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EXTENDED ABSTRACT

What are the predictors of clinical improvement in adolescents with chronic neck pain after pain neuroscience education and exercise? – secondary analysis of a randomized controlled trial

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Introduction:

Among the different painful chronic musculoskeletal conditions that affect adolescents, neck pain (NP) has emerged as one of the most prevalent, reaching up to 29.5% of adolescents aged 16 to 18 years old [1,2]. Several factors such as female gender, older age and high levels of disability have been associated with NP persistence and disability in this age group [3,4], raising doubts as to whether they influence the improvement of adolescents with NP in response to rehabilitation. Studies exploring NP management in adolescents are scarce [5]. A recent study by our team [6] suggested that interventions based on pain neuroscience education (PNE) and exercise are similarly effective. However, we were unable to find any studies that explored factors of treatment response in adolescents with NP. Thus, this study aimed to explore whether sociodemographic data, pain characteristics, physical activity, psychosocial factors, sleep, symptoms of central sensitization, pressure pain thresholds and neck muscles endurance at baseline predicted clinical improvement when using different standards: the Patient Global Impression of Change (PGIC) scale and the minimal change in the Numeric Pain Rating Scale (NPRS) for pain intensity and the Functional Disability Inventory (FDI) for disability, at post-intervention and 6-month follow-up.

Methods:

This study is a secondary analysis of a randomized controlled trial (6) conducted with 127 adolescents with chronic NP. Pain intensity, disability, physical activity, sleep, catastrophizing, fear of movement, and self-efficacy were assessed at baseline, post-intervention, and 6-month follow-up. Pressure pain thresholds and neck muscles endurance were assessed only at baseline and post-intervention. Impression of change (PGIC scale) was assessed at post-intervention and 6-month follow-up. To classify adolescents who improved from baseline to post-intervention and 6-month follow-up, different clinical improvement criteria were used: i) reporting a PGIC≥5 (moderately better, better, or a great deal better), ii) ≥50% reduction of pain intensity in the NPRS, iii) ≥50% reduction of disability in the FDI, and iv) ≥50% reduction in the NPRS and in the FDI, from baseline levels. Independent logistic-regression analyses were used to examine univariable and multivariable associations between the independent and dependent (clinical improvement) variables. The multivariable analyses were performed using Forward LR method and the significance level was set at $p<0.10$ and $p<0.05$ for univariable and multivariable analyses, respectively. The Nagelkerke R2 statistic was reported as an indication of the proportion of variance in the odds of a clinical improvement, which is explained by all of the significant variables in each multivariable model. The reported analyses were repeated for post-intervention and 6-month follow-up. All statistical analyses were performed using SPSS Software, version 22.0.

Results:

The characterization of adolescents with chronic neck pain is shown in table 1. At post-intervention, 72%(n=91) of the adolescents were classified as PGIC≥5, 52%(n=66) with improvements in the NPRS, 39%(n=50) with improvements in the FDI and 26%(n=33) with improvements in both NPRS and FDI. In the univariable models, i) older age was associated with decreased likelihood of improvement (OR=0.57, OR=0.70, $p<0.05$) using the PGIC and FDI scales, respectively and ii) moderate physical activity (OR=1.00, $p<0.10$) was associated with increased likelihood of improvement using the FDI. A multivariable model was found for the improvement of 50% in the FDI in which older age (OR=0.64, $p<0.05$) and

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moderate physical activity (OR=1.00, p<0.05) remained associated with decreased and increased likelihood of improvement, respectively (Nagelkerke R2 =0.12) (Table 2).

At 6-month follow-up, 69%(n=88) of the adolescents were classified as PGIC≥5, 54%(n=68) with improvements in the NPRS, 45%(n=57) with improvements in the FDI and 32%(n=40) with improvements in both NPRS and FDI. In the univariable models, i) older age (OR=0.70, p<0.10) was associated with decreased likelihood of improvement using the PGIC, ii) longer pain duration (OR=0.08, p<0.05), higher disability (OR=0.94, p<0.05) and more symptoms of central sensitization (OR=0.97, p<0.10) were associated with decreased likelihood of improvement and higher pressure pain thresholds (OR=1.04, p<0.10) was associated with increased likelihood of improvement using the NPRS, iii) having pain often (OR=0.21, p<0.05) was associated with decreased likelihood of improvement and higher neck flexors endurance (OR=1.07, p<0.10) with increased likelihood of improvement using the FDI, iv) having pain sometimes and often (OR=0.28 and OR=0.26, p<0.05) was associated with a decreased likelihood of improvement using NPRS and FDI. A multivariable model was found for the improvement of 50% in the NPRS ((Table 3) in which higher disability (OR=0.94, p<0.05) remained associated with decreased likelihood of improvement (Nagelkerke R2 =0.05) and for the improvement of 50% in the FDI (Table 2) in which having pain often (OR=0.23, p<0.05) and higher neck flexors endurance (OR=1.07, p<0.05) were associated with decreased and increased likelihood of improvement, respectively (Nagelkerke R2 =0.11).

Conclusions:

Taken together, our findings suggest that there are different factors associated with clinical improvement depending on the outcome used to categorize this improvement, but factors such as age, pain characteristics, disability, symptoms of central sensitization, pressure pain thresholds and neck muscle endurance seem to be relevant in the improvement of neck pain in adolescents at post-intervention and 6-month follow-up. However, considering the low explanatory percentage of the models found, other factors not included in this study should be considered in the assessment of these adolescents, such as parental factors.

Table 1 - Characterization of adolescents with chronic neck pain at baseline, post-intervention, and 6-month follow-up.

		Baseline (N=127)	**Post-intervention** (N=118)	**6-month follow-up** (N=117)
Sex	Female	109 (85.8%)	101 (85.6%)	99 (84.6%)
	Male	18 (14.2%)	17 (14.4%)	18 (15.4%)
Age (years)	Mean (SD)	16.06 (1.8)	16.44 (1.08)	16.92 (1.16)
BMI (Kg/m^2)	Mean (SD)	22.3 (4.0)	22.42 (4.1)	22.54 (3.8)
Scholar level (N, %)	10th	41 (32.3%)	39 (33.1%)	38 (32.5%)
	11th	52 (40.9%)	48 (40.7%)	48 (41.0%)
	12th	34 (26.8%)	31 (26.3%)	31 (26.5%)
Pain frequency (N, %)	Never	17 (13.4%)	26 (22.0%)	49 (41.9%)
	Sometimes	61 (48.0%)	59 (50.0%)	32 (27.4%)
	Oftentimes	36 (28.3%)	23 (19.5%)	29 (24.8%)
	Always	13 (10.2%)	10 (8.5%)	7 (6.0%)
Pain duration (N, %)	3 to 6 months	31 (24.4%)	--	--
	6 months to 1 year	24 (18.9%)		
	1 to 2 years	41 (32.3%)		
	2 to 5 years	24 (18.9%)		
	>5 years	7 (5.5%)		
Moderate PA (minutes/week)	Mean (SD)	197.05 (286.18)	185.00(198.02)	198.68 (237.08)
Vigorous PA (minutes/week)	Mean (SD)	137.65 (233.28)	140.85 (224.19)	166.45 (281.49)
NPRS (0-10)	Mean (SD)	4.51 (1.86)	2.44 (2.07)	2.24 (1.96)
FDI (0-60)	Mean (SD)	10.34 (6.55)	7.47 (7.02)	6.25 (6.92)
BaSIQS (0-28)	Mean (SD)	11.71 (4.63)	11.08 (4.72)	10.97 (4.72)
PCS (0-52)	Mean (SD)	13.48 (8.54)	11.29 (9.14)	9.63 (8.02)
TSK (13-52)	Mean (SD)	25.80 (5.52)	23.78 (5.96)	23.02 (5.90)
CSES (7-35)	Mean (SD)	17.17 (5.06)	15.83 (5.24)	15.50 (5.42)
CSI (0-100)	Mean (SD)	36.31 (12.90)	32.65 (13.55)	30.44 (13.94)
NPQ (0-12)	Mean (SD)	4.25 (1.84)	6.24 (2.32)	5.83 (2.50)
PPT (N/cm^2)	Right articular pillar C5/C6	21.10 (10.03)	--	--
	Left articular pillar C5/C6	19.37 (9.64)		
	Tibialis anterior	38.22 (13.89)		
Endurance tests (seconds)	Neck flexors	10.33 (6.00)		
	Neck extensors	116.54 (74.23)		
	Scapular stabilizers	33.56 (24.59)		

BMI, Body Mass Index; PA, Physical Activity (assessed with the International Questionnaire of Physical Activity for Adolescents); NPRS, Numeric Pain Rating Scale; FDI, Functional Disability Inventory; BaSIQS, Basic Scale on Insomnia complaints and Quality of Sleep; PCS, Pain Catastrophizing Scale; TSK, Tampa Scale of Kinesiophobia; CSES, Child Self-Efficacy Scale; CSI, Central Sensitization Inventory; NPQ, Pain Neurophysiology Questionnaire; PPT, Pressure Pain Thresholds

Table 2 - Results from univariable and multivariable models predicting ≥50% improvement in disability.

Predictors	Univariable models				Multivariable models			
	Post-intervention N=117		6-month follow-up N=118		Post-intervention Nagelkerke R^2=0.12		6-month follow-up Nagelkerke R^2=0.11	
	OR (95%CI)	*p*	OR (95%CI)	*p*	OR (95%CI)	*p*	OR (95%CI)	*p*
Female sex	1.42 (0.49-4.12)	0.53	0.55 (0.20-1.54)	0.26				
Age	0.70 (0.49-1.01)	0.05*	0.82 (0.59-1.15)	0.26	0.64 (0.44-0.93)	0.02**		
BMI	1.02 (0.93-1.12)	0.69	0.95 (0.87-1.05)	0.30				
Pain frequency								
Sometimes	1.43 (0.48-4.29)	0.53	0.39 (0.12-1.25)	0.11				
Oftentimes	0.51 (0.15-1.76)	0.29	0.24 (0.07-0.84)	0.03**			0.23 (0.06-0.82)	0.02**
Always	1.71 (0.37-7.92)	0.49	0.50 (0.10-2.43)	0.39				
Pain duration								
6 months to 1 year	0.93 (0.32-2.77)	0.90	0.63 (0.21-1.88)	0.40				
1 to 2 years	1.05 (0.39-2.78)	0.93	0.81 (0.31-2.14)	0.68				
2 to 5 years	0.98 (0.32-3.03)	0.97	0.81 (0.26-2.54)	0.72				
>5 years	0.52 (0.09-3.14)	0.48	0.33 (0.05-1.96)	0.22				
NPRS	0.91 (0.74-1.11)	0.33	1.04 (0.85-1.26)	0.72				
Moderate PA	1.00 (0.99-1.00)	0.07*	1.00 (0.99-1.00)	0.71	1.00 (1.00-1.01)	0.04**		
Vigorous PA	1.00 (0.99-1.00)	0.35	1.00 (0.99-1.00)	0.58				
FDI	0.99 (0.94-1.05)	0.84	0.96 (0.91-1.01)	0.14				
BaSIQS	1.04 (0.96-1.13)	0.35	0.99 (0.92-1.07)	0.84				
PCS	0.96 (0.92-1.01)	0.11	1.00 (0.96-1.05)	0.87				
TSK	0.98 (0.92-1.05)	0.58	0.99 (0.92-1.06)	0.69				
CSES	0.97 (0.90-1.05)	0.49	1.01 (0.94-1.09)	0.73				
CSI	1.00 (0.98-1.03)	0.79	0.99 (0.96-1.02)	0.46				
NPQ	1.16 (0.95-1.41)	0.15	1.00 (0.82-1.21)	0.96				
PPT-Right articular pillar C5/C6	1.00 (0.96-1.03)	0.90	1.01 (0.98-1.05)	0.48				
PPT-Left articular pillar C5/C6	1.00 (0.96-1.04)	0.91	1.03 (0.99-1.07)	0.17				
PPT-Tibialis anterior	0.99 (0.96-1.02)	0.44	1.00 (0.98-1.03)	0.77				
Endurance tests								
Neck flexors	1.05 (0.98-1.12)	0.14	1.07 (0.99-1.14)	0.06*			1.07 (1.00-1.15)	0.046**
Neck extensors	1.00 (0.99-1.01)	0.24	1.00 (0.99-1.01)	0.13				
Scapular stabilizers	1.00 (0.99-1.02)	0.74	1.01 (0.99-1.03)	0.22				

*p ≤ 0.1, **p<0.05. OR, Odds Ratio; CI, Confidence Interval; BMI, Body Mass Index; PA, Physical Activity (assessed with the International Questionnaire of Physical Activity for Adolescents); NPRS, Numeric Pain Rating Scale; FDI, Functional Disability Inventory; BaSIQS, Basic Scale on Insomnia complaints and Quality of Sleep; PCS, Pain Catastrophizing Scale; TSK, Tampa Scale of Kinesiophobia; CSES, Child Self-Efficacy Scale; CSI, Central Sensitization Inventory; NPQ, Pain Neurophysiology Questionnaire; PPT, Pressure Pain Thresholds

Table 3 - Results from univariable and multivariable models predicting ≥50% improvement in pain intensity

Predictors	Univariable models				Multivariable models	
	Post-intervention N=117		6-month follow-up N=118		6-month follow-up Nagelkerke R^2=0.05	
	OR (95%CI)	*p*	OR (95%CI)	*p*	OR (95%CI)	*p*
Female sex	0.87 (0.31-2.47)	0.80	0.65 (0.23-1.88)	0.43		
Age	0.88 (0.63-1.23)	0.45	0.80 (0.57-1.13)	0.21	0.64 (0.44-0.93)	0.02**
BMI	1.00 (0.91-1.10)	0.99	1.00 (0.91-1.09)	0.97		
Pain frequency						
Sometimes	1.37 (0.46-4.10)	0.57	0.52 (0.16-1.66)	0.27		
Oftentimes	0.70 (0.22-2.26)	0.55	0.39 (0.11-1.36)	0.14		
Always	2.37 (0.46-12.14)	0.30	1.88 (0.29-11.97)	0.51		
Pain duration						
6 months to 1 year	0.77 (0.26-2.25)	0.63	0.49 (0.16-1.53)	0.22		
1 to 2 years		0.55	0.77 (0.28-2.15)	0.62		
2 to 5 years	0.70 (0.23-2.13)	0.53	0.55 (0.17-1.79)	0.32		
>5 years	1.02 (0.19-5.37)	0.98	0.08 (0.01-0.72)	0.03**		
NPRS	1.09 (0.89-1.33)	0.40	1.08 (0.89-1.32)	0.44		
Moderate PA	1.00 (0.99-1.00)	0.45	1.00 (0.99-1.00)	0.81		
Vigorous PA	1.00 (0.99-1.00)	0.19	1.00 (0.99-1.00)	0.67		
FDI	0.98 (0.93-1.04)	0.54	0.94 (0.89-1.00)	0.05*	0.94 (0.89-1.00)	0.049**
BaSIQS	1.02 (0.94-1.10)	0.68	0.95 (0.88-1.03)	0.22		
PCS	1.00 (0.96-1.05)	0.94	0.97 (0.93-1.02)	0.23		
TSK	0.96 (0.90-1.03)	0.27	0.97 (0.91-1.04)	0.42		
CSES	0.95 (0.88-1.03)	0.21	0.94 (0.87-1.02)	0.14		
CSI	0.98 (0.95-1.01)	0.14	0.97 (0.94-1.00)	0.06*		
NPQ	1.05 (0.87-1.28)	0.62	0.89 (0.73-1.09)	0.27		
PPT-Right articular pillar C5/C6	1.01 (0.98-1.05)	0.51	1.04 (0.996-1.08)	0.08*		
PPT-Left articular pillar C5/C6	1.01 (0.97-1.05)	0.56	1.04 (0.996-1.08)	0.08*		
PPT-Tibialis anterior	1.01 (0.99-1.04)	0.34	1.02 (0.995-1.05)	0.12		
Endurance tests						
Neck flexors	1.02 (0.96-1.08)	0.62	1.04 (0.97-1.11)	0.28		
Neck extensors	1.00 (0.99-1.00)	0.20	1.00 (0.99-1.01)	0.52		
Scapular stabilizers	1.00 (0.99-1.02)	0.86	1.00 (0.99-1.02)	0.71		

*p ≤ 0.1, **p<0.05. OR, Odds Ratio; CI, Confidence Interval; BMI, Body Mass Index; PA, Physical Activity (assessed with the International Questionnaire of Physical Activity for Adolescents); NPRS, Numeric Pain Rating Scale; FDI, Functional Disability Inventory; BaSIQS, Basic Scale on Insomnia complaints and Quality of Sleep; PCS, Pain Catastrophizing Scale; TSK, Tampa Scale of Kinesiophobia; CSES, Child Self-Efficacy Scale; CSI, Central Sensitization Inventory; NPQ, Pain Neurophysiology Questionnaire; PPT, Pressure Pain Thresholds

Ethics committee and informed consent:

The current research was approved by an independent ethics committee and subjects gave their informed consent before they were enrolled in the study.

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