p = 0.046) and trend towards significance for left caudate CBF (r = 0.56, p = 0.061) and right caudate CBF (r = 0.54, p = 0.072)

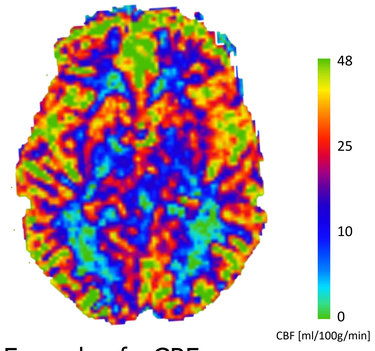
Material and Methods

Data acquisition:

- In a 3T MRI Philipps scanner using a 3D pseudo continuous arterial spin labelling sequence for perfusion imaging with the following parameters: FOV=240x240x96mm^3, voxel resolution= 3x3x6mm^3 , TR=4.1s, TE=11ms, PLD=1.8s, labelling, duration=1.8s, and 5 averages.

- Structural scans were acquired using a T1-weighted MPRAGE sequence with FOV =256x240x156mm^3, and an isotropic resolution of 1mm3 .

- Cognitive function was investigated using the Trail Making Test A, B and the Digit Span Memory test.



Example of a CBF map

Data analysis

- Cerebral blood flow (CBF) maps were derived using the BASIL toolbox from the FMRIB Software Library and corrected for partial volume effects (Chappell et al., 2011) following the White paper from Alsop (2015). ROI parcellation was based on Harvard-Oxford atlas.

- Group differences in CBF, controlling for age and gender, were investigated via ANCOVA using the SPSS statistical package.

- Associations between prematurity, CBF values and cognitive scores were investigated in the preterm group using partial correlations.

Conclusion / Discussion

- These preliminary results suggest long-lasting alterations in brain perfusion after preterm birth, particularly in subcortical structures.

- These subcortical brain perfusion alterations seem to be related to cognitive function such as working memory.

- Follow up studies with more participants are necessary to confirm these findings and to investigate the impact of neonatal complications such as intraventricular haemorrhage on these CBF differences.

References

Alsop, D. C., Detre, J. A., Golay, X.. et al. (2015). Recommended implementation of arterial spin-labeled perfusion MRI for clinical applications: A consensus of the ISMRM perfusion study group and the European consortium for ASL in dementia. *Magn Reson Med* 73(1), 102-116.
Brew, N., Walker, D., Wong, F.Y. (2014). Cerebral vascular regulation and brain injury in preterm infants. *Am J Physiol Regul Integr Comp Phys* 306, 773-786.
Chappell, M. A., Groves, A. R., MacIntosh, B. J et al. (2011). Partial volume correction of multiple inversion time arterial spin labeling MRI data. *Magn Reson Med* 65(4), 1173-1183.
Dubois, M., Leghouy, A., Corouge I. et al. (2021). Multiparametric analysis of cerebral development in preterm infants using magnetic resonance imaging. *Frontiers in Neuroscience* 15, 658002
Tortora, D., Mattei, P.A., Navarra R. et al. (2017). Prematurity and brain perfusion: Arterial spin labelling MRI. *Neuroimage Clinical* 15, 401-407.
Volpe, J.J. (2019): Dysmaturation of Premature Brain: Importance, Cellular Mechanisms, and Potential Interventions. *Pediatr Neurol* 95: 42–66.