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Mechanisms of recovery after neck-specific or general exercises in patients with cervical radiculopathy

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Abstract

Background: The mechanisms of action that facilitate improved outcomes after conservative rehabilitation are unclear in individuals with cervical radiculopathy (CR). This study aims to determine the pathways of recovery of disability with different exercise programs in individuals with CR.

Methods: We analysed a dataset of 144 individuals with CR undergoing conservative rehabilitation. Eleven variables collected at baseline, 3, 6 and 12 months follow-up were used to build a Bayesian Network (BN) model: treatment group (neck-specific vs. general exercises), age, sex, self-efficacy, catastrophizing, kinesiophobia, anxiety, neck–arm pain intensity, headache pain intensity and disability. The model was used to quantify the contribution of different mediating pathways on the outcome of disability at 12th months.

Results: All modelled variables were conditionally independent from treatment groups. A one-point increase in anxiety at 3rd month was associated with a 2.45-point increase in 12th month disability ($p < .001$). A one-point increase in head pain at 3rd month was associated with a 0.08-point increase in 12th month disability ($p < .001$). Approximately 83% of the effect of anxiety on disability was attributable to self-efficacy. Approximately 88% of the effect of head pain on disability was attributable to neck–arm pain.

Conclusions: No psychological or pain-related variables mediated the different treatment programs with respect to the outcome of disability. Thus, the specific characteristics investigated in this study did not explain the differences in mechanisms of effect between neck-specific training and prescribed physical activity. The present study provides candidate modifiable mediators that could be the target of future intervention trials.

Significance: Psychological and pain characteristics did not differentially explain the mechanism of effect that two exercise regimes had on disability in individuals with cervical radiculopathy. In addition, we found that improvements in self-efficacy was approximately five times more important than that of neck–arm pain intensity in mediating the anxiety-disability relationship. A mechanistic understanding of

recovery provides candidate modifiable mediators that could be the target of future intervention trials.

Trials registration: ClinicalTrials.gov identifier: NCT01547611.

1 | INTRODUCTION

Cervical radiculopathy (CR) is a disorder most commonly caused by a cervical disc herniation or spondylosis resulting in nerve root impingement and/or inflammation (Radhakrishnan et al., 1994). The annual incidence of CR is 83.2 per 100,000, with an increase in prevalence through the fifth decade of life (Radhakrishnan et al., 1994). A more recent study from the United States military found an incidence of 1.79 per 1,000 person-years (Schoenfeld et al., 2012). While most cases are self-limiting, some are refractory to conservative care, and may require surgical intervention (Radhakrishnan et al., 1994). It is thought that persistent physical deficits, such as reduced neck muscle endurance and cervical range of motion (ROM) (Peolsson et al., 2013), could exacerbate pain-related disability in individuals with CR (Engquist et al., 2015; Peolsson et al., 2013; Wibault et al., 2017, 2018). In other words, physical deficits may represent candidate treatment mediators to improve clinical outcomes.

Surprisingly, exercise programs designed specifically to target the aforementioned physical deficits are only just as equally effective as general physical activity, in improving pain and disability in individuals with CR (Dedering et al., 2018; Wibault et al., ,2017, 2018). A 12-week neck-specific training program did not significantly improve outcomes of pain, disability and psychological outcomes in conservatively managed individuals with CR, compared to a general physical activity program (Dedering et al., 2018). Similar equipoise of treatment efficacy was reported between neck-specific versus general physical activity prescription in the post-surgical rehabilitation of individuals with CR (Peolsson et al., 2019; Wibault et al., ,2017, 2018).

Comparable effectiveness between different exercise programs could occur because 1) similar mechanisms were targeted by different programs, or 2) competing mechanisms were influenced such that the total differential effect between the programs is zero (Hayes, 2017). To date, no studies to our knowledge have investigated the mechanism(s) of action (if any) which different exercise programs act upon to improve recovery in individuals with CR. In other spinal musculoskeletal pain disorders, different exercise programs have been shown to reduce pain-related disability by influencing catastrophizing (Hall et al., 2016; Smeets et al., 2006) and self-efficacy levels (Liew et al., 2019; O'Neill et al., 2020; Sherman et al., 2013).

To understand the mechanisms of action of different treatments, structured equations modelling (*SEM*) (Fordham et al., 2017; Mansell et al., 2016) and linear regression models (Hall et al., 2016; O'Neill et al., 2020) have been used. Both methods can be seen as particular cases of Bayesian Networks (BNs) (Nagarajan et al., 2013), a probabilistic graphical modelling approach used increasingly in the medical field (Farmer, 2014; Takenaka & Aono, 2017; Thanathornwong, 2018). BNs emphasize learning pathways directly from data, as opposed to considering problems with a fixed structure like linear regression (i.e. which variable is the dependent and which are the independent variables) and they are the foundation upon which counterfactual causal inference was built (Pearl, 2009). BNs can be used to "learn" and quantify the relationships between multiple variables (Scutari et al., 2017) and the ensuing model can be used to understand the mechanisms of action (if any) on recovery of different treatment programs.

An understanding of the mediators of recovery of pain-related disability could potentially enable researchers and clinicians to better design specific interventions to manage a complex disorder such as CR. The principal aim of the present secondary analysis was to determine the pathways (if any) to the recovery of disability of different exercise programs in the management of individuals with CR. Similar to other musculoskeletal disorders, as presented earlier, we hypothesized that psychological features of catastrophizing and self-efficacy would mediate the relationship between different exercise programs and pain-related disability.

2 | METHODS

2.1 | Study design

The present analysis was undertaken on a dataset collected from a multicentre, parallel-grouped, randomized controlled trial, the methodological details of which have been previously reported (Dedering et al., 2014, 2018). The trial was registered prospectively (ClinicalTrials.gov NCT01831271).

2.2 | Participants

Patients with CR were recruited from a regional neurosurgical department from October 2010 to November 2012. Patients were consecutively screened for eligibility by a neurosurgeon. They were eligible if the following criteria were fulfilled: (1) magnetic resonance imaging (MRI)

evidence of cervical nerve root compression; and (2) neck and/or arm pain, verified with a Spurling test or a neuro-dynamic provocation test (Tong et al., 2002). Potential participants were excluded if they had a previous cervical fracture, subluxation or surgery; spinal infection and malignancy; known drug abuse; diagnosed psychiatric disorders; other diseases or disorders contraindicating the participation of the prescribed interventions; and unfamiliarity with the Swedish language. The study was approved by the Regional Board of Ethics, with written informed consent sought prior to study enrolment. Of the 160 screened patients, 144 agreed to participate.

2.3 | Interventions (12 weeks)

Once randomization was complete, individuals received either the (1) neck-specific training (NST) or (2) prescribed physical activity (PPA). Both interventions included a cognitive behavioural approach, which was delivered continuously through the entire program for the NST group but only at the first session for the PPA group. Treating physiotherapists received written information about the elements to be included in the interventions, that is, pain physiology, consequences of stress and exercise, relaxation techniques, coping strategies and ergonomic advice. This information was standardized and similar for the two groups. The treating therapists in the NST group were given instructions stating when the elements were to be delivered – meaning during the early, intermediate or late phase of the intervention period. All participants were requested to train or exercise 3 times per week.

2.3.1 | Neck-specific training (NST)

In addition to the aforementioned common treatment, patients and physiotherapists in this group received a manual on the standardized neck-specific training program, including instructions for progression (see details in http://liu.diva-portal.org/smash/record.jsf?pid=diva2%3A785214&dswid=-9089). The training was provided by experienced physiotherapists in primary care who delivered three sessions per week. The program focused on improving sensorimotor function, neck muscle endurance and pain reduction. Briefly, participants started with gentle isometric muscle contractions of the deep cervical muscles, progressing to low-load endurance training in the gym. The neck-specific training was individually tailored for each participant regarding the choice of exercises and the progression rate. Progression was based on the participant's pain and neck movement quality, but also on the fulfilment of a specified criteria number of sets and repetitions to be completed. The neck-specific training also included a continuous physiotherapist-guided behavioural

approach targeting management of pain and stress, coping, education on breathing, relaxation, pacing and ergonomics.

2.3.2 | Prescribed physical activity (PPA)

The PPA intervention included one individual participant counselling session which led to a written prescription of physical activity. The counselling consisted of a motivational interview with a cognitive behavioural approach at the first session, an approach to facilitate behaviour change, to survey the patient's health state, history of physical activity, potential risk factors, patient's motivation and need of support for physical activity and training. Participants received individual prescriptions recommending general aerobic and/or muscular physical activity or training, but no neck-specific training. In addition, they were encouraged to perform at least 30 min of physical activity at moderate intensity at least 3 days per week. Patients in the PPA group were offered a physiotherapy contact in primary care to facilitate the implementation of the physical activity prescription. Three patients in this group initiated their PPA after the initial counselling session without the additional primary care physiotherapy contact; with the remaining initiating their PPA after the additional physiotherapy contact.

2.4 | Outcome measures

All continuous variables (i.e. variables 4 to 11 below) were assessed at baseline (pre-intervention), and at 3, 6 and 12 months follow-ups. The following 11 variables were used to form a BN:

1. Treatment: the randomized allocation into the two groups arms (NST vs. PPA).
2. Gender: men or women
3. Age: in years
4. Self-efficacy scale (SES): a measure to evaluate each participant's confidence in their ability to perform 20 activities of daily living. Score ranges from 0 (not confident) to 200 (very confident) (Altmaier et al., 1993; Bunketorp et al., 2005).
5. Pain Catastrophizing Scale (PCS): measures the magnitude of pain catastrophizing. Score ranges from 0 (no catastrophizing) to 52 (maximal catastrophizing) (Sullivan et al., 1995).
6. Tampa Scale for Kinesiophobia short form (TSK-11): measures fear of movement and (re)injury. Score ranges from 11 (no fear) to 44 (maximal fear) (Miller et al., 1991).
7. Hospital Anxiety and Depression Scale, anxiety sub-score (Anx): measures anxiety in a general medical

population. Total score ranges from 0 (absent anxiety) to 21 (maximal anxiety) (Zigmond & Snaith, 1983).

8. Hospital Anxiety and Depression Scale, depression sub-score (Dep): measures depression in a general medical population. Total score ranges from 0 (absent depression) to 21 (maximal depression) (Zigmond & Snaith, 1983).

9. Neck–arm pain intensity: average of two self-reported measures of current neck and arm pain intensities, each measured on the 0–100 visual analogue scale (VAS). Score ranges from 0 (no pain) to 100 (worst imaginable pain).

10. Headache pain intensity: a self-reported measure of current headache pain intensity on the VAS. Score ranges from 0 (no pain) to 100 (worst imaginable pain).

11. Neck disability index (NDI): a measure to quantify disability attributed to neck pain. Score ranges from 0 (no activity limitations) to 50 (maximal activity limitations).

2.5 | Approach to data analysis

2.5.1 | Unfolding of repeated outcome measures

To quantify the time-dependent change in variables against the outcome of disability, we "unfolded" the variables in the following method:

1. The 3rd and 6th month value of variables 4 to 10 were used as potential mediators, giving a total of 17 variables. Variables reflecting the 3rd and 6th month values were suffixed with "_3" and "_6" respectively.
2. The 12th month value of NDI was treated as an outcome, and this was suffixed with "_12".
3. Baseline variables of allocation group, age and gender remain unchanged.

The specific nature of the unfolding enabled us to quantify which variables needed to change and when, to alter the reduction in disability. Descriptive summary measures of mean and standard deviation (SD) for all continuous variables 4 to 11 as described above were calculated for each follow-up time point.

2.5.2 | Missing data handling

Forty-seven participants had complete missing data for the unfolded variables (4–10) at the 3rd and 6th month follow-up, and variable 11 at the 12th month follow-up; and they were excluded from analysis. The missing data were due to a discontinuation of participation from the 3rd month follow-up, and the main reasons for the discontinuation were patients' lack of time and interest (Dedering et al., 2018; Halvorsen et al., 2016).

There were no significant differences in gender, age, neck and arm pain intensity, between patients who dropped out before 3 months of follow-up and those retained in the trial. Ninety-seven participants were included into the BN analysis. The proportion of missing data for each unfolded variable can be found in Figure S1 of the supplementary material.

2.5.3 | Bayesian network analysis

All analyses were performed in R software [38] using the bnlearn package (Scutari, 2010), with codes and results available on GitHub (https://github.com/bernard-liew/2020_cxrad_bn). BN is a graphical modelling technique (Nagarajan et al., 2013), used increasingly in the health sciences to understand causal relationships.

BN quantifies the relationships among a set of variables $X = \{X_1, ..., X_N\}$, where N is the number of different variables, using a directed acyclic graph (DAG). Each variable is associated with a node and directed arcs represent conditional dependencies between pairs of nodes. Building a BN model using a data-driven approach involve two stages: 1) structural learning – identifying which arcs are present in the DAG; and 2) parameter learning – estimating the parameters that regulate the strength and the sign of the corresponding relationships.

In principle, a BN model can be built entirely with a sufficiently large dataset. However, inherent "noise" with real world clinical data means that spurious relationships (false positive), even relationships which violate biological truths may be found; and also real relationships may be missed (false negative). More informative models can be built by including prior knowledge, sourced from the literature and experts, during the model building process. In the BN framework, prior knowledge can be included in the model as blacklist and whitelist arcs. Blacklist arcs are those which contravene known biological/physical mechanisms. For example, depression does not influence age. We blacklisted all arcs which point backwards in time (e.g. from NDI_12 to PCS_6). We also blacklisted arcs pointing between the nodes of age and gender; and pointing from NDI to all other variables – since we were interested in understanding the pathways that explain pain-related disability as an outcome.

We made use of model averaging to reduce the potential of including spurious relationships in the BN, using bootstrap resampling (B = 200) and performing structure learning on each of the resulting sample using Structural Expectation Maximization (EM) (Friedman, 1997). Structural EM is a technique which can build BN models in the presence of missing data (Friedman, 1997). It does so by building an initial empty BN model using the original complete data, using it to impute missing data, rebuilding the BN model using the imputed complete data and repeating this sequence until convergence.

We computed an "average" consensus DAG by selecting those arcs that have a frequency of > 70% in the bootstrapped samples, to create a sparse and interpretable network (Scutari & Nagarajan, 2013). To determine the validity of the trained model, validation was performed using nested 10-fold cross-validation (CV). A nested 10-fold CV iteratively splits the training set into 10 approximately equal folds, trains the model on 9 folds using bootstrap resampling (as described above) and evaluates the model's performance on the 10th fold. Model performance was defined by computing the correlation coefficient between the predicted and observed values of each continuous variable. The strength of correlation was categorized as negligible ($|r| \leq 0.30$), low ($|r| = 0.31$ to 0.50), moderate ($|r| = 0.51$ to 0.70), high ($|r| = 0.71$ to 0.90) and very high ($|r| = 0.91$ to 1) (Hinkle et al., 2003). A model with high predictive performance should have as high a positive correlation as possible in the testing dataset. A nested 10-fold CV provides a more conservative means of model validation, since a model would perform well on the data it was exactly trained on. After validation, a final BN model was built using bootstrap resampling on the entire dataset ($n = 97$).

2.5.4 | Conditional probability queries

The derived averaged BN model can be considered an "expert system", which provides a set of decisions given a set of evidence. We can generate a large number of samples (i.e. values of any variables) from the model given a set of evidence (i.e. values of a set of variables in the model). Thereafter, we can calculate the conditional probabilities of observing a set of samples with the relevant outcomes given some evidence. For each conditional probability query, we generated 10^4 samples of the variables of interest in order to obtain precise probability estimates. We used a technique known as belief updating, which estimates the posterior probability of an outcome based on the available evidence on the values of certain variables. We adopted a specific method of belief updating known as logic sampling (Nagarajan et al., 2013). Essentially, logic sampling sequentially generates samples of values of the variables guided by their conditional distributions in the BN. The algorithm then weights the number of samples that contain both the desired set of outcome and given evidence, against the number of samples with the desired outcomes only, thus providing an updated belief of the probability of a particular outcome given the evidence.

3 | RESULTS

The mean (SD) values for all continuous variables 3 to 11 at each follow-up time point is reported in Figure 1. The baseline characteristics of the participants included ($n = 97$), and those

excluded from the BN analysis ($n = 47$) are found in Table 1. Figure 2 shows the averaged BN consensus model learnt from 200 networks constructed from the data, with arcs appearing at least in 70% of the networks kept. The predictive correlations for all variables are included in Table 2, which varied from high to very high.

Evidenced by the absence of a direct or indirect path passing from the variable Group to NDI_12, the effect of NDI_12 was found to be independent from group, conditional on the remaining variables. All pathways leading into NDI_12 passed through neck–arm_pain_3 and SES_6, while originating from head_pain_3 and Anx_3. This implies that headache pain intensity and anxiety at the 3rd month influenced pain-related disability at 12th month follow-up, through the path of neck–arm pain intensity at the 3rd month and self-efficacy levels at the 6th month respectively (Figure 2). From the sampled posterior distribution, a 1-point increase in Anx_3 was associated with a 2.45-point increase in NDI_12 ($t = 77.06$, $p < .001$) (Figure 3); while a one-point increase in head_pain_3 was associated with a 0.08-point increase in NDI_12 ($t = 11.23$, $p < .001$) (Figure 4).

To probe the relationship between Anx_3 and NDI_12, we simulated a scenario when SES_6 and/or neck–arm_pain_3 was not dependent on Anx_3. When the Anx_3 - SES_6 arc was removed by fixing the value of the SES_6 regression coefficients in the local distributions to zero, the effect of Anx_3 of NDI_12 reduced to a $\beta = 0.39$ ($t = 16.31$, $p < .001$) (Figure 5). When the Anx_3–neck–arm_pain_3 arc was removed by fixing the value of neck–arm_pain_3, the effect of Anx_3 of NDI_12 reduced to a $\beta = 2.05$ ($t = 72.30$, $p < .001$) (Figure 5). When both of the aforementioned arcs were removed by fixing the value of the neck–arm_pain_3 and SES_6, the effect of Anx_3 of NDI_12 was removed $\beta = -0.004$ ($t = -0.18$, $p = .85$). Hence, approximately, 16% $\left(\frac{0.39}{2.45}\right)$ of the effect of Anx_3 on NDI_12 was attributable to the anxiety → neck–arm pain → NDI pathway; while approximately 83% $\left(\frac{2.05}{2.45}\right)$ was attributable to the anxiety → self-efficacy → NDI pathway (Figure 5).

To probe the relationship between head_pain_3 and NDI_12, we simulated a scenario where neck–arm_pain_3 was not dependent on head_pain_3, by removing the head_pain_3–neck–arm_pain_3 arc. The scenario was simulated by fixing the value of the neck–arm_pain_3 regression coefficients in the local distributions to zero. When fixing the value of neck–arm_pain_3 to zero, the β coefficient reduced to 0.01 ($t = 1.56$, $p = .119$). Thus, approximately 88% $\left(\frac{0.01}{0.08}\right)$ of the effect of head_pain_3 on NDI_12 was attributable to the head pain → neck–arm pain → NDI pathway.

4 | DISCUSSION

Understanding the mechanisms of action of therapeutic interventions on pain-related disability has the potential to enable
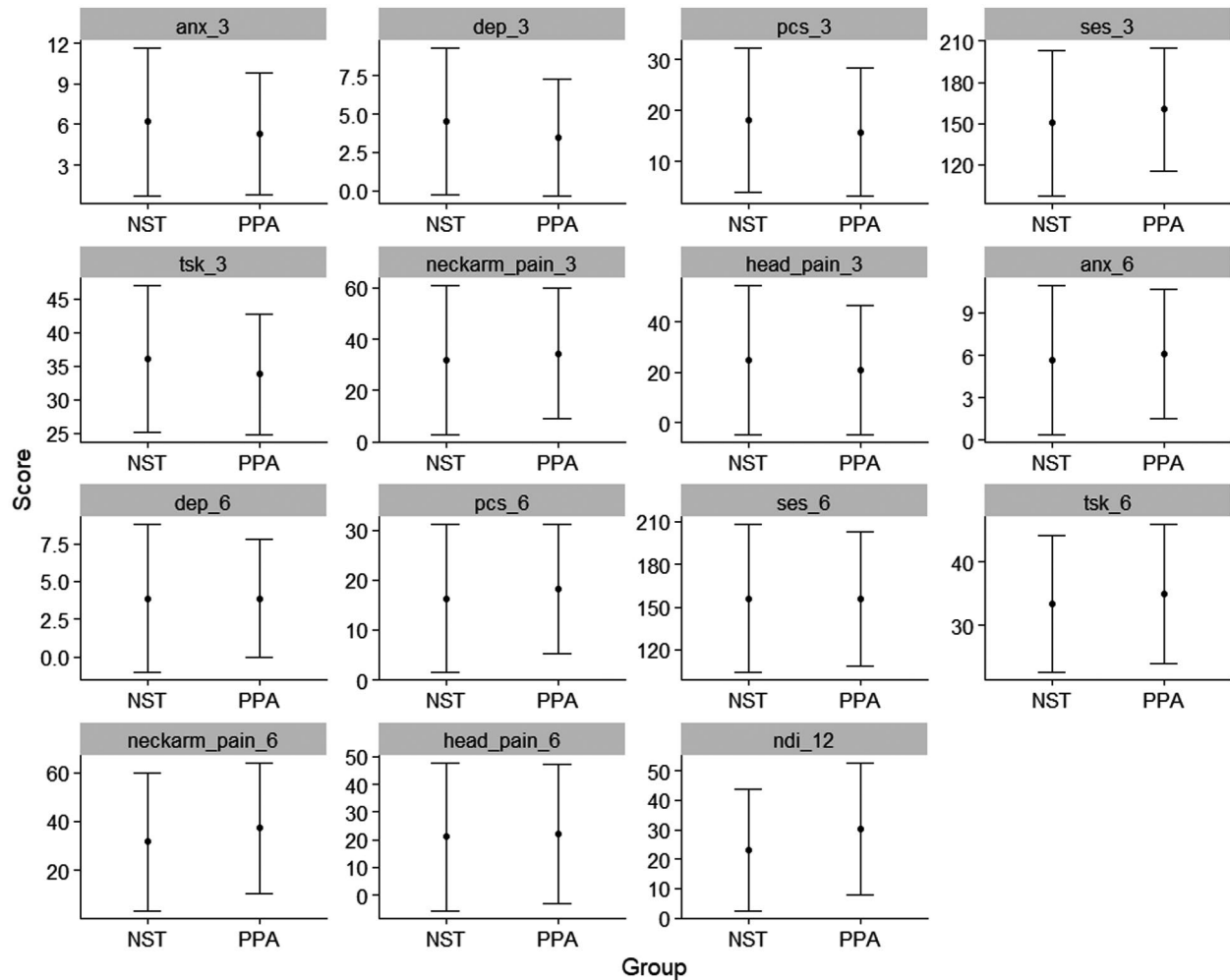
FIGURE 1 Mean and standard deviation of clinical variables used in Bayesian Network model. Abbreviation: Suffix with "_3", variables at 3rd month follow-up; Suffix with "_6", variables at 6th month follow-up; Suffix with "_12", variables at 12th month follow-up; Anx, Hospital Anxiety and Depression Scale, anxiety sub-score; Dep, Hospital Anxiety and Depression Scale, depression sub-score; SES, self-efficacy scale score; PCS, pain catastrophizing scale score; NDI, neck disability index; NST, Neck-Specific Training; PPA, Prescribed Physical Activity

researchers and clinicians to better design specific interventions to manage a complex disorder such as CR. In contrast to our hypothesis, no psychological and pain features mediated the relationship between different therapeutic exercise programs and disability. Interestingly, self-efficacy at 6th months and neck–arm pain at the 3rd month mediated the influence of 3rd month anxiety and headache pain intensity on 12th month disability.

Given that in the original study a significant main effect of time was reported for the effects of anxiety and head pain (Dedering et al., 2018), it would mean that the two presently prescribed interventions were similarly effective in targeting the purported mediators. This could explain why no psychological and pain variables mediated the different treatment programs with respect to the outcome of disability – a finding which contrasted with previous studies investigating different spinal pain disorders (Mansell et al., 2016; Smeets et al., 2006; Spinhoven et al., 2004). In a study on low back pain (LBP) recovery, the mediating influence of catastrophizing was greater when comparing cognitive-based therapy versus no

intervention, than when comparing physical-based rehabilitation versus no intervention (Smeets et al., 2006). However, a direct comparison of the mediating effect of catastrophizing between cognitive-based versus. physical-based treatment was not performed in Smeets et al. (2006). In a psychologically-informed treatment program of individuals with LBP, psychological distress mediated up to 80% of the treatment's effect (relative to an as-needed routine physiotherapy group) on pain-specific disability (Mansell et al., 2016). It maybe that the differential mediating role of psychological variables on disability may be magnified when comparing two contrasting treatment paradigms, such as psychologically informed against activity-based interventions. Not only were the two present treatments activity-based, but both groups received treatment elements (e.g. coping in NST and motivational interviewing in PPA) that could similarly target the presently investigated mediators.

Interestingly, our study revealed the relative greater importance of improvements in self-efficacy than neck–arm pain reductions as a mediator between anxiety and disability.

In contrast to the present finding, a study on chronic whiplash associated disorders (WAD) using BNs reported that self-efficacy partially mediated the greater effect a neck-specific training had on neck pain intensity compared to a general physical activity program (Liew et al., 2019). The different findings between the present study and Liew et al. (2019) occurred despite both studies incorporating similar cognitive behavioural components into the neck-specific training

programs (Dedering et al., 2014; Peolsson et al., 2014). This suggests that the same training program may have different mechanism of action in different musculoskeletal disorders affecting the same spinal region. This may not be surprising given that individuals with CR have different physical deficits and symptoms compared to individuals with WAD.

An important difference between the present finding and that of prior studies is in the relationship that self-efficacy was reported to mediate. For example, self-efficacy mediated the pain intensity–disability relationship in WAD (Söderlund & Åsenlöf, 2010), LBP (Costa Lda et al., 2011), general musculoskeletal chronic pain disorders (Arnstein, 2000; Arnstein et al., 1999) and the fear–disability relationship in LBP (Woby et al., 2007). These studies used traditional regression-based approaches which require testing of a pre-specified structural relationship, the knowledge of which, is driven by theory and the literature (Mansell et al., 2013). This is in contrast where we presently used BNs, a technique which couples both data-driven and theory-driven approaches to uncover structural relationships.

By synergising data- and theory-driven approaches, the present study reported that self-efficacy mediated the anxiety–disability relationship, which has indirect support from the literature. Pain-related anxiety has been conceptualized as a future-oriented emotion that occurs in anticipation of nociception (e.g. the potential of pain from performing a certain task) (Carleton & Asmundson, 2009). One approach

TABLE 1 Mean (standard deviation) of baseline characteristics of cohort

Variables	Included (*n* = 97)	Excluded (*n* = 47)
Age	47.74 (10.05)	49.23 (8.77)
Anxiety	7.04 (5.27)	6.32 (3.75)
Depression	4.85 (4.5)	3.81 (2.55)
Head pain intensity	27.69 (27.21)	23.96 (29.42)
Neck–arm pain intensity	41.72 (25.31)	37.07 (22.41)
Pain catastrophizing	21.42 (12.74)	20.59 (10.68)
Self-efficacy	140.78 (55.11)	153.64 (36.78)
Kinesiophobia	36.53 (9.31)	36.63 (7.62)

Note: Included – included into the network analysis; Excluded – excluded from network analysis
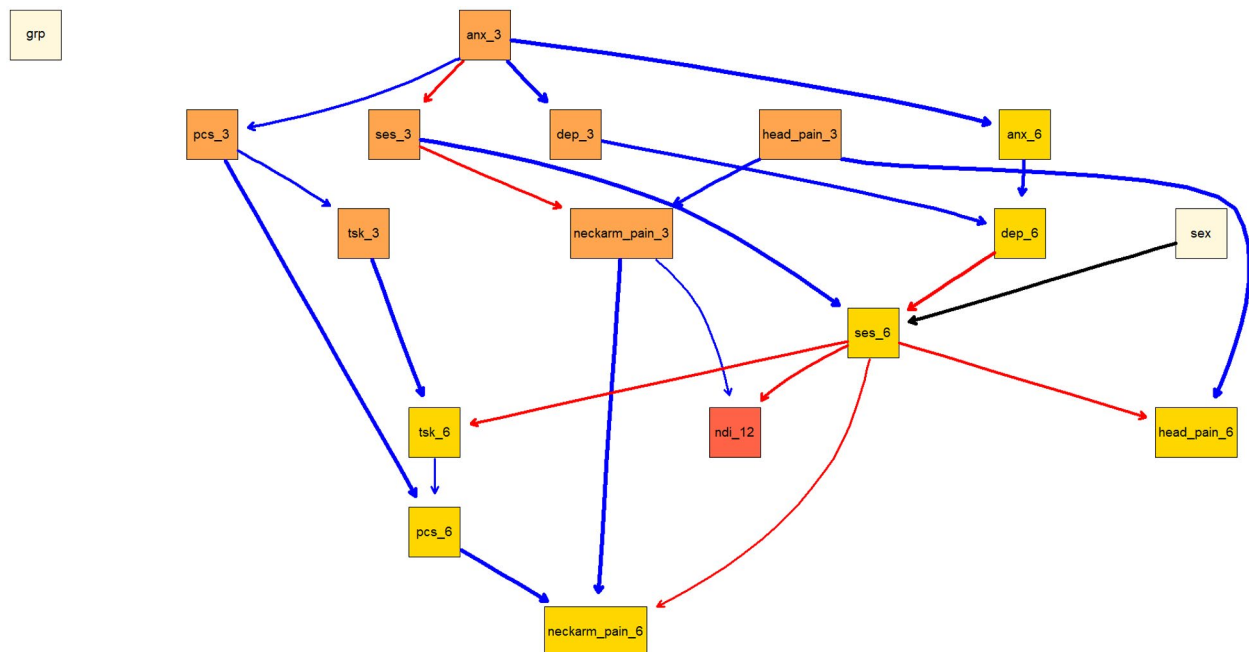
FIGURE 2 The directed acyclic graph (DAG) underlying the consensus Bayesian Network of learned from the variables across 97 participants. Abbreviation: Suffix with "_3", variables at 3rd month follow-up; Suffix with "_6", variables at 6th month follow-up; Suffix with "_12", variables at 12th month follow-up; Anx, Hospital Anxiety and Depression Scale, anxiety sub-score; Dep, Hospital Anxiety and Depression Scale, depression sub-score; SES, self-efficacy scale score; PCS, pain catastrophizing scale score; NDI, neck disability index; Grp, group. Arrows in blue indicate a positive β correlation relationship (i.e. positive relationship), while arrows in red indicate a negative β correlation relationship. Arrow sex -> ses_6 is black as sex is a categorical variable

to managing pain-related anxiety is Acceptance and Commitment Therapy (ACT) which focuses on concepts of mindfulness, acceptance and values-based action (Carleton & Asmundson, 2012). There is some evidence that changes in self-efficacy is a mechanism by which ACT positively influenced the outcome of disability in a heterogeneous cohort of individuals with musculoskeletal pain disorders (Craner et al., 2020), although it is inconsistent (Wicksell et al., 2010).

Independent studies from a heterogeneous group of individuals with musculoskeletal pain disorders have identified self-efficacy as an important mechanism driving recovery (Fordham et al., 2017; Liew et al., ,2019, 2020; Mansell

TABLE 2 Correlation between observed and predicted values

Variable	Value	Strength
anx_3	0.92	very high
dep_3	0.89	high
pcs_3	0.88	high
ses_3	0.94	very high
tsk_3	0.83	high
neckarm_pain_3	0.71	high
head_pain_3	0.83	high
anx_6	0.91	very high
dep_6	0.86	high
pcs_6	0.90	high
ses_6	0.97	very high
tsk_6	0.85	high
neckarm_pain_6	0.88	high
head_pain_6	0.83	high
ndi_12	0.86	high

Abbreviations: anx, anxiety; dep, depression; pcs, pain catastrophizing; ses, self-efficacy; tsk, kinesiophobia; NDI, neck disability index; _3, 3rd month follow up; _6, 6th month follow-up; _12, 12th month follow-up.
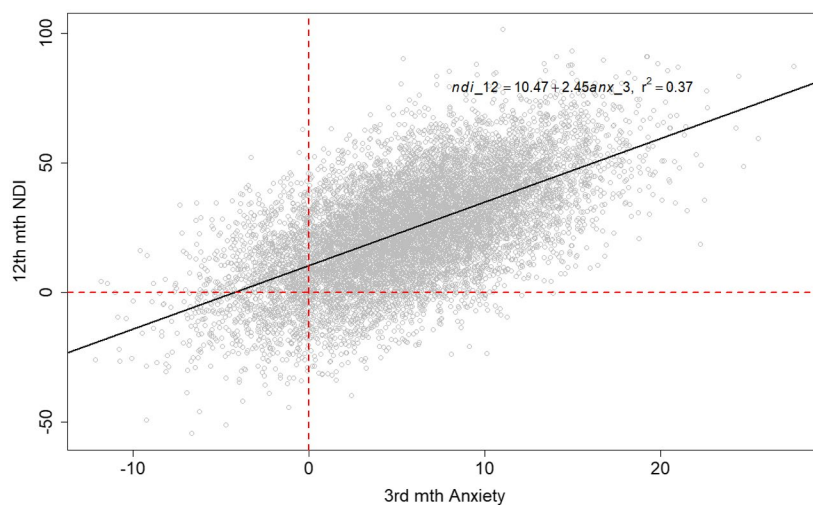
et al., 2016; O'Neill et al., 2020; Sherman et al., 2013). Given its importance, it may be prudent to speculate on the reasons underpinning the importance of self-efficacy as a mediator. Given that self-efficacy reflects a person's confidence about their abilities to successfully perform a task, it may be that individuals with higher self-efficacy have higher treatment adherence than those with lower self-efficacy. Greater treatment adherence results in greater therapeutic dosage, which may improve recovery (Hayden et al., 2005). Alternatively, greater self-efficacy may modulate the sensory pain processing mechanisms to confer a greater pain tolerance threshold to patients (Bandura et al., 1987; Dolce et al., 1986; Söderlund & Sterling, 2016). An under investigated area of research is the potential influence of self-efficacy in modulating the motor pathways. For example, individuals with high fear of movement experience greater trunk stiffness, increasing spinal loads, thus contributing to pain (Karayannis et al., 2013). It may be that individuals who are confident in moving, do so with more optimal motor control which optimizes tissue loading, thus aiding in recovery.

Despite the novelty of the present findings, the study is not without limitations. An important limitation is that we have not included all candidate variables into the BN model, particularly physical factors (e.g. cervical mobility). Realistically, the number of variables included into a BN model must depend not only on prior knowledge but should also consider the burden on patients when collecting a large battery of outcome measures. Hence, we view the relationships learnt in this study within a modular framework, as a component within a potentially more complex causal network of relationships (Fenton & Neil, 2012), which potentially encompasses biological, psychological and sociological factors. Future mediation studies would benefit from the present study's methods, given the capacity to build and compare competing models, to evaluate which model best fits the data.

$$ndi\_12 = 10.47 + 2.45anx\_3, \quad r^2 = 0.37$$

FIGURE 3 Posterior samples of neck disability index at 12th month (NDI_12) and anxiety at 3rd month (Anx_3) of the Bayesian Network model, with associated linear relationship. Each data point represents a simulated sample from the BN model

FIGURE 4 Posterior samples of neck disability index at 12th month (NDI_12) and headache pain at 3rd month (headpain_3) of the Bayesian Network model, with associated linear relationship. Each data point represented a simulated sample from the BN model

The plot shows: $ndi\_12 = 22.44 + 0.08 head\_pain\_3$, $r^2 = 0.01$
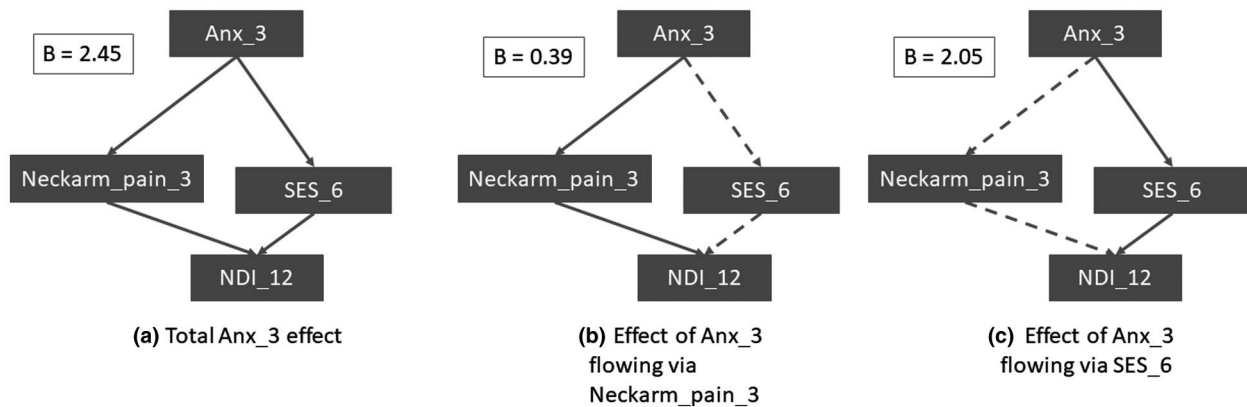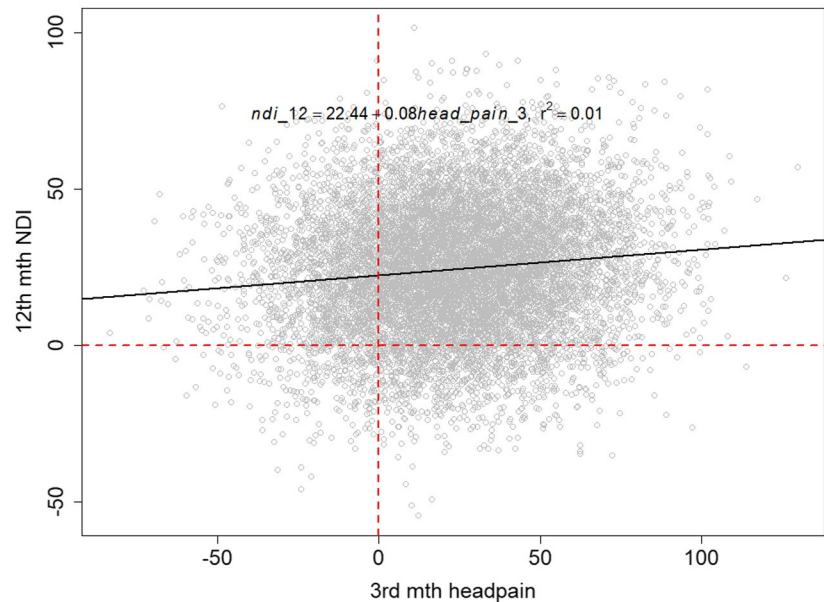
FIGURE 5 Contribution of different pathways from Anx_3 to NDI_12. (a) Total effect Anx_3 has on NDI_12, (b) effect Anx_3 has on NDI_12 flowing through neckarm_pain2 and (c) effect Anx_3 has on NDI_12 flowing through SES_6. Abbreviation: _3, 3rd month value; _6, 6th month value; _12, 12th month value; SES, Self-Efficacy Scale; Neckarm_pain, combined neck and arm pain intensity; NDI, Neck disability index

5 | CONCLUSIONS

No psychological or pain-related variables mediated the different treatment programs with respect to the outcome of disability. Thus, the specific characteristics investigated in this study did not explain the differences in mechanisms of effect between neck-specific training and prescribed physical activity. Improvements in self-efficacy were more important than the reduction in neck–arm pain intensity in mediating the anxiety–disability relationship. The present study provides candidate modifiable mediators that could be the target of future intervention trials. Given the growing evidence of the importance of self-efficacy as a mechanism driving recovery in musculoskeletal pain disorders, future studies should investigate the reasons underpinning its action.

CONFLICT OF INTEREST
The authors have no conflicts of interest to declare.

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