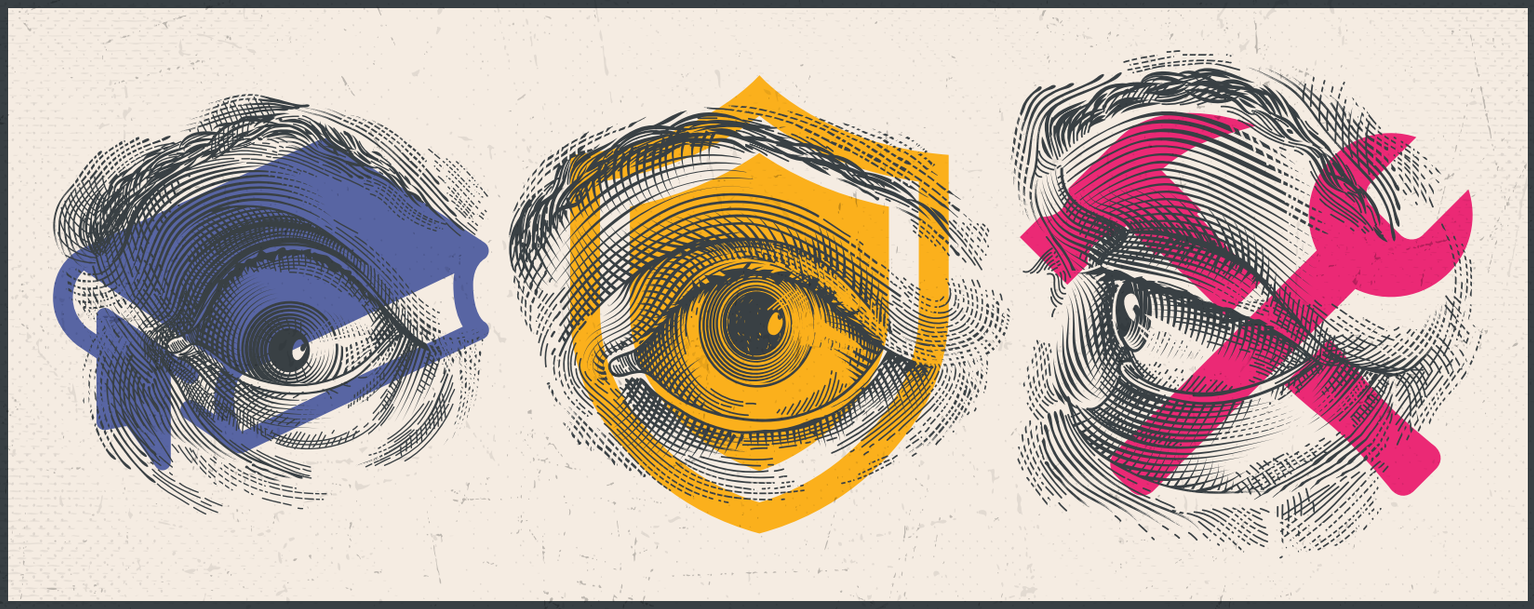


UNDERSTANDING NEUROLOGIC DRY EYE

Unraveling the complex connection between the ocular surface and nerves will enhance your patient care.

BY JACQUELINE THEIS, OD, FAAO, FNAP

Dry eye disease is a common condition that affects millions of people worldwide, causing ocular discomfort, burning, stinging, irritation, and a range of other nonspecific symptoms, including blur and photosensitivity, that can affect daily life. Dry eye is a multifactorial disease that can be incredibly frustrating for both patients and providers to treat, as the objective ocular signs don't always match the subjective ocular symptoms, making it an elusive diagnosis.

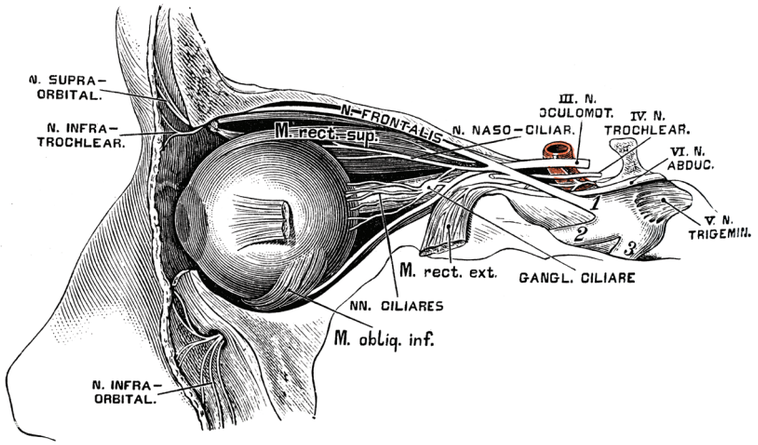
MAKING THE CONNECTION

Believe it or not, as a provider who mostly sees patients with vision problems such as diplopia secondary to neurologic conditions (eg, brain injury and stroke), dry eye plagues my clinic. Although most people associate dry eye with systemic diseases such as rosacea, Sjögren disease, and thyroid eye disease, dry eye is also common in neurologic conditions. In fact, a meta-analysis of US military veterans revealed that patients with a history of traumatic brain injury (TBI) are more likely to have a diagnosis of dry eye (37.2%) than their counterparts without TBI (29.1%).[1] Dry eye is also common in patients with migraine and other pain disorders, including chronic regional pain syndrome, fibromyalgia, and psychiatric conditions such as depression and anxiety.[2] Although the general population over 50 years of age has a prevalence of dry eye ranging from 5% to 35%, the prevalence of dry eye in patients with Parkinson disease is as high as 53% to 60%.[3,4]

The most common patient referred to my clinic complains of light sensitivity, double vision, and blurry vision post-TBI. Although oftentimes these complaints stem from post-traumatic headache and/or oculomotor dysfunction such as traumatic convergence and/or accommodative insufficiency, there is a large subset of patients who also have or *only* have dry eye. Interestingly, the majority of these patients deny having a history of dry eye before their TBI. In fact, they all swear that the symptoms started within a few days or weeks after their injury. I also have seen cases where dry eye signs and symptoms improve after the patient has cervical decompression surgery or starts treatment with levodopa for newly diagnosed Parkinson disease. How can TBI, Parkinson disease, and cervicogenic whiplash injury cause or exacerbate dry eye?

THE NEUROLOGIC LINK

Dry eye occurs when there is an imbalance in the production, maintenance, and drainage of tears, leading to loss of homeostasis of the tear film, tear film instability, hyperosmolarity, ocular surface inflammation and damage, and/or neurosensory abnormalities, all of which ultimately lead to inadequate



lubrication and damage to the eye's surface.[5] Neurologic dry eye represents a subset of dry eye disease, where the primary etiology or dysfunction lies in the neural pathways controlling tear production, blinking, and the corneal neurosensory pathway.

REGULATION OF TEAR PRODUCTION AND BLINKING

The cornea is the most densely innervated tissue in the body.[6] Corneal branches of the nasociliary nerve, a branch of the ophthalmic division of the trigeminal nerve, have different nociceptors at their nerve endings, including mechanoreceptors, polymodal receptors, and cold receptors, that when directly activated by touch, temperature changes, chemicals/gases, pH changes, and/or toxins, send a signal down the afferent ophthalmic division of the trigeminal nerve to the spinal trigeminal nucleus in the brain stem. This leads to activation of second- and third-order neurons that perpetuate the pain signal to the midbrain, thalamus, and somatosensory cortex and activate the trigeminal corneal reflex. The trigeminal corneal reflex leads to rapid innervation of the Edinger-Westphal nucleus, facial nerve nucleus, and lacrimal nucleus, leading to iris sphincter-mediated miosis, orbicularis oculi-mediated reflexive blinking, and parasympathetic lacrimal gland secretion.[6,7]

Secretion by the meibomian glands is also regulated by the parasympathetic system.[8] Thus, when a patient has damage to the neurosensory pathway innervating the eye, which can occur in stroke, traumatic brain or brain stem injury, cranial neuropathy—specifically CN V (trigeminal) or CN VII (facial)—or reduced inhibition of the superior colliculus due to damage in the substantia nigra as occurs in Parkinson disease, you may see abnormal blinking (increased or decreased) and lacrimal gland secretion (increased or decreased). This can then lead to ocular signs and symptoms of evaporative dry eye, blurry vision, glare sensitivity, and epiphora.

Depending on the neuropathophysiology, my patients often present with at least one—sometimes more—of the following: neurotrophic keratitis, neuropathic corneal pain (keratoneuralgia), and secondary dry eye.

Neurotrophic Keratitis

Neurotrophic keratitis is a condition in which there is damage to the trigeminal nerve, which causes corneal desensitivity, and ultimately leads to decreased activation of the trigeminal corneal reflex. This causes reduced tear film secretion, blinking, and corneal trophic supply. If left untreated, this progressive condition causes corneal epithelial breakdown and impaired healing, which can lead to corneal ulceration, perforation, and permanent vision loss.[9]

Neuropathic Corneal Pain

Neuropathic corneal pain can occur as a result of lesions in the peripheral and/or central nervous system. It can also occur because of pain sensitization from persistent inflammation or nerve damage, which subsequently alters the nociceptors, causing reduced firing thresholds and increased responsiveness of the pain-signaling neurons. Persistent abnormal firing of the first-order

AT A GLANCE

- Although seemingly simple on the surface, dry eye is a multifactorial disease that can be incredibly frustrating for both patients and providers to treat.
- Most people associate dry eye with systemic diseases such as rosacea, Sjögren disease, and thyroid eye disease, but it is also commonly seen in neurologic conditions.
- Everyone's experience with neurologic dry eye is unique, and personalized medicine approaches aim to tailor treatments based on specific neural and inflammatory profiles.

neurons from the eye to the brain stem (peripheral sensitization) can lead to chronic alterations in the second- and third-order nerve firing (central sensitization). Peripheral neuropathic pain can be reversed with resolution of the inciting trigger (eg, treating ocular surface disease), but central neuropathic eye pain is more recalcitrant to treatment and may require referral to a pain specialist.

Secondary Dry Eye

Sometimes, the patient doesn't necessarily have neurologic damage to the aforementioned neurosensory pathways, but has dry eye secondary to comorbidities of the neurologic disorder. For example, sleep dysfunction, dysautonomia, stress, depression, anxiety, migraine, and introduction of new medications to treat neurologic and systemic disease can have side effects that influence or exacerbate dry eye.[1-3,7,10,11] It is important to take a comprehensive patient history to understand what the inciting factors of dry eye may be, as the ultimate treatment of neurologic dry eye may not improve with topical ocular treatment, but rather referral for treatment of underlying systemic or neurologic disease and/or comorbidities.

Neuropathic corneal pain and neurotrophic keratitis share several underlying causes or risk factors, such as dry eye disease, herpetic keratitis, infectious keratitis, corneal chemical exposure, chemotherapy, autoimmune disease (eg, Sjögren syndrome), diabetes, TBI, and stroke.[9,10,12]

DIAGNOSIS AND MANAGEMENT

A neurologic dry eye workup should include comprehensive medication and medical history, slit-lamp examination of the anterior segment, including the surface of the eye and adnexa, vital dye staining, Schirmer test, tear film osmolarity, tear breakup time, and corneal sensitivity testing.[5,7,9,10,12] The Proparacaine Challenge Test can be useful to establish the origin of pain, central or peripheral (Figure).[10] Treatment for each condition varies depending on the type of neurosensory abnormality and the etiology and severity of the dry eye.[13]

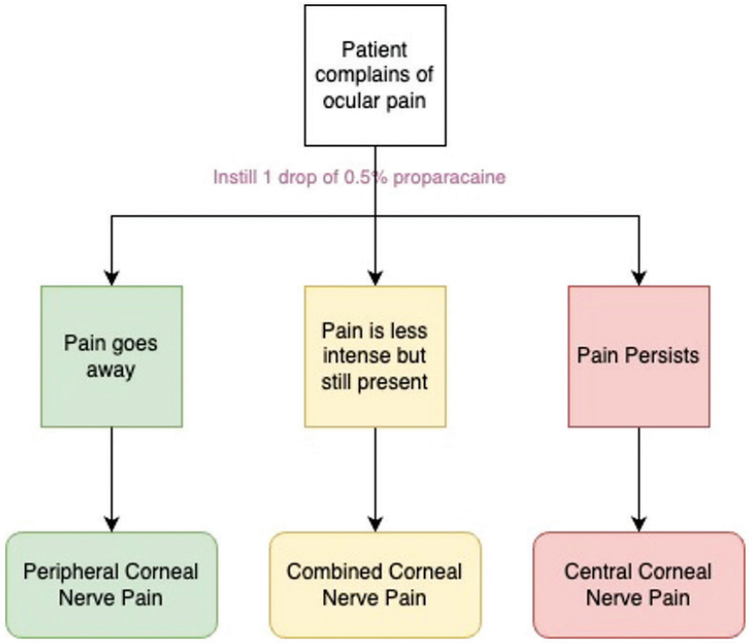


Figure. The Proparacaine Challenge Test can help pinpoint the origin of ocular pain.

PERSONALIZED MEDICINE

As research progresses, the identification of specific neural pathways involved in dry eye's pathogenesis and the development of targeted interventions hold immense potential for revolutionizing the management of this condition. Each individual's experience with neurologic dry eye is unique, and personalized medicine approaches aim to tailor treatments based on specific neural and inflammatory profiles. This individualized approach incorporates advanced diagnostic tools and multidisciplinary care and holds the potential to optimize therapeutic outcomes and improve the overall quality of life for those affected by neurologic dry eye. ■

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