Into the eye of the storm: childhood maltreatment and retinal markers of risk for major psychiatric disorders

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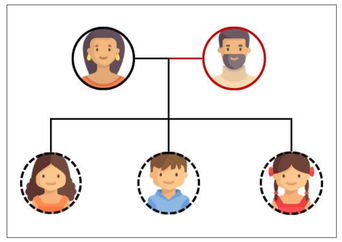
INTRODUCTION

Retina as a window to the brain

- The retina shares structural and developmental origins with the brain, making it a unique and accessible window for studying brain processes in a non-invasive manner (Gagne et al.,2020; Maziade & Silverstein, 2020).
- Retinal abnormalities have been consistently reported in adults with psychopathologies, including schizophrenia (SZ) and bipolar disorder (BD) (Lizano et al., 2020).



Familial high-risk paradigm to understand the developmental origins of psychiatric disorders

- Children and adolescents at familial high risk (FHR)—offspring of a parent with SZ or BP—have a 10–20-fold increased risk of developing these disorders. This underserved population offers a unique opportunity to investigate the developmental origins of major psychiatric disorders (Maziade, 2017).
- Consistent with this perspective, FHRs show early alterations across several developmental domains that parallel features observed in adult with SZ or BP, including specific cognitive deficits (Berthelot et al., 2015; 2022; Maziade et al., 2009).
- Recent findings from our group suggest that retinal abnormalities reported in adults with SZ or BP may have developmental origins, as similar alterations can already be detected during childhood in FHR youth (Maziade et al., 2026).

Trauma as a crucial risk factor

- Childhood maltreatment is a risk factor for the later development of major psychiatric disorders, including SZ and BP, and is associated with long-term alterations in brain structure and function (Teicher et al., 2022).
- Optical coherence tomography (OCT) may offer a non-invasive and preventive approach for detecting biological traces associated with childhood maltreatment that could contribute to the emergence of severe psychiatric disorders.
- The association between childhood maltreatment and retinal anomalies in children and adolescents remains largely unexplored to date.

OBJECTIVE. This study examined, for the first time, the association between **childhood maltreatment** and **retinal structures** in FHRs, as well as the association between **retinal structures** and **cognitive risk markers** in FHRs.

We **hypothesized** that cumulative exposure to childhood maltreatment would be associated with greater retinal thinning and that retinal thinning would be associated with greater accumulation of cognitive deficits among maltreated FHR youth.

METHOD

Sample of 38 FHRs (M_{age} = 13.86, SD = 3.92, 43% male), including 12 FHRs (31.7%) exposed to childhood trauma. A subsample (n = 24) also completed a cognitive battery assessing four cognitive domains associated with SZ and BP.

Measures

1) **Childhood trauma :** *Traumatic Events Screening Inventory*. Assesses five types of childhood maltreatment before the age of 18: physical abuse, sexual abuse, emotional abuse, neglect and domestic violence.
2) **Retinal morphology :** *Optical Coherence Tomography* (OCT). Revo 60 device and SOCT software 11.0.5 were used to measure the thickness of retinal nerve fiber layer (RNFL).
3) **Cognitive deficits :** 1) Processing speed—*Digit symbol Substitution Task* (WISC/WAIS) and *Category Fluency: animal naming*; 2) Episodic memory—*California Verbal Learning Test* (CVLT-II) delayed recall and *Rey Complex Figure* (RCF) delayed recall; 3) Working memory—*Digit span* (WISC/WAIS) and *Spatial Span*; 4) Executive functioning—*Wisconsin Card Sorting Test* total errors and *Tower of London* (TOL) number of problems solved in minimum moves.

Analysis

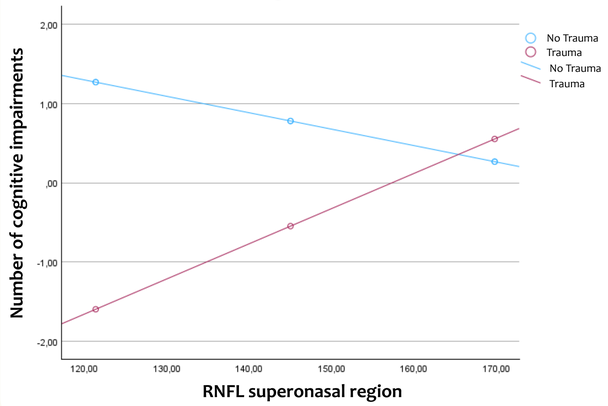
Regression and moderation analyses were conducted.

RESULTS

Table 1. Significant associations between childhood cumulative trauma and retinal nerve fiber layer (RNFL) subregions.

Predictor	Outcomes	β	*p*	95% CI	R^2 adjusted
Childhood trauma	RNFL Superior	.515	.001	[6.04 ; 21.71]	.26
	RNFL Superonasal	.374	.025	[1.28 ; 18.09]	.08
	RNFL Temporoinferior	.327	.054	[-.07 ; 6.77]	.03
	RNFL Inferotemporal	.309	.069	[-.58 ; 14.99]	.02

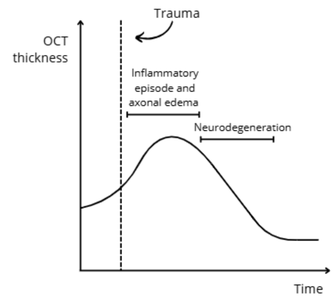
Figure 1. Interaction plot illustrating the moderating effect of childhood trauma on the association between retinal structures and cognitive impairments.



Results revealed a **significant moderation by trauma in the association between superonasal RNFL thickness and cognitive deficits** (t = 3.12, p = 0.005). In participants with trauma, thicker RNFL was associated with greater cognitive deficits (b = 0.03, p = 0.034), whereas the opposite pattern was observed in those without trauma (b = –0.018, p = 0.030).

DISCUSSION

- Results showed that **greater cumulative exposure to maltreatment** was associated with **increased RNFL thickness** on OCT. **Retinal thickening** was, in turn, associated with more pronounced **cognitive deficits** among FHRs with childhood maltreatment, whereas **no such association was observed in non-maltreated FHRs**.
- One possible interpretation is that **trauma-related inflammatory processes may induce transient axonal edema, leading to increased retinal thickness**. Such inflammatory processes has been documented in both animal and human studies as an early response to neural injury and may precede axonal degeneration and subsequent thinning of retinal structures (Kupersmith et al., 2011; Ziemssen et al., 2013; Ma et al., 2024).
- Taken together, these findings suggest that **childhood maltreatment may contribute to early retinal alterations** detectable by OCT, potentially **reflecting inflammatory processes** that **precede later neurodegenerative** changes (Blose, 2024) associated with vulnerability to major psychiatric disorders.
- This study may pave the way for earlier detection and preventive interventions in FHRs aimed at mitigating these emerging inflammatory processes.



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