

Sleep apnea and the eye

From floppy eyelid to NAION, what should ophthalmologists know about the association between OSA and ocular disease?

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Obstructive Sleep Apnea

What's the significance?

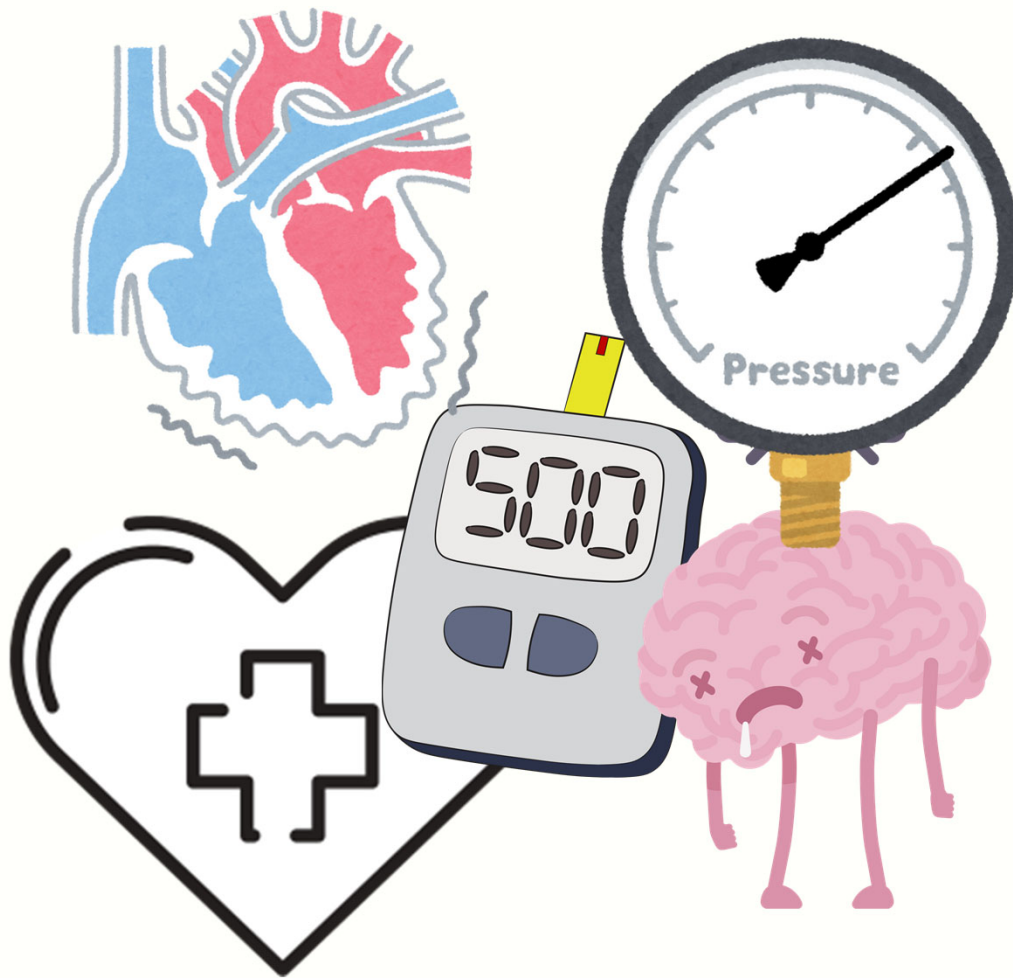
1) It affects our patients

Prevalence of 20-40% of the
general population

Possibly as high as 80% in
those over 70 years old.

2) We can help diagnose it

... possibly changing the patient's
life.



Systemic Associations

- Obesity
- Heart attack
- Stroke
- HTN
- Depression
- Cardiac arrhythmias
- Overall cardiovascular mortality
- Metabolic dysfunction



Presentation Framework

Ocular conditions affected by OSA

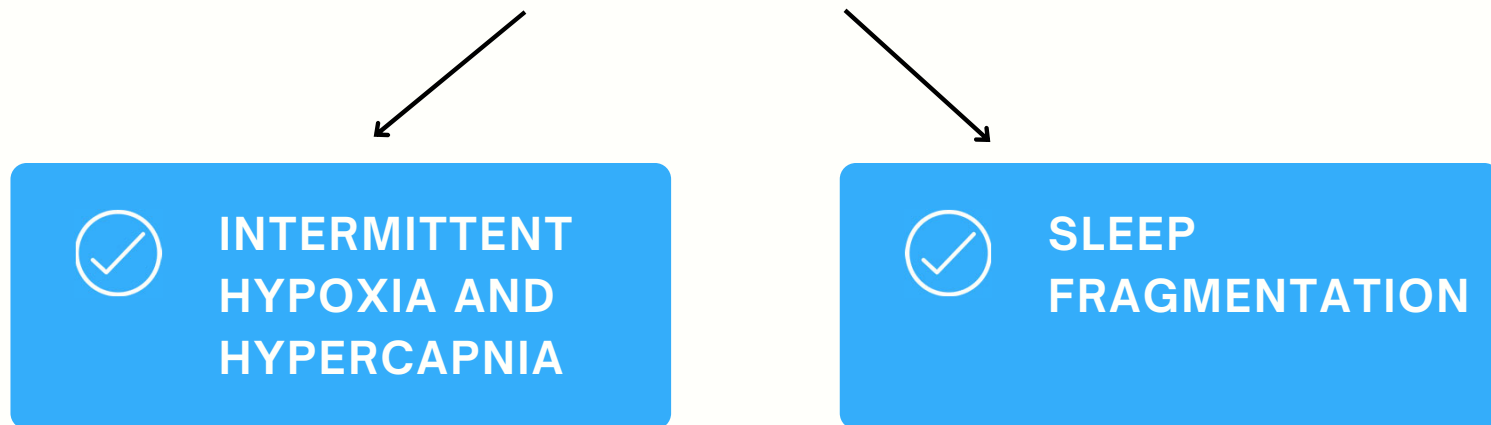
- Floppy eyelid syndrome
- Ocular surface disease
- POAG
- Papilledema
- NAION
- Diabetic retinopathy
- ARMD
- CSCR
- other retinal vascular changes

Quick Overview of OSA

Defined by:

multiple obstructive apneic/hypopneic episodes during sleep caused by repetitive partial or complete collapse of upper airway. [>5 events per hour = OSA]

Apneic episodes cause



Quick Overview of OSA



INTERMITTENT HYPOXIA AND HYPERCAPNIA

- Inflammation
- Oxidative stress
- Mitochondrial dysfunction and RBC death
- Increased ICP
- Increased sympathetic activity



SLEEP FRAGMENTATION

Increased sympathetic activity

Vasoconstriction & autonomic dysfunction

Decreased perfusion

Floppy Eyelid Syndrome



FES AND OSD

PATHOPHYSIOLOGY

TISSUE INJURY FROM MECHANICAL TRAUMA AND HYPOXIA



INCREASE IN MMPS (ESPECIALLY MMP-9)



ELASTIN DEGREDDATION



POOR TONE IN THE UPPER EYELID TARSAL PLATE



EYELID MALPOSITION



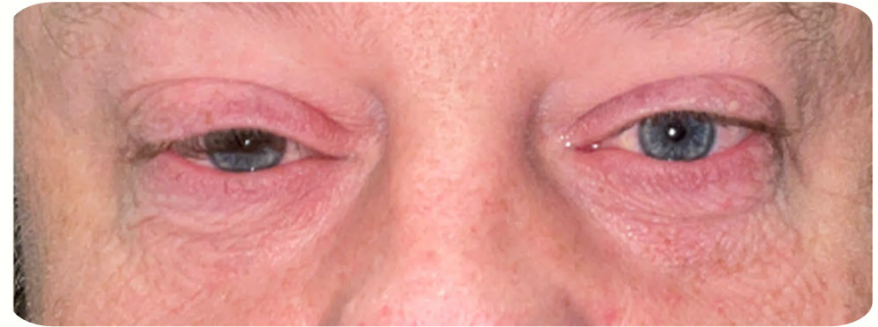
DISRUPTION OF THE INTERFACE OF THE LIDS
AND OCULAR SURFACE



CHRONIC IRRITATION AND CONJUNCTIVITIS

• Floppy Eyelid Syndrome classic findings

Are you missing these patients in your clinic?



- Easily everted lids
- Eyelash ptosis - pathognomonic
- “Velvety” papillary reaction of upper lid palpebral conjunctiva
- Ocular surface disease

Treatment (besides treating OSA)

NON-INVASIVE

Goal: limit exposure and irritation

- Ointment while sleeping
- Goggles or eye shields while sleeping
- No rubbing eyelids!
- Treat ocular surface disease

SURGICAL

Goal: Horizontal Tightening

- Lateral tarsal strip procedure
- Full Thickness Wedge Excision
- Canthal tendon plication
- Often need ptosis repair with blepharoplasty +/- repair of lash ptosis

Other: conjunctivoplasty with amniotic membrane fornix reconstruction

FES and OSA



HISTOLOGICAL STUDIES

- meibomian gland abnormalities including decreased lipid production
- duct widening and impaction
- atrophy of muscles of Riolo
- granuloma formation



CLINICAL STUDIES SHOW SIGNIFICANTLY WORSE:

- tear break up time (TBUT)
- Schirmer's scores
- ocular surface disease index (OSDI) scores
- meibomian gland dropout
- corneal staining



Other ocular surface disease considerations

Other exam findings

- corneal scarring
- corneal neovascularization
- recurrent corneal erosions
- corneal thinning and/or ectasia



Other ocular surface disease considerations

It is important to check on CPAP/BIPAP use in your patients.

Air leaking from treatment masks makes OSD worse.

Ask about symptoms worst in morning and if they notice mask leak.

Recommend a mask fitting or changing to another device if needed.



Can we reverse floppy eyelid syndrome?

Maybe

- no controlled trials
- One small study suggested that FES was reversed in about half of newly-diagnosed patients after 6 months of CPAP therapy
 - BUT there was no control group.
- A different small study found no difference in eyelid laxity between CPAP-treated vs untreated subjects.

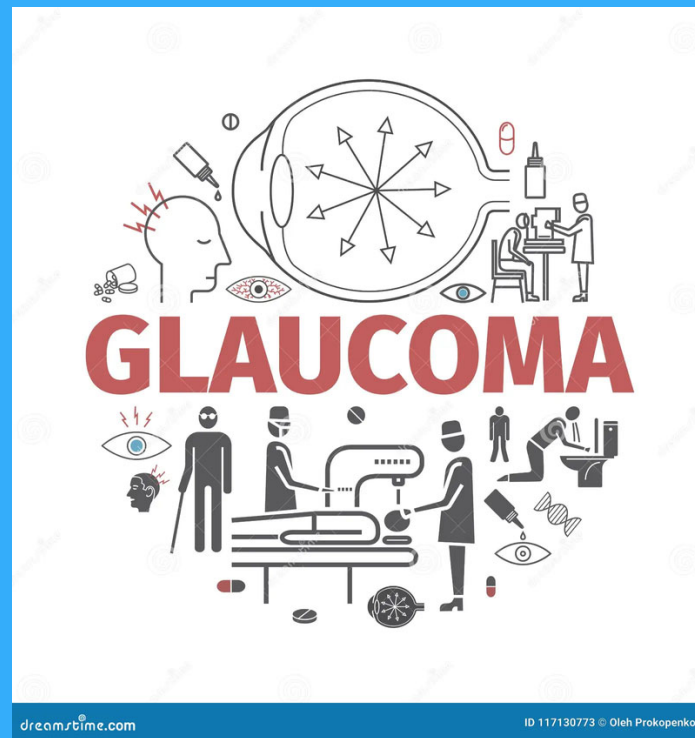


OSA and Floppy Eyelid Syndrome



SUMMARY SLIDE

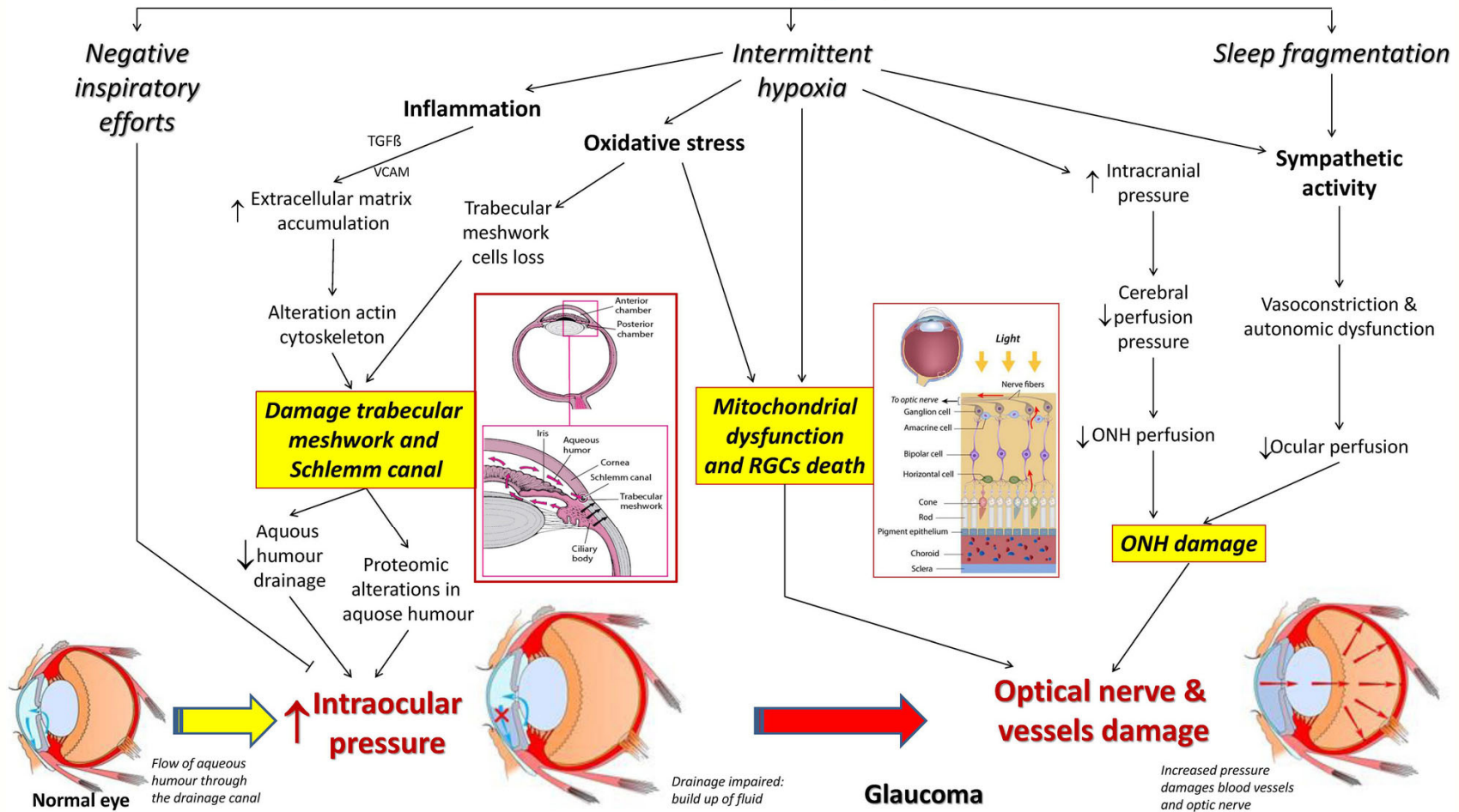
- **Floppy Eyelid Syndrome is the ocular finding that is most linked to OSA, as well as the most specific --- we can help diagnose OSA**
- **Get away from the slit lamp and touch the eyelids**
- **Treatment is mostly surgical**
- **Don't neglect the ocular surface disease**



dreamstime.com

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Obstructive Sleep Apnea

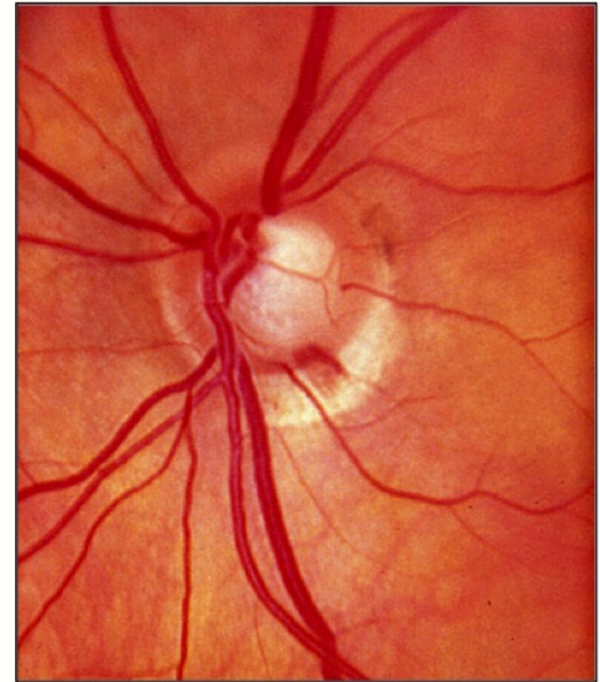


Floppy eyelid syndrome is also associated with decreased corneal hysteresis

Does OSA increase the risk of glaucoma?

Maybe

- Studies have been low quality
 - (poor patient selection, small size, comorbidities)
- OR of 1.0 to 2.5, but better quality studies being on the low end



https://eyewiki.org/Normal_Tension_Glaucoma

• In those with glaucoma and OSA, does OSA predict outcomes?



Yes

- Retrospective study (32 patients) by Fan et al reported those with moderate OSA or worse were 8x more likely to have RNFL thinning
- Another study by Wozniak et al showed twice as much RNFL loss over a 3 year period in patients with OSA



Does treating OSA decrease glaucoma progression?

We don't know yet

- CPAP theoretically improves nerve perfusion BUT ALSO INCREASES IOP
- Smaller studies suggest better outcomes with CPAP use
- A large retrospective study (12,000 patients) reported that CPAP-treated and untreated patients with OSA had similar levels of increased glaucoma risk, relative to a comparison cohort (HR = 1.65 and 2.15, respectively).
However, those who had undergone surgical treatment did not have an elevated risk of glaucoma compared with the controls



Glaucoma and OSA

QUICK SUMMARY SLIDE

Studies suggest OSA may be associated with primary open-angle glaucoma (POAG).

Having OSA does seem to be a risk factor for glaucoma progression.

We are still unsure if treating OSA with CPAP helps with glaucoma treatment.

Conflicting evidence exists, and more research is needed.

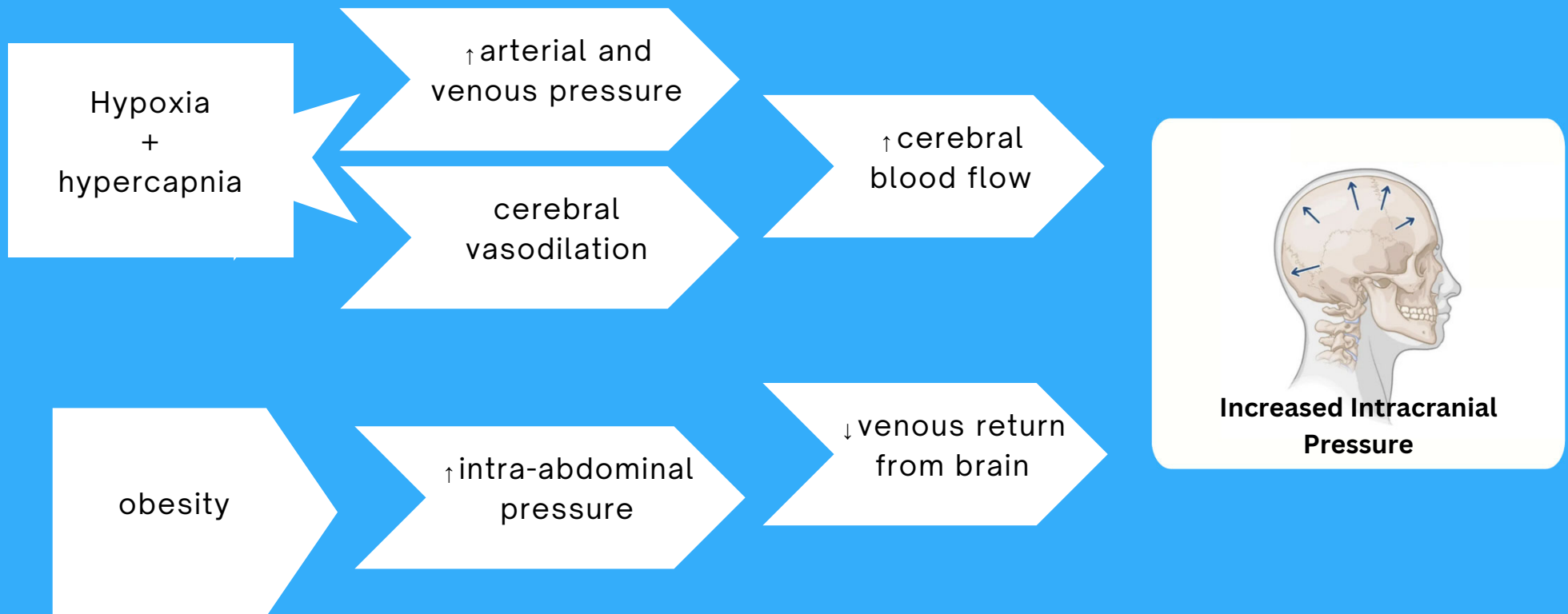
Papilledema and OSA



edema is characterized by Loss of major vessels as the

<https://www.opthalmologyreview.org/articles/papilledema>

Proposed pathophysiology



Association between papilledema/IIH and OSA

DATA IS CONFLICTING AND
MORE STUDIES ARE NEEDED

- A large cohort study by Stein et al showed a **hazard risk of 1.3-2** over patients without OSA.
 - comorbidities were not accounted for
- Other studies showed **no increased prevalence of OSA** in newly diagnosed IIH patients



<https://entokey.com/nonarteritic-anterior-ischemic-optic-neuropathy/>

NAION

2-4x

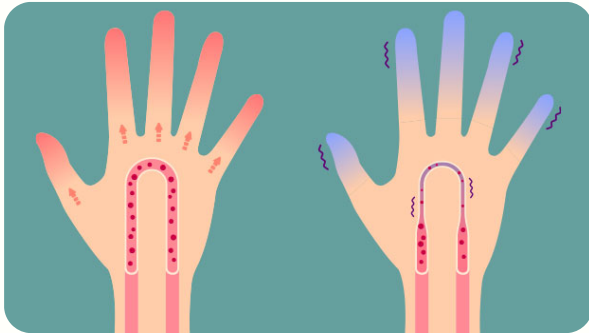
MORE LIKELY IN THOSE
WITH OSA

6x

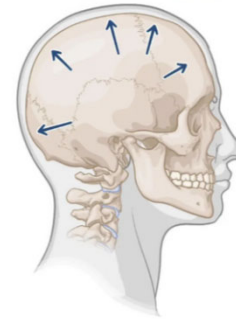
MORE LIKELY IN THOSE
WITH OSA UNDER 40
YEARS OLD

NAION and OSA: Proposed pathophysiology

Optic nerve and retinal hypoxic hypoperfusion



Elevated intracranial pressure

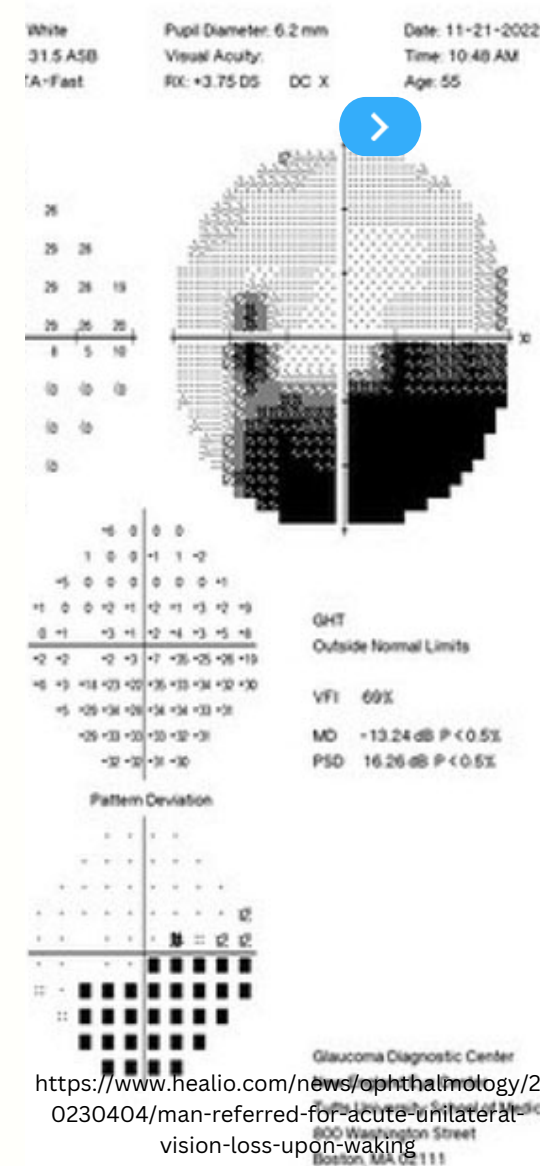


Does treating with CPAP decrease risk of NAION?

PROBABLY

In a small study of 67 patients with unilateral NAION and OSA, patients with **poor compliance to CPAP therapy** had **significantly higher risk of a second eye involvement, with a HR of 5.5.**

One study showed that those treated with CPAP had the same incidence of NAION as those WITHOUT OSA.





NAION and OSA

QUICK SUMMARY SLIDE

OSA increases the risk of NAION.

Patients with untreated OSA have a higher risk of second-eye involvement.

Personal opinion: all patients with NAION should get a sleep study or get re-investigated to make sure current CPAP settings are effective.



OSA and Retinal Disease

**Diabetic
Retinopathy**

Age-related
Macular
Degeneration

Central Serous
Chorioretinopathy

Macular Edema

Retinal Vein
Occlusions



Proposed pathophysiology of the association between OSA and retinal disease



“An increase in risk of **systemic hypertension** in individuals with OSA is hypothesized to be due to the OSA-induced hypoxia and hypercapnia, which result in **sympathetic activation, oxidative stress, vessel endothelial damage, and increased blood coagulation**, all of which are drivers of vascular disease.” - Lee S, et al



Proposed pathophysiology



- Increased inflammation and oxidative stress leads to glucose dysregulation.
- Oxidative stress is a key driver of macular degeneration.
- Increased intracranial pressure and venous pressure in the head found in OSA may hinder retinal blood flow.
- Hypoxia may lead to upregulation of VEGF in the eye
- Increased sympathetic activity and elevated serum cortisol leads to CSCR

OSA and diabetic retinopathy

- There is consistent evidence of an association between OSA and diabetes.
- OSA is associated with more severe DR or progression.
- Those with DM + OSA are 3x more likely to have macular edema.



OSA and macular degeneration

33-44% increased risk of AMD

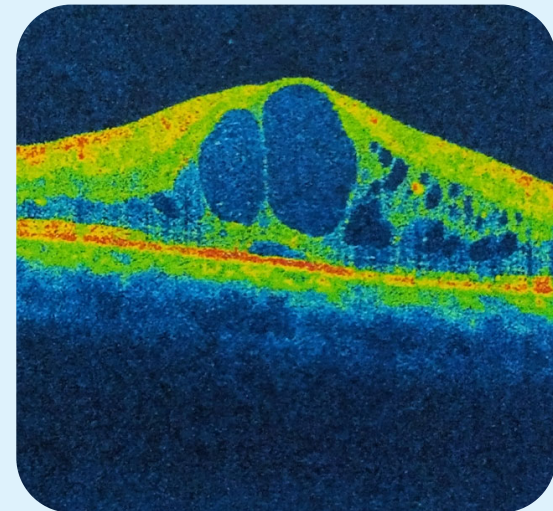
**(even after accounting for confounders
and comorbidities)**



OSA and macular edema (diabetic or macular degeneration)

In a case-controlled study of 38 patients with OSA and anti-VEGF injections for exudative AMD:

- the patients with untreated **OSA required double the number of injections** compared with those treated with CPAP (mean of 16 vs. 8 injections)
- Untreated OSA group had poorer:
 - final visual acuity (20/100 vs. 20/40)
 - thinner maculas (macular thickness: 322 vs. 254 μm)
 - despite having similar baseline measures prior to anti-VEGF therapy.



OSA and macular edema

(diabetic or macular degeneration)

In a case-controlled study of 133 patients with AMD or DMO:

- 78%–88% of patients with DME who required two or more consecutive anti-VEGF injections had symptoms and risk factors of OSA
 - vs only 50% who required less than 2 injections

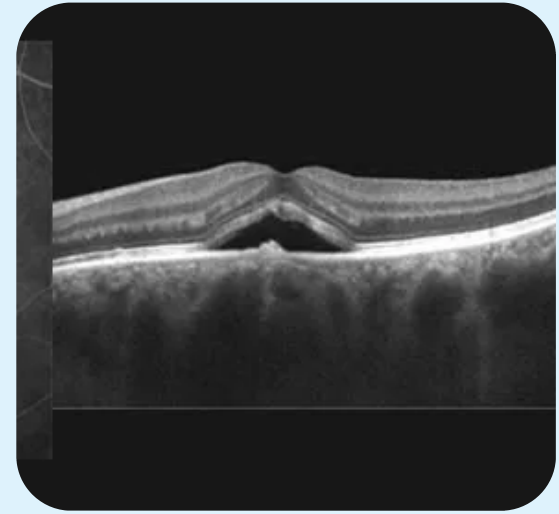
- 79% of patients with nAMD with poor response to anti-VEGF therapy had symptoms and other risk factors of OSA
 - vs < 50% in the other groups

OSA and Central Serous Chorioretinopathy

Overall, there is conflicting evidence.

CPAP use may decrease risk.

There is a case report of a patient with bilateral CSCR that rapidly resolved with CPAP therapy.



Retinal vascular disease and vein occlusions

Moderate-to-severe OSA had higher rates of vascular changes even after correcting for systemic BP.

A study of over 35,000 patients reported **double the rate of retinal vein occlusions** in those with sleep apnea.

Further studies are needed to determine if sleep apnea treatments affect RVOs.





Retinal disease and OSA



QUICK SUMMARY SLIDE

- OSA exacerbates retinal damage in diabetic patients and increases risk for DME
- Increased AMD risk
- Increased risk for resistance to anti-VEGF therapy
- More likely to develop RVO.
- Treating OSA with CPAP may decrease risk of developing CSCR or help treat it



Effects of OSA treatment on eye health



QUICK SUMMARY SLIDE

- **Continuous Positive Airway Pressure (CPAP) Therapy:**
 - May slow glaucoma progression but can increase IOP.
 - Reduces risk of NAION progression.
 - Likely improves retinal outcomes in treating SRF/IRF.
- CPAP mask leaks may cause ocular surface irritation.
- Surgical treatments for OSA may offer better ocular benefits than CPAP.



Summary



- **OSA is increasing in prevalence. You are definitely seeing affected patients in your clinic**
- **Look for floppy eyelid. Step away from the slit lamp.**
- **OSA influences multiple eye diseases including FES, OSD, glaucoma, NAION, and retinal vascular disease**
- **Due to poor screening in primary care, you may be the doctor who initiates a sleep apnea workup based on ocular signs -- potentially saving your patient from cardiovascular events or worsening chronic disease!**



When to refer a patient for a sleep study

- Any patient with floppy eyelid syndrome.
- Any patient who gets an NAION
- Consider in:
 - glaucoma patients who are progressing faster than expected based on their IOP
 - If a patient is responding poorly to anti-VEGF injections
 - Vein occlusions

REVIEW

Clinical & Experimental Ophthalmology WILEY

Sleep and eye disease: A review

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Abstract

There is a growing body of literature on the effects of sleep disorders, in particular obstructive sleep apnoea (OSA), on ocular health, with consistent evidence of an increased risk of floppy eyelid syndrome, non-arteritic anterior ischaemic optic neuropathy, diabetic macular oedema, and other retinal vasculature changes in individuals with OSA. However, reports on OSA's associations with glaucoma, papilloedema, diabetic retinopathy, central serous chorioretinopathy, and keratoconus have been conflicting, while links between OSA and age-related macular degeneration have only been described fairly recently. Despite numerous suggestions that OSA treatment may reduce risk of these eye diseases, well-designed studies to support these claims are lacking. In particular, the ocular hypertensive effects of continuous positive airway pressure (CPAP) therapy for OSA requires further investigation into its potential impact on glaucoma risk and management. Reports of ocular surface complications secondary to leaking CPAP masks highlights the importance of ensuring good mask fit. Poor sleep habits have also been linked with increased myopia risk; however, the evidence on this association remains weak.

KEYWORDS

age-related macular degeneration, eye disease, glaucoma, sleep, sleep apnoea

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Thank you for your attention



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