Mobility and Postural Testing in Patients with Rod-Cone Dystrophy Enrolled in the Prospective Natural History Study PHENOROD2

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Purpose

Rod-cone dystrophies (RCD) are a group of rare inherited retinal disorders whose etiology and clinical manifestations are heterogeneous. RCD gravely burden the patient's quality of life, and the disease impact on functional vision is not well characterized.

PHENOROD2 is an ongoing prospective natural history study **assessing RCD progression**, to help select relevant clinical efficacy endpoints for the evaluation of novel therapies.

Methods

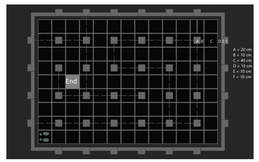
A subset of **30 subjects** enrolled in the PHENOROD2 study performed mobility and postural tests using the Artificial Street platform at the Streetlab facility (Paris, France).

The locomotion test consisted of a **modular maze** including 3 obstacles on the floor and 2 suspended obstacles. The mobility course was performed under binocular and monocular conditions, at 5 out of 14 possible light levels. A **performance score (0 to 100)** was computed considering trial duration and mobility errors (Authié *et al.*).

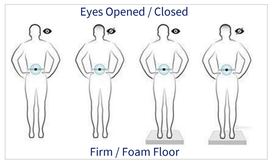
BCVA was measured with the ETDRS chart, mean sensitivity (MS) was measured on the Octopus perimeter, and foveal sensitivity on the MAIA perimeter.

The postural test consisted of the Sensory Organization Test (SOT), performed on the Opal Mobility Lab System (APMD Wearable Technologies).

Modular maze (5.2 x 3.6m)



SOT



Results

- At enrollment, visual function was **mildly to moderately affected**:
  - Mean BCVA was equivalent to Snellen 20/27
  - Mean foveal sensitivity was about 30% lower than normal values (Fujiwara *et al.* reported a mean normal central sensitivity of 27.2 dB with MAIA perimetry).
  - Mean MS was about 30% lower than normal values (Calixto *et al.* reported a mean normal MS of 26.8 dB on the Octopus perimeter).

Mobility Assessment

- At BSL, mean binocular performance score was **75 out of 100**, indicating mild to moderate impairment of mobility. Mean monocular scores were slightly lower, due to the loss of stereopsis.
- The mean change from baseline (CFB) of performance score was **negligible** at Year 1 and Year 2 (-2 and -1 respectively).
- **No significant difference** was reported between the 3 **genotypes** (Quade test).
- A threshold of "change detection" was determined based on the test-retest variability of the MOST mobility test (Authié *et al.*). A difference > 20 was considered to reflect disease progression. Only 1 subject was above that threshold at Y1, but not at Y2.
- **Monocular performance score correlated**:
  - Moderately with LogMAR BCVA (r^2 = -0.53)
  - Well with **foveal sensitivity (r^2 = 0.66)**
  - Strongly with **MS (r^2 = 0.73)**
- Binocular performance score correlated mildly with age (r^2 = -0.28).

Postural Assessment

- Romberg ratios (EC/EO) showed a **mild impact of vision** on **sway** area and movement fluidity (**jerk**), that did not change over time.
- No significant difference was reported between the 3 genotypes (Quade test).

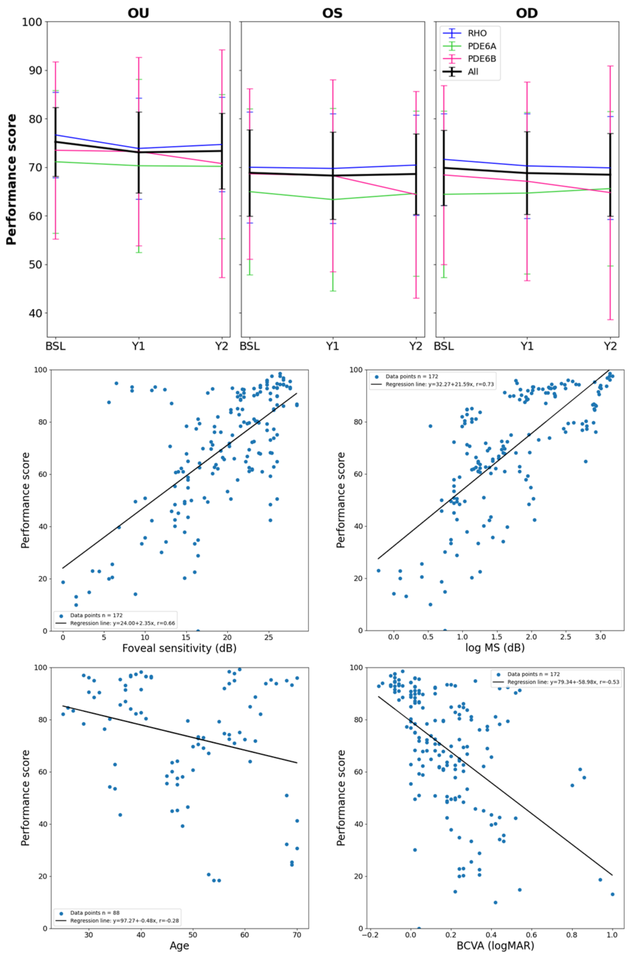
Cohort Characteristics

Genotype - n (%)	**N = 30**	
RHO	21 (70%)	
PDE6A	6 (20%)	
PDE6B	3 (10%)	
Demographics	**N = 30**	
Male : female ratio	15 : 15	
Age (years) - mean ± SD	46.9 ± 12.5	
BSL Visual Function - mean ± SD	**OD**	**OS**
BCVA (LogMAR)	0.15 ± 0.17	0.18 ± 0.24
Foveal sensitivity (dB)	19.1 ± 6.2	18.2 ± 6.8
Mean sensitivity (dB)	7.5 ± 6.0	7.6 ± 6.1

Mobility Performance Score Over Time

	OD	**OS**	**OU**
BSL (n = 30)			
Mean ± SD	69 ± 21	68 ± 24	75 ± 19
Min-Max	14 ; 96	0 ; 97	20 ; 98
Year 1 (n = 29)			
Mean ± SD	68 ± 23	68 ± 25	73 ± 23
Min-Max	10 ; 96	13 ; 98	18 ; 97
CFB @ Y1 (n = 29)			
Mean ± SD	0 ± 5	0 ± 7	-2 ± 6
Min-Max	-10 ; 13	-17 ; 30	-25 ; 5
Year 2 (n = 27)			
Mean ± SD	69 ± 21	69 ± 20	74 ± 19
Min-Max	25 ; 95	20 ; 97	30 ; 99
CFB @ Y2 (n = 27)			
Mean ± SD	-1 ± 6	0 ± 10	-1 ± 4
Min-Max	-15 ; 12	-10 ; 49	-13 ; 4

One patient was lost to follow-up after BSL assessment, two after Year 1.



Conclusions

Overall, **no substantial change** was reported for mobility or postural assessment after **2 years** of follow-up. The MOST-based mobility test could be used to **indirectly assess cone function**; however it may not be able to capture short-term changes in patients with slowly progressive RCD. **Long-term follow-up** may allow to detect changes in disease progression and inform on potential treatment effect in interventional clinical trials.

References

- Authié C, Poujade M, Talebi A, Defer A, Zenouda A, Coen C, Mohand-Said S, Chaumet-Riffaud P, Audo I, Sahel J-A. Development and validation of a novel mobility test for IRDs, from reality to virtual reality. medRxiv 2023.02.01.23285189.
- Calixto N, Santos RM, Cronemberger S. Visual field (Octopus 1-2-3) in normal subjects divided into homogeneous age-groups. Arq Bras Oftalmol. 2006 Sep-Oct;69(5):637-43. PMID: 17187126.
- Fujiwara A, Shiragami C, Manabe S, Izumibata S, Murata A, Shiraga F. [Normal values of retinal sensitivity determined by macular integrity assessment]. Nippon Ganka Gakkai Zasshi. 2014 Jan;118(1):15-21. PMID: 24505931.

Abbreviations: BCVA = best-corrected visual acuity ; BSL = baseline ; CFB = change from baseline ; :MS = mean sensitivity ; OD = *oculus dexter* (right eye); OS = *oculus sinister* (left eye) ; OU = *oculus uterque* (both eyes) ; RP = retinitis pigmentosa ; VF = visual field ; Y1/Y2 = Year 1/Year2. Disclosures: MP, CA: none ; LB, DC, ALM, KN, AC = (E) ; JAS = (I)(P) ; IA = (C). Contact: mylene.poujade@streetlab-vision.com