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Electroretinogram Findings in Early Stage Sickle Cell Retinopathy According to Hemoglobin type

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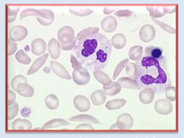
Purpose: To characterize full-field electroretinogram (ffERG) in patients with early sickle-cell retinopathy according to hemoglobin type.



2 x HbS → Xr 11 [Glu→Val] ⟶ **HbSS HOMOZYGOUS**

1 x HbC →Xr 11 [Glu→Lys]
1 x HbS → Xr 11 [Glu→Val] ⟶ **HbSC DOUBLE HETEROZYGOUS**

1x Normal
1 x HbS → Xr 11 [Glu→Val] ⟶ **HbAS Simple heterozygous**

Eaton JW, et al., eds. Sickle cell disease: basic principles and clinical practice. New York: Raven Press Ltd. 1994.

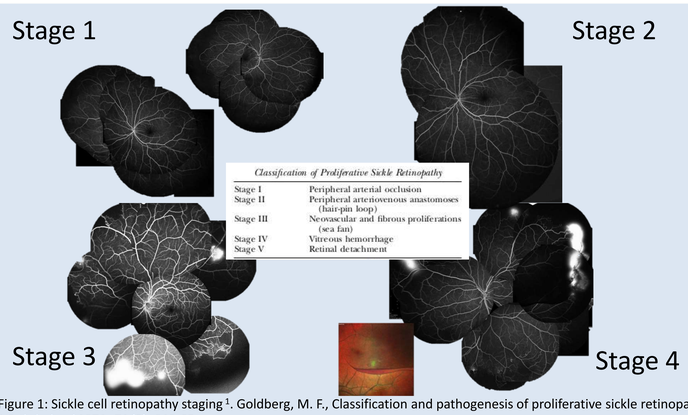


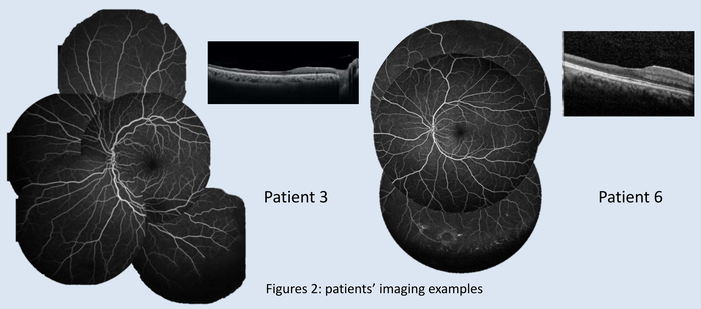
Figure 1: Sickle cell retinopathy staging [1]. Goldberg, M. F., Classification and pathogenesis of proliferative sickle retinopathy. *Am J Ophthalmol* **1971,** *71* (3), 649-65.

Methods: Rétrospective study, in Centre hospitalier intercommunal de Créteil, France
3 groups: SS, SC and control
Patient inclusion criteria
- Non proliferative sickle cell retinopathy (stage 1/2) (fig 2)
- Preserved VA

Patient exclusion criteria
- Other ophtalmological issue, laser treatment history

Control inclusion criteria:
- Aged matched, no ophthalmological history

Performed: VA, fundus, FA, OCT and ffERG



Figures 2: patients' imaging examples

		DA0.01 bw	DA3.0 aw	DA3.0 bw	DA3.0 b/a	SOPs 3.0	DA10.0 aw	DA10.0 bw	DA10.0 b/a	LA3.0 aw	LA3.0 bw	Fl30Hz
HbSS and HbSC groups	Total Median	184	214	334.5	1.6	120	253.5	368.5	1.42	37.1	119.5	86.6
	Q1-Q3	118-211.5	172.5-241.5	276-391.5	1.3-2	92-163.4	228.5-303	301.9-437	1.15-1.55	33.2-40.3	109-132	76.3-107
	SS Median	178.5	217.5	287.5	1.3	92	267	321.5	1.2	38	119.5	86.6
	Q1-Q3	137-213.5	202.5-239	263.2-365.5	1.1-1.6	76.2-134.3	238.5-313.5	285.4-377.5	0.97-1.4	35-39.9	91.4-131	75-106.4
	SC Median	188.5	194.5	355.5	2.0	141.5	241.5	400.5	1.55	35.1	119	85.6
	Q1-Q3	114-211	162.5-241.5	328.5-462.5	1.67-2.25	119.3-212.7	214.5-282	363.5-467.5	1.45-1.75	29.4-45.5	112.5-133	76.3-126.5
	P* (SS vs SC)	0.92	0.21	0.07	0.002*	0.07	0.15	0.07	0.02*	0.92	0.52	0.15
Control group	Median	220	282	418	1.5	135.9	345	455	1.3	45.4	139.2	116
	Q1-Q3	199-266	219-306	391-444	1.4-2	115-199.2	282-402	411-505	1.1-1.5	39.3-53.7	119-162.4	101.3-164
	P* (vs SS)	0.02*	0.14	0.003*	0.09	0.09	0.12	0.005*	0.56	0.03*	0.09	0.01*
	P* (vs SC)	0.18	0.03*	0.35	0.08	0.73	0.01*	0.26	0.10	0.03*	0.29	0.14
	P* (vs SS+SC)	0.04*	0.04*	0.06	0.91	0.15	0.02*	0.04*	0.74	0.01*	0.11	0.0*2

Table 1. Amplitudes in µV of the dark-adapted and light-adapted full-field electroretinogram (ffERG) responses.
a-wave component (aw), b-wave component (bw),b/a-ratio in dark-adapted (DA),light-adapted (LA) ffERGs and the sum of DA 3.0 oscillatory potentials (SOPs) in µV .
* P<0,05; P was assessed using mixed linear regression models adjusted for age.
Medians, first and third (Q1-Q3) quartiles from the HbSS, HbSC and control groups.Intensities in cd.s.m^{-2}.

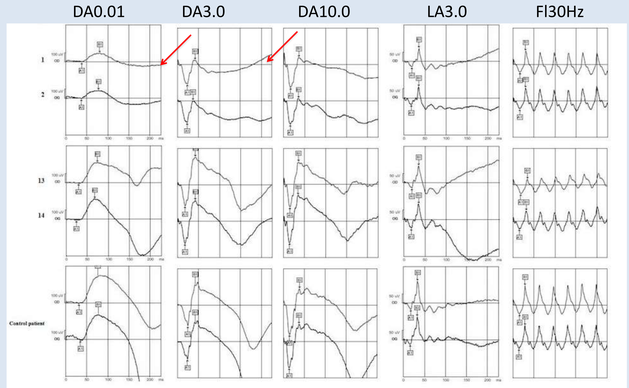


Fig 3: Full-field electroretinogram (ffERG) responses from one HbSS sickle cell patient (eyes 1 and 2), one HbSC sickle cell patient (eyes 13 and 14) and one control patient.
Recordings conform to ISCEV standards. Note reduced amplitudes in HbSS sickle cell patient (eyes 1 and 2) for the DA 3.0 and DA 10.0 cd.s.m^{-2} stimulations.

Results: Twenty-four eyes from 12 patients (6 HbSS and 6 HbSC) and twelve eyes from six controls were included.
FfERG results are visible in tables 1 (amplitudes) and in figure 3.
Significant alterations were found for amplitudes between the 3 groups:
- **Patients from HbSS group** showed a dramatic decrease of b-wave amplitudes for all dark-adapted ffERG responses (↙) but also reduced flicker 30Hz amplitudes and a-wave amplitudes for light-adapted ffERG responses,
- **Patients from the HbSC group** showed reduced a-wave amplitudes for all dark-adapted and light-adapted ffERG responses, compared with the control group.
- **Patients from the HbSS+HbSC group** exhibited reduced a-wave amplitudes for all dark-adapted and light-adapted ffERG responses, reduced flicker 30Hz amplitudes and reduced b-wave amplitudes for DA 0.01 and DA 10.0 responses compared with the control group.

Discussion:

This is the first report on eletrophysiological alterations in HbSS and HbSC patients, occurring so early in the evolution of sickle cell retinopathy
In 1987, Peachy *et al.*[2] studied retinal function in sickle cell disease patients and could not find any ERG modifications in sickle cell patients without proliferative lesions; however, they did not differentiate between SS and SC patients and the methods preceded the ISCEV standards era.
In this study:
- In HbSC patients: The significantly decreased a-wave amplitude found for ffERG responses are likely related to outer retina damage, as seen in chronic retinal ischemia.[3]
- In HbSS patients: The significant decrease of the dark-adapted b-wave amplitudes was not associated with a significant a-wave reduction, suggesting inner retina dysfunction.[4,5] The trend toward reduced OPs is another strong argument for this latter hypothesis in HbSS patients[6].

Recent imaging studies demonstrated significant thinning of the inner retina and vascular abnormalities in the superficial and deep capillary plexus to be common and early features in sickle cells patients; even before severe peripheral retinopathy[7,8,9].

Conclusions:

The main limitation of this study is the small number of patients included. Of course, to be able to support our hypothesis, larger studies are needed. It would also be of interest to compare ffERG results to OCT-Angiography findings; however, current systems mostly cover the area of the central retina, while ffERG collects responses from the whole retina. Evaluating ffERG responses of sickle cell patients would help determining possible correlations between global retinal function and the severity of vascular systemic complications

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