Editors' Note: WriteClick comments regarding Drs. Hawley and Weiner's August 2nd article consider additional pathophysiologic mechanisms that may play a role in peripheral trauma inciting focal dystonia. Dr. Butler supports a case for aberrant thalamic plasticity being involved and suggests further PET studies to evaluate this hypothesis. Dr. Van Gerpen cites several examples of patients with focal dystonia presenting after peripheral trauma or surgery, all of whom later proved to have a *THAP1* gene mutation, and questions whether the peripheral event may have provoked the presentations in susceptible patients. The authors respond to Dr. Van Gerpen that a correlation between peripheral trauma and any dystonia-associated genetic disorder is still unknown.

Megan Alcauskas, MD, and Robert C. Griggs, MD

PSYCHOGENIC DYSTONIA AND PERIPHERAL TRAUMA

Jay A. Van Gerpen, Rochester, MN: I read the article by Drs. Hawley and Weiner, who frequently equate fixed, painful postures that abruptly occur after peripheral trauma as a sine qua non of peripheral-induced dystonia.¹ In table 2,¹ they indicate that these are not universal features of this condition.

Therefore, I ask the authors to consider the following case: A man with a left L5/S1 radiculopathy gradually developed persistent "tightness, like a bow string" in his left gastrocnemius ambulating only with eventual hypertrophy of this muscle. In addition, when this patient's father was in his late adolescence, he gradually developed stable, nonfixed "torticollis" after a "whiplash" injury. The patient's paternal aunt had the insidious onset of persistent "neck shaking" after a thyroidectomy. Each of these individuals has a c.446 T greater than C sequence variant in their *THAP1* gene.²

Do the authors believe that there is "ample evidence" to support a link between *THAP1* mutations and dystonia^{3,4}? If so, what would be the most likely explanation for these patients developing symptoms and signs consistent with organic dystonia in areas of their body associated with trauma?

Tracy Butler, New York: Drs. Hawley and Weiner¹ note that there is little evidence of a pathophysiologic mechanism for peripheral trauma inducing or provoking focal dystonia. One mechanism that could be considered involves aberrant thalamic plasticity.

In a study of patients with peripheral limb or nerve injury, PET using [¹¹C]PK11195—a ligand of the translocator protein expressed by activated microglia—revealed long-lasting microglial activation in the thalamus contralateral to injury.⁵ The degree of microglial activation in patients with peripheral injury is comparable to that seen in CNS disorders such as epilepsy.⁶ Microglia cells, in addition to their role as the brain's resident immune cells, are increasingly understood to be key mediators of synaptic plasticity and remodeling.⁷

Given that thalamic injury is well known to cause focal dystonia,⁸ it is conceivable that an abnormally intense, widespread or otherwise dysregulated thalamic microglial response to peripheral injury may lead to focal dystonia in some patients, and other problems such as pain.

Future studies using [¹¹C]PK11195 PET can evaluate this hypothesis. Additionally, it is important to point out that "nonorganic" is not a synonym for "psychogenic"; psychogenic disorders are also brain disorders, and elucidating their neural basis is critical to optimizing treatment.

Author Response: Jason S. Hawley, Washington, DC; William J. Weiner, Baltimore: We appreciate Dr. Van Gerpen's interest in our article. We do not dispute that *THAP1* mutations are associated with dystonia; however, Dr. Van Gerpen suggests that focal trauma or surgery has provoked dystonia in his patients with a *THAP1* mutation. We would question this likely chance association and the causality of peripheral trauma inciting the dystonia. In our review, we explored the "mechanisms" for peripheral trauma provoking dystonia, and we simply showed that the evidence to date for a mechanism for trauma causing dystonia is nonexistent. In most case reports and case series reporting traumatically induced "dystonia," the patients do not have a family history of dystonia or a known genetic disorder associated

with dystonia. Based on our review, we would only counter that it is currently unknown as to an association for peripheral trauma in an individual with a genetic disorder known to cause dystonia.

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