Sarah brought her new horse home in December. Westley, an 8-year-old Thoroughbred cross, was wellbehaved and showed real potential as the pair spent the winter months training in the indoor arena. It was only when warmer weather arrived that their troubles began. The first time Westley flipped his nose up, jerking the reins from her hands, Sarah thought he had been bothered by an insect she didn't see. But then he did it again. And again. Within minutes, Westley was having a full-on meltdown: tossing his head up and down frantically, snorting, and rubbing his nose on his front legs. He became so agitated that he was unsafe to ride. Sarah hopped off and wondered what had happened to her easy-going horse. It would be a weeks of veterinary visits before she had the devastating answer: Westley was a headshaker.

very horse shakes his head on occasion—after all, it's an effective method for evading flies and other pests. In some cases, however, headshaking is signal that a horse is uncomfortable or in pain. Repetitive headshaking can be caused by poorly fitted tack, a heavy-handed rider, tooth abscesses, tumors, ear mites, cysts or infections around the eyes or in the sinuses. The behavior is disruptive, but once the source of trouble is identified and addressed, it stops.

Far more frustrating are cases of headshaking that have no identifiable





cause. When tack fits, the rider is skilled and the veterinary exam reveals no physical issues. What happens then?

These cases were once called "idiopathic headshaking"—meaning that the cause is unknown-and there was little that could be done. Owners often experimented for years with fly masks, supplements and management techniques (see "What Can Help," page 51) to provide their horses with relief. Sometimes they would succeed in halting chronic headshaking but more often they didn't. Persistent headshaking can have dire consequences. In the most extreme cases, horses were

**Triggers for trigeminal**mediated headshaking are still not fully understood but may include exercise, as well as exposure to sunlight or wind.

euthanatized because they were in a constant state of agitation or became a danger to work around. Idiopathic headshaking cases were often heartbreaking, for owners and veterinarians alike.

About two decades ago, however, veterinarians who shared their experiences in veterinary journals and at professional meetings began to notice patterns among cases of idiopathic headshakers. The headshaking itself, for instance, was nearly always quick flips, up and down, of the nose, rather than a sideto-side motion. The affected horses often seemed anxious or surprised, not willful or stubborn. They would snort repeatedly and rub their muzzles on their forelegs or other objects. For many horses, exercise seemed to be a trigger. Some horses avoided sunlight, even hiding their heads against a herdmate's flank when shade wasn't available.

Eventually, researchers were able to connect the dots between the equine

cases and a similar condition in human neurology, and consensus emerged on the source of the pain: the trigeminal nerve, which runs along each side of a horse's head and carries sensations from the face to the brain. Dysfunction of this nerve, researchers now believe, causes the horse to feel chronic neuropathic pain, which is sensation originating from the nerve itself, rather than an external cause.

"It's very, very rare that these headshaking cases are related to tooth abscesses, tumors or other problems," says John Madigan, DVM, DACVIM, of the University of California, Davis. "These do occur, but by and large the problem is caused by changes in the way the trigeminal nerve functions."

Knowing this means that researchers are one step closer to finding more effective treatments to ease, or even to stop, the neuropathic pain that leads to what is now called "trigeminal-mediated headshaking." Researchers in California and in England are both working on different treatment approaches that are already

> offering at least some horses relief from this maddening condition.

## **PROMISING** RESEARCH **FINDINGS POINT**

AUTUMN 2019

shaking in horses was once thought to be similar to a human condition called trigeminal neuralgia (also called tic douloureux), which is pain stemming from the trigeminal nerve. However, Madigan and the UC Davis group found many

#### **NEURAL ANATOMY**

A horse has two trigeminal nerves, one on each side of his head, which carry sensory information back to the brain. Each one divides into three main branches: the ophthalmic nerve, which covers the region around the eye; the maxillary nerve, which extends down over the muzzle; and the mandibular nerve, which runs down over the lower jaw.

differences between the equine and human disorders. In people, the nerve is oversensitive, firing in response to minor stimuli so that even mild contact, such as a brush on the cheek, can cause a jolt of pain. People describe sensations ranging from severe stabbing pain to constant itching, burning, tingling or aching. Horses with persistent headshaking have signs of neuropathic pain, burning, tingling, itching-like sensations, but the triggers are different.

Researchers over the past few years have sought to identify the role of the trigeminal nerve in equine headshaking. In a 2013 study from UC Davis, veterinary neurologist Monica Aleman, DVM, PhD, put 12 mature geldings under anesthesia and placed electrodes on their faces to measure the reactions of their sensory nerves. Six of geldings had idiopathic headshaking and six were non-headshaking "control" geldings. The researchers found that when electrical stimulation was applied to the gums behind the upper canine teeth of the study horses, the nerves of the headshakers fired at a much lower threshold than did those in the control group. This was the first proof that the trigeminal nerve was functioning differently in headshaking horses.

In the same study, the structures of the trigeminal nerves were also analyzed using detailed histopathology, and no changes in the nerve were observed. This suggests that headshaking is functional and could then be reversible, which explains the off-and-on signs often seen in horses with headshaking, says Madigan.

In people, trigeminal neuralgia is caused by physical damage to the myelin sheath, the outer surface of the nerve cell. Aleman in 2013 published detailed histopathology of the trigeminal nerve of six horses with headshaking and confirmed there was no abnormal activity of the nerve and found no damage to its myelin sheath or other physical changes.

The group in England repeated these studies and reached the same conclusion. "I worked with a human pathologist who did a lot of work in similar conditions in people," Roberts says. "We looked at the nerve from front to back in normal horses and compared them to headshaking horses, and the nerve is completely normal in the headshaking horses. So, what you are looking at is a nerve that is structurally normal but functionally abnormal. And that's very encouraging."

Physical damage to the nerve would have been difficult, if not impossible, to treat, explains Roberts. "The fact that the nerve is only functionally abnormal suggests that somehow a switch has been flicked to make it work badly, and maybe we can flick that switch back," she says. "What we don't know is what the switch is and how it got flicked in the first place."

These findings about the hypersensitivity of the trigeminal nerve are opening new avenues of research toward potential treatment options. "What we are trying to do is make the nerve behave as normally as we can," says Madigan. "So we are looking to identify specific abnormalities in the pathways that regulate the change in threshold for firing the nerve." Once researchers understand why the nerve misfires, it is hoped, they will be able to find a way to fix the headshaking at its source. So far, the following three areas of research have produced the most promising results.



# POTENTIAL THERAPY: MAGNESIUM SUPPLEMENTS

Madigan and other researchers in the Equine and Comparative Neurology Research Group (ECNRG) at UC, Davis have been investigating the role of nutrition in headshaking. Specifically, they have been looking into how varying blood levels of electrolytes—ionized minerals that play a role in many functions throughout the body—might affect neural function.

For a study published in the journal *Animals* in June 2018, the UC Davis researchers looked into the effects of temporarily altering a horse's blood pH and composition by administering intravenous fluids with varying levels of electrolytes. In horses who received a test solution that increased blood pH, headshaking behavior was reduced by 58 percent compared to controls. The

effects, however, lasted only about an hour because the body's regulatory mechanisms tend to "normalize" its blood levels of salts and minerals.

Nevertheless, says Madigan, "this study showed that altering a horse's chemical balance, such as might be achieved with diet, can make the nerve behave more normally."

This study also yielded a surprise finding: All six of the headshaking horses had low levels of ionized magnesium in their blood before the trial started. "We were not specifically looking at ionized magnesium at this point," says UC Davis equine nutritionist Shara Sheldon, PhD, who led the study. "The hay that the horses were being fed was tested and should have provided the 13 mg/kg requirement for magnesium, so we didn't think it would be an issue."

Sheldon specifies that, "our [study] horses had normal total magnesium

but their ionized magnesium was low. The ionized magnesium test is relatively new. Before, there was only a total magnesium test. We thought ionized magnesium was important because that is the active form in the blood that can work on nerves firing."

To investigate further, in a followup study published in January 2019, the research team administered intravenous magnesium sulfate to six horses with trigeminal-mediated headshaking. Several blood electrolyte levels changed in response to the treatment and headshaking behavior was reduced by 29 percent, compared to horses that were not treated.

Again, the effects of intravenous treatments were relatively short-lived, but now it was clear that altering a horse's levels of ionized magnesium can reduce headshaking behavior. Which led researchers to ask if it would be possible to produce the same effect

50 EQUUS 499

### **VOICES OF EXPERIENCE**

Managing a horse with trigeminal-mediated headshaking can be frustrating. The problem occurs in horses of virtually all breeds, disciplines, ages and genders.

Researchers have determined that an oversensitivity of the trigeminal nerve is the likely cause of neuropathic pain in an affected horse's face, triggering the evasive behavior. But they still don't understand why the nerve misfires. Until more is learned about this dysfunction—and, of course ways to prevent it—there will be no "cure" for this type of headshaking.

In the meantime, it's important to determine whether something else is causing the behavior. If a horse starts

headshaking, ask your veterinarian to examine him for tooth abscesses, guttural pouch infections, tumors or other issues that might cause pain or discomfort in or around the head. It's also a good idea to check the horse's tack for fit. In cases like these, eliminating the underlying problem is likely to stop the behavior.

When other potential causes have been ruled out, however, headshaking is considered neuropathic and associated with an overly reactive trigeminal nerve. At this point, it's helpful to begin a journal of the headshaking incidents you observe. This can help you to identify patterns in the behavior and perhaps to pinpoint the triggers that affect your horse.

The specific triggers that cause neuropathic headshaking vary among affected horses. More than half are "photic

headshakers," meaning that the behavior occurs when they are exposed to bright sunlight. Photic headshakers are more likely to be worse in the spring and summer months; the attacks may ease or stop entirely on overcast or rainy days or during the fall and winter. About 50 percent of affected horses show the behavior only during exercise, with or without a rider. Other potential triggers can include exposure to the wind as well as loud noises or smells.

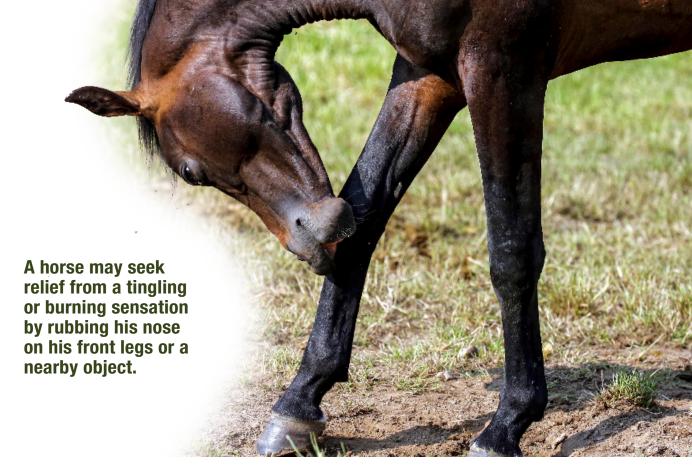
Therein lies a problem: A number of treatments and management strategies can help to alleviate the signs of headshaking, but because the triggers can vary from horse to horse, there is no one approach that is effective for all cases. It generally takes some trial and error to find a strategy that might work with each affected horse. Here are

some of the approaches owners have tried:

- Management changes. If headshaking is most pronounced when the horse is outside in direct sunlight, the best option might be to keep him inside during the days and turn him out only at night. A fly mask that blocks high levels of ultraviolet radiation might also be helpful.
- Physical coverings, such as nose nets, mesh sheets for a horse's muzzle or devices that dangle over a horse's nostrils can help to reduce headshaking in some horses who are triggered by exercise. How they help isn't clear, but in one trial with 36 owners, 75 percent reported at least some improvement with different types of nets.



- **Dietary supplements** including melatonin, a hormone that is involved in regulating the horse's sleep-wake cycles, may help horses who are seasonally affected by tricking their bodies into behaving as if it is always wintertime. Supplementing with magnesium, an electrolyte involved in nerve function, has been proven to be helpful. However if you want to try magnesium, your veterinarian will need to perform blood tests periodically to monitor your horse's blood levels of the mineral to guard against overdoses.
- **Medications** including cyproheptadine (an antihistamine), carbamazepine (an anti-seizure drug), hydroxyzine (an antihistamine) and phenobarbital (barbiturate) have reduced headshaking in some horses; however, they all have potentially serious side effects.



by altering a horse's diet alone.

In a third study, published in the spring 2019, the research team used 12 horses—six headshakers and six normal controls—and divided them into three groups to receive hay along with one of three dietary combinations: pelleted grain feed, pelleted grain with magnesium, or pelleted grain with magnesium combined with the mineral boron.

"With the grain-hay combination plus magnesium supplementation, there was a 52 percent reduction in headshaking behavior across all headshaking horses," reports Sheldon. "With the grain combination plus magnesium and boron, there was a 64 percent reduction in the behavior across all headshaking horses." The long-term effects of the dietary change have not yet been evaluated. Nevertheless, she says, "This is the first solid indication that diet may be involved in the trigeminal nerve firing in horses with headshaking. It is a new insight."

Anecdotal reports from some owners had previously suggested the magnesium supplements might be helpful for some headshaking horses. While this isn't a "cure-all," Sheldon says, "it is one more thing that you can try that has been scientifically tested. It depends on the horse and what they are being fed and what their ionized magnesium levels are."

For horse owners interested in trying this approach, Sheldon says, "it would be helpful to have your veterinarian run the test for ionized magnesium, and then add magnesium and boron and see if it helps."

Of course, it's always a good idea to consult your veterinarian before making any changes in your horse's diet. "Magnesium can cause diarrheal effects, so it would be best to go slow and see if this happens," explains Sheldon. "In our study, we did not see diarrhea in control or headshaking horses with the magnesium or magnesium-boron supplement."

# POTENTIAL TREATMENT: **ELECTRICAL STIMULATION**

Roberts and other British researchers have been exploring different ways of "resetting" the trigeminal nerve through electrical stimulation. One technology under investigation is called EquiPENS, based on PENS (percutaneous electrical nerve stimulation) neuromodulation therapy, which is used to treat neuropathic pain in people.

Roberts, along with other researchers from the University of Bristol's School of Veterinary Sciences as well as neurologists from Southmead Hospital in Bristol, England, published a study in 2016 about the use of EquiPENS in seven horses, following a similar protocol as is used to treat people. "Our first question was, was it safe for horses, and the second was, does it work," says Roberts.

52 EQUUS 499

For the procedure, the horse is sedated, and a small area on the face is anesthetized. Then, with ultrasound guidance, a disposable probe is inserted under the skin and pushed forward alongside the target nerve. Once the probe is in place, a low-voltage electric current is run through it in alternating frequencies, as is done in human treatments, for 25 minutes.

The treatment is then repeated on the other side of the horse's head. The neurologic pain may subside for hours or up to a week or so after the first treatment. If the treatment is repeated when signs return, the effects usually last longer—sometimes for months after a third or fourth treatment.

Roberts notes that electrical stimulation does not deliver pain relief to all human patients. "In people, you do a minimum of three procedures before you decide it's not going to work," she says. "So we thought we'd do at least three procedures in the horses and see what happens."

All seven of the study horses tolerated the treatments well, although three developed mild bruising at the site where the probe was inserted. The headshaking grew worse for the first few days in two of the horses, but ultimately six of the seven horses had a positive response to the first treatment. Median remission times were 3.8 days after the first treatment, 2.5 weeks after the second, and 15.5 weeks after the third. Two of the horses received a fourth treatment, which produced a remission of 20 weeks.

"We got five of the horses back to ridden work after their third procedure," says Roberts. "We're not claiming to have found a solution but we're barking up the right tree."

A second, larger clinical study of the procedure is currently underway at multiple clinics in the United Kingdom, Sweden and Denmark. So far, 168 horses have received a total of more than 530 treatments. "It's safe," Roberts reports. "Very, very low numbers are getting hematomas, and I had 10 occasions out of the 530 that were a little bit worse for a few days. Those all got better either on their own or with a steroid. I suspect that they had some nerve inflammation after we stimulated the nerve." Two horses refused to accept the treatment, even with sedation.

As for results, 53 percent of the study horses had remission of headshaking after initial treatment. "About 50 percent failed, which is pretty depressing except that that's by far the best results anyone has had for any procedure," says Roberts. "The next question is how long will it work. Some [horses] go back to work for a few weeks. Some go back to work for a few years. The longest followup I had is from 2014 because that's when we started. So, I've got some horses in work for four years after their procedures." A few of the horses who began headshaking again received a fourth procedure—in this group, the remission rate was 80 percent. "You would actually expect to get 100 percent on the fourth one because you are treating a population that responded in the past," Roberts says. "It's the same in people—it doesn't always keep on working."

The specific technology Roberts used is not currently available for use in the United States. "The equipment we use is not currently FDA-approved, but it's in the process," she says.

#### POTENTIAL TREATMENT: **ELECTROACUPUNCTURE**

Inspired by the successes shown by the EquiPENS, Sue Devereux, BVSc, MRCVS, who owns a practice called Equine Acupuncture & Chiropractic Referrals in Salisbury, Wiltshire, England, undertook a study to see if she could get similar results with a slightly different method for stimulating the trigeminal nerve with electricity: electroacupuncture.

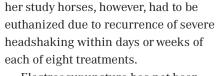
For this procedure, with the horse lightly sedated, two Chinese-style acupuncture needles are inserted, one under the target nerve and the other into the brachiocephalic muscle at the base of the neck on the same side. An electrical source is attached to each needle, and once the correct intensity is established, the stimulation continues for 25 minutes. The procedure is repeated on the opposite side of the head. As with the EquiPENS, the treatment is repeated as signs return.

For her study, published in 2017. Devereux treated six horses four warmbloods and two ponieswith this protocol. All six tolerated the treatment well, and all showed some improvement, as reported by their owners. The headshaking diminished in all six after the first treatment, for a period ranging from four to 13 days; although one horse showed an exacerbation of the clinical signs for 2 days. Treatments

returned, and the duration of the remissions increased. Two of the horses reached complete remission. defined as six months without recurrence, after a fifth treatment and one after a sixth.

Overall, Devereux reports, her results have been mixed: "Of the six horses used for my research which started in April 2015, two needed a single treatment in spring of 2016 and have not needed any further treatment since—that is, they remained asymptomatic for 2017, 2018 and 2019 with no further treatments. One horse continues to need a single treatment at the beginning of the headshaking season each year, and she remains asymptomatic for the rest of the year," she says. One of

With luck, research efforts will soon bring relief for horses with trigeminal-mediated headshaking.



Electroacupuncture has not been attempted in as many horses as EquiPENS has, but Devereux says, "in my hands it has worked for some horses really well and others not at all. Overall, 50% of my patients have shown a good response to the treatment with long periods of remission.

Devereux does not recommend electroacupuncture as a primary treatment for headshaking. "I think that nose nets and masks should be the first line of treatment," she says. "In my trial I insisted that the horses wear these, and I recommend that they continue to be worn whilst undergoing EA treatment."

Electroacupuncture is less invasive than the EquiPENS procedure, and the equipment is more widely available. A trained practitioner can administer the treatment on the farm. To date, no one has done a study to compare the efficacy of electroacupuncture versus EquiPENS.

Regarding either approach, Madigan says, "It's not a permanent cure, but it may be worth trying because it does give some horses some relief."

cure for trigeminal-mediated **A**headshaking is still on the horizon, but research results like these provide hope. "I am very confident we are going to have a more specific ideas of how to treat headshaking in the future," Madigan says. "We need more people doing basic research, more people trying novel therapies, and more people exploring medications." With luck, those efforts will soon bring relief to horses for whom headshaking isn't just an occasional way to deal with flies.

