Revealing the whole iceberg—

Visuopathy of prematurity

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On September 28, 2023, Sigrid Hegna Ingvaldsen defended her thesis, "Visuopathy of prematurity: Brain MRI alterations, neurodevelopment, and visual outcomes in children and adults born preterm," at the Faculty of Medicine and Health Sciences, Norwegian University of Science and Technology (NTNU). The Ph.D. project was conducted at the Dept. of Ophthalmology, St. Olav's Hospital, Trondheim. The supervisors were Associate Professor Tora Sund Morken, NTNU; Professor Dordi Austeng, NTNU; and Professor Olaf Dammann, Tufts University, Boston.

Key points:

- People born prematurely show visual problems even without a history of retinopathy of prematurity.
- Reduced visual function is associated with structural alterations along the visual pathway that can be revealed by clinical markers from optical coherence tomography.
- Clinical markers on brain MRI indicate that the observed visual problems may have a neural source.

Approximately 15 million babies are born preterm (<37 weeks of gestation) every year. Due to underdeveloped organs and bodily functions, several postnatal consequences of being born preterm can follow these infants into adulthood. One such consequence is retinopathy of prematurity (ROP), a disease characterized by abnormal blood vessel growth in the retina, causing reduced vision. Modern ROP screening identifies infants born preterm who require early postnatal treatment, and severe ROP is rarely seen in high-income countries with screening. However, even without ROP, children and adults born preterm still show adverse visual outcomes, including reduced visual function and visual processing along the visual pathway.

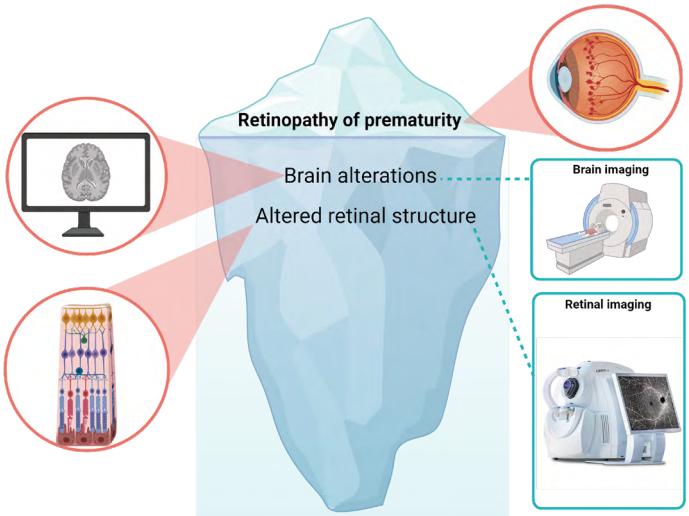

Figure 1. The visuopathy of prematurity (VOP) entity illustrates that retinopathy of prematurity (top right) is just the tip of the iceberg of a larger entity of adverse visual outcomes that could be explained by brain alterations and altered retinal structure (left). Right: Brain imaging using magnetic resonance imaging and retinal imaging using optical coherence tomography might reveal clinical imaging markers of VOP. ©Sigrid Hegna Ingvaldsen (2023).

Since ROP cannot solely explain the adverse visual outcomes in individuals born preterm, the idea behind this project was that ROP might be just the tip of the iceberg of a larger entity of visual problems, termed visuopathy of prematurity (VOP). VOP includes brain alterations and altered retinal structures along the visual pathway, which could explain the adverse visual outcomes. We aimed to explore the hallmarks of VOP and assess whether optical coherence tomography (OCT) and brain magnetic resonance imaging (MRI) could be used to find clinical imaging markers of VOP (**Figure 1**).

We assessed differences in the visual function (visual acuity and contrast sensitivity), the structure (retinal layers) and function (visual evoked potentials) of the visual pathway, and the visual processing regions of the brain matter (white and grey matter alterations) in a group of children born extremely preterm (EP; gestational age ≤28 weeks) and a group of adults born preterm with very low birthweight (VLBW: birthweight ≤1,500 g) in central Norway.

We found several hallmarks of VOP in the EP children and VLBW adults, including reduced contrast sensitivity, altered retinal structure (thicker central layers and thinner peripheral layers), small foveal avascular zone, delayed visual pathway signaling, and brain matter alterations in visual processing regions. Moreover, VLBW adults displayed brain MRI alterations along the visual pathway that predicted reduced visual function, and EP children showed altered retinal structures associated with delayed visual pathway signaling. The findings indicate that brain MRI could help localize the neural source of adverse visual outcomes and that OCT could be a useful tool for discovering structural clinical imaging markers of VOP in the retina.

Future directions:

- A multidisciplinary approach using clinical imaging markers and visual function testing could give a better understanding of the mechanisms underlying visuopathy of prematurity.

References

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