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Enhancing the Neurologist's Role in Complex Regional Pain Syndrome

G. Lorimer Moseley, PhD,[1,2] Michael Thacker, PhD,[3] and Herta Flor, PhD[4]

We applaud Oaklander and Fields' comprehensive review[1] of the literature concerning the role of small-fiber neuropathy in complex regional pain syndrome (CRPS). The review builds on a body of elegant work by Oaklander's group and others, and presents a compelling argument that many clinical features of CRPS are consistent with persistent dysfunction of C and Aδ fibers. The review culminates in treatment recommendations, and states that rehabilitation and physical therapy are critical. Unfortunately, what constitutes "rehabilitation" or "physical therapy" is not considered. This is like stating that medications are critical but not considering which ones. Oaklander and Fields[1] are by no means the first to make this oversight; guidelines the world over recommend "physical therapy" or "rehabilitation" for CRPS but make no attempt to sort the wheat from the chaff. This issue is of utmost importance because many and varied treatments for CRPS are undertaken under the banner of "rehabilitation," but most of them are probably not helpful. It is not that empirical data do not exist (see Daly and Bialocerkowski[2] for review); for example, several randomized, controlled trials show that graded motor imagery reduces pain and disability in chronic CRPS.[2] The number needed to treat for a 50% decrease in pain and a 4-point decline on a 10-point scale of disability is about 4,[3] which compares favorably with any other treatment for chronic CRPS, including spinal cord stimulators, for which Oaklander and Fields[1] state there is documented efficacy and they are indicated for CRPS. Oaklander and Fields[1] go on to note the absence of data for pharmacological treatment of CRPS and turn to the results of randomized, controlled trials for other neuralgias. Randomized, controlled trials also show that cognitive-behavioral programs reduce pain and disability in other neuralgias (see Turk[4] for review), and that sensory discrimination training reduces pain in chronic phantom limb pain.[5] Sensory discrimination training has already been extended to patients with chronic CRPS, where preliminary data appear supportive.[6] Oaklander and Fields[1] compiled a rigorous and discerning review of the role of small-fiber pathology in CRPS, which provided a strong basis for their proposal that neurologists should return to a central role in CRPS care. We humbly suggest that this role would be greatly enhanced, and most importantly, patient outcomes would be improved, if the same rigor and discernment were applied to evaluating evidence-based treatment options that fall under the broad category of "rehabilitation."

[1]Prince of Wales Medical Research Institute, [2]Faculty of Medicine, University of New South Wales, Sydney, Australia, [3]Academic Department of Physiotherapy and Wolfson Centre for Age Related Diseases, King's College London, London, United Kingdom, and [4]Department of Clinical and Cognitive Neuroscience, University of Heidelberg, Heidelburg, Germany

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Reply to: SNCA Variants Are Associated With Increased Risk of Multiple System Atrophy

Owen A. Ross, PhD,[1] Carles Vilariño-Güell, PhD,[1] Zbigniew K. Wszolek, MD,[2] Matthew J. Farrer, PhD,[1] and Dennis W. Dickson, MD[1]

Parkinson disease (PD) and multiple system atrophy (MSA) are disorders distinguished by pathologic accumulation of α-synuclein in neurons and glia. A common variation in the gene for α-synuclein (*SNCA*) is known to be associated with PD, but its role in MSA is unclear. Recently, Scholz et al reported a single-nucleotide polymorphism (SNP) (rs111931074) in the 3′ region of *SNCA* , originally identified in a genome-wide association study in PD, that increased the risk for MSA by nearly 6-fold in a subset of pathologically confirmed cases.[1] Our studies assessing the influence of *SNCA* variation in PD have examined the frequency of this SNP in a PD patient-control series from Ireland, Serbia, and Germany.[2,3] Although significant association was observed across the *SNCA* locus, rs111931074 was not associated with increased risk of PD, with a very low frequency (<1%) of minor allele homozygotes found in both patients and controls.

The association observed by Scholz et al of *SNCA* rs111931074 with MSA was most pronounced under a recessive model, especially in pathologically confirmed MSA. A frequency of the TT minor allele homozygote was 2% in a clinical series (n = 308) and 6% in a pathological series (n = 92) of MSA patients, compared with 0.6% in controls (n = 3,889). The effect of this variant appears to be most pronounced in pathologically confirmed MSA, with a dilution of the signal in clinical samples. The high diagnostic error in MSA may be the reason