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Machine Learning Approaches Applied in Spinal Pain Research

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Abstract

The purpose of this narrative review is to provide a critical reflection of how analytical machine learning approaches could provide the platform to harness variability of patient presentation to enhance clinical prediction. The review includes a summary of current knowledge on the physiological adaptations present in people with spinal pain. We discuss how contemporary evidence highlights the importance of not relying on single features when characterizing patients given the variability of physiological adaptations present in people with spinal pain. The advantages and disadvantages of current analytical strategies in contemporary basic science and epidemiological research are reviewed and we consider how analytical machine learning approaches could provide the platform to harness the variability of patient presentations to enhance clinical prediction of pain persistence or recurrence. We propose that machine learning techniques can be leveraged to translate a potentially heterogeneous set of variables into clinically useful information with the potential to enhance patient management.

The burden of musculoskeletal spinal pain

The 2019 Global Burden of Disease Study has highlighted the enormous global burden of spinal pain disorders. Low back pain (LBP) and neck pain (NP) disorders are the largest contributors to all spinal pain disorders (Urwin et al. , 1998), hence, are the focus of this review. The prevalence of LBP and NP increased between 15-20% from 2005 to 2015, reaching a current estimate of 539 and 358 million people, respectively (Hurwitz et al. , 2018). LBP and NP have been reported to be the 4th and 19th leading causes of disability in 2019 (Vos et al. , 2020), with current estimates of years lived with disability (YLDs) reported to be a combined total of 94 million years (Hurwitz, Randhawa, 2018). Most new episodes of spinal pain recover rapidly within the first 6 to 12 weeks from onset (Costa et al. , 2012, Hush et al. , 2011), although up to 30% of individuals report incomplete recovery after one year from baseline (Henschke et al. , 2008).

The societal and economic costs of spinal pain disorders are high, driven largely by a small fraction of individuals with persistent pain (Carroll et al. , 2008). The total cost for LBP was estimated at AUD $9 billion in 2001 in Australia (Maetzel and Li, 2002, Walker et al. , 2003), with similar proportions observed in the Netherlands and the United Kingdom (Dagenais et al. , 2008, Maniadakis and Gray, 2000, van Tulder et al. , 1995) In the Netherlands, the total health care cost in 1996 for NP was estimated at €485million (Borghouts et al. , 1999). Considering the rising costs of health care, it is plausible that these estimates would be higher today.

The high prevalence and significant burden of spinal pain disorders have resulted in a proliferation of research over the past three decades (Wang and Zhao, 2018). However, even though several treatments have been investigated for the management of spinal pain, the long-term effect sizes of these interventions are modest at best (Foster, 2011, Patel et al. , 2013). A critical factor that explains the small average treatment effect that has generated a

surge in research and clinical interest in the last decade is the concept of "heterogeneity" (Foster et al. , 2013) or "variability" (van Dieen et al. , 2019) – two words with the same meaning, but used in a different research context. Clinical heterogeneity is a term used to reflect the wide range of individual responses to specific treatments. Physiological variability is a term used to reflect the variation in individual and contextual physiological or psychological responses to pain or injury. Surprisingly, little research has attempted to directly bridge the study of physiological variability to develop therapeutic strategies and decision-making systems that manage the issue of clinical heterogeneity.

Research in spinal pain disorders has evolved to encompass a breadth of scientific disciplines, varying from basic science (Falla et al. , 2004, Hodges et al. , 1999) to epidemiological research (Saragiotto et al. , 2016a). Basic science investigations have ranged from studying individual muscle activity (Falla, Jull, 2004, Hodges, Cresswell, 1999), multi-muscle synergies (Gizzi et al. , 2015, Liew et al. , 2020a, Liew et al. , 2018), motor-unit (Falla et al. , 2010, Yang et al. , 2016a), spinal (Yu et al. , 2017) and supraspinal activation (Hodges et al. , 2009, Jacobs et al. , 2010, Tsao et al. , 2008). Epidemiological research has also encompassed a wide range of methodologies from cross-sectional diagnostic (Kim et al. , 2018), longitudinal prognostic (Costa, Maher, 2012), longitudinal trajectory analysis (Kongsted et al. , 2016), randomized controlled clinical trials (Griffin et al. , 2017, Marin et al. , 2017, Saragiotto et al. , 2016b), stratified care (Foster, Hill, 2013, Kent et al. , 2010), and causal mediation analysis (Lee et al. , 2015).

We argue that the dearth of translational research that maps variability from the bench to patient heterogeneity at the bedside could come from the challenge of managing and using high-dimensional multivariate data. The primary purpose of this review aims to address this gap in translational spinal pain research that sits at the nexus of basic science and epidemiology. We intend to achieve this aim by (1) reviewing current knowledge of the

physiological adaptations present in people with spinal pain, (2) the advantages and disadvantages of current analytical strategies in contemporary basic science and epidemiological research, (3) a critical reflection of new analytical machine learning (ML) approaches that could provide the platform to harness variability in translational research, and lastly (4) ending the review with a short commentary of the potential clinical implications that could emanate from this review.

Physiological adaptations in spinal pain

There is an extensive body of literature describing neuromuscular and biomechanical changes in people with spinal pain. Some of the more common changes in motor output observed in people with chronic symptoms compared to asymptomatic individuals include reduced strength and endurance (Conway et al. , 2018, Lindstroem et al. , 2012, Moreno Catalá et al. , 2018, Sanderson et al. , 2019b; Bech et al., 2017) and poorer force steadiness (Muceli et al. , 2011), as well as decreased range, speed, accuracy, variability, and smoothness of movement (Alsubaie et al. , 2021, Dideriksen et al. , 2014, Falla et al. , 2017, Gizzi et al. , 2019, Salehi et al. , 2021, Vaisy et al. , 2015; Bauer et al., 2017). Studies utilizing electromyography (EMG) have revealed various changes in muscle behaviour which likely contribute to such variation in motor output including changes in motor unit behaviour (Falla, Lindstrøm, 2010, Yang et al. , 2016b), delayed muscle responses to perturbations (Boudreau and Falla, 2014, Falla, Jull, 2004, Hodges and Richardson, 1996, Knox et al. , 2018), an altered distribution and loss of variability of muscle activity (Falla and Gallina, 2020, Falla et al. , 2014, Sanderson et al. , 2019a), greater myoelectric manifestations of fatigue (Beneck et al. , 2013, Falla et al. , 2003, Roy et al. , 1989),increased muscle co-activation (Bonilla-Barba et al. , 2020, Falla et al. , 2013), and altered muscle synergies (Liew, Del Vecchio, 2018). Additionally, there is evidence of changes in brain organization including the convergence of brain representations for multiple muscles (Tsao et al. , 2011) and modification of the size and

location of cortical representations (Elgueta-Cancino et al. , 2018, Tsao, Galea, 2008). Collectively this research suggests that there are some neuromuscular adaptations to pain that may be more consistent amongst people with spinal pain even though there can be considerable heterogeneity between individuals (Figure 1).

What is evident however from the existing literature is the massive amount of discrepancy in study findings which is likely at least partly explained by the variation in experimental methods, tasks examined, and clinical status of the patients tested (e.g. varying levels of pain intensity/disability and presence or absence of psychological features) amongst other factors. These discrepancies are evident from the conclusions of systematic reviews examining changes in neuromuscular or biomechanical features in people with musculoskeletal pain where heterogeneity across studies is identified such that meaningful conclusions cannot be drawn (Sanderson et al. , 2021, Wernli et al. , 2020). However, such discrepancy can also be attributed to the physiological variability described above. Indeed, studies that have examined subject-specific responses often reveal variability in neuromuscular adaptations in people with spinal pain. For example, in a recent study, we showed that people with chronic non-specific LBP, on average, activate more cranial regions of the lumbar erector spinae compared to asymptomatic individuals when they perform the Ito test sustained until exhaustion (main effect for group; $F = 44.00$, $P < 0.001$, $\eta p2 = 0.65$; Figure 2A). However, when reviewing individual responses, it was evident that several of the participants with chronic LBP performed the task with the same distribution of erector spinae activity as seen in asymptomatic people i.e. a more diffuse distribution of activity (Figure 2B). Given this variability, it is unlikely that the same findings of any study on people with spinal pain could be entirely replicated on a completely different cohort.

Such variation between individuals may relate to several factors including the redundancy of the muscle system, anthropometric features, the magnitude of pain intensity

and disability, extent of peripheral or central sensitisation, and the presence of psychological features such as the extent of fear of movement. Although there is some evidence to support an association between the extent of pain and/or disability and the extent of physiological adaptations (Alsultan et al. , 2020, Falla et al. , 2011, Jacobs et al. , 2017, O'Leary et al. , 2011, Salehi, Rasouli, 2021, Schabrun et al. , 2017) which can explain some variation in amongst people with spinal pain, this relationship doesn't always hold (Jacobs et al. , 2016, Steele et al. , 2014). Likewise, there are examples where the extent of psychological factors such as fear of movement, catastrophizing, and anxiety are associated with physiological features (Alsubaie, Martinez-Valdes, 2021, Alsultan, De Nunzio, 2020, Vaisy, Gizzi, 2015, Van Damme et al. , 2014), but again, this is not always the case (Lima et al. , 2018, Veeger et al. , 2020).

Evidence to support the individual-specific reorganization of the motor strategy to complete a given task when in pain comes from experimental pain studies. Studies have shown that the injection of a noxious stimulus in a single muscle can trigger subject-specific adaptations allowing individuals to complete a motor task when in pain albeit with a unique redistribution of muscular activity (Gizzi, Muceli, 2015, Hodges et al. , 2013). These findings help to explain the individual responses seen in clinical populations.

What has become particularly evident from the body of research on physiological adaptations in people with spinal pain is that we cannot rely on single features given the variability of neuromuscular adaptations in people with spinal pain.

Limitations of current analytical approaches

Scalar vs functional variables

$$Y = f(X) + \epsilon \quad (1)$$

In the majority of research undertaken in contemporary spinal pain research, data are collected on one or more outcomes (Y, also termed as dependent variables), at each unique value of a set of covariates (X, also termed predictors or independent variables). A statistical model is created (Eqn 1), to estimate the function f which maps X to Y, and ϵ being the error. There are two primary reasons why researchers may be interested in estimating f – for inference or prediction.

Statistical inference (e.g. null-hypothesis significance testing), seeks primarily to estimate the uncertainty of the relationship (i.e. f), producing estimates such as the confidence interval. This paradigm is at the heart of much spinal pain research seeking to either test competing theories of altered neuromuscular function with pain (Falla, Jull, 2004), or to test the effectiveness of competing therapies on clinical outcomes (Poquet et al. , 2016, Saragiotto, Machado, 2016a). Statistical prediction, on the other hand, focuses on how accurate the outcome Y can be estimated based on knowing the value of the predictors X. Statistical prediction has also been termed as prognostic modelling (Steyerberg et al. , 2013). Statistical prediction is typically undertaken because the outcome cannot be easily measured, but the predictors are more easily obtained. At the heart of statistical prediction is not necessarily knowing the structure of the function f, but achieving a prediction of the outcome that exceeds a clinically desirable accuracy threshold.

Regardless of whether statistics are used for inference or prediction purposes, many traditional statistical methods, such as the Analysis of Variance (ANOVA) and linear regression, rely on the presence of variables to lie on the scalar domain. Scalar variables are those that take on discrete variables – e.g. range of motion (ROM) and maximal strength. In contrast to scalar variables, functional variables are those with values that change as a function of time and/or space (distance). It is argued that many variables collected in spinal pain research are collected across time and space, thus making them functional. For example,

muscle activation magnitude can be collected over a gait cycle (van den Hoorn et al. , 2015) and different regions of the lumbar spine (Murillo et al. , 2019), pain intensity can be recorded daily for over a year (Kongsted et al. , 2017), and strength can be collected over a joint's ROM (Suryanarayana and Kumar, 2005). The functional nature of many routinely collected variables in spinal pain research precludes the use in their original form within traditional statistical models.

To use functional variables in traditional statistics, they must first be transformed to lie on the scalar domain. Some transformations include extracting the peak value, taking the average, or finding the difference between the maximum and minimum value of functional variables. The primary advantage of using scalar variables is that it opens up many more statistical models to be available to the researcher. Another advantage of scalar variables is the inherent interpretability of the model's solution – a necessity in inferential problems. Interpretability is also a necessity if clinicians were to depend on such models for clinical decision-making (2018). For example, in linear regression, the β coefficient can be easily understood as a change in Y for a unit change in X. Despite its obvious advantages, transforming functional to scalar variables removes a significant amount of information contained within the original variables. This could lead to potential false-negative findings during statistical inference or lack of an impact in improving a model's accuracy during prediction.

p>>n in the era of Big data

In both statistical inference and prediction, when there are more covariates p, than the sample size n, the model cannot be estimated with conventional fitting methods (e.g. OLS) as the corresponding algorithm for parameter estimation suffers from a singular matrix. In addition, traditional statistical models rely on the presence n being much greater than p, so that the estimated model's solutions have a low variance. For inferential problems, a low

variance provides a study with adequate statistical power to detect a true effect; whilst for prediction problems, a low variance allows the model to generalize well in performance beyond the original data used to develop the model.

Technological advancement has meant that it is becoming easier to collect more data than could easily exceed sample size. For example, up to 126 biomechanical variables can be extracted from a single accelerometer (Benson et al. , 2018). The issue of big p is not restricted to laboratory based research, but can be quite common in contemporary clinical epidemiological research (Ford et al. , 2018). For example, a typical practice is to treat the aggregate score of a psychological questionnaire into a single value (Miller et al. , 1991, Sullivan et al. , 1995). For psychological assessments, it is quite conceivable that two individuals can have the same aggregate score, but have different individual items' scores. A previous study reported that individual item responses from a questionnaire resulted in the identification of more clinical subgroups than using the aggregate score of the questionnaire (Nielsen et al. , 2016). Whilst data aggregation techniques often simplify the subsequent analysis, it may result in the loss of subject-specific information.

Managing high-dimensional data using machine learning

ML in spinal pain research has proliferated over the last decade (Azimi et al. , 2020, Tagliaferri et al. , 2020), more so in LBP than in NP. ML has been used in research that revolves around the themes of diagnosis and prediction, image segmentation, movement and muscle assessment in spinal pain disorders, causal analysis, and identifying clinical subgroups with homogeneous clinical characteristics. In the present section, we focus the discussion on how ML can be used to manage the issues related to to collinearity as well as measuring functional variables in a high-dimensional space, and consequently optimize the clinical prediction of the status and/or progression of spinal pain disorders.

Contemporary machine learning models

ML models for clinical prediction can be used to predict quantitative (e.g. pain intensity on a visual analog scale) or qualitative (e.g. recovered vs non-recovered) outcomes. The former is termed regression whilst the latter is termed classification. ML models vary in their flexibility in estimating the function f which maps the predictors X to predict the outcome Y. A model's flexibility is typically inversely related to the interpretability of the function f. For example, an example of a low flexibility ML model is OLS, where the outcome Y is a linear function of the estimated parameters (β coefficient). The low flexibility means that the function f is explicitly known (i.e. β coefficient), but at the expense that potentially non-linear relationships may be overlooked. For example, using stepwise linear regression, a 1% point increase in neck disability index (NDI) at baseline resulted in a 0.9% point increase at 12-month follow-up in a clinical cohort of individuals with cervical radiculopathy (Liew et al. , 2020b). In contrast, some of the most flexible ML models such as artificial neural networks (ANN), can model highly non-linear relationships, but at the expense that the function f is essentially a "BlackBox". For example, one study reported that artificial neural networks (ANN) (96.9%) resulted in more accurate prediction in 2-year post-surgical satisfaction in patients with lumbar spinal stenosis, compared to logistic regression (88.4%) (Azimi et al. , 2014). Most ML research in spinal pain have used highly flexible ML models - support vector machine (SVM) (Ashouri et al. , 2017, Jiang et al. , 2017, Lamichhane et al. , 2021, Lee et al. , 2019, Silva et al. , 2015), and ANN (Fidalgo-Herrera et al. , 2020, Hu et al. , 2018, Magnusson et al. , 1998). However, what constitutes the most important variable or the magnitude of effect each variable has on the prediction remains "hidden" in the ANN model.

The physiological data used for prediction in spinal pain ML studies typically consist of temporal (Ashouri, Abedi, 2017, Fidalgo-Herrera, Martínez-Beltrán, 2020, Hu, Kim, 2018,

Magnusson, Bishop, 1998), spatial (Lamichhane, Jayasekera, 2021), and spatio-temporal functional variables (Jiang, Luk, 2017). An important pre-processing step in many ML methods is that the variables are required to lie on a scalar domain. Some studies use Principal Components Analysis (PCA) (Ashouri, Abedi, 2017) on functional data to extract scalar features, whilst others directly extract scalar features from the original variables (Fidalgo-Herrera, Martínez-Beltrán, 2020, Jiang, Luk, 2017, Lamichhane, Jayasekera, 2021, Magnusson, Bishop, 1998). An important limitation of using dimension reduction techniques like PCA on functional data is a loss in spatial and/or temporal information, and often there is no strong prior knowledge as to what are the most important features to select.

Newer machine learning models

Functional data boosting

Functional data boosting (FDboost) (Brockhaus et al. , 2020) is a ML method that produces intrinsically interpretable model solutions. FDboost does not only allow modelling linear, smooth non-linear, and random effects as known from classical statistics but can also incorporate functional variables, both as an outcome or predictor without any pre-processing or loss of information. These user-specified effects are estimated in FDboost using a gradient boosting algorithm, which comes with an inherent variable selection. FDboost can thus also deal with settings where p>>n due to its penalized estimation algorithm. For example, from 94 scalar and functional candidate covariates on 46 participants, FDboost was able to select 3 covariates to classify individuals with and without NP with an area under the Receiver Operating Characteristic curve (AUC) of 80.8% (Liew et al. , 2020c). In a classification study on LBP, FDboost was not only able to achieve excellent prediction performance (> 90% AUC), but it could quantify when within the movement cycle a covariate was driving the prediction (Liew et al. , 2020d).

Patients in clinical research are traditionally assessed only at baseline or at few follow-up time points (Costa, Maher, 2012). Recently, research has begun tracking daily (Bedson et al. , 2019) and weekly (Irgens et al. , 2020) pain reports, as well as duration of spinal motion (Lagersted-Olsen et al. , 2016) of patients by leveraging mobile phone short messaging services or applications. In addition, the emergence of personal wearable sensor technologies means that data can be collected almost continuously (Burns et al. , 2021). To date, researchers have largely used dimension-reduction strategies such as clustering (Irgens, Kongsted, 2020), to identify homogeneous clinical subgroups from their pain trajectory patterns. We argue that the richness of pain trajectory patterns, or indeed any functional data, in explaining and predicting the course of spinal pain can be better harnessed using techniques such as FDboost.

Deep learning

Deep learning are a special field of ML where models consist of deep ANN (DNN), i.e., neural networks with many hidden intermediate layers. An ANN has typically few intermediate layers (e.g. 1-3), whereas DNNs are made by many more hidden layers (e.g. 11 to 19) (Simonyan and Zisserman, 2015). DNNs can deal with various model inputs such as images, texts, and also functional data (Perdices et al. , 2021). The larger number of intermediate layers in DNNs provides the capacity to learn multiple levels of abstraction of the input data. DNNs have yielded outstanding results in a wide range of research fields, including audio classification, natural language processing, or image recognition among many others, and in some cases, outperforming traditional ML models (Esteva et al. , 2019, Faust et al. , 2018). Although DNNs are still underexploited in spinal pain research, some studies have applied them to LBP classification or chronic pain syndromes, both with good to excellent performance (97% and 86%, respectively) (Hu, Kim, 2018, Santana et al. , 2019).

A disadvantage of DNNs in clinical research is their lack of interpretability. However, there is an increasing number of post-modelling techniques, such as DeepLIFT (Shrikumar et al. , 2017), that can inform end-users on the relative importance of each covariate in the outcome prediction. An exciting new extension to DNNs that could generate high performance, yet interpretable model solutions is the so-called "wide-and-deep", or semi-structured neural networks (Rügamer et al. , 2021). Semi-structured neural networks combine a "BlackBox" DNN, alongside a wide and interpretable network. Semi-structured deep regression follows this idea by embedding most of the commonly known statistical regression models in a neural network (Rügamer, Shen, 2021). Semi-structured regression models would fit well in a scenario whereby clinicians desire high interpretability of the relationship of some variables (e.g. effect of fear on long-term disability) but require less interpretability on the relationship of others (e.g. facial expression images of pain on long-term disability) (Bargshady et al. , 2020). Variables can make a useful contribution to a model's overall predictive performance, but because the specific nature of such relationships to the outcome may not be as important to a clinician, a "Blackbox" approach could be used to model these variables.

Emerging evidence of physiological predictors in spinal pain research

Biomarkers such as biomechanical or electrophysiological variables can be related to and influence the clinical presentation of people with spinal pain. Clinically, these markers appear to be ideal candidate variables that could be leveraged for clinical prediction and inform therapeutic management. For example, a study reported that 11 kinematic features obtained during gait selected by Neighbourhood Component Analysis could discriminate between individuals with and without NP with an accuracy of 90% (Jiménez-Grande et al. , 2021) (Figure 3). In addition, another study reported that seven EMG functional variables collected during a low-load lifting task could discriminate individuals with and without LBP

with the area under the receiver operator curve (AUC) of 90.4% (Liew, Rugamer, 2020d) (Figure 4).

Although most studies have assessed people with current pain, preliminary findings demonstrate that kinematic and neuromuscular features can also differentiate asymptomatic people from people with recurrent pain who are in a period of remission (Devecchi et al. , 2021, Liew, Rugamer, 2020d). For example, individuals in remission of NP could be discriminated from asymptomatic controls with an AUC of 87%, using 6 variables, namely velocity and smoothness of neck movement (in extension, flexion, and lateral flexion), endurance in neck flexion, co-contraction of the neck flexors, and kinesiophobia (Devecchi et al. , 2020) (Figure 5). In a further example, nine EMG functional variables were able to discriminate between individuals in remission of their LBP against asymptomatic controls with an AUC of 91.2% (Liew, Rugamer, 2020d). Interestingly, three EMG variables used to discriminate healthy from individuals in remission, also were found to discriminate healthy from individuals with LBP (Liew et al., 2020). This suggests that physical impairments may persist despite pain resolution, which could place an individual at a greater risk of recurrence. Overall, these findings promote the need to consider biomechanical and electrophysiological biomarkers as potential predictors of pain persistence or recurrence.

Clinical implications

Given the significant variability in the physiological and psychological response to spinal pain, an important issue is how ML can be used to leverage high-dimensional features to optimize clinical management. We provide a few clinically oriented examples.

LBP and NP daily pain recovery trajectories exhibit substantial inter-subject variation (Irgens, Kongsted, 2020, Kongsted, Hestbaek, 2017), which consequently benefit from the derivation of clinical subgroups. It is acknowledged that for both LBP and NP, most of the

recovery occurs within the first six weeks (Carroll, Hogg-Johnson, 2008, Costa, Maher, 2012) and that those who experience a little reduction in symptoms during this period, go on to experience persistent pain. A previous study reported that visual trajectory patterns could be used as a qualitative predictor of 12 weeks recovery, providing indirect evidence that early recovery phase pain trajectories could play an important role in long-term clinical prediction (Myhrvold et al. , 2020). It may be that intensive pain recording during the first six weeks after symptom onset could be used to objectively quantify "early recovery trajectory", such that each participant would have an associated functional trajectory. Such trajectories can subsequently be used in functional data techniques like FDboost, to quantitatively predict long-term recovery status.

Physiological variables have not been largely been considered as candidate predictors when developing statistical models in spinal pain, perhaps based on the assumption that they often exhibit prohibitively large inter-individual variability (Gizzi, Muceli, 2015, Hodges, Coppieters, 2013). An excellent example is that of static spinal alignment and its poor association with spinal pain (Hanten et al. , 2000, Mitchell et al. , 2008, Widhe, 2001). Clinicians will have significant difficulty in distinguishing a patient from a healthy subject from a static image of the patient's spinal alignment. Yet, most clinicians would have little difficulty identifying a person in pain from their movements. For example, individuals with LBP consistently lift slower than healthy individuals (Nolan et al. , 2019). In addition, static postures often correlate poorly with dynamic movements (Paterson et al. , 2015). We argue that because dynamic movement variables provide greater subject-specific insights to a complex system than static variables, the former would provide greater opportunities to develop personalized management strategies.

Conclusion

Spinal pain disorders are highly prevalent and disabling, with significant individual and societal costs. It is well established that pain can affect multiple levels of the human physiological and psychological systems. However, physiological variables have rarely been used directly in clinical epidemiological studies, likely due to two reasons – significant inter-individual variation and high-dimensionality of the data. We presented the case in this review of how ML techniques can be leveraged to translate a potentially heterogeneous set of variables into clinically useful information that can ultimately improve patient management.

Figure Legends

Figure 1: Common physiological adaptations and changes in motor output observed in people with spinal pain

Figure 2: A. Examples of a topographical map of lumbar erector spinae EMG amplitude recorded from a control participant and person with chronic non-specific LBP as they performed the Ito test sustained until exhaustion. The centroid of the EMG amplitude map is depicted by the crosshair and the scale is indicated in μV. **B.** Absolute mean locations (standard error) of the y-coordinate of the centroid of the EMG amplitude map for controls (CON) and people with chronic non-specific LBP throughout the endurance contraction. Note that people with chronic non-specific LBP, on average, activated more cranial regions of the lumbar erector spinae compared to asymptomatic individuals when they perform the Ito test sustained until exhaustion. **C.** When considering individual responses, it was evident that several of the participants with chronic LBP performed the task with the same distribution of erector spinae activity as seen in asymptomatic people i.e. a more diffuse distribution of activity. Reprinted from Sanderson et al., 2019 with permission.

406 **Figure 3:** Classification performance of curvilinear (left) and rectilinear gait (right). **A.**
407 Curvilinear and rectilinear tasks performed by subjects wearing reflective markers on their
408 head, trunk, shank, ankle, and foot to capture body kinematics **B.** Accuracy of the classifiers
409 (SVM, K-NN, and LDA) using the gait kinematic features selected by the feature filter,
410 Neighbour component analysis (NCA). The two data tips marked show the highest accuracy
411 achieved for each gait. **C**. Optimal hyperplane learned by SVM based on jerk data extracted
412 from head movement during gait. Reprinted from Jiménez-Grande et al., 2021 with
413 permission.

414 **Figure 4:** Mapping electromyography (EMG) alterations in individuals with LBP compared
415 to controls in a lifting task, onto resultant class probabilities. FDboost first identifies the time-
416 varying β-coefficient of each functional predictor, which represents the change in log odds
417 for a unit change in predictor value from the control group. Second, the cumulative change
418 over time in log-odds is determined for each functional predictor, and the cumulative change
419 over predictors are combined additively and transformed to class probabilities. * reflects the
420 instance where the EMG differences between groups are maximally different, which
421 corresponds to the instance where the β-coefficient has the highest magnitude.

422 **Figure 5:** Classification conducted to discriminate individuals in remission of neck pain and
423 asymptomatic controls. **A** Feature selection and their importance are obtained from a random
424 forest algorithm (selected features presented in black). **B** Example of one individual (test
425 observation represented by the grey circle) classified in one of the two groups using the k-
426 nearest neighbor (KNN) classifier.To classify the test observation, the closest *k* individuals
427 (circles pointed by the arrows) in the Control or Neck Pain Remission groups were
428 considered ($k = 5$). Classification conducted using the features previously selected (A). For
429 the graphical purpose, the high-dimensional space obtained from the six selected features has

been reduced using locally linear embedding (LLE). MQ, movement quality (obtained from velocity and smoothness of neck movements); SCM, sternocleidomastoid muscle.

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