What Is In A Name?

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Published in:
Movement Disorders

DOI (link to publication from Publisher):
10.1002/mds.29943

Publication date:
2024

Document Version
Publisher's PDF, also known as Version of record

Citation for published version (APA):
Ciampi de Andrade, D., Mylius, V., & Perez Lloret, S. (2024). What Is In A Name? *Movement Disorders*, *39*(9), 1651-1652. https://doi.org/10.1002/mds.29943

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We read with interest the OXYDOPA study by Brefel-Courbon et al,[1] where central pain in people with Parkinson's disease (PwP) was treated by prolonged-release oxycodone, increase in levodopa, or placebo. The authors should be complimented for conducting such a complex multicenter trial on a topic that needs urgent new data and that extended itself through times of coronavirus disease pandemics. Bravo.

Pain is among the most burdensome non-motor symptoms of Parkinson's disease (PD) and to date no effective evidence-based treatment exists for its control. Different pain types have different mechanisms of disease, which respond differently to therapeutic interventions. This means that clinicians should first assess the pain type PwP have and then proceed to a specific therapy.

To do that, three steps need to be completed. First, clinicians need to ascertain that pain is chronic (ie, being present most of the days for more than 3 months). Interestingly, several classification systems for pain in PD do not ascertain that pain is chronic. Second, since pain affects at least 20% of the general population, one needs to ascertain that chronic pain in PwP is related to PD. By ignoring this point, one risks misclassifying, for example, migraine, or previously existing fibromyalgia as PD-related pain. More than 20% of PwP have pains not related to the disease. Third, the classification should acknowledge general classification frameworks and previous knowledge generated by the field of PD and pain.[2]

The present study aimed at chronic pain in PwP, therefore, fulfilling the first step. However, it classified PD-related pain using a classification system that has not yet been validated. There was no reference to the relationship between patient's pain and PD. Therefore, the study sample may have included PwP with different pain mechanisms.

TABLE 1 *Mechanistic classification of chronic pain*

1. Nociceptive
Pain related to somatic tissue lesions, where activation of nociceptors leads to development and persistence of chronic pain (eg, shoulder pain in a person with Parkinson disease where tendinitis pain co-occurs with rigidity of the limb).
2. Neuropathic
Pain with neuropathic characteristics occurs in a body region where signs of sensory deficit (or allodynia in some cases) exist. Pain is in the region neuroanatomically related to the lesion site to the somatosensory system. Most instances of neuropathic pain reported in people with Parkinson's disease to date is peripheral and occurred in the same proportion (~7%) as found in the general population.
3. Nociplastic
Pain existing when central gain in nociceptive processing alone is the major driver of chronic pain. Lesions to the somatosensory nervous system or to somatic tissues either do not exist or cannot explain the pain. Current definitions of central parkinsonian pain fit this mechanistic descriptor. Different from neuropathic pain, that is specially localized to a body area where sensory deficit is detected, nociplastic pain in people with Parkinson's disease is frequently ill-localized, may be periabdominal or even diffuse, migrating from time to time. It frequently takes place in context of dopamine agonist withdraw syndrome or dopamine dysregulation syndrome, where pain coexists with intense dysphoria, motor restlessness/choreiform dyskinesia, anxiety, and autonomic activation.

What is more problematic is the use of "central neuropathic pain." Central neuropathic pain because of PD does not stand with any current classification of central neuropathic pain (see Table 1).[3] There is no doubt that the clinical phenotype described as being of central neuropathic pain exists in PwP, but it is rare.[4]

The authors also mixed the concept of "central neuropathic pain" with "central parkinsonian pain." The problematic definition of the pain type under study makes the results of this study difficult to apply to the clinical practice.

"Central parkinsonian pain" fits the definition of nociplastic pain (as suggested in the very same paper used for pain classification in the present study)[5] (Table 1). The classification of PD-related pains according to its mechanistic descriptors (nociceptive, neuropathic, and nociplastic) has been validated clinically, has shown to provide different profiles of somatosensory and cortical excitability changes in PwP,[6] and recently shown to be useful when performing neuromodulation strategies for pain relief in PwP.[7] The

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Relevant conflicts of interest/financial disclosures: There were no conflicts of interest relevant to this letter to declare.
Funding agencies: The Center for Neuroplasticity and Pain (CNAP) is supported by the Danish National Research Foundation (DNRF121). D.C.A. is supported by a Novo Nordisk grant NNF21OC0072828 and ERC Horizon Europe Consolidator grant PersoNINpain 101087925.

Received: 25 June 2024; **Accepted:** 27 June 2024

Published online in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/mds.29943

study of pain is an area of rich intersection between fields and the use of proper nomenclature and validated classification frameworks will only make the field of pain in PD move faster, for the sake of patients.

Acknowledgements: The Center for Neuroplasticity and Pain (CNAP) is supported by the Danish National Research Foundation (DNRF121). D.C.A. is supported by a Novo Nordisk grant NNF21OC0072828 and ERC Horizon Europe Consolidator grant PersoNINpain 101087925. We are thankful for the colleagues interested in the field of non-motor symptoms and in particular pain in PD who have laid the ground for important advances in the field.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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Adapted from

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Reply to: "What Is in a Name"

We are grateful for the opportunity to respond to the letter entitled "What is in a name" from Daniel Ciampi de Andrade, Veit Mylius, and Santiago Perez Lloret regarding our recent article.[1] We thank these authors for providing the three steps necessary to identify pain in Parkinson's disease (PD). They are an essential prerequisite for proposing appropriate treatment of pain in PD. As the authors note, our study focused on chronic pain in PD, therefore, fulfilling the first step. The second step was also respected, because we eliminated patients suffering from pain unrelated to PD (called concomitant pain) as defined by the Marques's algorithm.[2] Finally, in our case, the third step was to classify and diagnose parkinsonian central pain (PCP). We applied our classification[2] that is very close to that of Mylius et al,[3] which was published later. Based on this proposed classification, we used an algorithm aimed at disentangling PCP from other subtypes of chronic pain in PD by specifically and sequentially eliminating what is not PCP. Therefore, by respecting these different steps, we believe we have included mainly PCP patients and not patients suffering from other pain mechanisms.

Before the definition of nociplastic pain, older classifications of pain in PD defined and classified PCP as "central neuropathic pain" and described as boring, constant, ineffable, and diffuse, not limited to a dermatome or specific neural distribution.[4,5] We agree with the authors that the term "central neuropathic pain," which corresponds to a lesion of the central

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Relevant conflicts of interest/financial disclosures: The authors do not report any conflict of interest related to this article.
Funding agency: There is no funding during the research.

Received: 9 July 2024; **Accepted:** 10 July 2024

Published online in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/mds.29944