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Is spinal disinhibition a dominant mechanism in neuropathic pain?

Aims: Spinal disinhibition is one potential mechanism, which could explain the conundrum of painful symptoms in people otherwise characterized by loss of peripheral sensation. The present study aimed to explore whether impaired rate-dependent depression of the Hoffman reflex, a putative biomarker of spinal disinhibition, is associated with distinct phenotypes in people with painful diabetic neuropathy.
Methods: The study included a total of 93 participants with diabetic neuropathy in an observational, cross-sectional design. The participants underwent detailed clinical phenotyping including five distinct questionnaires, corneal confocal microscopy, and quantitative sensory testing in addition to testing of Hoffmann reflex rate-dependent depression. The latter was evaluated by tibial nerve stimulation using 1-ms square wave pulses delivered using surface electrodes located in the popliteal fossa. The H-wave responses were recorded in trains of ten stimuli delivered at 1-3 Hz, and the Hoffmann reflex rate-dependent depression was calculated as the mean value of stimuli 2-5 and expressed as the percentage of the first recorded H-reflex amplitude in the train.
Results: The study found that people with painful diabetic peripheral neuropathy had impaired Hoffmann reflex rate-dependent depression at 1, 2 and 3 Hz compared to people with painless diabetic peripheral neuropathy. In addition, the painful group exhibited an overall profile characterized by loss of function on quantitative sensory testing, while a cluster analysis performed within the same group revealed an association between greater spinal disinhibition and greater mechanical pain sensitivity, relative heat hyperalgesia and higher ratings of spontaneous burning pain.
Conclusion: Overall, the present study provides evidence that spinal disinhibition might be an important mechanism in the pathophysiology of some phenotypes of painful diabetic peripheral neuropathy.

Comments. The present study provides additional insight into the interplay between the peripheral and the central nervous system and the role of spinal disinhibition in the pathophysiology of painful diabetic peripheral neuropathy. This interplay is of particular importance when trying to understand the enigma that is painful diabetic peripheral neuropathy and is another step towards future personalized treatment regimens based on deep sensory profiling.
The study excels due to its mechanistic approach, deep sensory profiling and hypothesis-driven nature, and is an important proof-of-concept study for future studies to build upon. The limitations of the study include bias induced by neuropathic pain medication, potential selection bias due to the participant needing to have only mild/moderate neuropathy for the Hoffmann reflex rate-dependent depression to be detectable, and the cross-sectional nature of the study design.
To further investigate the impact of spinal disinhibition on the presence of painful symptoms in distinct phenotypes, future studies should also explore other peripheral and centrally mediated mechanisms and ultimately its therapeutic implications.

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