Natural History of the Refractive Errors in Patients with Congenital Stationary Night Blindness

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Introduction

- **Congenital stationary night blindness (CSNB)** is a group of retinal genetic disorders that primarily affect the signal transmission from the photoreceptors to the bipolar cells.[1]
- Complete (cCSNB) and incomplete CSNB (inCSNB) are linked to high myopia, but little is known about the natural history of refractive errors and the effect of genotype.
- This study assesses a SickKids cohort of CSNB patients to fill this knowledge gap.

Methods

- **Study design:** Retrospective observational longitudinal study.
- **Participants:** 78 patients with genetically confirmed diagnoses *(CACNA1F, TRPM1, NYX, CABP4, and GPR179* mutations*)* of CSNB .
- **Time period:** from 2009 to present.
- **Inclusion criteria:** ≥ 2 refractive error measurements be available.
- **Data collected:** age, gender, CSNB sub-type (based on electroretinogram), genotype, spherical equivalent of refraction (SER), presence of nystagmus.
- **Data analysis:** The SER range, mean, median and rate of progression at different ages were compared between the different genotypes.

Results

Gene (Number of patients)	SER range across all ages.	Mean SER across all ages.	Median SER across all ages.	AGE of the youngest myopic patient / mean SER at first visit / mean SER at last visit / number of visits
CACNA1F (N= 52)	+9.00 D to -20.50 D	- 3.45 D	- 3.38 D	5 months old / first visit SER = -0.75 D OU / progressed to -9 at age of 13 years / 9 visits
TRPM1 (N= 14)	-2.50 D to -18.25 D	- 9.00 D	- 9.38 D	4 months old / first visit SER = -2.5 D OU / progressed to -8.5 OU at age of 7 years / 6 visits
NYX (N= 9)	-1.75 D to -17.50 D	-10.03 D	- 4.50 D	5 years old / first visit SER = -1.75 D OU / progressed to -6 at age of 10 years / 6 visits
CABP4 (N= 2)	+5.00 D to -8.50 D	-0.28 D	+ 3.62 D	30 years old / first visit SER = -7.38 D OU / progressed to -7.65 OU at age of 31 years / 2 visits
GPR179 (N= 1)	-8.25	-8.09 D	- 8.25 D	1 year and a half / First visit SER = -8.25 D OU / regressed to -7.80 OU at age of 2 years / 2 visits

Table 1: SER Range, Mean, Median across all age groups in different genotype

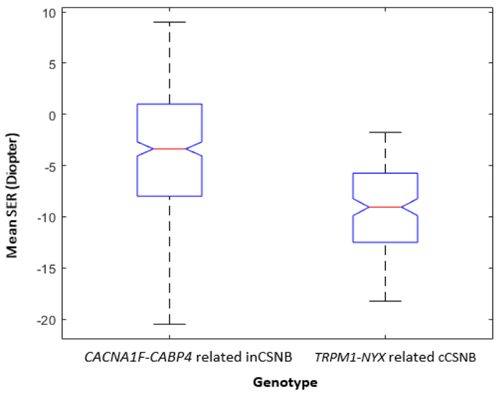

Figure 1: Mean SER of incomplete CSNB and complete CSNB

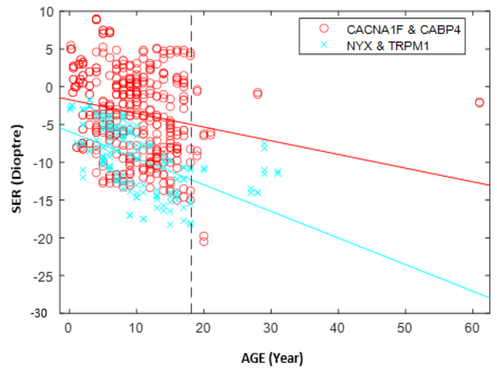

Figure 2: The slope of SER progression per age between cCSNB and inCSNB.

- Myopia was seen in 32/52 (61.54%) patients with *CACNA1F* mutations, 14/14 (100%) patients with *TRPM1*, 9/9 (100%) patients with *NYX* mutations, 1/2 (50%) patients with *CABP4* mutations, and 1/1 (100%) patient with *GPR179* mutation.
- SER across all ages, varied among genotypes (table 1).
- Mean SER was different between the *CACNA1F-CABP4* related inCSNB and *TRPM1-NYX* related cCSNB, with the latter showing more myopia (figure 1).
- There was a statistically significant difference in the rate of SER progression per age between the two sub-groups of CSNB (P-value: 0.0143); in patients with cCSNB, the rate of SER progression of myopisation was faster (figure 2).
- Nystagmus was observed in 36/54 (66.67%) cases with inCSNB and 10/23 (43.48%) cases of cCSNB.
- A chi-square test of independence was used to examine the relationship between the CSNB groups and nystagmus. The relation between these variables was significant (P-value: 0.0285).
- Prevalence of nystagmus is unrelated to the type and degree of refractive errors.

Conclusions

- Patients with cCSNB had a higher rate of myopia, compared to those with inCSNB.
- *CACNA1F* and *TRPM1* were the most prevalent genes mutated, followed by *NYX*.
- The estimated rate of SER progression per year was - 0.54 D, - 0.16 D, and - 0.20 D for *CACNA1F*, *TRPM1*, and *NYX*, respectively.

References

1. Zeitz C, Robson AG, Audo I. Congenital stationary night blindness: an analysis and update of genotype-phenotype Correlations and pathogenic mechanisms. *Prog Retin Eye Res*. 2015;45:58-110

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