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# Case report AOSLO imaging in poppers maculopathy shows high resolution loss of central macular cones



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ARTICLE INFO	A B S T R A C T
Keywords: Adaptive optics OCT Poppers maculopathy Toxic retinopathy Imaging Cones	Purpose: To use new adaptive optics scanning laser ophthalmoscopy (AOSLO) technology to better image macular pathology in poppers maculopathy.     Observations: A 40-year-old patient was found to have poppers maculopathy. Best corrected visual acuity was decreased to 20/40 OD and 20/50 OS, spectral domain optical coherence tomography found outer retinal disruption of the fovea, and AOSLO imaging showed significant decrease in cone density of the fovea of both eyes.     Conclusions and importance: Poppers maculopathy is a rare, but visually significant, complication of popper abuse. AOSLO technology demonstrates significant cone damage in poppers maculopathy. The striking loss of cones revealed by AOSLO imaging shows how AOSLO imaging can elucidate macular pathology.

#### 1. Introduction

Poppers are recreational drugs used for their psychoactive effects and are particularly common among men having sex with men (MSM) because of their ability to induce euphoria and myorelaxation. The most common type of poppers inhalant is amyl nitrite. One study revealed popper use among the general population in the UK, Australia, USA and Eurozone was around 7.6 % within the past year, whereas a study in Ireland showed that 35 % of MSM have used poppers in the same period.<sup>1,2</sup> Importantly, poppers use amongst MSM is also associated with increased incidence of unprotected sex and HIV transmission.<sup>3</sup>

Historically, poppers were thought to be relatively benign, with transient side effects including presyncope, syncope, hypotension, and flushing due to vasodilation.<sup>4</sup> More recently, poppers have been implicated as a cause of vision loss commonly characterized by central scotomas.<sup>5,6</sup> Our report describes a case of poppers maculopathy using newer generation adaptive optics scanning laser ophthalmoscopy (AOSLO; Apaeros System, Boston Micromachines, Boston USA).

## 2. Case report

A 40-year-old male with HIV disease well controlled on HAART was referred to our retina service with a 6 month history of progressive

blurring of vision OU. He had no prior ocular or relevant family history. On presentation, the patient's best corrected visual acuity (BCVA) was 20/40 OD and 20/50 OS. Anterior segment exam was unremarkable. A complete dilated eye examination revealed no obvious pathology (Fig. 1A), however, spectral-domain optical coherence tomography (SD-OCT) of the macula showed a small, central defect in the ellipsoid zone OU (Fig. 1B). Autofluorescence (AF), near infrared reflectance (NIR), and fluorescein angiography (FA) were all normal. Humphrey visual field 10–2 was without focal deficits.

Further history was elucidated inquiring about environmental exposures and the patient denied any sun-gazing but did endorse using "poppers" most days for the past 2 years. Given the relatively mild SD-OCT findings, yet significant decrease in best corrected visual acuity, we used AOSLO as an additional modality to assess the extent of retinal damage. Notably, AOSLO revealed extensive damage to the central cones of both eyes. In these images, the central dark elliptical zone denotes an area with absent cone outer segment signal. This is surrounded by normal reflecting outer segments in the perifovea (Fig. 2B and C). This is more apparent when compared to the central high density of cones that is seen in a healthy control (Fig. 2A).

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Fig. 1. Retinal Imaging: A- Fundus photography revealing normal appearing posterior pole OU; B- SD-OCT through fovea OU with focal defect of outer retina OU.

## 3. Discussion

Poppers maculopathy is a rare but visually significant maculopathy that is poorly understood with yellow foveal discoloration and disruption of the outer segments of foveal photoreceptors. Poppers maculopathy generally presents with bilateral central vision blurring that can present over the course of days to months. The prognosis of poppers maculopathy is poorly understood given the paucity of cases in the literature that have long term follow up. In a case series in 2014, Pahlitzsch et al. showed only 1 of the 3 patients recovered any visual acuity following initial presentation.<sup>7</sup> More recently a case series by Hui et al. showed complete recovery of visual acuity in the only patient that had long term follow up.<sup>8</sup>

Damage appears to be confined to the photoreceptors, with a few proposed mechanisms.

One hypothesis suggests that alkyl nitrates are directly toxic to photoreceptors while others have proposed that alkyl nitrates make photoreceptors more susceptible to photopic damage, explaining the similarity in appearance to solar retinopathy. Still others have speculated that poppers may disrupt blood flow to the photoreceptors via vasodilation.<sup>5,9</sup>

Abnormalities of the ellipsoid layer are the most common feature on OCT imaging as demonstrated in our case. Because of the relative paucity of findings, the characteristic OCT abnormalities are usually necessary to make the diagnosis. While OCT is a high definition modality to assess macular pathology, it is limited in its ability to fully delineate photoreceptor damage. AOSLO is an emerging technology that shows promise in the imaging of photoreceptors. By combining deformable adaptive optics mirrors with scanning laser ophthalmoscopy, AOSLO can generate high definition images by correcting for the optical aberrations of the imaged eve. AOSLO can provide high definition imaging of cones in vivo making it an ideal technology to further delineate the extent of damage caused to photoreceptors in poppers maculopathy. Geogiou et al. corroborate this point with their observation that SD-OCT was limited in fully describing the structural damage compared with AOSLO in patients with CNGA3-associated achromatopsia.<sup>10</sup> Similarly, Wu et al. described the structural changes that occur in solar retinopathy

using AOSLO demonstrating foveal cone photoreceptor mosaic disturbances.  $^{11}$ 

Only one other report in the literature in 2011 by Audo et al. has described AOSLO imaging in poppers maculopathy.<sup>6</sup> AOSLO imaging in this study also suggested central cone loss, however, the resolution of the older AOSLO technology is significantly limited compared to the newer images presented in this report, and there was no control eye for comparison. Our study report is the first to image the retina in poppers maculopathy using newer AOSLO technology demonstrating significant central loss of cones supporting a more focal maculopathy. Clemens et al. have suggested decreased signal on full field ERG may indicate a more widespread retinopathy while the normal ERG results demonstrated by Audo et al. indicated a more focal, central macular pathology.<sup>6,12</sup> Our AOSLO findings of significant central loss of cones point towards a more focal maculopathy.

#### 4. Conclusion

Our study underscores the importance of recognizing this entity as a possible cause for loss of vision and the utility of AOSLO to provide insight into central photoreceptor damage that may not be as apparent with other, more widely used, ophthalmic imaging techniques. Future studies with AOSLO imaging may inform as to the reversibility or progression of these changes through long term follow-up of patients. Enhancing public awareness and recognition of this rare entity is critical.

## Patient consent

Case reports are exempt from consent per our IRB.

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Fig. 2. AOSLO Imaging: A- Demonstrates normal control; B- Demonstrates OD/OS of case patient with loss of cones centrally.

## Authorship

All the authors attest that they meet the ICMJE criteria for Authorship.

## Declaration of competing interest

The following authors have no financial disclosures: CNR, AAF, MKG.

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#### References

- Davies AJ, Kelly SP, Naylor SG, et al. The prevalence of visual symptoms in poppers users: a global survey. *BMJ Open Ophthalmology*. 2017;1(1). https://doi.org/ 10.1136/bmjophth-2016-000015, 1–1.
- Barrett P, O'Donnell K, Fitzgerald M, et al. Drug use among men who have sex with men in Ireland: prevalence and associated factors from a national online survey. *Int J Drug Pol.* 2019;64:5–12. https://doi.org/10.1016/j.drugpo.2018.11.011.

- Deininger R, Muller R, Guggenmoos-Holzmann I, et al. Behavioral characteristics and laboratory parameters in homo and bisexual men in West Berlin: an evaluation of five years of testing and counseling on AIDS. *Klin Wochenschr.* 1990;68:906–913.
  O'Malley G, O'Malley R. "Volatile Nitrites - Special Subjects." Merck Manuals
- O'Malley G, O'Malley R. "Volatile Nitrites Special Subjects." Merck Manuals Professional Edition, Merck Manuals, www.merckmanuals.com/professional/ special-subjects/recreational-drugs-and-intoxicants/volatile-nitrites.
- Davies AJ, Kelly SP, Naylor SG, et al. "Adverse ophthalmic reaction in poppers users: case series of 'poppers maculopathy. *Eye*. 2012;26(11):1479–1486. https://doi.org/ 10.1038/eye.2012.191.
- Audo I, Sanharawi M, Vignal-Clermont, et al. Foveal damage in habitual poppers users. Arch Ophthalmol. 2011;129(6):703. https://doi.org/10.1001/ archophthalmol.2011.6.
- Pahlitzsch M, Mai C, Joussen A, Bergholz R. Poppers maculopathy: complete restitution of macular changes in OCT after drug abstinence. *Semin Ophthalmol.* 2014:1–6. https://doi.org/10.3109/08820538.2014.962175.
- Hui M, Galvin J, Chilov M, et al. Popper maculopathy. *Retin Cases Brief Rep.* 2020;14 (2):195–199. https://doi.org/10.1097/icb.00000000000650.
- Fajgenbaum MAP. "Is the mechanism of 'poppers maculopathy' photic injury? Eye. 2013;27(12):1420–1421. https://doi.org/10.1038/eye.2013.218.
- Georgiou M, Litts KM, Kalitzeos A, et al. Adaptive optics retinal imaging in CNGA3associated achromatopsia: retinal characterization, interocular symmetry, and intrafamilial variability. *Invest Ophthalmol Vis Sci.* 2019 Jan 2;60(1):383–396. https://doi.org/10.1167/iovs.18-25880. PMID: 30682209; PMCID: PMC6354941.
- Wu CY, Jansen ME, Andrade J, et al. Acute solar retinopathy imaged with adaptive optics, optical coherence tomography angiography, and en face optical coherence tomography. JAMA Ophthalmol. 2018;136(1):82–85. https://doi.org/10.1001/ jamaophthalmol.2017.5517.
- Clemens C, Alten F, Loos D, et al. Poppers maculopathy or retinopathy? *Eye*. 2015; 29:148–149. https://doi.org/10.1038/eye.2014.252.