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LETTER TO THE EDITOR

Response: A Systematic Evaluation of Burst Spinal Cord Stimulation for Chronic Back and Limb Pain

To the Editor:

With great interest we read the manuscript by Hou and colleagues, *"A Systematic Evaluation of Burst Spinal Cord Stimulation for Chronic Back and Limb Pain"* (1). The authors are to be congratulated on attempting to clarify whether there is strong evidence to use burst spinal cord stimulation. This is a valuable approach that should be welcomed, and more studies like this should be encouraged, as many novel stimulation designs are reaching the market: HF 10K, alternative burst modalities, High Density Stimulation, and so forth. However, there are three important methodological issues related to this paper.

First, and most importantly, the question can be raised if we can directly apply the American Academy of Neurology (AAN) guidelines for analyzing the evidence of neuromodulation trials, irrespective of whether this disorder is typically treated by neurologists, such as Parkinson's disease, or by anesthesiologists, such as chronic pain. In the setting of treatments for neurological disorders, the AAN guidelines have primarily been developed for medication trials; the criteria for classification have, therefore, been adapted to this. In invasive neuromodulation, effect sizes tend to be larger, and the treatment usually applied to medically intractable patients. Patients can effectively be used as their own control when (1) the study design has a sufficiently large washout period and (2) the study design includes a placebo control for the same patients. These differences might require a set of criteria or methodology for collecting evidence which is different from those created for typical medication trials. From a neuromodulation point of view it is strange to see that the authors classified two placebo controlled studies (2,3) as class IV, that is, the lowest possible kind of evidence, whereas they are the first placebo controlled studies ever performed in the history of neuromodulation, and the studies compared different stimulation designs and placebo, with the patients as their own controls. From a neuromodulation point of view, this looks like a rigid and scientifically sound way of analyzing trials. It is of course correct that the studies had a short follow up (from two weeks to one year) and low numbers of patients ($N = 12–48$), but the question is how to do better? Adding larger number of patients will give a higher reliability and validity as will a longer period of follow-up. However, the major point is whether the methodology used by the authors is ideal. Should we use guidelines from the ANN for neuromodulation trials, or should we, the neuromodulation community, develop our own guidelines for classifying evidence which can then be translated into useful guidelines for clinicians? If we are to continue to use the AAN guidelines for all the new and existing stimulation designs, we will always have to admit that there is no evidence from a AAN scientific point of view, but this negative result might be only the consequence of applying a nonadapted methodology.

Second, the question can be asked what the scientific value is of a systematic review of a treatment that is not even FDA approved yet. By definition, there will not be a completed noninferiority study, because if so, it would most likely be FDA approved. So what is the scientific benefit of a systematic review, before it is needed or required. And this leads to a very important third question.

Early systematic reviews on new therapies might undermine innovation. In Thomas Kuhn's seminal book on scientific innovation, "The Structure of Scientific Revolutions" (4), it is explained that all innovations go through three stages: first the scientific innovation is adopted by some early followers who embrace the innovation for its "beauty," as there is no available proof yet. Subsequently these early followers will perform studies that prove or disprove the value of the innovation, followed by acceptance or non-acceptance of the innovation through further confirmation/rejection by larger studies. Similar phases can be recognized in medical research, inclusive of neuromodulation research. All new therapies will start with pilot studies, case series and the like that help in the design of the larger prospective trial work with a higher evidence level. We therefore do not see the advantage of a systematic evidence review of a new therapy that is still in its early phase. It would have been scientifically of more interest to wait for the published data of the phase three multicenter study which, in preliminary form, has been presented in at the North American Neuromodulation Society (NANS) Annual Meeting in December 2015, but is yet to be published. Therefore, this systematic evaluation may be misinterpreted by the neuromodulation community at large and undermine the development and growth of all novel neuromodulation treatments, whether HF10K, high density stimulation or alternative burst designs. What the neuromodulation

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community needs is innovation, and therefore guidelines in how to come up with the best way of providing the data and evidence that novel neuromodulation designs/techniques are beneficial or not. We, therefore, plead to the International Neuromodulation Society to set up a committee with the task to develop mechanisms analogous to those of the AAN, but that are better adapted to the field of neuromodulation, so that the guidelines are more reflective of the specific characteristics of neuromodulation research.

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REFERENCES

1. Hou S, Kemp K, Grabois M. A systematic evaluation of burst spinal cord stimulation for chronic back and limb pain. *Neuromodulation* 2016;19:398–405.
2. De Ridder D, Plazier M, Kamerling N, Menovsky T, Vanneste S. Burst spinal cord stimulation for limb and back pain. *World Neurosurg* 2013;80:642–649.
3. Schu S, Slotty PJ, Bara G, von Knop M, Edgar D, Vesper J. A prospective, randomised, double-blind, placebo-controlled study to examine the effectiveness of burst spinal cord stimulation patterns for the treatment of failed back surgery syndrome. *Neuromodulation* 2014;17:443–450.
4. Kuhn T. *The structure of scientific revolutions*, 3rd ed. London: University of Chicago Press,1962.

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