Editors’ Note: Dr. Oaklander contends that in a recent article, “Bilateral somatosensory cortex disinhibition in complex regional pain syndrome type I (CRPS-I),” some contributory nerve and spinal cord effects were not recognized, specifically those from small-fiber nerve injury and contralateral input. The authors, Lenz et al., respond that unrecognized small-fiber neuropathy was likely not a confounding factor in their study as both small- and large-nerve fiber dysfunction were measured via quantitative sensory testing and there was no significant difference between the control and CRPS groups. They agree that the mirror effects described by Dr. Oaklander may partially explain their findings of bilateral somatosensory cortex disinhibition in CRPS.

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BILATERAL SOMATOSENSORY CORTEX DISINHIBITION IN COMPLEX REGIONAL PAIN SYNDROME TYPE I

Anne Louise Oaklander, Boston: The recent report of bilateral cortical disinhibition in complex regional pain syndrome type I (CRPS-I) neglects likely contributory nerve and spinal cord effects. The authors claim to have excluded patients with nerve lesions from among CRPS-I subjects by examination but do not specify how, precluding independent verification. They additionally rely on nerve conduction study to exclude nerve injury but this is insensitive to the small-fiber axonopathy identified in CRPS-I patients. Furthermore, myriad data demonstrate peripheral cross-midline coupling of small-fiber–mediated functions (e.g., in bones and kidney) likely to build and maintain body symmetry. Thus, unilateral injuries often subtly affect contralateral mirror-image tissues via damaged peripheral motor, sensory, and autonomic nerve fibers. Mirror effects are particularly associated with neuropathic pain conditions including CRPS-I, regardless of whether or not patients have contralateral symptoms. For instance, patients with unilateral postherpetic neuralgia after unilateral zoster had 47% fewer PGP9.5-immunoreactive axons in asymptomatic mirror-contralesional skin, a finding reproduced in some unilateral injury rodent models of CRPS-I. The focality of mirror changes excludes bloodborne signaling and their localization implicates nerves and spinal cord, perhaps involving the roughly half of dorsal horn neurons with bilateral, symmetric, receptive fields. Bilateral supraspinal responses to unilateral trauma in CRPS-I and elsewhere are best considered in conjunction with these findings.

Author Response: M. Lenz, E. Krumova, O. Hoefkken, P. Stude, S. Lissek, P. Schwenkreis, A. Reinersmann, J. Frettloeh, H. Richter, M. Tegenthoff, C. Maier, Bochum, Germany: We appreciate the comments of Dr. Oaklander. Experienced neurologists excluded nerve lesions using clinical examination, ENG, and SEP data. Additionally, quantitative sensory testing (QST), assessing small and large nerve fibers, revealed an isolated small-fiber dysfunction in only 17% of the CRPS patients, and in 34% combined small- and large-fiber dysfunction. A total of 18% of the control patients presented isolated small-fiber dysfunction and 18% combined small- and large-fiber dysfunction. However, QST cannot differentiate between peripheral neuropathy and dysfunction due to central plasticity, a potential finding in CRPS, as previously shown. Unrecognized small-fiber neuropathy is probably not an important confounding factor in our study, because the sensory loss assessed in QST was comparable in both groups. Nevertheless, even if small-fiber neuropathy was present in some subjects, to our knowledge, SEP are unaffected by small-fiber axonopathy. Consequently, we neither would expect paired-pulse SEP to be affected. The mirror effects addressed by Dr. Oaklander may partially explain our findings. Bilateral cortical changes in the motor system were found only in CRPS, while in other neuropathic pain conditions cortical excitability is affected unilaterally. In our study, we described a similar phenomenon for the somatosensory cortex with bilateral disinhibition only in CRPS.

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Bilateral Somatosensory Cortex Disinhibition in Complex Regional Pain Syndrome
Type I
Anne Louise Oaklander, M. Lenz, E. Krumova, et al.
Neurology 2012;78;606-607
DOI 10.1212/WNL.0b013e31824ab936

This information is current as of February 20, 2012