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**BHBI-Funded Research\*****Abstract 10****Complex Regional Pain Syndrome (CRPS I):  
A Systemic Disease of the Autonomic Nervous System****Kamal Chemali, MD;<sup>1</sup> Robert Shields, MD;<sup>1</sup> Lan Zhou, MD, PhD;<sup>1</sup>  
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Our study aims to assess the extent of systemic autonomic dysfunction in the autonomic pain syndrome known as complex regional pain syndrome type I (CRPS I). This condition, formerly known as reflex sympathetic dystrophy (RSD), is notorious for its pathophysiological complexity. On one hand, it occurs in only certain people after a minor trauma or insignificant trigger and behaves like a focalized pain syndrome to one limb with prominent local autonomic manifestations, such as edema, vasomotor changes, trophic changes, pain, and allodynia. A more recent theory speaks about somatic-autonomic coupling as an explanation for the above, and the most recent consensus seems to be that CRPS I is a disease of the central nervous system that manifests peripherally. Through this study we would like to investigate further the possibility that the autonomic nervous system involvement in this disorder is generalized rather than localized to the painful limb and, in a more general way, to try to open new windows on the role of the autonomic nervous system in generating and maintaining pain.

The study is a bicenter research project at Cleveland Clinic and University Hospitals of Cleveland that will include 20 patients with CRPS I. The control group will consist of 10 patients with small fiber neuropathy (a neuropathic pain condi-

tion similar in certain aspects to CRPS I), 10 patients with limb pain due to osteoarthritis of the knee (a nonneuropathic pain), and 10 healthy volunteers. All subject will undergo comprehensive autonomic testing, skin biopsies, pupillometry, and Doppler flowmetry to assess the autonomic nervous system at various levels of the body. Results will be compared between the patients with CRPS I and the control group and subgroups.

To date, one patient has been enrolled, a 27-year-old female with CRPS I of the left foot following a traumatic injury. After consenting to the research protocol, the patient underwent a washout from all medications known to affect the autonomic nervous system for 5 half-lives prior to testing. She then underwent a series of tests of the autonomic nervous system and a skin biopsy. Preliminary data revealed the following:

1. Decreased cardiac response to deep breathing, suggesting a cardiovagal abnormality
2. Abnormal vasomotor sympathetic response characterized by postural tachycardia, consistent with the diagnosis of postural orthostatic tachycardia syndrome (POTS)
3. Abnormal quantitative sudomotor axon reflex test (QSART) results consistent with an underlying small fiber neuropathy
4. A 35% reduction of small fiber at the left distal leg (sympathetic) compared to the contralateral asymptomatic leg
5. Abnormal pupillary response to light in constriction parameters in the right eye, consistent with a parasympathetic pupillary abnormality.

These data, from a single patient, are consistent with our hypothesis that CRPS I is a generalized (systemic) disorder of the autonomic nervous system.

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\* BHBI = Bakken Heart-Brain Institute