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.

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

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)¹ 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.² 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.³ 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 asymptom-

atic mirror-contralateral skin,⁴ a finding reproduced in some unilateral injury rodent models of CRPS-I.⁵ The focality of mirror changes excludes bloodborne signaling and their localization implicates nerves and spinal cord,⁶ 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. Hoeffken, P. Stude, S. Lissek, P. Schwenkreis, A. Reinersmann, J. Frettlöeh, 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,⁷ 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.⁸ 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.^{9–11} In our study, we described a similar phenomenon for the somatosensory cortex with bilateral disinhibition only in CRPS.

Copyright © 2012 by AAN Enterprises, Inc.

1. Lenz M, Höffken O, Stude P, et al. Bilateral somatosensory cortex disinhibition in complex regional pain syndrome type I. *Neurology* 2011;77:1096–1101.
2. Oaklander AL, Fields HL. Is reflex sympathetic dystrophy/complex regional pain syndrome type I a small-fiber neuropathy? *Ann Neurol* 2009;65:629–638.
3. Koltzenburg M, Wall PD, McMahon SB. Does the right side know what the left is doing? *Trends Neurosci* 1999;22:122–127.
4. Oaklander AL, Romans K, Horasek S, et al. Unilateral post-herpetic neuralgia is associated with bilateral sensory neuron damage. *Ann Neurol* 1998;44:789–795.
5. Oaklander AL, Brown JM. Unilateral nerve injury produces bilateral loss of distal innervation. *Ann Neurol* 2004;55:639–644.
6. Kolston J, Lisney SJ, Mulholland MN, Passant CD. Transneuronal effects triggered by saphenous nerve injury on one side of a rat are restricted to neurones of the contralateral, homologous nerve. *Neurosci Lett* 1991;130:187–189.
7. Rolke R, Baron R, Maier C, et al. Quantitative sensory testing in the German Research Network on Neuropathic Pain (DFNS): standardized protocol and reference values [erratum in 2006;125:197]. *Pain* 2006;123:231–243.
8. Maihofner C, Handwerker HO, Neundorfer B, Birklein F. Cortical reorganization during recovery from complex regional pain syndrome. *Neurology* 2004;63:693–701.
9. Maihofner C, Baron R, DeCol R, et al. The motor system shows adaptive changes in complex regional pain syndrome. *Brain* 2007;130:2671–2687.
10. Schwenkreis P, Janssen F, Rommel O, et al. Bilateral motor cortex disinhibition in complex regional pain syndrome (CRPS) type I of the hand. *Neurology* 2003;61:515–519.
11. Schwenkreis P, Scherens A, Ronnau AK, Hoffken O, Tegenthoff M, Maier C. Cortical disinhibition occurs in chronic neuropathic, but not in chronic nociceptive pain. *BMC Neurosci* 2010;11:73.

Neurology®

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

Updated Information & Services

including high resolution figures, can be found at:
<http://n.neurology.org/content/78/8/606.full>

References

This article cites 11 articles, 3 of which you can access for free at:
<http://n.neurology.org/content/78/8/606.full#ref-list-1>

Permissions & Licensing

Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
http://www.neurology.org/about/about_the_journal#permissions

Reprints

Information about ordering reprints can be found online:
<http://n.neurology.org/subscribers/advertise>

Neurology® is the official journal of the American Academy of Neurology. Published continuously since 1951, it is now a weekly with 48 issues per year. Copyright © 2012 by AAN Enterprises, Inc.. All rights reserved. Print ISSN: 0028-3878. Online ISSN: 1526-632X.