Editorial

The potential and challenges of artificial intelligence and machine learning in the study of pain

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In their article published in the current issue of *Clinical and Experimental Rheumatology*, Zhang *et al*. published an interesting paper investigating the molecular mechanisms underlying the connection between COVID-19 and fibromyalgia (FM) (1), a connection that has recently been explored even more deeply in the literature (2). Using blood transcriptome data from COVID-19 and FM patients, the authors employed a variety of analysis techniques, including Limma, GSEA, Wikipathway, KEGG, GO, and machine learning analysis, to identify common pathogenesis and key genes for the diagnosis of COVID-19 related FM. The study found 2505 differentially expressed genes (DEGs) in the FM dataset, with functional enrichment analysis revealing an intimate association between FM and viral infection. WGCNA analysis identified 243 genes firmly associated with the pathological process of COVID-19, and 50 common genes were screened between COVID-19 and FM, primarily involving immune-related pathways. The authors were able to identify three key genes for the diagnosis of COVID-19 related FM using machine learning and developed a diagnostic nomogram to predict the risk of FM occurrence. Finally, the study screened potential drugs that interact with the key genes, revealing their relevance to immune cells.

This study is important in shedding light on the molecular mechanisms underlying the connection between COVID-19 and FM and identifying potential biomarkers for further clinical research. One of the major strengths of the study is their use of a comprehensive approach to identify common molecular mechanisms between COVID-19 and FM. This approach is important as it allows for the identification of potential biomarkers and targets for further

clinical research, which is particularly valuable in this field. Another strength of the study is the development of a diagnostic nomogram to predict the risk of FM occurrence in COVID-19 patients. The nomogram showed excellent predictive performance, indicating that it could be a valuable tool in clinical practice. Diagnostic nomograms were already developed mainly for predicting the severity of COVID-19 in affected patients (3, 4); this is the first example of a diagnostic nomogram which could potentially help clinicians identify COVID-19 patients who are at risk of developing FM. Furthermore, the study's identification of three key genes that are closely relevant to immune cells and screened potential drugs that interact with the key genes is particularly promising. In fact, current research is focusing on immune alterations and dysautonomia related to COVID-19 infection, which has a lot of pathogenetic mechanisms in common with FM and ME/CFS (5, 6).

However, there are several limitations to the study that must be considered. One limitation is the small sample size, as only a limited number of patients were included in it. The sample sizes of both the COVID-19 and FM datasets were relatively small, which may limit the generalisability of the results. Another limitation is the use of transcriptome data, which only provides a snapshot of gene expression at a given time and may not fully capture the complex molecular processes underlying the connection between COVID-19 and FM (7). In addition, the study relied on publicly available data, which may have inconsistencies in terms of data quality and patient characteristics. Another potential limitation of the study is the reliance on bioinformatic analysis. While the use of machine learning and

bioinformatic techniques can provide valuable insights into complex datasets, these approaches may also introduce biases and errors that can affect the interpretation of results. It is important to carefully validate and cross-reference the findings of bioinformatic analysis with experimental data (8). Furthermore, the study focused on identifying biomarkers for the diagnosis of COVID-19 related FM but did not explore potential treatment options for patients with COVID-19 related FM. Future studies should aim to identify novel therapeutic targets and interventions for this patient population.

The study by Zhang *et al.* highlights the potential of using machine learning techniques to identify key genes and biomarkers associated with chronic pain. The use of machine learning in pain research has several advantages, including the ability to analyse large amounts of data quickly and efficiently, identify patterns and correlations that may not be apparent through traditional statistical analysis, and generate predictive models for patient outcomes. The diagnostic nomogram developed by Zhang *et al.* showed excellent predictive performance, suggesting the potential for machine learning techniques to improve the accuracy of pain diagnosis. However, the application of machine learning in pain research also has limi-

tations, including the potential for bias in the training data, the need for high-quality and standardised data to ensure accuracy and generalisability, and the ethical considerations surrounding the use of patient data (9). Additionally, the complexity of chronic pain and the multifactorial nature of its pathophysiology may limit the ability of machine learning techniques to capture the full spectrum of pain mechanisms and therapeutic targets.

Despite these limitations, the study provides a promising example of the potential of machine learning in pain research and highlights the need for continued research and development in this area. Future studies could explore the use of machine learning in larger and more diverse patient populations, as well as the integration of multiple data types, such as imaging and clinical data, to provide a more comprehensive understanding of pain mechanisms and treatment responses. Continued research in this area could lead to improved pain diagnosis, personalised treatment approaches, and ultimately better outcomes for patients suffering from chronic pain.

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