On the diagnosis of pain in Parkinson disease: a mechanism-based approach

Letter to Editor:

We read with interest the article entitled “Pain in the neurodegenerating brain: insights into pharmacotherapy for Alzheimer disease and Parkinson disease” from Timothy Lawn et al.[7] Their review summarized the current findings on pain processing as well as on pharmacotherapy of pain in both diseases. It further emphasizes the importance of mechanistic research for evidence-based pain medicine.

We would like to comment on the experimental findings and on the importance of a mechanism-based approach in Parkinson disease (PD) after the correct diagnosis of PDrelated pain has been made because a mechanism-based approach has been already validated.[14] Concerning experimental pain sensitivity, studies revealed increased pain sensitivity when tested in the medication defined off phase,[10,12] whereas converse observations were made in the on phase.[15] Increased pain sensitivity can be reversed by L-dopa or deep brain stimulation.[3–5]

This is an important point because the definition of PD-related pain relies in part on these observations. The distinction of PDrelated and PD-unrelated pain is crucial because PD-unrelated pains occur with high frequency from 20% to 60% in the elderly (and is considered to have higher intensity in one study).[8,14] Pain in the off phase and pain improvement by dopaminergic medication are 2 of the relevant factors related to pain along with pain onset at disease onset (or pain aggravation with disease progression), and pain during dyskinesia already described in our first proposal.[11] These factors were previously ascribed by Quinn et al. for the definition of PD-related pain, in the Non-Motor Symptoms Scale, and used in the recent validation study by Mylius et al.[2,14,16]

The last point is that a mechanism-based approach for pain in PD has already been suggested by Marques et al.[9] and validated by Mylius et al.[14] in an international validation study of the PD-Pain Classification System (PD-PCS) questionnaire. After the diagnosis of PD-related pain has been made on behalf of 1 of 4 factors mentioned above, it summarises all PDrelated pains under the respective pain mechanism (neuropathic, nociceptive, and nociplastic), allowing for a mechanism-

based therapeutic approach.[13,14] Nociplastic pain was included as a third descriptor for pains presenting also with neuropsychiatric symptoms due monoaminergic or dopaminergic depletion after the exclusion of neuropathic (by using the Douleur Neuropathique questionnaire[1]) and nociceptive pains.[6,14] The PD-PCS is a validated pain questionnaire for PD-related and PD-aggravated pains. It is one of the first questionnaires validated using a hierarchical algorithm to detect the respective pain mechanism as suggested by the International Association for the Study of Pain.[14]

We recently reviewed the literature with respect to mechanism based pain therapy in PD.[13] Optimizing the dopaminergic schedule should be the first step before using non dopaminergic drugs, physiotherapy, or invasive therapies. We agree with Timothy Lawn et al.,[7] that mechanism-based studies are lacking so far. Therefore, we suggest to examine the effects of dopaminergic and nondopaminergic drugs on the different pain mechanisms in forthcoming studies by using dedicated questionnaires addressing PD-related and PD-unrelated pains and the respective pain mechanisms.

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