Universidade de Aveiro

ANO 2021

Rosa Maria de Sousa Andias

DOR CERVICAL CRÓNICA EM ESTUDANTES DO SECUNDÁRIO: CARACTERIZAÇÃO E EFETIVIDADE DA EDUCAÇÃO EM NEUROCIÊNCIA DA DOR E EXERCÍCIO

CHRONIC NECK PAIN IN HIGH SCHOOL STUDENTS: CHARACTERIZATION AND EFFECTIVENESS OF PAIN NEUROSCIENCE EDUCATION AND EXERCISE

Universidade de Aveiro Escola Superior de Saúde

ANO 2021

Rosa Maria de Sousa Andias

DOR CERVICAL CRÓNICA EM ESTUDANTES DO SECUNDÁRIO: CARACTERIZAÇÃO E EFETIVIDADE DA EDUCAÇÃO EM NEUROCIÊNCIA DA DOR E EXERCÍCIO

CHRONIC NECK PAIN IN HIGH SCHOOL STUDENTS: CHARACTERIZATION AND EFFECTIVENESS OF PAIN NEUROSCIENCE EDUCATION AND EXERCISE

Tese apresentada à Universidade de Aveiro para cumprimento dos requisitos necessários à obtenção do grau de Doutor em Ciências da Reabilitação, realizada sob a orientação científica da Doutora Anabela Gonçalves da Silva, Professora Adjunta da Escola Superior de Saúde da Universidade de Aveiro.

This work is part of a PhD scholarship from the Portuguese Foundation for Science and Technology (FCT- Fundação para a Ciência e Tecnologia) (SFRH/BD/119528/2016).

o júri

presidente

Prof. Doutor António Manuel Melo de Sousa Pereira
Professor Catedrático da Universidade de Aveiro

Prof. Doutor Eduardo José Brazete Carvalho Cruz
Professor Coordenador da Escola Superior de Saúde de Setúbal – Instituto Politécnico de Setúbal

Prof. Doutor Felipe José Jandre dos Reis
Professor Associado do Instituto Federal do Rio de Janeiro

Prof. Doutora Maria Amélia Alves do Paço
Professor Adjunta Principal da Escola Superior de Saúde do Vale do Ave

Prof. Doutor Mário Alexandre Gonçalves Lopes
Professor Adjunto da Universidade de Aveiro

Prof. Doutora Anabela Gonçalves da Silva (Orientadora)
Professor Adjunta da Universidade de Aveiro

Acknowledgements

O presente projeto de investigação não teria sido possível sem a ajuda, incentivo e colaboração de diversas pessoas e instituições, às quais não posso deixar de proferir o que profundo agradecimento.

À minha orientadora Professora Doutora Anabela Silva por me ter dado a oportunidade de a acompanhar em mais 4 anos de aprendizagem! Muito obrigada pela extensa partilha de conhecimentos, orientação e disponibilidade, por ter acreditado, ainda antes de mim, que este caminho seria possível de percorrer. Foi também com carinho e com o dom da palavra que tranquilizou os momentos de maior dificuldade e sem ela eu não teria chegado até aqui.

Aos meus pais, Lurdes e Luís, e ao meu irmão, Luís, os meus pilares e fontes de inspiração que foram mais uma vez o grande suporte e o abraço de aconchego deste longo caminho. Ao meu Engenheiro Tomé, mais um pilar basilar da minha vida e deste projeto. O Tomé dedicou muito tempo a ajudar-me a otimizar várias das ferramentas e recursos deste projeto e foi também com a sua sabedoria e apoio incondicional que alcancei os objetivos a que me propus. À Bianca, a amiga e designer que, para além do apoio e das palavras de incentivo, criou todas as ilustrações usadas neste projeto. À Dra. Annina Schmid e à sua equipa de investigação que me receberam em Oxford numa semana repleta de aprendizagens e ao colega Carlos que me orientou em todo esse percurso. A toda a minha restante família e família do coração, os meus amigos, que nunca deixaram de estar presentes para me apoiar e motivar, mesmo nos períodos de maior ausência. A todas as minhas estrelinhas do céu que guiam e iluminam o meu caminho todos os dias. A todos os colegas e amigos de trabalho pelo apoio constante, com um especial obrigada às fisioterapeutas Patrícia e à Ana que ainda dispensaram algum do seu tempo a ajudar-me nas recolhas iniciais deste projeto. E por fim, mas não menos importante, à direção, professores, auxiliares educativas e alunos participantes de todas as escolas envolvidas neste projeto. Sem a ajuda, dedicação e paciência de todas estas pessoas, nada teria sido possível de realizar

A todos vós, um Muito Obrigada de coração por terem tornado este caminho possível e mais fácil de percorrer!

Este projeto foi financiado por uma bolsa de doutoramento da Fundação para a Ciência e Tecnologia, Portugal (SFRH/BD/119528/2016).

Palavras-chave Dor Cervical Crónica; Adolescentes; Fatores Psicossociais; Fatores Funcionais; Exercício; Educação em Neurociência da Dor

Resumo

A prevalência da dor cervical crónica idiopática em jovens está a aumentar e é a principal queixa de dor musculoesquelética em adolescentes. A dor cervical resulta em limitações das atividades da vida diária e é um fator de risco para dor cervical na idade adulta. Esta condição também tem sido associada a fatores funcionais e psicossociais, incapacidade, alterações do sono e sensibilização central. No entanto, são escassos os estudos que caracterizam os adolescentes com dor cervical comparativamente a assintomáticos ou adolescentes com outras condições de dor musculoesquelética, ou exploram os fatores associados à dor cervical atual e futura e à incapacidade. Também existe falta de evidência sobre a efetividade da fisioterapia na gestão da dor cervical em adolescentes. Assim, os dois principais objetivos deste projeto de investigação foram i) caracterizar a dor cervical e as alterações psicossociais e funcionais associadas, incapacidade, sono e sintomas auto-referidos de sensibilização central, em adolescentes e ii) avaliar a efetividade da Educação em Neurociência da Dor (END) e exercício versus exercício em adolescentes com dor cervical. Este projeto de pesquisa consiste em duas revisões sistemáticas da literatura (Capítulos 3 e 4), que revisaram as evidências sobre a associação entre alterações funcionais e psicossociais, sono e sensibilização central e dor cervical em adolescentes; três estudos observacionais (Capítulos 5, 6 e 7), que exploraram os fatores associados à dor cervical e incapacidade (Capítulo 5), os fatores associados à persistência de dor cervical e incapacidade no acompanhamento de 6 meses (Capítulo 6) e com o novo início da dor cervical aos 6 meses de acompanhamento em adolescentes (Capítulo 7); e um ensaio clínico randomizado (Capítulo 8) que avaliou a eficácia do END e do exercício versus exercício, no pós-intervenção e no acompanhamento de 6 meses, em adolescentes com dor cervical, em contexto escolar. Nos capítulos 3 e 4 foram encontradas evidências muito limitadas a limitadas sugerindo que a depressão, ansiedade e stress, catastrofização, baixa autoeficácia, alterações do sono, alterações musculares e propriocetivas e baixos limiares de dor estão associados à dor cervical em adolescentes. Os Capítulos 5 e 6 destacaram que o sexo feminino, fatores psicossociais, incapacidade, atividade física, sono e sintomas auto-referidos de sensibilização central estão associados à dor cervical e incapacidade e à sua persistência aos 6 meses, e o Capítulo 7 destacou a associação destes fatores com o novo início de dor cervical, especificamente, o sono e sintomas auto-referidos de sensibilização central. O Capítulo 8 sugeriu que o exercício e exercício mais END foram igualmente eficazes no tratamento de adolescentes com dor cervical. Esses achados apoiam a inclusão dos fatores psicossociais, incapacidade, atividade física, sono e sintomas auto-referidos de sensibilização central na avaliação de adolescentes com dor cervical, e a necessidade da sua avaliação preventiva em adolescentes assintomáticos. Além disso, incentiva a aplicação de intervenções baseadas em exercício e exercício mais END para a gestão da dor cervical crónica em adolescentes, no ambiente escolar.

Keywords Chronic Neck Pain; Adolescents; Psycosocial factors; Functional factors; Exercise; Pain Neuroscience Education

Abstract

The prevalence of chronic idiopathic neck pain (NP) in young people is increasing and it is the leading musculoskeletal complaint in adolescents. NP results in limitations of daily living activities and is a risk factor for having NP in adulthood. It has also been reported to be associated with functional and psychosocial factors, disability, impaired sleep, and central sensitization. However, studies characterizing adolescents with NP compared to asymptomatic or to adolescents with other musculoskeletal pain conditions or exploring the factors associated with current and future NP and disability are scarce. There is also a lack of evidence on the effectiveness of physical therapy management of NP in adolescents. Therefore, the two main aims of this research project were i) to characterize NP and associated psychosocial and functional changes, disability, sleep, and self-reported symptoms of central sensitization in adolescents and ii) to assess the effectiveness of Pain Neuroscience Education (PNE) and exercise compared to exercise only for adolescents with NP. This research project consists of two systematic reviews of the literature (Chapters 3 and 4), which reviewed the evidence on the association between functional and psychosocial changes, sleep, and central sensitization and NP in adolescents; three observational studies (Chapters 5, 6, and 7), which explored the factors associated both with NP and disability (Chapter 5), the factors associated with the persistence of chronic NP and disability at 6-month follow-up (Chapter 6) and with the new onset of NP at 6-month follow-up in adolescents (Chapter 7); and one randomized controlled trial (Chapter 8) which assessed the effectiveness of PNE and exercise compared to exercise only at post-intervention and at 6-month follow-up in adolescents with NP, at the school setting. Chapters 3 and 4 found very limited to limited evidence suggesting that depression, anxiety and stress, catastrophizing, poor self-efficacy, sleep impairments, deficits in muscle function and proprioception, and low pain thresholds are associated with NP in adolescents. Chapters 5 and 6 highlighted that female sex, psychosocial factors, disability, physical activity, sleep, and self-reported symptoms of central sensitization are associated with chronic NP and disability and its persistence at 6 months, and Chapter 7 further highlighted the association of these factors for the new onset of NP, specifically, sleep and self-reported symptoms of central sensitization. Chapter 8 suggested that exercise and exercise plus PNE were similarly effective in treating adolescents with NP. These findings support the inclusion of psychosocial factors, disability, physical activity, sleep, and self-reported symptoms of central sensitization in the assessment of adolescents with NP, and the need for their preventive assessment in asymptomatic adolescents. Furthermore, it encourages the application of interventions based on exercise and exercise plus PNE for the management of chronic NP in adolescents, at the school setting.

Publications within the scope of the thesis

Articles published and submitted to peer-reviewed journals

- Andias, R. & Silva, AG. (2019). “A systematic review with meta-analysis on functional changes associated with neck pain in adolescents”. Musculoskeletal Care, 17(1):23-26.
- Andias, R. & Silva, AG. (2019). Psychosocial variables and sleep associated with neck pain in adolescents: a systematic review. Physical & Occupational Therapy in Pediatrics, 40(2):168-191.
- Andias, R.; Monteiro J.; Santos, B. & Silva, AG. (2019). European Portuguese version of the Functional Disability Inventory: translation and cultural adaptation, validity and reliability in adolescents with chronic spinal pain. Disability and Rehabilitation, 10:1-8.
- Andias, R. & Silva, AG. (2020). European Portuguese version of the Child Self-Efficacy Scale: a contribution to cultural adaptation, validity and reliability testing in adolescents with chronic musculoskeletal pain. Musculoskeletal Science & Practice, 49:1-7.
- Andias, R. & Silva, AG. (2020). “Cross-cultural adaptation and psychometric properties of the European Portuguese version of the Central Sensitization Inventory in adolescents with musculoskeletal chronic pain”. Pain Practice, 20(5):480-490.
- Andias, R. & Silva, AG. (2021). “Factors associated with pain and pain associated disability in adolescents with chronic neck pain compared to chronic back and limb pain”. Pain Medicine *(submitted and revised).*
- Andias, R. & Silva, AG. (2021). “Predictors of pain persistence and disability in high school students with chronic neck pain at 6 months follow-up”. Quality of life research. 1-14.

- Andias, R. & Silva, AG. (2021). “The onset of chronic pain in high-school adolescents: associated factors and the role of symptoms of central sensitization”. Physical Therapy *(submitted and revised).*
- Andias, R., Sá-Couto, P. & Silva, AG. (2021). “Blended-learning pain neuroscience education and exercise in high school students with chronic neck pain - a randomized controlled study”. Physical Therapy *(submitted and revised).*

Posters in conferences

- Andias R & Silva AG. Are there differences in psychosocial variables and sleep between adolescents with and without neck pain? A systematic review. “17th *World Congress on Pain*”, International Association for the Study of Pain, 12 a 16 setembro de 2018, Boston (EUA).
- Andias R & Silva AG. Are there differences in posture, muscle and sensory function between adolescents with and without neck pain? A systematic review and meta-analysis. 2018. “17th *World Congress on Pain*”, International Association for the Study of Pain, 12 a 16 setembro de 2018, Boston (EUA).
- Andias, R & Silva, AG. Psychosocial variables and sleep in adolescents with neck pain? A systematic review with meta-analysis. "Statistics on health decision making: state of the art ", Universidade de Aveiro, 10 de maio 2019.
- Andias R & Silva AG. Validity and reliability of the european portuguese version of the functional disability inventory. “11th *Congress of the European Pain Federation EFIC*”, 4 a 7 setembro de 2019, Valência (Espanha).
- Andias, R & Silva, AG. What are the factors associated with the persistence of neck pain and disability in adolescents after 6-months follow-up. "Statistics on health decision making: state of the art ", Universidade de Aveiro, 22 julho de 2021.

- Andias, R & Silva, AG. Baseline factors of pain and disability for regional and multisite pain in adolescents with chronic musculoskeletal pain. VII Congresso da Associação Portuguesa para o Estudo da Dor (APED), "Prevenção é o Futuro", 15 e 16 outubro 2021, Lisboa.
- Andias, R & Silva, AG. Blended-learning pain neuroscience education and exercise using WhatsApp in adolescents with chronic neck pain - a randomized controlled study. VII Congresso da Associação Portuguesa para o Estudo da Dor (APED), "Prevenção é o Futuro", 15 e 16 outubro 2021, Lisboa.

Oral presentations

- Andias R & Silva AG. Baseline determinates of pain and disability in subgroups of adolescents with chronic pain. "*World Physiotherapy Congress 2021 online*", 9 a 11 Abril de 2021.
- Andias R & Silva AG. Are psychosocial factors, sleep and central sensitization predictive of persistent pain adolescents with neck pain?. "*World Physiotherapy Congress 2021 online*", 9 a 11 Abril de 2021.
- Andias R & Silva AG. What are the factors associated with the onset of musculoskeletal pain and disability in adolescents?. "*World Physiotherapy Congress 2021 online*", 9 a 11 Abril de 2021.

Table of contents

List of figures

List of tables

List of abbreviations

NP	Neck Pain
PNE	Pain Neuroscience Education
IASP	International Association of Study of Pain
PAG	Periaqueductal Grey Matter
NMDA	N-Methyl-D-Aspartate
PRISMA	Preferred Reporting Items for Systematic Review and Meta-Analyses
NOS	Newcastle Ottawa Scale
SD	Standard Deviation
OR	Odd Ratio
WMD	Weighted Mean Difference
CI	Confidence Interval
FHP	Forward Head Posture
ROM	Range of Motion
JPE	Joint Repositioning Error
UT	Upper Trapezius
CE	Cervical Extensors
SCM	Sternocleidomastoid
PPT	Pressure Pain Threshold
ICC	Intraclass Correlation Coefficient
α	Cronback's Alpha
SPSS	Statistical Package for Social Sciences
BMI	Body Mass Index
VIF	Variance Inflation Factor
SEM	Standard Error of Measurement
SDC	Smallest Detectable Change
AIC	Akaike's Information Criterion

1. CHAPTER 1: GENERAL INTRODUCTION

1.1. Introduction

Chronic musculoskeletal pain is a common complaint in adolescents and its prevalence has been increasing over the last decades. Recent studies report prevalence rates of up to 40% in children and adolescents (Hoftun, Romundstad, Zwart, & Rygg, 2011; King et al., 2011). In late adolescence, chronic musculoskeletal pain tends to approach the prevalence reached in adults (Kamper, Henschke, Hestbaek, Dunn, & Williams, 2016). Previous studies reported that chronic pain negatively influences psychosocial development, interfering with school attendance, family, and social engagement (Gauntlett-Gilbert & Eccleston, 2007; Hoftun et al., 2011; Roth-Isigkeit, Thyen, Stöven, Schwarzenberger, & Schmucker, 2005). In addition, a significant percentage of these adolescents maintain their complaints at long-term follow-up (Mikkelsson, Salminen, Sourander, & Kautiainen, 1998; Paananen, Taimela, et al., 2010). The most common painful body sites in adolescents aged between 16 and 18 years are the neck (20.9%), followed by the low back (17.5%), upper back (11.5%), lower extremities (8.6%), and upper extremities (3.9%) (Hoftun et al., 2011).

Adolescents with chronic neck pain (NP) show functional (Oliveira & Silva, 2016; Park et al., 2012; Sá & Silva, 2017), psychosocial (Diepenmaat, Van Der Wal, De Vet, & Hirasing, 2006; Rees, Smith, O'Sullivan, Kendall, & Straker, 2011; Sá & Silva, 2017) and sleep-related differences when compared to asymptomatic adolescents as well as a generalized hypersensitivity suggesting a contribution of the central nervous system (Sá & Silva, 2017). However, the amount of literature aiming to characterize adolescents with NP is scarce and important factors seen in adults with NP have not been explored in this population. Similarly, and to the best of our knowledge, studies exploring pain treatment and management in adolescents with chronic NP are also

scarce. However, pain interventions based on pain neuroscience education (PNE) have emerged as promising (Louw, Zimney, Puentedura, & Diener, 2016; Watson et al., 2019). PNE consists of educational sessions describing the neurophysiology of pain and the nervous system's ability to modulate the pain experience (Louw, Zimney, O'Hotto, & Hilton, 2016). It promotes the patients' understanding of chronic pain and changes unadjusted thoughts and cognitions, which are important barriers to active therapy and exercise (Meeus, Nijs, Van Oosterwijck, Van Alsenoy, & Truijen, 2010; Neto, Andias, & Silva, 2018). A recent systematic review (Siddall et al., 2021), comparing studies that explored the effect of combining PNE and exercise for patients with chronic musculoskeletal pain versus exercise only, concluded that a combined intervention results in a greater reduction in pain intensity, disability, catastrophizing, and fear-of-movement compared to exercise only. However, studies included in this systematic review were in adults and only one of the included studies used adults with chronic NP (Matias, Vieira, Pereira, Duarte, & Silva, 2019). The systematic review of Dragotta et al. (2019) on the available evidence on the intervention of physical therapy in adolescents with NP, found only two studies which were both carried out by our research team (Andias, Neto, & Silva, 2018; Neto et al., 2018). The findings of the quantitative study suggest that PNE and exercise decrease pain and catastrophizing and improve neck muscles endurance (Andias et al., 2018). The qualitative study suggested that PNE is perceived by adolescents as a facilitator of behavior change towards exercise and self-management (Neto et al., 2018). However, the small sample, the inclusion of a control group that did not perform any treatment, and the lack of medium and long-term follow-up, highlighted the need for more studies exploring the effectiveness of PNE in adolescents with NP.

In summary, the increasing prevalence of chronic NP in adolescents, its negative impact, and the lack of studies that comprehensively characterize chronic NP in adolescents and investigate the effectiveness of PNE interventions justify the need to

perform this PhD research project. Throughout this thesis, the term adolescents will be used as a replacement for the term high school students present in the title of this research project.

1.2. Research aims

This research project has two main aims: i) to characterize chronic idiopathic NP and associated psychosocial and functional changes, disability, sleep, and self-reported symptoms of central sensitization in adolescents; ii) to design and assess the effectiveness of PNE and exercise compared to exercise only in adolescents with chronic NP.

1.3. Research objectives

The objectives of this thesis were:

- To provide the current definition of chronic NP and adolescence, and contextualize the evidence on functional and psychosocial changes, sleep, and symptoms of central sensitization associated with NP, and current interventions (Chapter 2);
- To systematically review and critically assess the evidence on functional and psychological changes, sleep, and symptoms of central sensitization associated with NP in adolescents (Chapter 3 and 4);
- To characterize adolescents with chronic NP in terms of i) sociodemographic characteristics, ii) disability, iii) physical activity, iv) psychosocial factors, v) sleep and vi) self-reported symptoms of central sensitization (Chapter 5);
- To explore the factors associated both with NP and disability and compare these between adolescents with NP and adolescents with back and limb pain (Chapter 5);

- To explore whether i) sociodemographic characteristics, ii) physical activity, iii) psychosocial factors, iv) sleep and v) self-reported symptoms of central sensitization at baseline, were associated with the persistence of chronic NP and disability at 6-month follow-up in adolescents, and whether there are differences between girls and boys (Chapter 6);
- To explore whether sociodemographic characteristics, depression, anxiety and stress, sleep, and self-reported symptoms of central sensitization at baseline in asymptomatic adolescents were associated i) with new onset of chronic musculoskeletal pain and ii) with new onset of chronic NP, at 6-month follow-up (Chapter 7);
- To assess the effectiveness of PNE and exercise compared to exercise only at post-intervention and at 6-month follow-up in adolescents with chronic NP (Chapter 8);
- To make recommendations for clinical practice and future research regarding chronic NP assessment and treatment in adolescents (Chapter 9).

A schematic outline of the research project is presented in Figure 1.

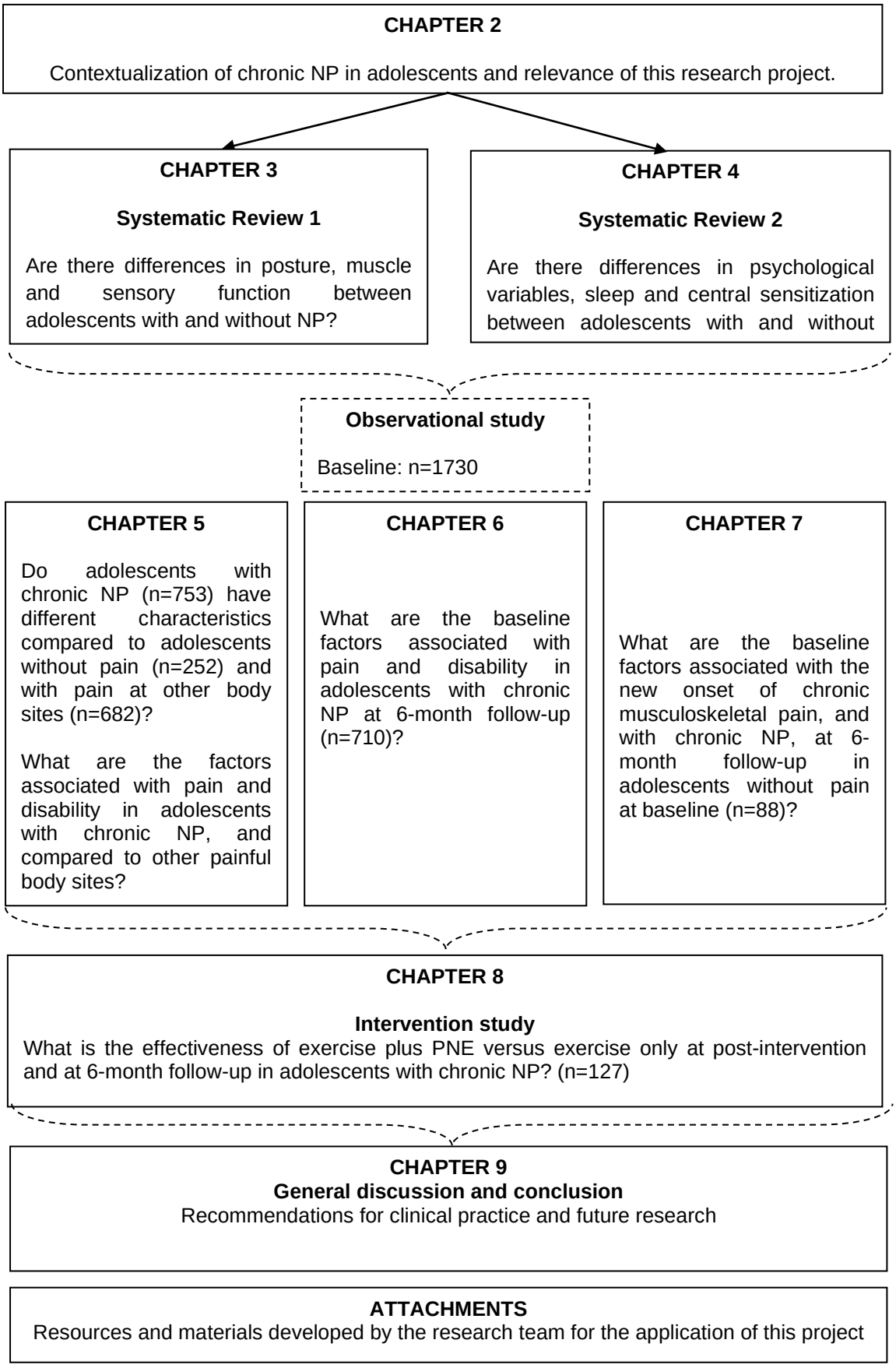


Figure 1. Schematic representation of the chapters presented in this research project.

2. CHAPTER 2: BACKGROUND

2.1. Musculoskeletal pain prevalence and associated disability in adolescents

Adolescence is a period of several physical and psychosocial changes that point to the transition from childhood to adulthood (Berenbaum, Beltz, & Corley, 2015). According to the American Academy of Pediatrics, the period of adolescence between 11 and 21 years old may be divided into early (11–14 years old), middle (15–17 years old), and late (18–21 years old) adolescence (Hardin & Hackell, 2017; Williams et al., 2012).

Pain is one of the most common complaints among adolescents (Steven J. Kamper & Williams, 2017; Perquin et al., 2000; Zapata, Moraes, Leone, Doria-Filho, & Silva, 2006). Considering the individual meaning and the sensory and emotional complexity associated with the experience of pain, its definition has been revised over the years. Recently, a new update from the International Association of Study of Pain (IASP) defined pain as "*an unpleasant sensory and emotional experience associated with or resembling that associated with, actual or potential tissue damage"* (Raja et al., 2020). As for the duration, it might be defined as acute, when maintaining its protective role generally defined for up to 3 months, or chronic, when it persists beyond 3 months (Raja et al., 2020; Treede et al., 2019). When pain complaint is reported in the joints, bones, muscles, or surrounding structures involving the areas of the neck, shoulders, wrists/hands, upper back, lower back, hips/thighs, knees, ankles/feet, it is defined as musculoskeletal pain (IASP, 2009; Steve J. Kamper et al., 2016).

The prevalence of chronic musculoskeletal pain is high and has been estimated to reach up to 65% of children and adolescents (Eckhoff, Straume, & Kvernmo, 2017; King et al., 2011; Silva, Pitangui, Xavier, Correia-Júnior, & De Araújo, 2016; Swain et

al., 2014). According to Hoftun et al. (2011), in adolescents aged between 13 and 15 years, the most common painful body sites are the neck (14.3%), followed by the lower extremities (12.8%), low back (10.9%), upper back (8.1%) and upper extremities (4.0%). Similarly, in the age group of 16 to 18 years old, the most common painful body sites are the neck (20.9%), followed by the low back (17.5%), upper back (11.5%), lower extremities (8.6%) and upper extremities (3.9%) (Hoftun et al., 2011).

In addition to the high prevalence, chronic musculoskeletal pain has a negative impact in several domains of life, with present and future consequences. Mano et al. (2020) reported that adolescents aged 12 to 17 years old with chronic musculoskeletal pain have impaired executive functions, including decreased working memory, ability to control attention, and cognitive flexibility when compared to asymptomatic adolescents. These changes in executive functioning, in turn, are also associated with greater functional disability, school absences, restrictions on social and recreational functioning, and higher levels of anxiety and depression (Gauntlett-Gilbert & Eccleston, 2007; Hoftun et al., 2011; Konijnenberg et al., 2005). Adolescents' pain also has a negative impact in life and emotional functioning of their parents and family members such as distress, burden, and interruption of daily routines (Eccleston, Crombez, Scotford, Clinch, & Connell, 2004; Palermo, 2000; Palermo & Chambers, 2005). Regarding future implications of pain, Murray et al. (2020) in a longitudinal study with 12 years of follow-up and a sample of 14 790 adolescents reported that adolescents with musculoskeletal chronic pain grew into adulthood with lower levels of education, poor vocational functioning, and increased social losses compared to asymptomatic adolescents. Furthermore, adolescents with chronic pain are likely to experience chronic pain when adults (Brattberg, 2004; Hanvold, Veiersted, & Wærsted, 2010). Thus, chronic musculoskeletal pain is a complaint with current and long-term high impact on the daily life of adolescents.

2.2. Neck pain definition and prevalence

Among the several chronic idiopathic musculoskeletal pain syndromes, NP is the most commonly reported in adolescents (Gustafsson, Laaksonen, Aromaa, Löyttyniemi, & Salanterä, 2018; Hoftun et al., 2011; Stahl, El-Metwally, & Rimpelä, 2014). NP might be anatomically defined as pain perceived anywhere in the posterior region of the neck, from the superior nuchal line to the first thoracic vertebra, bounded laterally by the lateral margins of the neck (Misailidou, Malliou, Beneka, Karagiannidis, & Godolias, 2010). To be considered as chronic pain, NP must persist for more than 3 months, a commonly defined time for the normal tissue healing process (Treede et al., 2019). NP may be related to injury, such as sports-related injuries or whiplash, surgery, chronic disease, or rarely serious pathology, e.g. infections and neoplasms (Becker, Heathcote, Timmers, & Simons, 2018; Misailidou et al., 2010). However, in most cases, no discernible cause of NP can be identified (Hoftun et al., 2011) and it is termed idiopathic NP, defined as NP not associated with any known injury or disease (Misailidou et al., 2010).

The prevalence rates of NP in adolescents are high and have been increasing over the last decades, with girls showing higher NP prevalence than boys (Hakala, Rimpelä, Salminen, Virtanen, & Rimpelä, 2002; Hoftun et al., 2011; Minghelli, 2019; Stahl et al., 2014). Hakala et al. (2002), in a survey with 189 894 adolescents aged 14 to 16 years old reported that NP prevalence in the last 6 months increased from 29% to 36% in girls and from 15% to 20% in boys, between 1991 and 2001. At 18-years old the increase was from 36% to 45% for girls and from 14% to 20% for boys (Hakala et al., 2002). Similarly, Stahl et al. (2014) also showed an increasing prevalence of NP in adolescents aged 12 to 14 years old from 1991 to 2011, from 11.1% to 18.5% in girls and from 4.8% and 5.9% in boys. At the age of 16 to 18 years old, the prevalence increased from 22.7% to 29.5% in girls and from 7.1% to 10.7% in boys over the same

decade (Stahl et al., 2014). These numbers also show that NP prevalence is higher at the later phases of adolescence. This has also been reported in other studies (Gustafsson et al., 2018; Hoftun et al., 2011). Furthermore, NP is often not reported as a single body site and adolescents with NP tend to report pain complaints in multiple body sites (Auvinen et al., 2017; Auvinen et al., 2009; Paananen, Auvinen, et al., 2010).

Neck pain also has a negative impact on adolescents' daily routines. Two studies were found that assessed disability in adolescents with chronic NP (Oliveira & Silva, 2016; Sá & Silva, 2017). Oliveira & Silva (2016) in a sample of 35 adolescents with NP reported that 48.6% of adolescents responded that NP interfered with their daily activities. Sá & Silva (2017) in a sample of 40 adolescents with NP found that 49.1% of adolescents with NP reported difficulties during physical education classes, 29.1% reported difficulties in performing their leisure activities, 27.5% reported difficulties sitting during classes, 23.7% reported difficulties falling asleep and that NP disturbed their sleep, and 8.7% reported difficulties to walk more than 1 km. No other studies were found that specifically assessed disability in adolescents with NP.

Overall, NP prevalence in adolescents exceeds the prevalence of other common painful complaints such as low back pain. Thus, a better characterization of NP and associated factors in adolescents emerges as particularly relevant for its appropriate management at an early stage.

2.3. Biopsychosocial characterization of adolescents with neck pain

Different biological, psychological, and social factors are associated with NP and modulate the experience of pain in adolescents (Koechlin, Locher, & Prchal, 2020; Liossi & Howard, 2016). The extent of the impact of each of these factors vary from person to person (Liossi & Howard, 2016).

From a biological perspective, being a female (Dianat, Alipour, & Asgari Jafarabadi, 2018; Pourbordbari, Riis, Jensen, Olesen, & Rathleff, 2019; Vikat et al., 2000) and of older ages (Vikat et al., 2000) are commonly reported in the literature as being associated with the presence of NP in adolescents. In a recent study, Richard et al. (2021) found that female sex and having chronic NP at 17 years of age were associated with chronic NP at 22 years of age. Also, adolescents with chronic NP show several functional changes, including decreased endurance of the neck flexor and extensor muscles (Oliveira & Silva, 2016), increased activity of the superficial muscles, such as the sternocleidomastoid and trapezius muscles (Park et al., 2012), and impaired joint position sense (Sá & Silva, 2017) when compared to asymptomatic adolescents. Previous studies have also explored the association between posture and NP, but results are conflicting with a few reporting NP to be associated with head posture deviations (Straker, O'Sullivan, Smith, & Perry, 2009), while others reported no differences between adolescents with and without NP (Cheung, Shum, Tang, Yau, & Chiu, 2009; Richards, Beales, Smith, O'Sullivan, & Straker, 2016). Oliveira & Silva (2016) also added that adolescents with chronic NP have less forward head posture than asymptomatic adolescents.

Studies have also shown that adolescents with chronic NP report daytime tiredness and sleep disorders (Auvinen et al., 2010; Gustafsson et al., 2018). Furthermore, Stahl et al. (2008) reported that daytime tiredness, difficulty falling asleep, and waking up during the night predicted the onset and maintenance of weekly NP at a 4-year follow-up. Similarly, Auvinen et al. (2010) found that insufficient quantity and quality of sleep at 16 years old was a risk factor for NP at 18 years old, but only in girls. And Gustafsson et al. (2018) reported that daytime tiredness at 10 years old predicted the presence of NP at the age of 15 years old.

In addition to the already presented factors, Sá & Silva (2017) reported that adolescents with chronic NP have increased pain sensitivity in the neck region, but also at a distant body site (the lower leg), suggesting a possible presence of central sensitization mechanisms. Central sensitization is characterized by an augmented and maintained neuronal responsiveness on central pain pathways to their normal or sub-threshold afferent input, which translates into pain hypersensitivity and may reflect increased activity of nociceptive facilitatory pathways, decreased activity of descending inhibitory pathways, and modified sensory processing in the brain, with increased activity of the brain neuromatrix (Harte, Harris, & Clauw, 2018; Latremoliere & Woolf, 2009; Woolf, 2011). Central sensitization seems to have a key role in modulating the development of chronic pain, facilitating its persistence over time, and negatively influencing its management (Nijs et al., 2021, 2014; Staud, 2013; Woolf, 2011).

Concerning psychological factors, adolescents with chronic NP have been shown to report higher levels of depression (Dolphens et al., 2016; Myrtveit et al., 2014), anxiety, and stress (Niemi, Levoska, Rekola, & Keinänen-Kiukaanniemi, 1997; Sá & Silva, 2017), pain catastrophizing (Sá & Silva, 2017), and poorer self-efficacy (Niemi et al., 1997) than asymptomatic adolescents. These factors are believed to play an important role in the onset and maintenance of pain and disability. Stahl et al. (2008) reported that self-reported physical and psychological symptoms, including headache, abdominal pain, and depressive mood predicted the onset and maintenance of weekly NP at a 4-year follow-up. Also, Mikkelsson et al. (1999) and Feldman et al. (2002) suggested that psychological symptoms, such as depressive symptoms and lower mental health, might contribute to the onset of NP and to its transition from localized chronic NP to widespread pain, at 1-year follow-up among adolescents. Siivola et al. (2004) found that abdominal pain, headache, fatigue, and anxiety in adolescents aged 15 to 18 years old predicted the onset of NP at 22 to 25 years of age. Recently, a systematic review of prognostic factors for musculoskeletal pain in adolescents

highlighted the relevance of depressive symptoms, multisite pain, female sex, and daily tiredness as baseline factors associated with the long-term persistence of NP (Pourbordbari et al., 2019).

In the context of social factors, adolescents who do not live with both of their parents (Diepenmaat et al., 2006) and who have antisocial/isolation behaviors at school and with their peers (Rees et al., 2011) are more likely to report NP lasting 1-month. Also, Batley et al. (2019), found higher levels of loneliness and lower levels of peer acceptance in adolescents with spinal pain, including NP, compared to asymptomatic adolescents. A high percentage of adolescents with chronic NP report poor communication skills (82%) and decreased school marks (64%) (Fares, Fares, & Fares, 2017). Physical activity has also been reported to be associated with NP in adolescents (Myrtveit et al., 2014; Niemi, Levoska, Kemilä, Rekola, & Keinänen-Kiukaanniemi, 1996; Vikat et al., 2000), but other studies reported no association (Dianat et al., 2018; Diepenmaat et al., 2006). Vikat et al. (2000) suggested that both lack and excess of physical activity might increase the likelihood of reporting chronic NP in adolescents. Niemi et al. (1996) suggested that physical activity involving dynamic loading of upper limbs had a protective effect for NP, in girls with NP aged 15 to 18 years old, compared with activities involving static postures of the upper limb or other types of physical activity. Myrtveit et al. (2014) also suggested that performing physical activity at least 1-3 days a week has a protective effect for NP in a sample of 1797 adolescents with chronic NP. However, Diepenmaat et al. (2006) suggested that physical activity was not associated with NP in a sample of 427 adolescents with NP, categorized as lasting 1 month and occurring at least once a week. Similarly, Dianat et al. in a sample of 460 adolescents with NP found no association between NP and physical activity.

All biological, psychological, and social factors are components of the biopsychosocial model of chronic pain that suggests that pain and pain-associated behavior are the results of the dynamic interaction of these domains (Liossi & Howard, 2016). Thus, a comprehensive biopsychosocial assessment of adolescents with chronic NP seems to be crucial to determine the most appropriate pain management strategy. However, in this preliminary search, we were unable to find studies that comprehensively assessed the psychosocial and sleep factors in adolescents with chronic NP. Furthermore, no study was found that assessed fear of movement in adolescents. Additionally, although no studies have been found in adolescents that assessed central sensitization or symptoms of central sensitization, studies in adults have suggested that both psychosocial factors and sleep impairments might contribute to central sensitization (Courtney, Fernández-de-las-Peñas, & Bond, 2017; Nijs, Van Houdenhove, & Oostendorp, 2010; van Wilgen et al., 2018). The mechanisms underlying this relationship are not entirely clear and understood. However, it is known that psychosocial factors might contribute to the dysregulation of the descending inhibitory and facilitatory nociceptive pathways sending outputs from activated areas involved in the processing of emotions and cognitions, such as the anterior cortex cingulate, the pre-frontal cortex, the amygdala, and the thalamus to the periaqueductal grey matter (PAG) (Bushnell, Ceko, & Low, 2013). Also, increased levels of adrenaline and dysregulation of the autonomic nervous system (Dimitriadis, Kapreli, Strimpakos, & Oldham, 2015), increased activation of brain areas related to anticipation of pain and attention to pain (Bushnell et al., 2013; Gracely et al., 2004; Sullivan et al., 2001) and changes in neurotransmitter concentrations at the supraspinal areas and in the gray matter volume (Wippert & Wiebking, 2018), have been some of the changes reported in the presence of increased levels of depression, anxiety, catastrophizing, and stress. On the other hand, sleep deprivation is associated with the dysregulation of the endogenous opioid system, attenuation of its analgesic capacity, and negative changes

in mood and emotions (Finan, Goodin, & Smith, 2013). More recently, evidence has been suggested that sleep impairments and high levels of stress result in abnormal glial activation and a low-grade neuroinflammation state, which in turn contributes to the development and maintenance of central sensitization (Nijs et al., 2017). Thus, all these processes might contribute to altered pain processing and facilitate the central hyperexcitability of the central nervous system and its high responsiveness to various stimuli (Othman et al., 2021).

Apart from all the described biological and psychosocial factors associated with chronic NP, it is important to note that adolescence itself is a phase characterized by several neurobiological, psychosocial, and behavioral changes, so, controlling pain at this stage is essential to minimize its negative impact on the transition into adulthood (Casey, Giedd, & Thomas, 2000; Griffin, 2017; Rosenbloom, Rabbitts, & Palermo, 2017).

2.4. Neck pain management

A variety of interventions have been reported in previous literature reviews designed to identify current evidence for the best management of chronic pain in children and adolescents, including pharmacological, psychological, and/or physical therapy and other specific interventions, such as education (e.g. pain education), lifestyle counseling, relaxation, and parent coaching, and complementary interventions, such as music therapy, integrated into a multimodal intervention or as a single treatment (Caes, Fisher, Clinch, & Eccleston, 2018; Harrison et al., 2019; Simons & Basch, 2016).

In the context of physical therapy, exercise is identified as a key intervention (Caes et al., 2018; Harrison et al., 2019), but a few studies also report school-based back education programs, based on the education of the correct spinal posture, as an

intervention and preventive strategy for children and adolescents (Dolphens et al., 2011; Koh et al., 2014; Steele, Dawson, & Hiller, 2006). Steele et al. (2006) in a systematic review aiming to synthesize the effectiveness of these school-based interventions in students under the age of 18 years old, found 12 studies of low methodological quality, that included education on spinal anatomy and physiology, risk factors for injuries, and strategies to incorporate a correct posture into daily routines. The authors concluded that the evidence for this type of intervention is weak, and it is not possible to conclude whether there is any behavior change in adolescents who receive this type of intervention, but there appears to be an increase in knowledge about spinal care and a decrease in the prevalence of spinal pain up to 1 year follow up. Dolphens et al. (2011) assessed the long-term effectiveness (8-year follow-up) of a 6-week school-based back education program focused on posture and spine biomechanics compared to a control group that performed no-intervention, in 96 schoolchildren aged 9 to 11 years old. Although there was a significant increase in knowledge about back care until adulthood, the intervention did not change the spine care behavior or increase self-efficacy in early adulthood, and the prevalence of back pain, including NP, was significantly higher in the group that received the education program (Dolphens et al., 2011). Thus, the findings of these studies suggest that there might be no long-term positive impact of school-based back education programs and that there might be a worsening of back pain, including NP, with this type of intervention. Nevertheless, none of these studies specifically targeted adolescents with NP. A systematic review from Dragotta et al. (2019), which aimed to assess the evidence on the physical therapy management of NP in children and adolescents, identified only two intervention studies, both performed by our research team (Andias et al., 2018; Neto et al., 2018), suggesting scarcity of evidence on this topic. Andias et al. (2018) compared PNE and exercise against no intervention in 21 adolescents aged 17.4±1.4 years old and reported a significant improvement in knowledge of pain

neuroscience and endurance capacity of neck extensors, and a non-statistically significant tendency to decreased pain intensity, anxiety, and catastrophizing, and increased endurance of neck flexors and scapular muscles in the group that received the intervention when compared to the control group (Andias et al., 2018). In the same sample of adolescents and using a qualitative approach, Neto et al. (2018) reported that PNE was perceived as a facilitator of both pain reconceptualization and exercise, overcoming maladjusted thoughts and cognitions, which were barriers to exercise. The intervention used follows the current international guidelines for the management of chronic pain in young people. PNE consists of explaining to individuals the pain neurophysiology simultaneously with the role of the brain and emotions in the interpretation and processing of pain by the nervous system, and this knowledge seems to have a role in modulating the pain experience and the emotional response to pain (Louw, Zimney, O'Hotto, et al., 2016; Robins, Perron, Heathcote, & Simons, 2016). PNE sessions can be applied in different formats, from individual sessions, in groups, or using short videos, with contents and materials (e.g. metaphors, drawings, leaflets) always adapted to the target population (Robins et al., 2016). The main aim of PNE is to make pain understandable for the patients and disrupt pain-related misconceptions, such as catastrophizing and fear-avoidance behaviors (Kim & Lee, 2020; Louw, Zimney, Puentedura, et al., 2016; Watson et al., 2019). In this sense, it uses principles and strategies of cognitive-behavioral therapies (Fisher et al., 2014; Moseley & Butler, 2015).

Recently, the World Health Organization developed a guideline regarding the management of chronic pain in children and adolescents and recommended that pain interventions should follow the biopsychosocial model, integrating a biological but also a psychological and a social component, according to individual needs (Ezeanosike et al., 2020). The guideline was based on a systematic review that included 24

randomized controlled trials about physical interventions, 63 randomized controlled trials about psychological interventions, and 29 randomized controlled trials about pharmacological interventions. Overall, very low evidence recommends physical therapies, such as exercise, and moderate evidence recommends cognitive-behavioral therapies, in a face-to-face format or combined with a remote intervention (Ezeanosike et al., 2020).

Exercise, as a common and widely recommended intervention in adults with chronic NP, is relevant to increase function (Blanpied et al., 2017; O'Riordan, Clifford, Van De Ven, & Nelson, 2014), but also to facilitate desensitization of the nervous system (Nijs, Lluch Girbés, Lundberg, Malfliet, & Sterling, 2015). Sluka et al (2018) reviewed the mechanisms by which exercise reduces pain and highlighted the activation of the endogenous inhibitory systems in the central nervous system; decreased central hyperexcitability, for example, by decreased expression of ionic receptors that facilitate pain, such as *N*-methyl-D-aspartate (NMDA) receptor; modulation of neuroimmune signaling, for example, facilitating the balance between inflammatory and anti-inflammatory cytokines and consequently reducing the activation of nociceptors; promotion of tissue regeneration; and improvement of general well-being and mental health. There are specific recommendations for the prescription of exercise for chronic NP in adults (Ferro Moura Franco et al., 2021; O'Riordan et al., 2014), however, to our knowledge, there are no specific recommendations for children or adolescents with NP. Theoretical studies have suggested that multimodal interventions including self-management strategies, pain education, such as PNE, and active based-movement interventions, such as exercise, appear to be relevant in the management of pain and disability in adolescents with chronic musculoskeletal pain (Eccleston et al., 2021; Robins, Perron, Heathcote, & Simons, 2016; Stinson, Connelly, Kamper, Herlin, & Toupin, 2016). Harrison et al. (2019), in a review of the best evidence for the

rehabilitation of pediatric pain, also highlighted the need to use multimodal interventions combining strategies based on the understanding of pain neuroscience and managing negative and maladaptive thoughts and cognitions often associated with pain (e.g. psychoeducation, relaxation techniques, and behavioral exposures), and exercise and exercise education. A recent systematic review of Siddall (2021), which aimed to compare the effect of PNE in combination with exercise versus exercise only in adults with chronic musculoskeletal pain, found 5 randomized controlled trials classified with high methodological quality and concluded that combining PNE and exercise results in a greater reduction in pain intensity, disability, catastrophizing, and fear-of-movement compared to exercise only. However, only one of the included studies was specific to adults with chronic NP (Matias et al., 2019). We were unable to find any study that attempted to compare the effectiveness of an intervention based on PNE and exercise versus exercise only, in children or adolescents with pain in general or NP in particular. Thus, despite the increasing prevalence of NP in adolescents, few studies have explored the effectiveness of physical therapy. Thus, no clear recommendations exist to guide and inform clinical practice. PNE associated with exercise appears to be a promising intervention, but existing studies are scarce and of a small size, suggesting that further studies are needed.

2.5. Summary

The high and growing prevalence of chronic NP at younger ages, particularly in the age range of 16 to 18 years old, its tendency to persist into adulthood, and the apparent lack of studies focusing on adolescents with NP highlight the need to better characterize this population. Few studies characterizing the functional and psychosocial factors associated with chronic NP in adolescents seem to have been published. Furthermore, most of them are cross-sectional studies and do not assess potentially relevant factors, such as fear of movement or the presence of symptoms of

central sensitization. Nevertheless, and to the best of our knowledge, a synthesis of existing evidence on the characteristics of adolescents with NP has not been performed. Conceivably, a better characterization of adolescents with chronic NP, following a biopsychosocial model, will allow the design of more effective interventions. Therefore, to have an in-depth understanding of existing evidence on the functional and psychological characteristics associated with NP in adolescents, two systematic reviews of the literature were performed, which are presented in the next two chapters of this research project.

3. CHAPTER 3: A SYSTEMATIC REVIEW WITH META-ANALYSIS ON FUNCTIONAL CHANGES ASSOCIATED WITH NECK PAIN IN ADOLESCENTS

Based on the systematic review from Andias, R. & Silva, AG. (2019). “A systematic review with meta-analysis on functional changes associated with neck pain in adolescents”. Musculoskeletal Care, 17 (1):23-26.

3.1. Introduction

Adolescents with NP seem to have decreased endurance of the neck flexor and extensor muscles (Oliveira & Silva, 2016) and increased activity of the superficial muscles (Park et al., 2012), impaired joint position sense and increased pain sensitivity (Sá & Silva, 2017) when compared to asymptomatic adolescents. The evidence in regard to posture is contradictory (Hellstenius, 2009; Oliveira & Silva, 2016; Richards et al., 2016). However and to the best of our knowledge, studies on functional changes associated with NP in young people have not been systematically reviewed, assessed, and synthetized. A better understanding and characterization of NP and associated changes in young people is essential to improve assessment, intervention and, potentially, minimize the consequences of NP in adolescence and adulthood. Thus, the aim of the present systematic review is to identify and critically assess the evidence on the functional changes associated with NP, in adolescents, specifically for: i) posture, ii) postural control iii) range of motion, iv) proprioception, v) muscle function, vi) sensory threshold, and vii) central sensitization.

3.2. Methods

3.2.1. Registration of the systematic review protocol

This review was registered in the PROSPERO, with the ID CRD42018089518.

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed in this review (Moher et al., 2009).

3.2.2. Search strategy and study selection

From September to November 2017 an electronic search was conducted in Pubmed, ScienceDirect, Web of Science, PEdro, Scielo, Scopus and Academic Search Premier databases. Additionally, the list of references of all included studies was analysed to check for another relevant studies not identified by the electronic searches.

A combination of words was used in the search strategies, including NP, adolescents and specific terms regarding NP function. Pubmed was searched using MeSH terms and filters for age and article type. Data searches were conducted for publications available since database inception and for studies published in English, Spanish, French or Portuguese.

To be included in this review, studies had to compare aspects of neck function in adolescents with and without NP, in line with the following criteria:

- Age range of included participants between 12 and 18 years (Williams et al., 2012);
- Report on acute or chronic NP not related to any known pathology or injury (Merskey & Bogduk, 2002; Misailidou et al., 2010);
- Compare any of following variables between adolescents with and without NP: range of motion, proprioception, muscle strength/endurance, sensory threshold and/or central sensitization, posture and/or postural control;
- Be full articles published in peer reviewed journals.

Studies in adolescents with nervous system pathology, rheumatic pathology, and major structural pathology (i.e. infection, neoplasms, systemic disease) were excluded from this review.

3.2.3. Data extraction

All retrieved references were imported into the reference software EndNote X5 (Clarivate Analytics, Philadelphia, United States) and checked for duplicates. The principal investigator (RA) screened titles and abstracts against the inclusion and exclusion criteria. Then, full texts of potentially eligible studies were retrieved and screened for inclusion independently by the authors of this review (RA and AGS). Discrepancies between reviewers were resolved by discussion until consensus was reached. The principal investigator (RA) extracted study characteristics using standardized forms. The extracted data was verified independently by the second reviewer (AGS) and any disagreement was resolved by discussion.

3.2.4. Methodological quality assessment

Methodological quality of included studies was independently assessed by the two reviewers using the Newcastle-Ottawa Scale (NOS) for case control studies (Lo, Mertz, & Loeb, 2014; Wells, Shea, & O'Connell, 2014), which is recommended by the Cochrane Collaboration (Higgins & Green, 2011). Disagreements were resolved by discussion until reaching a consensus. Agreement was measured using a Cohen's kappa with linear weighting. Values between 0-0.20 indicate no agreement, 0.21-0.39 minimal agreement, 0.40-0.59 weak agreement, 0.60-0.79 moderate agreement, 0.80-0.90 strong agreement and above 0.90 almost perfect agreement (McHugh, 2012). The NOS score varies between 0 and 9, with higher scores indicating lower risk of bias (Wells et al., 2014). The quality rating is interpreted as good quality (score ≥7), fair (score ≥5) and poor (score <5) (Mcpheeters et al., 2012).

3.3. Data synthesis and analysis

Outcomes were described according to the measured variable (posture, postural control, range of motion, proprioception, muscle function and sensory threshold). Data

were presented as mean ± standard deviation (SD), or odd ratio (OR) or percentage difference (%). To discuss the results, the weighted mean difference (WMD) and respective 95% confidence interval (CI) were calculated for each study that presented the results with mean ± SD. These calculations were performed using the Meta XL software (Epigear International, Australia; http://www.epigear.com) with population size, mean and SD as input data.

A meta-analysis was performed for studies that measured forward head posture, since only in this case there were at least 3 studies using similar measurements. The meta-analysis was also performed using Meta XL. Statistical heterogeneity of the studies was assessed using the Cochran's Q test (defined as $p<0.05$) and the I^2 statistic (interpreted as 0% to 40% might not be important; 30% to 60% may represent moderate heterogeneity; 50% to 90% may represent substantial heterogeneity and 75% to 100% considerable heterogeneity) (Higgins & Green, 2011; Israel & Richter, 2011). The results were tested with the random-effect model. Forest plots were used to present the WMD and CI for the individual studies of the meta-analysis and for overall analysis (Barendregt & Doi, 2011). Finally, we defined the "levels of evidence" according to the recommendations of van Tulder et al. (van Tulder, Furlan, Bombardier, & Bouter, 2003) and Barton et al. (Barton, Lack, Malliaras, & Morrissey, 2013) as strong, moderate, limited, very limited and conflicting evidence.

3.4. Results

3.4.1. Study selection

Searches resulted in 1150 references. After removing duplicates (n=457), 693 references were screened based on title and abstract and 26 full articles were retrieved. Of these, 10 articles were eligible for inclusion (Figure 2). The main reasons for exclusion were: studies without reference to NP in adolescents (n=13), no between group comparisons (n=1), no data on functional changes (n=2).

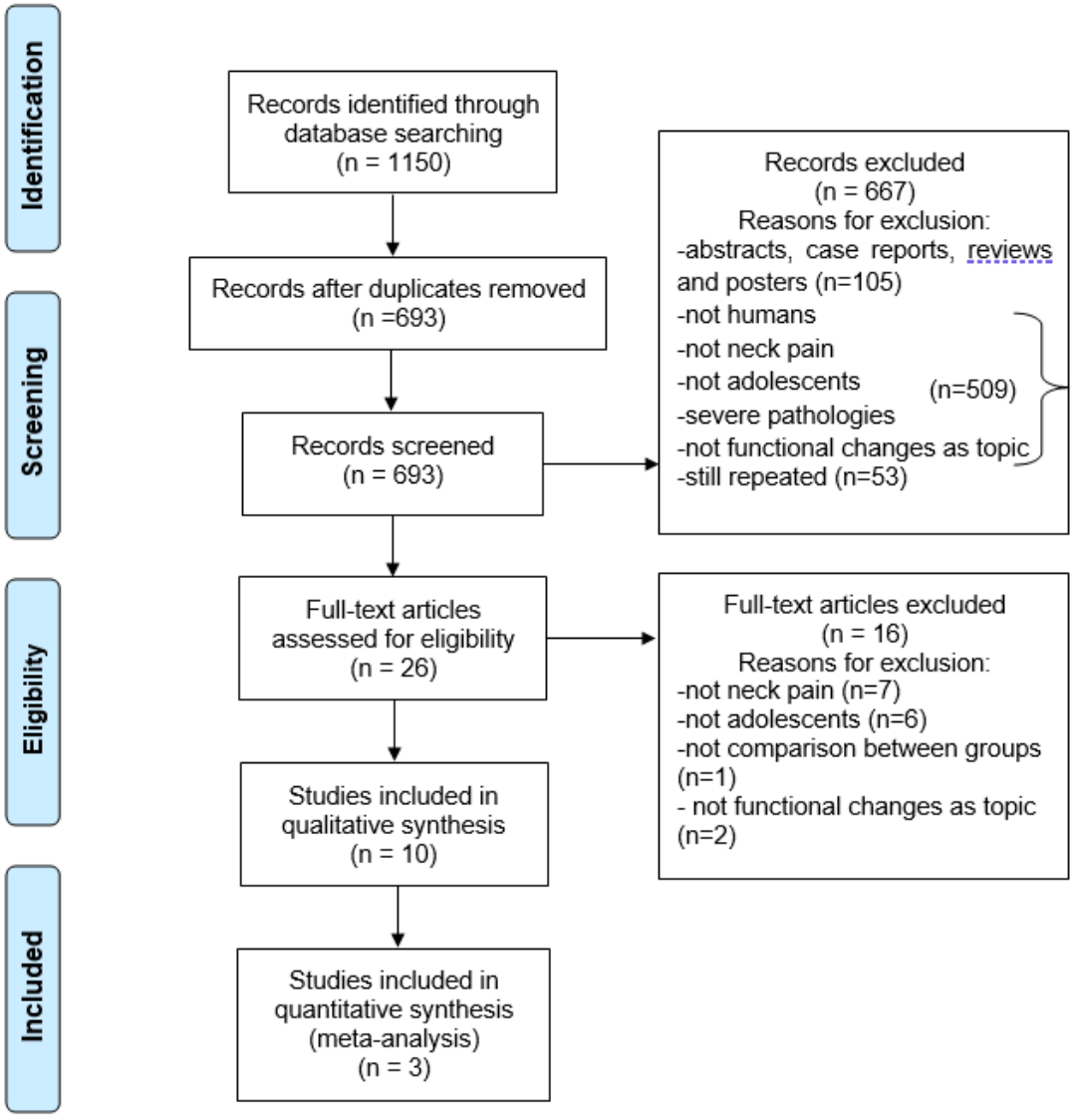


Figure 2. Study flowchart (PRISMA).

3.4.2. General overview of included studies

Nine out of the 10 included studies were case-control studies and one (Mikkelsson et al., 2006) was a prospective longitudinal study. Five of the 10 studies assessed more than one variable and, therefore, a total of 15 comparisons between adolescents with and without NP were made on different variables: posture (n=7), muscle function (n=3), range of motion (n=3), joint repositioning error (n=1) and pressure pain threshold (n=1). No studies were found on postural control. Only 5 of the included studies clarify the

duration of NP. The remaining studies did not specify its duration. A detailed characterization of included studies is presented in Table 1.

3.4.3. Methodological quality

Cohen's k for reviewer's agreement was 0.63, 95% CI (0.47; 0.78). Total score for the 10 included studies varied between 3 (n=3) and 6 (n=3) (Table 2), out of a maximum of 9 points (i.e., no study reached the cut off point for good quality ≥7).

Only one paper had participants interviewed by an experienced physical therapist for their NP (Cheung et al., 2009). All studies used participants that were representative of the population of adolescents with NP and community controls, but only 5 of them defined the criteria for being a control (Dolphens et al., 2016; Hellstenius, 2009; Oliveira & Silva, 2016; Richards et al., 2016; Sá & Silva, 2017). Only 4, out of the 10 included studies met criteria 5 (adjusted for age/gender) and 6 (adjusted for additional factors), regarding comparability of cases and controls (Dolphens et al., 2016; Mikkelsson et al., 2006; Richards et al., 2016; Straker et al., 2009). Only two of the 10 included studies performed a structured interview with an blind assessor (Hellstenius, 2009; Straker et al., 2009). All included studies assessed cases and controls using the same method. No study reported on non-response rate.

3.4.4. Posture

Details on measurement procedures and study results can be found in Tables 3 and 4. A total of 7 studies compared posture between adolescents with and without NP. Three of these studies characterized head posture through the angle between C7, the tragus of the ear and the horizontal (indicative of forward head posture (FHP) using the Head Posture Spinal Curvature Instrument (Cheung et al., 2009), the universal goniometer (Oliveira & Silva, 2016) and photogrammetry (Ruivo, Pezarat-Correia, & Carita, 2014). Another study characterized FHP in relation to a plumb line crossing the lateral

malleolus and the external auditory meatus (Hellstenius, 2009). Of these 4 studies, 2 with poor to fair methodological quality, found no difference (Cheung et al., 2009; Hellstenius, 2009) between adolescents with and without NP; one study with fair quality reported adolescents with NP to have significantly less FHP than asymptomatic controls (Oliveira & Silva, 2016) and the other study, assessed as poor, found adolescents with NP to have significantly more FHP than asymptomatic controls (Ruivo et al., 2014). The results of the meta-analysis with the 3 studies that assessed FHP through the angle between C7, the tragus and the horizontal showed statistically significant heterogeneity across studies (Q=13, p=0.00; I^2=85%) in a random-effect model. After pooled the results showed no statistically significant differences in FHP between adolescents with and without NP (WMD=1.1°; 95% CI -2.1°; 4.2°) (see Figure 3). Straker et al. (2009) and Richards et al. (2016), both with fair methodological quality, assessed head and spinal sitting posture using a 2D photographic method. Richards et al. (2016) found no statistically significant difference for head posture between adolescents with and without NP. In contrast, Straker et al. (2009) reported adolescents with NP to have significantly lower cervicothoracic angle (anterior angle formed between the lines of tragus to C7 and C7 to T12) when compared to adolescents without NP, indicating a more flexed cervicothoracic posture (WMD=-2.2°; 95% CI=-4.2°; -0.2°). However, when subdividing the sample according to gender these differences were no longer significant. Therefore, limited evidence suggests that there are neither differences in cervicothoracic posture, nor more specifically in FHP between adolescents with and without NP.

Straker et al. (2009) also reported a significantly lower trunk angle, indicating a more extended posture of the trunk (WMD= -3.0°; 95% CI=-6.0°; -0.1°); a significantly lower lumbar angle, indicating a greater lordosis (WMD= -6.4°; 95%CI=-10.7°; -2.1°) and a higher angle of pelvic tilt, indicating a greater anterior pelvic tilt (WMD=5.2°; 95%CI=1.5°; 9.1°) in adolescents with NP compared to asymptomatic adolescents.

After analysis by gender these differences remained only for the lumbar angle and anterior pelvic tilt. Dolphens et al. (2016), in a study with fair methodological quality, used the Spinal Mouse instrument to assess standing posture and found that adolescents with NP have a greater backward trunk lean than adolescents without NP. Furthermore, they also suggested an increased probability of NP in the presence of these characteristics (OR; 95% CI= 1.2; 1.1-1.3).

Thus, there is i) very limited evidence suggesting that adolescents with NP have a lower lumbar angle and higher angle of pelvic tilt in sitting posture than adolescents without NP and ii) very limited evidence that adolescents with NP have a smaller trunk angle (i.e., tendency for a greater extension of the trunk).

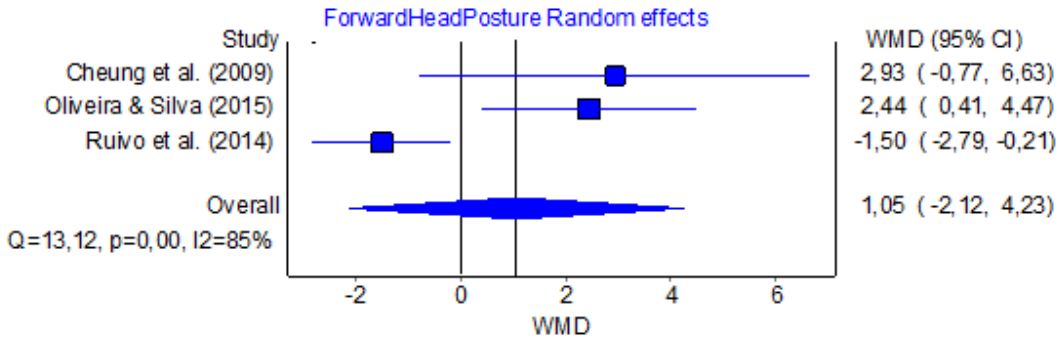


Figure 3. Forest plot of Forward Head Posture.

Note: Positive values indicate that adolescents with NP have a lower FHP compared to asymptomatic adolescents.

3.4.5. Range of motion

A total of 3 studies compared range of motion (ROM) between adolescents with and without NP (Tables 5 and 6). Two studies assessed neck range of motion (Hellstenius, 2009; Park et al., 2012) and one study (Dolphens et al., 2016) assessed thoracic and lumbar extension movement. Hellstenius (2009), with fair methodological quality, used a cervical collar goniometer to measure neck rotation and reported no significant differences between adolescents with and without NP. Park et al. (2012), with poor

methodological quality, assessed all movements of the neck using a three-dimensional ultrasonic motion analysis system and reported that adolescents with NP have a greater range of motion of left lateral bending (WMD=9.4°; 95%CI=2.8°; 16.0°) and left rotation (WMD=5.5°; 95% CI=0.8°; 10.2°), and a lower right axial rotation (WMD=-9.6°; 95%CI=-18.2°; -1.1°) and left axial rotation (WMD=-14°;95%CI=-21.1°; -6.9°), compared to adolescents without NP. Thus, very limited evidence indicates that there are differences in neck movements between adolescents with and without NP. Dolphens et al. (2016), with fair methodological quality, used the Spinal Mouse instrument to assess the extension movement of the thoracic and lumbar spine in standing posture and, although weak, found a statistically significant association for the movement of thoracic and lumbar extension suggesting that adolescents with higher levels of extension have more probability of NP (OR; 95% CI=0.98; 0.96–1.00 and 0.96; 0.93–1.00, respectively). Thus, very limited evidence suggests that a greater movement of extension of the thoracic and lumbar spine is associated with NP.

3.4.6. Proprioception

A single study (Tables 7 and 8), with fair methodological quality, used a laser pointer and the left and right rotation movements of the cervical spine to determine the joint repositioning error (JPE) (Sá & Silva, 2017). They showed that adolescents with NP have a higher JPE compared to adolescents without NP (WMD=1.9°; 95%CI=0.8°; 2.9° and 2.4° (1.3°; 3.5°) for right and left rotation, respectively). Therefore, very limited evidence suggests that adolescents with NP have a higher JPE than adolescents without NP.

3.4.7. Muscle endurance and strength

Two studies compared muscle endurance and strength between adolescents with and without NP (Tables 9 and 10). One of these studies (Oliveira & Silva, 2016), with fair

methodological quality, assessed the endurance of the deep flexors and extensors of the neck. The other study (Park et al., 2012), with poor methodological quality, measured the superficial electromyographic activity of the upper trapezius (UT), superficial cervical extensors (CE) and sternocleidomastoid (SCM) muscles while adolescents with and without NP were playing violin. The first study reported adolescents with NP to have a lower neck flexor (WMD=-11.4; 95%CI=-21.8; -0.9 seconds) and extensor (WMD=-42; 95%CI=-77.8; -6.3 seconds) muscles endurance capacity compared to adolescents without NP. The second study concluded that adolescents with NP have a higher activity (in % maximal voluntary isometric contraction) than adolescents without NP (WMD=9.7; 95%CI=5.0; 14.5 in left UT, 7.3 (3.8; 10.8) in right CE, 4.9 (0.9; 8.9) in left CE, 6.6 (1.8; 11.4) in right SCM and 6.2 (4.1; 8.4) in left SCM). Limited evidence indicates that adolescents with NP have lower endurance capacity of deep neck flexors and extensors and higher activity of larger superficial muscles. Regarding general muscle strength, in a prospective study with fair methodological quality, Mikkelsson et al. (2006) suggested that normal strength in adolescent was associated with lower probability of NP (OR; 95% CI=0.6; 0.4–0.9) in women adulthood.

3.4.8. Sensory Threshold

A single study (Sá & Silva, 2017), with fair methodological quality, used the pressure algometer to assess the pressure pain threshold (PPT) (Table 11 and 12) and reported adolescents with NP to have a lower pressure pain threshold than adolescents without NP (WMD=-14.2; 95%CI=-17.2; -11.2 N/cm² in right UT, -15.6 (-18.5; -12.8) in left UT, -9.3 (-11.3; -7.2) in right articular pillar C1/C2, -10.3 (-12.7; -7.8) in left articular pillar C1/C2, -11.1 (-13.8; -8.4) in right articular pillar C5/C6, -11.4 (-14.1; -8.7) in left articular pillar C5/C6 and -13.4 (-16.8; -10.0) in tibialis anterior). Thus, very limited evidence

suggests that adolescents with NP have higher local (neck) and distant pressure pain threshold than adolescents without NP.

3.5. Discussion

The purpose of this review was to identify and critically assess the evidence on functional changes associated with NP in adolescents. A total of 10 articles performing 15 comparisons between adolescents with and without NP for functional changes, including posture, range of motion, proprioception, muscle function and sensory threshold, were included. Overall, results suggest i) limited to very limited evidence that there are no differences for cervicothoracic posture between adolescents with and without NP; ii) very limited evidence that there are differences in neck movements between adolescents with and without NP; iii) very limited evidence that adolescents with NP have a higher JPE than adolescents without NP; iv) limited evidence that adolescents with chronic NP have a lower endurance of the deep neck muscles; and iv) very limited evidence that adolescents with NP have higher local and distant sensory pain threshold than adolescents without NP. These findings suggest that more high-quality research is needed and that it is very likely to change the conclusions and confidence we have in the findings of this review.

To our knowledge this is the first systematic review aiming to characterize NP associated with functional changes. Therefore, comparisons will be made against studies on adults with chronic idiopathic neck pain. Concerning posture, a previous systematic review in adults (Silva, Sharples, & Johnson, 2010), concluded that there was insufficient good quality evidence to determine whether head posture differs between participants with NP and asymptomatic participants. In our review it was possible to perform a meta-analysis with 3 studies comparing FHP between adolescents with and without NP and the overall results pointed towards no difference.

Nevertheless, the few studies included, their poor methodological quality and high heterogeneity (I^2=85%) may impact the accuracy of the findings (Israel & Richter, 2011) and therefore caution should be taken when interpreting them. In addition, the procedures and equipment used for postural assessment varied considerably among studies, which may explain some differences found between studies. In addition, all studies use external landmarks to characterize posture, what may not reflect the true alignment of the structures, as verified in a recent study that classified cervical spine alignment using internal radiological landmarks (Daffin, Stuelcken, & Sayers, 2017). Concerning ROM, the only study that reported values on this outcome (Park et al., 2012) suggested that ROM was significantly higher in the adolescents with NP for left lateral bending (WMD=9.4°) and left rotation (WMD=5.5°) and significantly lower for right and left axial rotation (WMD=-9.6°) and (WMD=-14.0°). These findings are different from those reported for adults as a recent systematic review concluded that adults with NP have significantly decreased ROM for all cervical motions when compared to asymptomatic participants (Crone & Dahl, 2012). However, the poor methodological quality of the study of Park et al. (2012), the small sample size and the fact of having assessed a specific population (i.e. adolescents who played violin) may have influenced the results. Therefore, more studies in adolescents are needed to explore the association between NP and ROM.

We found very limited evidence suggesting that adolescents with chronic NP have a lower endurance of the deep flexors (WMD=-11.4) and extensors (WMD=-42.0) of the neck and a higher activity of superficial muscles compared to adolescents without NP. The same study (Oliveira & Silva, 2016) found a standard error of measurement (SEM) of 9.50 and 12.18 seconds for deep neck flexor endurance test and 45.45 and 48.46 seconds for deep neck extensor endurance test, in adolescents with and without NP, respectively. Thus, the deep flexors endurance is the only test that may also represent

clinical relevance. In adults, these changes have been well documented (Caneiro et al., 2010; Falla, Jull, & Hodges, 2004; Jull, Kristjansson, & Dall'Alba, 2004; Shahidi, Johnson, Curran-Everett, & Maluf, 2012). Although the magnitude of the differences between individuals with and without NP tends to be higher in adults (Shahidi et al., 2012), these differences may be related to different methodologies of studies and characteristics of the population (for example, NP is of higher duration and intensity in adults compared to adolescents) (Oliveira & Silva, 2016). It has been suggested, in adults, that the increased activity of superficial muscles may be occurring to compensate the deficit in deep muscles or changes in motor control, which may result from a decreased activity of painful muscles or a more vigilant response from the individual to protect against pain and movement (Falla, Bilenkij, & Jull, 2004; Falla & Farina, 2007; Johnston, Jull, Souvlis, & Jimmieson, 2008; Nederhand, Jzerman, Hermens, Baten, & Zilvold, 2000).

Finally, very limited evidence was found that JPE is increased and pressure pain threshold is decreased in adolescents with chronic NP based on the findings of one study only (Sá & Silva, 2017). Two systematic reviews reported that adults with NP have impaired sense of head position when compared to asymptomatic participants (de Vries et al., 2015; Stanton, Leake, Chalmers, & Moseley, 2016). In the present study, the WMD for JPE between adolescents with and without NP was 1.9° and 2.4° for right and left rotation, respectively. In the review of Vries et al. (2015) in adults, JPE ranged from 3.7° and 6.1° for rotation movement. The lower JPE found for adolescents with NP when compared to adults with NP may be related to the different NP characteristics, which are of lower intensity and duration in adolescents (Sá & Silva, 2017). In addition, some mechanisms that have been reported in adults, as deficits in the vestibular system, degenerative and sensitivity changes in joints and muscles of the neck region and the influence of pain in local nociceptive activity and in central

nervous system can contribute to greater differences in JPE (Armstrong, McNair, & Taylor, 2008; Le Pera et al., 2001; Tsay, Allen, Proske, & Giummarra, 2015). A reorganization of the somatosensory cortex associated with the presence of chronic pain may also change the representation of body sites with pain and influence the JPE (Tsay et al., 2015). The same study (Sá & Silva, 2017) also suggests the presence of central sensitization in adolescents with NP as indicated by a decreased pressure pain threshold measured in the tibialis anterior when compared to adolescents with NP. Central sensitization has been reported not only by involving the sensitization of the nociceptors and segmental areas but also the entire central nervous system and endogenous pain modulation mechanisms (Roussel et al., 2013; Woolf, 2011). However, a systematic review on studies on adults concluded that there was a lack of evidence for the presence of central sensitization in adults with chronic idiopathic NP (Malfliet et al., 2015).

3.5.1. Limitations

We made no attempt to contact original study authors for clarifications. Studies of low and moderate methodological quality were included in this review and due to the small number of studies a separate analysis was not possible. In general, the studies included in this review were very heterogeneous regarding the population, definition of NP, measurement instruments and procedures, which may decrease the confidence in the findings. The limited number of studies for some of the outcomes of interest prevented a meta-analysis.

3.5.2. Implications for clinical practice and research

Limited and very limited evidence was found for all variables assessed in this review. This highlights the clear need for further research characterizing motor and sensory changes associated with NP in adolescents that overcome the methodological

limitations of included studies. In particular, future studies should clearly defined NP, clarify inclusion and exclusion criteria and perform a priori sample size calculations. They may also consider, comparing NP with asymptomatic adolescents and with adolescents with pain at other body sites to better characterize the potential between group differences. Such information will contribute to improve the characterization of NP in young people. The limited evidence found, also limits the strength of the recommendations for clinical practice. Nevertheless, based on the findings and on the strength of evidence we cautiously suggest that including posture and, particularly, head posture as part of the assessment and treatment of adolescents with NP is unlikely to be of relevance. In contrast, we cautiously suggest the inclusion of the remaining variables as of relevance when assessing adolescents with NP to inform treatment.

3.6. Conclusion

This systematic review found limited evidence that there are no differences in cervicothoracic posture between adolescents with and without NP as well as limited evidence that adolescents with NP have lower endurance capacity of the deep neck flexors and extensors, and increased activity of the larger superficial muscles and, very limited evidence that adolescents with NP have changes in neck range of motion, JPE and sensory pain thresholds when compared to adolescents without NP.

Table 1. Characteristics of included studies.

Study	Sample characteristics of NP group (mean ±SD)	Definition/Characteristics of Neck Pain	Sample characteristics of control group (mean ±SD)	Definition/Characteristics of asymptomatic participants	Measured Variables
Mikkelsson et al. (2006)	N=1125 (605 F, 520 M)	Tension Neck: a pain syndrome related to tightened neck musculature	No reference	No reference	Strenght
Cheung et al. (2009)	N=30 (17F, 13M) Age=14.47 ± 0.20y Weight= 52.36 ±1.43 kg Height=1.62 ±1.77m	Neck pain: experienced pain over neck region in the past three months.	N=30 (13F, 17M) Age=14.43 ± 0.18y Weight= 57.25 ±2.14 kg Height=1.65 ±1.43m	No reference	Forward Head Posture
Hellstenius (2009)	N=52 Age= 10-11y (9F e 9M) Age=11-12y (4F e 4M) Age=12-13y (15F e 11M)	Neck pain: students who answered “I have neck pain” when asked on the questionnaire if they experienced neck pain. Usual pain score:4 ±2.4 (Likert scale 0-11) Worst pain score:6.3 ±2.6 (Likert scale 0-11) (*) Intensity and frequency for NP and/or headaches	N=79	Students who answered “I never have neck pain”, or “I only have neck pain when I am sick” on the questionnaire.	Forward Head Posture Cervical Range of Motion (rotation to the right/left)
Straker et al. (2009)	N=74	Prolonged neck/shoulder pain (NSP): NSP in the past month and at least one episode that had lasted three or more months.	N=1394	Without NSP	Sitting spinal posture
Park et al. (2012)	N=9 (F) Age=17.88±0.33y BMI=52.11 ±7.94kg Height=157.78 ±6.12cm	Neck pain: Students who reported pain above 3 cm on the VAS after violin practice. Pain Score=5.89 ±0.78(VAS)	N=9 (F) Age=17.11±0.33y BMI=50.67 ±6.54kg Height=155.33 ±6.28cm	No reference	Electromyographic activity Cervical range of motion (flexion, extension, lateral bending, rotation and axial rotation)
Ruivo et al. (2014)	N=105 (81F, 24M)	Neck pain: Students were asked to answer yes or no to the following question: "Do you feel neck pain regularly?"	N=170 (72F, 98M)	No reference	Standing posture of the cervical and shoulder (including Forward head posture)
Oliveira &Silva (2016)	N=35 (25F, 10M) Age=16.6 ± 0.7y Weight= 59.9 ±11.2 kg Height=168.4 ±8.9 cm	Chronic idiopathic neck pain: pain felt dorsally between the inferior margin of the occiput and T1 not related to trauma or any known pathology that was present at least once a week during the last 3 months. Pain Score=3.7±2.2(VAS)	N=35 (22F, 13M) Age=16.7 ± 0.7y Weight= 64.5 ±14.4 kg Height=167.0 ±9.6 cm	Asymptomatic participants who had no current pain and reported that they had never NP.	Forward Head Posture Neck flexors/extensors muscles endurance

Dolphens et al. (2016)	N=77 Age (?)=10.6±0.47y (F)/ 12.6±0.54y (M)	Spinal pain: a discomfort or pain, in the back or neck that is considered to be a local, uncomfortable feeling in the back or neck, with the possibility of radiation to other parts of the body. Can be intermittent or constant, gradually developed or with a sudden onset.	N=765 Age (?)=10.6±0.47y (F)/ 12.6±0.54y (M)	No reference	Standing posture (trunk lean, sacral inclination) Range of motion (mobility of the thoracic and lumbar spine)
Richard et al. (2016)	N=219 (persistent NP) N=140 (NP worse with sitting) Age=17.0±0.2y	Neck pain: adolescents were asked to look at a picture depicting NP as pain in the neck and upper trapezius region and to answer four questions: "Have you ever had neck/shoulder pain?", "Has your neck/shoulder pain lasted more than 3 months continuously?", "Has your neck/shoulder pain ever lasted for more than 3 months off an on?", "Has sitting ever made your neck/shoulder pain worse?"	N=653 (?)	No reference	Sitting posture (neck, head and thoracic)
Sá &Silva (2017)	N=40 (21F, 19M) Age=17.2±0.56y	Chronic idiopathic neck pain: pain felt dorsally between the inferior margin of the occiput and T1 not related to trauma or any known pathology that was present at least once a week during the last 3 months. Pain Score: 3.39±1.84(VAS)	N=40 (21F, 19M) Age=17.2±0.56y	Asymptomatic participants: no current neck pain and reported that they had never had neck pain.	Pressure Pain Threshold Joint repositioning error

Legend: (?) Not clear in the study; F (Female); M (Male); y (years); kg (kilograms); cm (centimeters); NP (Neck Pain); NSP (Neck /Shoulder Pain); VAS (Visual Analogic Scale)

Table 2. Newcastle-Ottawa Quality Assessment Scale for case-control studies.

Criteria methodological quality	Selection				Comparability		Exposure			Total (9)	Quality rating
	Criterion 1	Criterion 2	Criterion 3	Criterion 4	Criterion 5	Criterion 6	Criterion 7	Criterion 8	Criterion 9		
Mikkelsson et al. (2006)	0	1	1	0	1	1	0	1	0	5	Fair
Cheung et al. (2009)	1	1	1	0	0	0	0	0	0	3	Poor
Hellstenius (2009)	0	1	1	1	0	0	1	1	0	5	Fair
Straker et al. (2009)	0	1	1	0	1	1	1	1	0	6	Fair
Park et al. (2012)	0	1	1	0	0	0	0	1	0	3	Poor
Ruivo et al. (2014)	0	1	1	0	0	0	0	1	0	3	Poor
Oliveira &Silva (2015)	0	1	1	1	1	0	0	1	0	5	Fair
Dolphens et al. (2016)	0	1	1	1	1	1	0	1	0	6	Fair
Richard et al. (2016)	0	1	1	1	1	1	0	1	0	6	Fair
Sá &Silva (2017)	0	1	1	1	1	0	0	1	0	5	Fair

Legend: 0 (criterion not fulfilled); 1 (criterion fulfilled); Criterion 1 (Case definition adequate); Criterion 2 (Representativeness of the cases); Criterion 3 (Selection of controls); Criterion 4 (Definition of controls) Criterion 5 (Study controls for age/gender); Criterion 6 (Study controls for any additional factor); Criterion 7 (Ascertainment of exposure); Criterion 8 (Same method of ascertainment for cases and controls); Criterion 9 (Non-Response rate)

Table 3. Studies that compared posture between adolescents with and without NP.

Study	Variable of interest	Measurements	Results of NP group (mean ±SD or OR (95% CI) or %)	Results of control group (mean ±SD or OR (95% CI) or %)	WMD (95% CI)	Main conclusions
Cheung et al. (2009)	Forward Head Posture (degrees)	Craniovertebral angle	60.03 ±9.05	57.10 ±5.00	2.9 (-0.8; 6.6)	No significant differences between adolescents with and without NP.
Hellstenius, S. (2009)	Forward Head Posture	Plumb line	Standing: 53% had FHP Sitting: 50% had FHP		.	No significant differences between adolescents with and without NP.
Straker et al. (2009)	Sitting spinal posture (degrees)	Head flexion angle (ahead)	71.0 (±11.1) F: 70.0 (±9.0) M: 72.5 (±13.8)	71.4 (±9.7) F: 71.3 (±9.4) M: 71.5 (±9.9)	-0.4 (-3.0; 2.2) -1.3 (-4.0; 1.4) 1.0 (-4.0; 6.1)	Adolescents with NP, looking ahead, have a more flexed cervicothoracic posture and a more extended posture of the trunk than adolescents without NP. They also have a greater lordosis and anterior pelvic tilt, and these differences remain after analysis by gender and when tested looking down.
		Head flexion angle (down)	108.8 (±15.7) F: 104.9 (±13.9) M: 107.2 (±18.3)	105.7 (±13.3) F: 104.1 (±13.1) M: 107.2 (±13.3)	3.1 (-0.5; 6.7) 0.8 (-3.4; 5.0) 0 (-6.7; 6.7)	
		Neck flexion angle (ahead)	51.8 (±8.6) F: 51.1 (±7.5) M: 52.8 (±10.1)	52.4 (±8.7) F: 51.3 (±7.1) M: 53.4 (±9.9)	-0.6 (-2.6; 1.4) -0.2 (-2.5; 2.1) -0.6 (-4.3; 3.1)	
		Neck flexion angle (down)	68.5 (±11.0) F: 67.7 (±9.8) M: 69.7 (±12.7)	69.3 (±10.6) F: 67.1 (±9.2) M: 71.4 (±11.3)	-0.8 (-3.4; 1.8) 0.6 (-2.3; 3.5) -1.7 (-6.4; 3.0)	
		Craniocervical angle (ahead)	160.8 (±12.7) F: 161.2 (±11.6) M: 160.2 (±14.6)	161.0 (±12.4) F: 160.0 (±12.3) M: 161.8 (±12.3)	-0.2 (-3.2; 2.8) 1.2 (-2.3; 4.7) -1.6 (-7.0; 3.8)	
		Craniocervical angle (down)	142.7 (±11.2) F: 142.9 (±8.9) M: 142.4 (±14.1)	143.6 (±12.0) F: 143.0 (±12.4) M: 144.2 (±11.7)	-0.9 (-3.5; 1.8) -0.1 (-2.9; 2.7) -1.8 (-7.0; 3.4)	
		Cervicothoracic angle (ahead)	146.9 (±8.6) * F: 144.2 (±7.6) M: 151.1 (±8.6)	149.1 (±8.3) F: 145.4 (±6.9) M: 152.5 (±8.0)	-2.2 (-4.2; -0.2) -1.2 (-3.5; 1.1) -1.4 (-4.6°; 1.8)	
		Cervicothoracic angle (down)	132.5 (±10.7) F: 129.8 (±9.7) M: 136.6 (±11.1)	134.1 (±9.2) F: 131.2 (±8.0) M: 136.7 (±9.4)	-1.6 (-4.1; 0.9) -1.4 (-4.3; 1.5) -0.1 (-4.2; 4.0)	
		Trunk angle (ahead) *	229.4 (±12.5) F: 223.8 (±10.2) M: 238.0 (±10.8)	232.4 (±12.8) F: 225.9 (±10.8) M: 238.3 (±11.5)	-3.0 (-6.0; -0.1) -2.1 (-5.2; 1.0) -0.3 (-4.3; 3.8)	
		Trunk angle (down)	231.5 (±12.6) F: 226.1 (±10.3) M: 239.8 (±11.5)	234.4 (±13.0) F: 227.7 (±10.9) M: 240.6 (±11.6)	-2.9 (-5.9; 0.1) -1.6 (-4.7; 1.5) -0.8 (-5.1; 3.5)	

		Lumbar angle (ahead)	123.2 (±18.6) F: 118.7 (±17.9) * M:130.1 (±17.8)	129.6 (±18.4) F:124.4 (±16.1) M:134.3 (±19.1)	-6.4 (-10.7; -2.1) -5.7 (-11.1; -0.3) -4.2 (-10.8; 2.4)	
		Lumbar angle (down)	123.9 (±18.7) F: 119.6 (±17.9) * M: 130.6 (±18.2)	129.9 (±18.4) F: 124.7 (±16.1) M: 134.6 (±19.0)	-6.0 (-10.4; -1.6) -5.1 (-10.5; 0.3) -4.0 (-10.8; 2.8)	
		Pelvic tilt (ahead)	9.7 (±16.4) F: 13.9 (±14.5) * M: 3.1 (±17.4)	4.4 (±15.6) F: 8.9 (±13.6) M: 0.3 (±16.1)	5.3 (1.5; 9.1) 5.0 (0.6; 9.4) 2.8 (-3.6; 9.2)	
		Pelvic tilt (down)	9.3 (±16.7) F: 13.2 (±14.6) * M: 3.3 (±18.1)	4.1 (±15.6) F: 8.5 (±13.7) M: 0.1 (±16.2)	5.2 (1.5; 9.1) 4.7 (0.3; 9.1) 3.2 (-3.6; 9.2)	
Ruivo et al. (2014)	Standing posture of the cervical and shoulder (degrees)	Sagittal head tilt angle (HT)	16.4±5.7 F: 15.8±5.5 M: 18.1±6.3	17.6±5.7 F: 16.5±5.1 M:18.5±6.0	-1.2 (-2.6; 0.2) -0.7 (-2.4; 1.0) -0.4 (-3.2; 2.4)	No significant differences between adolescents with and without NP for the HT.
		Cervical angle	46.5±5.6 F: 45.8 ±5.6 * M: 48.6 ±5.5	48.0 ±4.8 F: 47.4 ±4.8 * M: 48.4 ±4.8	-1.5 (-2.8; -0.2) -1.6 (-3.2; -0.1) 0.3 (-2.1; 2.6)	Girls with NP have a higher FHP than girls without NP.
		Shoulder angle (SH)	52.2 ±9.1 F: 51.4 ±8.8 M: 55.0 ±9.9	51.0 ±8.2 F: 50.7 ±7.7 M:51.1 ±8.4	1.3 (-0.8; 3.4) 0.7 (-1.9; 3.3) 3.9 (-0.4; 8.2)	No significant differences between adolescents with and without NP.
Oliveira &Silva (2016)	Forward Head Posture (degrees)	Angle between C7, tragus and the horizontal	46.6 ±4.9	44.2±3.6	2.4 (0.4; 4.5)	Adolescents with NP have less FHP than adolescents without NP.
Dolphens et al. (2016)	Standing posture	Global body alignment (leaning-forward vs neutral)	OR:1.5 (0.9-2.6)			No significant differences, the global body alignment was not associated with NP.
		Trunk lean	OR:1.2 (1.1-1.3)			Adolescents with a higher backward trunk lean and levels of pelvic retroversion, have a greater probability to have NP.
		Sacral inclination in backward bend position	OR:1.0 (0.9-1.0)			
Richard et al. (2016)	Sitting posture	Cervicothoracic posture in persistent NP	OR cluster 2: 0.8 (0.5-1.4) OR cluster 3:0.7 (0.4-1.3) OR cluster 4:0.9 (0.6-1.3)			No significant differences between adolescents with and without NP.
		Cervicothoracic posture in NP worse with sitting	OR cluster 2:1.1 (0.6-2.0) OR cluster 3:0.7 (0.4-1.5) OR cluster 4:1.4 (0.9-2.2)			

Legend: F (Female); M (Male); NP (Neck Pain)

Table 4. Measurement procedures used in the assessment of posture.

Study	Variable of interest	Measuring instrument	Measurement procedure
Cheung et al. (2009)	Forward Head Posture	Head Posture Spinal Curvature Instrument	i) Participants were asked to stand in a relaxed posture. ii) The C7 spinous process was marked and the instrument placed adjacent to the left shoulder. With the axis at the spinous process of C7, the stationary arm was aligned parallel to the floor, which was confirmed by the spirit level attached. Then the movable arm of the instrument was aligned to the tragus of the left ear. iii) The craniovertebral angle is the angle formed between C7, the tragus of the ear and the horizonal. (In this study, this angle was measured in unloaded and carrying backpack 5%, 10%, 15%, 20%, 25% and 30% of their body weights).
Hellstenius (2009)	Forward Head Posture	Plumb line test for postural alignment	i) The base point was fixed anterior to the lateral malleolus and forward head posture was recorded when the external auditory meatus (EAM) is anterior to the plumb line. ii) Participants was instructed to sit upright with their buttocks positioned at the back of a school chair and their arms relaxed at their sides. iii) The midpoint of the body laterally was used for a fixed point and the position of the EAM was assessed in relation to the plumb line. FHP was noted when the EAM was anterior to the plumb line.
Oliveira &Silva (2015)	Forward Head Posture	Universal goniometer and bubble level	i) Participants were instructed to stand in their stocking feet in a position they feel is “natural” for them and were instructed to have a similar distribution of body weight through each foot, to place their feet slightly apart and have their arms by their sides. ii) The spinous process of C7 was identified by palpation and marked with tape. To facilitate the natural head posture that is sought, participants were asked to tilt their head forwards and backwards with decreasing amplitude until they felt that a natural FHP is reach. iii) FHP was characterized with the angle between C7, the tragus of the ear and the horizonal. Decreasing values indicative of a more FHP.
Ruivo et al. (2014)	Standing posture of the cervical and shoulder	Photogrammetry and PAS/SAPO software	i) Participants were instructed to stand comfortably in a normal standing position and to look straight ahead aligned perpendicular to the camera. ii) Landmarks were placed on the floor in front of the camera and in front t a white wall. A camera was supported on a tripod three meters away of the participant's position line and all necessary calibration was performed. The height of the tripod was adjusted so the middle of the objective lens was 130 cm above the ground. Before photographing, was placed reflective markers on right side of participant's body: tragus of the ear, lateral canthus of the eye, spinous process of C7 and midpoint of the humerus to help the measure of the angles. iii) Angles definition: Sagittal head tilt angle (HT), the angle formed at the intersection of a horizontal line through the tragus of the ear and a line joining the tragus of the ear and the lateral canthus of the eye; Cervical angle (CV), the angle formed between C7, the tragus of the ear and the horizontal line (if

			the angle was less than 50°, the participant was considered to have FHP) and the Shoulder angle (SH), the angle formed at the intersection of the line between the midpoint of the humerus and spinous process of C7 and the horizontal line through the midpoint of the humerus (the angle of 52° was the reference angle).
Dolphens et al. (2016)	Standing posture	Photographic postural, digital inclinometer and Spinal Mouse	i)Participants were assessed regarding gross body segment orientations, specific spinopelvic characteristics and magnitude of spinal curves (in this study the description of the photographic postural and the digital inclinometer procedure was referenced for consultation in another study, Dolphens et al. 2012). ii) Angle definition: trunk lean, defined as a greater angle between the vertical and a line joining C7 to the greater trochanter and sacral inclination with respect to the vertical, where the positive values indicated a forward inclination of the sacrum and negative values the backward inclination.
Richard et al. (2016)	Sitting posture (neck, head and thoracic)	2D photographic postural	i) Photographic reflective markers were placed on bony landmarks on the participant's right side. Landmarks apply are the outer canthus, tragus and the C7 and T12 spinous processes. A 25cm plumb line is hung from the stool, to calibrate distance and determine vertical. ii) A camera was placed on a tripod 80cms from the floor and 250cm perpendicular to the participant. iii) Right-sided lateral photographs were taken as participants sit on a stool with thighs horizontal and knees flexed to 90 degrees.
Straker et al. (2009)	Sitting spinal posture	2D photographic postural	i) Retro-reflective markers were placed on the right outer canthus, right tragus, C7 and T12 spinous processes, anterior superior iliac spine and greater trochanter. ii) Lateral photographs were taken with each child sit on a stool (adjusted to their popliteal height) during three different static sit postures: (a) to look straight ahead, (b) to look down at their lap, and (c) to sit slumped. The camera was positioned on a tripod 80 cm from the floor and 250 cm from the subject, with the subject align so they are face perpendicular to camera. Posteriorly the standard head/neck/thoracic angles were calculated. iii) Angles definition: Head flexion angle, formed between the vertical and the line from canthus to tragus; neck flexion angle, angle between the vertical and the line of tragus to C7; craniocervical angle, angle between the lines of canthus to tragus and tragus to C7; cervicothoracic angle, angle between the lines of tragus to C7 and C7 to T12; trunk angle, posterior angle formed between the lines of C7 to T12 and T12 to greater trochanter; lumbar angle, posterior angle formed between the lines of T12 to anterior superior iliac spine (ASIS) and ASIS to greater trochanter and pelvic tilt, angle between the vertical and the line of greater trochanter to ASIS.

Table 5. Studies that compared range of motion between adolescents with and without NP.

Study	Variable of interest	Measurements	Results of NP group (mean ±SD or OR (95% CI)	Results of control group (mean ±SD or OR (95% CI)	WMD (95% CI)	Main conclusions
Hellstenius (2009)	Cervical range of motion	Rotation to the right and left	No reference	No reference	No reference	No significant differences between adolescents with and without NP.
Park et al. (2012)	Cervical range of motion (degrees)	Flexion	46.4 ± 11.0	55.4 ± 15.12	-9.0 (-21.2; 3.3)	Adolescents have a greater range of motion of left lateral bending and left rotation, and a lower axial rotation, than adolescents without NP.
		Extension	64.5 ± 15.4	62.5 ± 16.2	2.0 (-12.6; 16.6)	
		Right lateral bending	44.5 ± 10.8	36.9 ± 4.0	7.6 (0.0; 15.1)	
		Left lateral bending	47.8 ± 8.8	38.4 ± 4.9	9.4 (2.8; 16.0)	
		Right rotation	57.2 ± 5.7	52.9 ± 3.5	4.4 (0.0; 8.7)	
		Left rotation	59.2 ± 4.2	53.7 ± 5.9	5.5 (0.8; 10.2)	
		Right axial rotation	37.5 ± 11.1	47.1 ± 6.9	-9.6 (-18.2; -1.1)	
		Left axial rotation	25.2 ± 3.6	39.2 ± 10.3	-14.0 (-21.1; 6.9)	
Dolphens et al. (2016)	Range of motion	Extension of the thoracic spine	OR:0.98 (0.96-1.00)			Adolescents with a higher extension motion levels of the thoracic and lumbar spine, have a greater probability to have NP.
		Extension of the lumbar spine	OR:0.96 (0.93-1.00)			

Legend: NP (Neck Pain)

Table 6. Measurement procedures used in the assessment of range of motion.

Study	Variable of interest	Measuring instrument	Measurement procedure
Hellstenius (2009)	Cervical Range of Motion (rotation to the right/left)	Cervical collar goniometer	i) Participants were instructed to be sit erect and to rotate their head to each side as far as they comfortably could without moving their shoulders. ii) The examiner to stand in behind them with fingers rest on their shoulders to feel if when shoulder movement is engaging. iii) Rotation was measured in degrees to the right and to the left before shoulder activity is engage.
Park et al. (2012)	Active cervical range of motion (flexion, extension, lateral bending, rotation and axial rotation)	Three-dimensional ultrasonic motion analysis system	i) Participant were asked to sit upright in a chair with her feet on the floor, look straight ahead and to assume a neutral (anatomical) position. ii) One triple-active marker was attached over the head. Before record data for neck ROM, the motions (flexion, extension, rotation, axial rotation, lateral bending) were explained and demonstrate by the examiner. iii) Each participant was instructed to move her head in each direction and continue the motion until she felt the end of the range of neck flexion, extension, lateral bending, rotation and axial rotation on both sides. During axial rotation, the examiner's hand was placed on the participant's chin to maintain a chin-tuck position. The participant was asked to move her head at a self-selected comfortable speed. iv) Five repetitions were performed.
Dolphens et al. (2016)	Range of motion (mobility of the thoracic and lumbar spine)	Spinal Mouse	i) The full flexion and extension position, the thoracic and lumbar spine, and trunk and sacral inclination of each participant were recorded using the skin-surface electromechanical device.(In this study the description of the procedure was referenced for consultation in another study, Dolphens et al. 2012).

Table 7. Studies that compared joint repositioning error between adolescents with and without NP.

Study	Variable of interest	Measurements	Results of NP group (mean ±SD)	Results of control group (mean ±SD)	WMD (95% CI)	Main conclusions
Sá &Silva (2017)	JPE (degrees)	Right rotation	5.2±2.6	3.4±1.9	1.9 (0.8; 2.9)	Adolescents with NP showed impaired joint position sense when compared to adolescents without NP.
		Left rotation	6.2±2.7	3.8±2.7	2.4 (1.3; 3.5)	

Legend: NP (Neck Pain)

Table 8. Measurement procedures used in the assessment of joint repositioning error.

Study	Variable of interest	Measuring instrument	Measurement procedure
Sá &Silva (2017)	JPE	Laser point	i) A laser pointer was fixed on the top of a helmet that participants used during measurements. Participants were seated in a standard chair placed 90 cm away from a wall where the target (a A3 sheet of millimetric paper) was fixed and had their eyes close. ii) Rotation movements were used to the right and to the left. Before the beginning of the test, participants were asked to have their head in neutral position, which was marked on the target (correspond to where the light of the laser pointer is on the sheet of paper). From this position participants were asked to fully rotate their head to the left or right and return to the initial neutral position that was remarked on the target. iii) Between each trial, the examiner manually adjusts the participant's head to match the original start position and gave no feedback on accuracy. One familiarization trial for each side (one right and one left) was conducted before measurements. iv) There were performed 3 movements to the left and 3 movements to the right.

Table 9. Studies that compared muscle function between adolescents with and without NP.

Study	**Variable of interest**	**Measurements**	**Results of NP group (mean ±SD or OR (95%CI)**	**Results of control group (mean ±SD or OR (95%CI)**	**WMD (95% CI)**	**Main conclusions**
Mikkelsson et al. (2006)	Strenght	Intermediate	(F) OR: 0.7 (0.5-1.1) (M) OR: 1.1 (0.6-2.0)			No significant differences, high strength was not associated with NP.
		High	(F) OR:0.6 (0.4-0.9) (M) OR:1.1 (0.6-2.0)			A normal strength in adolescent may help to decrease the risk of NP in adult women.
Park et al. (2012)	Electromyographic activity (%MVIC, maximal voluntary isometric contraction)	UT of the right side	9.8 ± 5.2	7.7 ± 4.2	-7.7 (-12.0; -3.3)	Adolescents with NP have a higher activity of the left UT, bilateral CEs and bilateral SCMs than adolescents without NP.
		UT of the left side	24.3 ± 3.6	14.5 ± 6.3	-9.7 (5.0; 14.5)	
		CE of the right side	19.3 ± 4.3	12.0 ± 3.3	7.3 (3.8; 10.8)	
		CE of the left side	21.5 ± 5.5	16.7 ± 2.7	4.9 (0.9; 8.9)	
		SCM of the right side	15.7 ± 4.4	9.1 ± 5.9	6.6 (1.8; 11.4)	
		SCM of the left side	10.4 ± 2.6	4.2 ± 2.1	6.2 (4.1; 8.4)	
Oliveira &Silva (2016)	Neck flexors/extensors endurance (seconds)	Deep neck flexor endurance test	24.5 ±23	35.9±21.5	-11.4 (-21.8; -0.9)	Adolescents with NP have less neck flexor endurance capacity when compared to adolescents without NP.
		Deep neck extensor endurance test	126.6±77.9	168.7±74.8	-42.0 (-77.8; -6.3)	Adolescents with NP have less neck extensor muscle endurance capacity when compared to adolescents without NP.

Legend: F (Female); M (Male); NP (Neck Pain); UT (Upper Trapezius), CE (superficial Cervical Extensors) and Sternocleidomastoid (SCM)

Table 10. Measurement procedures used in the assessment of muscle function.

Study	Variable of interest	Measuring instrument	Measurement procedure
Oliveira &Silva (2015)	Neck flexors/extensors endurance	Deep neck flexor endurance test	i) Participants were placed in the supine position with their arms by their side. ii) They were asked to flex the upper cervical spine, moved their heads away from the couch approximately 2.5 cm and then maintain this position for as long as possible. The examiner had a chronometer in one hand while the other hand is kept beneath the participant's head. iii) The test finished when participants drop their heads or lose the craniocervical flexion. Head drop was assessed by observe the position of the head and feel it touch the examiner's hand, loss of craniocervical flexion was assessed by examine the position of the mandible in relation to the neck and by observe the skin folders posterior to the mandible formed when the head is in craniocervical flexion. A change in the thickness of this skin fold or visible motion of the chin was interpreted as a loss of craniocervical flexion and was resulted in finish of the test. iv) Test was repeated twice with a 5 min interval between repetitions.
		Neck extensor endurance test	i) Participants were placed in the prone position, head neutral, arms by their sides and a 10 cm stabilizing velcro was placed at the 6th dorsal vertebra level. ii) An inclinometer and a 5 cm strap were placed around the participants head with 2 Kg weight hanging from it. Participants were asked to support this weight for as long as possible while maintaining the neutral head position. The weight and the participants' head were supported until the beginning of the test. iii) The test finished when the head moved more than 5° from the neutral position or a maximum of 5 minutes was reached. iv) The test was repeated twice with a 5 minutes interval between repetitions.
Mikkelsson et al. (2005)	Strenght	Sit up test	i)Participants were instructed to lie down in their backs with knees flexed at a right angle and with hands on the back of the neck. ii) An examiner kept the participant's heels in contact with the floor. iii) For 30 seconds participants were continually sit up to touch their knees with their elbows.
Park et al. (2012)	Electromyographic activity	Electromyograph	i) The skin at the electrode sites were prepared by shave the area and then clean with rubbing alcohol. Surface electrode pairs were positioned at an interelectrode distance of 2 cm. The reference electrode was placed on the spinous process of C7. ii) EMG data was collected for the following muscles: bilateral upper trapezius (UT) (2 cm lateral to the midline drawn between the C7 spinous process and the posterolateral acromion), the sternal head of the sternocleidomastoids (SCM) (half the distance between the mastoid process and suprasternal notch), and the cervical extensors (CE) (parallel to the spine, approximately 2 cm apart, over the muscle belly at approximately C4). iii) EMG signal was recorded three times for 30-seconds, with a 5- minute rest between trials.

Table 11. Studies that compared pain sensory threshold between adolescents with and without NP.

Study	**Variable of interest**	**Measurements**	**Results of NP group (mean ±SD)**	**Results of control group (mean ±SD)**	**WMD (95% CI)**	**Main conclusions**
Sá &Silva (2017)	Pressure Pain Threshold (*N/cm²)	Right upper trapezius	20.7±5.1	34.9±8.1	-14.2 (-17.2; -11.2)	Adolescents with NP showed increase pain sensitivity than adolescents without NP.
		Left upper trapezius	20.5±5.1	36.1±7.6	-15.6 (-18.5; -12.8)	
		Right articular pillar C1/C2	15.5±4.2	24.7±5.2	-9.3 (-11.3; -7.2)	
		Left articular pillar C1/C2	16.5±5.5	26.8±5.7	-10.3 (-12.7; -7.8)	
		Right articular pillar C5/C6	16.7±5.2	27.8±7.0	-11.1) (-13.8; -8.4)	
		Left articular pillar C5/C6	20.1±6.1	31.5±6.1	-11.4 (-14.1; -8.7)	
		Tibialis anterior	41.4±8.5	54.8±7.0	-13.4 (-16.8; -10.0)	

Legend: NP (Neck Pain)

Table 12. Measurement procedures used in the assessment of sensory threshold.

Sá &Silva (2017)	Pressure Pain Threshold	Algometer	i) Participants were instructed to be place in the prone position, with the head aligned and as relaxed as possible (except for the tibialis anterior, which was measured with the patient in supine). ii) The algometer allowed to measure PPT at both the right and left upper trapezius (at the mid distance between the posterior angle of the acromion and C7), the right and left articular pillar between C1 and C2 (approximately 1 cm lateral and above the spinous process of C2), the right and left articular pillar of C5/C6 (approximately 1 cm lateral to the mid distance between the spinous processes of C5 and C6, which was identified by palpation) and over the right tibialis anterior. Before measurements on these points were taken, PPT measurement was demonstrated in the hand to familiarize the patient with the procedure. (lateral to the medial malleolus). iii) Participants were instructed to say “stop” when the sensation change from pressure to pain. A probe of 0.5 cm of diameter and pressure was applied at a rate of approximately 3N/s up to a maximum of 60N, which is not exceed because of the risk of tissue damage. iv) Three measurements were taken at each point. A 30-s resting period was allowed between each measurement.

4. PSYCHOSOCIAL VARIABLES AND SLEEP ASSOCIATED WITH NECK PAIN IN ADOLESCENTS: A SYSTEMATIC REVIEW

Based on the systematic review from Andias & Silva (2019). “Psychosocial variables and sleep associated with neck pain in adolescents: a systematic review. Physical & Occupational Therapy in Pediatrics, 40 (2):168-191.

4.1. Introduction

In addition to the functional changes reported in Chapter 3, psychosocial factors and sleep-related changes also seem relevant in adolescents with NP. Adolescents with NP have been found to report higher rates of depression and perceived stress (Diepenmaat et al., 2006), anxiety (Rees et al., 2011), catastrophizing (Sá & Silva, 2017), defined as an exaggerated negative mental set used during the actual or anticipated pain experience (Sullivan et al., 2001), and poor self-efficacy, defined as an individual resilience mechanism, which activated in response to pain, may positively influence pain management capacity (Tomlinson, Cousins, Mcmurtry, & Cohen, 2017), when compared to asymptomatic adolescents. Psychosocial variables have also been related to altered sleep patterns which, in turn, have been found to be a risk factor for the onset of NP (Andreucci, Campbell, & Dunn, 2017). Furthermore, as previously suggested, sleep impairments and psychosocial variables might contribute to altered pain processing and facilitate the central hyperexcitability of the central nervous system (Othman et al., 2021). However and to the best of our knowledge, studies on psychosocial changes, and sleep impairments associated with NP in young people have not been systematically reviewed, assessed, and synthetized. Thus, the aim of the present systematic review is to identify and critically assess the evidence on the association between NP and psychosocial variables (depression, anxiety,

catastrophizing, stress, disability, fear of movement, self-efficacy) and sleep, in adolescents with NP.

4.2. Methods

4.1.1. Registration of systematic review

The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines were followed in this review (Moher et al., 2009) and the protocol was registered in PROSPERO (CRD42018089533).

4.2.1. Search strategy and study selection

An electronic search was conducted in Pubmed, ScienceDirect, Web of Science, PEdro, Scielo, Scopus and Academic Search Premier (EBSCO host) databases in the period of 1 December 2017 to January 2018. A combination of words was used in the search strategies, including: neck pain, adolescents, psychosocial, depression, anxiety, catastrophizing, stress, fear of movement, sleep and self-efficacy. Pubmed was searched using MeSH terms and filters for age and article type (to exclude reviews, systematic reviews and books). No date limit was used but languages of publication were limited to English, Spanish, French and Portuguese. The list of references of all included studies was checked for additional studies not identified by electronic searches.

To be included in this systematic review, studies had to:

- Compare at least one of the following variables: depression, anxiety, catastrophizing, stress, fear of movement, sleep and self-efficacy between adolescents with and without NP;
- Use participants aged between 12 and 18 years old (Williams et al., 2012);
- Report on acute or chronic NP not related to any known pathology or injury (Merskey & Bogduk, 2002; Misailidou et al., 2010);

- Be full text articles published in peer reviewed journals.

In this systematic review, studies in adolescents with nervous system pathology, rheumatic pathology or any major structural pathology (i.e. infection, neoplasms, systemic disease) in addition to NP or as a cause of NP were excluded.

4.2.2. Data extraction

Articles were imported from databases into the EndNote X5 (Clarivate Analytics, Philadelphia, United States) and checked for duplicates. Then, titles and abstracts were screened by the first author (RA) against the inclusion and exclusion criteria. Potential eligible manuscripts were then retrieved and screened for inclusion by the two authors (RA and AGS). Data were extracted by the first author (RA) using a standardized form including author, sample characteristics, NP characteristics, outcomes of interest and results. The extracted data was checked by the second author (AGS) and the disagreements between authors at any point in the process were resolved through discussion until consensus was achieved.

4.2.3. Methodological quality assessment

The assessment of methodological quality of included studies was performed using the NOS for case control studies (Lo et al., 2014; Wells et al., 2014) by the two authors, independently. Any disagreement was resolved by discussion until reaching a consensus. Agreement was measured using a Cohen's K. Values below 0.20 indicate no concordance, between 0.21 and 0.39 minimal concordance, between 0.40 and 0.59 weak concordance, between 0.60 and 0.79 moderate concordance, between 0.80 and 0.90 strong concordance and above 0.90 almost perfect concordance (McHugh, 2012). The NOS scale is recommended by the Cochrane Collaboration (Higgins & Green, 2011) and allows the assessment of risk of bias in three domains: 1) selection of study groups (maximum of 4 points); 2) comparability of groups (maximum of 2 points); and

3) ascertainment of exposure and outcomes (maximum of 3 points). Each item of the scale is assigned with 1 point (study meets the criteria of the item) or 0 points (study does not meet the criteria, or the item is not described). The total score can range from 0 to 9 points, with higher scores indicating lower risk of bias. This scale also allows a quality rating: 1) good quality (score ≥7), 2), fair quality (score ≥5 and <7) and 3) poor quality (score <5) (Mcpheeters et al., 2012).

4.3. Data synthesis and analysis

Data was extracted from each study by the first author and then checked by the second author. For studies that reported data as mean ± SD, the WMD and respective 95% CI were calculated using Meta XL software (Epigear International, Australia; http://www.epigear.com). Two separated meta-analysis were performed, one aggregating studies that measured depression and other aggregating studies on sleep, using Meta XL and the random-effect model. The small number of studies for the remaining variables (less than 3) prevented meta-analysis for the remaining variables. Statistical heterogeneity was assessed using the Cochran's Q test (defined as $p<0.05$) and the I^2 statistic (interpreted as 0% to 40% might not be important; 30% to 60% may represent moderate heterogeneity; 50% to 90% may represent substantial heterogeneity and 75% to 100% considerable heterogeneity) (Higgins & Green, 2011; Israel & Richter, 2011). Forest plots were used to present the individual studies' results and the overall analysis (Barendregt & Doi, 2011). For studies reporting results as OR results were interpreted as: exposure does not affect odds of outcome (OR=1), exposure associated with a higher odd of outcome (OR>1) and exposure associated with lower odd of outcome, i.e., has a protective effect (OR<1) (Chang & Hoaglin, 2017; Szumilas, 2010). Finally, after analyzing the results, we defined the "levels of evidence" as strong evidence, moderate evidence, limited evidence, very limited

evidence and conflicting evidence, in line with vanTulder et al. (2003) modified by Barton et al. (2013).

- Strong evidence: pooled results must derive from three or more studies, with a minimum of two studies of good methodological quality in NOS, which are statistically homogeneous ($p>0.05$);
- Moderate evidence: statistically significant pooled results must derive from multiple studies, with at least one study with a good methodological quality in NOS, which are statistically heterogeneous ($p<0.05$), or from multiple studies with poor/fair methodological quality in NOS, which are statistically homogeneous ($p>0.05$);
- Limited evidence: results from multiple studies with poor/fair methodological quality in NOS, which are statistically heterogeneous ($p<0.05$) or from one study with good methodological quality;
- Very limited evidence: results from one study with poor/fair methodological quality;
- Conflicting evidence: pooled insignificants results and derived from multiple studies, which are statistically heterogeneous ($p<0.05$).

4.4. Results

4.4.1. Study selection

In total, 5064 references were retrieved from electronic databases. After removing duplicates (n=1923), 3141 references were screened based on title and abstract and 56 full articles were considered as potentially eligible. Of the 56 full manuscripts retrieved, 13 met the eligibility criteria and were included in this systematic review (Figure 4). Reasons for exclusion were: duplicated data (n=4), participants were outside the age range considered in this review (n=37), no control group (n=1) and written in Chinese language (n=1). One study was included after checking the

references of included studies. Therefore, a total of 14 studies were included in this systematic review.

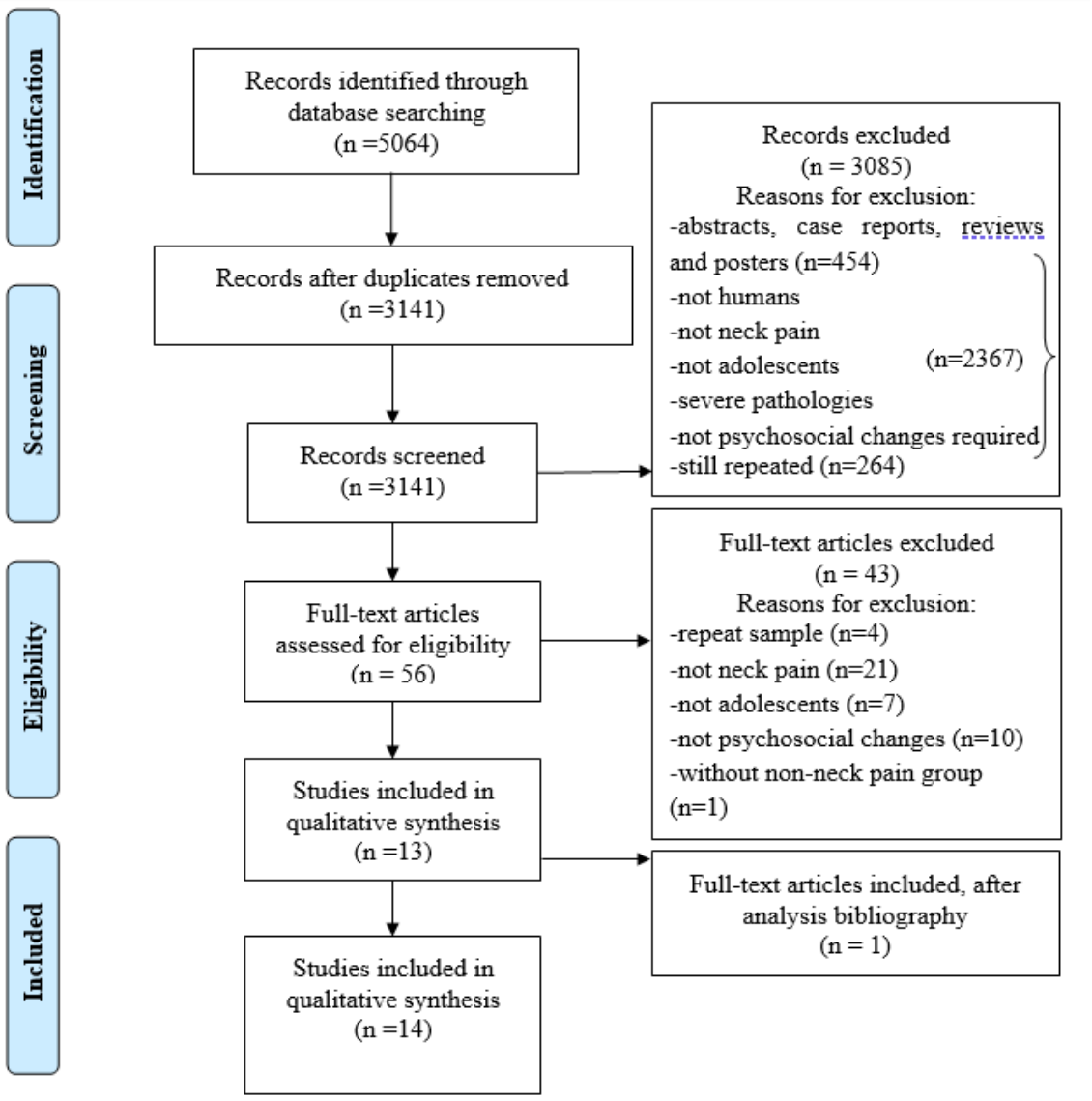


Figure 4. Flow chart (PRISMA).

4.4.2. General overview of included studies

Twelve of the 14 included studies were cross-sectional and the remaining 2 (Auvinen et al., 2010; Ståhl et al., 2008) were longitudinal studies. Six of the included studies assessed more than one variable of interest totaling 20 comparisons (out of 14 studies) between adolescents with and without NP: depression (n=7), anxiety (n=2), catastrophizing (n=1), stress (n=2), sleep (n=6) and self-efficacy (n=2). No studies

were found on fear of movement. Three of the included studies did not specify the duration of NP (Dolphens et al., 2016; dos Passos et al., 2017; Paiva, Gaspar, & Matos, 2015). The remaining studies used different definitions of NP. Lastly, three studies reported the intensity of pain (Sá & Silva, 2017; Shan et al., 2014; Silva et al., 2017) and one the frequency (Shan et al., 2014). The characterization of the studies can be found in table 13.

4.4.3. Methodological quality

Total score for the 14 included studies varied between 2 (n=1) and 6 (n=8), out of a maximum of 9 points (Table 14). Cohen's k for reviewer's agreement was 0.79, 95% CI (0.69; 0.89). No study met criterion 1 (subjects were interviewed by an experienced physical therapist for their history of NP). All but one study met criterion 2 (representativeness of the population of adolescents with NP) because its sample included adolescents who practiced sport only. All studies (n=14) used community controls (criterion 3), but 2 of them did not state the criteria for being a control (dos Passos et al., 2017; Myrtveit et al., 2014) (criterion 4). Only 9 studies met criteria 5 (control for age/gender) and 6 (control for additional factors) (Auvinen et al., 2010; Diepenmaat et al., 2006; Dolphens et al., 2016; Myrtveit et al., 2014; Niemi et al., 1997; Paiva et al., 2015; Pollock et al., 2011; Shan et al., 2014; Silva et al., 2017). None of the included studies performed a structured blinded interview to participants (criterion 8) or reported the non-response rate (criterion 9).

4.4.4. Depression

Seven studies with fair methodological quality assessed depression using a total of 6 different measurement instruments, and all studies reported adolescents with NP to have higher depressive symptoms than asymptomatic adolescents (Tables 15 and 16). All studies included boys and girls, but only 5 performed separated analysis (Härmä,

Kaltiala-Heino, Rimpelä, & Rantanen, 2002; Myrtveit et al., 2014; Niemi et al., 1997; Pollock et al., 2011; Ståhl et al., 2008). The meta-analysis (figure 5) with 3 studies that did not perform an analysis by gender (Diepenmaat et al., 2006; Dolphens et al., 2016; Pollock et al., 2011), showed significant heterogeneity across studies (Q=55.18, p=0.00; I^2=96%) and no statistically significant difference for depression between adolescents with and without NP (OR=2.00; 95% CI=1.00, 3.98). In contrast, when pooling the studies that analysed data by gender, the meta-analysis showed that depression was significantly associated with increased odds of reporting NP, both in girls (OR= 2.36; 95% CI=1.26, 4.42) and boys (OR=2.26; 95% CI=1.06, 4.84). However, there was significant heterogeneity across studies (Q=118.24, p=0.00; I^2=97% and Q=82.07, p=0.00; I^2=96%, respectively for girls and boys). An additional study not included in the previous meta-analysis (Niemi et al., 1997), also showed girls with NP to have more depressive symptoms than girls without NP (WMD=0.63; 95% CI=1.40, 0.85 points). Therefore, limited evidence suggests that the presence of depressive symptoms is significantly associated with increased odds of reporting NP both for girls and boys. Stahl et al. (2008) using a specific question to assess depression, still found that depressive mood predicted the occurrence of NP for the 4 following years (OR=1.14; 95% CI=1.03,1.26 and OR=1.25; 95% CI=1.11,1.41, respectively for girls and boys an average age of 10 and 12 years).

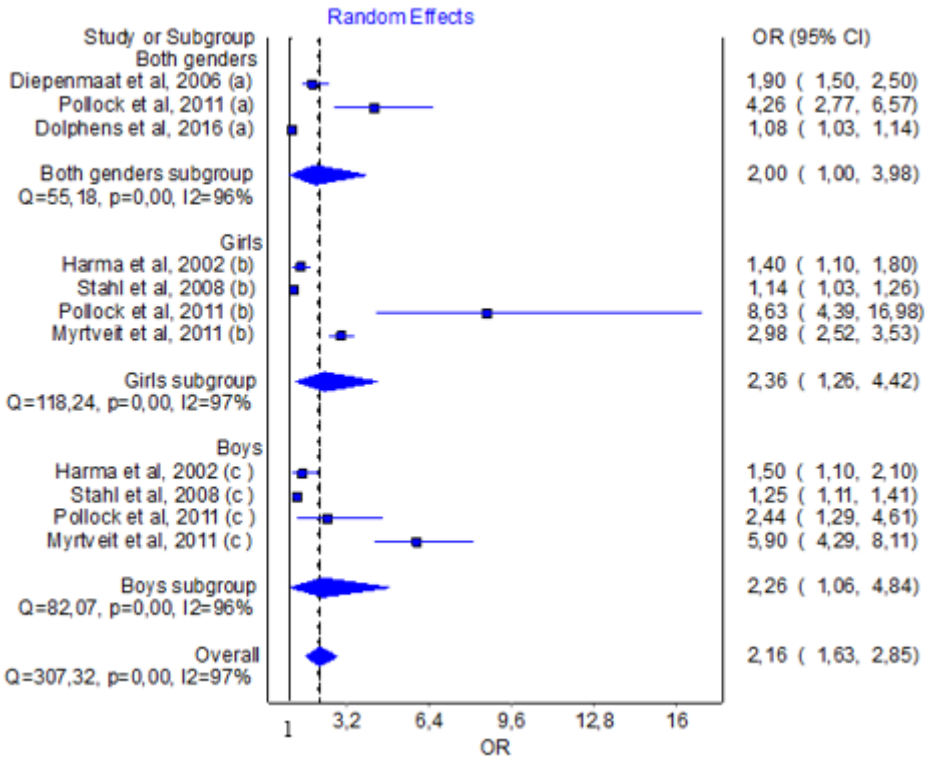


Figure 5. Forest plot of random-effect model for depression in adolescents with and without NP.

Note: OR>1 represents a higher odd od reporting NP in presence of depression.

4.4.5. Anxiety

Two studies with fair methodological quality assessed anxiety with two different measurement instruments (Rees et al., 2011; Sá & Silva, 2017) (Tables 17 and 18). Sá & Silva (2017) assessed the trait and state anxiety and showed that adolescents with NP have higher levels of trait and state anxiety than adolescents without NP (WMD=3.80; 95% CI=-0.55, 8.15 and WMD=6.75; 95% CI=3.09, 10.41 for state anxiety and trait anxiety, respectively). Rees et al. (2011) reported that anxiety/depression was significantly associated with increased odds of reporting NP (OR=1.43; 95% CI=1.20, 1.70). This study used the Youth Self Report Scale of the Child Behavior Check List which assesses anxiety and depression simultaneously. Thereby, very limited evidence

suggests that adolescents with NP have higher levels of anxiety than adolescents without NP.

4.4.6. Catastrophizing

Catastrophizing was assessed in a single study (Sá & Silva, 2017), with fair methodological quality (Tables 19 and 20), which found that adolescents with NP had higher levels of catastrophizing compared to adolescents without NP (WMD=3.45; 95% CI=1.89, 5.01 points for rumination, WMD=0.05; 95% CI=-0.92, 1.02 for magnification, WMD=3.10; 95% CI=1.53, 4.67 for helplessness and WMD=6.60; 95% CI=3.07, 10.13 for total score of the pain catastrophizing scale). Thereby, very limited evidence suggests that adolescents with NP have higher levels of catastrophizing than adolescents without NP.

4.4.7. Stress

Two studies with fair methodological quality assessed stress (Diepenmaat et al., 2006; Niemi et al., 1997) (Tables 21 and 22). Niemi et al. (1997) assessed stress symptoms and found that adolescents with NP had significantly more symptoms of stress than adolescents without NP (WMD=1.87; 95% CI=1.33, 2.40 and WMD=0.89; 95% CI=0.13, 1.65 for girls and boys, respectively). Diepenmaat et al. (2006) reported that feeling stressed regularly/always was significantly associated with increased odds of reporting NP (OR=2.00; 95% CI=1.50, 2.70). Thereby, very limited evidence suggests that adolescents with NP have more stress symptoms than adolescents without NP.

4.4.8. Sleep

Five studies with fair methodological quality (Auvinen et al., 2010; Paiva et al., 2015; Shan et al., 2014; Silva et al., 2017; Ståhl et al., 2008) and 1 study with poor methodological quality (dos Passos et al., 2017) assessed sleep using a total of 6 different measurement instruments (Tables 23 and 24). Two of these studies were

longitudinal (Auvinen et al., 2010; Ståhl et al., 2008). Stahl et al. (2008) used a specific question about daytime tiredness, difficulty falling asleep and waking up during the night and found that sleep difficulties predicted the occurrence of NP within the 4 following years (OR=1.14; 95% CI=1.03, 1.26 and OR1.25; 95% CI=1.11,1.41 for girls and boys, respectively). Auvinen et al. (2010) assessed sleep at 16 and 18 years of age with a postal questionnaire derived from the Youth Self-Report, subdividing the variable sleep into quantity of sleep and quality of sleep. They found that insufficient quantity and quality of sleep at 16 years in girls was significantly associated with increased odds of reporting NP at 18 years (OR=3.20; 95% CI=1.54, 6.68). The results of the meta-analysis (figure 6) with the remaining 4 cross-sectional studies (dos Passos et al., 2017; Paiva et al., 2015; Shan et al., 2014; Silva et al., 2017), showed significant differences in quantity and quality of sleep between adolescents with and without NP (OR=1.63; 95% CI=1.23, 2.18). However, there was significant heterogeneity across studies (Q=11.46, p=0.00; I^2=74%). Thereby, limited evidence suggests that insufficient quantity and quality of sleep is significantly associated with increased odds of having NP in adolescents.

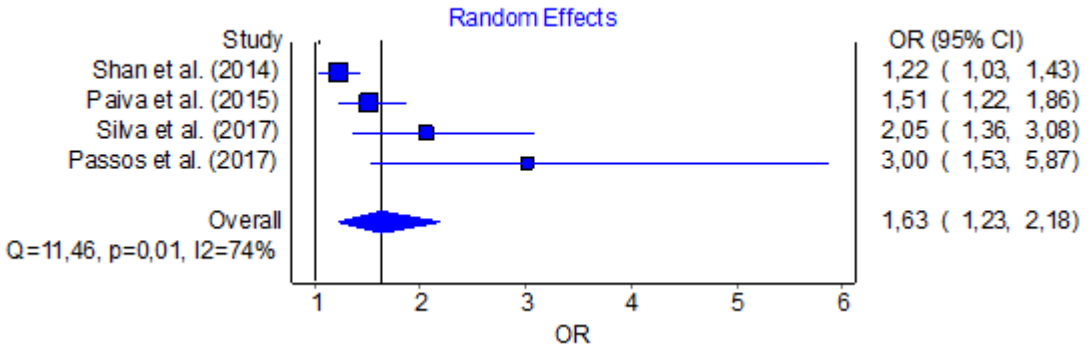


Figure 6. Forest plot of random-effect model of the sleep in adolescents with and without NP.

Note: OR >1 represent a higher odd of reporting NP in presence of sleep impairments.

4.4.9. Self-efficacy

Two studies with fair methodological quality assessed self-efficacy (Niemi et al., 1997; Pollock et al., 2011) (Tables 25 and 26). Niemi et al. (1997) found that girls with NP had significantly lower self-efficacy than girls without NP (WMD=-1.18; 95% CI=0.70, 2.28). In contrast, Pollock et al. (2011) found no significant differences in perceived self-efficacy between adolescents with and without NP (OR=0.87; 95% CI=0.65, 1.17 and OR=0.73; 95% CI=0.52, 1.03, respectively for medium and high levels of self-efficacy). Thereby, there is conflicting evidence on whether self-efficacy varies between girls with and without NP.

4.5. Discussion

A total of 14 studies performing 20 comparisons between adolescents with and without NP for depression, anxiety, catastrophizing, stress, sleep and self-efficacy were included in this systematic review. Very limited evidence suggests that adolescents with NP have higher levels of anxiety, catastrophizing and stress than adolescents without NP; limited evidence suggests that depressive symptoms and sleep impairments are associated with NP; and there is conflicting evidence on whether self-efficacy differs between adolescents with and without NP. No studies were found on fear of movement.

In spite of the low levels of evidence, previous studies support the findings of this systematic review by suggesting an association between psychosocial factors and several musculoskeletal pain conditions (Eccleston et al., 2004; Harrison, Wilson, & Munafó, 2016; Simons & Kaczynski, 2012). A recent study in adolescents with musculoskeletal pain found depressive symptoms, fear of pain, pain catastrophizing and poor sleep quality to be predictors of the transition from acute to persistent musculoskeletal pain (Holley, Wilson, & Palermo, 2017). Catastrophizing is also

pointed as a predictor of pain and pain intensity and both catastrophizing and anxiety are predictors of disability (Tran et al., 2015). Some physiological explanations for the association between pain and higher levels of these psychosocial variables have been suggested. Sensory pathways of pain share the same brain regions involved in mood management (Bushnell et al., 2013; Sheng, Liu, Wang, Cui, & Zhang, 2017), and the increased levels of adrenaline, hypervigilance to pain, muscle tension and pain sensitivity associated to psychosocial aspects, may facilitate maladaptive pain processing and promote peripheral and central sensitization (i.e. a generalized hypersensitivity of the somatosensory system) (Beesdo et al., 2009; Dimitriadis et al., 2015; Sullivan et al., 2001; Wippert & Wiebking, 2018). Therefore, the findings that depression, anxiety, catastrophizing and stress are higher in adolescents with NP when compared to those without NP is of relevance as these factors may contribute to the maintenance of NP and its impact. Nevertheless, studies included in the present systematic review and in the meta-analysis showed high heterogeneity, which may have an impact on the accuracy of the results (Israel & Richter, 2011).

Regarding sleep, the findings of our systematic review are in line with those found in a recent review that explored sleep as a risk factor for the onset of musculoskeletal pain, which concluded that sleep problems are a risk factor for the onset of NP in girls (Andreucci et al., 2017). Further, sleep impairments have been associated with decreased endogenous pain inhibition, increased responses of hyperalgesia and increased catastrophizing and negative emotions (Finan et al., 2013; Harrison, Wilson, & Munafò, 2014).

Finally, conflicting results were found for self-efficacy based on the findings of only two studies (Niemi et al., 1997; Pollock et al., 2011), which may be related to differences in NP duration. The study that reported no differences assessed adolescents with acute NP (Pollock et al., 2011) while the other used adolescents with chronic NP (Niemi et

al., 1997). However, self-efficacy has been suggested as a mediator factor between pain and disability in adults with acute and chronic NP (Lee et al., 2015; Martinez-Calderon, Zamora-Campos, Navarro-Ledesma, & Luque-Suarez, 2018) and in adolescents with various forms of chronic pain, such as headache and abdominal pain, where higher levels of self-efficacy have been associated with less disability, lower levels of depression and somatic symptoms (Bursch, Tsao, Meldrum, & Zeltzer, 2006; Kalapurakkel, Carpino, Lebel, & Simons, 2015). A relevant question that emerges from these contradictory findings is whether changes in self-efficacy may be subsequent to pain.

In addition, this systematic review findings show that only a few studies present a comprehensive characterization of study samples, in terms, for example, of NP characteristics, such as its intensity (Sá & Silva, 2017; Shan et al., 2014; Silva et al., 2017) or frequency (Shan et al., 2014), aspects that have been reported in the literature as being fundamental in chronic pain assessment (Fillingim, Loeser, Baron, & Edwards, 2016; Liossi & Howard, 2016). The latest published guideline on NP in adults already enhanced the importance of assessing not only the intensity of pain, but also the levels of self-reported disability and catastrophizing associated to pain in individuals with NP (Blanpied et al., 2017). Another relevant point is the limited number of variables assessed in each study, what limits the possibility of exploring the association and confounding among variables.

4.5.1. Limitations

All studies included in this review were of poor to fair methodological quality, which may impact the accuracy of findings. Most studies do not provide a comprehensive characterization of the sample, particularly for aspects of NP. Studies also fail to report on the reliability and validity of instruments when used in adolescents with NP or use

questionnaires developed for the purpose of their study, and, therefore, the validity and reliability of their findings is unclear. The high heterogeneity and the small number of studies included in the meta-analysis suggest that further studies are likely to impact the results or, at least, the degree of confidence on the findings (Israel & Richter, 2011). Although two of the included studies in this review were longitudinal, it was not possible to assess a cause-effect relationship.

4.5.2. Implications for clinical practice and research

The results of this systematic review suggest that psychosocial aspects such as depression, anxiety, catastrophizing, stress, sleep, and self-efficacy should be considered when assessing adolescents with NP and when designing interventions targeting adolescents with NP. However, the limited number of studies, the high heterogeneity and low to fair methodological quality suggest that these findings should be taken with caution and that more studies are needed. Furthermore, the findings of this systematic review highlight the need of more high-quality research on the association between psychosocial factors and NP. Specifically, studies should clarify the criteria of eligibility for both asymptomatic and adolescents with NP, provide a comprehensive characterization of NP, use valid and reliable measurement instruments, and assess more than one psychosocial variable and explore association and confounding. Comparing NP both with asymptomatic adolescents and with adolescents with pain at other body sites will also inform community-based interventions.

4.6. Conclusion

This review found very limited evidence that adolescents with NP show higher scores for anxiety, pain catastrophizing and stress than adolescents without NP and limited evidence that the presence of depression and sleep impairments are associated with

an increased odd of having NP. Moreover, this review found conflicting evidence on whether self-efficacy differs between adolescents with and without NP. However, the limited number of studies, the high heterogeneity and low to fair methodological quality suggest that these findings should be taken with caution and that further studies aiming to characterize NP in adolescents and associated variables are needed.

Table 13. Characteristics of included studies.

Study	Sample characteristics of NP group (mean ±SD)	Definition/Characteristics of Neck Pain	Sample characteristics of control group (mean ±SD)	Definition/Characteristics of asymptomatic participants	Measured Variables
Niemi et al. (1997)	N= 111 (84F;27M)	"Disturbing symptoms": have neck and shoulder symptoms once or more often during a week over the past 12 months.	N= 550 (308F;242M)	"No disturbing symptoms": no neck shoulder symptoms or had more rarely than once a week over the past 12 months.	Stress Depression Self-efficacy
Härmä et al. (2002)	N=15965 (7850F,8115M) Age=15.3±0.6y	The adolescents were asked: ‘‘During the past six months, did you experience any of the following symptoms?" (neck and shoulder pain, low back pain, stomach-ache and headache) and "How frequently?’’ (symptoms occurring once a week or daily or almost daily was considered frequent).			Depression
Diepenmaat et al. (2006)	N= 399 (249F;150M)	The adolescents were asked: “In the past month have you experienced pain lasting a day or longer in the indicated shaded area?” (yes/no) and if the response was affirmative: “How long, in terms of days, did you experience pain in this area during the past month?” To meet neck/shoulder, low back, or arm pain criteria, participants had to experience pain for 4 days per month in the neck/shoulder, low back, or arm area.	N=3086 (1510F;1576M)	The adolescents were questioned: “In the past month have you experienced pain lasting a day or longer in the indicated shaded area?” (yes/no).	Depression Stress
Stahl et al. (2008)	N= 308 (NP once a month) N=191 (NP at least once a week) Age=9.8 (0.4)y/11.8 (0.4)y (?)	The adolescents were asked about the presence of pain in seven different areas of the body. Pain symptoms were asked by using a five-level frequency classification (pain seldom or never, once a month, once a week, more than once a week, almost daily) during the preceding three months. Based on the frequency of NP reported during the follow-up adolescents with fluctuating (frequency varied from no pain to once a month to at least once a week) and persistent (NP at least once a week at all three evaluation points) NP were identified.	N=769 Age=9.8(0.4)y/ 11.8 (0.4)y (?)	Based on frequency of NP reported during follow up, adolescents without pain were identified as pain-free (no NP at any evaluation point).	Depression Sleep

Auvien et al. (2010)	Age=16y N=756 (485F;271M) Age= 18y N= 1098 (718F; 380M)	The adolescents answered “yes” a postal questionnaire including questions: ‘‘Have you had any aches or pains during the last 6 months in the following areas of your body?’’ (neck or occipital area, shoulders and low back).	Age=16y N=996 (488F;508M) Age= 18y N= 644 (254F; 390M)	The adolescents answered “no” a postal questionnaire including questions: ‘‘Have you had any aches or pains during the last 6 months in the following areas of your body?’’ (neck or occipital area, shoulders and low back).	Sleep
Pollock et al. (2011)	N= 345 (211F;134M) Age=14.1±0.18y (?)	The adolescent answered “yes” to a question based on the Nordic Musculoskeletal Questionnaire: “Has your neck/shoulder been painful in the last month?"	N= 913 (410F; 503M) Age=14.1±0.18y (?)	The adolescents answered "no" to a question based on the Nordic Musculoskeletal Questionnaire: “Has your neck/shoulder been painful in the last month?"	Depression Self-efficacy
Rees et al. (2011)	N=245 (134F, 111M) Age=14.1±0.2y (?)	The adolescents were asked, with two questions based on the Nordic Pain Questionnaire, about their experience of NSP described as pain in the area of the posterior neck and upper trapezius: (i) "Have you ever had NSP?", and if they reported pain ever, (ii) "Has your neck/shoulder been painful in the last month?".	N=886 (404F, 482M) Age=14.1±0.2y (?)	The adolescents were asked, with two questions based on the Nordic Pain Questionnaire, about their experience of NSP described as pain in the area of the posterior neck and upper trapezius: (i) "Have you ever had NSP?", and if they reported pain ever, (ii) "Has your neck/shoulder been painful in the last month?".	Anxiety/ Depression
Myrtveit et al. (2014)	N= 1797 (1354F,443M) Age=17.8y (?)	The adolescents were asked how often they had suffered from NSP during the last 6 months. Who answered, “more than once a week” and “more or less every day” were included in the group with frequent NSP.	N= 7193 (3477F,3716M) Age=17.8y (?)	The adolescents were asked how often they had suffered from NSP during the last 6 months. Who answered “every week", “every month” and "seldom/never" were included in the group with no frequent NSP.	Depression
Shan et al. (2014)	N=1167 (653F;514M)	The adolescents were asked “For the past 6 months, I have felt pain or discomfort in my neck/shoulder?” Participants who answered “yes” were asked more questions concerning pain characteristics (frequency, duration and degree). Pain score (VAS) Mild pain (1–3 pts): 369F; 313M Moderate pain (4–6 pts):228F; 162M Heavy pain (7–8 pts): 49F; 31M Severe pain (9–10 pts):7F; 8M	N=1675 (825F;850M)	The adolescents were asked “For the past 6 months, I have felt pain or discomfort in my neck/shoulder?” Participants who answered “no” were included in this group.	Sleep

Paiva et al. (2015)	N=624 (?) Age=14.9±1.26y (?)				Sleep
Dolphens et al.(2016)	N=77 Age=10.6±0.47y (F)/ 12.6±0.54y (M) (?)	"Spinal pain": a discomfort or pain, in the back or neck that is considered to be a local, uncomfortable feeling in the back or neck, with the possibility of radiation to other parts of the body. Can be intermittent or constant, gradually developed or with a sudden onset.	N=765 Age=10.6±0.47y (F)/ 12.6±0.54y (M) (?)		Depression
Passos et al. (2017)	N=197 Age= 14.15±2.11y (?)	The adolescents pointed out the places that felt pain/discomfort in a body diagram of Corlett.	N=112		Sleep
Silva et al. (2017)	N= 969 Age=15.6±1.8y Weight=57.3±11.9 kg Height=1.64±0.11 cm	The adolescents were asked if they felt pain during the past 7 days in the neck, shoulders, elbows, wrists/hands, mid back, lumbar region, hips, knees and ankles/feet using adapted version of the Nordic Musculoskeletal Questionnaire. Pain (VAS)=3.9±1.8 (F); 3.6±1.8 (M) Number of pain sites [1;9]:2.1 ± 1.3			Sleep
Sá &Silva (2017)	N=40 (21F,19M) Age=17.2±0.56y	"Chronic idiopathic NP": pain felt dorsally between the inferior margin of the occiput and T1 not related to trauma or any known pathology that was present at least once a week during the last 3 months. Pain Score (VAS): 3.39±1.84	N=40 (21F, 19M) Age=17.2±0.56y	"Asymptomatic participants": no current NP and reported that they had never had NP.	Catastrophizing Anxiety

Legend: (?) Not clear in the study; F (Female); M (Male); y (years); kg (kilograms); cm (centimeters); NP (Neck Pain); NSP (Neck /Shoulder Pain); VAS (Visual Analogic Scale)

Table 14. Newcastle-Ottawa Quality Assessment Scale for case-control studies.

Criteria methodological quality	Selection				Comparability		Exposure			Total (9)	Quality rating
	Criterion 1	Criterion 2	Criterion 3	Criterion 4	Criterion 5	Criterion 6	Criterion 7	Criterion 8	Criterion 9		
Niemi et al. (1997)	0	1	1	1	1	1	0	1	0	6	Fair
Härmä et al. (2002)	0	1	1	1	1	0	0	1	0	5	Fair
Diepenmaat et al. (2006)	0	1	1	1	1	1	0	1	0	6	Fair
Stahl et al. (2008)	0	1	1	1	1	0	0	1	0	5	Fair
Auvinen et al. (2010)	0	1	1	1	1	1	0	1	0	6	Fair
Pollock et al. (2011)	0	1	1	1	1	1	0	1	0	6	Fair
Rees et al. (2011)	0	1	1	1	1	0	0	1	0	5	Fair
Myrtveit et al. (2014)	0	1	1	0	1	1	0	1	0	5	Fair
Shan et al. (2014)	0	1	1	1	1	1	0	1	0	6	Fair
Paiva et al. (2015)	0	1	1	1	1	1	0	1	0	6	Fair
Dolphens et al. (2016)	0	1	1	1	1	1	0	1	0	6	Fair
Passos et al. (2017)	0	0	1	0	0	0	0	1	0	2	Poor
Silva et al. (2017)	0	1	1	1	1	1	0	1	0	6	Fair
Sá & Silva (2017)	0	1	1	1	1	0	0	1	0	5	Fair

Legend: 0 (criterion not fulfilled); 1 (criterion fulfilled); Criterion 1 (Case definition adequate); Criterion 2 (Representativeness of the cases); Criterion 3 (Selection of controls); Criterion 4 (Definition of controls) Criterion 5 (Study controls for age/gender); Criterion 6 (Study controls for any additional factor); Criterion 7 (Ascertainment of exposure); Criterion 8 (Same method of ascertainment for cases and controls); Criterion 9 (Non-Response rate)

Table 15. Studies that compared depression between adolescents with and without NP.

Study	Measuring instrument	Results of NP group WMD (95% CI) or OR (95% CI)	Results of control group WMD (95% CI) or OR (95% CI)	Adjusted confounding factors	Main conclusions
Niemi et al. (1997)	Depressive Symptoms (sum score)	**Female** WMD: 0.63 (1.40-0.85) * **Male** WMD: 0.22 (0.14-0.57		N/A	Girls with NP have more depressive symptoms than girls without NP.
Harma et al. (2002)	13-item version of the Beck Depression Inventory (score)	**Female** Weekly neck symptoms: 1.4 (1.1–1.8) * 1 weekly pain symptom: 2.3 (1.8-2.8) * 2 weekly pain symptoms: 3.5 (2.7-4.4) * 3 weekly pain symptoms: 6.4 (4.8-8.6) * 4 weekly pain symptoms: 11.0 (7.2-16.7) * **Male** Weekly neck symptoms: 1.5 (1.1–2.1) * 1 weekly pain site: 2.6 (2.0-3.4) * 2 weekly pain site: 4.0 (2.9-5.6) * 3 weekly pain site: 5.9 (3.6-9.6) * 4 weekly pain site: 10.7 (5.2-21.9) *		Age Anxiety	Adolescents with NP are significantly associated with increased odds of having depression. Having more than one region of pain also increases the likelihood of depression.
Diepenmaat et al. (2006)	Center for Epidemiologic Studies Depression Scale (score)	1.9 (1.5–2.5) *****		N/A	Adolescents with depressive symptoms are significantly associated with increased odds of having NP.
Stahl et al. (2008)	Specific question about depressive mood (score)	**Female** 1.14 (1.03-1.26) * **Male** 1.25 (1.11-1.41) * (note: OR values considering the value of the sum of 1 to 6 psychosomatic symptoms)		N/A	Having other psychological symptoms, such as depressive mood, with a frequency of at least once a week at baseline predicted the occurrence of weekly NP in both genders, within the 4 following years.
Pollock et al. (2011)	Beck Depression Inventory for Youth (score)	**Both (Female and Male)** Medium BDI-Y: 2.29 (1.59 -3.29) * High BDI-Y: 4.26 (2.77-6.57) * **Female** Medium BDI-Y: 4.28 (2.31 -7.92) * High BDI-Y: 8.63 (4.39- 16.98) * **Male** Medium BDI-Y: 1.56 (0.98-2.50) High BDI-Y: 2.44 (1.29 -4.61) *		Gender and covariates (global self-worth, physical working capacity)	Adolescents with medium or high depressed mood are significantly associated with increased odds of reporting NP pain than adolescents with low depressed mood. When analysed by gender, girls with medium and high depressed mood and boys with high depressed mood have more likely to report NP.

Myrtveit et al. (2014)	Short Mood and Feelings Questionnaire (score)	**Female** 2.98 (2.52-3.53) * **Male** 5.90 (4.29-8.11) *	Sociodemographic (age, school situation, family economy)	Adolescents with depressive symptoms are significantly associated with increased odds of having NP.
Dolphens et al. (2016)	Short version of the Depression Questionnaire for Children (score)	1.08 (1.03–1.14) *	N/A	Adolescents with high scores on the depression questionnaire are significantly associated with increased odds of having NP.

Legend: NP (Neck Pain); N/A (Not applicable); BDI-Y (Beck Depression Inventory for Youth); * (statistically significant results)

Table 16. Measurement procedures used in the assessment of depression.

Study	Measuring instrument	Measurement procedure
Niemi et al. (1997)	Specific questions to determine Depressive Symptoms Sum Score (DSS)	i) Participants were assessed with specific questions including the presence and frequency of difficulty sleeping, fatigue, and lack of energy, which are considered common depressive symptoms (according to American Psychiatric Association, 1980); ii) The range of the DSS can range from 0-3.
Härmä et al. (2002)	13-item version of the Beck Depression Inventory	i) Participants were assessed using a modified 13-item version of this scale which has been shown to be a valid measure for detecting depression in adolescents, with good psychometric properties; ii) Students scored from 0 to 7 were classified as having no depression to mild depression, and those who had scores of 8 to 39 were classified as having moderate to severe depression; (In this study adolescents with a score greater than 8 will be considered as having depression).
Diepenmaat et al. (2006)	Center for Epidemiologic Studies Depression Scale (CES-D)	i) Participants were assessed with a 20-item self-report scale that was designed to measure depressive symptoms in the general population. The CES-D has been validated previously in adolescents; ii) The total score ranges from 0 to 60 and is calculated by summing all items. Adolescents who scored 16 were classified as being depressed.
Stahl et al. (2008)	Specific question about depressive mood	i) Participants were assessed with a question about depressive mood using the same frequency categorization as for musculoskeletal pain symptoms (none/once a month/ at least once a week); ii) All symptoms appearing at least once a week were considered positive.
Pollock et al. (2011)	Beck Depression Inventory for Youth (BDI-Y)	i) Participants were assessed using this inventory with 20 items to assess depressed mood in early adolescence. The BDI-Y converges with the Children's Depression Inventory has high internal consistency and excellent test-retest reliability over 7 days. ii) Depressed mood was characterized by BDI-Y as low (<1.79), medium (1.79-10.60) and high (>10.60) to increase the sensitivity of analysis compared with using clinical depression cut offs (mild,17-20, moderate, 21-28, and severe, 29-60, in 11-14 year old).
Myrtveit et al. (2014)	Short Mood and Feelings Questionnaire	i) Participants were assessed with this questionnaire which measure depressive symptoms with 13 items on feelings, thoughts, and actions the last 2 weeks. Each item has three levels differentiating between "true," "sometimes true," and "not true"; ii) Each of the 13 statements could vary from 0 to 2 and the questionnaire range from 0 to 26.
Dolphens et al. (2016)	Short version of the Depression Questionnaire for Children, described by *De Wit CAM (1987)*	In this study the description of the procedure was referenced for consultation study in another study, De Wit CAM (1987).

Table 17. Studies that compared anxiety between adolescents with and without NP.

Study	**Measuring instrument**	**Results of NP group (Mean ±SD), WMD (CI 95%) or OR(95% CI)**	**Results of control group (Mean ±SD), WMD (CI 95%) or OR(95% CI)**	**Adjusted confounding factors**	**Main conclusions**
Rees et al. (2011)	The Youth Self Report scale of the Child Behaviour Check List (score)	NP only: 1.43 (1.20-1.70) * NP and Back Pain: 1.94 (1.64-2.30) *		Gender	Adolescents with higher anxious/depressed state are significantly associated with increased odds of reporting NP in isolation, and simultaneously with neck and back pain.
Sá &Silva (2017)	Staite-Trait Anxiety Inventory (score)	State anxiety: 32.05 ± 9.07 Trait anxiety: 39.98 ± 10.53	State anxiety: 28.25 ± 10.71 Trait anxiety: 33.23 ± 5.36	N/A	Adolescents with chronic NP have a more trait and state anxiety than adolescents without NP.
		WMD state anxiety: 3.80 (-0.55;8.15) * WMD trait anxiety: 6.75 (3.09;10.41) *			

Legend: NP (Neck Pain); N/A (Not applicable); * (statistically significant results)

Table 18. Measurement procedures used in the assessment of anxiety.

Study	Measuring instrument	Measurement procedure
Härmä et al. (2002)	13 items of the Finnish modified S-BDI	i) Participants were asked to rate the alternative that best described them today: I don't easily lose my nerve or get anxious (=0); I don't feel anxious or nervous (=0); I get anxious and nervous rather easily (=1); I very easily get distressed, anxious or nervous (=2); I am constantly anxious and distressed, my nerves are always on edge (=3); ii) Only responses at the most severe range, scores 2 and 3, were considered significant anxiety.
Rees et al. (2011)	The Youth Self Report (YSR) scale of the Child Behaviour Check List (CBCL)	i) Participants were assessed with the 118 items of the YSR form with 8 syndrome scales: Somatic Complaints, Anxious/Depressed, Withdrawn, Aggressive Behaviour, Rule-breaking Behaviour, Social Problems, Thought Problems and Attention Problems. Prior second order factor analysis identified 2 broad-band scales: Internalising (reflecting problems of Anxiety/Depression, Withdrawal and Somatic Complaints scales) and Externalising (reflecting Rule-breaking and Aggressive Behaviour); ii) Raw scores for the 8 YSR syndrome scales were used for analysis as recommended by Achenbach (1991).
Sá &Silva (2017)	Staite-Trait Anxiety Inventory (STAIC)	i) Participants were assessed with this instrument that distinguishes between a tendency to anxious behavior rooted in the personality (trait) and the short-term anxiety common to some situations (state), each measured using a 20-item scale; ii) Each scale prompts the participant to rate each of the 20 statements from hardly ever true to often true. A separate score is produced for the State Scale and the Trait Scale. Scores range from 20 to 80 for each scale and higher scores are associated with higher levels of anxiety.

Table 19. Studies that compared catastrophizing between adolescents with and without NP.

Study	Measuring instrument	Results of NP group (Mean ±SD)	Results of control group (Mean ±SD)	WMD (CI 95%)	Main conclusions
Sá &Silva 2017	Pain Catastrophizing Scale (score)	Rumination: 6.40 ± 3.57 Magnification: 4.00 ± 2.25 Helplessness: 5.93 ± 3.85 Catastrophizing (Total):16.33 ± 8.47	Rumination: 2.95 ± 3.57 Magnification: 3.95 ± 2.19 Helplessness: 2.83 ± 3.31 Catastrophizing (Total): 9.73 ± 7.61	3.45 (1.89;5.01) * 0.05 (-0.92;1.02) * 3.10 (1.53;4.67) * 6.60 (3.07;10.13) *	Adolescents with chronic NP have increased levels of catastrophizing than adolescents without NP.

Legend: NP (Neck Pain); * (statistically significant results)

Table 20. Measurement procedures used in the assessment of catastrophizing.

Study	Measuring instrument	Measurement procedure
Sá &Silva (2017)	Pain Catastrophizing Scale	i) Participants were assessed with this instrument that is composed of 13 statements. Participants was prompted to indicate the degree to which they experience each of them when experiencing pain, on 5-point scales with the end points (0) not at all and (4) all the time. The 13 statements are grouped into 3 subscales: rumination (4 items), magnification (3 items) and helplessness (6 items); ii) Total score ranges from 0 to 52 and higher scores are indicative of higher catastrophizing.

Table 21. Studies that compared stress between adolescents with and without NP.

Study	Measuring instrument	Results of NP group WMD (95% CI) or OR (95% CI)	Results of control group WMD (95% CI) or OR (95% CI)	Adjusted confounding factors	Main conclusions
Niemi et al. (1997)	17-item questionnaire about presence and frequency of physiologic symptoms considered a manifestation of mental stress (score)	**Female** WMD: 1.87 (1.33-2.40) ***** **Male** WMD: 0.89 (0.13-1.65) *****		N/A	Adolescents with NP have more stress symptoms than adolescents without NP.
Diepenmaat et al. (2006)	Specific question about stress	Feeling stress regularly/always 2.0 (1.5–2.7) *****		N/A	Adolescents with feeling stress regularly/always are significantly associated with increased odds of having NP than adolescents without stress symptoms.

Legend: NP (Neck Pain); N/A (Not applicable); * (statistically significant results)

Table 22. Measurement procedures used in the assessment of stress.

Study	Measuring instrument	Measurement procedure
Niemi et al. (1997)	17-item questionnaire about the presence and frequency of physiologic symptoms considered a manifestation of mental stress	i) Participants were assessed with 17-item questionnaire about the presence and frequency of psychophysiological symptoms considered a manifestation of mental stress (Aro H., 1988); ii) Stress symptoms sum score was calculated after scoring the values of 1-2 (no or occasional symptoms) as 0 and the values of 3-4 (fairly often and often or constantly) as 1. The range of the sum score can range from 0-17.
Diepenmaat et al. (2006)	Specific question about stress	i) Participants were assessed with a question: “Have you experienced stress in the past week” (no= never/sometimes; yes=often/always).

Table 23. Studies that compared sleep between adolescents with and without NP.

Study	Measuring instrument	Results of NP group (Mean ±SD) or OR (95% CI)	Results of control group (Mean ±SD) or OR (95% CI)	Adjusted confounding factors	Main conclusions
Stahl et al. (2008)	Specific question about daytime tiredness, difficult falling asleep and waking up during the night (score)	**Female** 1.14 (1.03-1.26) * **Male** 1.25 (1.11-1.41) * (note: OR values considering the value of the sum of 1 to 6 psychosomatic symptoms)		N/A	Having other psychological symptoms, such us more tiredness, difficulty falling sleep and waking up during the night at baseline predicted the occurrence of weekly NP in both genders, within the next 4 years.
Auvinen et al. (2010)	Postal questionnaire (derived from the Youth Self- Report) - Average hours spent sleeping	**Female** 7 h or less: 1.44 (0.90–2.43) 9h: 1.02 (0.66-1.57) 10h or more: 1.55 (0.84-2.87) **Male** 7h or less: 1.40 (0.86–2.30) 9h: 0.98 (0.64-1.50) 10h or more: 0.86 (0.52-1.44)		Pain at 16 years	Despite in girls sleep less than 7h at 16 years increase the likelihood of having NP at 18 years, when adjusted for the presence of pain, the increased risk disappears.
	Postal questionnaire (derived from the Youth Self- Report) - I have sleeping problems	**Female** Sometimes or often: 1.67 (1.00–2.78) **Male** Sometimes or often: 0.83 (0.48-1.44)		Pain at 16 years	Despite in girls have sleeping problems “sometimes or often” at 16 years increase the likelihood of having NP at 18 years, when adjusted for the presence of pain, the increased risk disappears.
	Composite variable	Insufficient sleep **Female:** 3.20 (1.54-6.68) ***** **Male:**1.60 (0.82-3.12) Intermediate sleep **Female:** 1.36 (0.88-2.11) **Male:** 1.47 (1.00-2.14)		Pain at 16 years	Insufficient quantity or quality of sleep at 16 years in girls is significantly associated with the increased odds of reporting NP at 18 years.
Shan et al. (2014)	Questionnaire for school factors and lifestyle	Before 12 am: 1.22 (1.03-1.43) * Before 1 am: 1.55 (1.20-2.00) * Later: 1.05 (0.66-1.67)		Gender and family history	Lie down before 12 am and 1 am increases the risk of NP.
Paiva et al. (2015)	Health Behaviour in School-Aged Children Questionnaire (score)	1.51 (1.22-1.86) *		N/A	The presence of sleep deprivation in adolescents is significantly associated with increased odds of having NP.
Silva et al. (2017)	Specific question about hours of sleep	2.05 (1.36-3.08) *		Gender, age, sleeping, using mobile phone and using computer	Sleeping 7h or less are significantly associated with increased odds of reporting NP.

Passos et al. (2017)	Brazilian version of the Pittsburgh Sleep Quality Index (score)	Sleep duration:7.43h	Sleep duration: 7.73h	N/A	No statistical difference between adolescents with and without NP.
		3.00 (1.53-5.87) *			Adolescents with NP are significantly associated with increased odds of reporting poor sleep quality.

Legend: NP (Neck Pain); N/A (Not applicable); * (statistically significant results)

Table 24. Measurement procedures used in the assessment of sleep.

Study	Measuring instrument	Measurement procedure
Stahl et al. (2008)	Specific question about daytime tiredness, difficult falling asleep and waking up during the night	i) Participants were assessed with a question about daytime tiredness, difficulty falling asleep and waking up during the night using the same frequency categorization as for musculoskeletal pain symptoms (none/once a month/ at least once a week); ii) All symptoms appearing at least once a week were considered positive.
Auvinen et al. (2010)	Postal questionnaire (derived from the Youth Self- Report (YSR)	i) Participants were assessed with the 118 items of the YSR form with 8 syndrome scales: Somatic Complaints, Anxious/Depressed, Withdrawn, Aggressive Behaviour, Rule-breaking Behaviour, Social Problems, Thought Problems and Attention Problems. Prior second order factor analysis identified 2 broad-band scales: Internalising (reflecting problems of Anxiety/Depression, Withdrawal and Somatic Complaints scales) and Externalising (reflecting Rule-breaking and Aggressive Behaviour); ii) Raw scores for the 8 YSR syndrome scales were used for analysis as recommended by Achenbach (1991).
Shan et al. (2014)	Specific questionnaire	i) Questionnaire divided into three parts where one of them was specific for school factors and lifestyle.
Paiva et al., (2015)	Health Behaviour in School-Aged Children Questionnaire	i) Participants were assessed with questions about sleep duration during the weeknights and weekends, and sleep deprivation (defined as a difference in sleep duration equal to or more than 3h between weeknights and weekends) and health complaints (headaches, backache, fatigue, sadness, irritability, anxiety and difficulty in falling asleep). The questions were either closed or likert scale types; ii) Sleep deprivation (Yes/No) was defined as the difference hours of sleep, in weeknights and weekends, of 3h or more.
Silva et al. (2017)	Closed question	i) Participants were assessed with a specific question: "On average, how many hours per day do you sleep?" with the following response options: i) less than 6 h; ii) 6 to 7 h; iii) 8 to 9 h; iv) 10 h or more.
Passos et al. (2017)	Brazilian version of the Pittsburgh Sleep Quality Index (PSQI)	i) Participants were assessed with this questionnaire that was validated to Portuguese and can assess sleep quality and presence of sleep disorders in a period of 1 month. It is an instrument composed of seven components (subjective quality, sleep latency, duration of sleep, sleep efficiency, sleep disorders, use of drugs, daily impairment); ii) Each component receive score from 0 to 3, with a total score that vary from 0 to 21 points. The scores >5 indicate poor quality of sleep.

Table 25. Studies that compared self-efficacy between adolescents with and without NP.

Study	Measuring instrument	Results of NP group WMD (95% CI) or OR (95% CI)	Results of control group WMD (95% CI) or OR (95% CI)	Adjusted confounding factors	Main conclusions
Niemi et al. (1997)	Measured on a 7-item scale developed by *Helenius and Lyttinen (1974)* (score)	**Female** WMD: -1.18 (0.70-2.28) ***** **Male** WMD: 0.81 (-1.02-2.64)		N/A	Girls with NP have less self-efficacy than girls without NP.
Pollock et al. (2011)	Modified version of the Perceived Self-Efficacy Scale by *Cowen et al., (1991)* (score)	**Both (Female and Male)** Medium PSE: 0.87 (0.65- 1.17) High PSE: 0.73 (0.52-1.03)		N/A	No significant differences in adolescents were found between perceived self-efficacy and NP.

Legend: NP (Neck Pain); N/A (Not applicable); PSE (Perceived Self-efficacy); * (statistically significant results)

Table 26. Measurement procedures used in the assessment of self-efficacy.

Study	Measuring instrument	Measurement procedure
Niemi et al. (1997)	Measured on a 7-item scale developed by Helenius and Lyttinen (1974).	i) Participants were asked to judge the extent (1-5 scale) to which the statements referring to self-efficacy applied to their present situation; Ii) A sum score for self-efficacy will be calculated and can range from 7-35.
Pollock et al. (2011)	Modified version of the Perceived Self-Efficacy Scale (PSE) by Cowen et al. (1991)	No reference.

5. CHARACTERIZATION OF ADOLESCENTS WITH CHRONIC NECK PAIN AND FACTORS ASSOCIATED WITH NECK PAIN AND DISABILITY, COMPARED TO CHRONIC BACK AND LIMB PAIN

Based on the study from Andias, R. & Silva, AG. (2021). “Factors associated with pain and pain associated disability in adolescents with chronic neck pain compared to chronic back and limb pain”. Pain Medicine *(submitted)*

5.1. Introduction

In Chapters 2 and 4 we concluded that there are few studies, with low methodological quality, characterizing psychosocial, and sleep factors in adolescents with chronic NP. Furthermore, no studies were found that assessed fear of movement. Among the studies found in Chapter 3, only one assessed central sensitization in adolescents with chronic NP and reported lower sensory thresholds both at the neck region and at a point distant from the neck when compared against asymptomatic adolescents, suggesting central sensitization (Sá & Silva, 2017). This study of Sá & Silva (2017) also found that 80% of adolescents with NP reported disability and suggested a positive and moderate correlation between pain and disability and anxiety and catastrophizing, further highlighting the relevance of psychosocial factors. Despite the negative interference of chronic NP with the daily activities of adolescents, as suggested in the studies from Oliveira & Silva (2016) and Sá & Silva (2017), disability has been poorly explored in this population as these were the only studies found reporting disability in the systematic reviews of Chapters 3 and 4.

The focus of the systematic reviews reported in Chapters 3 and 4 was the functional and psychosocial changes associated with chronic NP, and the variable physical

activity was not included. However, as reported in chapter 2, there is inconsistency in the literature regarding its association with the presence of NP. Also, only 50% of the studies included in the systematic review of Chapter 4 compared adolescents with NP with adolescents with pain at other body sites, such as the lower back and/or the thoracic spine (Auvinen et al., 2010; Diepenmaat et al., 2006; Dolphens et al., 2016; Härmä et al., 2002; Paiva et al., 2015; Rees et al., 2011; Silva et al., 2017), but none included the comparison against limb pain. Nevertheless, it has been suggested that, despite some similarities, the factors associated with the presence of pain and disability appear to be different depending on the painful body site. While limb pain is believed to be predominantly traumatic, pain in the spine, specifically in the neck region, tends to be idiopathic and, therefore, more related to psychosocial factors than limb pain (El-Metwally, Salminen, Auvinen, Kautiainen, & Mikkelsson, 2006; El-Metwally, Salminen, Auvinen, MacFarlane, & Mikkelsson, 2007; Silva et al., 2017). A more detailed analysis of chronic NP in adolescents, including a comparison with adolescents with pain at other body sites, will allow a better understanding of the factors that should be considered when planning the assessment and intervention for adolescents with NP and on its specificities. Thus, the study presented in this Chapter aimed to i) characterize adolescents with chronic NP in terms of i.i) sociodemographic characteristics, i.ii) disability, i.iii) physical activity, i.iv) psychosocial factors, i.v) sleep and i.vi) self-reported symptoms of central sensitization; ii) to explore the factors associated with both NP and disability and iii) to compare adolescents with NP with adolescents with back and limb pain.

5.2. Methods

5.2.1. Study design and participants

This study was approved by the Council of Ethics and Deontology of the University of Aveiro. Participants were recruited from 4 Portuguese secondary schools, and all

students who attended the 10th, 11th, and 12th grades were invited to participate. Six high schools were initially invited, but only 4 accepted to participate in the study. The total number of students that met the inclusion criteria was 2410 and 2300 were invited. The study was first presented to the school director and then to all students in one of the physical education classes. Students were informed that the study involved filling in an online questionnaire at the beginning of a physical education class. This was previously arranged with the physical education teacher. Legal guardians were also informed about the study by an informative document. Written informed consent was obtained from all participants and for participants under 18 years old, written informed consent of the legal guardian was also obtained. All adolescents who reported no pain or who reported neck, back, and/or limb pain in the last 3 months, at least once a week, were included (between October 2018 and January 2019). Adolescents with pathology of the nervous or rheumatic system were excluded. Adolescents were screened for these exclusion criteria before filling the online questionnaire, with an initial screening dichotomous question.

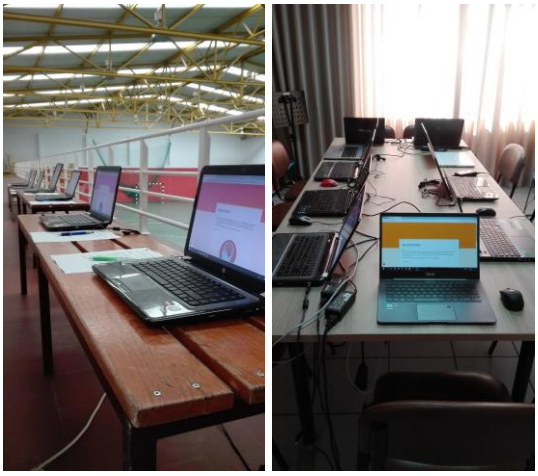


Figure 7. Illustrative pictures of the data collection set up.

5.2.2. Measurement instruments

Adolescents were asked to provide information on gender, age, weight, height, scholar level and family situation (who they lived with) and to complete an online questionnaire (Figure 7) including the measurement instruments detailed below:

Nordic Musculoskeletal Questionnaire

The Nordic Musculoskeletal Questionnaire consists of 27 “Yes or No” questions and was used to assess the presence of pain in any of nine anatomic regions: neck, shoulders, wrists/hands, thoracic region, lumbar region, hips/thighs, knees, and ankles/feet. To facilitate the identification of the body areas, the questionnaire includes an illustrative body diagram (Mesquita, Ribeiro, & Moreira, 2010). To meet the recent definition of chronic pain, the questions of the Nordic Musculoskeletal Questionnaire were adapted as follows: “Had some troubles or pain in the last 3 months, at least once a week, in the following body areas?”, “During the last 3 months did you have to avoid your daily activities due to problems in the following body areas?”, “Did you have some troubles or pain in the last 7 days?”). The European Portuguese version of the Nordic Musculoskeletal Questionnaire was considered valid and reliable (*Kuder-Richarson*=0.86 and Cohen’s kappa between 0.8 to 1) (Mesquita et al., 2010).

For this study, and considering the responses to the Nordic Musculoskeletal Questionnaire, adolescents who reported no pain in the last 7 days and no pain in the last 3 months were considered asymptomatic. Those that only reported pain in the last 7 days were considered to have acute pain and the remaining had chronic pain. Based on pain location, adolescents with chronic pain were grouped into the following mutually exclusive groups: i) NP, ii) thoracic and low back pain, and iii) limb pain (including lower and upper limb pain). Although the groups were mutually exclusive, adolescents with NP may also experience pain in the back or limbs, adolescents with

back pain may also experience pain in the limbs and adolescents with limb pain only experience pain in the limbs.

International Physical Activity Questionnaire for Adolescents

Physical activity was assessed with the International Physical Activity Questionnaire for Adolescents. This questionnaire is divided into four parts and assesses the performance of moderate and vigorous physical activities in the last 7 days during school hours, housework, activities related to transportation, and in the context of leisure time. For each of the four domains, adolescents reported on the number of days per week and periods per day spent walking, performing moderate physical activity, and vigorous physical activity (De Cocker et al., 2011; Ferro-Lebres, Silva, Moreira, & Ribeiro, 2018). According to previous studies, a minimum of 10 minutes per activity was considered when adolescents reported activity in the past week and each intensity was truncated to a maximum of 180 minutes per day (De Cocker et al., 2011; Sjostrom et al., 2005). To avoid unrealistic high values, the physical activity scores were also truncated in the different domains: i) 1800 minutes/week for school hours, ii) 1680 minutes/week for housework and leisure time, iii) 1290 minutes/week for transportation, iv) 1260 minutes/week for each intensity levels of physical activity (walking, moderate and vigorous) and v) 2540 minutes/week for total physical activity (De Cocker et al., 2011; Sjostrom et al., 2005). In our study, the International Physical Activity Questionnaire for Adolescents data were reported in minutes/week. The first validation of the European Portuguese version of the International Physical Activity Questionnaire for Adolescents suggested a significant correlation between the International Physical Activity Questionnaire for Adolescents and accelerometer for the total physical activity and moderate to vigorous physical activity in boys, with an agreed percentage of 42.3% (Ferro-Lebres et al., 2018).

Functional Disability Inventory

This inventory consists of 15 items related to perceptions of activity limitations during the past 2 weeks measured with a 5-point Likert scale (“No trouble” to “Impossible”). Total score ranges from 0 to 60 points and higher scores indicate greater disability (Claar & Walker, 2006; Walker & Engle, 2015). Cut-offs for the Functional Disability Inventory in adolescents were established as no/minimal (0 to 12), moderate (13 to 29), and severe disability (≥30) in a sample of 1300 youngers (mean age=14.2±2.4) (Kashikar-Zuck et al., 2011). The European Portuguese version of the Functional Disability Inventory was considered valid and showed good test-retest reliability (Intraclass Correlation Coefficient - ICC=0.86) in adolescents with chronic musculoskeletal pain (Andias & Silva, 2019a).

Depression, Anxiety and Stress Scale for Children

This scale is a self-report instrument composed of 21 items distributed in three subscales: i) depression, ii) anxiety, and iii) stress. Each item is classified on a scale of 4 points, rated from 0= “Did not apply to me at all” and 3 = “Applied to me very much, or most of the time”. Total score ranges from 0 to 21 points for each subscale, and higher scores indicate more negative affective conditions (Leal, Antunes, Passos, Pais-Ribeiro, & Maroco, 2009; Pais-Ribeiro, Honrado, & Leal, 2004). The European Portuguese version of the Depression, Anxiety and Stress Scale for Children showed a good internal consistency (Cronbach's alpha (α)=0.78, α=0.74, and α=0.75) for depression, stress, and anxiety subscales, respectively, for the younger population (age between 8 and 15 years old) (Leal et al., 2009). This scale is often used in adolescents and Jovanovic et al. (2019) assessed its structural validity in adolescents (mean age=16.54±0.95) and suggested that the subscales of the Depression, Anxiety and Stress scale of 21 items can differentiate depression, anxiety, and stress in adolescents.

Basic Scale on Insomnia complaints and Quality of Sleep

The quality of sleep was assessed with the Basic Scale on Insomnia complaints and Quality of Sleep. This is a self-report scale composed of 7 items covering the assessment of difficulties with sleep onset and maintenance and the quality and depth of sleep during the last month and considering a normal week of classes. Total score ranges from 0 to 28 points and higher scores are associated with poor quality of sleep. The cut-off point to distinguish good from poor sleepers was defined as 9 or more points (Allen Gomes et al., 2015). The European Portuguese version of the Basic Scale on Insomnia complaints and Quality of Sleep was shown to be valid and reliable (ICC ≥ 0.8) for students (mean age=19.6±2.2) (Allen Gomes et al., 2015) and was also applied to students aged 17 to 25 years (Allen Gomes, Tavares, & Pinto de Azevedo, 2009).

Pain Catastrophizing Scale

Pain catastrophizing was assessed with the Pain Catastrophizing Scale. This is a 13 items self-report scale that assesses catastrophic thinking and inappropriate coping strategies about pain, distributed in three subscales: i) rumination, ii) magnification, and iii) helplessness. Each item is classified on a 5-point Likert scale, rated from 0= “never” and 4= “always”, with higher scores indicating elevated levels of catastrophizing (Jacome & Cruz, 2004). Cut-offs for the Pain Catastrophizing Scale in children were established as low (0 to 14), moderate (15 to 25), and high (≥26) catastrophizing (Pielech et al., 2014). The European Portuguese version of the Pain Catastrophizing Scale showed construct validity and high internal consistency (α=0.91) (Jacome & Cruz, 2004). A recent systematic review with meta-analysis established acceptable psychometric properties of Pain Catastrophizing Scale in children and adolescents, with test-retest reliability of 0.71 (Fisher, Heathcote, Eccleston, Simons, & Palermo, 2018).

Tampa Scale of Kinesiophobia

This scale consists of 13 items related to fear of movement and the degree of confidence for the movement, measured on a 4-point Likert scale (1= “strongly disagree” and 4= “strongly agree”). The total score ranges from 13 to 52 points and higher scores indicate increased levels of fear of movement (Cordeiro, Pezarat-Correia, Gil, & Cabri, 2013). Cut-offs for the Tampa Scale of Kinesiophobia in adults with chronic pain were established as subclinical (13 to 22), mild (23 to 32), moderate (33 to 42), and severe (43 to 52) (Neblett, Hartzell, Mayer, Bradford, & Gatchel, 2016). The European Portuguese version of the Tampa Scale of Kinesiophobia showed good psychometric properties in adults (α=0.82; ICC= 0.99) (Cordeiro et al., 2013).

Child Self-Efficacy Scale

This scale consists of 7 items that assess children's self-efficacy to maintain their normal routines when they are in pain. Each item is classified on a 5-point Likert scale rated from 1 (“very certain”) to 5 (“very uncertain”). Total score ranges from 7 to 35 points and higher scores are associated with lower self-efficacy (Bursch et al., 2006). The European Portuguese version of the Child Self-Efficacy Scale was considered valid and showed good test-retest reliability (ICC=0.83) in adolescents with chronic musculoskeletal pain (Andias & Silva, 2020b).

Central Sensitization Inventory

The somatic and emotional symptoms associated with central sensitization were assessed with Central Sensitization Inventory. This inventory consists of 25 items to assess health-related symptoms that are common in central sensitization conditions, where each item can be scored on a 5-point Likert scale ranging from “never” (0) to “always” (4). The total score ranges from 0 to 100 points and higher scores are associated with more symptoms of central sensitization (Mayer et al., 2012). Central

Sensitization Inventory severity levels were established by Neblett et al. (Neblett et al., 2013) as i) subclinical (0 to 29 points), ii) mild (30 to 39 points), iii) moderate (40 to 49 points), severe (50 to 59 points) and extreme (60 to 100 points). The European Portuguese version of the Central Sensitization Inventory was considered valid and showed good test-retest reliability (ICC=0.94) in adolescents with chronic musculoskeletal pain (Andias & Silva, 2020a).

5.3. Statistical analysis

Statistical analyses were performed using Statistical Package for Social Sciences (SPSS) Software, version 22.0. Summary statistics were used to describe characteristics of the sample using means and standard deviations for continuous variables and counts (n), and percentages (%) for categorical variables. Differences between adolescents with i) chronic NP, ii) chronic back pain, iii) chronic limb pain, and iv) adolescents without pain were explored using chi-square tests for categorical variables and One-Way ANOVAs for continuous variables. The criteria for normality of residues and homogeneity of variances were tested. Since the normality of the residues was not verified in any of the variables, the Kruskal – Wallis test was performed. However, for all analyses the nonparametric equivalent corroborated the parametric statistics, and, therefore, the parametric test results are reported.

Independent logistic-regression analyses were used to examine univariable and multivariable associations between the independent variables (sociodemographic characteristics: gender, age, Body Mass Index (BMI), and family situation; physical activity; psychosocial factors: anxiety, depression, and stress, catastrophizing, fear of movement, self-efficacy; sleep, and self-reported symptoms of central sensitization) and the dependent variables (presence of chronic neck, back and limb pain). The results for each independent variable were presented in OR and 95% CI. Independent linear regression analyses were used to explore univariable and multivariable

associations between the same independent variables plus the number of painful body sites and the total score of the Functional Disability Inventory as the dependent variable.

The univariable analyses were performed using the enter method and a $p \leq 0.10$ required for variables to enter the multivariable models. The multivariable analyses were performed using the stepwise method. The assumptions for the regression models (Hosmer and Lemeshow test for logistic regression and normality of the residuals for linear regression) were met. Significance was set at $p<0.05$.

5.4. Results

A total of 1730 adolescents (76.2%) answered the online questionnaire. Of these, 753 (43.5%) adolescents were classified in the group with chronic NP (mean age ± SD=16.30±1.14; 73.3% female), 384 (22.2%%) in the group with chronic back pain (mean age ± SD=16.29±1.19; 60.7% female), 298 (17.2%) in the group with chronic limb pain (mean age ± SD=16.30±1.23; 46.3% female), and 252 (14.6%) did not report pain (mean age ± SD=16.50±1.22; 32.1% female). Adolescents with acute pain (n=43) were excluded from this analysis due to the small sample size. A detailed characterization of the subgroups is presented in Table 27.

5.4.1. Characteristics of adolescents with NP and comparison with asymptomatic adolescents

Adolescents with NP reported higher levels of disability ($p<0.001$), catastrophizing ($p<0.001$), fear of movement ($p<0.001$), anxiety, depression, and stress ($p<0.001$), and symptoms of central sensitization ($p<0.001$), poorer quality of sleep ($p<0.001$), and lower self-efficacy ($p<0.001$) than asymptomatic adolescents.

5.4.2. Comparison of adolescents with NP with adolescents with back and limb pain

Comparisons among the 3 groups of adolescents with pain, revealed that the group of adolescents with chronic NP reported higher levels of disability ($p<0.001$), anxiety, depression, and stress ($p<0.001$), and self-reported symptoms of central sensitization ($p<0.001$) when compared to the other two groups. Adolescents with chronic NP had poorer quality of sleep ($p<0.001$), higher levels of catastrophizing ($p=0.02$), and lower levels of self-efficacy ($p<0.001$) compared to adolescents with limb pain, but similar to those with back pain ($p>0.05$). No other significant differences were found. These comparisons are illustrated in Figures 8-14.

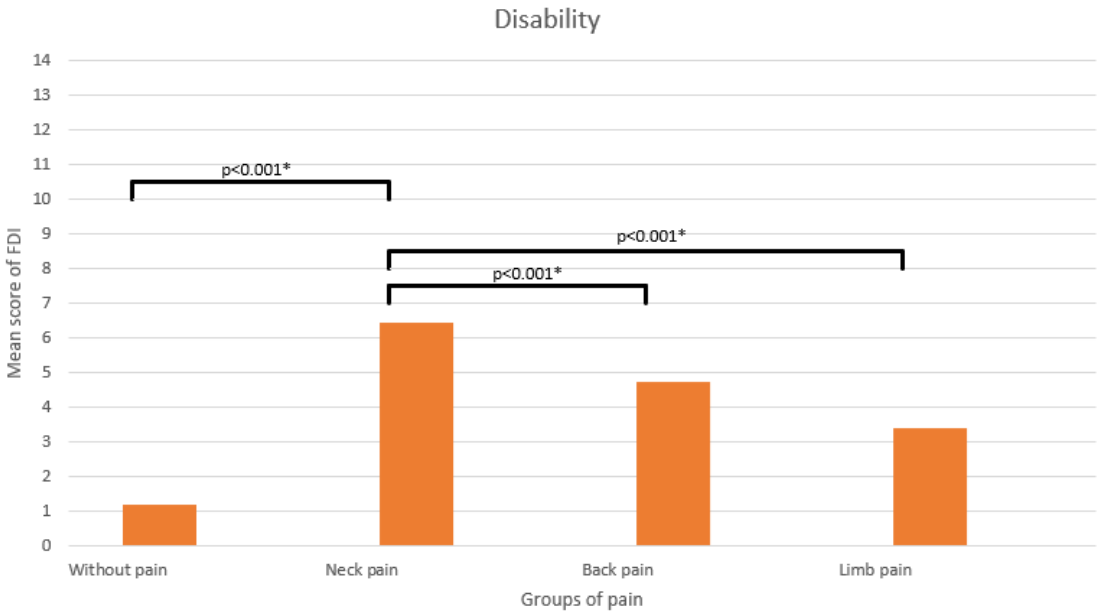


Figure 8. Mean scores of the Functional Disability Inventory and results of the comparisons among the groups with NP and without pain, back and limb pain.

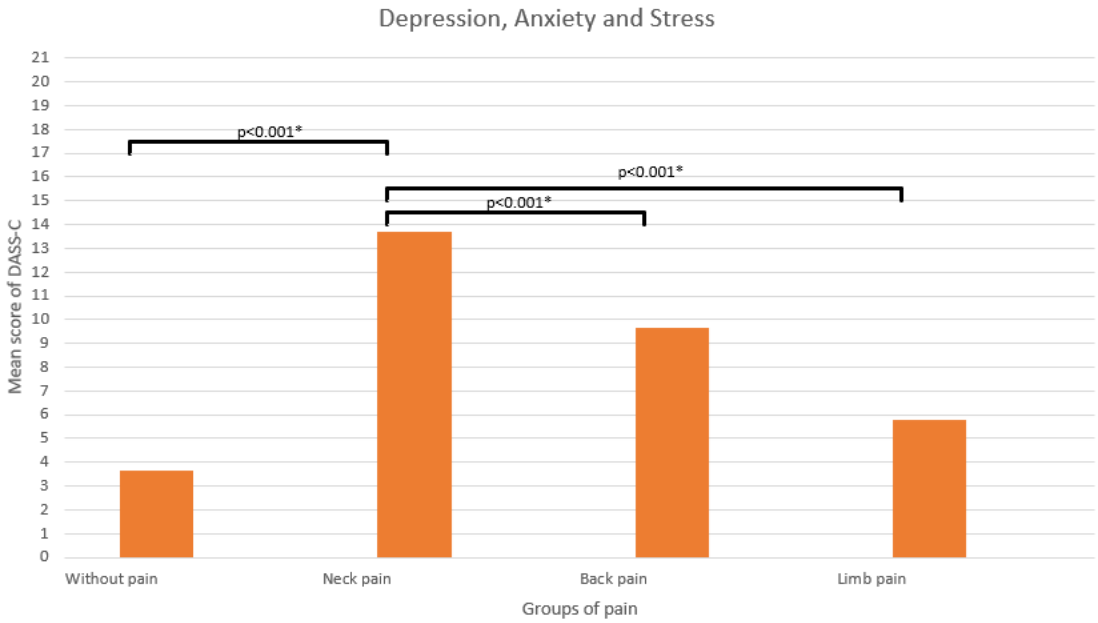


Figure 9. Mean scores of the Depression, Anxiety and Stress Scale for Children and and results of the comparisons among the groups with NP and without pain, back and limb pain.

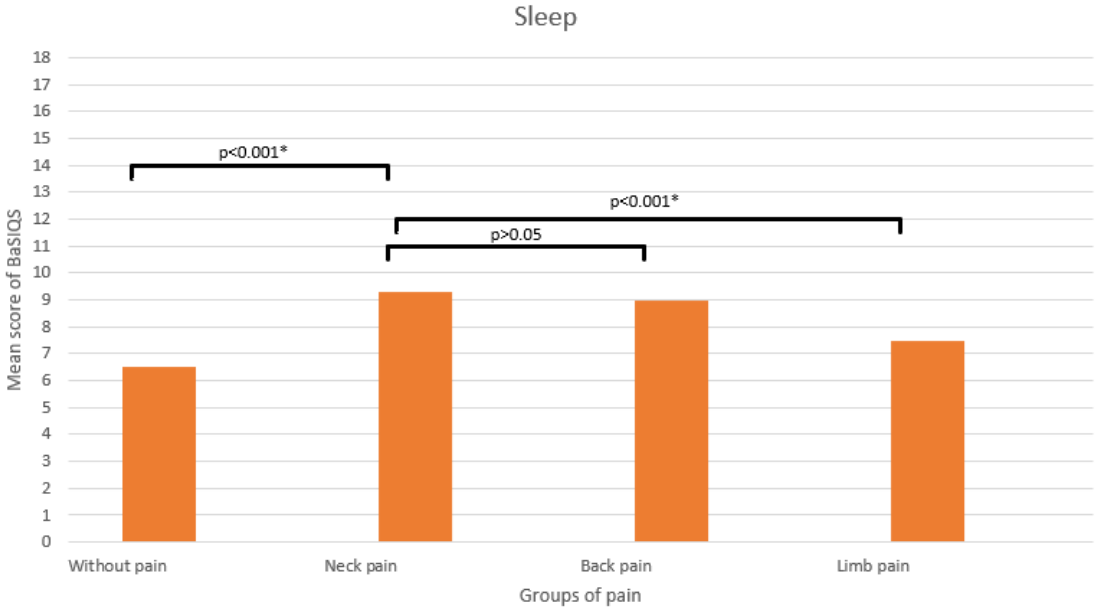


Figure 10. Mean scores of the Basic Scale on Insomnia complaints and Quality of Sleep and results of the comparisons among the groups with NP and without pain, back and limb pain.

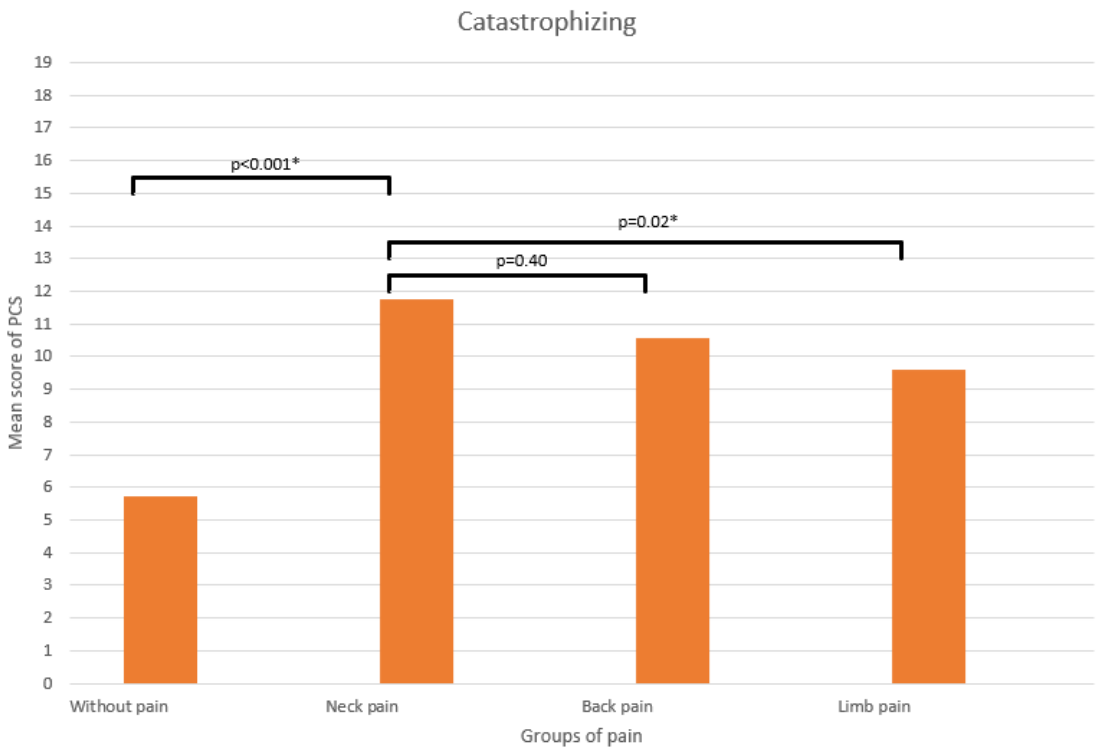


Figure 11. Mean score of the Pain Catastrophizing Scale and results of the comparisons among the groups with NP and without pain, back and limb pain.

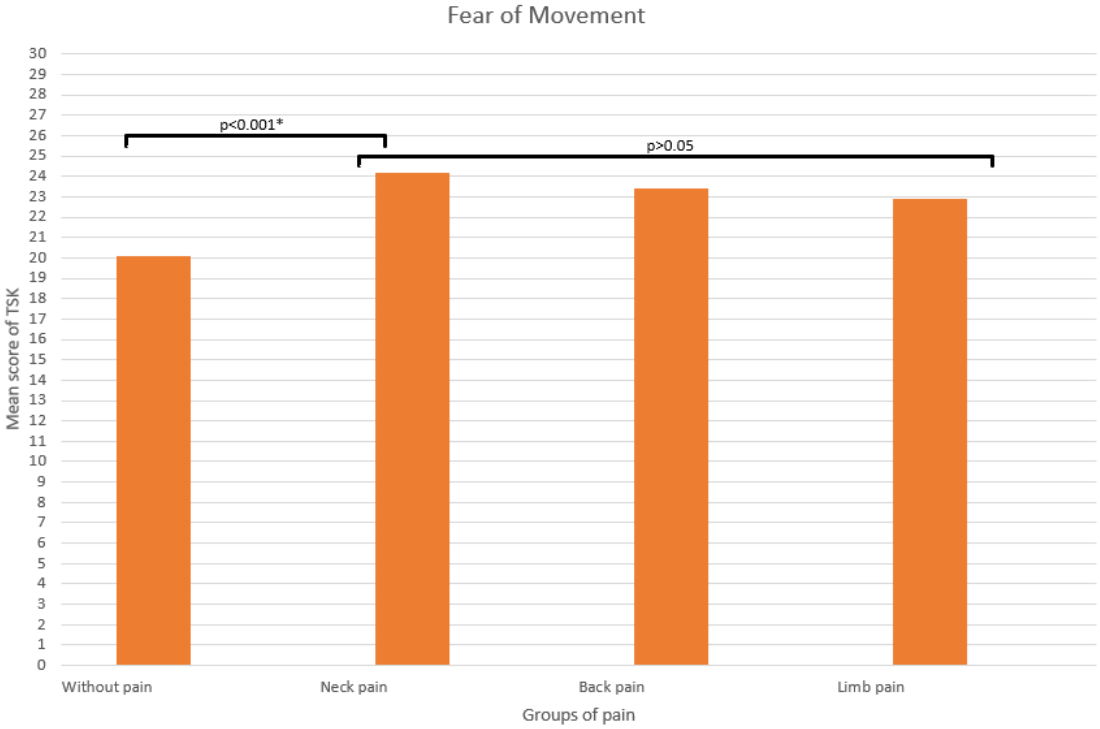


Figure 12. Mean score of the Tampa Scale of Kinesiophobia and results of the comparisons among the groups with NP and without pain, back and limb pain.

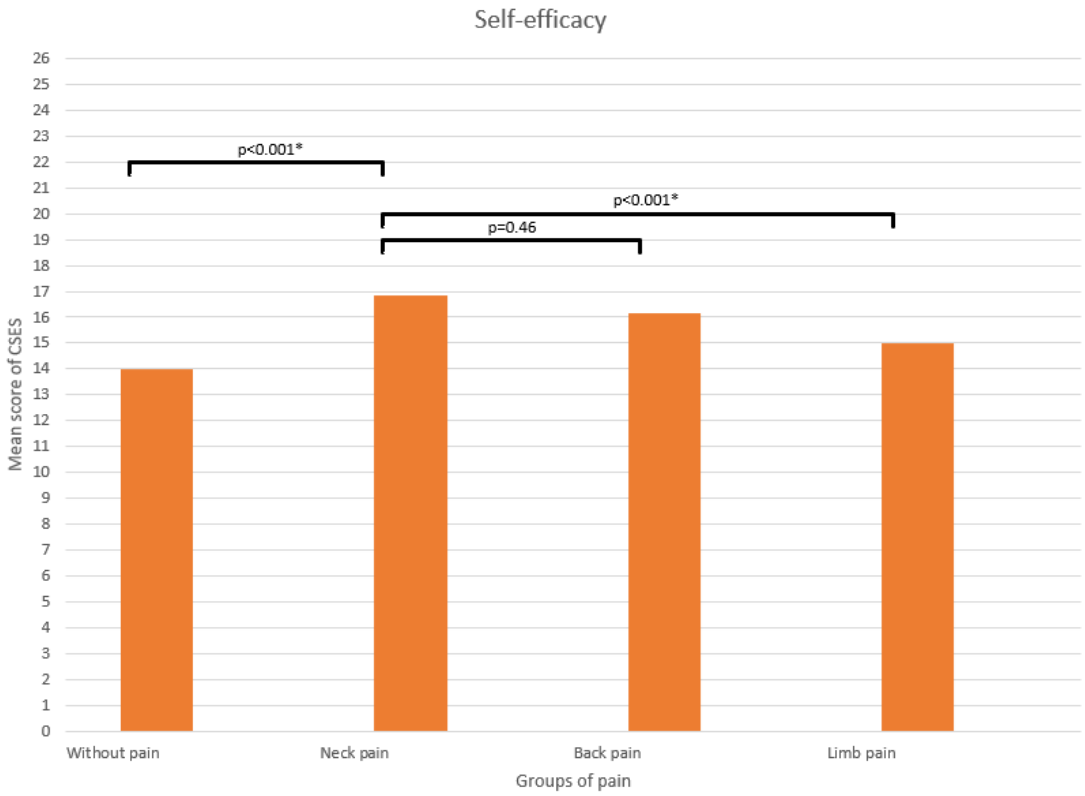


Figure 13. Mean scores of the Child Self-Efficacy Scale and results of the comparisons among the groups with NP and without pain, back and limb pain.

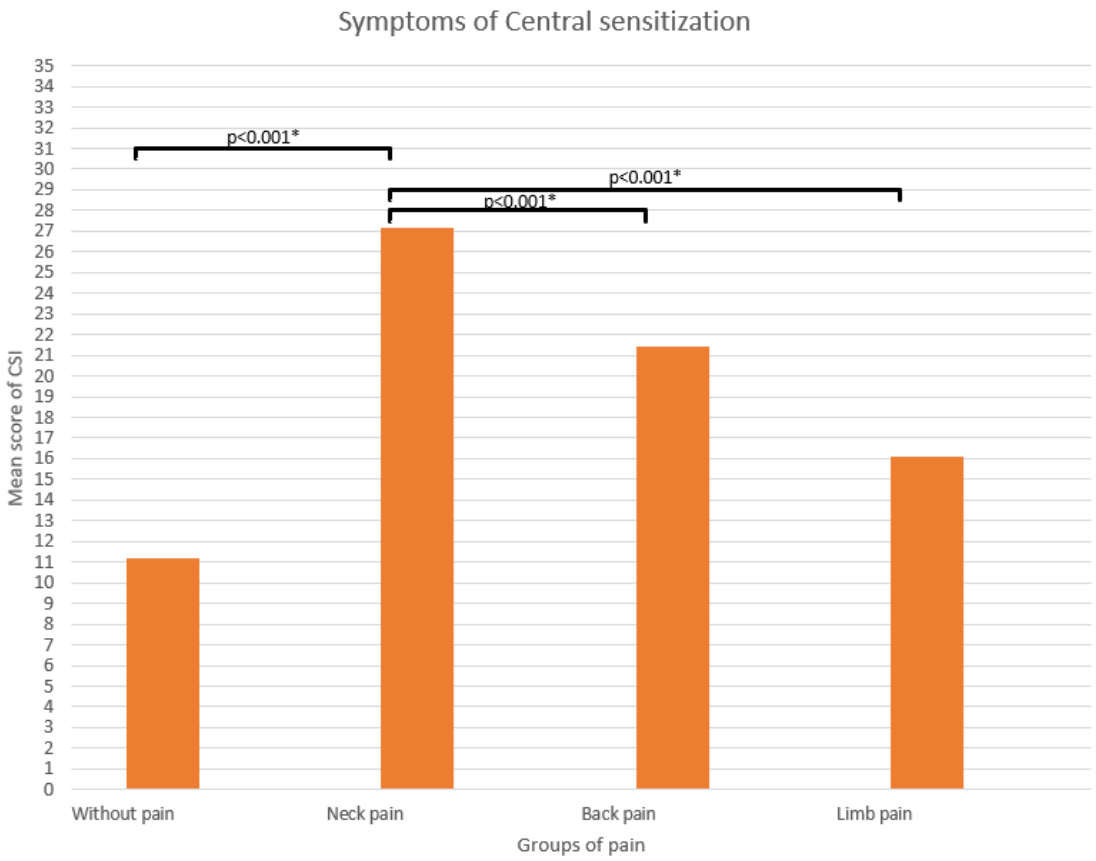


Figure 14. Mean scores of the Central Sensitization Inventory an results of the comparisons among the groups with NP and without pain, back and limb pain.

5.4.3. Univariable association between NP and sociodemographic variables, physical activity, psychosocial factors, sleep, and symptoms of central sensitization and comparison with back and limb pain

The univariable model showed that being a female (OR=5.80, p<0.05), reporting moderate (OR=2.51, p<0.05) and high (OR=4.55, p<0.05) catastrophizing, mild (OR=2.35, p<0.05), and moderate (OR=4.77, p<0.05) fear of movement, lower levels of self-efficacy (OR=2.31, p<0.05), poor quality of sleep (OR=3.22, p<0.05) and mild (OR=9.24, p<0.05) or moderate (OR=42.11, p<0.05) self-reported symptoms of central sensitization, significantly increased the odds of reporting chronic NP. Similarly, these

factors significantly increased the odds of reporting back and limb pain. Higher levels of anxiety, depression, and stress (OR=9.90, $p<0.05$) were associated with NP, and also with back pain, but not with limb pain ($p>0.05$), and severe self-reported symptoms of central sensitization were associated with increased odds of reporting NP (OR=8.16, $p<0.05$), but not back or limb pain (Table 28).

5.4.4. Multivariable association between NP and sociodemographic variables, psychosocial factors, sleep, and symptoms of central sensitization and comparison with back and limb pain

Being a female significantly increased the odds of reporting chronic NP (OR=3.88, $p<0.05$), as well as back and limb pain. Mild and moderate self-reported symptoms of central sensitization (OR=5.25, $p<0.05$) and poorer sleep (OR=1.58, $p<0.05$) increased the odds of NP and also back pain, but not of limb pain ($p>0.05$). None of the other variables were associated with NP ($p>0.05$). However, kinesiophobia was associated with back pain (OR=1.77 for mild fear of movement, $p<0.05$) and limb pain (OR=1.99 and 2.51 for mild and moderate fear of movement, respectively, $p<0.05$). The Nagelkerke R^2 was 0.31, 0.24, and 0.07 in the multivariable model of the neck, back and limb pain, respectively (Table 28). Figure 15 illustrates the factors associated with neck, back, and limb pain.

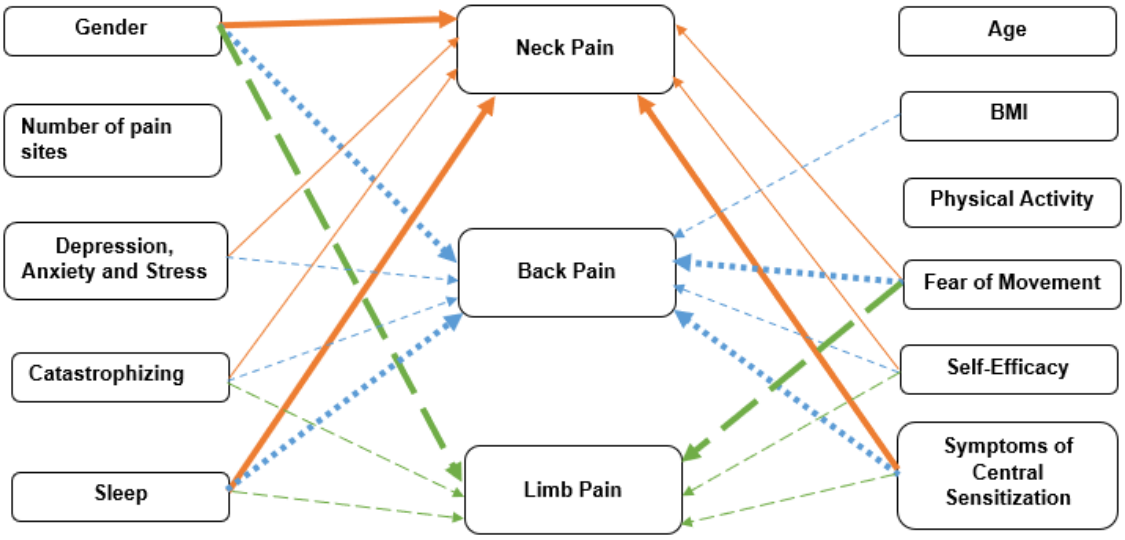


Figure 15. Similarities and differences between the groups of with neck, back, and limb pain for the factors associated with the presence of pain.

The continuous orange lines represent the factors associated with NP, the dotted lines in blue represent the factors associated with back pain, and the dashed lines in green represent the factors associated with limb pain in the univariate analysis. The thicker lines represent the factors that remained in the multivariable analysis.

5.4.5. Univariable association between disability and sociodemographic variables, number of pain sites, physical activity, psychosocial factors, sleep, and symptoms of central sensitization in NP and comparison with back and limb pain

The univariable model showed that in the group of adolescents with NP disability was significantly associated with higher levels of anxiety, depression, and stress ($p<0.05$), catastrophizing ($p<0.05$), fear of movement ($p<0.05$), and self-reported symptoms of central sensitization ($p<0.05$), poor quality of sleep ($p<0.05$), lower levels of self-efficacy ($p<0.05$) and a higher number of painful body sites ($p<0.05$). Similarly, these factors were significantly associated with disability in the groups of adolescents with back and limb pain. In addition, being a female was associated with disability in the group of adolescents with neck and back pain ($p<0.05$) but not with limb pain ($p>0.10$).

In contrast, higher BMI was associated with disability in the group with limb pain ($p<0.05$) but not in the group with NP (Table 29 and Figure 16).

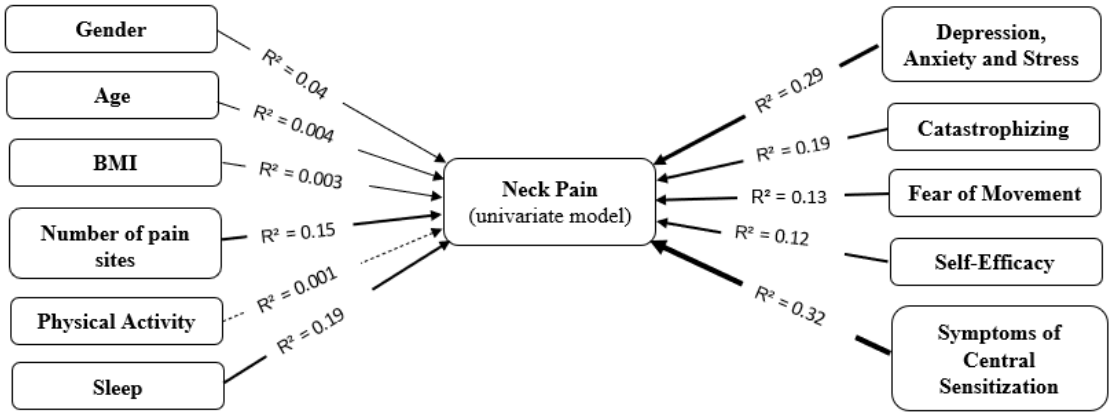


Figure 16. Variables associated with disability: the plots show the adjusted R^2 values for univariate regression analyses for the NP group.
The thickness of the arrows represents the strength of the association measured by the R^2, with dotted lines representing non-significant associations ($p>0.05$).

5.4.6. Multivariable association between disability and sociodemographic variables, number of pain sites, physical activity, psychosocial factors, sleep, and symptoms of central sensitization in NP and comparison with back and limb pain

In the group of adolescents with chronic NP, disability was significantly associated with higher levels of anxiety, depression, and stress, catastrophizing and self-reported symptoms of central sensitization, poorer quality of sleep, lower levels of self-efficacy, and a higher number of painful body sites. The model was statistically significant ($F=91.64$; $p<0.001$) with an adjusted R^2 of 0.42, suggesting that 42% of disability variance was explained by these variables. The same variables were significantly associated with disability in the group of adolescents with back pain, except for self-efficacy and self-reported symptoms of central sensitization, and the model was also statistically significant ($F=40.28$; $p<0.001$) with an adjusted R^2 of 0.34. In the group of

adolescents with limb pain, disability was associated with sleep impairments, catastrophizing, a larger number of painful body sites, and also a higher BMI and higher levels of fear of movement. The model was statistically significant (F=19.56; p<0.001) with an adjusted R^2 of 0.24 (Table 29). Figure 17 illustrates the different factors associated with disability in the groups with neck, back, and limb pain.

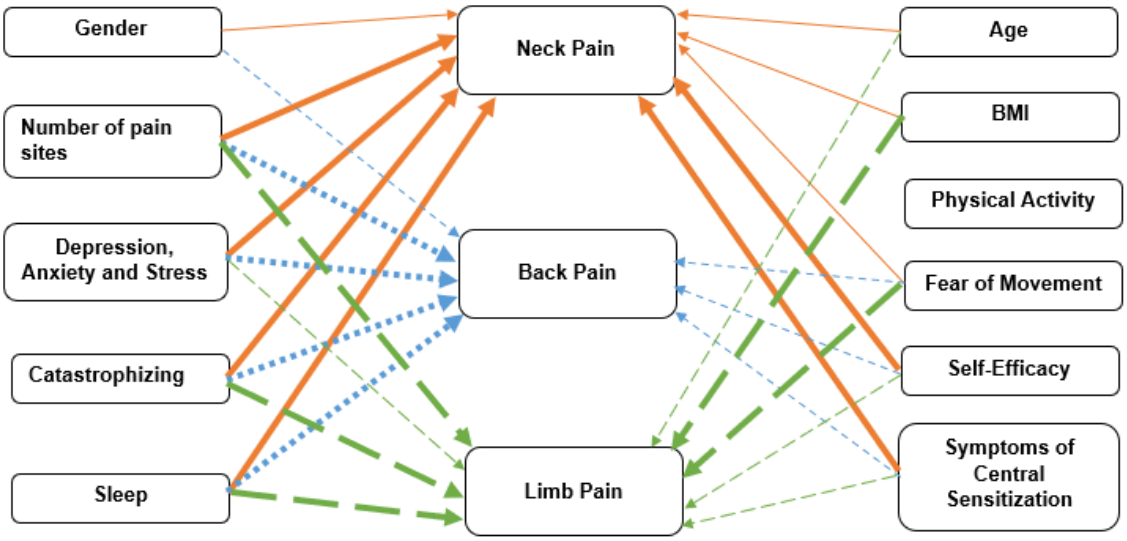


Figure 17. Similarities and differences between the groups with neck, back, and limb pain for the factors associated with disability.

The continuous orange lines represent the factors associated with disability in the group of adolescents with NP, the dotted lines in blue represent the factors associated with disability in the group of adolescents with back pain and the dashed lines in green represent the factors associated with disability in the group of adolescents with limb pain in the univariable analysis. Thicker lines represent the factors that remained in the multivariable analysis.

5.5. Discussion

This study characterized a sample of adolescents with chronic NP, assessed the variables associated with both the presence of chronic NP and disability and compared these with a group of adolescents with chronic back, and limb pain. To the best of our

knowledge, this is the first study exploring a wide range of variables including psychosocial (depression, anxiety, and stress, catastrophizing, fear of movement, self-efficacy), disability, physical activity, sleep, and self-reported symptoms of central sensitization in adolescents with NP and directly comparing them with adolescents with pain at other body sites.

5.5.1. Characteristics of adolescents with chronic NP and comparison with adolescents with chronic back and limb pain

Our findings suggested that adolescents with NP report more disability, anxiety, depression, and stress, catastrophizing, fear of movement, and self-reported symptoms of central sensitization, and lower sleep quality and self-efficacy than asymptomatic adolescents. These findings are in line with previous studies. A recent systematic review (Andias & Silva, 2019b) found that adolescents with NP have higher levels of depression, anxiety, stress, catastrophizing, and sleep impairments compared to adolescents without pain. This review also reported that for self-efficacy there is conflicting evidence on whether there are differences between adolescents with and without NP and no studies were found for fear of movement. The association between pain and psychosocial symptoms has also been reported for musculoskeletal pain in general. Noel et al. (2016) found that adolescents with chronic musculoskeletal pain, headache, and stomachache (mean age ± SD=16.0±0.12) reported significantly higher anxiety and depressive symptoms, insufficient sleep, and poorer general health compared to asymptomatic adolescents. Taken together, these findings highlight the importance of assessing psychosocial factors, disability, sleep, and self-reported symptoms of central sensitization in adolescents with chronic NP.

When compared to the groups that reported back and limb pain, the group of adolescents with NP reported higher disability, depression, anxiety, stress, and self-

reported symptoms of central sensitization, and poorer quality of sleep, but there are no differences between adolescents with neck and back pain regarding catastrophizing, self-efficacy, and sleep. Looking at the characteristics of adolescents with NP, it is possible to see that they also reported a higher mean number of painful body sites, which has been linked to a negative impact on physical and mental health in this age group (Harrison et al., 2016; Paananen et al., 2011) and might contribute to explain the differences found between the three groups of adolescents with pain.

5.5.2. Factors associated with chronic NP and comparison with chronic back and limb pain

Regarding the variables associated with NP, results suggest that in the univariable analysis, 6 of the 11 variables used for the regression models were associated with an increased odds of reporting NP and also back, and limb pain. These were: gender, sleep, catastrophizing, fear of movement, self-efficacy, and self-reported symptoms of central sensitization. Also, depression, anxiety, and stress were significantly associated with an increased odds of reporting neck and back pain, but not limb pain. However, when these variables were included in the multivariable models, i) only gender remained common to all the three groups, ii) self-reported symptoms of central sensitization and sleep impairments remained associated with increased odds of reporting neck and back pain, and iii) higher levels of fear of movement remained associated with higher odds of pain in back and limbs. While the univariable model only establishes the association between an independent variable and a specific outcome, the multivariable model allows us to examine the association of a set of variables with the outcome and, consequently, determines those that are the most important factors associated with the outcome (Katz, 2011). Thus, our results suggest that gender, self-reported symptoms of central sensitization, and sleep impairments are the variables that most determine the increased odds of reporting neck and back pain. We also

found that, among our variables of interest, gender, and fear of movement are those that are most associated with the increased odds of reporting limb pain. Besides, fear of movement also seems to be an important determinate for low back pain. Therefore, we can suggest that there are similar factors associated with the presence of neck, back, and limb pain, but there are also differences that should be considered when assessing and treating adolescents with different chronic pain complaints.

In the literature, several studies showed that girls are more likely to have chronic musculoskeletal pain in general (El-Metwally et al., 2007; Martin, McGrath, Brown, & Katz, 2007; Stahlschmidt, Hübner-Möhler, Dogan, & Wager, 2019) and also neck/shoulder and back pain (Diepenmaat et al., 2006). However, a few studies have reported that gender was not associated with the presence of pain in the lower limbs (El-Metwally, Salminen, Auvinen, Kautiainen, & Mikkelsson, 2005; El-Metwally et al., 2006). In our study, the group of adolescents with limb pain had not only lower limb pain but also upper limb pain, which may have contributed to the significant association with gender. Self-reported symptoms of central sensitization and sleep were associated with increased odds of reporting neck and back pain. Although no studies have been found in adolescents, studies in adults have reported the impact of central sensitization on chronic musculoskeletal pain (Nijs et al., 2010; Roussel et al., 2013). Central sensitization related to chronic pain has been associated with an abnormal increase of pain as a consequence of several mechanisms including neuronal hyperexcitability, malfunctioning of nociceptive pathways, and altered sensory processing in the brain (Nijs et al., 2010; Woolf, 2011). Moreover, central sensitization is also characterized by multiple painful body sites, as found in the groups with neck and back pain. Poor sleep has been found to be associated with chronic non-specific musculoskeletal pain in adolescents (Auvinen et al., 2010; Badawy, Law, & Palermo, 2019; Harrison et al., 2016). A recent systematic review (Andias & Silva, 2019b) also reported that sleep

impairments are associated with increased odds of reporting NP in adolescents. Additionally, Evans et al. (2017) explored the indirect effect of sleep on pain in adolescents with chronic pain, including musculoskeletal, headache, and abdominal pain (mean age ± SD=14.5±2.4). Sleep quality was a significant predictor of chronic pain, but also a significant predictor of negative emotions, which, in turn, were a significant predictor of pain. In general, poor sleep may promote a set of biopsychosocial consequences, including increased pain catastrophizing and a decrease in the effectiveness of endogenous pain mechanisms, which also contribute to pain (Finan et al., 2013; Valrie, Bromberg, Palermo, & Schanberg, 2013).

In the multivariable analysis, there is no common determinate of pain among the group of adolescents with neck and limb pain, besides gender. Fear of movement remained associated with the presence of pain in the group of adolescents with limb and back pain. According to the fear-avoidance model of pain, fear and catastrophic thoughts in response to pain increase the risk of developing chronic musculoskeletal pain (Leeuw et al., 2007; Turk & Wilson, 2010). A theoretical study in children and adolescents explored that the fear-avoidance cycle is characterized by avoidance, emotional suffering, and dysfunction, which also have a negative influence on pain (Asmundson, Noel, Petter, & Parkerson, 2012). No study was found that investigated the association between fear of movement and chronic pain in adolescents. In adults, a few studies have found an association between kinesiophobia and an increased likelihood of reporting chronic low back pain (Comachio, Magalhães, Campos, Silva, & Marques, 2018; Picavet, Vlaeyen, & Schouten, 2002). The finding that fear of movement was the only determinate, in addition to gender, that was associated with pain in the limbs may be explained by its likely traumatic origin and the fear of reinjury. El-Metwally et al. (2006) suggested that risk factors and consequences of traumatic and non-traumatic lower limb pain were different in preadolescents. Traumatic lower limb pain was more

associated with physical activities while non-traumatic pain was more associated with psychosocial variables. This reason may also help to explain the non-association of fear of movement with NP that tends to have a non-traumatic origin and the low Nagelkerke R^2 (0.07) for the model in the group of adolescents with limb pain. Other factors, such as the type and intensity of physical activity (El-Metwally et al., 2006; Guddal et al., 2017), which were not included in this analysis, may be associated with limb pain. On the other hand, the association of fear of movement in the group of adolescents with back pain may be related to more common negative beliefs in avoiding movement associated with the back (O'Sullivan, Smith, Beales, & Straker, 2017), and perhaps an increased need for higher range of motion for daily activities compared to the neck region.

Finally, in our study, physical activity was not associated with neck, back or limb pain, as reported in previous studies (Malmborg et al., 2019; Stommen, Verbunt, Gorter, & Goossens, 2012), but contrary to others (Heikkala, Paananen, Taimela, Auvinen, & Karppinen, 2019; Long, Palermo, & Manees, 2008). The use of different measurement instruments between studies (objective measurements versus self-report) and the different levels of physical activity of the sample may contribute to the differences between studies.

5.5.3. Factors associated with disability in chronic NP and comparison with chronic back and limb pain

Similarly to pain, our results suggest common factors associated with disability among the three groups, but also differences. Our findings showed that in the univariable analysis, 7 of the 11 variables used in the regression models were significantly associated with disability in the group of adolescents with NP, and also in the groups of adolescents with back and limb pain. These were: higher levels of anxiety, depression,

and stress, catastrophizing, fear of movement, number of painful body sites, self-reported symptoms of central sensitization, poorer sleep, and lower self-efficacy. Still, in the univariable analysis, female gender was significantly associated with disability in the groups of adolescents with neck and back pain, but not in the group of adolescents with limb pain. Older age and higher BMI were also associated with disability in the groups of adolescents with neck and limb pain, but not in the group of adolescents with back pain. However, in the multivariable models, i) self-reported symptoms of central sensitization and lower levels of self-efficacy remained associated with disability in the group of adolescents with NP only, ii) higher levels of anxiety, depression, and stress remained associated with disability in the group of adolescents with NP, and also in the group of adolescents with back pain, iii) catastrophizing, number of painful body sites and sleep remained associated with disability in the group of adolescents with NP, and also in the groups of adolescents with back and limb pain, and iv) BMI and higher levels of fear of movement were associated with disability in the group of adolescents with limb pain. The amount of variance explained by the models was higher in the groups of adolescents with neck (R^2 of 0.42) and back pain (R^2 of 0.34), compared to the group of adolescents with limb pain (R^2 of 0.24). Other variables that may have an impact on disability, such as parents' pain behavior or pain intensity (Palermo, Valrie, & Karlson, 2014) were not investigated in this study and may account for some of the unexplained variance. No studies were found in adolescents with chronic NP that explored the R^2 in multivariate models of disability. Lynch et al. (2006) in adolescents with back pain associated with other painful body sites reported an R^2 of 0.43 for a model of explained disability including gender, pain intensity, catastrophizing, and family history of chronic pain. Gauntlett-Gilbert & Eccleston (2007) found an R^2 of 0.36 in a model of disability including pain intensity and depression in 110 adolescents with complex regional pain syndrome, head, and abdominal pain. Differences in the sample characteristics, as well as in the type and number of variables included, and in the

method chosen for the regression analysis, must be taken into account when comparing these studies.

Lynch et al. (2006) in 65 adolescents (mean age± SD=14.9±2.6) with chronic back pain, including NP, found that catastrophizing was the most strong determinate of functional disability. Exaggerated and negative thoughts and expectations in response to a painful or potentially painful experience have been associated with a decrease in management and control capacity of pain, which, in turn, influences negatively the participation in daily activities, resulting in increased functional disability (Simons & Kaczynski, 2012; Tran et al., 2015). Sleep is both a predictor of disability and of negative emotions which, in turn, are also a predictor of disability (Evans et al., 2017). Anxiety, depression, and stress remained associated with disability in adolescents with neck and back pain, but not with limb pain, suggesting that these factors are more relevant in those painful conditions, potentially due to the more idiopathic nature of the pain. In previous studies depression, anxiety and stress were also associated with disability in adolescents with neck and back pain (Kashikar-Zuck, Goldschneider, Powers, Vaught, & Hershey, 2001; Simons, Sieberg, & Claar, 2012; Stommen, Verbunt, Gorter, & Goossens, 2012). Regarding self-efficacy and self-reported symptoms of central sensitization, these were only associated with disability in the group of adolescents with NP. Although the NP group has similar values of self-efficacy compared to the back pain group, once again the fact that the NP group could also have back and limb pain, and consequently multiple painful body sites, may explain this association. Nevertheless, it may suggest that the combination of neck and back pain is associated with lower levels of self-efficacy (61% of adolescents in the NP group also had back pain) to a greater extent than lower back or limb pain only and than both back and limb pain combined. Lower levels of self-efficacy have been associated with higher levels of functional disability (Kalapurakkel et al., 2015). Self-efficacy is a

protective resilience factor that increases confidence to perform actions and activities, which has been reported as an important factor associated with disability in adolescents with different chronic pain conditions (Carpino, Segal, Logan, Lebel, & Simons, 2014; Kalapurakkel et al., 2015).

The presence of self-reported symptoms of central sensitization was also higher in the NP group compared to the other two groups, and these remained associated with disability in the NP group. Again, the combination of neck and back pain may be a relevant factor that contributes to this association. Despite the lack of evidence in adolescents concerning central sensitization, Tanaka et al. (Tanaka et al., 2019) suggested that higher levels in the Central Sensitization Inventory predicted higher disability in a sample of 553 adults with musculoskeletal pain. Clinical symptoms tend to be worse with increasing Central Sensitization Inventory scores, thus increasing disability levels (Tanaka et al., 2019).

Similarly to the findings for factors associated with pain, fear of movement was associated with disability in the group of adolescents with limb pain only. A recent systematic review explored the role of the kinesiophobia on disability, in adults with chronic musculoskeletal pain, and reported that moderate evidence indicates that kinesiophobia predicts the progression of disability (Luque-Suarez, Martinez-Calderon, & Falla, 2019). Similarly, Martin et al. (2007) in a small sample of adolescents (mean age±SD= 14.2±2.2) with chronic pain, including musculoskeletal, abdominal, head and neuromuscular pain, suggested that fear of pain accounted for 39.9% of the variance in pain-related disability. This finding might suggest that the presence of pain only in the limbs is associated with higher levels of fear of movement to a greater extent than their combination with other areas.

5.5.4. Factors simultaneously associated with pain and disability in chronic NP and comparison with chronic back and limb pain

Interestingly, when comparing the factors associated with pain and disability, some factors are common to both models but there are also differences. In the group of adolescents with NP, self-reported symptoms of central sensitization and sleep impairment were associated with both pain and disability. In the groups of adolescents with back and limb pain, only sleep and fear of movement, respectively, were associated with both pain and disability. In contrast, i) gender was associated with pain in all groups, ii) catastrophizing and number of painful body sites were associated with disability in all groups, iii) depression, anxiety and stress were associated with disability in the groups of adolescents with neck and back pain, and iv) BMI was associated with disability in the group of adolescents with limb pain only. These findings emphasize the importance of assessing these variables in adolescents with chronic musculoskeletal pain and suggest that when designing interventions targeting both pain and disability, all these variables should be considered.

5.5.5. Clinical Implications

Our findings highlight the need to consider depression, anxiety and stress, catastrophizing, fear of movement, self-efficacy, sleep, and self-reported symptoms of central sensitization when assessing and treating adolescents with chronic NP, but also with back, and limb pain. Furthermore, the findings suggest the presence of similar factors associated with pain and disability among adolescents with neck, back, and limb pain, but also differences according to the painful body area. Regarding the presence of pain, special attention should be paid to the assessment of self-reported symptoms of central sensitization and sleep in adolescents with neck and back pain, as well as to fear of movement in adolescents with limb and back pain. Concerning disability, catastrophizing, sleep, and the number of painful body sites should be

considered independently of pain location. In addition, anxiety, depression, and stress should be taken into account in adolescents with neck and back pain, and fear of movement in limb pain. Results suggest that interventions targeting adolescents with chronic pain may have a common structure, independent of painful body site, but also specific components that target additional relevant factors associated with pain and disability that depend on the painful body region. Furthermore, our findings suggest a need for preventive strategies and early interventions targeting pain that should be delivered at schools to reach a high number of (virtually all) adolescents.

5.5.6. Limitations and future research

The findings of this study should be analysed in light of its limitations. The sample was divided into 3 mutually exclusive groups. Nevertheless, adolescents in each group had other painful body sites: adolescents in the NP group could have back and limb pain; adolescents in the back group could have limb pain but not NP, and adolescents with limb pain only had limb pain. This is likely to have impacted the number of painful body sites in each of the groups and consequently the results. However, adolescents with NP (which were the focus of this study) have multiple painful body sites and, therefore, including other painful body sites in this group better represents the reality and facilitates the comparison between adolescents with NP and adolescents without NP but with pain at other body sites. Nevertheless, the results suggest that the combination of different painful body sites may influence the identification of the most relevant factors. This should be explored in future studies, eventually grouping participants by their chief pain complaint. The transversal nature of this study does not allow for a cause-effect determination. Longitudinal studies are needed to inform on the long-term predictive value of these variables both for the appearance and maintenance of NP. Also, the sample in this study is community-based, and cannot be generalized to adolescents in clinical settings.

5.6. Conclusion

In summary, our findings suggest that chronic NP in adolescents is a common complaint and that there are common and distinctive factors associated with both the presence of NP pain and with disability. Similarly, there are also commonalities and differences between adolescents with NP and adolescents with chronic back and limb pain that should be considered when designing assessment and intervention strategies. Our results further highlight the relevance of psychosocial factors, sleep, and self-reported symptoms of central sensitization in pain and disability in adolescents with chronic NP and musculoskeletal pain in general. Future studies should explore its relevance to the long-term maintenance of chronic NP.

Table 27. Characterization of adolescents without musculoskeletal pain, with chronic neck, back, and limb pain.

Variables		**Without pain (n=252)**	**Chronic pain**			***p*-value**
			Neck Pain (n=753)	**Back Pain** (n=384)	**Limb Pain** (n=298)	
Gender	Girls	81 (32.1%)	552 (73.3%)	233 (60.7%)	138 (46.3%)	<0.001
	Boys	171(67.9%)	201 (26.7%)	151 (39.3%)	160 (53.7%)	
Age (years)		16.50±1.22	16.30±1.14	16.29±1.19	16.30±1.23	0.105
BMI (Kg/m^2)		21.26±3.21	21.77±7.56	22.03±6.11	21.72±3.47	0.500
Scholar level	10th	82 (32.5%)	260 (34.5%)	145 (37.8%)	117 (39.3%)	0.574
	11th	77 (30.6%)	236 (31.3%)	115 (29.9%)	91 (30.5%)	
	12th	93 (36.9%)	257 (34.1%)	124 (32.3%)	90 (30.2%)	
Family situation (Lives with…)	Father and mother	174(69.0%)	504 (66.9)	254 (66.1%)	206 (69.1%)	0.788
	Mother	54 (21.4%)	151 (20.1%)	79 (20.6%)	57 (19.1%)	
	Father	7 (2.8%)	19 (2.5%)	7 (1.8%)	8 (2.7%)	
	Other	17 (6.7%)	79 (10.5%)	44 (11.5%)	27 (9.1%)	
Number of painful body sites (mean±SD)		-	3.81±1.68	2.56±1.24	1.65±0.82	<0.001
Search for health care because of pain	Yes	-	347 (46.1%)	195 (50.9%)	137 (46.0%)	<0.001
	No	-	406 (43.9%)	189 (49.1%)	161 (54.0%)	
IPAQ-A (0-2540 minutes/week)	Total score	1001.14±759.21	1095.02±744.72	1033.48±708.92	1120.42±755.72	0.148
	School Physical Activity	278.00±309.03	279.11±260.54	265.69±233.93	296.09±279.36	0.533
	Transportation	262.52±328.40	332.04±378.16	308.94±360.48	312.35±360.55	0.074
	Housework	127.90±255.54	152.35±235.82	129.71±237.05	141.10±223.33	0.340
	Leisure Time	426.28±477.74	403.46±455.58	402.92±442.10	468.52±479.00	0.184
FDI (0-60)	Total score	1.18±2.91	6.44±6.62	4.75±5.61	3.41±4.95	<0.001
	No/minimal (≤12)	247 (98.0%)	641 (85.1%)	354 (92.2%)	285 (95.6%)	
	Moderate (13-29)	5 (2.0%)	107 (14.2%)	27 (7.0%)	13 (4.4%)	
	Severe (≥30)	0 (0.0%)	5 (0.7%)	3 (0.8%)	0 (0.0%)	
DASS-C (0-63)	Total score	3.66±5.98	13.68±12.55	9.65±10.16	5.77±6.89	<0.001
	DASS-C ≤ 21	245 (97.2%)	587 (78.0%)	340 (88.5%)	286 (96.0%)	
	DASS-C >21	7 (2.8%)	166 (22.0%)	44 (11.5%)	12 (4.0%)	
	Anxiety (subscale score DASS-C)	0.80±1.64	3.55±4.13	2.48±3.17	1.22±1.79	<0.001
	Depression (subscale score	1.44±2.68	5.02±4.98	3.70±4.21	2.28±3.23	<0.001

	DASS-C)					
	Stress (subscale score DASS-C)	1.42±2.41	5.11±4.60	3.47±3.89	2.27±2.96	<0.001
BaSIQS (0-28)	Total score	6.52±3.81	9.29±4.91	8.98±4.71	7.47±3.84	<0.001
	Good sleepers (<9)	191 (75.8%)	371 (49.3%)	201 (52.3%)	193 (64.8%)	
	Poor sleepers (≥9)	61 (24.2%)	382 (50.7%)	183 (47.7%)	105 (35.2%)	
PCS (0-52)	Total score	5.71±8.22	11.74±10.89	10.55±9.98	9.62±10.57	<0.001
	Low (≤14)	221 (87.7%)	528 (70.1%)	283 (73.7%)	232 (77.9%)	
	Moderate (15-25)	23 (9.1%)	138 (18.3%)	64 (16.7%)	41 (13.8%)	
	High (≥26)	8 (3.2%)	87 (11.6%)	37 (9.6%)	25 (8.4%)	
	Rumination (subscale)	2.20±3.39	4.27±4.18	3.93±3.96	3.54±4.16	<0.001
	Magnification (subscale)	1.22±1.99	2.64±2.77	2.38±2.49	2.23±2.70	<0.001
	Helplessness (subscale)	2.29±3.46	4.83±4.83	4.24±4.45	3.85±4.59	<0.001
TSK (13-52)	Total score	20.10±7.63	24.15±7.11	23.43±7.04	22.88±7.29	<0.001
	Subclinical (13-22)	168 (66.7%)	331 (44.0%)	165 (43.0%)	146 (49.0%)	
	Mild (23-32)	70 (27.8%)	324 (43.0%)	182 (47.4%)	126 (42.3%)	
	Moderate (33-42)	10 (4.0%)	94 (12.5%)	36 (9.4%)	23 (7.7%)	
	Severe (43-52)	4 (1.6%)	4 (0.5%)	1 (0.3%)	3 (1.0%)	
CSES (7-35)	Total score	13.98±6.69	16.84±5.89	16.16±6.13	15.01±6.09	<0.001
	CSES ≤14	139 (55.2%)	262 (34.8%)	153 (39.8%)	143 (48.0%)	
	CSES >14	113 (44.8%)	491 (65.2%)	231 (60.2%)	155 (52.0%)	
CSI (0-100)	Total score	11.17±10.28	27.13±14.95	21.39±13.21	16.09±10.88	<0.001
	Subclinical (0-29)	240 (95.2%)	456 (60.6%)	291 (75.8%)	264 (88.6%)	
	Mild (30-39)	9 (3.6%)	158 (21.0%)	55 (14.3%)	23 (7.7%)	
	Moderate (40-49)	1 (0.4%)	80 (10.6%)	25 (6.5%)	8 (2.7%)	
	Severe (50-59)	2 (0.8%)	31 (4.1%)	9 (2.3%)	3 (1.0%)	
	Extreme (>60)	0 (0.0%)	28 (3.7%)	4 (1.0%)	0 (0.0%)	

BMI, Body Mass Index; NP, Neck Pain; IPAQ-A, International Questionnaire of Physical Activity for Adolescents; FDI, Functional Disability Inventory; DASS-C, Depression, Anxiety and Stress Scale for Children; 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

Table 28. Odds ratios and 95% confidence intervals for univariable and multivariable associations with chronic neck, back, and limb pain.

		Neck pain Nagelkerke R^2=0.31		**Back pain** Nagelkerke R^2=0.24		**Limb pain** Nagelkerke R^2=0.07	
Variables		Univariable OR; CI95%	Multivariable OR; CI95%	Univariable OR; CI95%	Multivariable OR; CI95%	Univariable OR; CI95%	Multivariable OR; CI95%
Gender	Male	1		1		1	
	Female	5.80; [4.25;7.90]**	3.88; [2.79;5.38]**	3.26; [2.33;4.55]**	2.71; [1.90;3.87]**	1.82; [1.29;2.58]**	1.72; [1.20;2.45]**
Age		0.86; [0.76;0.98]**		0.87; [0.76;0.99]**		0.88; [0.76;1.01]*	
BMI		1.03; [0.98;1.07]		1.05; [0.99;1.10]*		1.04; [0.99;1.10]	
IPAQ-A	School related PA	1.00; [0.99;1.00]		1.00; [1.00;1.00]		1.00; [1.00;1.00]	
	Transportation	1.00; [1.00;1.00]		1.00; [1.00;1.00]		1.00; [1.00;1.00]*	
	Housework	1.00; [1.00;1.00]**		1.00; [1.00;1.00]		1.00; [1.00;1.00]	
	Leisure Time	1.00; [1.00;1.00]		1.00; [1.00;1.00]		1.00; [1.00;1.00]	
DASS-C	DASS-C score (≤21)	1		1		1	
	DASS-C score (>21)	9.90; [4.58;21.39]**		4.53; [2.01;10.23]**		1.47; [0.57;3.79]	
BaSIQS	BaSIQS (<9)	1		1		1	
	BaSIQS (≥9)	3.22; [2.34;4.45]**	1.58; [1.10;2.27]**	2.86; [2.01;4.05]**	2.07; [1.42;3.02]**	1.70; [1.17;2.48]**	
PCS	Low (≤14)	1		1		1	
	Moderate (15-25)	2.51; [1.57;4.01]**		2.17; [1.31;3.61]**		1.70; [0.99;2.92]*	
	High (≥30)	4.55; [2.17;9.55]**		3.61; [1.65;7.91]**		2.98; [1.32;6.74]**	
TSK	Subclinical (13-22)	1		1		1	
	Mild (23-32)	2.35; [1.71;3.23]**	1.36; [0.94;1.94]	2.65; [1.87;3.76]**	1.77; [1.21;2.59]**	2.07; [1.44;2.99]**	1.99; [1.37;2.88]**
	Moderate (33-42)	4.77; [2.42;9.40]**	1.89; [0.89;3.99]	3.67; [1.76;7.63]**	1.68; [0.74;3.83]	2.65; [1.22;5.74]**	2.51; [1.15;5.47]**
	Severe (43-52)	0.51; [0.13;2.06]	0.21; [0.03;1.32]	0.26; [0.03;2.30]	0.25; [0.03;2.53]	0.86; [0.19;3.92]	0.83; [0.18;3.80]
CSES	CSES (≤14)	1		1		1	
	CSES (>14)	2.31; [1.73;3.08]**		1.86; [1.35;2.56]**		1.33; [0.95;1.87]*	
CSI	Subclinical (0-29)	1		1		1	
	Mild (30-39)	9.24; [4.64;18.41]**	5.25; [2.56;10.76]**	5.04; [2.44;10.41]**	3.49; [1.64;7.45]**	2.32; [1.05;5.12]**	
	Moderate (40-49)	42.11; [5.82;304.46]**	20.34; [2.76;149.99]**	20.62; [2.77;153.28]**	8.63; [1.11;67.22]**	7.27; [0.90;58.58]*	
	Severe (50-59)	8.16; [1.94;34.38]**	4.50; [0.98;20.57]	3.71; [0.79;17.34]	2.30; [0.44;12.08]	1.36; [0.23;8.23]	
	Extreme (60-100)	-		-		-	

*p < 0.1; ** p < 0.05

OR, Odd Ratio; BMI, Body Mass Index; NP, IPAQ-A, International Questionnaire of Physical Activity for Adolescents; FDI, Functional Disability Inventory; DASS-C, Depression, Anxiety and Stress Scale for Children; 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.

Table 29. Factors associated with disability in the subgroups of adolescents with chronic neck, back, and limb pain.

	Neck Pain						Back Pain						Limb Pain					
	Univariable linear regression			Multivariable linear regression (R^2=0.42)			Univariable linear regression			Multivariable linear regression (R^2=0.34)			Univariable linear regression			Multivariable linear regression (R^2=0.24)		
Variables	B-coefficient (95% CI)	β	*p*	B-coefficient (95% CI)	β	*p*	B-coefficient (95% CI)	β	*p*	B-coefficient (95% CI)	β	*p*	B-coefficient (95% CI)	β	*p*	B-coefficient (95% CI)	β	*p*
Gender (f)	3.05 (2.00; 4.10)	0.20	<0.001				1.70 (0.56; 2.84)	1.15	0.004				0.8 (0.33;1.93)	0.08	0.17			
Age	0.42 (0.01; 0.84)	0.07	0.05				0.16 (-0.32; 0.63)	0.03	0.52				0.43 (-0.03; 0.88)	0.12	0.07			
BMI	0.06 (-0.002; 0.12)	0.07	0.06				0.005 (-0.09; 0.10)	0.01	0.92				0.25 (0.09; 0.41)	0.18	0.002	0.16 (0.02; 0.31)	0.12	0.03
Number of pain sites	1.53 (1.27; 1.79)	0.39	<0.001	0.64 (0.40; 0.87)	0.16	<0.001	1.28 (0.85; 1.72)	0.28	<0.001	0.76 (0.37; 1.14)	0.17	<0.001	1.17 (0.50; 1.84)	0.20	0.001	0.81 (0.20; 1.41)	0.13	0.01
IPAQ-A	0.00 (0.00; 0.001)	0.00	0.23				6.04E-02 (-0.001;0.001)	0.01	0.88				0 (-0.001;0.001)	-0.03	0.62			
DASS-C	0.28 (0.25; 0.31)	0.53	<0.001	0.10 (0.06; 0.15)	0.2	<0.001	0.24 (0.19; 0.29)	0.44	<0.001	0.11 (0.06; 0.17)	0.21	<0.001	0.14 (0.06; 0.22)	0.19	0.001			
BaSIQS	0.6 (0.51; 0.68)	0.04	<0.001	0.26 (0.17; 0.35)	0.19	<0.001	0.47 (0.36; 0.58)	0.40	<0.001	0.25 (0.15; 0.36)	0.21	<0.001	0.46 (0.32; 0.59)	0.35	<0.001	0.34 (0.21; 0.47)	0.27	<0.001
PCS	0.27 (0.22; 0.31)	0.44	<0.001	0.08 (0.03; 0.12)	0.12	<0.001	0.25 (0.20; 0.30)	0.44	<0.001	0.12 (0.06; 0.18)	0.21	<0.001	0.16 (0.11; 0.21)	0.34	<0.001	0.09 (0.04; 0.14)	0.19	0.001
TSK	0.34 (0.28; 0.40)	0.37	<0.001				0.28 (0.21; 0.36)	0.36	<0.001	0.08 (0.001; 0.16)	0.1	0.05	0.21 (0.14; 0.29)	0.31	<0.001	0.10 (0.03; 0.18)	0.15	0.01
CSES	0.39 (0.31; 0.46)	0.35	<0.001	0.10 (0.03;0.17)	0.09	0.007	0.24 (0.15; 0.33)	0.26	<0.001				0.13 (0.04; 0.22)	0.16	0.006			
CSI	0.25 (0.22; 0.28)	0.56	<0.001	0.07 (0.03; 0.11)	0.16	0.001	0.20 (0.16; 0.23)	0.46	<0.001				0.13 (0.08; 0.18)	0.29	<0.001			

B-coefficient, Unstandardized Regression Coefficient; β-coefficient, Standardized regression coefficient; BMI, Body Mass Index; NP, Neck Pain; IPAQ-A, International Questionnaire of Physical Activity for Adolescents; FDI, Functional Disability Inventory; DASS-C, Depression, Anxiety and Stress Scale for Children; 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

6. PREDICTORS OF PERSISTENT PAIN AND DISABILITY IN HIGH SCHOOL STUDENTS WITH CHRONIC NECK PAIN AT 6 MONTHS FOLLOW-UP

Based on the study from Andias, R. & Silva, AG. (2021). “Predictors of pain persistence and disability in high school students with chronic neck pain at 6 months follow-up”. Quality of Life Research *(submitted and revised).*

6.1. Introduction

In Chapter 5, we found that being a female, and reporting sleep impairments, and more self-reported symptoms of central sensitization increase the likelihood of reporting current chronic NP in adolescents. We also found that a higher number of painful body sites, higher levels of anxiety, depression, and stress, catastrophizing, and self-reported symptoms of central sensitization, and sleep impairments, and lower levels of self-efficacy were associated with current levels of disability in adolescents with chronic NP. However, the study described in the previous Chapter was a transversal study and did not allow for the assessment of the role of these variables in the long-term maintenance of NP. Thus, following the findings of Chapter 5 and considering that only two of the studies included in the systematic review of Chapter 4 were longitudinal studies in adolescents with NP, this chapter analysed the impact of psychosocial factors, disability, sleep impairments, physical activity, and self-reported symptoms of central sensitization at baseline in the maintenance of chronic NP at 6-month follow-up.

A recent systematic review of prognostic factors for musculoskeletal pain in adolescents included three studies on NP (Pourbordbari et al., 2019). The results of these three studies suggested that the baseline factors associated with the long-term persistence of NP were female sex, depressive symptoms, multisite pain, and daily

tiredness (Pourbordbari et al., 2019). However, none of these studies explored the predictive capacity of aspects such as catastrophizing, fear of movement, self-efficacy, or self-reported symptoms of central sensitization, which might have an important role in the development and maintenance of chronic pain (Edwards, Dworkin, Sullivan, Turk, & Wasan, 2016). In line with the pediatric fear-avoidance model of chronic pain (Asmundson et al., 2012), negative thoughts and beliefs in confront with pain lead to a vicious cycle of poor expectations of recovery, that might be intensified with increased catastrophizing levels, higher levels of pain-related fear, hypervigilance, avoidance behaviors, depression, and anxiety, which in turn lead to increased fear-avoidance behaviors, pain perpetuation, and loss of functioning (Asmundson et al., 2012).

Considering that disability is one of the main consequences of pain, the long-term impact of those variables on disability was also explored. Furthermore, a recent systematic review found no longitudinal studies exploring the predictors of long-term disability in community adolescents with musculoskeletal pain (Pate et al., 2020). Thus, this study aimed to explore whether i) sociodemographic characteristics, ii) physical activity, iii) psychosocial factors, iv) sleep, and v) self-reported symptoms of central sensitization at baseline, were associated with the persistence of chronic NP at 6-month follow-up and with disability at 6-month follow-up in adolescents with persistent NP. Also, considering the finding in the previous Chapter that being a female increased the odds of reporting chronic NP, a secondary aim was to explore these associations separately for boys and girls.

To our knowledge, this is the first longitudinal study exploring the role of such a comprehensive set of factors for both pain and disability persistence in adolescents with chronic NP. Knowledge of the predictive factors for persistence of pain and disability in adolescents with NP will help define assessment and intervention

strategies more adjusted to this population, which, conceivably, will lead to better outcomes.

6.2. Methods

6.2.1. Study design and participants

This is a longitudinal component of the study conducted in the 4 Portuguese secondary schools approved by the Council of Ethics and Deontology of the University of Aveiro. All students attending the 10th, 11th, and 12th grades that in Chapter 5 reported having chronic idiopathic NP, defined as pain non-related to any known pathology or injury, perceived anywhere between the superior nuchal line and the spinous process of T1, which occurs weekly and persist for more than 3 months (Misailidou et al., 2010), were included in this study.

Six months after the baseline assessment, adolescents with chronic NP repeated the online questionnaire. Data collection procedures were as described in Chapter 5, also at school, and in the presence of the same researcher (RA).

6.2.2. Measurement instruments

As reported in Chapter 5, the online questionnaire included sociodemographic data (age, sex, school year, and family situation, i.e., who they lived with), self-reported weight and height, and the following measuring instruments: i) the Nordic Musculoskeletal Questionnaire, ii) the Numeric Pain Rating Scale ranging from 0 (“no pain”) to 10 (“the worst imaginable pain”) to assess NP intensity (Castarlenas, Jensen, von Baeyer, & Miró, 2017); pain intensity was only collected from adolescents with NP and therefore, data on NP intensity was not used in the previous Chapter, iii) the International Physical Activity Questionnaire for Adolescents, iv) the Functional Disability Inventory, v) the Depression, Anxiety and Stress Scale for Children, vi) the Basic Scale on Insomnia complaints and Quality of Sleep, vii) the Pain Catastrophizing

Scale of 13 items, viii) the Tampa Scale of Kinesiophobia of 13 items, ix) the 7-items Child Self-Efficacy Scale, and x) the Central Sensitization Inventory. The full description of these instruments can be found in Chapter 5.

6.2.3. Categorization of participants

Adolescents that, at baseline, reported to have pain in the neck region (as defined in the Nordic Musculoskeletal Questionnaire) at least once a week every week for the last 3 months, were considered as reporting chronic NP. Based on the progression of NP from baseline to the 6-month follow-up, each adolescent with chronic NP at baseline was categorized as:

i) having persistent NP, if the adolescent reported NP at baseline and follow-up and did not achieve at least 50% improvement in NP intensity from baseline to follow-up (calculated subtracting pain intensity at baseline from pain intensity at 6-month follow-up);
ii) recovered, if the adolescent did not report pain in the neck at follow-up or reported pain in the neck but reported at least 50% improvement in NP intensity from baseline to follow-up.

This categorization was based on a classification previously used in a longitudinal study by Holley et al. (2017) in a sample of children and adolescents with musculoskeletal pain.

6.3. Statistical analysis

Descriptive statistics (mean and standard deviation for continuous data and frequencies and percentages for categorical data) were used to describe the characteristics of the sample. Differences between subgroups of adolescents with NP (persistent pain vs recovered) were explored using S*tudent's t-tests* for continuous data and *chi-square* tests for categorical data. All adolescents completed the questionnaire

and there was no missing data. To determine possible factors associated with the persistence of chronic NP, independent logistic-regression analyses were used to explore univariable and multivariable associations between the independent variables (baseline data for sociodemographic characteristics: sex, age, BMI, and family situation; mean number of painful body sites; disability; physical activity; psychosocial factors: anxiety, depression, and stress, catastrophizing, fear of movement, self-efficacy; sleep, and self-reported symptoms of central sensitization) and the dependent variable (persistent NP vs recovered NP at 6 months). Similarly, to explore the predictors of disability at 6-month follow-up, in the group with persistent NP, univariable and multivariable independent linear regression analyses between the pre-specified independent variables and the total score of the Functional Disability Inventory at 6-months, which was the dependent variable. The enter method was used for the univariable analyses and $p \leq 0.10$ was required for variables to enter the multivariable models. The multivariable analyses were performed using the stepwise method. The variables that entered into the models were checked for multicollinearity using Variance Inflation Factor (VIF) ≤5 and the respective tolerance value (Marôco, 2014). The reported analyses were also repeated on girls and boys separately. Significance was set at $p<0.05$. All statistical analyses were performed using SPSS Software, version 22.0.

6.4. Results

Of the 753 adolescents that reported chronic NP at baseline, 710 (94.3%) participated in the follow-up assessment and entered this study. Of these, 334 (47.0%) (mean age ± SD= 16.18±1.11; 79.3% female) were classified as reporting “persistent” NP and 361 (50.8%) (mean age ± SD= 16.30±1.12; 68.7% female) adolescents reported either no NP or at least a 50% reduction in their NP intensity and were classified as “recovered” at 6-month follow-up. Adolescents with persistent NP reported a mean (±SD) NP

intensity of 2.16±2.30 at baseline and 3.12±2.28 at 6-month follow-up and mean disability of 7.00±6.41 and 7.49±7.60, respectively. The group of recovered adolescents reported a mean (±SD) pain intensity of 2.43±2.31 at baseline and 0.41±0.91 at 6-months follow-up and mean disability was 5.79±6.52 and 5.11±7.02, respectively.

6.4.1. Comparison between persistent and recovered NP

Comparisons at baseline between adolescents that reported persistent NP and those categorized as recovered at 6-month follow-up, showed that adolescents with persistent NP reported a higher number of painful body sites (p=0.002), higher levels of disability (p=0.01), depression, anxiety, and stress (p=0.005), sleep impairments (p=0.02) and more self-reported symptoms of central sensitization (p<0.001) than recovered adolescents (Table 30).

Subgroup analysis for boys and girls revealed that girls who reported persistent NP showed more self-reported symptoms of central sensitization at baseline than girls recovered at 6-month follow-up (p=0.01) and boys that reported persistent NP showed a higher number of painful body sites (p=0.01), sleep impairments (p=0.01), higher levels of catastrophizing (p=0.04) and more self-reported symptoms of central sensitization (p=0.02) at baseline than boys who recovered at 6-month follow-up (Table 31).

6.4.2. Predictors of persistent NP at 6-month follow-up

In the univariable analysis, being female (OR=1.75, p<0.05), having a higher number of painful body sites (OR=1.15, p<0.05), reporting higher levels of anxiety, depression, and stress (OR=1.02, p<0.05), reporting sleep impairments (OR=1.04, p<0.05) and more self-reported symptoms of central sensitization were significantly associated with persistent NP at 6-month follow-up (Table 32).

In the multivariable model, the female sex (OR=1.47, p=0.04) and the self-reported symptoms of central sensitization (OR=1.02, p=0.001) were the only predictive factors for persistent NP at 6-month follow-up. The Nagelkerke R^2 was 0.04 (Table 32).

When exploring the predictive factors by sex, the self-reported symptoms of central sensitization (OR=1.02, p=0.03) were the only predictive factor for persistent NP at 6-month follow-up in girls (Nagelkerke R^2=0.02). In boys, the number of painful body sites (OR=1.22, p=0.046) and sleep impairments (OR=1.08, p=0.047) were both predictive factors for persistent NP at 6-month follow-up in boys (Nagelkerke R^2=0.08) (Table 33).

6.4.3. Predictors of disability at 6-month follow-up in the persistent NP group

The univariable model showed that disability at 6-month follow-up was significantly associated with being female (<0.05), reporting a higher number of painful body sites (p<0.001), higher levels of pain intensity (p<0.001), higher levels of disability (p<0.001), more time of physical activity (p<0.05), poor quality of sleep (p<0.05), higher levels of anxiety, depression, and stress (p<0.001), catastrophizing (p<0.001), fear of movement (p<0.001) and self-reported symptoms of central sensitization (p<0.001) and lower levels of self-efficacy (p<0.001) at baseline (Table 34).

In the multivariable analysis, disability at 6-month follow-up was significantly associated only with higher levels of disability and more self-reported symptoms of central sensitization at baseline. The model was statistically significant (F=105.72; p<0.001) with an adjusted R^2 of 0.40 (Table 34).

When exploring the predictive factors by sex, disability at 6-month follow-up in girls was also significantly associated with higher levels of disability and more self-reported symptoms of central sensitization at baseline. The model was statistically significant (F=89.49; p<0.001) with an adjusted R^2 of 0.64. In boys, disability at 6-month follow-up was significantly associated with higher levels of physical activity and more self-

reported symptoms of central sensitization at baseline (F=10.00; p<0.001; adjusted R^2=0.48) (Table 35).

Table 36 include a distribution of adolescents by the 25th, 50th, and 75th quartiles of the Central sensitization Inventory baseline scores.

6.5. Discussion

6.5.1. Recovery versus persistence rates

This longitudinal study explored the factors associated with the persistence of chronic NP and disability at 6-months follow-up. To our knowledge, this is the first prospective study that specifically assessed the factors associated with maintenance of chronic NP and disability at 6-months follow-up in adolescents (age from 15 to 18 years old), including a large range of variables, such as catastrophizing and fear of movement, self-efficacy, sleep impairments, self-reported symptoms of central sensitization and physical activity. In this study, 47.2% of adolescents maintained their NP complaints at a 6-month follow-up and were categorized as reporting persistent NP. A similar percentage was found in the study by Stahl et al. (2008), who reported that 48.6% of preadolescents aged 9 to 12 years old maintained their chronic NP at 1 year of follow-up. These findings highlight the persistence of chronic NP at younger ages and the need to study the factors that may contribute to it.

6.5.2. Predictors of persistent NP at 6-month follow-up

In the multivariable model for the whole sample, only female sex and self-reported symptoms of central sensitization remained significantly associated with the persistence of NP. In the recent systematic review of Pourbordbari et al. (2019), the female sex was the prognostic factor most frequently identified in primary studies as being associated with persistent musculoskeletal pain, and specifically with NP, at 1-year follow-up in adolescents. Also Mikkelsson et al. (1998) in a study with 452

preadolescents with persistent musculoskeletal pain at baseline and mean age of 11.8±0.37, reported that being female increased the odds of pain persisting at 1-year follow-up (OR=1.78; 1.18-2.69) compared to boys. A novel finding of our study was that self-reported symptoms of central sensitization at baseline were associated with persistent NP at 6-month follow-up. To our knowledge, no other studies investigated the association between self-reported symptoms of central sensitization and persistence of neck or other musculoskeletal pain in adolescents. However, current knowledge of the impact of central sensitization on pain may help explain this association. Central sensitization has been described as a neurophysiological state related to amplified pain facilitator mechanisms and/or reduced pain inhibitory mechanisms (Woolf, 2011).

The Central Sensitization Inventory does not directly assess central sensitization, but it is used as an indirect measurement tool to assess symptoms associated with central sensitization, such as fatigue, sleep and emotional disorders, and altered sensitivity to environmental stimuli, e.g. bright light and odors (Mayer et al., 2012; Smart, Blake, Staines, Thacker, & Doody, 2012). Thus, it points towards the potential existence of central sensitization, and the need to direct the intervention towards the central nervous system (Neblett, 2018; Nijs, Paul van Wilgen, Van Oosterwijck, van Ittersum, & Meeus, 2011). The presence of central sensitization is often associated with maladaptive beliefs related to the pain experience and may contribute to the enhancement of the pain experience and its persistence (Chimenti, Frey-Law, & Sluka, 2018; Graven-Nielsen & Arendt-Nielsen, 2002; Nijs, Goubert, & Ickmans, 2016). However, future studies should further explore this association, particularly using more objective and direct measures of central sensitization.

The number of painful body sites, higher levels of anxiety, depression, and stress, and sleep impairments were significantly associated with NP persistence only in the

univariable model. However, previous systematic reviews suggested its association with the persistence of general musculoskeletal pain in adolescents (Huguet et al., 2016; Pourbordbari et al., 2019). Only one of the included studies, Stahl et al. (2008) used pre-adolescents with NP and explored the baseline factors associated with NP persistence at 4-year follow-up. They reported a significant tendency for persistent NP when adolescents simultaneously experienced pain at other body sites in addition to the neck, reported depressive symptoms, or sleep impairments at baseline. No longitudinal study was found that explored the potential role of fear of movement or catastrophizing in NP persistence in adolescents. However, fear of movement and catastrophizing are predictors of the persistence of chronic pain in adults with chronic neck and/or upper limb pain (Karels et al., 2007). None of the studies found report the value of Nagelkerke R^2, but the Nagelkerke R^2 for the 6-month pain persistence predictor model in our study was low, suggesting that there are other important predictors of NP persistence that were not considered in this study, such as the history of parents with chronic pain (Palermo & Chambers, 2005), or the quantity of sleep and weekly day tiredness (Pate et al., 2020).

Considering that gender remained an important factor associated with NP persistence in our study, an analysis by gender was also performed. While in girls the findings associated with the symptoms of central sensitization were highlighted, in boys, only the number of painful body sites and sleep impairments remained associated with the persistence of pain. These results agree with the differences found among the boys at the baseline, where boys with persistent NP reported more painful body sites and more sleep impairments than boys in the recovered group, although there are no differences between boys and girls at baseline. Previous studies in adolescents also support these findings. Harrison et al. (2014) reported that sleep impairments in adolescents aged 15 years are associated with the presence of chronic musculoskeletal pain at 17 years of

age. Silva et al. (2017) reported that sleeping 7h or less was associated with chronic NP in adolescents aged 15.6 ± 1.8 years. The only study found exploring the association between sleep and the presence of chronic musculoskeletal pain in adolescents, by sex, highlighted that sleep impairments increased the odds of chronic musculoskeletal pain in boys, but not in girls (Andreucci et al., 2020). Several theoretical studies have described the relationship between sleep and pain, namely its importance for the regulation of the endogenous pain system (Andreucci, Groenewald, Rathleff, & Palermo, 2021; Badawy et al., 2019; Finan et al., 2013). Silva et al. (2018) also highlighted the relevance of multiple body sites in adolescents, reporting that the likelihood of chronic NP increases in the presence of other painful body sites, specifically thoracic, lumbar, shoulder and wrist/hand pain.

6.5.3. Predictors of disability in adolescents with persistent NP

Functional Disability Inventory scores found in this study were lower than those previously reported in clinical studies with adolescents with musculoskeletal chronic pain (Guite, McCue, Sherker, Sherry, & Rose, 2011; Kashikar-Zuck et al., 2011). According to Kashikar-Zuck et al. (2011) the Funtional Disability Inventory scores corresponded to the level of disability of no to minimal disability ranging from 0 to 12 points). However, the fact that the sample of the present study included adolescents from the community might explain these differences. Concerning disability, our study results suggest that, in the univariable analysis, disability at follow-up was significantly associated with all variables assessed in this study, except age and BMI. However, when these variables were entered in the multivariable model, only higher levels of disability at baseline and more self-reported symptoms of central sensitization remained significantly associated with disability, with an adjusted R^2 of 0.40. Basch et al. (2018), in a clinical sample of 195 adolescents with chronic musculoskeletal pain (mean age=13.8±2.42), but also with headache, neuropathic and abdominal pain,

explored the association between a set of variables including the number of pain sites, anxiety, depression, and functional disability at baseline and disability at 4-month follow-up. They reported that disability and number of pain sites at baseline emerged as predictors of disability at 4-month follow-up, with an adjusted R^2 of 0.26. Despite the differences regarding pain complaints, both studies suggest that baseline disability is a predictor of disability at follow-up.

Similar to what was previously reported for pain persistence, no previous studies were found that explored the association between disability and self-reported symptoms of central sensitization in adolescents. However, self-reported symptoms of central sensitization at baseline were found to be associated with disability in adults at a 3-month follow-up (Tanaka et al., 2019). According to the authors, as Central Sensitization Inventory severity levels increase, clinical symptoms tend to worsen, and this may be a possible explanation for this association with disability (Tanaka et al., 2019). On the other hand, as reported above, the presence of symptoms associated with central sensitization may influence an exaggerated and maladaptive response to pain that, therefore, may negatively influence long-term pain persistence and self-reported disability.

The remaining variables (anxiety, depression, and stress, catastrophizing, quality of sleep, self-efficacy, and multiple painful body sites) did not remain in the multivariable model, but were found to be significantly associated with disability in previous cross-sectional studies of adolescents with several chronic musculoskeletal pain conditions (Evans et al., 2017; Gauntlett-Gilbert & Eccleston, 2007; Kalapurakkel et al., 2015; Tran et al., 2015).

The subgroup analysis by sex, revealed that for boys, higher levels of symptoms of central sensitization and physical activity at baseline were the factors associated with disability at 6 months. According to the characteristics of the sample at the baseline, the score of the International Physical Activity Questionnaire for adolescents was higher in boys with persistent pain than in girls with persistent NP, which might explain its greatest impact in this group. Also, Malmborg et al. (2019) found statistically higher levels of physical activity on the International Physical Activity Questionnaire in boys compared to girls.

6.5.4. Clinical implications

Self-reported symptoms of central sensitization emerged as a relevant determinant of both NP persistence and disability, suggesting that it should be included in the assessment of adolescents with NP and be a target for early interventions as an attempt to minimize its future impact on pain persistence and disability. The results of this study also suggest that there are similar but also different predictors of pain and disability among boys and girls. Therefore, these variables should also be considered when assessing and designing interventions for adolescents with NP. Finally, this study results suggest the need to implement school-based screening actions to identify those at risk of persistent NP, followed by appropriate interventions as an attempt to minimize the long-term persistence and impact of NP.

6.5.5. Limitations and future research

Our findings should be interpreted considering the study limitations. The sample of adolescents with chronic NP at baseline was divided into two groups at follow-up, i.e., “persistent” NP and “recovered”. However, as the adolescents had multiple painful body sites, those who reported being recovered from NP might still experience pain in other body regions. Nevertheless, adolescents with NP, commonly report pain at other

body sites (Auvinen et al., 2009; Paananen et al., 2010). We also did not classify adolescents with regional vs widespread pain and the predictive factors in these two groups might be different (Mikkelsson et al., 1999; Paananen et al., 2010).

To meet the recent definition of chronic pain, the pain reference time point in the Nordic Musculoskeletal Questionnaire was adapted from 12 months to 3 months although no additional validation was performed. As previously reported the Central Sensitization Inventory is not a direct indicator of central sensitization, but rather assesses a set of symptoms potentially associated with central sensitization. Although there is currently no gold standard for central sensitization diagnosis, assessing pain thresholds or conditioned pain modulation would have helped confirm the presence of central sensitization. However, the time needed to perform these assessments prevented us from using them in the current study. The strength of our study is the longitudinal approach, and the assessment of a wide set of variables seldom explored in previous studies with adolescents with NP. In this sense, future studies with longer longitudinal approaches are needed to further explore the findings reported in this study and the impact of early screening of these relevant variables on the prevention of NP onset.

6.6. Conclusion

Self-reported symptoms of central sensitization at baseline and female sex seem to be associated with NP persistence at a 6-month follow-up. Self-reported symptoms of central sensitization and disability at baseline seem to be associated with disability at a 6-month follow-up in those adolescents with persistent NP. Furthermore, there are common but also different predictive factors associated with the persistence of NP and disability in girls and boys, which include the number of painful body sites, sleep impairments, and physical activity at baseline, in addition to self-reported symptoms of central sensitization.

Table 30. Characterization of the groups with NP (persistent and recovered) considering the baseline characteristics.

Variables		**Neck Pain**		**p-value**
		Persistent (n=334)	**Recovered** (n=361)	
Gender	Girls	265 (79.3%)	248 (68.7%)	0.002
	Boys	69 (20.7%)	113 (31.3%)	
Age (years)		16.18±1.11	16.30±1.12	0.14
BMI (Kg/m^2)		21.53±3.34	21.95±10.30	0.47
Scholar level	10th	119 (35.6%)	124 (34.3%)	0.89
	11th	106 (31.7%)	113 (31.3%)	
	12th	109 (32.6%)	124 (34.3%)	
Family situation (Lives with…)	Father and mother	219 (65.6%)	254 (70.4%)	0.60
	Mother	69 (20.7%)	65 (18.0%)	
	Father	8 (2.4%)	8 (2.2%)	
	Other	38 (11.4%)	34 (9.4%)	
Number of painful body sites	mean±SD	3.98±1.64	3.59±1.68	0.002
	1	15 (4.5%)	38 (10.5%)	0.02
	2	54 (16.2%)	70 (19.4%)	
	3	72 (21.6%)	71 (19.7%)	
	4	62 (18.5%)	79 (21.9%)	
	5 or more	131 (39.2%)	103 (28.5%)	
NPRS (0-10)		2.16±2.30	2.43±2.31	0.12
IPAQ-A (0-2540 minutes/week)		1071.21±733.62	1100.07±748.12	0.61
FDI (0-60)		7.00±6.41	5.79±6.52	0.01
DASS-C (0-63)		15.16±13.44	12.45±11.70	0.005
BaSIQS (0-28)		9.65±4.88	8.80±4.83	0.02
PCS (0-52)		12.17±10.79	11.09±10.54	0.18
TSK (13-52)		24.25±6.80	23.80±7.18	0.39
CSES (7-35)		16.96±5.73	16.47±5.86	0.27
CSI (0-100)		29.41±15.04	24.62±14.48	<0.001

BMI, Body Mass Index; NP, Neck Pain; NPRS, Numeric Pain Rating Scale; IPAQ-A, International Questionnaire of Physical Activity for Adolescents; FDI, Functional Disability Inventory; DASS-C, Depression, Anxiety and Stress Scale for Children; 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

Table 31. Subgroup characterization of persistent and recovered adolescents by sex and for baseline data.

Variables		**Girls**			**Boys**		
		Persistent NP (n=265)	**Recovered** (n=248)	p-value	**Persistent NP** (n=69)	**Recovered** (n=113)	**p-value**
Age (years)		16.16±1.09	16.27±1.13	0.26	16.25±1.18	16.37±1.10	0.47
BMI (Kg/m^2)		21.69±3.35	22.25±12.26	0.47	20.92±3.24	21.30±2.95	0.42
Scholar level	10th	93 (35.1%)	91 (36.7%)	0.82	26 (37.7%)	33 (29.2%)	0.45
	11th	88 (33.2%)	76 (30.6%)		18 (26.1%)	37 (32.7%)	
	12th	84 (31.7%)	81 (32.7%)		25 (36.2%)	43 (38.1%)	
Family situation (Lives with…)	Father and mother	175 (66.0%)	173 (69.8%)	0.51	44 (63.8%)	81 (71.7%)	0.29
	Mother	52 (19.6%)	49 (19.8%)		17 (24.6%)	16 (14.2%)	
	Father	6 (2.3%)	6 (2.4%)		2 (2.9%)	2 (1.8%)	
	Other	32 (12.1%)	20 (8.0%)		6 (8.7%)	14 (12.3%)	
Number of painful body sites	mean±SD	4.03±1.62	3.81±1.69	0.14	3.78±1.71	3.11±1.57	0.01
	1	12 (4.5%)	21 (8.5%)	0.33	3 (4.4%)	17 (15.0%)	0.19
	2	39 (14.7%)	42 (16.9%)		15 (21.8%)	28 (24.8%)	
	3	55 (20.8%)	44 (17.7%)		17 (24.6%)	27 (23.9%)	
	4	51 (19.2%)	57 (23.0%)		11 (15.9%)	22 (19.5%)	
	5 or more	108 (40.8%)	84 (33.9%)		23 (33.3%)	19 (16.8%)	
NPRS (0-10)		2.27±2.35	2.56±2.36	0.17	1.75±2.05	2.16±2.18	0.22
IPAQ-A (0-2540 minutes/week)		1022.90±705.22	1088.78±732.63	0.30	1256.72±812.86	1124.87±783.82	0.28
FDI (0-60)		7.60±6.66	6.79±6.75	0.17	4.70±4.73	3.59±5.40	0.16
DASS-C (0-63)		16.86±13.88	15.10±12.30	0.13	8.64±9.07	6.62±7.53	0.11
BaSIQS (0-28)		9.87±4.83	9.60±5.05	0.55	8.81±5.02	7.03±3.76	0.01
PCS (0-52)		12.76±11.23	12.86±10.85	0.92	9.88±8.60	7.19±8.65	0.04
TSK (13-52)		24.67±6.91	24.73±7.27	0.93	22.65±6.16	21.74±6.55	0.35
CSES (7-35)		17.49±5.51	17.32±5.60	0.73	14.94±6.14	14.62±6.01	0.73
CSI (0-100)		31.22±14.92	27.63±14.47	0.01	22.46±13.50	18.02±12.18	0.02

BMI, Body Mass Index; NP, Neck Pain; NPRS, Numeric Pain Rating Scale; IPAQ-A, International Questionnaire of Physical Activity for Adolescents; FDI, Functional Disability Inventory; DASS-C, Depression, Anxiety and Stress Scale for Children; 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

Table 32. Factors associated with persistent chronic NP (n=334) compared to the recovered group (n=361).

		Neck pain (R Nagelkerke=0.04)	
Variables		Univariable OR; CI95%	Multivariable OR; CI95%
Gender	Male	1	1
	Female	1.75; [1.24;2.47] *	1.47; [1.02;2.11] *
Age		0.90; [0.79;1.03]	
BMI		0.99; [0.97;1.02]	
Family Situation	Both Parents	1	
	Alternative (mother, father or other)	1.25; [0.91;1.72]	
Number of pain sites		1.15; [1.05;1.26] *	
NPRS		0.95; [0.89;1.01]	
FDI		1.03; [1.01;1.05] *	
IPAQ-A		1.00; [0.99;1.00]	
DASS-C		1.02; [1.01;1.03] *	
BaSIQS		1.04; [1.01;1.07] *	
PCS		1.01; [0.99;1.02]	
TSK		1.01; [0.99;1.03]	
CSES		1.02; [0.99;1.04]	
CSI		1.02; [1.01;1.03] *	1.02; [1.01;1.03] *

*p <0.05

BMI, Body Mass Index; NPRS, Numeric Pain Rating Scale; FDI, Functional Disability Inventory; IPAQ-A, International Questionnaire of Physical Activity for Adolescents; DASS-C, Depression, Anxiety and Stress Scale for Children; 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

Table 33. Factors associated with persistent chronic NP compared to the recovered group by girls and boys.

		Girls (n=513)		**Boys** (n=182)	
		Neck pain (R Nagelkerke=0.02)		**Neck pain** (R Nagelkerke=0.08)	
Variables		Univariable OR; CI95%	Multivariable OR; CI95%	Univariable OR; CI95%	Multivariable OR; CI95%
Age		0.91; [0.78;1.07]		0.91; [0.69;1.18]	
BMI		0.99; [0.97;1.02]		0.96; [0.87;1.06]	
Family Situation	Both Parents	1		1	
	Alternative (mother, father or other)	1.19; [0.82;1.72]		1.44; [0.76;2.73]	
Number of pain sites		1.08; [0.97;1.20]		1.29; [1.07;1.55]**	1.22; [1.01;1.49]**
NPRS		0.95; [0.88;1.02]		0.91; [0.79;1.06]	
FDI		1.02; [0.99;1.05]		1.04; [0.98;1.10]	
IPAQ-A		1.00; [0.99;1.00]		1.00; [0.99;1.00]	
DASS-C		1.01; [0.99;1.02]		1.03; [0.99;1.07]	
BaSIQS		1.01; [0.98;1.05]		1.10; [1.02;1.18]**	1.08; [1.01;1.16]**
PCS		0.99; [0.98;1.02]		1.04; [1.01;1.07]**	
TSK		0.99; [0.98;1.02]		1.02; [0.98;1.07]	
CSES		1.01; [0.98;1.04]		1.01; [0.96;1.06]	
CSI		1.02; [1.01;1.03] **	1.02; [1.01;1.03] **	1.03; [1.01;1.05] **	

*p ≤ 0.1; ** p < 0.05

BMI, Body Mass Index; NPRS, Numeric Pain Rating Scale; FDI, Functional Disability Inventory; IPAQ-A, International Questionnaire of Physical Activity for Adolescents; DASS-C, Depression, Anxiety and Stress Scale for Children; 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

Table 34. Multivariable regression analyses of baseline variables predicting disability at 6-month follow-up for persistent NP (n=334).

	Univariable linear regression			Multivariable linear regression (R^2=0.40)		
Variables	B-coefficient (95% CI)	β	*p*	B-coefficient (95% CI)	β	*p*
Gender (f)	3.34 (1.35; 5.33)	0.18	0.001			
Age	0.02 (-0.72; 0.76)	0.003	0.96			
BMI	0.15 (-0.10; 0.39)	0.07	0.23			
Number of pain sites	1.49 (1.01; 1.96)	0.32	<0.001			
NPRS	0.78 (0.43;1.12)	0.24	<0.001			
FDI	0.68 (0.58; 0.79)	0.68	<0.001	0.50 (0.38; 0.62)	0.41	<0.001
IPAQ-A	0.002 (0.001; 0.003)	0.17	0.002			
DASS-C	0.24 (0.19; 0.30)	0.43	<0.001			
BaSIQS	0.50 (0.35; 0.66)	0.32	<0.001			
PCS	0.25 (0.18; 0.32)	0.36	<0.001			
TSK	0.35 (0.24; 0.47)	0.32	<0.001			
CSES	0.41 (0.27; 0.54)	0.31	<0.001			
CSI	0.26 (0.21; 0.31)	0.52	<0.001	0.14 (0.09; 0.20)	0.28	<0.001

B-coefficient, Unstandardized Regression Coefficient; β-coefficient, Standardized regression coefficient; BMI, Body Mass Index; NPRS, Numeric Pain Rating Scale; IPAQ-A, International Questionnaire of Physical Activity for Adolescents; FDI, Functional Disability Inventory; DASS-C, Depression, Anxiety and Stress Scale for Children; 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

Table 35. Multivariable regression analyses of baseline variables predicting disability at 6-month follow-up for persistent NP for girls (n=256) and boys (n=69).

	Girls						**Boys**					
	Univariable linear regression			Multivariable linear regression (R^2=0.64)			Univariable linear regression			Multivariable linear regression (R^2=0.48)		
Variables	B-coefficient (95% CI)	β	*p*	B-coefficient (95% CI)	β	*p*	B-coefficient (95% CI)	β	*p*	B-coefficient (95% CI)	β	*p*
Age	-0.05 (-0.93; 0.83)	-0.01	0.91				0.42 (-0.69; 1.53)	0.09	0.45			
BMI	0.11 (-0.18; 0.40)	0.05	0.46				0.13 (-0.28; 0.53)	0.08	0.54			
Number of pain sites	1.63 (1.07; 2.19)	0.33	<0.001				0.77 (0.02; 1.52)	0.24	0.04			
NPRS	0.81 (0.41;1.21)	0.24	<0.001				0.32 (-0.32;0.96)	0.12	0.32			
FDI	0.70 (0.59; 0.82)	0.59	<0.001	0.51 (0.38; 0.64)	0.43	<0.001	0.41 (0.15; 0.67)	0.36	0.003			
IPAQ-A	0.002 (0.001; 0.003)	0.16	0.01				0.003 (0.001; 0.004)	0.38	0.001	0.002 (0.001; 0.004)	0.37	0.001
DASS-C	0.24 (0.18; 0.31)	0.42	<0.001				0.16 (0.02; 0.30)	0.26	0.03			
BaSIQS	0.52 (0.33; 0.71)	0.32	<0.001				0.36 (0.11; 0.60)	0.33	0.01			
PCS	0.26 (0.18; 0.34)	0.36	<0.001				0.14 (-0.01; 0.29)	0.22	0.06			
TSK	0.36 (0.22; 0.49)	0.31	<0.001				0.23 (0.03; 0.44)	0.26	0.03			
CSES	0.43 (0.26; 0.60)	0.30	<0.001				0.21 (-0.03; 0.41)	0.23	0.05			
CSI	0.28 (0.23; 0.34)	0.53	<0.001	0.16 (0.10; 0.22)	0.29	<0.001	0.12 (0.03; 0.22)	0.32	0.01	0.12 (0.03; 0.21)	0.30	0.03

B-coefficient, Unstandardized Regression Coefficient; β-coefficient, Standardized regression coefficient; BMI, Body Mass Index; NPRS, Numeric Pain Rating Scale; IPAQ, International Questionnaire of Physical Activity; FDI, Functional Disability Inventory; DASS-C, Depression, Anxiety and Stress Scale for Children; 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

Table 36. Distribution of adolescents by the 25th, 50th, and 75th quartiles of the Central Sensitization Inventory baseline scores.

CSI quartiles	**Persistent neck pain**			**Recovered**		
	Total sample (n=334)	Girls (n=265)	Boys (n=69)	Total sample (n=361)	Girls (n=248)	Boys (n=113)
25%	18 points (n=87; 26.0%)	21 points (n=71; 26.8%)	13 points (n=17; 24.6%)	13 points (n=90; 24.9%)	17 points (n=65; 26.2%)	9 points (n=29; 25.7%)
25%-**50%**	19-28 points (n=88; 26.3%)	22-29 points (n=63; 23.8%)	14-20 points (n=18; 26.2%)	14-23 points (n=98; 27.1%)	18-27 points (n=62; 25.0%)	10-16 points (n=31; 27.4%)
50% -**75%**	29-38 points (n=82; 24.6%)	30-39 points (n=65; 24.5%)	21-30 points (n=17; 24.6%)	24-33 points (n=83; 23.1%)	28-36 points (n=59; 23.8%)	17-24 points (n=26; 23.0%)
75%	>38 points (n=77; 23.1%)	>39 points (n=66; 24.9%)	>30 points (n=17; 24.6%)	>33 points (n=90; 24.9%)	>36 points (n=62; 25.0%)	>24 points (n=27; 23.9%11)
p-value (*)	0.01	0.18	0.11	p<0.001	0.09	0.14

(*) Note: Pearson's chi-squared between persistent vs recovered group using the different cut-offs points of the central sensitization inventory established at the baseline

.

7. THE ONSET OF CHRONIC MUSCULOSKELETAL PAIN, INCLUDING NECK PAIN, IN HIGH SCHOOL ADOLESCENTS: ASSOCIATED FACTORS AND THE ROLE OF SYMPTOMS OF CENTRAL SENSITIZATION

Based on the study from Andias, R. & Silva, AG. (2021). “The onset of chronic pain in high-school adolescents: associated factors and the role of symptoms of central sensitization”. Physical Therapy *(submitted and revised).*

7.1. Introduction

In previous Chapters 5 and 6, female sex, sleep, and self-reported symptoms of central sensitization were the factors that remained associated with the presence of chronic NP and its persistence at 6-month follow-up, in the multivariable analyses. Depression, anxiety and stress at baseline were also simultaneously associated with the presence of pain and its persistence at the 6-month follow-up in the univariable analyses. None of the other psychosocial variables were simultaneously associated with chronic NP and its persistence at the 6-month follow-up. Furthermore, female sex was simultaneously associated with the presence of back and limb pain in the multivariable analyses, and sleep, self-reported symptoms of central sensitization, depression, anxiety, and stress in the univariable analyses also for the presence of pain in these painful body sites. These similarities between baseline and follow-up, as well as between different painful body sites, reinforce the importance of considering these variables when exploring potential predictors of new onset of pain, which is the focus of this Chapter. Although the focus of this research project was on chronic NP, the percentage of adolescents without pain at baseline (Chapter 5) was very low (n=252; 14.6%). Thus, we decided to include in this study all adolescents with a new onset of pain, independently of the painful body site, as we anticipated that the number of

adolescents with a new onset of chronic NP at 6-month follow-up would be small. Nevertheless, and considering that the main focus of this thesis is NP, we performed a sub-analysis for adolescents who reported a new onset of chronic NP at 6 months.

The high percentage of adolescents with a new onset of chronic musculoskeletal pain, including NP reported in previous studies (El-Metwally, Salminen, Auvinen, Kautiainen, & Mikkelsson, 2004; Ståhl et al., 2008) highlight the need to explore its predisposing factors. In the study of El-Metwally (2004), of the 403 adolescents without musculoskeletal pain at baseline, 53.8% (n=217) reported a new onset of chronic musculoskeletal pain at a 1-year follow-up. For chronic NP, in particular, Stahl et al. (2008) found that of 769 adolescents without NP at baseline, 50% reported a new onset of chronic NP at a 4-year follow-up. A previous systematic review of the factors that are associated with the onset of musculoskeletal pain in childhood and adolescence found 10 studies (Huguet et al., 2016) and reported very low-quality evidence suggesting that being a female is a significant risk factor for the new onset of pain, moderate-quality evidence for negative emotional symptoms, including depression, mental distress, and emotional functioning and high-quality evidence for low sociodemographic status (Huguet et al., 2016). Another systematic review assessing the evidence of sleep impairments as a risk factor for the onset of musculoskeletal pain in children and adolescents reported moderate evidence that sleep quality is not a risk factor for general musculoskeletal pain onset, but strong evidence that girls with poor sleep quality and daytime tiredness have a higher risk of NP onset (Andreucci et al., 2017). Similarly, Stahl et al. (2008) reported the link between sleep impairments and the onset of NP and highlighted that depressive mood also predicted the onset of weekly NP at a 4-year follow-up. Three more studies were found that related depression and anxiety to the onset of NP in adolescents (Feldman et al., 2002; Marja Mikkelsson et al., 1998; Siivola et al., 2004).

The role of central sensitization as a predictor of new onset of pain in adolescents has not been explored, but our results from Chapters 5 and 7 and previous evidence highlighting its contribution to both the transition from acute to chronic pain and the maintenance over time (Chimenti et al., 2018; Nijs et al., 2016) suggest that it might be relevant. Mayer et al. (2012) in the first validation of the Central Sensitization Inventory pointed out that considering the variability of the self-reported symptoms of central sensitization, it is likely that these symptoms may be present before pain, i.e., in asymptomatic individuals. Thus, this study aimed to explore whether sociodemographic characteristics, depression, anxiety and stress, sleep, and self-reported symptoms of central sensitization at baseline in asymptomatic adolescents were associated with new onset of chronic musculoskeletal pain at 6-month follow-up. A secondary objective was to explore the same associations for the group of adolescents with chronic NP. Understanding the factors that may predispose to the development of chronic musculoskeletal pain is of uttermost relevance to its prevention.

7.2. Methods

7.2.1. Study design and participants

This is a longitudinal component of the study conducted in the 4 Portuguese secondary schools approved by the Council of Ethics and Deontology of the University of Aveiro. All participants who reported no musculoskeletal pain at baseline (Chapter 5), were assessed at 6-month follow-up and were included in this study. The absence of musculoskeletal pain at baseline was assessed using the adapted version of the Nordic Musculoskeletal Questionnaire (Mesquita et al., 2010), in which the time point of reference was changed from reporting pain in the last year to reporting pain in the last 3 months, at least once a week. Adolescents were asked whether they reported pain in any of nine body segments both in the last 7 days and 3 months and had to report no pain at all to enter this study.

Measurement instruments

At 6-month follow-up asymptomatic adolescents completed a similar online questionnaire and data collection was performed similarly as reported in chapter 5, also at school, and in the presence of the same researcher (RA). This questionnaire covered: sociodemographic data (age, sex, school year, and family situation, i.e., who they lived with), and self-reported weight and height, the Depression, Anxiety and Stress Scale for Children (Leal et al., 2009), the Basic Scale on Insomnia complaints and Quality of Sleep (Allen Gomes et al., 2015), and the Central Sensitization Inventory (Andias & Silva, 2020a; Mayer et al., 2012). The full description of these instruments can be found in Chapter 5.

7.2.2. Categorization of participants

At 6-month follow-up adolescents were categorized as: i) having acute pain if reporting pain in the last 7 days in at least one body site but reporting no pain in the last 3 months; ii) having chronic pain if reporting pain in the last 3 months in at least one body site and as iii) asymptomatic if reporting no pain at all. Those with chronic NP were considered for the sub-analysis.

7.3. Statistical analysis

All statistical analyses were performed using SPSS Software, version 22.0. Descriptive characteristics of the sample were reported using means and standard deviation for continuous data, and frequencies and percentages for categorical data. S*tudent's t-tests* for continuous data and *chi-square* tests for categorical data were used to explore differences between subgroups of adolescents with and without pain. To determine possible factors associated with the onset of pain, independent logistic-regression analyses were used to explore univariable and multivariable associations between the dependent variable (new onset of pain vs no pain at 6 months) and the independent

variables at baseline (sex, age, BMI, family situation, physical activity, anxiety, depression, and stress, sleep, and self-reported symptoms of central sensitization). The enter method was used for the univariable analyses and p≤ 0.10 was required for variables to enter the multivariable model. A similar analysis was performed using the variable "new onset of NP vs no pain at 6 months" as the dependent variable. The variables that entered the models were also checked for multicollinearity using the VIF ≤5 and the respective tolerance value (Marôco, 2014). For multivariable analysis, all 7 logistic regression methods were tested, of which 6 showed consistent results. Considering the superior quality of adjustment (Nagelkerke R^2) we chose to report the results based on the Forward LR. C*hi-square* tests were used to compare individual score items of the Central Sensitization Inventory at baseline between the groups with and without chronic pain at 6-month follow-up. The significance level was set at $p<0.05$ for all statistical analyses.

7.4. Results

Of the 252 adolescents who reported no pain at baseline, 231 completed the assessment at 6-months follow-up (91.7% response rate). Of these, 127 (55.0%) reported no pain at 6-month follow-up, 16 (6.9%) reported pain in the last 7 days only (i.e. acute pain), and 88 (38.1%) reported a new onset of pain that had been present for at least 3 months (i.e., chronic pain). Of these 88 adolescents with chronic pain at follow-up, a subgroup of adolescents (n=29) specifically reported chronic NP. Due to the small size of the sample of adolescents with acute pain (n=16), this group was excluded from the analysis.

A detailed characterization of adolescents with and without pain is presented in Table 7.1. Baseline comparisons between the groups with new onset of pain and no pain at 6-month follow-up showed that adolescents with pain were younger (p=0.02) and reported higher scores in the Central Sensitization Inventory (p=0.002) than

adolescents without pain (Table 37). The results also suggested a tendency for adolescents with pain to have lower sleep quality (p=0.05). No statistically significant between-group differences were found for depression, anxiety, and stress (p>0.05).

The comparison between the subgroup with new onset of NP and without pain showed that adolescents with NP reported more self-reported symptoms of central sensitization compared to the group without pain at the baseline (Table 38).

7.4.1. Distribution and number of painful body sites at 6-month follow-up

At 6-month follow-up, of the 88 adolescents with chronic musculoskeletal pain, 29 (33.0%) of the adolescents reported NP, (18) 20.5% reported back pain, and 41 (46.5%) reported limb pain. Overall, 43 (48.9%) adolescents reported a single painful body site, 29 (33%) reported two painful body sites, 9 (10.1%) reported three painful body sites, and 7 (8.0%) reported more than 4 painful body sites. The mean±SD number of painful body sites was 1.81±1.04 (Table 39).

7.4.2. Baseline factors associated with chronic pain at 6-month follow-up

In the univariable analysis, being female (OR=2.69, p<0.05), reporting lower sleep quality (OR=1.07, p<0.10), and more self-reported symptoms of central sensitization (OR=1.05, p<0.05) were significantly associated with chronic pain at 6-month follow-up (Table 7.4). Being female (OR=2.34, 95%CI 1.28-4.27; p<0.05) and reporting more self-reported symptoms of central sensitization (OR=1.04, 95%CI 1.01-1.07; p<0.05) were the only factors that remained significantly associated with chronic pain at 6-month follow-up. The Nagelkerke R^2 of the final multivariable model was 0.10. For all analyses, the value of VIF and the respective tolerance value was 1.

For the subgroup with new onset of NP, reporting more self-reported symptoms of central sensitization (OR=1.04, 95%CI 1.00-1.09; p<0.05) was the only factor that

remained significantly associated with chronic pain at 6-month follow-up. The final multivariate model showed an Nagelkerke R^2 of 0.04 (Table 40).

7.4.3. Between-group comparison of the individual items of the Central Sensitization Inventory

Comparisons of the Central Sensitization Inventory items at baseline between the groups with and without pain at 6-month follow-up showed a statistically significant difference for items 16 ("*I feel sad or depressed"*), 22 *("My legs feel uncomfortable and restless when I am trying to go to sleep at night"*), and 23 (*"I have difficulty remembering things"*), showing that a higher percentage of adolescents with chronic pain marked these items at baseline (Figure 18 and Table 41).

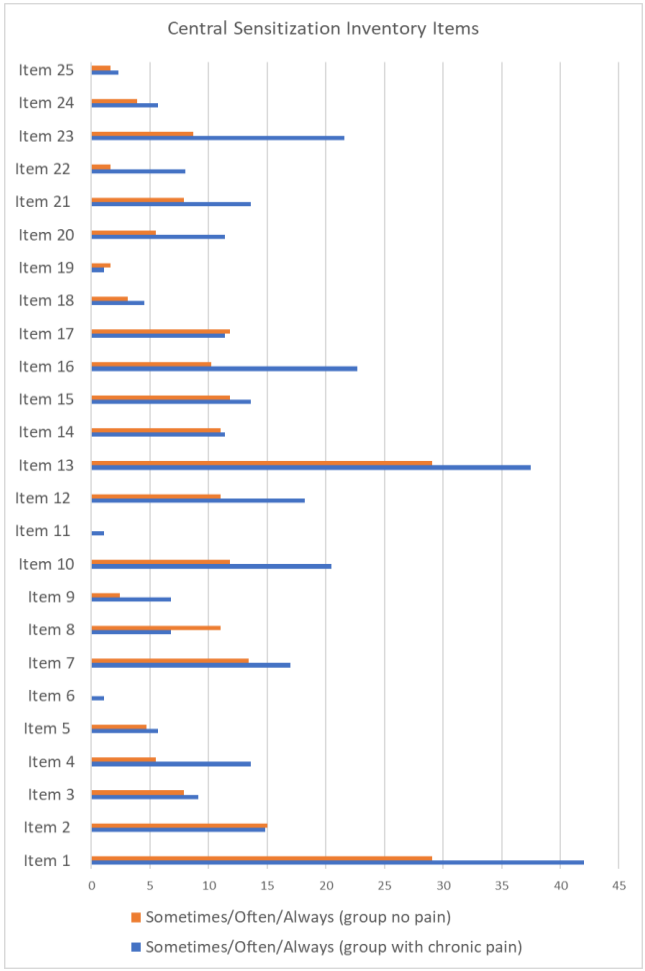


Figure 18. Central Sensitization Inventory Items.

Item 1: I feel tired and unrefreshed when I wake from sleeping; Item 2: My muscles feel stiff and achy; Item 3: I have anxiety attacks; Item 4: I grind or clench my teeth; Item 5: I have problems with diarrhea and/or constipation; Item 6: I need help in performing my daily activities; Item 7: I am sensitive to bright lights; Item 8: I get tired very easily when I am Physically active; Item 9: I feel pain all over my body; Item 10: I have headaches; Item 11: I feel discomfort in my bladder and/or burning when I urinate; Item 12: I do not sleep well; Item 13: I have difficulty concentrating; Item 14: I have skin problems such as dryness, itchiness, or rashes; Item 15: Stress makes my physical symptoms get worse; Item 16: I feel sad or depressed; Item 17: I have low energy; Item 18: I have muscle tension in my neck and shoulders; Item 19: I have pain in my jaw; Item 20: Certain smells, such as perfumes, make me feel dizzy and nauseated; Item 21: I have to urinate frequently; Item 22: My legs feel uncomfortable and restless when I am trying to go to sleep at night; Item 23: I have difficulty remembering things; Item 24: I suffered trauma as a child; Item 25: I have pain in my pelvic area.

7.5. Discussion

This longitudinal study explored the baseline factors that were associated with the reporting of chronic pain at 6-month follow-up in 252 adolescents who were asymptomatic at baseline. From baseline to follow-up, 38.1% of the adolescents reported a new onset of chronic pain lasting at least 3 months. Other longitudinal studies in adolescents found lower percentages. Malmborg et al. (2019) in a high school sample of 169 adolescents aged 16 years found that 15.6% reported pain at a 3-year follow-up. El-Metwally et al. (2007) reported that of 1113 preadolescents attending the third (mean age=9.8±0.4) and fifth (mean age=11.8±0.4) grade, 21.5% reported pain in at least one body site at 1-year follow-up. Although both studies have explored school communities like the present study, the use of different pain assessment questionnaires (e.g. pain questionnaires based on frequency and etiology

of pain) and longer periods of follow-up (e.g. as long as 3-year follow-up) might contribute to the differences found. In the present study, the most common painful body sites at 6-month follow-up were the neck (29.5%) followed by the lower back (28.4%), and the knees (21.6%). El-Metwally et al. (2007) also found in their study that the neck region was the most common painful body site. These findings are also in line with several prevalence studies that have suggested that chronic NP prevalence has been increasing in adolescents in the last decades (Hoftun et al., 2011; Stahl et al., 2014).

In this study, female sex, sleep impairments, and self-reported symptoms of central sensitization were significantly associated with the onset of chronic pain in the univariable analysis. However, of these, only the female sex and self-reported symptoms of central sensitization remained significantly associated with the onset of chronic pain in the multivariable model. In the analysis of the subgroup of adolescents with chronic NP, the symptoms of central sensitization also remained associated with the new onset of NP. In the systematic review of Huguet et al. (2016) insufficient quality of evidence was reported for the relationship between female sex and the onset of chronic musculoskeletal pain, finding a significant association only in studies that addressed exclusively chronic pain, such as the present study. Studies in adults have reported that gender differences concerning pain may be strongly related to biological (e.g. genetic and hormonal differences) and psychosocial factors (e.g. pain-coping differences and parents' behavioral influences) (Boerner, Schinkel, & Chambers, 2015; Mogil, 2012). Despite the individual and subjective perceptions underlying the phenomenon of pain, few studies have also explored possible sex differences in response to pain in children and adolescents (Boerner, Birnie, Caes, Schinkel, & Chambers, 2014; Schmitz, Vierhaus, & Lohaus, 2013). For instance, Schmitz et al. (2013) explored pain tolerance and pain-coping in adolescents and found that girls aged 15 to 17 years old reported lower pain threshold and higher levels of

catastrophizing compared to boys of the same age, who in turn reported higher levels of self-efficacy. These differences between girls and boys may contribute to this increased risk of chronic pain associated with being a female.

Previous studies reported an association of the psychological factors, such as depression and anxiety (Feldman et al., 2002; Marja Mikkelsson et al., 2008; Ståhl et al., 2008) and sleep impairments (Auvinen et al., 2010; El-Metwally et al., 2007) and the onset of chronic pain in adolescents. However, in this study, only self-reported symptoms of central sensitization assessed by the Central Sensitization Inventory emerged as a risk factor for the onset of chronic musculoskeletal pain and, specifically, of chronic NP. Looking at the total score of the Basic Scale on Insomnia complaints and Quality of Sleep (7.20±3.77 out of a maximum of 28 points), we verified that the mean score did not reach the cut-off of 9 used to distinguish good sleepers from poor sleepers, suggesting that, in general, adolescents reported good quality sleep. Also, in the present study, objective sleep quantity and daytime tiredness were not assessed. To our knowledge, no other study has investigated the association between self-reported symptoms of central sensitization and the onset of chronic pain neither in adolescents nor in other age groups. Considering that central sensitization may reflect a state of generalized hypersensitivity to pain, but also to other stimuli unrelated to the musculoskeletal system (e.g. environmental and chemical stimuli, emotional distress, sleep problems, stress, mental load) these symptoms may be present in the absence of pain (Mayer et al., 2012; Nijs et al., 2014) and predispose to pain onset. Harte et al. (2018) reported the t*op-down* central sensitization, in which the primary change may originate in supraspinal structures and does not require a nociceptive stimulus. According to these authors, in top-down central pain mechanisms, the onset of pain occurs at younger ages, predominantly following puberty, and among several

characteristics, the hypersensitivity to stimuli unrelated to pain is present (Harte et al., 2018).

Several mechanisms can be associated with the development and reinforcement of central sensitization. These mechanisms can be varied, ranging from neuronal hyperexcitability to increased activity of brain neuromatrix, which are influenced by cognitive-emotional factors and previous pain experiences (Neblett, 2018; Nijs et al., 2016; Woolf, 2011). This neurosignature in the brain, which can be activated independently of sensory inputs, may also influence the experience of pain (Melzack, 2001; Randy Neblett, 2018; Woolf, 2011). However, these findings have to be cautiously interpreted. Although there is no precise clinical test to assess central sensitization, quantitative sensory testing, e.g. pressure pain thresholds assessed with an algometer, should be used to semi-objectively reinforce central sensitization findings (Van Griensven, Schmid, Trendafilova, & Low, 2020). Moreover, a recent study in adults with shoulder pain reported a stronger association of the Central Sensitization Inventory with psychosocial measures than with quantitative sensory testing (Coronado & George, 2018), suggesting the need for a better understanding of the relationship between Central Sensitization Inventory and other measures suggestive of central sensitization.

In this study, an additional analysis of the Central Sensitization Inventory was performed to understand which items of this inventory were most reported by adolescents that developed pain at 6-month follow-up. Between-group differences were found only for three out of 24 items, including item 16 (“*I feel sad or depressed”)*, suggesting that symptoms of depression might precede chronic pain, contrary to what has been suggested in adults (Poole, White, Blake, Murphy, & Bramwell, 2009). However, the low score of the Depression, Anxiety, and Stress Scale (4.44 ± 6.03) in the group of adolescents with pain does not support this hypothesis. Comparison of the

present study with other studies is difficult due to differences in measurement instruments for depression and participants' age ranges, but previous studies reported moderate-quality evidence suggesting that depression and mental distress were associated with the onset of chronic musculoskeletal pain (Huguet et al., 2016). Finally, the Nagelkerke R^2 of the multivariable model was 0.10 and 0.04 in the group of musculoskeletal pain and NP, respectively, suggesting that the ability of the female sex and Central Sensitization Inventory to explain pain at 6-month follow-up is small. As previously suggested, other factors such as the presence of other non-musculoskeletal pain conditions, e.g. headaches, and day-time tiredness (El-Metwally et al., 2007) and having parents with chronic pain (Palermo & Chambers, 2005), which have been associated with pain in adolescents, were not assessed in the present study, and might predispose to new onset of chronic pain.

7.5.1. Clinical implications and future research

This study findings cautiously suggest that the assessment of the nervous system hypersensitivity might have a role in identifying adolescents at risk of developing chronic pain. However, further studies are needed using more objective indicators of central sensitization. Considering the increasing prevalence of chronic musculoskeletal pain in adolescents, the results of this study highlight the importance of identifying risk factors for the onset of chronic pain and suggest that self-reported symptoms of central sensitization as a target for these interventions. The assessment and intervention in the school context may facilitate access to a greater number of adolescents.

7.5.2. Strengths and limitations

The main strengths of this study were its longitudinal approach and the wide set of variables included at the baseline and follow-up assessments. The fact that the study was performed in a school context, with adolescents from the community and from

different geographical areas, is also a positive aspect to highlight. To overcome a limitation frequently reported in the review of Huguet et al. (2016), this study only included adolescents with chronic pain at follow-up and adolescents who remained without pain. However, some limitations should be noted. The Central Sensitization Inventory was used to assess the symptoms associated with central sensitization. In this sense, the conclusions of this study were given as a reference to these symptoms. To extend these conclusions to the condition of central sensitization, more objective measures, such as pain thresholds or conditioned pain modulation, need to be used (Van Griensven et al., 2020). The time point of reference for pain in the Nordic Musculoskeletal Questionnaire was adapted from 12 months to 3 months to meet the current definition of chronic pain and minimize memory bias, although no additional validation was performed. The measurement instruments used were validated for adolescents with pain, but not for pain-free adolescents. Although their questions do not focus on pain, additional validation may be necessary for its application in pain-free adolescents. In this study, it was not identified the possible origin for the onset of pain, e.g. traumatic vs. non-traumatic, and its severity, and the predictors of pain might vary depending on pain origin (El-Metwally et al., 2007). Furthermore, the study focused on musculoskeletal pain, and other common types of pain (e.g. headache, abdominal or menstrual pain) were not assessed in this study and could have acted as confounders. Also, no measure on the pubertal status of the adolescents was used. However, the progression of pubertal development involves a set of biopsychosocial changes that can influence pain complaints and behavior of adolescents. The absence of pain at baseline was assessed for the last 3 months, however, recurrent pain episodes before that were not considered. The follow-up period for this study was relatively short.

7.6. Conclusions

Being a female adolescent and reporting more symptoms in the Central Sensitization Inventory at baseline were associated with the onset of chronic musculoskeletal pain at 6-month follow-up. Furthermore, symptoms of central sensitization also remained associated with the new onset of chronic NP. Future studies are needed to further explore the possible role of central sensitization in a new musculoskeletal pain onset.

Table 37. Characterization of the groups with and without pain at 6-month follow-up for baseline data.

Variables		No pain (n=127)	With chronic musculoskeletal pain (n=88)	p-value
Sex	Girls	30 (23.6%)	40 (45.5%)	0.001
	Boys	97 (76.4%)	48 (54.5%)	
Age (years)		16.60±1.08	16.22±1.22	0.02
BMI (Kg/m^2)		21.23±3.03	20.80±2.72	0.28
Scholar level ª	10th	30 (23.6%)	41 (46.6%)	0.002
	11th	46 (36.2%)	24 (27.3%)	
	12th	51 (40.2%)	23 (26.1%)	
Family situation (Lives with…)	Father and mother	81 (63.8%)	66 (75.0%)	0.34
	Mother	32 (25.2%)	15 (17.0%)	
	Father	4 (3.1%)	3 (3.4%)	
	Other	10 (7.9%)	4 (4.5%)	
DASS-C (0-63)		3.17±5.90	4.44±6.03	0.13
BaSIQS (0-28)		6.14±3.90	7.20±3.77	0.05
CSI (0-100)		9.22±9.11	13.34±10.12	0.002

BMI, Body Mass Index; DASS-C, Depression, Anxiety and Stress Scale for Children; BaSIQS, Basic Scale on Insomnia complaints and Quality of Sleep; CSI, Central Sensitization Inventory

ª Scholar level represent the different years of schooling in high school.

Table 38. Characterization of the groups with and without NP at 6-month follow-up for baseline data.

Variables		No Pain (n=127)	With Neck Pain (n=29)	p-value
Sex	Girls	30 (23.6%)	12 (41.4%)	0.06
	Boys	97 (76.4%)	17 (58.6%)	
Age (years)		16.60±1.08	16.41±1.35	0.50
BMI (Kg/m^2)		21.23±3.03	21.25±2.38	0.97
Scholar level ª	10th	30 (23.6%)	14 (48.3%)	0.03
	11th	46 (36.2%)	6 (20.7%)	
	12th	51 (40.2%)	9 (31.0%)	
Family situation (Lives with…)	Father and mother	81 (63.8%)	23 (79.3%)	0.41
	Mother	32 (25.2%)	4 (13.8%)	
	Father	4 (3.1%)	0 (0.0%)	
	Other	10 (7.9%)	2 (6.9%)	
DASS-C (0-63)		3.17±5.90	5.21±7.50	0.18
BaSIQS (0-28)		6.14±3.90	6.55±3.24	0.56
CSI (0-100)		9.22±9.11	13.03±9.68	0.046

BMI, Body Mass Index; IPAQ-A, International Questionnaire of Physical Activity for adolescents; DASS-C, Depression, Anxiety and Stress Scale for Children; BaSIQS, Basic Scale on Insomnia complaints and Quality of Sleep; CSI, Central Sensitization Inventory

ª Scholar level represent the different years of schooling in high school.

Table 39. Painful body sites at 6-month follow-up.

Body area	Musculoskeletal pain n (%)*	Neck pain n (%)*
Neck	29 (33.0)	29 (100)
Shoulder	16 (18.2)	7 (24.1)
Elbow	2 (2.3)	0 (0.0)
Wrist	19 (21.6)	4 (13.8)
Thoracic	5 (5.7)	1 (3.4)
Lumbar	26 (29.5)	11 (37.9)
Hip	17 (19.3)	2 (6.9)
Knee	25 (28.4)	6 (20.7)
Ankle	19 (21.6)	8 (27.6)
Number of painful body sites (mean±SD)	1.81±1.04	2.34±1.34

*The percentages add up to more than 100% as participants could report more than one painful body site.

Table 40. Odds ratios and 95% confidence intervals for univariable and multivariable associations for the onset of musculoskeletal pain, and, particularly, NP.

		Musculoskeletal pain (n=88) (R Nagelkerke=0.10)		**Neck pain** (n=29) (R Nagelkerke=0.04)	
Variables		Univariable OR; CI95%	Multivariable OR; CI95%	Univariable OR; CI95%	Multivariable OR; CI95%
Gender	Male	1	1	1	
	Female	2.69; [1.50;4.84]**	2.34; [1.28;4.27]**	2.28; [0.98;5.31]*	
Age (years)		0.74; [0.58;0.95]**		0.86; [0.60;1.24]	
BMI (Kg/m^2)		0.95; [0.86;1.04]		1.00; [0.87;1.15]	
Family Situation	Both Parents	1		1	
	Alternative[a]	0.59; [0.32;1.07]*		0.46; [0.17;1.21]	
DASS-C (0-63)		1.04; [0.99;1.09]		1.05; [0.99;1.11]	
BaSIQS (0-28)		1.07; [1.00;1.15]*		1.03; [0.93;1.14]	
CSI (0-100)		1.05; [1.02;1.08]**	1.04; [1.01;1.07] **	1.04; [1.00;1.09]**	1.04; [1.00;1.09]**

*p < 0.1; ** p < 0.05

[a]Live only with mother, father or other.

BMI, Body Mass Index; IPAQ-A, International Questionnaire of Physical Activity for adolescents; DASS-C, Depression, Anxiety and Stress Scale for Children; BaSIQS, Basic Scale on Insomnia complaints and Quality of Sleep; CSI, Central Sensitization Inventory

Table 41. Between-group comparison (no pain vs chronic musculoskeletal pain) of the items of the Central Sensitization Inventory.

CSI item	No pain		Musculoskeletal pain		p-value
	Never/Rarely	Sometimes/Often	Never/Rarely	Sometimes/Often	
	N (%)	N (%)	N (%)	N (%)	
1. I feel unrefreshed when I wake up in the morning.	90 (70.9)	37 (29.1)	51 (58.0)	37 (42.0)	0.058
2. My muscles feel stiff and achy.	108 (85.0)	19 (15.0)	75 (85.2)	13 (14.8)	1
3. I have anxiety attacks.	117 (92.1)	10 (7.9)	80 (90.9)	8 (9.1)	0.81
4. I grind or clench my teeth.	120 (94.5)	7 (5.5)	76 (86.4)	12 (13.6)	0.05
5. I have problems with diarrhea and/or constipation.	121 (95.3)	6 (4.7)	83 (94.3)	5 (5.7)	1
6. I need help in performing my daily activities.	127 (100.0)	0 (0.0)	87 (98.9)	1 (1.1)	0.41
7. I am sensitive to bright lights.	110 (86.6)	17 (13.4)	73 (83.0)	15 (17.0)	0.56
8. I get tired very easily when I am physically active.	113 (89.0)	14 (11.0)	82 (93.2)	6 (6.8)	0.35
9. I feel pain all over my body.	124 (97.6)	3 (2.4)	82 (93.2)	6 (6.8)	0.17
10. I have headaches.	112 (88.2)	15 (11.8)	70 (79.5)	18 (20.5)	0.12
11. I feel discomfort in my bladder and/or burning when I urinate.	127 (100.0)	0 (0.0)	87 (98.9)	1 (1.1)	0.41
12. I do not sleep well.	113 (89.0)	14 (11.0)	72 (81.8)	16 (18.2)	0.16
13. I have difficulty concentrating.	90 (70.9)	37 (29.1)	55 (62.5)	33 (37.5)	0.24
14. I have skin problems such as dryness. itchiness or rashes.	113 (89.0)	14 (11.0)	78 (88.6)	10 (11.4)	1
15. Stress makes my physical symptoms get worse.	112 (88.2)	15 (11.8)	76 (86.4)	12 (13.6)	0.84
16. I feel sad or depressed.	114 (89.8)	13 (10.2)	68 (77.3)	20 (22.7)	0.02
17. I have low energy.	112 (88.2)	15 (11.8)	78 (88.6)	10 (11.4)	1
18. I have muscle tension in my neck and shoulders.	123 (96.9)	4 (3.1)	84 (95.5)	4 (4.5)	0.72
19. I have pain in my jaw.	125 (98.4)	2 (1.6)	87 (98.9)	1 (1.1)	1
20. Certain smells. such as perfumes. make me feel dizzy and nauseated.	120 (94.5)	7 (5.5)	78 (88.6)	10 (11.4)	0.13
21. I have to urinate frequently.	117 (92.1)	10 (7.9)	76 (86.4)	12 (13.6)	0.25
22. My legs feel uncomfortable and restless when I am trying to go to sleep at night.	125 (98.4)	2 (1.6)	81 (92.0)	7 (8.0)	0.03
23.I have difficulty remembering things.	116 (91.3)	11 (8.7)	69 (78.4)	19 (21.6)	0.01
24. I suffered trauma as a child.	122 (96.1)	5 (3.9)	83 (94.3)	5 (5.7)	0.74
25. I have pain in my pelvic area.	125 (98.4)	2 (1.6)	86 (97.7)	2 (2.3)	1

8. BLENDED-LEARNING PAIN NEUROSCIENCE EDUCATION AND EXERCISE IN HIGH SCHOOL STUDENTS WITH CHRONIC NECK PAIN - A RANDOMIZED CONTROLLED STUDY

Based on the study from Andias, R., Sá-Couto, P. & Silva, AG. (2021). “Blended-learning pain neuroscience education and exercise in high school students with chronic neck pain - a randomized controlled study”. Physical Therapy *(submitted and revised).*

8.1. Introduction

In Chapter 5 we found that 753 adolescents (43.5%) of a total of 1730 reported chronic NP, of which 334 (47.0%) reported persistent chronic NP at a 6-month follow-up (Chapter 6). Furthermore, of the 252 asymptomatic adolescents at baseline, 231 (91.7%) completed the 6-month follow-up and 29 (12.6.0%) reported a new onset of NP (Chapter 7). These findings highlight the high prevalence of NP and its persistent nature and the need for school-based interventions directed at NP and its associated factors. These factors were investigated and described in Chapters 3 to 6 and self-reported symptoms of central sensitization recurrently emerged as a relevant factor. However, other factors were reported as important, including psychosocial factors, sleep impairments, disability, and physical activity. In addition, Chapter 3 found limited evidence that adolescents with chronic NP have lower endurance of the deep neck muscles and very limited evidence that adolescents with NP have higher local and distant sensory pain thresholds than adolescents without NP. Therefore, both of these variables were assessed in this randomized controlled trial.

In this Chapter 8 we designed an intervention that targets the identified factors found to be associated with chronic NP in the previous Chapters of this thesis and assessed its

effectiveness. The intervention is based on PNE and exercise. As previously explored in Chapter 2, PNE aims to make pain understandable, explaining that it is not a direct reflection of tissue damage, but a brain output resulting from various interactions at the level of biological, psychological, and social processes (Louw, Zimney, O'Hotto, et al., 2016), promoting the reconceptualization of pain and maladaptive beliefs (Robins et al., 2016). We are unable to find studies on PNE for adolescents with NP other than the pilot study from our team (Andias et al., 2018), which compared 4 weeks of PNE and exercise against no intervention and found a significant improvement in knowledge of pain neuroscience and endurance capacity of neck extensors, and a non-significant trend towards a higher decrease in pain intensity, catastrophizing and anxiety, and increased muscle endurance in the PNE and exercise group. Moreover, the adolescents that received the intervention reported PNE as a facilitator of both pain reconceptualization and of a positive attitude towards exercise (Neto et al., 2018). Exercise is widely suggested in the literature as an intervention strategy to improve function in chronic NP (Blanpied et al., 2017; O'Riordan et al., 2014), but it is also recognized as a facilitator of the desensitization of the nervous system, commonly hyperexcitable and hypersensitive in chronic pain (Nijs et al., 2015).

Considering the relevance of previously explored biopsychosocial factors, particularly self-reported symptoms of central sensitization, and the pilot study mentioned above, both modalities of intervention seem relevant to improve NP management and function in adolescents. Furthermore, a recent systematic review of Siddall (2021), concluded that combining PNE and exercise results in a greater reduction in pain intensity, disability, catastrophizing, and fear-of-movement compared to exercise only. However, this systematic review included studies in adults only and only one of the included studies was specific to adults with chronic NP (Matias et al., 2019).

Several strategies for applying PNE and exercise have been reported in the literature. More recently, Malfliet et al. (2018) highlighted the potential of blended-learning in a sample of adults with chronic spinal pain. Sangrar et al. (2019) defined the blended-learning approach as a combination of face-to-face and online educational sessions using electronic devices or platforms, increasingly used as a method of healthcare education. Considering the potential benefits of digital solutions, such as WhatsApp, to provide accessible health information and its popularity and perceived usefulness among adolescents with chronic pain as an alternative to traditional face-to-face interventions (Beneitez, Nieto, Hernández, & Boixadós, 2020; Slater et al., 2016), a blended-learning strategy using WhatsApp was used for the present randomized controlled trial.

Thus, the main aim of this study was to compare the effectiveness of exercise and PNE versus exercise only on pain intensity of high school adolescents with chronic idiopathic NP at post-intervention and 6-month follow-up. The secondary aims were to assess the effectiveness of both interventions on disability, sleep, catastrophizing, fear of movement, self-efficacy, neck, and scapular muscle endurance, pressure pain thresholds, and knowledge on pain neuroscience at post-intervention and 6-month follow-up.

8.2. Methods

8.2.1. Study design

This randomized controlled trial was approved by the Council of Ethics and Deontology of the University of Aveiro and the trial protocol was registered at ClinicalTrials.gov (NCT04125901). The study was implemented as a two-arms intervention (a group of exercise versus a group of exercise plus PNE) with 3 assessment points: i) baseline, ii) 1-week post-intervention and iii) 6 months post-intervention and designed in a blended-

learning format with a combination of face-to-face sessions at schools and non-face-to-face online sessions using WhatsApp (WhatsApp Inc. of Mountain View, California).

8.2.2. Participants and randomization

Two secondary schools in the council of Aveiro, Portugal, were contacted to authorize the invitation of their students to this study. The inclusion criteria for this study were i) aged between 15 and 18 years old, ii) having idiopathic NP pain for at least 3 months, defined as pain non-related to any known pathology or injury, felt at least once a week for the past 3 months and perceived anywhere between the superior nuchal line and the spinous process of T1 (Misailidou et al., 2010), iii) having NP intensity in the numeric pain rating scale equal or greater than 2 points and iv) not currently receiving any treatment for NP (except occasional painkillers). All students in each class were invited to participate in the screening for inclusion criteria by completing an initial questionnaire in a physical education class, which included four questions related to the 4 inclusion criteria previously defined. Students with pathology of the nervous or rheumatological systems were excluded. Those who met the criteria to participate in the study received a written explanation of the study procedures for them and their legal guardians to read. Those students who agreed to participate signed written informed consent. For those aged less than 18 years old, informed consent from the legal guardian was also required. After all informed consents have been collected, randomization was performed. A researcher not involved in participant recruitment and treatment (AGS) used an online software (Research Randomizer; https://www.randomizer.org/) to randomly allocate each participant to one of the two intervention groups. To minimize the contamination effect, the randomization process was performed by classes, so that all possible participants in a specific class were part of the same group, and by areas of knowledge (e.g., sciences, economics, humanities, arts) to minimize the potential effect of baseline biology knowledge on the acquisition or

predisposition for PNE. It was not possible to blind the physiotherapist who performed the intervention.

8.2.3. Sample size

Sample size calculations were performed using the formula of Kirkwood & Sterne (Kirkwood & Sterne, 2003) for comparison of two means and based on the following assumptions: power at 95%, alpha at 5% two-tailed, SD of 2.03, and a between-group difference to be detected of 1.39 (30% of the pain intensity of adolescents with an average Numeric Pain Rating Scale of 4.64). This resulted in 110 participants, which was added by a possible loss to follow-up of 15%. The recruitment target was 127 participants. These values were based on the results obtained in the group of adolescents with chronic NP (n = 753) from the study reported in Chapter 5.

8.2.4. Outcome measures

At baseline, participants completed an online self-reported questionnaire that included sociodemographic information (sex, age, Body Mass Index, scholar level), pain characteristics, disability, sleep, catastrophizing, fear of movement, self-efficacy, symptoms of central sensitization, and knowledge on pain neuroscience. Also, participants were assessed for muscle function and PPT by a trained physiotherapist. The questionnaire was filled by the participants at baseline, post-intervention and at 6-month follow-up, while the muscle tests and PPT measurements were performed only at baseline and post-intervention. Due to the worldwide SARS-CoV-2 pandemic, it was not possible to complete the muscle tests and PPT measurements for all participants and all the 3 moments of assessment. The assessment of the individual's perception of change was also assessed at post-intervention and 6-month follow-up using the Patient’s Global Impression of Change. A full description of each measurement instrument and test used is described below, except for the Functional Disability

Inventory, Basic Quality Self-Reported Quality of Sleep, Pain Catastrophizing Scale, Tampa Scale of Kinesiophobia, Child Self-Efficacy Scale, and Central Sensitization Inventory, which were described in Chapter 5.

Characterization of pain

Pain intensity at the moment was assessed using the Numeric Pain Rating Scale from 0 (representing no pain) to 10 (representing the worst pain) (Castarlenas et al., 2017). Numeric Pain Rating Scale is valid in adolescents (Ruskin et al., 2014). For adolescents with chronic pain changes of 1 point on Numeric Pain Rating Scale have been suggested as clinically meaningful (Castarlenas et al., 2017). The duration of pain was also assessed at baseline with a closed question (*How long have you had neck pain?*). The frequency of pain in the last week was specified as i) never, ii) rarely (once a week), iii) occasionally (2 to 3 times a week), iv) frequently (more than 3 times a week), or v) always.

Pain Neurophysiology Questionnaire of 12 items

Knowledge of each participant about the mechanisms and assumptions of pain neuroscience was assessed using the Pain Neurophysiology Questionnaire (Neto et al., 2018). It is scored from 0 to 12 points and higher scores indicate greater knowledge of pain neuroscience (Catley, O'Connell, & Moseley, 2013). It has shown good psychometric properties (α=0.67) (Nogueira et al., 2018).

Patient's Global Impression of Change

Perception of improvement associated with the intervention was assessed using the Patient's Global Impression of Change. Participants were instructed to select on a scale from 1 ("No change or condition worsened") to 7 ("Much better, and with a considerable improvement that made all the difference") the statement that best

reflected the impact of the intervention on their condition (Domingues & Cruz, 2011; Dworkin et al., 2008). This is a valid instrument and a score of 5 or more is associated with a clinically significant improvement in the condition of participants (Domingues & Cruz, 2011; Hurst & Bolton, 2004).

Deep Neck Flexor Endurance Test

Participants were supine and gently flexed the upper cervical spine and moved their head away from the examiner's hand, approximately 2.5 cm, while maintaining the upper cervical flexion. The loss of the test position led to the end of the test (Andias et al., 2018; Edmondston et al., 2008; Oliveira & Silva, 2016). The SEM and smallest detectable change (SDC) are 9.50s. and 26.3s. respectively (Oliveira & Silva, 2016).

Cervical Extensor Endurance Test

Participants were prone and positioned their head over the end of the plinth, initially supported by the examiner. A weight of 2kg was suspended from a headband placed on the participant's head while the participant was asked to hold the cervical spine horizontal as measured by an inclinometer and the chin retracted. The loss of the test position in more than 5º or reaching the 5 minutes of the test led to the end of the test (Andias et al., 2018; Edmondston et al., 2008; Oliveira & Silva, 2016). The SEM and SDC in adolescents with NP are 45.45s. and 125.63s. respectively (Oliveira & Silva, 2016).

Scapular Muscle Endurance Test

Participants were positioned facing a wall, with shoulders and elbows flexed at 90°, and no contact with the wall. An analogical dynamometer was placed between the participant's hands, a ruler was held between their elbows, and scapulae were maintained in a neutral position. Participants were instructed to externally rotate the

shoulders to achieve a 1kg load and to maintain this force while also maintaining the test position. The loss of the ability to produce 1 kg force or of the test position led to the end of the test (Andias et al., 2018; Edmondston et al., 2008; Oliveira & Silva, 2016). The SEM and SDC are 10.87s. and 30.1s. respectively, in adults with NP (Edmondston et al., 2008).

For all muscle tests, participants first did a trial test and then performed each test twice with a 5-minute interval. The mean of these two measurements was used for statistical analysis.

Pressure Pain Threshold

PPT was assessed using a digital pressure algometer (JTECH Medical Industries, Salt Lake City, US) with a probe of 0.5 cm of diameter, applied perpendicular to the skin, at the right and left articular pillar of C5-C6 (approximately 1 cm lateral to the mid-distance between the spinous processes of C5 and C6, which were identified by palpation) and at the right tibialis anterior (approximately 2.5 cm lateral and 5 cm inferior to the tibial tubercle), at a rate of approximately 3N/s up to a maximum of 60N with 30 seconds resting period between each measurement (Sá & Silva, 2017; Walton et al., 2011). In the presence of pain or discomfort at rest on the right tibialis, the left tibialis was used. The participant was instructed to say “stop” as soon as the pressure sensation changed to pain. The participant first tried the procedure in the thenar region of the hand, then 3 measurements were taken at each of the 3 body sites.

8.2.5. Intervention – general information

Each of the two groups had weekly contacts with a physiotherapist (RA) for 8 weeks in a blended-learning format. Three to 5 of these contacts were face-to-face sessions with up to 45 minutes duration that took place at the school, and for the remaining the WhatsApp was used to facilitate the communication and monitoring of participants. The

first two sessions were always face-to-face. For those receiving 5 face-to-face sessions, these were interspersed with WhatsApp sessions and those receiving 3 face-to-face sessions had the 3rd and the 5th to 8th sessions via WhatsApp. The initial design of this study included 5 face-to-face sessions for all (Figure 8.1), but due to the worldwide SARS-CoV-2 pandemic and the closing of schools, while we were conducting the study, it had to be adapted. The face-to-face sessions at school were delivered in groups of 4 to 6 students usually from the same class. Face-to-face sessions were conducted by a physiotherapist (RA) with 5 years of experience in these programs. For the WhatsApp sessions, each group of participants shared a common WhatsApp account and was sent a 5-minute video showing how to perform the exercises for the respective session for both groups and activities on PNE for the exercise and PNE group. Also, WhatsApp allowed the exchange of weekly messages between the physiotherapist and participants. After the first two face-to-face sessions, illustrative pictures of the exercises performed in these sessions were also sent via WhatsApp to facilitate the performance of exercises at home. In the exercise plus PNE group, WhatsApp was also used for sharing PNE contents after each session. For both groups, two weekly reminders were sent at the beginning and end of the week, over 8 weeks, to remember the need to perform the proposed exercises and activities. Participants were also encouraged to use WhatsApp to ask questions and clarify doubts with the physiotherapist and provide feedback about home exercises. The exchange of information with participants was informed by behavior change techniques, such as instruction on how to perform a behavior, goal setting, demonstration of the behavior, feedback on behavior, and self-monitoring of behavior (Hynynen et al., 2016). A more detailed description of the exercise and PNE content is provided below.

8.2.6. Exercise

Both intervention groups performed the same exercises, but the number of sessions and the duration of the component of exercise varied. The exercise group performed exercises in all sessions (45 minutes exercise in face-to-face sessions), but the exercise plus PNE group begun exercises in the 2nd session. In this session, exercises were performed for 15 minutes and the time devoted to exercise increased up to 45 minutes in session 8th. All exercise sessions included i) warm-up: global exercises and full range mobility exercises of the body and particularly of the neck and shoulder, ii) neuromuscular control, endurance and strength exercises including for the deep neck flexor and extensor muscles and scapular stabilizer muscles, using body-weight, elastic bands, and balls, and iii) cooling-down: stretching exercises for neck and shoulder muscles (Blanpied et al., 2017; O'Riordan et al., 2014). Please see Tables 42 to 44 for details on the exercise intervention. The training volume was adjusted by increasing the number of repetitions from 2-3 sets of 8-12 repetitions to 3-5 sets of 8-12 repetitions, according to individual comfort. Participants were also instructed to work between the 4 (a little strong) and 6 (strong) effort levels of the Modified Borg Scale (Yildiz, Turgut, & Duzgun, 2018). There was a rest period of 1 minute between each series of exercises (Lloyd et al., 2014). During the exercise program, the principles of cognition-targeted exercise therapy were used, i.e., time-contingent exercises instead of a symptom-contingent exercise (Malfliet et al., 2017; Nijs et al., 2015). Participants were encouraged to perform exercises 2 to 3 times a week.

8.2.7. Pain Neuroscience Education

PNE was delivered to the exercise and PNE group only. Contents were in line with guidelines (Butler & Moseley, 2013; Louw & Puentedura, 2013) and previous studies in adolescents (Andias et al., 2018; Louw et al., 2018) and included the discussion of acute pain, the transition from acute to chronic pain, central sensitization, brain

plasticity, pain modulation and the importance of exercise, and the role of cognitions, emotions and sleep on pain. Pictures, diagrams, metaphors, and YouTube videos were used to facilitate the understanding of the concepts (Heathcote et al., 2019; Adriaan Louw, Puentedura, Diener, Zimney, & Cox, 2019; Adriaan Louw, Zimney, O'Hotto, et al., 2016). The 1st session was PNE only and lasted approximately 45-minutes. In the 2nd session, there were 30-minutes of PNE and the remaining 15-minutes was exercise. In the following 4th and 6th sessions 15 minutes of each session were used to clarify doubts and emphasize PNE concepts and strategies. The 8th session included exercise only. At the end of the face-to-face PNE sessions, an online information leaflet, written exclusively for this study by the research team, was sent via WhatsApp with an illustrated summary of the session and activities to be performed at home. In the WhatsApp sessions, in addition to the video with the exercises, participants received activities on PNE, such as crosswords or a link to a YouTube video (e.g. "What Is Pain Video" of the IMGinDC channel and recommended by Heathcote et al., (2019). Figure 19 shows illustrative pictures of the spaces provided by schools for the intervention and Figure 20 a general diagram of the intervention program. Please see Table 43 and attachments for details on the exercise plus PNE intervention.

Figure 19. Illustrative pictures of the spaces provided by schools for intervention.

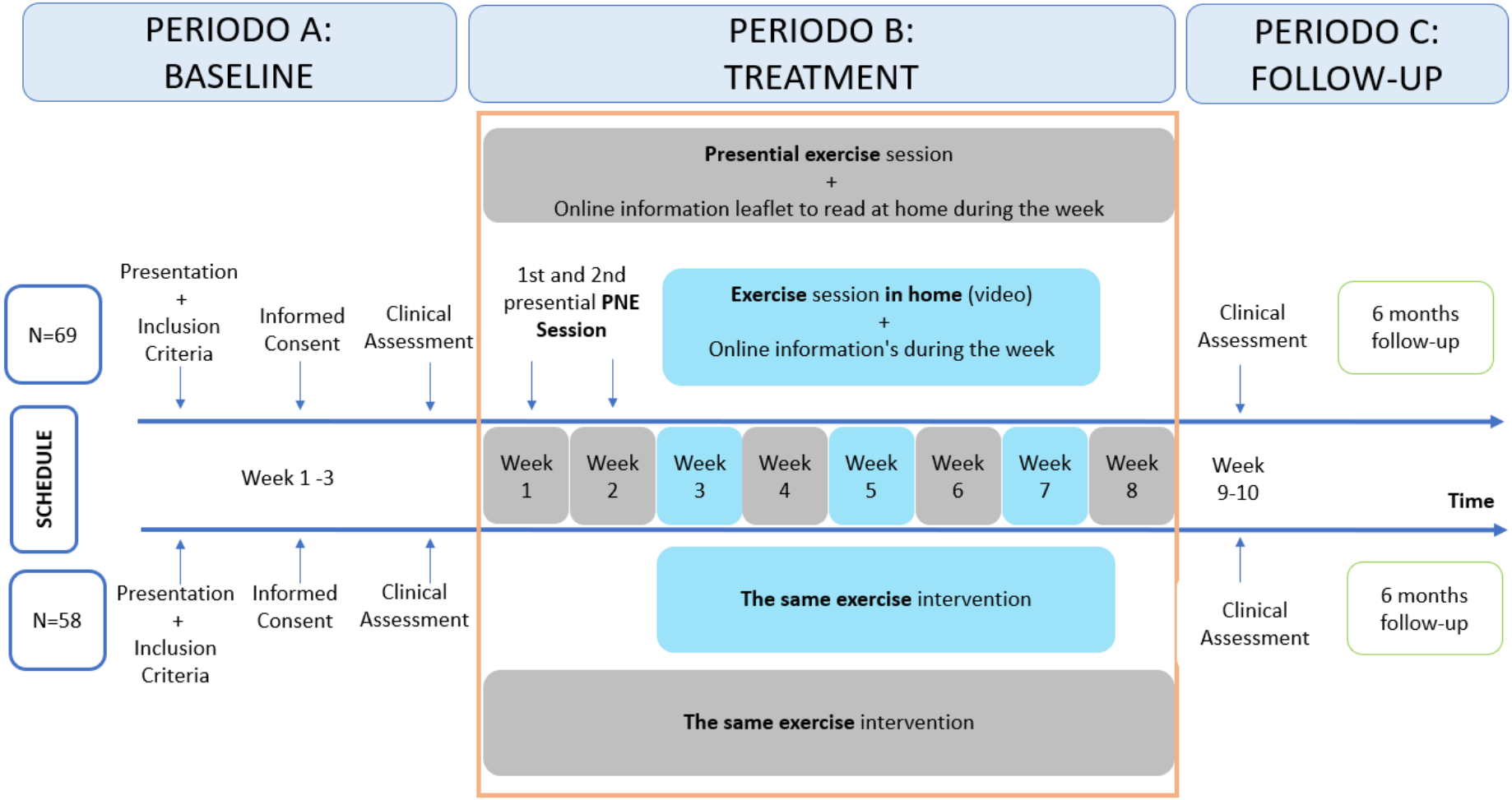


Figure 20. Illustrative diagram of the intervention program.

8.3. Data analysis

Participants' characteristics at baseline were summarized using descriptive statistics, including counts (n), and percentages (%) for categorical variables and mean and SD for continuous variables. Differences between groups (exercise versus exercise plus PNE) at baseline were explored using S*tudent's t-tests* for continuous data and *chi-square* tests for categorical data. Mann-Whitney tests were also performed when the normality of the data was not verified. However, nonparametric statistics corroborated the parametric, so, the parametric results were reported. The intention-to-treat principle was used in the data analysis. The main analyses, to assess the between-group differences in response to the interventions for variables pain intensity, disability, quality of sleep, catastrophizing, fear of movement, self-efficacy, symptoms of central sensitization, and knowledge on pain neuroscience were performed using *random coefficient linear mixed models.* The model included treatment (exercise versus exercise plus PNE), time (3 measurement points: i) baseline, ii) post-intervention and iii) 6-month follow-up), treatment by time and baseline values as fixed effects, and subject and time as a random effect, using an AR1 covariance structure. This model was selected because it obtained a better Akaike's Information Criterion (AIC) value. For the primary variable (pain intensity) and one of the secondary variables (disability) were performed a sensitivity analysis using the main analysis model: 1) without adjusting to the baseline values of the variable; 2) adjusting to sex, age, and Body Mass Index; and 3) using a complete-cases analysis. The residuals' normality was verified by visual inspection of QQ plot. For the muscle tests and Pressure Pain Threshold, the same analysis model was used but only with 2-time assessment points (baseline and post-intervention). Furthermore, the analysis of these functional variables was performed only with data from participants (n=33) who were not interrupted by the mandatory confinement due to the SARS-CoV-2 pandemic. Effect sizes were

calculated between baseline to post-intervention and baseline to 6-month follow-up, in each of the intervention groups, using the *Partial Eta Square* (*Partial eta²)* calculated from a one-way repeated-measures ANOVA. *Partial eta²* was interpreted as a very high effect (>0.5), high effect (0.25-0.5), medium effect (0.05-0.25), and small effect (≤0.05) (Cohen, 1988). All data analyses were conducted using SPSS software, version 22.0. The significance level was set at $p<0.05$ for all statistical analyses.

8.4. Results

This study took place between September 2019 and October 2020. Of 203 adolescents screened for eligibility, 127 (62.6%) met the inclusion criteria and accepted to enter the study (Figure 21). After randomization, 59 participants were allocated to the exercise group and 68 participants were allocated to the exercise plus PNE group. Forty (67.8%) and 42 (61.8%) participants in the exercise-only group and the exercise plus PNE group, received 5 face-to-face intervention sessions, respectively. The response rate at post-intervention and after 6-month follow-up was 98.3% and 94.9% in the exercise group and 88.2% and 89.7% in the exercise plus PNE group. At baseline, no between-group differences were found for sociodemographic characteristics or outcome measures (Table 45).

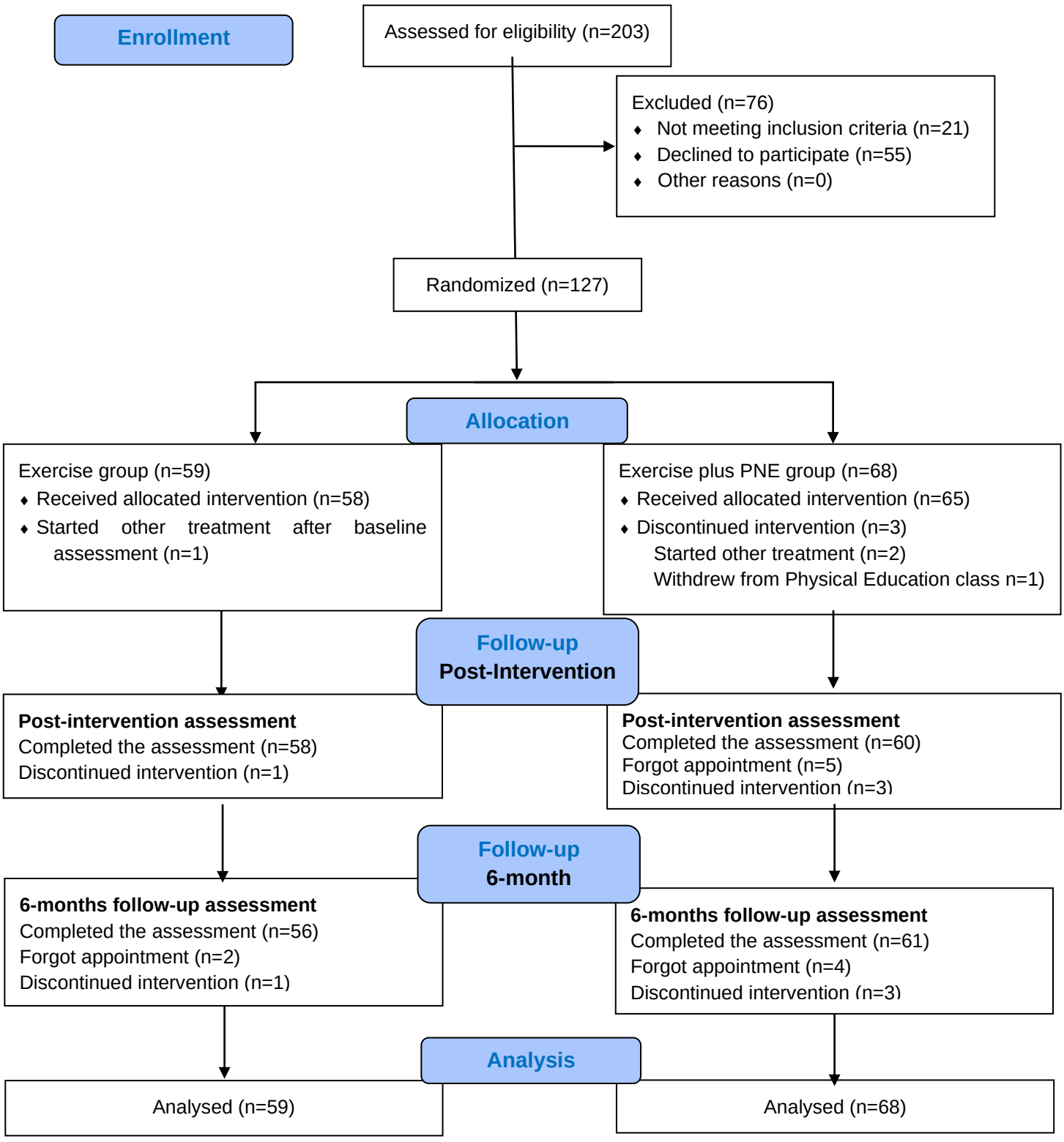


Figure 21. CONSORT Flow Diagram.

8.4.1. Pain intensity

There was a significant decrease in pain intensity from baseline to post-intervention and from baseline to follow-up in both groups (F(2;242.65)=87.84; *p*<0.001), but no between-group differences (F(1;123.38)=0.69; *p*=0.41), nor interaction between time and groups (F(2;242.65)=0.23; *p*=0.79) (Tables 46 and 47; Figure 22). Sensitivity analyses performed for the primary outcome resulted in findings similar to the main analysis (Table 46).

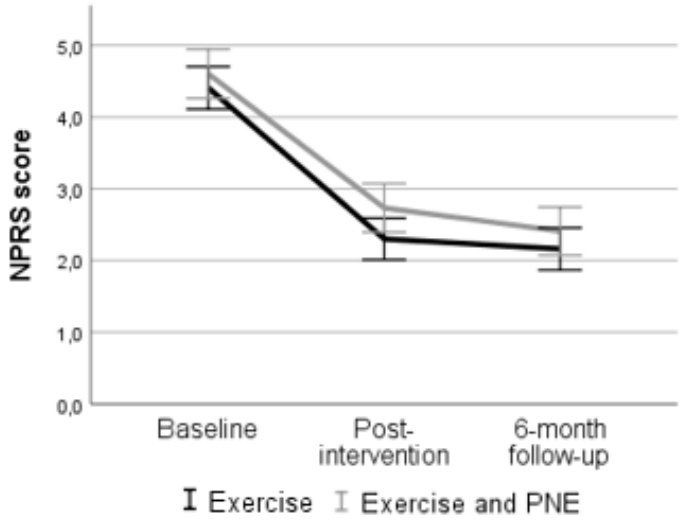


Figure 22. Predictive mean values for pain intensity, for both intervention groups.

8.4.2. Disability

There was a significant decrease in disability from baseline to post-intervention and from baseline to follow-up in both groups (F(2;414.88)=40.99; *p*<0.001), but no between-group differences (F(1;2616.03)=0.27; *p*=0.61), nor the interaction between time and groups (F(2;414.88)=2.51; *p*=0.08) (Tables 46 and 47; Figure 23). Sensitivity analyses performed for this secondary outcome resulted in findings similar to the main analysis (Table 46).

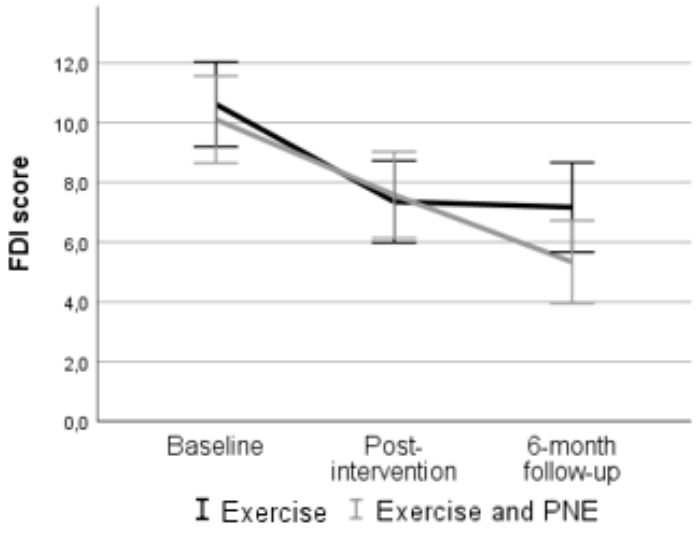


Figure 23. Predicted mean values for disability, for both intervention groups.

8.4.3. Sleep, psychosocial variables and symptoms of central sensitization

There was a significant improvement in quality of sleep ($F(2;245.86)=3.25$; $p<0.05$) and self-efficacy ($F(2;416.11)=8.83$; $p<0.001$), and a significant decrease in catastrophizing ($F(2;392.19)=18.99$; $p<0.001$), fear-of-movement ($F(2;413.62)=24.13$; $p<0.001$) and symptoms of central sensitization ($F(2;407.67)=19.06$; $p<0.001$), from baseline to post-intervention and from baseline to follow-up in both groups, but no between-group differences, nor interaction between time and groups (Tables 47 and 48; Figure 24).

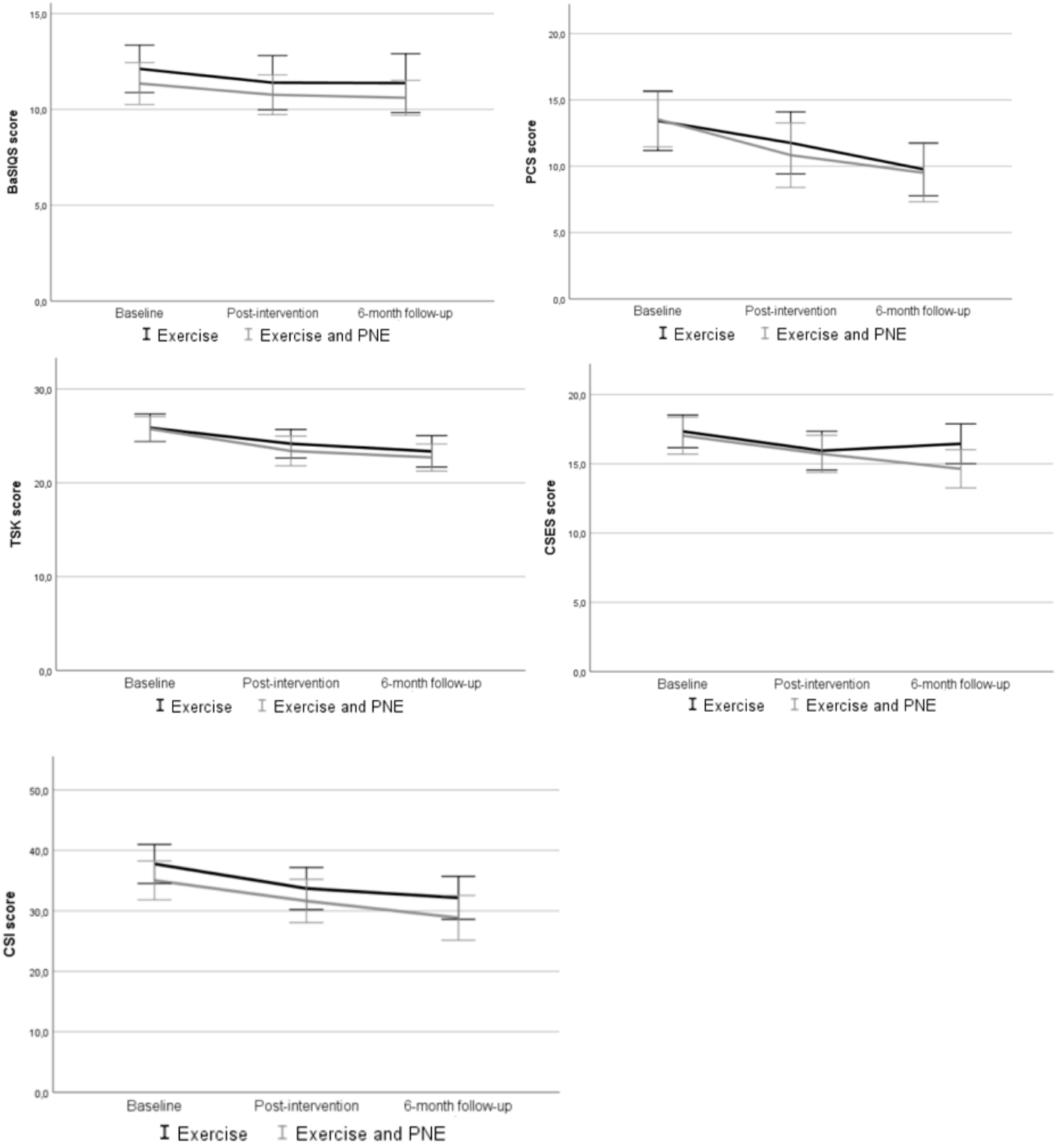


Figure 24. Predicted mean values for sleep (BaSIQS score), catastrophizing (PCS score), fear of movement (TSK score), self-efficacy (CSES score), and symptoms of central sensitization (CSI score), for both intervention groups.

8.4.4. Knowledge about pain neuroscience

The exercise plus PNE group showed a significant increase in the knowledge about pain neuroscience (F(2;241.12)=48.23; *p*<0.001) compared to the exercise group from baseline to post-intervention and from baseline to follow-up (Tables 47 and 48). For this outcome, there was statistical differences between groups (F(1;121.10)=60.23; *p*<0.001) and also, the interaction between time and groups was significant (F(2;241.12)=35.17; *p*<0.001), favourable for the exercise plus PNE group (Figure 25).

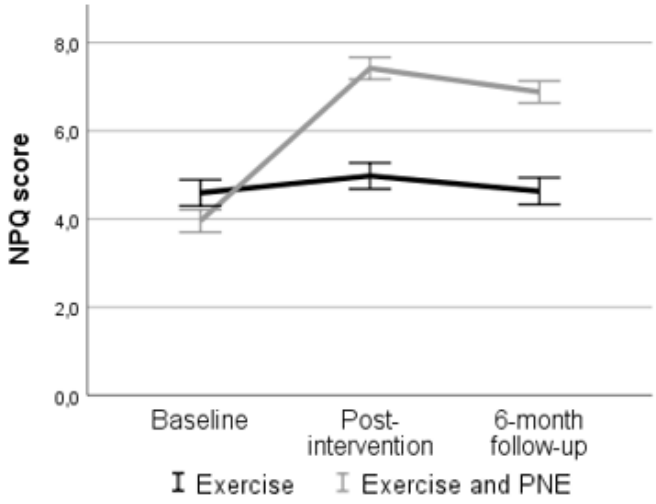


Figure 25. Predicted mean values for knowledge on pain neuroscience, for both intervention groups.

8.4.5. Pressure Pain Threshold and muscle endurance

There was a significant increase in PPT from baseline to post-intervention for the right pilar C5-C6 (F(1;64.60)=144.98; *p*<0.001), left articular pillar C5-C6 (F(1;64.64)=175.30; *p*<0.001) and tibialis anterior (F(1;127.00)=119.24; *p*<0.001) in both groups, but a significant between group difference (F(1;63.38)=5.71; *p*<0.05) and its corresponding interaction between time and group (F(1;64.64)=7.43; *p*<0.05) only for the left articular pillar C5-C6, with the exercise group showing higher increases in

PPT. There was also a significant increase in neck flexors (F(1;64.64)=150.14; *p*<0.001), neck extensors (F(1;64.60)=190.64; *p*<0.001) and scapular stabilizers (F(1;64.63)=67.22; *p*<0.001) in both groups, but no between group differences, nor interaction between time and groups (Table 49; Figure 26 and 27). For both groups, the effect size was very high for all PPT and muscle tests (*Partial eta*²=1).

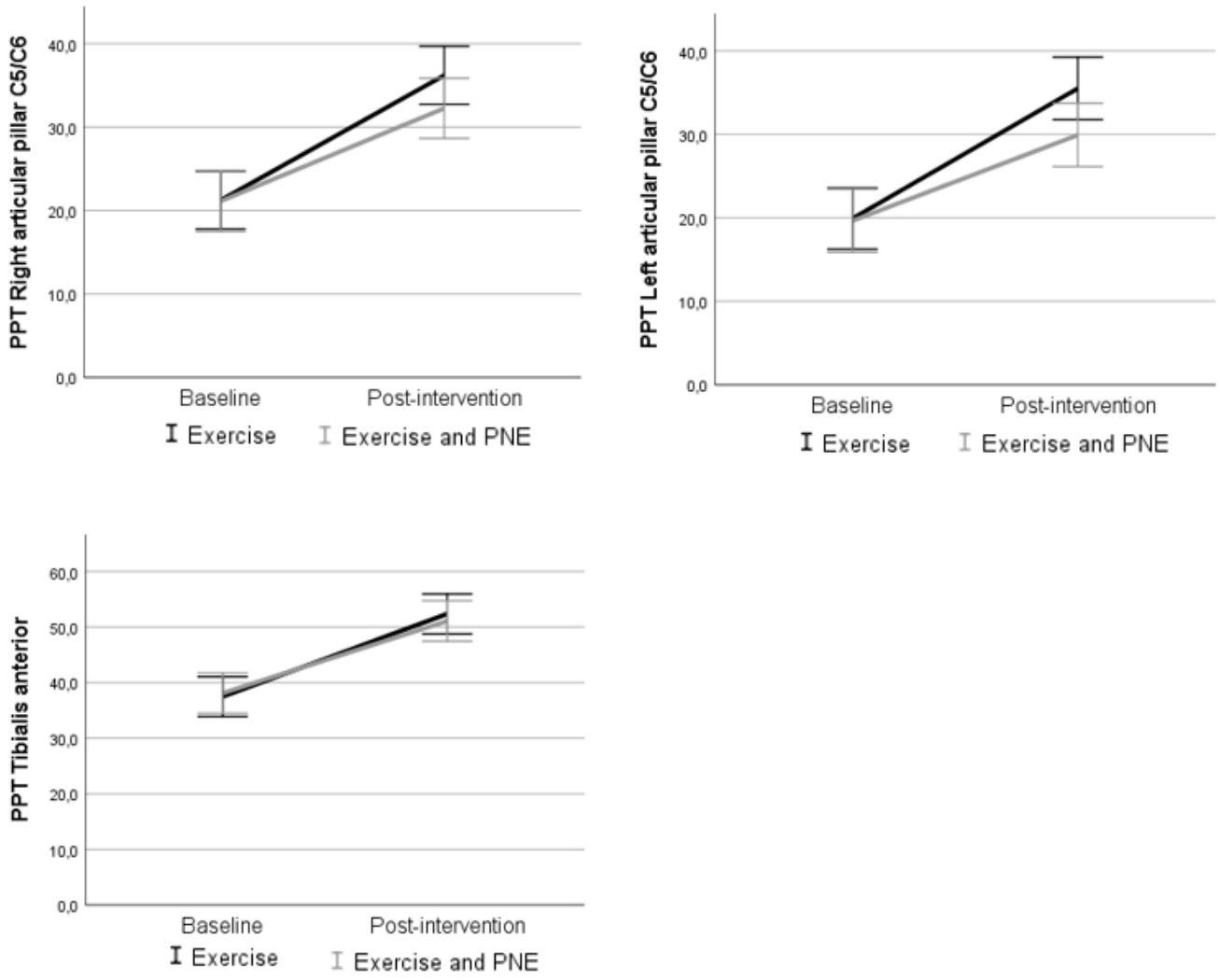


Figure 26. Predicted mean values of the pressure pain thresholds.

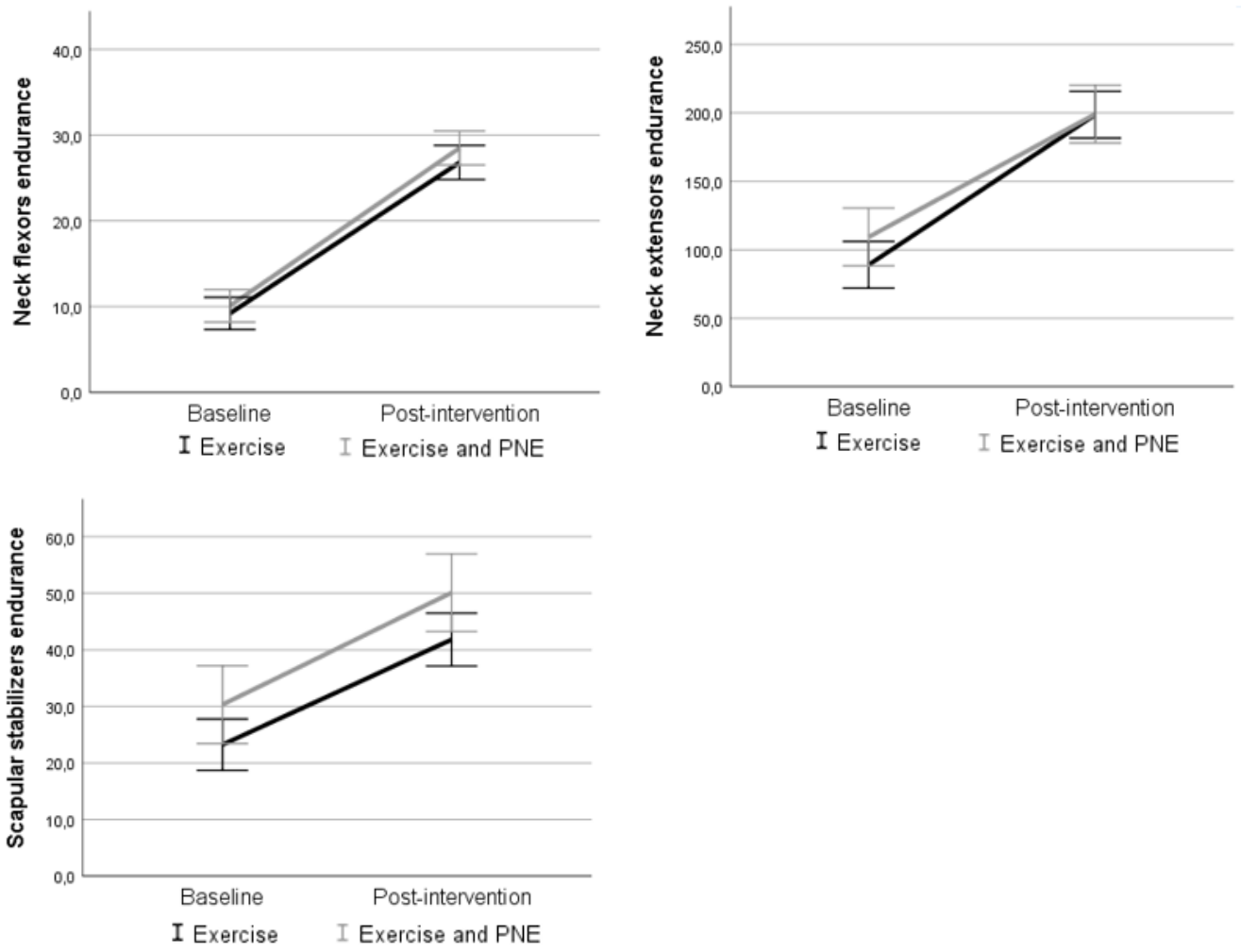


Figure 27. Predicted mean values of the muscle endurance tests.

8.4.6. Patient's Global Impression of Change

At post-intervention, 79.3% of the participants in the exercise group and 75% of the participants in the exercise plus PNE group reported being moderately better, better, or a great deal better. These percentages were similar at the 6-month follow-up (Table 50).

Supplementary Tables 51 and 52 show the unadjusted mean values (±SD) for each group at baseline, post-intervention, and 6-month follow-up.

8.5. Discussion

This randomized controlled study is the first to compare the effectiveness of a blended-learning intervention using exercise plus PNE versus exercise only in adolescents with NP. The findings suggest that both interventions reduce to a similar extend pain intensity, disability, catastrophizing, fear of movement, and symptoms of central sensitization and increase sleep quality, self-efficacy, PPT in the right articular pillar C5-C6 and tibialis anterior, and endurance of neck and scapulothoracic muscles, in the short term and at 6-month follow-up. Statistical differences between groups were found only for knowledge about pain neuroscience and PPT at the left articular pillar of C5-C6. Furthermore, the gains at post-intervention were maintained at 6-month follow-up.

In this study, baseline mean pain intensity was low, but the percentage of reduction was 47.4% and 50.6% in the exercise group and 41.5% and 48.8% in the exercise plus PNE group at post-intervention and at 6-month follow-up, respectively, suggesting that the statistically significant decreases in pain intensity were also clinically relevant. Andias et al. (2018) reported similar percentages of pain intensity reduction at post-intervention in a group of adolescents with NP receiving exercise and PNE for 4 weeks. Pack et al. (2018) also found a decrease in the Numeric Pain Rating Scale of 50% in adolescents with a central sensitization syndrome treated with 4-weeks of PNE and gradual exposure activity. None of the studies found in adolescents conducted a follow-up assessment. According to Hirschfeld et al. (2014), in adolescents with head, back/extremities, and abdominal chronic pain, changes of 1 point on Numeric Pain Rating Scale, or percent changes of 12.5%, should be considered clinically meaningful. Moreover, the high percentage of adolescents who reported a Patient's Global Impression of Change score of 5 or more in the present study reinforces the clinical relevance of our results.

Regarding disability, the mean decrease from baseline to post-intervention and 6-month follow-up was higher than the SEM of 2.50 but lower than the SDC of 6.93 (Andias & Silva, 2019a), raising doubts regarding its clinical relevance. Similarly, the mean increase in self-efficacy from baseline to 6months (-2.07, 95% CI: -2.59; -1.55) in the exercise plus PNE group reached a value close to the SEM of 2.49 for the CSES (Andias & Silva, 2020b), but lower than the SDC of 6.9. However, at 6-month follow-up, there is a trend towards a continuing decrease in pain disability and an increase in self-efficacy, particularly in the exercise plus PNE group as suggests the larger effect size. This might indicate that in the long-term this decrease in disability and the increase in self-efficacy might reach clinically relevant levels in this group. These findings might be related to the acquired knowledge of pain neuroscience. PNE aims to help individuals with pain to use their knowledge and set of strategies provided during PNE in pain self-management, promoting the retraining of their relationship with pain, triggering changes in their behaviors, and breaking the vicious cycle of fear-avoidance pain over time (Robins et al., 2016). Previous studies in adults with chronic pain have reported a positive effect of PNE in reducing disability for up to 1-year follow-up (Beltran-Alacreu, López-de-Uralde-Villanueva, Fernández-Carnero, & La Touche, 2015; Werner, Storheim, Lochting, Wisloff, & Grotle, 2016). However, the long-term impact of PNE remains to be investigated in future studies with longer follow-ups.

These study findings are also in line with previous studies on what refers to sleep quality, catastrophizing, and fear of movement. A systematic review synthesizing studies that assessed the influence of exercise on sleep concluded that exercise promotes increased sleep quality and duration (Dolezal, Neufeld, Boland, Martin, & Cooper, 2017). Andias et al. (2018) reported a decrease in catastrophizing from moderate catastrophizing (20.2 ± 10.3) to borderline low catastrophizing (14.1±11.2), after 4 weeks of exercise and PNE in adolescents with NP. Although no studies have

been found in adolescents for fear of movement, studies in adults with chronic musculoskeletal pain have reported a decrease with interventions based on exercise and PNE (Galan-Martin et al., 2020; Malfliet, Kregel, Meeus, Roussel, et al., 2018).

Contrary to what we expected, both groups reduced catastrophizing and fear of movement levels, symptoms of central sensitization, and improved sleep, similarly. The low scores of these variables at baseline may have contributed to the absence of differences between groups. Previously, it has been reported that PNE may be more effective in patients with high self-reported symptoms of central sensitization (Malfliet, Kregel, Meeus, Danneels, et al., 2018). To our knowledge, there are no intervention studies that have assessed the impact of any intervention on the Central Sensitization Inventory scores in children or adolescents. The mean decrease in both groups was higher than the SEM of 4.15 points but did not reach the SDC of 11.50 points (Andias & Silva, 2020a).

An increase in PPT of 15% has been reported as being clinically relevant in adults (Malfliet, Kregel, Coppieters, et al., 2018). To our knowledge, no values have been reported for adolescents, but both groups reached increases higher than 15%. Only one study, in children with abdominal pain, reported lower local pressure pain thresholds at 3-weeks after interventions of PNE and hypnotherapy (Pas et al., 2020). It should be noted that although statistical differences between groups were found for the PPT at the left articular pillar of C5-C6, considering that there were no differences for the contralateral side, a type I error may be present. Despite differences in the dose of exercise, both groups improved neck and scapular stabilizers' muscle endurance to an extent that was higher than the SEM found in previous studies (Oliveira & Silva, 2016), but lower than the SDC. For adults with NP, strength or endurance interventions need to be of a minimum 6-week duration, 2 to 3 times a week (Ferro Moura Franco et al., 2021). No indications were found for adolescents. Considering the blended-learning

format of the intervention, we were unable to control the adolescents' adherence to the exercise program at home. However, the increases were in line with a previous study in adolescents with NP with face-to-face sessions (Andias et al., 2018).

8.5.1. Clinical implications

Our findings support the design of interventions based on exercise or exercise plus PNE for the management of chronic NP in adolescents implemented at the school setting and using a blended-learning format. This was a low resource demanding intervention that can reach virtually all adolescents with NP as school attendance till 18 years is compulsory. Furthermore, the results of this study also suggest that similar interventions might be implemented to other painful syndromes.

8.5.2. Strengths, limitations, and further research

Study strengths include the sample size and few dropouts from baseline to post-intervention and follow-up. The results of the Neurophysiology Pain Questionnaire suggest that there was no contamination between groups regarding PNE. Some limitations should also be considered. The different number of face-to-face sessions within and between groups. However, as reported previously, it does not seem to have had a negative impact on results. Although depression, anxiety, and stress were also reported in Chapter 5 as being relevant to disability in adolescents with NP, which in turn was associated with disability at 6 months, the assessment of these variables was not included in this randomized controlled trial. The reduced number of schools used is likely to have decreased the heterogeneity of students, so some caution is needed when generalizing the study results. The assessor was not blinded to the study group. However, we believe that this had a negligible impact on results, particularly for the patient-reported outcomes as data was collected through an online questionnaire administered in the absence of the assessor (at post-intervention and 6-month follow-

up participants filled the questionnaires at home). Future research should consider comparing the impact of these two interventions for longer follow-up periods and into adulthood and for other painful conditions.

8.6. Conclusion

This study findings suggest that interventions based on exercise and exercise plus PNE, delivered at the school setting in a blended-learning format reduced pain intensity, disability, catastrophizing, fear of movement, symptoms of central sensitization and increased sleep quality, self-efficacy, PPTs, and endurance of neck and scapulothoracic muscles, at post-intervention and 6-month follow-up, in adolescents with NP. The addition of PNE to exercise seems to accentuate a trend towards the continued improvement of disability and self-efficacy from post-intervention to 6-month follow-up, but these differences were not significant. Future studies should compare these two interventions for longer follow-ups.

Table 42. Global structure of the exercise program.

Exercise session	**Intensity**	**In between sessions resources sent via WhatsApp**
Session 1 /week 1 (**Face-to-face)**		
-Initial presentation of the participants and introduction to the program -Explanation of the general benefits of exercise (e.g., promotion of functionality and sense of well-being) and Modified Borg Scale -Exercise program	2-3 sets of 8-12 repetitions (with contraction times of 3-5 seconds)	-Pictures of home exercises sent via WhatsApp -Two weekly reminders, to reinforce the importance of performing exercises at home, via WhatsApp
Session 2 / week 2 (**Face-to-face)**		
-Exercise program -Final reminder that the next session is at home with the support of a video sent via WhatsApp.	2-3 sets of 8-12 repetitions (with contraction times of 3-5 seconds)	-Pictures of home exercises sent via WhatsApp -Two weekly reminders, to reinforce the importance of performing exercises at home, via WhatsApp
Session 3 / week 3 (**WhatsApp**)		
-A video with a maximum 5 minutes duration, in which the physiotherapist showed how to perform the exercises -In the end, the video finished with some practical strategies for participants' to include the exercises in their daily routines	2-3 sets of 8-12 repetitions to 3-5 sets of 8-12 repetitions (with contraction time of at least 10 seconds)	-Two weekly reminders, to reinforce the importance of performing exercises at home, via WhatsApp
Session 4 / week 4 (**Face-to-face or WhatsApp)**		
Face to face -Exercise program, which finished with final relaxation -Final reminder that the next session is at home with the support of a video sent via WhatsApp. WhatsApp -A video with a maximum 5 minutes duration, in which the physiotherapist showed how to perform the exercises	2-3 sets of 8-12 repetitions to 3-5 sets of 8-12 repetitions (with contraction time of at least 10 seconds)	-Two weekly reminders, to reinforce the importance of performing exercises at home, via WhatsApp
Session 5 / week 5 (**WhatsApp)**		
- A video with a maximum 5 minutes duration, in which the physiotherapist showed how to perform the exercises - In the end, the video finished with some general back mobility and stretching exercises for participants' daily routines	3-5 sets of 8-12 repetitions (with contraction time of at least 10 seconds)	-Two weekly reminders, to reinforce the importance of performing exercises at home, via WhatsApp

Session 6 / week 6 (**Face-to-face or WhatsApp)**		
Face to face -Exercise program -Final reminder that the next session is at home with the support of a video sent via WhatsApp. WhatsApp - A video with a maximum 5 minutes duration, in which the physiotherapist showed how to perform the exercises	3-5 sets of 8-12 repetitions (with contraction time of at least 10 seconds)	-Two weekly reminders, to reinforce the importance of performing exercises at home, via WhatsApp
Session 7 / week 7 (**WhatsApp)**		
-A video with a maximum 5 minutes duration, in which the physiotherapist showed how to perform the exercises -In the end, the video finished with some practical strategies for participants' to include the exercises in their daily routines	3-5 sets of 8-12 repetitions (with contraction time of at least 10 seconds)	-Two weekly reminders, to reinforce the importance of performing exercises at home, via WhatsApp
Session 8 / week 8 (**Face-to-face or WhatsApp)**		
Face to face -Final considerations of the program -Exercise program, which finished with final relaxation WhatsApp - A video with a maximum 5 minutes duration, in which the physiotherapist showed how to perform the exercises -Final considerations of the program	3-5 sets of 8-12 repetitions (with contraction time of at least 10 seconds)	-Two weekly reminders, to reinforce the importance of performing exercises at home, via WhatsApp

Table 43. Detailed description of PNE topics, activities and materials.

Session	**Type**	**Topics**	**Duration** (minutes)	**Material/Strategies used (examples)**
1	In group at school	Introduction to the program	5	
		Assessment of patients' beliefs towards pain - Concept of "Pain is normal"	5	Questions to participants
		Acute pain processing	10	Diagrams/ images/metaphors Video: https://www.youtube.com/watch?v=PMZdkac4YLk-
		Concept of chronic pain and the role of peripheral and central sensitization	10	Diagrams/ images/metaphors
		Importance of the exercise	5	Scheme "Fear-avoidance cycle"
		Student perceptions about exercise		
		Indications for home exercise session 1 and explanation of the use of Modified Borg Scale	5	Booklet online sent via WhatsApp (Explanation of the video with instructions for home exercises Explanation of the diary of exercise
	Homework	Activity 1: Participants were invited to explain the neck discomfort process, considering what they learned in the session. Activity 2: Perform the exercises at home		Activity 1 was sent via WhatsApp. A weekly reminder was sent for the exercise.
2	In group at school	Clarification of doubts and revision concepts	5	
		Pain neuromatrix	5	Diagrams/ images
		Pain modulation: the role of cognitions in pain (depression, anxiety, stress, fear and catastrophizing)	10	Images/ -"Lion metaphor"
		The role of the sleep	5	
		Reinforcement of the importance of the self-efficacy and exercise	15	Booklet online sent via WhatsApp
		Exercise session 2		
		Indications for session 3 in home	5	Diary of exercise
	Homework	Activity 1: Participants were invited to explore their sleep routines. Activity 2: Perform the exercises at home		Activity 1 was sent via WhatsApp. A weekly reminder was sent for the exercise.
3	Individual at home	Exercise session 3	20	Video with instructions Diary of exercise
	Homework	Activity 1: Participants were invited to view the video sent by the researchers via WhatsApp. Activity 2: Perform the exercises at home		Video "What Is Pain Video": https://www.youtube.com/watch?v=GF2xhUKxzxY A weekly reminder will be sent for the exercise.
4	In group at school	Clarification of doubts and revision concepts	5	Questions of the Pain Neurophysiology Questionnaire (version 12 items)

		Others strategies to help to control pain/retraining pain memories: relaxation/ breathing techniques, sleep strategies, emotional control, do things to stay positive	10	Highlight strategies
		Exercise session 4	25	Booklet online sent via WhatsApp Diary of exercise
		Reinforcement of the importance of the exercise during the week		
	Homework	Activity 1: Participants were invited to comment the phrase "The pain in my neck is related to any changes that I have in my bones or muscles and so I can't move it" Activity 2:Perform the exercises at home		Activity 1 was sent via WhatsApp. A weekly reminder was sent for the exercise.
5	Individual at home	Exercise session 5	20	Video with instructions Diary of exercise
	Homework	Activity 1: Participants were invited to answer 6 True / False questions about pain neuroscience on google docs Activity 2: Perform the exercises at home		Activity 1 was sent via WhatsApp. A weekly reminder was sent for the exercise.
6	In group at school	Clarification of doubts and highlights of neuroscience of pain	10	Questions of the Pain Neurophysiology Questionnaire Possibility to show part of the video "The mysterious science of pain"
		Exercise session 6	30	Diary of exercise
	Homework	Activity 1: Participants were invited to found 6 cross words Activity 2: Perform the exercises at home		Activity 1 was sent via WhatsApp A weekly reminder was sent for the exercise.
7	Individual at home	Exercise session 7	20	Video with instructions Diary of exercise
	Homework	Activity 1: Participants were invited to view the video sent by the researchers via WhatsApp. Activity 2: Perform the exercises at home		Video: https://www.youtube.com/watch?v=e9BhNbluM6M A weekly reminder was sent for the exercise.
8	In group at school	Exercise session 8	30	
		Summary of key-points	10	Questions of the Pain Neurophysiology Questionnaire
		Program conclusion		

Table 44. Brief description of the specific exercises included in each of the 3 parts of the exercise program (warm-up, neck, and shoulder exercises and cool-down).

	Exercises	Intensity
Example of exercises used across sessions for warm-up		
Global warm-up exercises	• Jump rope (skipping rope interspersing support leg, double leg rope skipping, double leg rope skipping with higher speed, skipping rope with double leg while walking 10 meters) • Lateral and front jumping jacks • Partner wheelbarrow- 10-meter walk (*) • Walking back and forth with the upper limbs, in prone position, with a gymnastic ball under the hips region and both hands on the floor • Cat-cow spinal movement exercise • ROM neck exercises (flexion, extension, lateral flexion and rotation) and shoulder ROM exercises (elevation/depression, circumduction)	2 sets of 10 reps (*) 2-3 sets
Example of neck and shoulder specific exercises used across sessions		
Deep neck flexors	Individual exercises • Students lying supine on a mattress were asked to perform craniocervical flexion and hold this position for a few seconds Progression to: o While keeping craniocervical flexion raise the head from the mattress; o While keeping craniocervical flexion, raise the head from the mattress and perform diaphragmatic breathing; o While keeping craniocervical flexion, raise the head from the mattress and perform flexion and extension of each lower limb alternately; o While keeping craniocervical flexion, raise the head from the mattress and perform circumduction of each upper limb or pass an object from one hand to the other. • Students supine lying with both feet on the ground, the trunk/hip supported on a gymnastic ball and the neck unsupported were instructed to perform craniocervical flexion Progression to: o While keeping craniocervical flexion, perform flexion and extension of each upper limb alternately	2-3 sets of 8-12 repetitions to 3-5 sets of 8-12 repetitions Contraction times of 3-5 seconds to contraction times of at least 10 seconds
Deep neck extensors	Individual exercises • Craniocervical flexion-extension and rotation up to approximately 40º in a quadruped position • Students in a standing position, with head and back against a wall, were instructed to slowly walk forward while keeping the head against the wall • Similar to previous exercise but with a ball in between the students head and the wall • In a standing position, with shoulders and elbows at 90º flexion hold the theraband around the head and extend the	2-3 sets of 8-12 repetitions to 3-5 sets of 8-12 repetitions Contraction times of 3-5 seconds to contraction

	neck against theraband resistance	times of at least 10 seconds
Scapular stabilizers	Individual exercises • With both hands against the wall, elbows extended and shoulders at 90º flexion perform retraction and protraction of the shoulder girdle • Students in a standing position were instructed to hold a theraband in both hands, with elbows flexed at 90º and perform external rotation of both shoulders simultaneously • In a quadruped position, students were instructed to fix the theraband with one hand, while performing a horizontal shoulder abduction with the other against the theraband resistance • Push-ups on the wall Progression to: o Push-ups on a table (body inclination of 45º) o Push-ups on the floor o Push-ups on the floor with lateral walking with both hands and feet o Push-ups on a gymnastic ball	2-3 sets of 8-12 repetitions to 3-5 sets of 8-12 repetitions Contraction times of 3-5 seconds to contraction times of at least 10 seconds
Exercises targeting both neck and shoulder muscles	Competition between pairs • Walking around the room with a book on the top of the head for as long as possible • Walking in pairs, back against back, holding a small ball in between the back of the heads, back straight and hips and knees flexed • Two students positioned themselves face-to-face in standing, with the trunk tilted forward, arms extended, were instructed to maintain a plank position using each others' hands for support as long as possible • Two students were instructed to position themselves in a plank position with their hands on the floor, face-to-face, and alternately to raise one hand and touch each other's hands (competition between pairs) Individual exercises • Students lying down on a mattress in a prone position, shoulders at 90º abduction, elbows at 90º flexion, were instructed to raise the head, the upper limbs and the upper part of the trunk from the ground Progression to: o raise the head, the upper limbs and the upper part of the trunk from the ground while semi-extend the elbows in front in a first phase, and fully extend the elbows in a second phase • Students lying down on a mattress in supine position, feet on the floor, hips and knees at 45º flexion, and head resting on a book, were instructed to perform craniocervical flexion and press their head against the book while performing circular movements with the upper limbs Progression to: o While keeping craniocervical flexion and pressing the head against the book, perform scapular retraction	2-3 sets of 8-12 repetitions to 3-5 sets of 8-12 repetitions Contraction times of 3-5 seconds to contraction times of at least 10 seconds

	and protraction with the shoulders at 90º flexion • Students in a prone position with both hands on the ground and the hips supported on a gymnastic ball, were instructed to perform craniocervical flexion-extension and rotation up to approximately 40º • Students lying down in a supine position, with lower feet on the floor and hip and knees at 45º flexion, head resting on a semi-empty ball and in craniocervical flexion, were instructed to perform a bridge or semi-bridge • Students in a standing position, facing a wall, holding a small ball with the front of the head against the wall and a theraband in both hands, with elbows flexed at 90º, were asked to perform external rotation of both shoulders while pressing the ball against the wall • Students in a standing position, with their back facing a wall, holding a small ball with the back of the head against the wall and with a theraband fixed on the foot and hand, were asked to perform shoulder abduction against theraband resistance while pressing the ball against the wall • Horizontal plank exercise Progression to: o Horizontal plank with lower limb movement: abduction/adduction or knee and hip flexion/extension	
Cooling-down		
Stretching exercises	• Neck stretching for anterior, posterior and lateral muscle groups (standing or sitting on a gymnastic ball) • Stretching for posterior muscles of the trunk and anterior, posterior and lateral muscle groups of the shoulders (standing or sitting on the gymnastic ball)	3 sets of 20-30 seconds for each stretch

Table 45. Characterization of adolescents with chronic NP at baseline.

Variables		**Exercise group** (N=59)	**Exercise plus PNE group** (N=68)	***p***
Sex (N, %)	Female	50 (84.7)	59 (86.8)	0.80
	Male	9 (15.3)	9 (13.2)	
Age (years)	Mean (SD)	15.85 (2.35)	16.24 (1.17)	0.23
BMI (Kg/m^2)	Mean (SD)	22.20 (3.39)	22.34 (4.55)	0.84
Scholar level (N, %)	10th	19 (32.2)	22 (32.4)	0.20
	11th	20 (33.9)	32 (47.1)	
	12th	20 (33.9)	14 (20.6)	
Areas of knowledge	Sciences	23	22	--
	Economics	6	12	
	Humanities	9	18	
	Arts	21	14	
	Informatics	0	2	
Pain duration (N, %)	3 to 6 months	15 (25.4)	16 (23.5)	0.89
	6 months to 1 year	11 (18.6)	13 (19.1)	
	1 to 2 years	20 (33.9)	21 (30.9)	
	2 to 5 years	9 (15.3)	15 (22.1)	
	> 5 years	4 (6.8)	3 (4.4)	
Pain frequency (N, %)	Rarely	6 (10.2)	11 (16.2)	0.68
	Sometimes	30 (50.8)	31 (45.6)	
	Often/Always	23 (39)	26 (38.3	
NPRS (0-10)	Mean (SD)	4.41 (1.68)	4.60 (2.02)	0.56
FDI (0-60)	Mean (SD)	10.61 (6.22)	10.10 (6.86)	0.67
BaSIQS (0-28)	Mean (SD)	12.12 (4.75)	11.35 (4.53)	0.36
PCS (0-52)	Mean (SD)	13.42 (8.61)	13.53 (8.55)	0.95
TSK (13-52)	Mean (SD)	25.86 (5.67)	25.75 (5.43)	0.91
CSES (7-35)	Mean (SD)	17.34 (4.53)	17.03 (5.50)	0.73
CSI (0-100)	Mean (SD)	37.76 (12.38)	35.04 (13.29)	0.24
NPQ (0-12)	Mean (SD)	4.59 (1.79)	3.96 (1.84)	0.05
PPT (N/cm2) Mean (SD)	Right articular pillar C5/C6	21.19 (10.02)	21.02 (10.10)	0.92
	Left articular pillar C5/C6	19.12 (9.62)	19.59 (9.72)	0.78
	Tibialis anterior	37.98 (14.52)	38.43 (13.42)	0.86
Endurance tests (seconds) Mean (SD)	Neck flexors	10.48 (5.91)	10.19 (6.12)	0.78
	Neck extensors	117.27 (73.19)	115.90 (75.66)	0.92
	Scapular stabilizers	30.48 (20.23)	36.22 (27.70)	0.19

SD, Standard Deviation; PNE, Pain Neuroscience Education; 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, Neurophysiology of Pain Questionnaire; PPT, Pressure Pain Thresholds.

Table 46. Pain intensity and disability - estimated marginal means and sensitivity analysis.

Variables	Exercise group			Exercise plus PNE group			Statistical results
	Baseline (n=59) Mean (95% CI)	**Post-Intervention (n=58)** Mean (95% CI)	**6Mo Follow-up (n=56)** Mean (95% CI	**Baseline (n=68)** Mean (95% CI	**Post-Intervention (n=60)** Mean (95% CI	**6Mo Follow-up (n=61)** Mean (95% CI	
NPRS* (0-10)	4.43 (4.03-4.84)	2.33 (1.91-2.74)	2.19 (1.76-2.62)	4.51 (4.13-4.88)	2.64 (2.23-3.04)	2.31 (1.90-2.73)	Group:*p*=0.41; Time:*p*<0.001 Group*Time: *p*=0.79 Baseline value: *p*<0.001
Sensitivity analysis[a]	4.41 (3.92-4.90)	2.30 (1.79-2.80)	2.16 (1.62-2.70)	4.60 (4.15-5.06)	2.68 (2.19-3.17)	2.38 (1.87-2.90)	Group:*p*=0.35; Time:*p*<0.001 Group*Time: *p*=0.86
Sensitivity analysis[b]	4.31 (3.85-4.77)	2.20 (1.74-2.66)	2.06 (1.58-2.53)	4.37 (3.93-4.80)	2.50 (2.04-2.95)	2.17 (1.70-2.64)	Group:*p*=0.44; Time:*p*<0.001 Group*Time: *p*=0.79 Baseline value: *p*<0.001 Sex: *p*=0.18; Age: *p*=0.90; BMI: *p*=0.97
Sensitivity analysis[c]	4.40 (4.00-4.80)	2.27 (1.87-2.68)	2.15 (1.72-2.57)	4.38 (3.99-4.77)	2.55 (2.15-2.95)	2.27 (1.86-2.69)	Group:*p*=0.56; Time:*p*<0.001 Group*Time: *p*=0.65 Baseline value: *p*<0.001
FDI* (0-60)	10.41 (9.30-11.52)	7.16 (6.03-8.28)	6.97 (5.79-8.15)	10.30 (9.27-11.34)	7.78 (6.68-8.88)	5.53 (4.40-6.66)	Group:*p*=0.61; Time:*p*<0.001 Group*Time: *p*=0.08 Baseline value: *p*<0.001
Sensitivity analysis[a]	10.61 (8.96-12.26)	7.36 (5.68-9.03)	7.13 (5.34-8.92)	10.10 (8.57-11.64)	7.60 (5.98-9.21)	5.37 (3.66-7.08)	Group:*p*=0.50; Time:*p*<0.001 Group*Time: *p*=0.20
Sensitivity analysis[b]	10.20 (8.92-11.48)	6.95 (5.67-8.22)	6.79 (5.46-8.12)	10.10 (8.88-11.32)	7.60 (6.33-8.87)	5.37 (4.05-6.68)	Group:*p*=0.63; Time:*p*<0.001 Group*Time: *p*=0.08 Baseline value: *p*<0.001 Sex: *p*=0.55; Age: *p*=0.93; BMI: *p*=0.21
Sensitivity analysis[c]	10.39 (9.23-11.56)	7.36 (6.19-8.53)	7.02 (5.81-8.23)	10.28 (9.13-11.42)	7.65 (6.50-8.81)	5.45 (4.26-6.64)	Group:*p*=0.47; Time:*p*<0.001 Group*Time: *p*=0.13 Baseline value: *p*<0.001

CI, Confidence Interval; Mo, Months; PNE, Pain Neuroscience Education; NPRS; Numeric Pain Rating Scale; FDI, Functional Disability Inventory

* Linear mixed model including treatment (exercise and exercise plus PNE), time (baseline, post-intervention and 6-month follow-up) and treatment x time as fixed effects, baseline as covariate (fixed effects), and subject and time as random effect.

[a] Linear mixed model including treatment (exercise and exercise plus PNE), time (baseline, post-intervention and 6-month follow-up) and treatment x time as fixed effects, and subject and time as random effect.
[b] Linear mixed model including treatment (exercise and exercise plus PNE), time (baseline, post-intervention and 6-month follow-up) and treatment x time as fixed effects, baseline values, sex, age and Body Mass Index as covariate (fixed effects), and subject and time as random effect.
[c] Complete-cases analysis based on linear mixed model analysis of data from those who completed all three assessments. Linear mixed model including treatment (exercise and exercise plus PNE), time (baseline, post-intervention and 6-month follow-up) and treatment x time as fixed effects, baseline values as covariate (fixed effects), and subject and time as random effect.

Table 47. Values of *partial eta square* between baseline and post-intervention and between baseline and 6-month follow-up using the predictive values of the linear mixed model.

Variables	**Exercise group**		**Exercise plus PNE group**	
	Baseline to Post-intervention	Baseline to 6Mo Follow-up	Baseline to Post-intervention	Baseline to 6Mo Follow-up
NPRS (0-10)	0.99	0.98	0.99	0.98
FDI (0-60)	0.66	0.67	0.52	0.83
BaSIQS (0-28)	0.71	0.52	0.39	0.51
PCS (0-52)	0.98	0.99	0.99	0.99
TSK (13-52)	0.41	0.56	0.57	0.61
CSES (7-35)	0.32	0.18	0.22	0.49
CSI (0-100)	1.00	1.00	1.00	1.00
NPQ (0-12)	0.82	0.02	1.00	0.99

Mo, Months; PNE, Pain Neuroscience Education; 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, Neurophysiology of Pain Questionnaire.

Table 48. Sleep, psychosocial variables, symptoms of central sensitization and knowledge about pain neuroscience – estimated marginal means adjusted for the baseline values.

Variables	Exercise group			Exercise plus PNE group			Statistical results
	Baseline (n=59) Mean (95% CI)	**Post-Intervention (n=58)** Mean (95% CI)	**6Mo Follow-up (n=56)** Mean (95% CI)	**Baseline (n=68)** Mean (95% CI)	**Post-Intervention (n=60)** Mean (95% CI)	**6Mo Follow-up (n=61)** Mean (95% CI)	
BaSIQS (0-28)	11.73 (11.07-12.40)	11.00 (10.31-11.68)	10.98 (10.26-11.70)	11.62 (11.00-12.24)	11.23 (10.56-11.90)	10.97 (10.28-11.66)	Group: p=0.92; Time: p=0.04 Group*Time: p=0.82
PCS (0-52)	13.46 (12.07-14.85)	11.67 (10.25-13.08)	9.66 (8.21-11.11)	13.49 (12.20-14.78)	10.99 (9.61-12.38)	9.57 (8.18-10.96)	Group:p=0.72; Time:p<0.001 Group*Time: p=0.83
TSK (13-52)	25.87 (24.85-26.89)	24.05 (23.02-25.08)	23.29 (22.20-24.37)	25.85 (24.90-26.80)	23.48 (22.47-24.49)	22.76 (21.73-23.80)	Group:p=0.50; Time:p<0.001 Group*Time: p=0.77
CSES (7-35)	17.17 (16.22-18.12)	15.69 (14.73-16.65)	16.15 (15.14-17.17)	17.09 (16.20-17.98)	16.01 (15.07-16.95)	15.02 (14.05-15.98)	Group:p=0.56; Time:p<0.001 Group*Time: p=0.17
CSI (0-100)	36.47 (34.53-38.40)	32.13 (30.18-34.09)	30.68 (28.69-32.67)	36.05 (34.25-37.85)	32.92 (31.00-34.83)	30.64 (28.73-32.55)	Group:p=0.90; Time:p<0.001 Group*Time: p=0.80
NPQ (0-12)	4.42 (3.98-4.87)	4.81 (4.35-5.26)	4.46 (3.99-4.94)	4.13 (3.72-4.55)	7.60 (7.15-8.04)	7.06 (6.60-7.51)	Group:p<0.001;Time:p<0.001 Group*Time: p<0.001

CI, Confidence Interval; Mo, Months; PNE, Pain Neuroscience Education; 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, Neurophysiology of Pain Questionnaire.

Table 49. Muscle endurance tests and pressure pain thresholds – estimated marginal means for each group adjusted for the baseline values.

Variables	**Exercise group**		**Exercise plus PNE group**		**Statistical results**
	Baseline (n=33) Mean (95% CI)	**Post-Intervention (n=33)** Mean (95% CI)	**Baseline (n=33)** Mean (95% CI)	**Post-Intervention (n=33)** Mean (95% CI)	
PPT Right articular pillar C5C6 (N/cm2)	21.18 (18.92-23.43)	36.14 (33.85-38.43)	21.17 (18.91-23.43)	32.29 (30.00-34.58)	Group: p=0.12; Time: p<0.001 Group*Time: p=0.08
PPT Left articular pillar C5C6 (N/cm2)	19.78 (17.73-21.83)	35.36 (33.28-37.45)	19.79 (17.74-21.84)	30.05 (27.96-32.14)	Group: p=0.02; Time: p<0.001 Group*Time: p=0.01
PPT Tibialis anterior (N/cm2)	37.70 (35.18-40.23)	52.59 (50.07-55.12)	37.89 (35.36-40.41)	50.87 (48.35-53.40)	Group: p=0.55; Time: p<0.001 Group*Time: p=0.46
Neck flexors endurance (seconds)	9.62 (6.53-12.72)	27.22 (24.08-30.37)	9.66 (6.57-12.76)	28.07 (24.92-31.22)	Group: p=0.79; Time: p<0.001 Group*Time: p=0.78
Neck extensors endurance (seconds)	98.24 (83.10-113.37)	207.90 (192.54-223.26)	100.11 (84.97-115.25)	189.93 (174.57-205.29)	Group: p=0.33; Time: p<0.001 Group*Time: p=0.17
Scapular stabilizers endurance (seconds)	26.56 (21.62-31.50)	45.14 (40.12-50.16)	26.98 (22.04-31.92)	46.77 (41.75-51.79)	Group: p=0.71; Time: p<0.001 Group*Time: p=0.80

CI, Confidence Interval; PNE, Pain Neuroscience Education; PPT, Pressure Pain Thresholds

Table 50. Patient Global Impression of Change scores.

Patient Global Impression of Change	**Exercise group**				**Exercise plus PNE group**			
	Post-intervention n=58		Follow-up n=56		Post-intervention n=60		Follow-up n=61	
1. No change (or condition has got worse).	0 (0.0%)	12 (20.7%)	1 (1.8%)	11 (19.6%)	0 (0.0%)	15 (25.0%)	0 (0.0%)	18 (29.6%)
2. Almost the same, hardly any change at all.	1 (1.7%)		1 (1.8%)		2 (3.3%)		4 (6.6%)	
3. A little better, but no noticeable change.	4 (6.9%)		4 (7.1%)		7 (11.7%)		7 (11.5%)	
4. Somewhat better, but the change has not made any real difference.	7 (12.1%)		5 (8.9%)		6 (10.0%)		7 (11.5%)	
5. Moderately better, and a slight but noticeable change.	20 (34.5%)	46 (79.3%)	17 (30.4%)	45 (80.4%)	24 (40.0%)	45 (75.0%)	15 (24.6%)	43 (70.5%)
6. Better, and a definitive improvement that has made a real and worthwhile difference.	22 (37.9%)		25 (44.6%)		18 (30.0%)		16 (26.2%)	
7. A great deal better, and a considerable improvement that has made all the difference.	4 (6.9%)		3 (5.4%)		3 (5.0%)		12 (19.7%)	

Table 51. Unadjusted means (SD) for all Patient Report Outcome Measures.

Variables	**Exercise group**			**Exercise and PNE group**		
	Baseline (n=59) Mean (SD)	**Post-Intervention (n=58)** Mean (SD)	**6Mo Follow-up (n=56)** Mean (SD)	**Baseline (n=68)** Mean (SD)	**Post-Intervention (n=60)** Mean (SD)	**6Mo Follow-up (n=61)** Mean (SD)
NPRS (0-10)	4.41 (1.68)	2.29 (1.95)	2.16 (1.91)	4.60 (2.02)	2.58 (2.20)	2.31 (2.01)
FDI (0-60)	10.61 (6.22)	7.36 (6.34)	7.21 (7.26)	10.10 (6.86)	7.58 (7.68)	5.36 (6.51)
BaSIQS (0-28)	12.12 (4.75)	11.40 (5.38)	11.37 (5.75)	11.35 (4.53)	10.77 (4.01)	10.61 (3.55)
PCS (0-52)	13.42 (8.61)	11.76 (8.88)	9.77 (7.48)	13.53 (8.55)	10.83 (9.43)	9.51 (8.54)
TSK (13-52)	25.86 (5.67)	24.17 (5.81)	23.36 (6.23)	25.75 (5.43)	23.40 (6.13)	22.70 (5.62)
CSES (7-35)	17.34 (4.53)	15.95 (5.34)	16.45 (5.36)	17.03 (5.50)	15.72 (5.18)	14.64 (5.37)
CSI (0-100)	37.76 (12.38)	33.71 (13.24)	32.16 (13.27)	35.04 (13.29)	31.63 (13.88)	28.85 (14.45)
NPQ (0-12)	4.59 (1.79)	4.98 (2.02)	4.64 (2.38)	3.96 (1.84)	7.45 (1.93)	6.92 (2.09)

SD, Standard Deviation; M, Months; PNE, Pain Neuroscience Education; 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, Neurophysiology of Pain Questionnaire.

Table 52. Unadjusted means (SD) for muscle endurance tests and pressure pain thresholds.

Variables		**Exercise group**		**Exercise plus PNE group**	
		Baseline (n=33) Mean (SD)	**Post-Intervention (n=33)** Mean (SD)	**Baseline (n=33)** Mean (SD)	**Post-Intervention (n=33)** Mean (SD)
PPT (N/cm2)	Right articular pillar C5/C6	21.22 (10.42)	36.19 (14.78)	21.22 (10.42)	32.24 (10.72)
	Left articular pillar C5/C6	19.92 (9.90)	35.50 (15.55)	19.65 (10.53)	29.91 (11.54)
	Tibialis anterior	37.48 (14.42)	52.37 (10.92)	38.12 (14.61)	51.09 (9.35)
Muscular tests (seconds)	Neck flexors endurance	9.20 (5.20)	26.80 (12.19)	10.08 (5.55)	28.49 (14.95)
	Neck extensors endurance	89.01 (52.60)	198.67 (77.63)	109.34 (64.84)	199.16 (78.45)
	Scapular stabilizers Endurance	23.23 (13.16)	41.80 (24.16)	30.31 (20.59)	50.10 (26.30)

SD, Standard Deviation; PNE, Pain Neuroscience Education; PPT, Pressure Pain Thresholds

9. GENERAL DISCUSSION AND CONCLUSION

To our knowledge, this research project was the first to systematically explore the association between a set of functional, psychosocial, and sleep impairments, and symptoms of central sensitization and current and future pain and disability in adolescents with chronic NP and to investigate the effectiveness of exercise plus PNE compared to exercise only. Studies investigating the presence of functional and psychosocial factors associated with chronic NP in adolescents are scarce. Furthermore, in a preliminary search (Chapter 2), we were unable to find studies that assessed fear of movement or self-reported symptoms of central sensitization in adolescents with chronic NP. The absence of a literature review that systematized functional, psychosocial, sleep, and central sensitization changes in adolescents with NP was the starting point for Chapters 3 and 4.

The systematic review of studies comparing functional changes (Chapter 3) found a total of 10 studies, of which i) 5 out of 7 studies suggested that there are no differences in cervicothoracic posture between adolescents with and without NP, ii) 1 out of 3 studies suggested that there are restrictions in neck movements in adolescents with NP compared to adolescents without NP, iii) a single study suggested that adolescents with NP have a higher joint repositioning error and higher pain sensitivity than asymptomatic adolescents and iv) a single study suggested that adolescents with NP have a lower endurance of the deep neck muscles than asymptomatic adolescents. To the best of our knowledge, since the conclusion of the systematic review on functional factors associated with NP (Chapter 3), one more study was published (Richards et al., 2021). Results of this study reinforce the previous findings of Chapter 3, that neck

posture is not associated with NP in adolescents. Richards et al. (2021) re-evaluated the sample of 17-year-old adolescents with NP included in Richards et al. (2016), at 22 years of age, and reported that sitting neck posture at 17 years is not a risk factor for having persistent pain at 22 years of age. Furthermore, postures categorized as more relaxed (slumped thorax/forward head) compared to upright postures might be protective for NP in girls. Female sex and the presence of NP at 17 years of age were the only factors suggested by Richards et al. (2021) as risk factors for chronic NP at 22 years of age.

The second systematic review (Chapter 4) with emphasis on psychosocial variables and sleep found 14 studies, of which i) a meta-analysis of 4 studies showed that depression was associated with increased odds of reporting NP, both in girls and boys, ii) 2 studies suggested that adolescents with NP have higher levels of anxiety than asymptomatic adolescents, iii) 2 studies suggested that adolescents with NP have higher levels of stress than asymptomatic adolescents, iv) a single study suggested that adolescents with NP have higher levels of catastrophizing than asymptomatic adolescents, v) a meta-analysis of 4 studies showed that sleep impairments were associated with increased odds of reporting NP, and vi) 1 out of 2 studies suggested that adolescents with NP have less self-efficacy than asymptomatic adolescents. No studies were found on fear of movement. Again, was repeated the search since the date of the conclusion of the collection of articles included in the systematic review of psychosocial factors and sleep associated with NP, and we found two recent studies that explored the variables depression and quality of sleep in adolescents with NP (Richards et al., 2021; Scarabottolo et al., 2020). Scarabottolo et al. (2020) in a cross-sectional study found an association between poorer sleep quality and NP in girls (n=105) and boys (n=71), and these results reinforce the previous findings of Chapter 4. Richard et. al. (2021) reported that depression at age 17 was not a risk factor for

persistent NP at age 22, contrary to the findings of the Chapter 4, in which depressive mood was reported to predict the occurrence of NP for up to 4 years follow-up in girls and boys with 10 and 12 years. The difference between the adolescents' ages in both studies may help to explain these differences, highlighting the importance of this variable at younger ages.

Chapter 5 focused on the baseline characterization of adolescents with chronic NP, including sociodemographic data, physical activity, psychological factors (anxiety, depression, and stress, catastrophizing, fear of movement, self-efficacy), sleep, and self-reported symptoms of central sensitization, compared to adolescents without pain and adolescents with back (thoracic and/or lumbar) and/or limb (upper and/or lower limb) pain. The main findings of this Chapter were that: i) adolescents with chronic NP reported higher disability, anxiety, depression, and stress, catastrophizing, fear of movement, and self-reported symptoms of central sensitization, and lower sleep quality and self-efficacy than asymptomatic adolescents. Also, adolescents with neck and back pain reported similar levels of catastrophizing, self-efficacy, and sleep. Regarding factors associated with the presence of pain and disability at baseline, similarities but also differences were found between groups of adolescents with neck, back, and limb pain. Multivariable analyses showed that i) female sex remained as a factor associated with pain in the three groups, ii) self-reported symptoms of central sensitization and sleep impairments were associated with the increased odds of reporting neck and back pain, and iii) fear of movement was associated with higher odds of reporting pain in the back and limbs. As for disability, i) self-reported symptoms of central sensitization and lower levels of self-efficacy remained associated with disability in the group of adolescents with NP only, ii) higher levels of anxiety, depression, and stress remained associated with disability in the group of adolescents with NP, and also in the group of adolescents with back pain, iii) catastrophizing, number of painful body sites and sleep

remained associated with disability in the three groups, and iv) BMI and higher levels of fear of movement were associated with disability in the group of adolescents with limb pain. The similarity between the factors associated with NP and back pain might be partially explained by a similar origin of neck and back pain, often reported by adolescents as idiopathic, with no associated traumatic mechanism. This might also help explain the stronger relationship of psychosocial factors, sleep, and symptoms of central sensitization with neck and back pain as found in this study.

The relevance of psychosocial factors, sleep, and self-reported symptoms of central sensitization in adolescents with chronic NP (Chapters 4 and 5), pointed to the need to explore their association with NP maintenance and disability (Chapter 6). For Chapter 6, the sample of adolescents with chronic NP at baseline was divided into “persistent” or “recovered” at 6-month follow-up. Forty-seven percent of adolescents were categorized as having persistent NP at 6-month follow-up. The persistence of chronic NP in adolescents at 6-month follow-up was significantly associated with female sex and baseline self-reported symptoms of central sensitization in the multivariable analysis. Variables such as the number of painful body sites, depression, anxiety, and stress, and sleep were also significantly associated with NP persistence but only in the univariable analysis. Regarding disability, only disability and self-reported symptoms of central sensitization at baseline remained significantly associated with disability in adolescents with chronic NP at 6-month follow-up in the multivariable analysis. The results of this Chapter also suggest that there are differences in the factors associated with NP persistence at 6-month follow-up between boys and girls. The number of body sites with pain and sleep remained in the model for boys, but not for girls, while self-reported symptoms of central sensitization remained in the model only for girls. For disability persistence at 6-month follow-up, self-reported symptoms of central

sensitization at baseline emerged as a relevant factor for both boys and girls, but physical activity was only significant for boys.

Considering the lack of studies on factors associated with the new onset of chronic musculoskeletal pain, and specifically NP, in adolescents (as reported in Chapter 2), adolescents without pain at baseline were assessed at 6-month follow-up (Chapter 7). Multivariable analyses showed that i) female sex and self-reported symptoms of central sensitization remained significantly associated with the onset of chronic musculoskeletal pain in general and ii) self-reported symptoms of central sensitization also remained associated with the new onset of NP, showing that self-reported symptoms of central sensitization emerged again as a relevant factor for the new onset of pain in adolescents.

Comparing the results of all the analyses performed in Chapters 5, 6, and 7 for the presence of NP, some aspects are important to emphasize. The high percentage of adolescents with NP at baseline and adolescents with persistent NP at 6-month follow-up highlights the need for early assessment and management of NP in adolescents. For adolescents with chronic NP, self-reported symptoms of central sensitization emerged as a factor associated with both the presence of chronic NP and disability, as well as a predictor of its persistence at 6-month follow-up and of a new onset of pain at 6-month follow-up. Although this research project is the first to include the assessment of self-reported symptoms of central sensitization in adolescents, this finding is in line with the results from Sá & Silva (2017), which suggested the possible presence of central sensitization mechanisms in adolescents with chronic NP assessed through the measurement of pressure pain thresholds at a point distant from the neck. In addition, being female seems to increase the odds of both reporting NP at baseline and 6-month follow-up. However, looking at the Nagelkerke R^2 of the logistic regression models for

the presence of NP at baseline and 6-month follow-up, the baseline model had a higher predictive value (Nagelkerke R^2=0.31) compared to the persistence model of chronic NP at 6-month follow-up (Nagelkerke R^2 =0.04) and of new onset (Nagelkerke R^2 =0.04). These results suggest that other factors, not included in this analysis, may influence the persistence and new onset of NP such as the nature and history of adolescent' pain, history of parents with chronic pain (Palermo & Chambers, 2005), or the quantity of sleep and weekly day tiredness (Pate et al., 2020). Moreover, it suggests that the relevance of factors associated with current pain and its maintenance or new onset is different.

Similarly, results across Chapters 5 and 6 for disability show that at baseline it was associated with depression, anxiety and stress, sleep impairments, catastrophizing, self-efficacy, symptoms of central sensitization, and a higher number of painful body sites (Chapter 5). Furthermore, baseline disability was associated with disability at 6-month follow-up along with self-reported symptoms of central sensitization (Chapter 6). These findings suggest that the assessment and intervention targeting psychosocial factors, sleep, and self-reported symptoms of central sensitization at baseline is key to minimize not only current but also future levels of disability.

Furthermore, findings from Chapters 2 to 7 also highlighted the need for interventions targeting NP in adolescents. Therefore, the last study of this research project consisted of the design and assessment of the effectiveness of an intervention based on exercise plus PNE versus exercise only in adolescents with chronic NP. The results of this randomized controlled trial suggested that both interventions reduce to a similar extend pain intensity (primary outcome), disability, catastrophizing, fear of movement, and symptoms of central sensitization and increase sleep quality, self-efficacy, pressure pain thresholds, and endurance of the neck and scapulothoracic muscles (secondary

outcomes), at post-intervention and 6-month follow-up. As expected, the group of adolescents that performed exercise and PNE showed a significantly higher score in the Pain Neurophysiology Questionnaire compared to the group of adolescents that only performed exercise, both at post-intervention and 6-month follow-up. Despite the absence of statistically significant differences between the two groups, in the group of adolescents that received PNE, the decrease in disability and the increase in self-efficacy maintain a trend towards improvement at 6-month follow-up more marked than in the group of adolescents that only performed exercise, and the differences were closer to the SDC of the Functional Disability Inventory and Children Self-Efficacy Scale. These results might suggest that there is potentially a greater impact of long-term education on both variables, which requires further research.

International recommendations for exercise in adults with chronic NP suggest that endurance and strength training interventions need to be of a minimum 6-week duration, 2 to 3 times a week (O'Riordan et al., 2014). Considering these recommendations, and in the absence of recommendations for adolescents, the program applied in our randomized controlled trial was designed with a duration of 8 weeks, with a frequency of once a week in a blended-learning format. In addition to the exercise program sessions, adolescents were encouraged to perform the proposed exercises at least 2-3 more times a week. However, the study was interrupted by the worldwide SARS-CoV-2 pandemic, and this may have influenced the participation of some adolescents in the program considering that they suddenly needed to adapt to a new school, family, and social routine. According to recent studies in Portuguese adolescents, during confinement, the time available for physical activity was reduced (Francisco et al., 2020; Pombo, Luz, Rodrigues, Ferreira, & Cordovil, 2020; Pombo, Luz, Rodrigues, & Cordovil, 2021), and consequently, this may also have reduced the time allocated to perform the recommended exercises. Considering the blended-

learning format of the intervention, and although we were unable to control the adolescents' adherence to the exercise program at home, confinement might also have contributed to adolescents' lack of adherence to the frequency of sessions per week. This factor may also help explain that SCD was not achieved in the muscle endurance tests from baseline to post-intervention and 6-month follow-up. Furthermore, confinement also had a negative psychosocial impact on adolescents (Branquinho, Kelly, Arevalo, Santos, & Matos, 2020), which may also have influenced the overall results of this study.

In addition to the differences reported at post-intervention and 6-months follow-up in both groups, the effectiveness of both interventions for chronic NP management and their clinical impact on adolescents was highlighted in the Patient's Global Impression of Change Scale results. At post-intervention, 75% of the participants in the exercise plus PNE group and 79.3% of the participants in the exercise group reported being moderately better, better, or a great deal better and these percentages were similar at the 6-month follow-up, reinforcing that the impact of this intervention program is maintained over time, as well as its relevance for the treatment of adolescents with chronic NP as previously suggested in the pilot study from Andias et al. (2018) and Neto et al. (2018).

9.1. Strengths, limitations, and future research

Our research project was designed in view of the increasing prevalence of chronic NP in adolescents, but simultaneously due to the lack of characterization and intervention studies in this population. Overall, the strengths of this research project are the longitudinal approach, and the assessment of a wide set of variables seldom explored in previous studies with adolescents with chronic NP. The fact that the research project was performed in a school setting, with adolescents from the community and from

different geographical areas, is also a positive aspect to highlight. The methodology of the studies in this research project was also carefully designed, with a clear definition of the adolescents with and without chronic NP, the measurement instruments, and the study procedures. However, our findings should be analysed in light of some limitations.

Throughout the development of both systematic reviews included in this research project, the points that required greater attention in interpreting the results were similar. In general, the studies included in the systematic reviews were very heterogeneous regarding the population, definition of NP, measurement instruments, and procedures, which may decrease the confidence in the findings. All included studies were classified as low to fair methodological quality, which reinforces the caution in our findings.

The focus of this research project was on adolescents with chronic NP, which has been reported in the literature as having predominantly an idiopathic origin. However, in the characterization of adolescents in this research project, it was not assessed the cause or mechanisms of pain, which limited the comparison of NP against pain at other body sites (back and limb pain) in terms of the factors associated with the presence of pain and disability. Similarly, the structure of our characterization questionnaire did not allow to classify adolescents with regional vs widespread pain, and the factors associated with pain and disability in these two groups may be different. Thus, these aspects should be considered in future studies as well. In addition to the Nordic Musculoskeletal Questionnaire, no more questions were asked about non-musculoskeletal pain (e.g. headache, abdominal or menstrual pain), which might have acted as confounders.

For Chapter 5, the sample was divided into 3 mutually exclusive groups, however, adolescents in each group had other painful body sites. This is likely to have impacted the number of painful body sites in each of the groups, as well as some of the characteristics and factors found in the analysis. The same happened in Chapter 6 where those who reported being recovered from NP might still experience pain in other body regions. The online questionnaire containing the measurement instruments completed by the adolescents contained an open question for ranking pain according to their chief pain complaint, however, the absence of answers to this question by a high percentage of adolescents precluded its consideration in the statistical analysis. However, this could be a way for future studies to overcome this limitation.

Regarding the measurement instruments, the Basic Scale on Insomnia complaints and Quality of Sleep was selected to assess difficulties with sleep onset and maintenance and the quality and depth of sleep in this thesis, but this scale did not include the assessment of the amount of sleep and/ or daytime tiredness which have also been reported as factors associated with the presence and maintenance of chronic pain in adolescents. Thus, further studies may explore the impact of these factors on adolescents with chronic NP as well.

Although there is currently no gold standard for the assessment of central sensitization, the Central Sensitization Inventory is not a direct indicator of central sensitization but assesses a set of symptoms potentially associated with central sensitization. Therefore, other measures such as pain thresholds or conditioned pain modulation might be used to confirm our findings in adolescents with chronic NP. Chapter 7 also included the Central Sensitization Inventory to explore the impact of self-reported symptoms of central sensitization on new onset of pain in asymptomatic adolescents. However, studies found in the literature have focused on the assessment of symptoms

of central sensitization in different pain conditions and not specifically in asymptomatic individuals. Thus, the psychometric properties of its application in asymptomatic adolescents should be better explored.

Furthermore, other factors not included in this research project, such as the parents' history of chronic pain, might be associated with pain. For that reason, the inclusion of these factors should be considered in future investigations (McKillop & Banez, 2016) and, if a positive association emerges, perhaps a simultaneously intervention with the parents might have an important contribution to the management of chronic NP in adolescents (Koechlin et al., 2020; Palermo, Kashikar-Zuck, Friedrichsdorf, & Powers, 2019).

Regarding the randomized controlled trial (Chapter 8), some limitations also need considering. The reduced number of schools used is likely to have decreased the heterogeneity of students, so some caution is needed when generalizing the results. Furthermore, the results of this randomized clinical trial suggest that both interventions explored are effective in adolescents with chronic NP, but future research should consider exploring whether PNE makes a difference in adolescents with chronic NP at longer follow-up periods and into adulthood, namely, for variables such as disability and self-efficacy.

Future studies with longer longitudinal approaches are needed to further explore the findings reported in Chapters 5 to 8 and the impact of early screening and early interventions targeting psychosocial factors, disability, sleep, and self-reported symptoms of central sensitization, in preventing NP onset and its persistence over time. Early identification of the factors related to chronic NP and its persistence might guide physical therapists in designing appropriate management for this condition,

helping to reduce the consequences and burden of chronic NP at an early age. Harrison et al. (2019) recently suggested that intervention in children and adolescents with chronic pain complaints might be enhanced if the physiotherapist follows a risk screening instrument, such as the Pediatric Pain Screening Tool developed by Simons et al. (2015), which allows categorizing adolescents by risk levels for appropriate interventions. Therefore, future studies may consider the inclusion of this type of risk screening instrument.

9.2. Clinical implications

Our findings in this research project can inform clinical practice to maximize control and self-management of chronic NP by adolescents. We suggest the inclusion of the psychosocial factors, disability, physical activity, sleep, and self-reported symptoms of central sensitization in the assessment of adolescents with NP to inform treatment. The relevance that self-reported symptoms of central sensitization showed in this project with the association with both chronic NP and disability and its persistence at 6-month follow-up, highlights the need to assess it in adolescents with chronic NP and, to target it with early-stage interventions. Furthermore, its association with a new onset of NP emphasizes the need for its assessment also in asymptomatic adolescents, potentially informing preventive interventions in this population. We believe that a new vision for the treatment of chronic NP in children and adolescents is emerging, empowering them at an early stage with self-management and pain control strategies when they are asymptomatic. However, studies are needed to explore the effectiveness of preventive interventions in the short and long term, namely in decreasing NP prevalence.

The multiple painful body sites and the similarities found between factors associated with the presence of NP and disability and pain and disability for other painful body

sites suggest that there could be a common intervention for pain, which can be adjusted according to the particularities of each group of adolescents with pain at specific body sites.

We cautiously suggest that including posture and, particularly, head posture as part of the assessment and treatment of adolescents with NP is unlikely to be of relevance (Chapter 2).

Finally, our findings support the application of interventions based on exercise or exercise plus PNE for the management of chronic NP in adolescents, using a blended-learning format, and implemented at the school setting.

9.3. Conclusion

The assessment of adolescents with chronic NP at baseline should include psychosocial factors, disability, physical activity, sleep, and self-reported symptoms of central sensitization, considering its association with the persistence of NP and disability at 6-month follow-up. Sleep impairments and self-reported symptoms of central sensitization also emerged as relevant to the new onset of NP. These findings suggest that an early assessment of these factors might help prevent the persistence of NP and disability over time, but also its new onset. Furthermore, this research project suggests that interventions based on exercise and exercise plus PNE, administered at the school setting in a blended-learning format, are effective in decreasing pain intensity, disability, catastrophizing, fear of movement, symptoms of central sensitization and increasing sleep quality, self-efficacy, pressure pain thresholds, and muscle endurance, at post-intervention and 6-month follow-up, in adolescents with chronic NP. However, future studies should further explore the findings of this research project.

10. REFERENCES

Allen Gomes, A., Ruivo Marques, D., Meia-Via, A. M., Meia-Via, M., Tavares, J., Fernandes da Silva, C., & Pinto de Azevedo, M. H. (2015). Basic Scale on Insomnia complaints and Quality of Sleep (BaSIQS): Reliability, initial validity and normative scores in higher education students. *Chronobiology International*, *32*(3), 428–440. https://doi.org/10.3109/07420528.2014.986681

Allen Gomes, A., Tavares, J., & Pinto de Azevedo, M. H. (2009). Padrões de sono em estudantes universitários portugueses. *Acta Médica Portuguesa*, *22*, 545–552.

Andias, R., Neto, M., & Silva, A. G. (2018). The effects of pain neuroscience education and exercise on pain, muscle endurance, catastrophizing and anxiety in adolescents with chronic idiopathic neck pain: a school-based pilot, randomized and controlled study. *Physiotherapy Theory and Practice*, *34*(9), 682–691. https://doi.org/10.1080/09593985.2018.1423590

Andias, R., & Silva, A. G. (2019a). European Portuguese version of the Functional Disability Inventory: translation and cultural adaptation, validity and reliability in adolescents with chronic spinal pain. *Disability and Rehabilitation*, *in submiss*.

Andias, R., & Silva, A. G. (2019b). Psychosocial Variables and Sleep Associated With Neck Pain in Adolescents: A Systematic Review. *Physical & Occupational Therapy In Pediatrics*, *40*(2), 168–191. https://doi.org/10.1080/01942638.2019.1647328

Andias, R., & Silva, A. G. (2020a). Cross-Cultural Adaptation and Psychometric Properties of the European Portuguese Version of the Central Sensitization Inventory in Adolescents With Musculoskeletal Chronic Pain. *Pain Practice*, *20*(5), 480–490. https://doi.org/10.1111/papr.12875

Andias, R., & Silva, A. G. (2020b). European Portuguese version of the Child Self-Efficacy Scale: A contribution to cultural adaptation, validity and reliability testing in adolescents with chronic musculoskeletal pain. *Musculoskeletal Science and Practice*, *49*. https://doi.org/10.1016/j.msksp.2020.102176

Andreucci, A., Campbell, P., & Dunn, K. M. (2017, July 1). Are sleep problems a risk factor for the onset of musculoskeletal pain in children and adolescents? A systematic review. *Sleep*, Vol. 40. https://doi.org/10.1093/sleep/zsx093

Andreucci, A., Campbell, P., Mundy, L. K., Sawyer, S. M., Kosola, S., Patton, G. C., & Dunn, K. M. (2020). Sleep problems increase the risk of musculoskeletal pain in boys but not girls: a prospective cohort study. *European Journal of Pediatrics*. https://doi.org/10.1007/s00431-020-03667-8

Andreucci, A., Groenewald, C. B., Rathleff, M. S., & Palermo, T. M. (2021). The Role of Sleep in the Transition from Acute to Chronic Musculoskeletal Pain in Youth—A Narrative Review. *Children*, *8*(3), 241. https://doi.org/10.3390/children8030241

Armstrong, B., McNair, P., & Taylor, D. (2008). Head and neck position sense. *Sports Medicine*, Vol. 38, pp. 101–117. https://doi.org/10.2165/00007256-200838020-00002

Asmundson, G. J., Noel, M., Petter, M., & Parkerson, H. A. (2012). Pediatric fear-avoidance model of chronic pain: Foundation, application and future directions. https://doi.org/10.1155/2012/908061

Auvinen, J., Eskola, P. J., Ohtonen, H. R., Paananen, M., Jokelainen, J., Timonen, M., … Karppinen, J. (2017). Long-term adolescent multi-site musculoskeletal pain is associated with psychological distress and anxiety. *Journal of Psychosomatic Research*, *93*, 28–32. https://doi.org/10.1016/j.jpsychores.2016.12.006

Auvinen, J. P., Paananen, M. V. J., Tammelin, T. H., Taimela, S. P., Mutanen, P. O. A.,

Zitting, P. J., & Karppinen, J. I. (2009). Musculoskeletal Pain Combinations in Adolescents. *Spine*, *34*(11), 1192–1197. https://doi.org/10.1097/BRS.0b013e3181a401df

Auvinen, J. P., Tammelin, T. H., Taimela, S. P., Zitting, P. J., Järvelin, M. R., Taanila, A. M., & Karppinen, J. I. (2010). Is insufficient quantity and quality of sleep a risk factor for neck, shoulder and low back pain? A longitudinal study among adolescents. *European Spine Journal*, *19*(4), 641–649. https://doi.org/10.1007/s00586-009-1215-2

Badawy, S. M., Law, E. F., & Palermo, T. M. (2019, October 1). The interrelationship between sleep and chronic pain in adolescents. *Current Opinion in Physiology*, Vol. 11, pp. 25–28. https://doi.org/10.1016/j.cophys.2019.04.012

Barendregt, J. J., & Doi, S. A. (2011). MetaXL User Guide Version 5.3. *EpiGear International Pty Ltd.*

Barton, C. J., Lack, S., Malliaras, P., & Morrissey, D. (2013, March 1). Gluteal muscle activity and patellofemoral pain syndrome: A systematic review. *British Journal of Sports Medicine*, Vol. 47, pp. 207–214. https://doi.org/10.1136/bjsports-2012-090953

Basch, M. C., Chow, E. T., Logan, D. E., Borsook, D., Schechter, N. L., & Simons, L. E. (2018). Cumulative effects of multiple pain sites in youth with chronic pain. *European Journal of Pain (United Kingdom)*, *22*(6), 1134–1141. https://doi.org/10.1002/ejp.1201

Batley, S., Aartun, E., Boyle, E., Hartvigsen, J., Stern, P. J., & Hestbæk, L. (2019). The association between psychological and social factors and spinal pain in adolescents. *European Journal of Pediatrics*, *178*(3), 275–286. https://doi.org/10.1007/s00431-018-3291-y

Becker, A. J., Heathcote, L. C., Timmers, I., & Simons, L. E. (2018). Precipitating events in child and adolescent chronic musculoskeletal pain. *PAIN Reports*, *3*(7), e665. https://doi.org/10.1097/PR9.0000000000000665

Beesdo, K., Hoyer, J., Jacobi, F., Low, N. C. P., Höfler, M., & Wittchen, H. U. (2009). Association between generalized anxiety levels and pain in a community sample: Evidence for diagnostic specificity. *Journal of Anxiety Disorders*, *23*(5), 684–693. https://doi.org/10.1016/j.janxdis.2009.02.007

Beltran-Alacreu, H., López-de-Uralde-Villanueva, I., Fernández-Carnero, J., & La Touche, R. (2015). Manual Therapy, Therapeutic Patient Education, and Therapeutic Exercise, an Effective Multimodal Treatment of Nonspecific Chronic Neck Pain. *American Journal of Physical Medicine & Rehabilitation*, *94*, 887–897. https://doi.org/10.1097/PHM.0000000000000293

Beneitez, I., Nieto, R., Hernández, E., & Boixadós, M. (2020). Adolescents' social needs living with juvenile idiopathic arthritis and their views about digital resources. *Advances in Rheumatology*, *60*(1). https://doi.org/10.1186/s42358-020-00138-4

Berenbaum, S. A., Beltz, A. M., & Corley, R. (2015). The Importance of Puberty for Adolescent Development: Conceptualization and Measurement. In *Advances in Child Development and Behavior* (Vol. 48, pp. 53–92). https://doi.org/10.1016/bs.acdb.2014.11.002

Blanpied, P. R., Gross, A. R., Elliott, J. M., Devaney, L. L., Clewley, D., Walton, D. M., … Robertson, E. K. (2017). Neck Pain: Revision 2017. *Journal of Orthopaedic & Sports Physical Therapy*, *47*(7), 1–83. https://doi.org/10.2519/jospt.2017.0302

Boerner, K. E., Birnie, K. A., Caes, L., Schinkel, M., & Chambers, C. T. (2014). Sex differences in experimental pain among healthy children: A systematic review and

meta-analysis. *Pain*, *155*(5), 983–993. https://doi.org/10.1016/j.pain.2014.01.031

Boerner, K. E., Schinkel, M., & Chambers, C. T. (2015). It is not as simple as boys versus girls: the role of sex differences in pain across the lifespan. *Pain Management*, Vol. 5, pp. 1–4. https://doi.org/10.2217/pmt.14.42

Branquinho, C., Kelly, C., Arevalo, L. C., Santos, A., & Matos, M. G. de. (2020). “Hey, we also have something to say”: A qualitative study of Portuguese adolescents’ and young people’s experiences under COVID-19. *Journal of Community Psychology*, *48*(8), 2740–2752. https://doi.org/10.1002/JCOP.22453

Brattberg, G. (2004). Do pain problems in young school children persist into early adulthood? A 13-year follow-up. *European Journal of Pain*, *8*(3), 187–199. https://doi.org/10.1016/j.ejpain.2003.08.001

Bursch, B., Tsao, J. C. I., Meldrum, M., & Zeltzer, L. K. (2006). Preliminary validation of a self-efficacy scale for child functioning despite chronic pain (child and parent versions). *Pain*, *125*(1–2), 35–42. https://doi.org/10.1016/j.pain.2006.04.026

Bushnell, M. C., Ceko, M., & Low, L. A. (2013). Cognitive and emotional control of pain and its disruption in chronic pain. *Nature Reviews. Neuroscience*, *14*(7), 502–511. https://doi.org/10.1038/nrn3516

Butler, D., & Moseley, L. (2013). *Explain Pain*. Adelaide, Noigroup Publications.

Caes, L., Fisher, E., Clinch, J., & Eccleston, C. (2018). Current Evidence-Based Interdisciplinary Treatment Options for Pediatric Musculoskeletal Pain. *Current Treatment Options in Rheumatology*, *4*(3), 223–234. https://doi.org/10.1007/s40674-018-0101-7

Caneiro, J. P., O’Sullivan, P., Burnett, A., Barach, A., O’Neil, D., Tveit, O., & Olafsdottir, K. (2010). The influence of different sitting postures on head/neck posture and muscle activity. *Manual Therapy*, *15*(1), 54–60.

https://doi.org/10.1016/j.math.2009.06.002

Carpino, E., Segal, S., Logan, D., Lebel, A., & Simons, L. E. (2014). The interplay of pain-related self-efficacy and fear on functional outcomes among youth with headache. *The Journal of Pain : Official Journal of the American Pain Society*, *15*(5), 527–534. https://doi.org/10.1016/j.jpain.2014.01.493

Casey, B. J., Giedd, J. N., & Thomas, K. M. (2000). Structural and functional brain development and its relation to cognitive development. *Biological Psychology*, *54*(1–3), 241–257. https://doi.org/10.1016/S0301-0511(00)00058-2

Castarlenas, E., Jensen, M. P., von Baeyer, C. L., & Miró, J. (2017). Psychometric Properties of the Numerical Rating Scale to Assess Self-Reported Pain Intensity in Children and Adolescents. *The Clinical Journal of Pain*, *33*(4), 376–383. https://doi.org/10.1097/AJP.0000000000000406

Catley, M. J., O'Connell, N. E., & Moseley, G. L. (2013). How Good Is the Neurophysiology of Pain Questionnaire? A Rasch Analysis of Psychometric Properties. *The Journal of Pain*, *14*(8), 818–827. https://doi.org/10.1016/j.jpain.2013.02.008

Chang, B. H., & Hoaglin, D. C. (2017). Meta-analysis of odds ratios. *Medical Care*, *55*(4), 328–335. https://doi.org/10.1097/MLR.0000000000000696

Cheung, C. H., Shum, S. T., Tang, S. F., Yau, P. C., & Chiu, T. T. W. (2009). The correlation between craniovertebral angle, backpack weights, and disability due to neck pain in adolescents. *Journal of Back and Musculoskeletal Rehabilitation*, *22*(4), 197–203. https://doi.org/10.3233/BMR-2010-0259

Chimenti, R. L., Frey-Law, L. A., & Sluka, K. A. (2018). A mechanism-based approach to physical therapist management of pain. *Physical Therapy*, *98*(5), 302–314. https://doi.org/10.1093/ptj/pzy030

Claar, R. L., & Walker, L. S. (2006). Functional assessment of pediatric pain patients: Psychometric properties of the Functional Disability Inventory. *Pain*, *121*(1), 77–84. https://doi.org/10.1016/j.pain.2005.12.002

Cohen, J. (1988). *Statistical Power Analysis for the Behavioral Sciences*. New York: NY: Routledge Academic.

Comachio, J., Magalhães, M., Campos, P. de M., Silva, A., & Marques, A. (2018). A cross-sectional study of associations between kinesiophobia, pain, disability, and quality of life in patients with chronic low back pain. *Advances in Rheumatology*. https://doi.org/10.1186/s42358-018-0011-2

Cordeiro, N., Pezarat-Correia, P., Gil, J., & Cabri, J. (2013). Portuguese Language Version of the Tampa Scale for Kinesiophobia [13 Items]. *Journal of Musculoskeletal Pain*, *21*(1), 58–63. https://doi.org/10.3109/10582452.2012.762966

Coronado, R. A., & George, S. Z. (2018). The Central Sensitization Inventory and Pain Sensitivity Questionnaire: An exploration of construct validity and associations with widespread pain sensitivity among individuals with shoulder pain. *Musculoskeletal Science and Practice*, *36*, 61–67. https://doi.org/10.1016/j.msksp.2018.04.009

Courtney, C. A., Fernández-de-las-Peñas, C., & Bond, S. (2017). Mechanisms of chronic pain–key considerations for appropriate physical therapy management. *Journal of Manual and Manipulative Therapy*, *25*(3), 118–127. https://doi.org/10.1080/10669817.2017.1300397

Crone, E. A., & Dahl, R. E. (2012). Understanding adolescence as a period of social-affective engagement and goal flexibility. *Nature Reviews Neuroscience*, *13*(9), 636–650. https://doi.org/10.1038/nrn3313

Daffin, L., Stuelcken, M. C., & Sayers, M. G. L. (2017). The efficacy of sagittal cervical spine subtyping: Investigating radiological classification methods within 150 asymptomatic participants. *Journal of Craniovertebral Junction and Spine*, *8*(3), 231–238. https://doi.org/10.4103/jcvjs.JCVJS_84_17

De Cocker, K., Ottevaere, C., Sjöström, M., Maöreno, L. A., Wrnberg, J., Valtueña, J., … De Bourdeaudhuij, I. (2011). Self-reported physical activity in European adolescents: Results from the HELENA (Healthy Lifestyle in Europe by Nutrition in Adolescence) study. *Public Health Nutrition*, *14*(2), 246–254. https://doi.org/10.1017/S1368980010000558

de Vries, J., Ischebeck, B. K., Voogt, L. P., van der Geest, J. N., Janssen, M., Frens, M. A., & Kleinrensink, G. J. (2015, December 1). Joint position sense error in people with neck pain: A systematic review. *Manual Therapy*, Vol. 20, pp. 736–744. https://doi.org/10.1016/j.math.2015.04.015

Dianat, I., Alipour, A., & Asgari Jafarabadi, M. (2018). Risk factors for neck and shoulder pain among schoolchildren and adolescents. *Journal of Paediatrics and Child Health*, *54*(1), 20–27. https://doi.org/10.1111/jpc.13657

Diepenmaat, A. C. M., Van Der Wal, M. F., De Vet, H. C. W., & Hirasing, R. A. (2006). Neck/shoulder, low back, and arm pain in relation to computer use, physical activity, stress, and depression among dutch adolescents. *Pediatrics*, *117*(2), 412–416. https://doi.org/10.1542/peds.2004-2766

Dimitriadis, Z., Kapreli, E., Strimpakos, N., & Oldham, J. (2015). Do psychological states associate with pain and disability in chronic neck pain patients? *Journal of Back and Musculoskeletal Rehabilitation*, *28*(4), 797–802. https://doi.org/10.3233/BMR-150587

Dolezal, B. A., Neufeld, E. V., Boland, D. M., Martin, J. L., & Cooper, C. B. (2017).

Interrelationship between Sleep and Exercise: A Systematic Review. *Advances in Preventive Medicine*, *2017*. https://doi.org/10.1155/2017/1364387

Dolphens, M., Cagnie, B., Danneels, L., De Clercq, D., De Bourdeaudhuij, I., & Cardon, G. (2011). Long-term effectiveness of a back education programme in elementary schoolchildren: An 8-year follow-up study. *European Spine Journal*, *20*(12), 2134–2142. https://doi.org/10.1007/s00586-011-1856-9

Dolphens, M., Vansteelandt, S., Cagnie, B., Vleeming, A., Nijs, J., Vanderstraeten, G., & Danneels, L. (2016). Multivariable modeling of factors associated with spinal pain in young adolescence. *European Spine Journal*, *25*(9), 2809–2821. https://doi.org/10.1007/s00586-016-4629-7

Domingues, L., & Cruz, E. (2011). *Adaptação Cultural e Contributo para a Validação da Escala Patient Global Impression of Change*. Retrieved from http://www.ifisionline.ips.pt/media/3jan_vol2_n1/pdfs/artigo4_vol2n1.pdf

dos Passos, M. H. P., Silva, H. A., Pitangui, A. C. R., Oliveira, V. M. A., Gomes, G. C., & Araújo, R. C. (2017). Association between sleep quality and pain in the cervical region and scapular waist in adolescent athletes. *Sleep and Biological Rhythms*, *15*(2), 137–142. https://doi.org/10.1007/s41105-017-0093-y

Dragotta, K., Jang, B., Quinzi, B., Bosco, A., & Clewley, D. (2019). Physical therapy management of pediatric and adolescent neck pain: a call to action. *Physical Therapy Reviews*, *24*(5), 208–215. https://doi.org/10.1080/10833196.2019.1663979

Dworkin, R. H., Turk, D. C., Wyrwich, K. W., Beaton, D., Cleeland, C. S., Farrar, J. T., … Zavisic, S. (2008). Interpreting the Clinical Importance of Treatment Outcomes in Chronic Pain Clinical Trials: IMMPACT Recommendations. *The Journal of Pain*, *9*(2), 105–121. https://doi.org/10.1016/j.jpain.2007.09.005

Eccleston, C., Crombez, G., Scotford, A., Clinch, J., & Connell, H. (2004). Adolescent chronic pain: patterns and predictors of emotional distress in adolescents with chronic pain and their parents. *Pain*, *108*(3), 221–229. https://doi.org/10.1016/j.pain.2003.11.008

Eccleston, C., Fisher, E., Howard, R. F., Slater, R., Forgeron, P., Palermo, T. M., … Wood, C. (2021, January 1). Delivering transformative action in paediatric pain: a Lancet Child & Adolescent Health Commission. *The Lancet Child and Adolescent Health*, Vol. 5, pp. 47–87. https://doi.org/10.1016/S2352-4642(20)30277-7

Eckhoff, C., Straume, B., & Kvernmo, S. (2017). Multisite musculoskeletal pain in adolescence and later mental health disorders: a population-based registry study of Norwegian youth: the NAAHS cohort study. *BMJ Open*, *7*, 12035. https://doi.org/10.1136/bmjopen-2016

Edmondston, S. J., Wallumrød, M. E., MacLéid, F., Kvamme, L. S., Joebges, S., & Brabham, G. C. (2008). Reliability of Isometric Muscle Endurance Tests in Subjects With Postural Neck Pain. *Journal of Manipulative and Physiological Therapeutics*, *31*(5), 348–354. https://doi.org/10.1016/j.jmpt.2008.04.010

Edwards, R. R., Dworkin, R. H., Sullivan, M. D., Turk, D. C., & Wasan, A. D. (2016). The Role of Psychosocial Processes in the Development and Maintenance of Chronic Pain. *The Journal of Pain : Official Journal of the American Pain Society*, *17*(9 Suppl), T70-92. https://doi.org/10.1016/j.jpain.2016.01.001

El-Metwally, A., Salminen, J. J., Auvinen, A., Kautiainen, H., & Mikkelsson, M. (2004). Prognosis of non-specific musculoskeletal pain in preadolescents: A prospective 4-year follow-up study till adolescence. *Pain*, *110*(3), 550–559. https://doi.org/10.1016/j.pain.2004.03.021

El-Metwally, A., Salminen, J. J., Auvinen, A., Kautiainen, H., & Mikkelsson, M. (2005).

Lower limb pain in a preadolescent population: Prognosis and risk factors for chronicity - A prospective 1- and 4-year follow-up study. *Pediatrics*, *116*(3), 673–681. https://doi.org/10.1542/peds.2004-1758

El-Metwally, A., Salminen, J. J., Auvinen, A., Kautiainen, H., & Mikkelsson, M. (2006). Risk factors for traumatic and non-traumatic lower limb pain among preadolescents: A population-based study of Finnish schoolchildren. *BMC Musculoskeletal Disorders*, *7*(3), 1-9. https://doi.org/10.1186/1471-2474-7-3

El-Metwally, A., Salminen, J. J., Auvinen, A., MacFarlane, G., & Mikkelsson, M. (2007). Risk factors for development of non-specific musculoskeletal pain in preteens and early adolescents: A prospective 1-year follow-up study. *BMC Musculoskeletal Disorders*, *8*(46), 1-8. https://doi.org/10.1186/1471-2474-8-46

Evans, S., Djilas, V., Seidman, L. C., Zeltzer, L. K., & Tsao, J. C. I. (2017). Sleep Quality, Affect, Pain, and Disability in Children With Chronic Pain: Is Affect a Mediator or Moderator? *The Journal of Pain*, *18*(9), 1087–1095. https://doi.org/10.1016/j.jpain.2017.04.007

Ezeanosike, O., Kayungo, S. J., Mwashala, W., Namisango, E., Bustamante, Tuchez, L. M., … Yotani, N. (2020). Guidelines on the management of chronic pain in children.1-56. Retrieved March 14, 2021, from World Health Organization website: https://www.who.int/publications/i/item/9789240017870

Falla, D., Bilenkij, G., & Jull, G. (2004). Patients with chronic neck pain demonstrate altered patterns of muscle activation during performance of a functional upper limb task. *Spine*, *29*(13), 1436–1440. https://doi.org/10.1097/01.BRS.0000128759.02487.BF

Falla, D., & Farina, D. (2007, December). Neural and muscular factors associated with motor impairment in neck pain. *Current Rheumatology Reports*, Vol. 9, pp. 497–

502. https://doi.org/10.1007/s11926-007-0080-4

Falla, D. L., Jull, G. A., & Hodges, P. W. (2004). Patients with neck pain demonstrate reduced electromyographic activity of the deep cervical flexor muscles during performance of the craniocervical flexion test. *Spine*, *29*(19), 2108–2114. https://doi.org/10.1097/01.brs.0000141170.89317.0e

Fares, J., Fares, M. Y., & Fares, Y. (2017). Musculoskeletal neck pain in children and adolescents: Risk factors and complications. *Surgical Neurology International,* 8(72), 1-5. https://doi.org/10.4103/sni.sni_445_16

Feldman, D. E., Shrier, I., Rossignol, M., & Abenhaim, L. (2002). Risk factors for the development of neck and upper limb pain in adolescents. *Spine*, *27*(5), 523–528. https://doi.org/10.1097/00007632-200203010-00013

Ferro-Lebres, V., Silva, G., Moreira, P., & Ribeiro, J. C. (2018). Validation of the Portuguese Version of the International Physical Activity Questionnaire for Adolescents (IPAQA). *The Open Sports Sciences Journal*, *10*(1), 239–250. https://doi.org/10.2174/1875399x01710010239

Ferro Moura Franco, K., Lenoir, D., Santos Franco, Y. R., Jandre Reis, F. J., Nunes Cabral, C. M., & Meeus, M. (2021). Prescription of exercises for the treatment of chronic pain along the continuum of nociplastic pain: A systematic review with meta-analysis. *European Journal of Pain*, *25*(1), 51–70. https://doi.org/10.1002/ejp.1666

Fillingim, R. B., Loeser, J. D., Baron, R., & Edwards, R. R. (2016, September 1). Assessment of Chronic Pain: Domains, Methods, and Mechanisms. *Journal of Pain*, Vol. 17, 10–20. https://doi.org/10.1016/j.jpain.2015.08.010

Finan, P. H., Goodin, B. R., & Smith, M. T. (2013). The association of sleep and pain: An update and a path forward. *J Pain*, *14*(12), 1539–1552.

https://doi.org/10.1016/j.jpain.2013.08.007

Fisher, E., Heathcote, L. C., Eccleston, C., Simons, L. E., & Palermo, T. M. (2018). Assessment of Pain Anxiety, Pain Catastrophizing, and Fear of Pain in Children and Adolescents With Chronic Pain: A Systematic Review and Meta-Analysis. *Journal OfPediatric Psychology*, *43*(3), 314–325. https://doi.org/10.1093/jpepsy/jsx103

Fisher, E., Heathcote, L., Palermo, T. M., de C Williams, A. C., Lau, J., & Eccleston, C. (2014). Systematic Review and Meta-Analysis of Psychological Therapies for Children With Chronic Pain. *Journal of Pediatric Psychology*, *39*(8), 763–782. https://doi.org/10.1093/jpepsy/jsu008

Francisco, R., Pedro, M., Delvecchio, E., Espada, J. P., Morales, A., Mazzeschi, C., & Orgilés, M. (2020). Psychological Symptoms and Behavioral Changes in Children and Adolescents During the Early Phase of COVID-19 Quarantine in Three European Countries. *Frontiers in Psychiatry*, *11* (570164), 1-14. https://doi.org/10.3389/fpsyt.2020.570164

Galan-Martin, M. A., Montero-Cuadrado, F., Lluch-Girbes, E., Coca-López, M. C., Mayo-Iscar, A., & Cuesta-Vargas, A. (2020). Pain Neuroscience Education and Physical Therapeutic Exercise for Patients with Chronic Spinal Pain in Spanish Physiotherapy Primary Care: A Pragmatic Randomized Controlled Trial. *Journal of Clinical Medicine*, *9*(4), 1201. https://doi.org/10.3390/jcm9041201

Gauntlett-Gilbert, J., & Eccleston, C. (2007). Disability in adolescents with chronic pain: Patterns and predictors across different domains of functioning. *Pain*, *131*(1), 132–141. https://doi.org/10.1016/j.pain.2006.12.021

Gracely, R. H., Geisser, M. E., Giesecke, T., Grant, M. A. B., Petzke, F., Williams, D. A., & Clauw, D. J. (2004). Pain catastrophizing and neural responses to pain

among persons with fibromyalgia. *Brain*, *127*(4), 835–843. https://doi.org/10.1093/brain/awh098

Graven-Nielsen, T., & Arendt-Nielsen, L. (2002). Peripheral and central sensitization in musculoskeletal pain disorders: an experimental approach. *Current Rheumatology Reports*, Vol. 4, 313–321. https://doi.org/10.1007/s11926-002-0040-y

Griffin, A. (2017). Adolescent Neurological Development and Implications for Health and Well-Being. *Healthcare*, *5*(4),1-8. https://doi.org/10.3390/healthcare5040062

Guddal, M. H., Stensland, S. Ø., Småstuen, M. C., Johnsen, M. B., Zwart, J. A., & Storheim, K. (2017). Physical Activity Level and Sport Participation in Relation to Musculoskeletal Pain in a Population-Based Study of Adolescents: The Young-HUNT Study. *Orthopaedic Journal of Sports Medicine*, *5*(1),1-9. https://doi.org/10.1177/2325967116685543

Guite, J. W., McCue, R. L., Sherker, J. L., Sherry, D. D., & Rose, J. B. (2011). Relationships Among Pain, Protective Parental Responses, and Disability for Adolescents With Chronic Musculoskeletal Pain. *The Clinical Journal of Pain*, *27*(9), 775–781. https://doi.org/10.1097/AJP.0b013e31821d8fb4

Gustafsson, M. L., Laaksonen, C., Aromaa, M., Löyttyniemi, E., & Salanterä, S. (2018). The prevalence of neck-shoulder pain, back pain and psychological symptoms in association with daytime sleepiness - A prospective follow-up study of school children aged 10 to 15. *Scandinavian Journal of Pain*, *18*(3), 389–397. https://doi.org/10.1515/sjpain-2017-0166

Hakala, P., Rimpelä, A., Salminen, J. J., Virtanen, S. M., & Rimpelä, M. (2002). Back, neck, and shoulder pain in Finnish adolescents: National cross sectional surveys. *British Medical Journal*, *325*(7367), 743–745. https://doi.org/10.1136/bmj.325.7367.743

Hanvold, T. N., Veiersted, K. B., & Wærsted, M. (2010). A Prospective Study of Neck, Shoulder, and Upper Back Pain Among Technical School Students Entering Working Life. *Journal of Adolescent Health*, *46*(5), 488–494. https://doi.org/10.1016/j.jadohealth.2009.11.200

Hardin, A. P., & Hackell, J. M. (2017). Age Limit of Pediatrics. *American Academy of Pediatrics*. 1-3. Retrieved from www.aappublications.org/news

Härmä, A. M., Kaltiala-Heino, R., Rimpelä, M., & Rantanen, P. (2002). Are adolescents with frequent pain symptoms more depressed? *Scandinavian Journal of Primary Health Care*, *20*(2), 92–96. https://doi.org/10.1080/pri.20.2.92.96

Harrison, L. E., Pate, J. W., Richardson, P. A., Ickmans, K., Wicksell, R. K., & Simons, L. E. (2019). Best-Evidence for the Rehabilitation of Chronic Pain Part 1: Pediatric Pain. *Journal of Clinical Medicine*, *8*(9), 1-19. https://doi.org/10.3390/jcm8091267

Harrison, L., Wilson, S., & Munafó, M. R. (2016). Pain-related and psychological symptoms in adolescents with musculoskeletal and sleep problems. *Clinical Journal of Pain*, *32*(3), 246–253. https://doi.org/10.1097/AJP.0000000000000252

Harrison, L., Wilson, S., & Munafò, M. R. (2014). Exploring the associations between sleep problems and chronic musculoskeletal pain in adolescents: A prospective cohort study. *Pain Research and Management*, *19*(5),139–145. https://doi.org/10.1155/2014/615203

Harte, S. E., Harris, R. E., & Clauw, D. J. (2018). The neurobiology of central sensitization. *Journal of Applied Biobehavioral Research*, *23*(2),1-25. https://doi.org/10.1111/jabr.12137

Heathcote, L. C., Pate, J. W., Park, A. L., Leake, H. B., Lorimer Moseley, G., Kronman, C. A., … Simons, L. E. (2019). Pain neuroscience education on youtube. *PeerJ*, *2019*(3), 1-22. https://doi.org/10.7717/peerj.6603

Heikkala, E., Paananen, M., Taimela, S., Auvinen, J., & Karppinen, J. (2019). Associations of co-occurring psychosocial and lifestyle factors with multisite musculoskeletal pain during late adolescence—A birth cohort study. *European Journal of Pain (United Kingdom)*, *23*(8), 1486–1496. https://doi.org/10.1002/ejp.1414

Hellstenius, S. A. (2009). Recurrent Neck Pain and Headaches in Preadolescents Associated with Mechanical Dysfunction of the Cervical Spine: A Cross-Sectional Observational Study With 131 Students. *Journal of Manipulative and Physiological Therapeutics*, *32*(8), 625–634. https://doi.org/10.1016/j.jmpt.2009.08.025

Higgins, J., & Green, S. (2011). Cochrane Handbook for Systematic Reviews of Interventions-Version 5.1.0. *The Cochrane Collaboration*. https://doi.org/http://handbook-5-1.cochrane.org/

Hirschfeld, G., Wager, J., Schmidt, P., & Zernikow, B. (2014). Minimally clinically significant differences for adolescents with chronic pain - Variability of ROC-based cut points. *Journal of Pain*, *15*(1), 32–39. https://doi.org/10.1016/j.jpain.2013.09.006

Hoftun, G. B., Romundstad, P. R., Zwart, J.-A., & Rygg, M. (2011). Chronic idiopathic pain in adolescence – high prevalence and disability: The young HUNT study 2008. *Pain*, *152*(10), 2259–2266. https://doi.org/10.1016/j.pain.2011.05.007

Holley, A. L., Wilson, A. C., & Palermo, T. M. (2017). Predictors of the transition from acute to persistent musculoskeletal pain in children and adolescents: A prospective study. *Pain*, *158*(5), 794–801. https://doi.org/10.1097/j.pain.0000000000000817

Huguet, A., Tougas, M. E., Hayden, J., McGrath, P. J., Stinson, J. N., & Chambers, C. T. (2016, August 10). Systematic review with meta-analysis of childhood and

adolescent risk and prognostic factors for musculoskeletal pain. *Pain*, Vol. 157, 2640–2656. https://doi.org/10.1097/j.pain.0000000000000685

Hurst, H., & Bolton, J. (2004). Assessing the clinical significance of change scores recorded on subjective outcome measures. *Journal of Manipulative and Physiological Therapeutics*, *27*(1), 26–35. https://doi.org/10.1016/j.jmpt.2003.11.003

Hynynen, S. T., Van Stralen, M. M., Sniehotta, F. F., Araújo-Soares, V., Hardeman, W., Chinapaw, M. J. M., … Hankonen, N. (2016, January 1). A systematic review of school-based interventions targeting physical activity and sedentary behaviour among older adolescents. *International Review of Sport and Exercise Psychology*, Vol. 9, 22–44. https://doi.org/10.1080/1750984X.2015.1081706

IASP. (2009). *Musculoskeletal Pain*. Retrieved from http://www.bls.gov/iff/home.htm.

Israel, H., & Richter, R. R. (2011, July 1). A guide to understanding meta-analysis. *Journal of Orthopaedic and Sports Physical Therapy*, Vol. 41, 496–504. https://doi.org/10.2519/jospt.2011.3333

Jacome, C., & Cruz, E. (2004). Adaptação Cultural e contributo para a Validação da Pain Catastrophizing Scale (PCS). *Instituto Politécnico de Setúbal*.

Johnston, V., Jull, G., Souvlis, T., & Jimmieson, N. L. (2008). Neck movement and muscle activity characteristics in female office workers with neck pain. *Spine*, *33*(5), 555–563. https://doi.org/10.1097/BRS.0b013e3181657d0d

Jovanović, V., Gavrilov-Jerković, V., & Lazić, M. (2019). Can adolescents differentiate between depression, anxiety and stress? Testing competing models of the Depression Anxiety Stress Scales (DASS-21). *Current Psychology*, 1–12. https://doi.org/10.1007/s12144-019-00540-2

Jull, G., Kristjansson, E., & Dall'Alba, P. (2004). Impairment in the cervical flexors: A

comparison of whiplash and insidious onset neck pain patients. *Manual Therapy*, *9*(2), 89–94. https://doi.org/10.1016/S1356-689X(03)00086-9

Kalapurakkel, S., A. Carpino, E., Lebel, A., & E. Simons, L. (2015). “Pain Can’t Stop Me”: Examining Pain Self-Efficacy and Acceptance as Resilience Processes Among Youth With Chronic Headache. *Journal of Pediatric Psychology*, *40*(9), 926–933. https://doi.org/10.1093/jpepsy/jsu091

Kamper, Steve J., Henschke, N., Hestbaek, L., Dunn, K. M., & Williams, C. M. (2016). Musculoskeletal pain in children and adolescents. *Brazilian Journal of Physical Therapy*, *20*(3), 275–284. https://doi.org/10.1590/bjpt-rbf.2014.0149

Kamper, Steven J., & Williams, C. M. (2017, October 1). Musculoskeletal pain in children and adolescents: A way forward. *Journal of Orthopaedic and Sports Physical Therapy*, Vol. 47, 702–704. https://doi.org/10.2519/jospt.2017.0109

Karels, C. H., Bierma-Zeinstra, S. M. A., Burdorf, A., Verhagen, A. P., Nauta, A. P., & Koes, B. W. (2007). Social and psychological factors influenced the course of arm, neck and shoulder complaints. *Journal of Clinical Epidemiology*, *60*(8), 839–848. https://doi.org/10.1016/j.jclinepi.2006.11.012

Kashikar-Zuck, S, Goldschneider, K. R., Powers, S. W., Vaught, M. H., & Hershey, A. D. (2001). Depression and functional disability in chronic pediatric pain. *The Clinical Journal of Pain*, *17*(4), 341–349. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11783815

Kashikar-Zuck, Susmita, Flowers, S. R., Claar, R. L., Guite, J. W., Logan, D. E., Lynch-Jordan, A. M., … Wilson, A. C. (2011). Clinical utility and validity of the Functional Disability Inventory among a multicenter sample of youth with chronic pain. *Pain*, *152*(7), 1600–1607. https://doi.org/10.1016/j.pain.2011.02.050

Katz, M. H. (2011). *Multivariable Analysis A Practical Guide for Clinicians*. Cambridge

University Press.

Kim, H., & Lee, S. (2020). Effects of pain neuroscience education on kinesiophobia in patients with chronic pain: a systematic review and meta-analysis. *Physical Therapy Rehabilitation Science*, *9*(4), 309–317. https://doi.org/10.14474/ptrs.2020.9.4.309

King, S., Chambers, C. T., Huguet, A., MacNevin, R. C., McGrath, P. J., Parker, L., & MacDonald, A. J. (2011). The epidemiology of chronic pain in children and adolescents revisited: A systematic review. *Pain*, *152*(12), 2729–2738. https://doi.org/10.1016/j.pain.2011.07.016

Kirkwood, B., & Sterne, J. (2003). *Medical Statistics-second edition*.

Koechlin, H., Locher, C., & Prchal, A. (2020). Talking to Children and Families about Chronic Pain: The Importance of Pain Education—An Introduction for Pediatricians and Other Health Care Providers. *Children*, *7*(10), 179. https://doi.org/10.3390/children7100179

Koh, M. J., Park, S. Y., Park, E. J., Park, S. H., Jeon, H. R., Kim, M. G., … Kim, S. I. (2014). The effect of education on decreasing the prevalence and severity of neck and shoulder pain: A longitudinal study in Korean male adolescents. *Korean Journal of Anesthesiology*, *67*(3), 198–204. https://doi.org/10.4097/kjae.2014.67.3.198

Konijnenberg, A. Y., Uiterwaal, C. S. P. M., Kimpen, J. L. L., Van Der Hoeven, J., Buitelaar, J. K., & De Graeff-Meeder, E. R. (2005). Children with unexplained chronic pain: Substantial impairment in everyday life. *Archives of Disease in Childhood*, *90*(7), 680–686. https://doi.org/10.1136/adc.2004.056820

Latremoliere, A., & Woolf, C. J. (2009, September). Central Sensitization: A Generator of Pain Hypersensitivity by Central Neural Plasticity. *Journal of Pain*, Vol. 10, 895–

926. https://doi.org/10.1016/j.jpain.2009.06.012

Le Pera, D., Graven-Nielsen, T., Valeriani, M., Oliviero, A., Di Lazzaro, V., Tonali, P. A., & Arendt-Nielsen, L. (2001). Inhibition of motor system excitability at cortical and spinal level by tonic muscle pain. *Clinical Neurophysiology*, *112*(9), 1633–1641. https://doi.org/10.1016/S1388-2457(01)00631-9

Leal, I. P., Antunes, R., Passos, T., Pais-Ribeiro, J., & Maroco, J. (2009). Estudo da escala de Depressão, Ansiedade e Stress para Crianças (EADS- C). *Psicologia, Saúde & Doenças*, *10*(2), 277–284.

Lee, H., Hübscher, M., Moseley, G. L., Kamper, S. J., Traeger, A. C., Mansell, G., & McAuley, J. H. (2015). How does pain lead to disability? A systematic review and meta-analysis of mediation studies in people with back and neck pain. *Pain*, Vol. 156, 988–997. https://doi.org/10.1097/j.pain.0000000000000146

Leeuw, M., Goossens, M. E. J. B., Linton, S. J., Crombez, G., Boersma, K., & Vlaeyen, J. W. S. (2007, February 20). The fear-avoidance model of musculoskeletal pain: Current state of scientific evidence. *Journal of Behavioral Medicine*, Vol. 30, 77–94. https://doi.org/10.1007/s10865-006-9085-0

Liossi, C., & Howard, R. F. (2016). Pediatric Chronic Pain: Biopsychosocial Assessment and Formulation. *Pediatrics*, *138*(5), 1–16. https://doi.org/10.1542/peds.2016-0331

Lloyd, R. S., Faigenbaum, A. D., Stone, M. H., Oliver, J. L., Jeffreys, I., Moody, J. A., … Myer, G. D. (2014). Position statement on youth resistance training: The 2014 International Consensus. *British Journal of Sports Medicine*, *48*(7), 498–505. https://doi.org/10.1136/bjsports-2013-092952

Lo, C. K. L., Mertz, D., & Loeb, M. (2014). Newcastle-Ottawa Scale: Comparing reviewers' to authors' assessments. *BMC Medical Research Methodology*, *14*(1),

1–5. https://doi.org/10.1186/1471-2288-14-45

Long, A. C., Palermo, T. M., & Manees, A. M. (2008). Brief Report: Using Actigraphy to Compare Physical Activity Levels in Adolescents with Chronic Pain and Healthy Adolescents. *Journal of Pediatric Psychology*, *33*(6), 660-665. https://doi.org/10.1093/jpepsy/jsm136

Louw, Adriaan, Podalak, J., Zimney, K., Schmidt, S., & Puentedura, E. J. (2018). Can pain beliefs change in middle school students? A study of the effectiveness of pain neuroscience education. *Physiotherapy Theory and Practice*, *34*(7), 542–550. https://doi.org/10.1080/09593985.2017.1423142

Louw, Adriaan, Puentedura, E. J., Diener, I., Zimney, K. J., & Cox, T. (2019). Pain neuroscience education: Which pain neuroscience education metaphor worked best? *South African Journal of Physiotherapy*, *75*(1),1-7. https://doi.org/10.4102/sajp.v75i1.1329

Louw, Adriaan, Zimney, K., O'Hotto, C., & Hilton, S. (2016). The clinical application of teaching people about pain. *Physiotherapy Theory and Practice*, *32*(5), 385–395. https://doi.org/10.1080/09593985.2016.1194652

Louw, Adriaan, Zimney, K., Puentedura, E. J., & Diener, I. (2016). The efficacy of pain neuroscience education on musculoskeletal pain: A systematic review of the literature. *Physiotherapy Theory and Practice*, *32*(5), 332–355. https://doi.org/10.1080/09593985.2016.1194646

Louw, Adrian, & Puentedura, E. (2013). *Therapeutic Neuroscience Education. Teaching Patients About Pain - A Guide for Clinicians*. International Spine and Pain Institute.

Luque-Suarez, A., Martinez-Calderon, J., & Falla, D. (2019). Role of kinesiophobia on pain, disability and quality of life in people suffering from chronic musculoskeletal

pain: a systematic review. *Br J Sports Med*, *53*, 554–559. https://doi.org/10.1136/bjsports-2017-098673

Lynch, A. M., Kashikar-Zuck, S., Goldschneider, K. R., & Jones, B. A. (2006). Psychosocial Risks for Disability in Children With Chronic Back Pain. *Journal of Pain*, *7*(4), 244–251. https://doi.org/10.1016/j.jpain.2005.11.001

Malfliet, A., Kregel, J., Cagnie, B., Kuipers, M., Dolphens, M., Roussel, N., … Nijs, J. (2015). Lack of Evidence for Central Sensitization in Idiopathic, Non-Traumatic Neck Pain: A Systematic Review. *Pain Physician*, *18*, 223–235. Retrieved from www.painphysicianjournal.com

Malfliet, A., Kregel, J., Coppieters, I., De Pauw, R., Meeus, M., Roussel, N., … Nijs, J. (2018). Effect of pain neuroscience education combined with cognition-targeted motor control training on chronic spinal pain a randomized clinical trial. *JAMA Neurology*, *75*(7), 808–817. https://doi.org/10.1001/jamaneurol.2018.0492

Malfliet, A., Kregel, J., Meeus, M., Cagnie, B., Roussel, N., Dolphens, M., … Nijs, J. (2017). Applying contemporary neuroscience in exercise interventions for chronic spinal pain: treatment protocol. *Brazilian Journal of Physical Therapy*, *21*(5), 378–387. https://doi.org/10.1016/j.bjpt.2017.06.019

Malfliet, A., Kregel, J., Meeus, M., Danneels, L., Cagnie, B., Roussel, N., & Nijs, J. (2018). Patients With Chronic Spinal Pain Benefit From Pain Neuroscience Education Regardless the Self-Reported Signs of Central Sensitization: Secondary Analysis of a Randomized Controlled Multicenter Trial. *PM&R*, *10*(12), 1330-1343. https://doi.org/10.1016/j.pmrj.2018.04.010

Malfliet, A., Kregel, J., Meeus, M., Roussel, N., Danneels, L., Cagnie, B., … Nijs, J. (2018). Blended-Learning Pain Neuroscience Education for People With Chronic Spinal Pain: Randomized Controlled Multicenter Trial. *Physical Therapy*, *98*(5),

357–368. https://doi.org/10.1093/ptj/pzx092

Malmborg, J. S., Bremander, A., Olsson, M. C., Bergman, A.-C., Brorsson, A. S., & Bergman, S. (2019). Worse health status, sleeping problems, and anxiety in 16-year-old students are associated with chronic musculoskeletal pain at three-year follow-up. *BMC Public Health Volume*, *19*(1565), 1–11. https://doi.org/10.1186/s12889-019-7955-y

Mano, K. E. J., Beckmann, E. A., Fussner, L. M., & Kashikar-Zuck, S. (2020). Executive Functioning in Adolescents with Chronic Musculoskeletal Pain. *Children*, *7*(273), 1-12. https://doi.org/10.3390/children7120273

Marôco, J. (2014). *Análise estatística com o SPSS Statistics (6ª edição)*. ReportNumber.

Martin, A. L., McGrath, P. A., Brown, S. C., & Katz, J. (2007). Children with chronic pain: Impact of sex and age on long-term outcomes. *Pain*, *128*(1–2), 13–19. https://doi.org/10.1016/j.pain.2006.08.027

Martin, A. L., McGrath, P. A., Brown, S. C., Katz, J., Martin, A., Martin, A., … Katz, J. (2007). Anxiety sensitivity, fear of pain and pain-related disability in children and adolescents with chronic pain. In *Pain Res Manage*, 12(4), 267-272.

Martinez-Calderon, J., Zamora-Campos, C., Navarro-Ledesma, S., & Luque-Suarez, A. (2018, January 1). The Role of Self-Efficacy on the Prognosis of Chronic Musculoskeletal Pain: A Systematic Review. *Journal of Pain*, Vol. 19, 10–34. https://doi.org/10.1016/j.jpain.2017.08.008

Matias, B. A., Vieira, I., Pereira, A., Duarte, M., & Silva, A. G. (2019). Pain neuroscience education plus exercise compared with exercise in university students with chronic idiopathic neck pain. *International Journal of Therapy and Rehabilitation*, *26*(7), 1–14. https://doi.org/10.12968/ijtr.2018.0084

Mayer, T. G., Neblett, R., Cohen, H., Howard, K. J., Choi, Y. H., Williams, M. J., … Gatchel, R. J. (2012). The Development and Psychometric Validation of the Central Sensitization Inventory. *Pain Practice*, *12*(4), 276–285. https://doi.org/10.1111/j.1533-2500.2011.00493.x

McHugh, M. L. (2012). Interrater reliability: The kappa statistic. *Biochemia Medica*, *22*(3), 276–282. https://doi.org/10.11613/bm.2012.031

McKillop, H. N., & Banez, G. A. (2016). A Broad Consideration of Risk Factors in Pediatric Chronic Pain: Where to Go from Here? *Children,* 3(4),1-18. https://doi.org/10.3390/children3040038

Mcpheeters, M. L., Kripalani, S., Peterson, N. B., Idowu, R. T., Jerome, J. T., Potter, R. N., & Andrews, J. (2012). Quality Improvement Interventions to Address Health Disparities, Closing the Quality Gap: Revisiting the State of the Science | Request PDF. *Agency for Healthcare Research and Quality*, *208*, 1–475. Retrieved from https://www.researchgate.net/publication/259723571_Quality_Improvement_Interventions_to_Address_Health_Disparities_Closing_the_Quality_Gap_Revisiting_the_State_of_the_Science

Meeus, M., Nijs, J., Van Oosterwijck, J., Van Alsenoy, V., & Truijen, S. (2010). Pain physiology education improves pain beliefs in patients with chronic fatigue syndrome compared with pacing and self-management education: A double-blind randomized controlled trial. *Archives of Physical Medicine and Rehabilitation*, *91*(8), 1153–1159. https://doi.org/10.1016/j.apmr.2010.04.020

Melzack, R. (2001). Pain and the Neuromatrix in the Brain. *Journal of Dental Education*, *65*(12), 1378–1382. https://doi.org/10.1002/j.0022-0337.2001.65.12.tb03497.x

Merskey, H., & Bogduk, N. (2002). Classification of chronic pain descriptions of chronic

pain syndromes and definitions of pain terms. *International Association for the Study of Pain Press*, *2nd edition*, 1–238.

Mesquita, C. C., Ribeiro, J. C., & Moreira, P. (2010). Portuguese version of the standardized Nordic musculoskeletal questionnaire: cross cultural and reliability. *Journal of Public Health*, *18*(5), 461–466. https://doi.org/10.1007/s10389-010-0331-0

Mikkelsson, L., Nupponen, H., Kaprio, J., Kautiainen, H., Mikkelsson, M., & Kujala, U. M. (2006). Adolescent flexibility, endurance strength, and physical activity as predictors of adult tension neck, low back pain, and knee injury: A 25 year follow up study. *British Journal of Sports Medicine*, *40*(2), 107–113. https://doi.org/10.1136/bjsm.2004.017350

Mikkelsson, M., Sourander, A., Salminen, J. J., Kautiainen, H., & Piha, J. (1999). Widespread pain and neck pain in schoolchildren. A prospective one-year follow-up study. *Acta Paediatrica, International Journal of Paediatrics*, *88*(10), 1119–1124. https://doi.org/10.1080/08035259950168199

Mikkelsson, Marja, El-Metwally, A., Kautiainen, H., Auvinen, A., Macfarlane, G. J., & Salminen, J. J. (2008). Onset, prognosis and risk factors for widespread pain in schoolchildren: A prospective 4-year follow-up study. *Pain*, *138*(3), 681–687. https://doi.org/10.1016/j.pain.2008.06.005

Mikkelsson, Marja, Salminen, J. J., Sourander, A., & Kautiainen, H. (1998). Contributing factors to the persistence of musculoskeletal pain in preadolescents: A prospective 1-year follow-up study. *Pain*, *77*(1), 67–72. https://doi.org/10.1016/S0304-3959(98)00083-9

Minghelli, B. (2019). Musculoskeletal spine pain in adolescents: Epidemiology of non-specific neck and low back pain and risk factors. *Journal of Orthopaedic Science,*

25(5), 776-780. https://doi.org/10.1016/j.jos.2019.10.008

Misailidou, V., Malliou, P., Beneka, A., Karagiannidis, A., & Godolias, G. (2010). Assessment of patients with neck pain: a review of definitions, selection criteria, and measurement tools. *Journal of Chiropractic Medicine*, *9*(2), 49–59. https://doi.org/10.1016/j.jcm.2010.03.002

Mogil, J. S. (2012, December 20). Sex differences in pain and pain inhibition: Multiple explanations of a controversial phenomenon. *Nature Reviews Neuroscience*, Vol. 13, 859–866. https://doi.org/10.1038/nrn3360

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., Altman, D., Antes, G., … Tugwell, P. (2009, July). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PLoS Medicine*, 6(7),1-6. https://doi.org/10.1371/journal.pmed.1000097

Moseley, G. L., & Butler, D. S. (2015, September 1). Fifteen Years of Explaining Pain: The Past, Present, and Future. *Journal of Pain*, Vol. 16, 807–813. https://doi.org/10.1016/j.jpain.2015.05.005

Murray, C. B., Groenewald, C. B., de la Vega, R., & Palermo, T. M. (2020). Long-term impact of adolescent chronic pain on young adult educational, vocational, and social outcomes. *Pain*, *161*(2), 439–445. https://doi.org/10.1097/j.pain.0000000000001732

Myrtveit, S. M., Sivertsen, B., Skogen, J. C., Frostholm, L., Stormark, K. M., & Hysing, M. (2014). Adolescent neck and shoulder pain - The association with depression, physical activity, screen-based activities, and use of health care services. *Journal of Adolescent Health*, *55*(3), 366–372. https://doi.org/10.1016/j.jadohealth.2014.02.016

Neblett, R., Hartzell, M. M., Mayer, T. G., Bradford, E. M., & Gatchel, R. J. (2016).

Establishing clinically meaningful severity levels for the Tampa Scale for Kinesiophobia (TSK-13). *European Journal of Pain (United Kingdom)*, *20*(5), 701–710. https://doi.org/10.1002/ejp.795

Neblett, Randy. (2018). The central sensitization inventory: A user's manual. *Journal of Applied Biobehavioral Research*, *23*(2), 1-13. https://doi.org/10.1111/jabr.12123

Neblett, Randy, Cohen, H., Choi, Y., Hartzell, M. M., Williams, M., Mayer, T. G., & Gatchel, R. J. (2013). The Central Sensitization Inventory (CSI): Establishing Clinically Significant Values for Identifying Central Sensitivity Syndromes in an Outpatient Chronic Pain Sample. *The Journal of Pain*, *14*(5), 438–445. https://doi.org/10.1016/j.jpain.2012.11.012

Nederhand, M. J., Jzerman, M. J. I., Hermens, H. J., Baten, C. T. M., & Zilvold, G. (2000). Cervical muscle dysfunction in the chronic whiplash associated disorder Grade II (WAD-II). *Spine*, *25*(15), 1938–1943. https://doi.org/10.1097/00007632-200008010-00012

Neto, M., Andias, R., & Silva, A. G. (2018). Pain Neuroscience Education and Exercise for Neck Pain: A Focus Group Study on Adolescents' Views. *Pediatric Physical Therapy*, *30*(3), 196–201. https://doi.org/10.1097/PEP.0000000000000511

Niemi, S., Levoska, S., Kemilä, J., Rekola, K., & Keinänen-Kiukaanniemi, S. (1996). Neck and shoulder symptoms and leisure time activities in high school students. *Journal of Orthopaedic and Sports Physical Therapy*, *24*(1), 25–29. https://doi.org/10.2519/jospt.1996.24.1.25

Niemi, S. M., Levoska, S., Rekola, K. E., & Keinänen-Kiukaanniemi, S. M. (1997). Neck and shoulder symptoms of high school students and associated psychosocial factors. *Journal of Adolescent Health*, *20*(3), 238–242.

https://doi.org/10.1016/S1054-139X(96)00219-4

Nijs, J., George, S. Z., Clauw, D. J., Fernández-de-las-Peñas, C., Kosek, E., Ickmans, K., Curatolo, M. (2021). Central sensitisation in chronic pain conditions: latest discoveries and their potential for precision medicine. *The Lancet Rheumatology*, vol. 3, 1-10. https://doi.org/10.1016/S2665-9913(21)00032-1

Nijs, J., Goubert, D., & Ickmans, K. (2016, December 1). Recognition and treatment of central sensitization in chronic pain patients: Not limited to specialized care. *Journal of Orthopaedic and Sports Physical Therapy*, Vol. 46, 1024–1028. https://doi.org/10.2519/jospt.2016.0612

Nijs, J., Lluch Girbés, E., Lundberg, M., Malfliet, A., & Sterling, M. (2015). Exercise therapy for chronic musculoskeletal pain: Innovation by altering pain memories. *Manual Therapy*, *20*(1), 216–220. https://doi.org/10.1016/j.math.2014.07.004

Nijs, J., Loggia, M. L., Polli, A., Moens, M., Huysmans, E., Goudman, L., … Clauw, D. (2017). Sleep disturbances and severe stress as glial activators: key targets for treating central sensitization in chronic pain patients? *Expert Opinion on Therapeutic Targets*, *21*(8), 817–826. https://doi.org/10.1080/14728222.2017.1353603

Nijs, J., Paul van Wilgen, C., Van Oosterwijck, J., van Ittersum, M., & Meeus, M. (2011). How to explain central sensitization to patients with ‘unexplained’ chronic musculoskeletal pain: Practice guidelines. *Manual Therapy*, *16*(5), 413–418. https://doi.org/10.1016/j.math.2011.04.005

Nijs, J., Torres-Cueco, R., van Wilgen, C. P., Girbes, E. L., Struyf, F., Roussel, N., … Meeus, M. (2014). Applying modern pain neuroscience in clinical practice: criteria for the classification of central sensitization pain. *Pain Physician*, *17*(5), 447–457. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/25247901

Nijs, J., Van Houdenhove, B., & Oostendorp, R. A. B. (2010). Recognition of central sensitization in patients with musculoskeletal pain: Application of pain neurophysiology in manual therapy practice. *Manual Therapy*, *15*(2), 135–141. https://doi.org/10.1016/J.MATH.2009.12.001

Noel, M., Groenewald, C. B., Beals-Erickson, S. E., Gebert, J. T., & Palermo, T. M. (2016). Chronic pain in adolescence and internalizing mental health disorders: A nationally representative study. *Pain*, *157*(6), 1333–1338. https://doi.org/10.1097/j.pain.0000000000000522

Nogueira, L., De Oliveira Chaves, A., Oliveira, N., Santos De Almeida, R., José, F., Reis, J., … Catley, M. J. (2018). *Cross-cultural adaptation of the Revised Neurophysiology of Pain Questionnaire into Brazilian Portuguese language Adaptação transcultural do Questionário Neurofisiológico da Dor revisado para língua portuguesa do Brasil*.1-5. https://doi.org/10.1590/0047-2085000000215

O'Riordan, C., Clifford, A., Van De Ven, P., & Nelson, J. (2014). Chronic Neck Pain and Exercise Interventions: Frequency, Intensity, Time, and Type Principle. *Archives of Physical Medicine and Rehabilitation*, *95*(4), 770–783. https://doi.org/10.1016/j.apmr.2013.11.015

O'Sullivan, P., Smith, A., Beales, D., & Straker, L. (2017, October 1). Understanding adolescent low back pain from a multidimensional perspective: Implications for management. *Journal of Orthopaedic and Sports Physical Therapy*, Vol. 47, 741–751. https://doi.org/10.2519/jospt.2017.7376

Oliveira, A. C., & Silva, A. G. (2016). Neck muscle endurance and head posture: A comparison between adolescents with and without neck pain. *Manual Therapy*, *22*, 62–67. https://doi.org/10.1016/j.math.2015.10.002

Othman, R., Jayakaran, P., Swain, N., Dassanayake, S., Tumilty, S., & Mani, R. (2021,

February 1). Relationships Between Psychological, Sleep, and Physical Activity Measures and Somatosensory Function in People With Peripheral Joint Pain: A Systematic Review and Meta-Analysis. *Pain Practice*, Vol. 21, 226–261. https://doi.org/10.1111/papr.12943

Paananen, M., Taimela, S., Auvinen, J., Tammelin, T., Zitting, P., & Karppinen, J. (2011). Impact of Self-Reported Musculoskeletal Pain on Health-Related Quality of Life among Young Adults. *Pain Medicine*, *12*(1), 9–17. https://doi.org/10.1111/j.1526-4637.2010.01029.x

Paananen, M. V., Auvinen, J. P., Taimela, S. P., Tammelin, T. H., Kantomaa, M. T., Ebeling, H. E., … Karppinen, J. I. (2010). Psychosocial, mechanical, and metabolic factors in adolescents' musculoskeletal pain in multiple locations: A cross-sectional study. *European Journal of Pain*, *14*(4), 395–401. https://doi.org/10.1016/j.ejpain.2009.06.003

Paananen, M. V., Taimela, S. P., Auvinen, J. P., Tammelin, T. H., Kantomaa, M. T., Ebeling, H. E., … Karppinen, J. I. (2010). Risk factors for persistence of multiple musculoskeletal pains in adolescence: A 2-year follow-up study. *European Journal of Pain*, *14*(10), 1026–1032. https://doi.org/10.1016/j.ejpain.2010.03.011

Pack, R., Gilliland, R., & Mecham, A. (2018). The treatment of central sensitization in an adolescent using pain neuroscience education and graded exposure to activity: A case report. *Physiotherapy Theory and Practice*, 1–11. https://doi.org/10.1080/09593985.2018.1551454

Pais-Ribeiro, J. L., Honrado, A., & Leal, I. (2004). Contribuição para o estudo da adaptação portuguesa das escalas de Ansiedade, Depressão e Stress (EADS) de 21 items de Lovibond. *Psicologia, Saúde & Doenças*, *5*(2), 229–239.

Paiva, T., Gaspar, T., & Matos, M. G. (2015). Sleep deprivation in adolescents:

Correlations with health complaints and health-related quality of life. *Sleep Medicine*, *16*(4), 521–527. https://doi.org/10.1016/j.sleep.2014.10.010

Palermo, T. M. (2000). Impact of recurrent and chronic pain on child and family daily functioning: A critical review of the literature. *Journal of Developmental and Behavioral Pediatrics*, Vol. 21, 58–69. https://doi.org/10.1097/00004703-200002000-00011

Palermo, T. M., & Chambers, C. T. (2005, December 15). Parent and family factors in pediatric chronic pain and disability: An integrative approach. *Pain*, Vol. 119, 1–4. https://doi.org/10.1016/j.pain.2005.10.027

Palermo, T. M., Kashikar-Zuck, S., Friedrichsdorf, S. J., & Powers, S. W. (2019). Special considerations in conducting clinical trials of chronic pain management interventions in children and adolescents and their families. *Pain Reports*, *4*(3), 1-11. https://doi.org/10.1097/PR9.0000000000000649

Palermo, T. M., Valrie, C. R., & Karlson, C. W. (2014). Family and parent influences on pediatric chronic pain. *American Psychologist*, *69*(2), 142–152. https://doi.org/10.1037/a0035216

Park, K. N., Kwon, O. Y., Ha, S. M., Kim, S. J., Choi, H. J., & Weon, J. H. (2012). Comparison of electromyographic activity and range of neck motion in violin students with and without neck pain during playing. *Medical Problems of Performing Artists*, *27*(4), 188–192. https://doi.org/10.21091/mppa.2012.4035

Pas, R., Rheel, E., Van Oosterwijck, S., Foubert, A., De Pauw, R., Leysen, L., … Ickmans, K. (2020). Pain Neuroscience Education for Children with Functional Abdominal Pain Disorders: A Randomized Comparative Pilot Study. *Journal of Clinical Medicine*, *9*(6), 1797. https://doi.org/10.3390/jcm9061797

Pate, J. W., Hancock, M. J., Hush, J. M., Gray, K., Pounder, M., & Pacey, V. (2020).

Prognostic factors for pain and functional disability in children and adolescents with persisting pain: A systematic review and meta-analysis. *European Journal of Pain*, *24*(4), 722–741. https://doi.org/10.1002/ejp.1539

Perquin, C. W., Hazebroek-Kampschreur, A. A. J. M., Hunfeld, J. A. M., Bohnen, A. M., Van Suijlekom-Smit, L. W. A., Passchier, J., & Van Der Wouden, J. C. (2000). Pain in children and adolescents: A common experience. *Pain*, *87*(1), 51–58. https://doi.org/10.1016/S0304-3959(00)00269-4

Picavet, H. S. J., Vlaeyen, J. W. S., & Schouten, J. S. A. G. (2002). Pain Catastrophizing and Kinesiophobia: Predictors of Chronic Low Back Pain. Am J Epidemiol. 156(11), 1028-1034. https://doi.org/10.1093/aje/kwf136

Pielech, M., Ryan, M., Logan, D., Kaczynski, K., White, M. T., & Simons, L. E. (2014). Pain catastrophizing in children with chronic pain and their parents: Proposed clinical reference points and reexamination of the PCS measure. *Pain*, *155*(11), 2360–2367. https://doi.org/10.1016/j.pain.2014.08.035

Pollock, C. M., Harries, R. L., Smith, A. J., Straker, L. M., Kendall, G. E., & O'Sullivan, P. B. (2011). Neck/shoulder pain is more strongly related to depressed mood in adolescent girls than in boys. *Manual Therapy*, *16*(3), 246–251. https://doi.org/10.1016/j.math.2010.10.010

Pombo, A., Luz, C., Rodrigues, L. P., Ferreira, C., & Cordovil, R. (2020). Correlates of children's physical activity during the COVID-19 confinement in Portugal. *Public Health*, *189*, 14–19. https://doi.org/10.1016/j.puhe.2020.09.009

Pombo, André, Luz, C., Rodrigues, L. P., & Cordovil, R. (2021). Effects of COVID-19 Confinement on the Household Routines Of Children in Portugal. *Journal of Child and Family Studies*, *30*(7), 1664–1674. https://doi.org/10.1007/s10826-021-01961-z

Poole, H., White, S., Blake, C., Murphy, P., & Bramwell, R. (2009). Depression in Chronic Pain Patients: Prevalence and Measurement. *Pain Practice*, *9*(3), 173–180. https://doi.org/10.1111/j.1533-2500.2009.00274.x

Pourbordbari, N., Riis, A., Jensen, M. B., Olesen, J. L., & Rathleff, M. S. (2019, July 1). Poor prognosis of child and adolescent musculoskeletal pain: A systematic literature review. *BMJ Open*, 9(7), 1-10. https://doi.org/10.1136/bmjopen-2018-024921

Raja, S. N., Carr, D. B., Cohen, M., Finnerup, N. B., Flor, H., Gibson, S., … Vader, K. (2020). The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises. *Pain*, *161*(9), 1976–1982. https://doi.org/10.1097/j.pain.0000000000001939

Rees, C. S., Smith, A. J., O'Sullivan, P. B., Kendall, G. E., & Straker, L. M. (2011). Back and neck pain are related to mental health problems in adolescence. *BMC Public Health*, *11*(1), 1-8. https://doi.org/10.1186/1471-2458-11-382

Richards, K. V., Beales, D. J., Smith, A. J., O'Sullivan, P. B., & Straker, L. M. (2016). Neck posture clusters and their association with biopsychosocial factors and neck pain in Australian adolescents. *Physical Therapy*, *96*(10), 1576–1587. https://doi.org/10.2522/ptj.20150660

Richards, K. V, Beales, D. J., Smith, A. L., O'Sullivan, P. B., & Straker, L. M. (2021). Is Neck Posture Subgroup in Late Adolescence a Risk Factor for Persistent Neck Pain in Young Adults? A Prospective Study. *Physical Therapy*, *101*(3). https://doi.org/10.1093/ptj/pzab007

Robins, H., Perron, V., Heathcote, L., & Simons, L. (2016). Pain Neuroscience Education: State of the Art and Application in Pediatrics. *Children*, *3*(4), 1-17. https://doi.org/10.3390/children3040043

Rosenbloom, B. N., Rabbitts, J. A., & Palermo, T. M. (2017, September 1). A developmental perspective on the impact of chronic pain in late adolescence and early adulthood: Implications for assessment and intervention. *Pain*, Vol. 158, 1629–1632. https://doi.org/10.1097/j.pain.0000000000000888

Roth-Isigkeit, A., Thyen, U., Stöven, H., Schwarzenberger, J., & Schmucker, P. (2005). Pain Among Children and Adolescents: Restrictions in Daily Living and Triggering Factors. *PEDIATRICS*, *115*(2), 152–162. https://doi.org/10.1542/peds.2004-0682

Roussel, N. A., Nijs, J., Meeus, M., Mylius, V., Fayt, C., & Oostendorp, R. (2013). Central Sensitization and Altered Central Pain Processing in Chronic Low Back Pain. *The Clinical Journal of Pain*, *29*(7), 625–638. https://doi.org/10.1097/AJP.0b013e31826f9a71

Ruivo, R. M., Pezarat-Correia, P., & Carita, A. I. (2014). Cervical and shoulder postural assessment of adolescents between 15 and 17 years old and association with upper quadrant pain. *Brazilian Journal of Physical Therapy*, *18*(4), 364–371. https://doi.org/10.1590/bjpt-rbf.2014.0027

Ruskin, D., Lalloo, C., Amaria, K., Stinson, J. N., Hon, E. K., Campbell, F., … McGrath, P. A. (2014). Assessing pain intensity in children with chronic pain: Convergent and discriminant validity of the 0 to 10 numerical rating scale in clinical practice. *Pain Research and Management*, *19*(3), 141–148. https://doi.org/10.1155/2014/856513

Sá, S., & Silva, A. G. (2017). Repositioning error, pressure pain threshold, catastrophizing and anxiety in adolescents with chronic idiopathic neck pain. *Musculoskeletal Science and Practice*, *30*, 18–24. https://doi.org/10.1016/j.msksp.2017.04.011

Sangrar, R., Docherty-Skippen, S. M., & Beattie, K. (2019, October 1). Blended face-to-face and online/computer-based education approaches in chronic disease self-management: A critical interpretive synthesis. *Patient Education and Counseling*, Vol. 102, 1822–1832. https://doi.org/10.1016/j.pec.2019.05.009

Scarabottolo, C. C., Pinto, R. Z., Oliveira, C. B., Rodrigues Tebar, W., Thamyres, B., Saraiva, C., … Christofaro, D. (2020). Back and neck pain and poor sleep quality in adolescents are associated even after controlling for confounding factors: An epidemiological study. *Sleep Sci*, *13*(2), 107–112. https://doi.org/10.5935/1984-0063.20190138

Schmitz, A.-K., Vierhaus, M., & Lohaus, A. (2013). Pain tolerance in children and adolescents: Sex differences and psychosocial influences on pain threshold and endurance. *European Journal of Pain*, *17*(1), 124–131. https://doi.org/10.1002/j.1532-2149.2012.00169.x

Shahidi, B., Johnson, C. L., Curran-Everett, D., & Maluf, K. S. (2012). Reliability and group differences in quantitative cervicothoracic measures among individuals with and without chronic neck pain. *BMC Musculoskeletal Disorders*, *13*(1), 1–11. https://doi.org/10.1186/1471-2474-13-215

Shan, Z., Deng, G., Li, J., Li, Y., Zhang, Y., & Zhao, Q. (2014). How schooling and lifestyle factors effect neck and shoulder pain? A cross-sectional survey of adolescents in China. *Spine*, *39*(4), 276-283. https://doi.org/10.1097/BRS.0000000000000124

Sheng, J., Liu, S., Wang, Y., Cui, R., & Zhang, X. (2017, June 19). The Link between Depression and Chronic Pain: Neural Mechanisms in the Brain. *Neural Plasticity*, Vol. 2017, 1-11. https://doi.org/10.1155/2017/9724371

Siddall, B., Ram, A., Jones, M. D., Booth, J., Perriman, D., & Summers, S. J. (2021).

Short-term impact of combining pain neuroscience education with exercise for chronic musculoskeletal pain: a systematic review and meta-analysis. *Pain*, 1–11. https://doi.org/10.1097/j.pain.0000000000002308

Siivola, S. M., Levoska, S., Latvala, K., Hoskio, E., Vanharanta, H., & Keinänen-Kiukaanniemi, S. (2004). Predictive factors for neck and shoulder pain: A longitudinal study in young adults. *Spine*, *29*(15), 1662–1669. https://doi.org/10.1097/01.BRS.0000133644.29390.43

Silva, A. G., Couto, P. S., Queiros, A., Neto, M., & Rocha, N. P. (2018). Musculoskeletal multisite pain and patterns of association after adjusting for sleep, physical activity, and screen time in adolescents. *Spine*, Vol. 43, 1432–1437. https://doi.org/10.1097/BRS.0000000000002646

Silva, A. G., Sa-Couto, P., Queirós, A., Neto, M., & Rocha, N. P. (2017). Pain, pain intensity and pain disability in high school students are differently associated with physical activity, screening hours and sleep. *BMC Musculoskeletal Disorders*, 18(194), 1.11. https://doi.org/10.1186/s12891-017-1557-6

Silva, A. G., Sharples, P., & Johnson, M. I. (2010, February 1). Studies comparing surrogate measures for head posture in individuals with and without neck pain. *Physical Therapy Reviews*, Vol. 15, 12–22. https://doi.org/10.1179/174328810X12647087218631

Silva, G. R. R., Pitangui, A. C. R., Xavier, M. K. A., Correia-Júnior, M. A. V., & De Araújo, R. C. (2016). Prevalence of musculoskeletal pain in adolescents and association with computer and videogame use. *Jornal de Pediatria*, *92*(2), 188–196. https://doi.org/10.1016/j.jped.2015.06.006

Simons, L. E., & Basch, M. C. (2016). State of the art in biobehavioral approaches to the management of chronic pain in childhood. *Pain Management*, Vol. 6, 49–61.

https://doi.org/10.2217/pmt.15.59

Simons, L. E., & Kaczynski, K. J. (2012). The fear avoidance model of chronic pain: Examination for pediatric application. *Journal of Pain*, *13*(9), 827–835. https://doi.org/10.1016/j.jpain.2012.05.002

Simons, L. E., Sieberg, C. B., & Claar, R. L. (2012). Anxiety and impairment in a large sample of children and adolescents with chronic pain. *Pain Research & Management*, *17*(2), 93–97. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/22518371

Simons, L. E., Smith, A., Ibagon, C., Coakley, R., Logan, D. E., Schechter, N., … Hill, J. C. (2015). Pediatric pain screening tool: Rapid identification of risk in youth with pain complaints. *Pain*, *156*(8), 1511–1518. https://doi.org/10.1097/j.pain.0000000000000199

Sjostrom, M., Ainsworth, B., Bauman, A., Bull, F., Hamilton-Craig, C., & Sallis, J. (2005). Guidelines for data processing analysis of the International Physical Activity Questionnaire (IPAQ) - Short and long forms. 1-15. Retrieved July 3, 2020, from https://www.scienceopen.com/document?vid=b223350f-d159-4043-9b48-e2031f210a3c

Slater, H., Jordan, J. E., Chua, J., Schütze, R., Wark, J. D., & Briggs, A. M. (2016). Young people's experiences of persistent musculoskeletal pain, needs, gaps and perceptions about the role of digital technologies to support their co-care: A qualitative study. *BMJ*, *6*(12), 1-11. https://doi.org/10.1136/bmjopen-2016-014007

Smart, K. M., Blake, C., Staines, A., Thacker, M., & Doody, C. (2012). Mechanisms-based classifications of musculoskeletal pain: Part 1 of 3: Symptoms and signs of central sensitisation in patients with low back (±leg) pain. *Manual Therapy*, *17*(4), 336–344. https://doi.org/10.1016/J.MATH.2012.03.013

Stahl, M., El-Metwally, A. A. S., & Rimpelä, A. H. (2014). Time trends in single versus concomitant neck and back pain in finnish adolescents: results from national cross-sectional surveys from 1991 to 2011. *BMC Musculoskeletal Disorders*, *15*(296), 1–7.

Ståhl, M., Kautiainen, H., El-Metwally, A., Häkkinen, A., Ylinen, J., Salminen, J. J., & Mikkelsson, M. (2008). Non-specific neck pain in schoolchildren: Prognosis and risk factors for occurrence and persistence. A 4-year follow-up study. *Pain*, *137*(2), 316–322. https://doi.org/10.1016/j.pain.2007.09.012

Stahlschmidt, L., Hübner-Möhler, B., Dogan, M., & Wager, J. (2019). Pain Self-Efficacy Measures for Children and Adolescents: A Systematic Review. *Journal of Pediatric Psychology*, *44*(5), 530–541. https://doi.org/10.1093/jpepsy/jsz002

Stanton, T. R., Leake, H. B., Chalmers, K. J., & Moseley, G. L. (2016, June 1). Evidence of impaired proprioception in chronic, idiopathic neck pain: Systematic review and meta-analysis. *Physical Therapy*, Vol. 96, 876–887. https://doi.org/10.2522/ptj.20150241

Staud, R. (2013). The important role of CNS facilitation and inhibition for chronic pain. *International Journal of Clinical Rheumatology*, Vol. 8, 639–646. https://doi.org/10.2217/ijr.13.57

Steele, E. J., Dawson, A. P., & Hiller, J. E. (2006, January). School-based interventions for spinal pain: A systematic review. *Spine*, Vol. 31, 226–233. https://doi.org/10.1097/01.brs.0000195158.00680.0d

Stinson, J., Connelly, M., Kamper, S. J., Herlin, T., & Toupin April, K. (2016, June 1). Models of Care for addressing chronic musculoskeletal pain and health in children and adolescents. *Best Practice and Research: Clinical Rheumatology*, Vol. 30, 468–482. https://doi.org/10.1016/j.berh.2016.08.005

Stommen, N. C., Verbunt, J. A., Gorter, S. L., & Goossens, M. E. (2012). Physical activity and disability among adolescents and young adults with non-specific musculoskeletal pain. *Disability and Rehabilitation*, *34*(17), 1438–1443. https://doi.org/10.3109/09638288.2011.645112

Straker, L. M., O'Sullivan, P. B., Smith, A. J., & Perry, M. C. (2009). Relationships between prolonged neck/shoulder pain and sitting spinal posture in male and female adolescents. *Manual Therapy*, *14*(3), 321–329. https://doi.org/10.1016/j.math.2008.04.004

Sullivan, M. J. L., Thorn, B., Haythornthwaite, J. A., Keefe, F., Martin, M., Bradley, L. A., & Lefebvre, J. C. (2001). Theoretical perspectives on the relation between catastrophizing and pain. *Clinical Journal of Pain*, *17*(1), 52–64. https://doi.org/10.1097/00002508-200103000-00008

Swain, M. S., Henschke, N., Kamper, S. J., Gobina, I., Ottová-Jordan, V., & Maher, C. G. (2014, May 13). An international survey of pain in adolescents. *BMC Public Health*, 14(447), 1-7. https://doi.org/10.1186/1471-2458-14-447

Szumilas, M. (2010). Explaining odds ratios. *Journal of the Canadian Academy of Child and Adolescent Psychiatry*, *19*(3), 227–229. Retrieved from http://www.csm-oxford.org.uk/

Tanaka, K., Murata, S., Nishigami, T., Mibu, A., Manfuku, M., Shinohara, Y., … Ono, R. (2019). The central sensitization inventory predict pain-related disability for musculoskeletal disorders in the primary care setting. *European Journal of Pain (United Kingdom)*, *23*(9), 1640–1648. https://doi.org/10.1002/ejp.1443

Tomlinson, R. M., Cousins, L. A., Mcmurtry, C. M., & Cohen, L. L. (2017). The power of pain self-efficacy: Applying a positive psychology framework to pediatric pain. *Pediatric*, Vol. 19, 1-5. Retrieved from: www.pubmed.gov/11194620

Tran, S., Jastrowski Mano, K., Hainsworth, K., Medrano, G., Anderson Khan, K., Weisman, S., & Davies, W. (2015). Distinct Influences of Anxiety and Pain Catastrophizing on Functional Outcomes in Children and Adolescents With Chronic Pain. *Journal of Pediatric Psychology*, *40*(8), 1-10. https://doi.org/10.1093/JPEPSY/JSV029

Treede, R. D., Rief, W., Barke, A., Aziz, Q., Bennett, M. I., Benoliel, R., … Wang, S. J. (2019, January 1). Chronic pain as a symptom or a disease: The IASP Classification of Chronic Pain for the International Classification of Diseases (ICD-11). *Pain*, Vol. 160, 19–27. https://doi.org/10.1097/j.pain.0000000000001384

Tsay, A., Allen, T. J., Proske, U., & Giummarra, M. J. (2015, May 1). Sensing the body in chronic pain: A review of psychophysical studies implicating altered body representation. *Neuroscience and Biobehavioral Reviews*, Vol. 52, 221–232. https://doi.org/10.1016/j.neubiorev.2015.03.004

Turk, D. C., & Wilson, H. D. (2010, April 3). Fear of pain as a prognostic factor in chronic pain: Conceptual models, assessment, and treatment implications. *Current Pain and Headache Reports*, Vol. 14, 88–95. https://doi.org/10.1007/s11916-010-0094-x

Valrie, C. R., Bromberg, M. H., Palermo, T., & Schanberg, L. E. (2013, February). A systematic review of sleep in pediatric pain populations. *Journal of Developmental and Behavioral Pediatrics*, Vol. 34, 120–128. https://doi.org/10.1097/DBP.0b013e31827d5848

Van Griensven, H., Schmid, A., Trendafilova, T., & Low, M. (2020). Central sensitization in musculoskeletal pain: Lost in translation? *Journal of Orthopaedic and Sports Physical Therapy*, *50*(11), 592–596. https://doi.org/10.2519/jospt.2020.0610

van Tulder, M., Furlan, A., Bombardier, C., & Bouter, L. (2003). Updated Method Guidelines for Systematic Reviews in the Cochrane Collaboration Back Review Group. *Spine*, *28*(12), 1290–1299. https://doi.org/10.1097/01.brs.0000065484.95996.af

van Wilgen, C. P., Vuijk, P. J., Kregel, J., Voogt, L., Meeus, M., Descheemaeker, F., … Nijs, J. (2018). Psychological Distress and Widespread Pain Contribute to the Variance of the Central Sensitization Inventory: A Cross-Sectional Study in Patients with Chronic Pain. *Pain Practice*, *18*(2), 239–246. https://doi.org/10.1111/papr.12600

Vikat, A., Rimpelä, M., Salminen, J. J., Rimpelä, A., Savolainen, A., & Virtanen, S. M. (2000). Neck or shoulder pain and low back pain in Finnish adolescents - PubMed. *Scand J Public Health*, *28*(3), 164–173. Retrieved from https://pubmed.ncbi.nlm.nih.gov/11045747/

Walker, L. S., & Engle, J. M. (2015). Manual for the Functional Disability Inventory (FDI). *Department of Pediatrics, Vanderbilt University*, 1–11.

Walton, D., Macdermid, • Joy, Nielson, • Warren, Teasell, R., Chiasson, • Marco, & Brown, • Lauren. (2011). Reliability, Standard Error, and Minimum Detectable Change of Clinical Pressure Pain Threshold Testing in People With and Without Acute Neck Pain. *Journal of Orthopaedic & Sports Physical Therapy® Downloaded from Www.Jospt.Org at On*, *41*(9), 644–650. https://doi.org/10.2519/jospt.2011.3666

Watson, J. A., Ryan, C. G., Cooper, L., Ellington, D., Whittle, R., Lavender, M., Martin, D. J. (2019). Pain Neuroscience Education for Adults With Chronic Musculoskeletal Pain: A Mixed-Methods Systematic Review and Meta-Analysis. *The Journal of Pain*, 20(10), 1-22 https://doi.org/10.1016/J.JPAIN.2019.02.011

Wells, G., Shea, B. J., & O'Connell, J. (2014). The Newcastle-Ottawa Scale (NOS) for Assessing The Quality of Nonrandomised Studies in Meta-analyses | Request PDF. *Ottawa Hospital Research Institute*. Retrieved from https://www.researchgate.net/publication/288802810_The_Newcastle-Ottawa_Scale_NOS_for_Assessing_The_Quality_of_Nonrandomised_Studies_in_Meta-analyses

Werner, E. L., Storheim, K., Lochting, I., Wisloff, T., & Grotle, M. (2016). Cognitive patient education for low back pain in primary care: A cluster randomized controlled trial and cost-effectiveness analysis. *Spine*, *41*(6), 455–462. https://doi.org/10.1097/BRS.0000000000001268

Williams, K., Thomson, D., Seto, I., Contopoulos-Ioannidis, D. G., Ioannidis, J. P. A., Curtis, S., … StaR Child Health Group. (2012). Standard 6: Age Groups for Pediatric Trials. *Pediatrics*, *129*(Supplement 3), 153–160. https://doi.org/10.1542/peds.2012-0055I

Wippert, P.-M., & Wiebking, C. (2018). Stress and Alterations in the Pain Matrix: A Biopsychosocial Perspective on Back Pain and Its Prevention and Treatment. *International Journal of Environmental Research and Public Health*, *15*(4), 785, 1-11. https://doi.org/10.3390/ijerph15040785

Woolf, C. J. (2011). Central sensitization: Implications for the diagnosis and treatment of pain. *Pain*, *152*(Supplement), 2–15. https://doi.org/10.1016/j.pain.2010.09.030

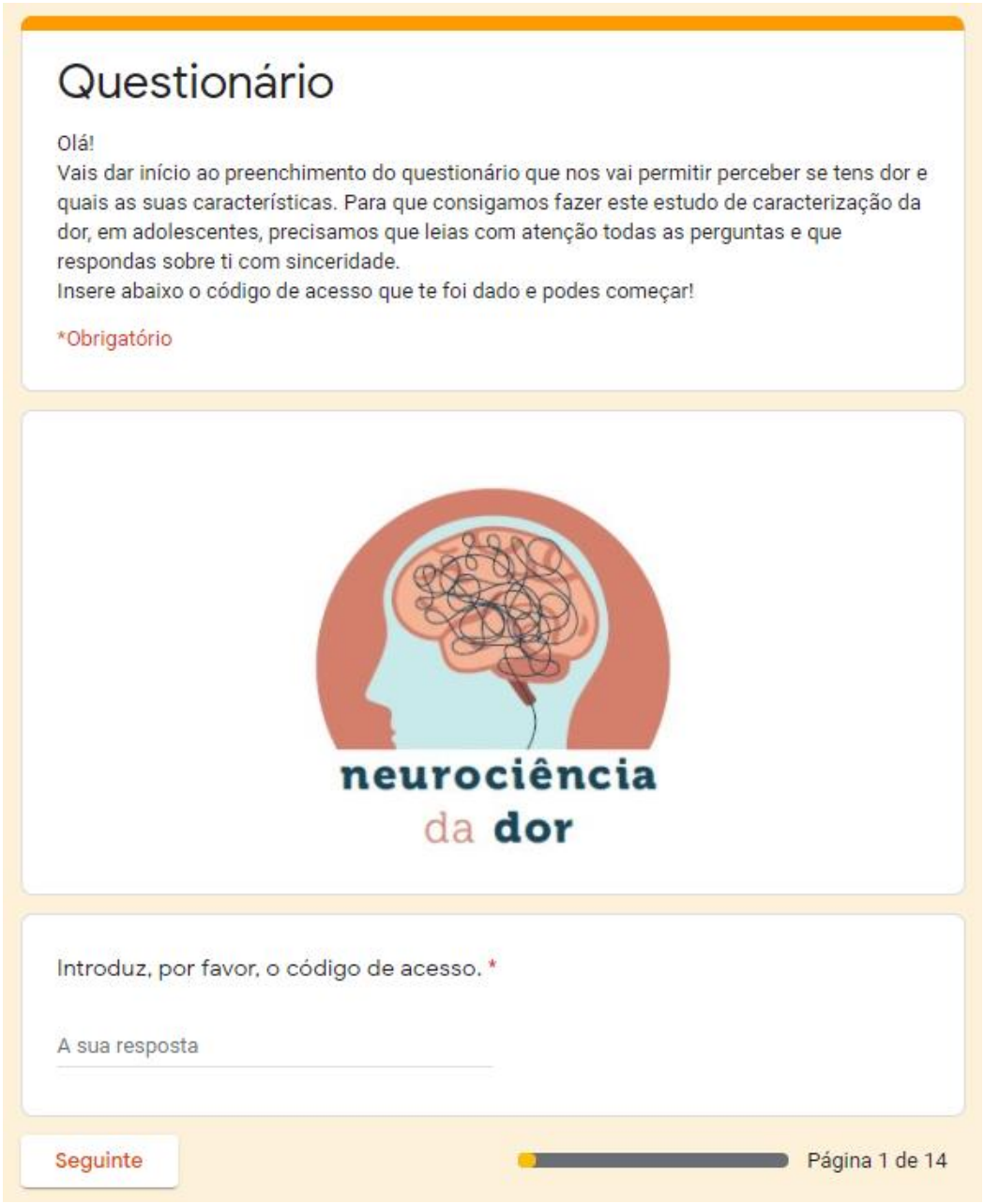
Yildiz, T. I., Turgut, E., & Duzgun, I. (2018). Neck and scapula-focused exercise training on patients with nonspecific neck pain: A randomized controlled trial. *Journal of Sport Rehabilitation*, *27*(5), 403–412. https://doi.org/10.1123/jsr.2017-0024

Zapata, A. L., Moraes, A. J. P., Leone, C., Doria-Filho, U., & Silva, C. A. A. (2006). Pain and musculoskeletal pain syndromes in adolescents. *Journal of Adolescent Health*, *38*(6), 769–771. https://doi.org/10.1016/j.jadohealth.2005.05.018

11. APPENDICES

11.1. Appendix 1

Layout of the online questionnaire used in the characterization studies and in the baseline, post-intervention, and 6-month follow-up assessment of the randomized controlled trial.



11.2. Appendix 2

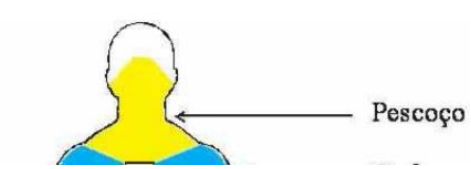
Inclusion criteria of the randomized controlled trial.

"Dor cervical crónica idiopática em adolescentes do ensino secundário"

Para conseguirmos perceber se tens dor ou não na região do pescoço, pedimos-te que respondas às duas questões que te colocamos a seguir. Lembra-te que a tua participação neste questionário é totalmente voluntária e se não quiseres preencher, poderás não o fazer sem dar qualquer justificação.

Por favor, responde a cada uma das perguntas assinalando com um **X** a **resposta que se aplica a ti ou indicando a informação solicitada**.

A.1 Dor



A.1.1 N**os últimos 3 meses**, tiveste **dor ou desconforto** na região do pescoço e sentiste essa dor ou desconforto pelo menos uma vez por semana?

Sim [ ] Não [ ]

Se assinalaste **"não"** o questionário termina por aqui. **Muito obrigada!**

A.1.2 Se assinalaste **"sim" na resposta anterior,** indica em baixo o valor que representa a intensidade da tua dor neste momento, sendo que 0 significa "Sem Dor" e 10 significa "Dor máxima"

Sem Dor	0	1	2	3	4	5	6	7	8	9	10	Dor Máxima

Se referiste dor no pescoço e assinalaste **"sim"** na primeira pergunta, preenche os teus dados abaixo:

Nome:_____

Qual o teu ano de escolaridade? (assinala só uma opção)

[ ] 10º ano

[ ] 11º ano

[ ] 12ºano

Qual a tua turma:_____

Código do Participante: [ ] **(a preencher pela investigadora)**

(Para destacar)

Código do Participante: [ ] **(a preencher pela investigadora)**

Ano:_____ **Turma**:_____

11.3. Appendix 3

Example guide to the first session of pain neuroscience education used in the randomized controlled trial.

1ª SESSÃO

Objetivos da sessão

-Breve apresentação e introdução ao programa;
-Compreender a neurofisiologia básica e a origem da dor no sistema nervoso;
-Compreender a evolução da dor aguda para a dor crónica e o papel dos mecanismos de sensitização periférica e central;
-Introdução das estratégias para controlo da dor crónica: a importância do exercício.

Parte 1: Introdução do Programa de Educação

- Apresentação das fisioterapeutas investigadoras e participantes;
    - Nome, idade, o que esperas do programa?
    - Eu sou a Rosa, sou Fisioterapeuta e estou a desenvolver este projeto no âmbito do meu doutoramento com a Prof. Dra. Anabela Silva.

- Motivação breve para o programa;
    - Como já te dissemos, este programa vai ajudar-te a compreender melhor a tua dor, e poderá ajudar a melhorar a tua dor! Para isso construímos um programa de 8 sessões (5 presenciais aqui na escola e 3 que vais poder ver e realizar em casa com os vídeos que construímos). Nas primeiras duas sessões vamos abordar alguns conceitos importantes para perceberes a tua dor e à medida que vamos avançando nas sessões, vamos introduzindo alguns exercícios para a tua dor no pescoço. Por isso esperamos que gostes destas 8 semanas! Para atingirmos os resultados do programa é muito importante a tua presença e participação em todas as sessões. Apenas conhecendo as tuas dúvidas e opiniões é que poderemos ajustar a informação ao que realmente é importante para ti!

Parte 2: Introdução aos conceitos

1. **A dor é normal!**
    - Como estamos aqui hoje para falar sobre a vossa dor no pescoço, temos de perceber o que é a dor! **Vocês sabem o que é a dor?**
    - **Como é que vocês acham que têm dor? É sempre um sinal de aviso? (2 minutos de discussão)**

(Deixar que os participantes respondam! O Ft faz pequenos apontamentos das respostas dadas (palavras-chave), para utilizarmos ao longo da sessão, e ir percebendo se eles acham que a dor é algo positivo ou negativo)

Quando te magoas/lesionas, como por exemplo, torces um pé (Já alguém torceu um pé? Senão podemos dar outro exemplo, como queimar-se num fogão), vais sentir dor e vais provavelmente lembrar-te do incidente várias vezes e, talvez, para o resto da tua vida! Vais recontar a história em inúmeros encontros de amigos e familiares e, provavelmente, mudar a forma como eles pensam também.

Imagina se não fosses avisado pelo corpo quando te magoavas! A dor alerta-te para retirares a parte do corpo do perigo. Quando fazes uma simples entorse, a dor impede-te de realizar alguns movimentos para não piorares, protegendo os teus tecidos de uma nova agressão. Conseguimos perceber assim que, **a dor é normal e funciona como um sinal de alerta!**

Agora, para sentires dor, o teu sistema nervoso tem de estar a funcionar bem. O teu sistema nervoso é um sistema contínuo que funciona como um sistema de alarme - projetado para te avisar do perigo. Como falámos, no caso de torceres um pé, te queimares ou pisares um prego (*ajustar de acordo com o que os participantes nos referirem no início da sessão*), o teu pé começa a doer! Alertar-te para o perigo é normal, faz parte da nossa sobrevivência.

(*mostrar poster grande+ imagens*)

O sistema nervoso é constituído por vários neurónios, interligados entre si, que levam a informação da ameaça/perigo dos recetores especiais de perigo, nociceptores, (mecânicos, térmicos e químicos, classificados pela modalidade do estímulo ambiental ao qual responde ou é sensível) até à medula espinhal e ao cérebro, para este processar e enviar uma resposta ativando o sistema de alarme. No caso de queimares a mão, ele envia uma mensagem descendente pela rede do sistema nervoso, para

sentires dor e retirares a mão do lume (*ver se eles no geral perceberam o circuito da dor: recetores→medula espinhal→cérebro (que deteta o que acontece na periferia, se está quente, frio, morno*)

Contudo, em cada um destes locais, acontecem pequenos fenómenos que permitem a transmissão da mensagem de perigo! Vamos agora então ver como tudo se processa em cada um destes!

Processamento da dor (*com o poster ir explicando o processamento normal da dor aguda após um estímulo externo e as estruturas que estão envolvidas e usar as pequenas imagens e legendas para ir construindo o esquema completo*)

1. Exemplo: Se queimares a mão, os recetores especiais da temperatura vão detetar o estímulo nocivo, transformá-lo em energia elétrica, e vão dar origem a diferentes mensagens no nosso sistema nervoso, dependendo da quantidade da estimulação do estímulo ambiental em causa;

2. Se a quantidade de energia elétrica for suficiente para atingir o limiar (valor limite de estimulação), (exemplo: se eu estiver perto do fogo, vou sentir mais quente, mas não acontece nada. Agora, se eu me aproximar, permanecer e o tocar, vou sentir alguma coisa!) um potencial de ação vai ser produzido, os nervos ficam excitados e enviam uma mensagem, normalmente, de perigo! *(se necessário, desenhar numa folha/no quadro o gráfico com a atividade do nervo, o tempo e o potencial de ação)*

3. Esta mensagem (sob a forma de potencias de ação) vai ser transportada ao longo dos teus neurónios, utilizando sinapses – abertura de portões (canais iónicos) na parede do nervo;

4. A mensagem é enviada ao longo do nervo, que está em constante atividade elétrica, até à medula espinhal e só depois transmitida até ao cérebro, para ser interpretada;

5. O cérebro envia mensagens pelos neurónios descendentes para a tua medula espinhal, que podem aumentar a informação nociceptiva (mensagens de perigo) que sobe pela tua medula espinhal.

6. Assim, estes neurónios podem trazer respostas inibitórias (para diminuir a tua dor), excitatórias (aumentar a tua dor) ou para a manter.

7. Em todo este processo, os teus nervos podem adaptar-se produzindo mais portões (canais iónicos) e aumentar o seu nível de excitação em repouso (ou seja, mais facilmente serão ativados).

Quando o estímulo de perigo cessar, o normal é que corpo regresse à sua condição de repouso normal!

Paragem: Questionar os participantes se perceberam e o que perceberam! Pedir-lhes para explicar o processo com um exemplo.

Atividade: Retirar as imagens e as legendas do poster e pedir aos alunos para as voltarem a colocar no local que acham correto de acordo com o que perceberam.

Assim, **como podes ver, é no cérebro que a dor é compreendida. Sem cérebro não havia dor!**

Consolidação de conhecimentos: mostrar vídeo do processamento normal da dor sem som! (https://www.youtube.com/watch?v=PMZdkac4YLk- ao mesmo tempo vamos fazendo nós a descrição do filme)

E, numa primeira fase, como foste capaz de ver, a dor é boa, é útil! Contudo, quando se mantém como a vossa, deixa de ter utilidade!
Mas então, porque é que a dor se manteve no vosso caso por tanto tempo? É isso que vamos tentar perceber agora!

2. A evolução para a dor crónica

Lançar algumas questões para perceber o que pensam da sua dor no pescoço:

- Quando é que ela surge/surgiu? Em que momentos do dia-a-dia?
- Sentes que surge quando estás mais nervoso ou agitado?
- Que estratégias utilizas para aliviar essa dor?

(Deixar que os participantes respondam! O Ft faz pequenos apontamentos numa folha/quadro das respostas dadas (palavras-chave))

À medida que vão respondendo às questões acima, levar os participantes a pensar em algumas situações onde existem diferentes perceções de dor:
- Quando tiramos sangue e já temos dor ainda a enfermeira não espetou a agulha! Situações em que há dor, e não há lesão!
- Quantas vezes estamos com dor de cabeça, e se nos distraímos, parece que ela diminui, e até mesmo desparece!
-Quantas vezes nos lesionamos (ex. a praticar um desporto, a correr para chegar a algum local) e só passado algum tempo nos começa a doer (o nosso corpo numa primeira instância reage para nos defender de uma ameaça maior. Em função do contexto, a dor é variável)

-O mesmo acontece com o vosso desconforto no pescoço e /ou ombros, existe uma dor sem lesão, ou uma lesão que não é diretamente proporcional à vossa dor!

Explicação da dor crónica: No vosso caso, o desconforto no pescoço já surge há alguns dias, semanas e meses, e já afeta algumas das vossas atividades do dia-a-dia! Neste caso, ela já não é um sinal de alerta ou de lesão, contrariamente ao que falámos há pouco! Vamos então perceber a razão de ela permanecer!

Desenvolvimento da dor crónica

- Está presente há mais de 3 meses (ao contrário da dor aguda, ultrapassa já o tempo que o nosso corpo necessita para recuperar de uma lesão!)
- Como persistiu, o sistema nervoso foi-se tornando cada vez mais especialista a transmiti-la e ocorreram um conjunto de alterações no teu sistema nervoso, tornando os teus recetores mais sensíveis à transmissão da mensagem de perigo:
    1. Na periferia vamos ter um aumento do número de canais iónicos (portões) nos recetores especiais da dor (nociceptores) e, portanto, vão ser mais a responder mais prontamente à mensagem de perigo (a energia necessária para os ativar também é mais baixa do que era anteriormente);
    2. A transmissão da mensagem de perigo ao longo do nervo vai ser muito mais eficaz, pois as sinapses (comunicação entre neurónios) também se estão a realizar de forma mais eficaz;
    3. Assim, a quantidade de informação que está a ascender ao cérebro, pela nossa medula espinhal (que a amplia), também é em maior e, portanto, o cérebro vai estar a constantemente ativo a tentar responder a estas mensagens de perigo (no cérebro, mais áreas vão estar ativadas e a responder à mensagem).

(Nota: Se necessário usar o exemplo da queimadura em contacto com a água fria)

- Com os nervos sensibilizados e a disparar facilmente, o sistema nervoso central e o teu cérebro não podem deixar de se interessar (excitando-se também), pois como já dissemos, o sistema nervoso, é um sistema contínuo. Mais uma vez - isto é normal. Assim sendo, para entenderes a tua dor agora, **precisas entender o teu cérebro.**
- Ao longo do tempo foi-se criando uma memória de dor no teu cérebro, que tende a responder de forma mais exagerada aos estímulos de dor, diminuindo

a capacidade de enviar respostas que a consigam acalmar! Vamos perceber esta “memória” na próxima sessão e o papel que as nossas emoções e pensamentos podem ter na nossa perceção de dor!

3. Relativamente à tua dor cervical e à importância do exercício

Há algum movimento que vos causa mais desconforto quando movimentam o pescoço? *(explorar as opiniões de todos os participantes)*

Por exemplo: Quando dobras (ou usar outro movimento relatado pelos participantes) o pescoço um pouco, dizes logo: "dói", mesmo que até às vezes seja só um desconforto mais pequeno. Porque tens medo de dobrar, os recetores especiais da dor e os nervos estão mais sensíveis e ativam-se com pouco estímulo. Por outro lado, o cérebro já está alerta porque tem a memória de que esse movimento(s) é doloroso! Neste caso, o cérebro vai interpretar esse movimento como uma ameaça, ativar mais áreas cerebrais e desencadear uma resposta dolorosa. **Mas lembra-te, com o tempo que já decorreu, eles estão mais sensíveis do que o normal**.

Nota:

Homúnculo

Lembram-se de falarmos das pessoas que podem ter dor mesmo quando não têm uma parte do corpo? Isso acontece porque no nosso cérebro há uma representação de cada uma das partes do nosso corpo. Entre outras coisas, estes mapas permitem-nos saber onde está cada uma das partes do nosso corpo. Por exemplo, se eu vos pedir para fechar os olhos e tocar com o dedo indicador no nariz, vocês conseguem. Nas pessoas que não têm dor cada parte do corpo está representada no cérebro de forma bem definida**. Quando a dor afeta uma parte do corpo, a representação dessa parte do corpo no cérebro fica desfocada. Quanto mais desfocada, maior é a dor. Mexer a parte do corpo com dor ajuda a redefinir a representação dos segmentos corporais no nosso cérebro.** Assim, é preciso mexer o nosso corpo, fazer exercício de forma gradual e progressiva. Compreender a dor também ajuda a redefinir as partes do corpo. Quando for muito doloroso ou difícil mover um segmento corporal, pode ajudar imaginar essa parte do corpo a mexer de forma lenta e gradual. Por exemplo, se pensarmos que os músicos e os atletas têm que repetir os movimentos vezes e vezes sem conta até serem muito bons no que estão a fazer, por isso percebemos a importância do exercício!

Agora percebes que, no teu caso, o desconforto que sentes não é um sinal de lesão ou dano nos tecidos. O teu pescoço pode estar doloroso, sensível ou mesmo com pouca força, mas não existir nenhuma lesão nos tecidos.

Ligação com a prática de exercício: Desta forma, a prática de exercício físico é importante no alívio da dor crónica!

- Mostrar e explicar esquema da Teoria do medo- evitamento

O exercício ajuda o sistema nervoso a ficar menos sensível e ajuda o corpo a combater a dor. O exercício ajuda no aumento da produção dos nossos próprios analgésicos endógenos (ex. as endorfinas, os nossos próprios bem-u-rons).

(Para consolidar esta ideia questionar os participantes como se sentem depois de dançar, jogar um jogo de futebol ou outro exercício que gostem).

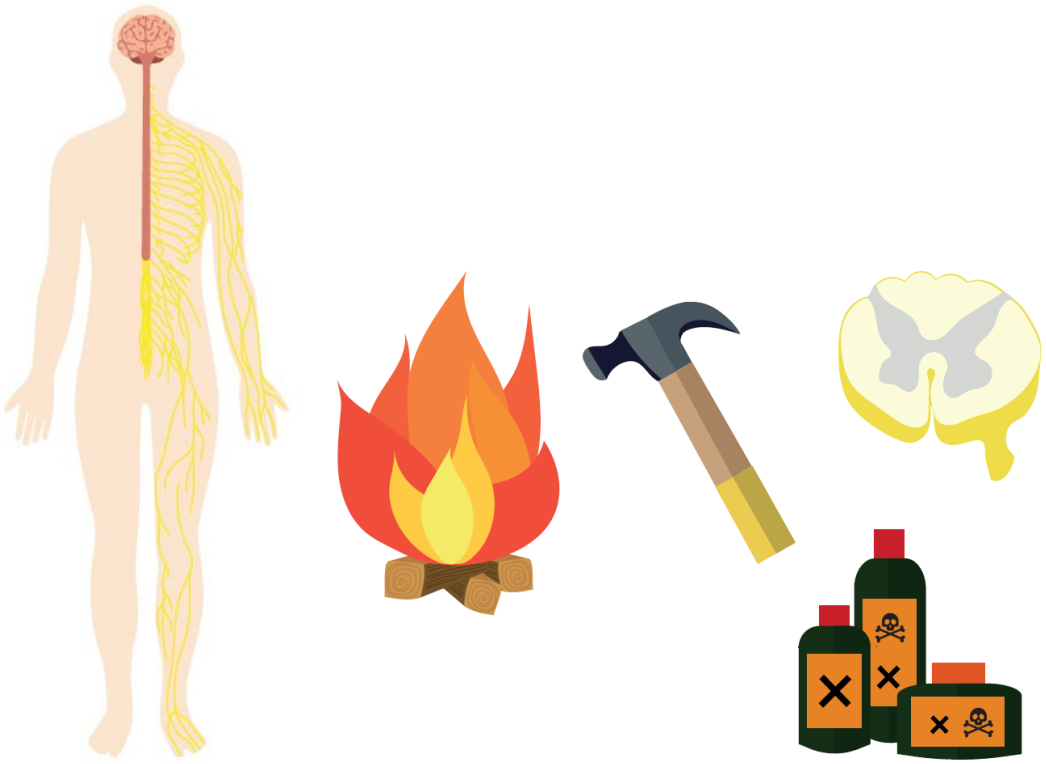
Agora, peço-te que faças o mesmo movimento que disseste que te incomodava, por exemplo, dobrar o teu pescoço para frente - recebes mensagens de perigo, mas as mensagens de perigo correm até ao cérebro, percorrem o mapa, mas não te sentes ameaçado por isso. Agora entendes que esta dor não te faz mal. O mapa ainda é percorrido, mas pode não haver dor, ou se existe, a dor é mais bem compreendida e, portanto, menos ameaçadora. Portanto, podes avançar dobrando gradualmente mais o teu pescoço.

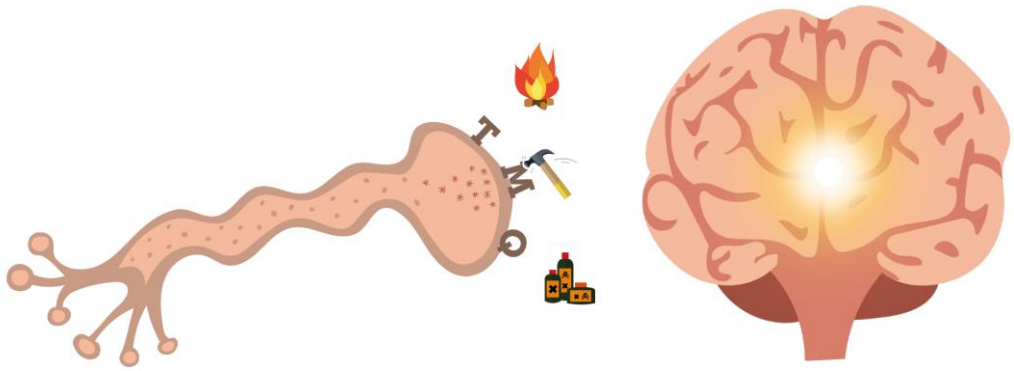
Resumo: No vosso caso, vocês desenvolveram um desconforto no pescoço que permanece há já algum tempo, e desenvolveu-se porque os vossos nervos tornaram-se muito sensíveis, porque o vosso sistema nervoso é um grande sistema que funciona como um todo, e o "sistema" manteve-se acordado. A boa notícia é que nós podemos explicar isto e quanto mais vocês entenderem sobre isso, mais os vossos nervos se vão acalmar.
É isto que vamos fazer ao longo destas sessões! Perceber como este desconforto surgiu e ao mesmo tempo realizar exercícios que vão ajudar a melhorar a tua condição e favorecer o alívio desse desconforto!

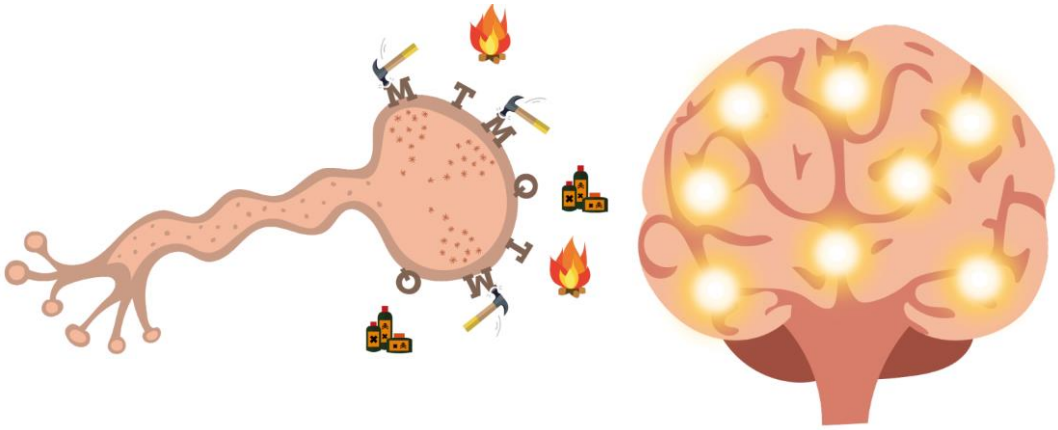
Finalizar a sessão com a questão: O que aprenderam de novo hoje? (para percebermos que mensagem lhes deixámos)

- Explicar documento que será enviado com 3 exercícios para fazerem em casa durante a semana (exemplificar brevemente)
- Explicar que irão receber os primeiros pontos-chave da sessão para relembrarem em casa com a correspondente atividade de casa (explicar). Pedir para trazerem na próxima sessão!

Pictures used throughout the first PNE session:



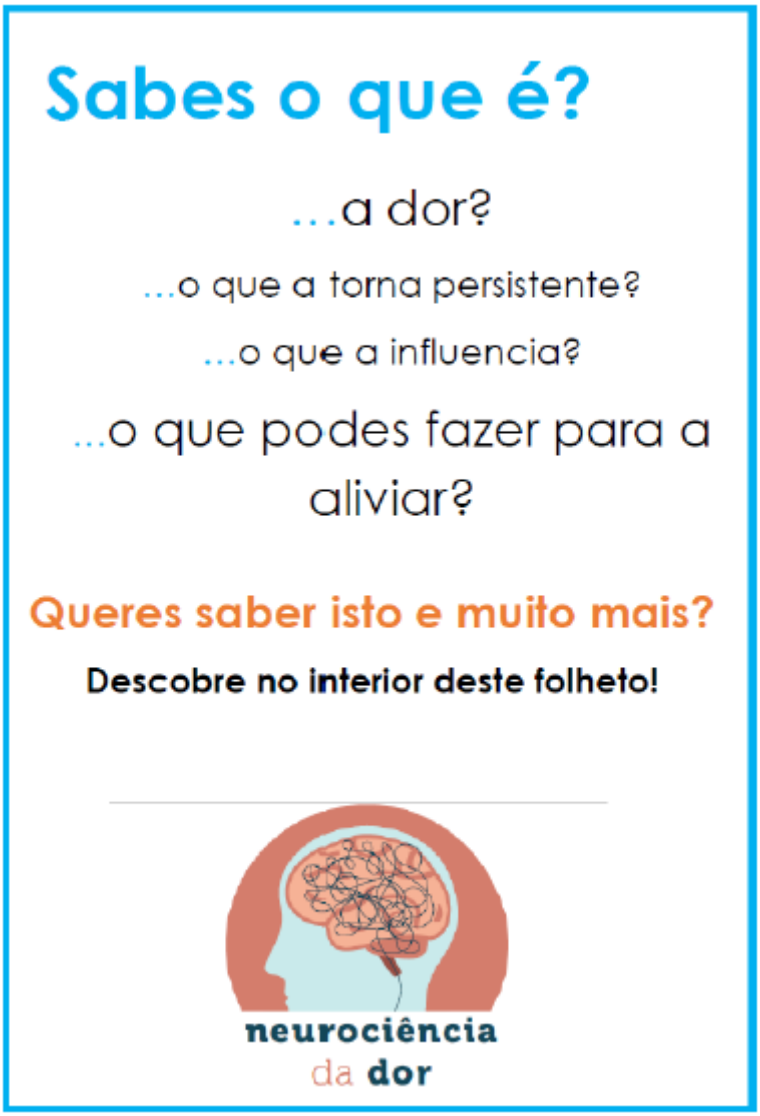




Illustrations by Bianca Silva

11.4. Appendix 4

Illustrative Brochure developed for the pain neuroscience education sessions of the randomized controlled trial by the research team.



1. A dor aguda é normal!

Quando te magoas ou lesionas, como por exemplo, queimas uma mão, sentes dor! Imagina o que aconteceria se não fosses avisado pelo corpo quando te magoavas... A dor alerta-te para não voltares a colocar a tua mão em perigo e evitar que te queimes. Como vês, **a dor é normal, funciona como um sinal de alerta e faz parte da nossa sobrevivência!**

Para isso, o teu sistema nervoso (SN) tem de estar a funcionar bem! O SN, constituído por vários neurónios, tem recetores nos tecidos (que respondem a estímulos mecânicos, térmicos e químicos) que detetam o perigo. Depois de detetarem o perigo, enviam mensagens de perigo, através dos nervos, para a medula e depois através desta para o cérebro. E só aqui, no cérebro, é que estas mensagens de perigo vão ser interpretadas e, se este achar necessário, produzida a sensação de dor! No caso de te magoares o cérebro envia uma mensagem pelos neurónios descendentes para sentires dor e não voltares a magoar-te. **Vê como ocorre o processamento normal da dor:**

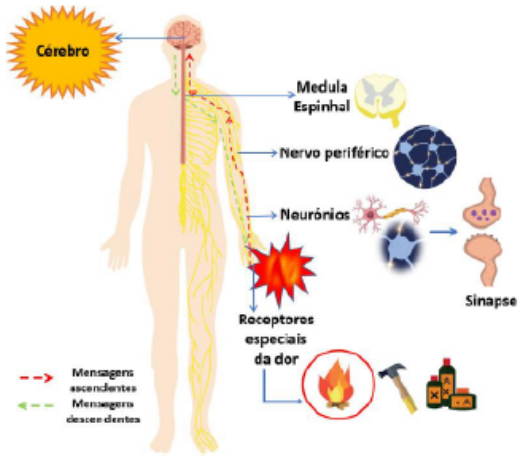


Figura 1: (Circuito de) Processamento da dor

1. Se queimares a mão, os recetores especiais de perigo para a temperatura vão detetar o estímulo e transformá-lo em energia elétrica;

2. Se a quantidade de energia elétrica for suficiente, dá origem a um potencial de ação, que é transmitido pelos nervos até à medula e passa de estrutura nervosa em estrutura nervosa através das sinapses – abertura de portões (canais iónicos) na parede do nervo;

4. A mensagem é enviada ao longo do nervo, até à medula espinhal e só depois é transmitida até ao cérebro, para ser interpretada. O cérebro interpreta a informação tendo em conta as tuas experiências anteriores, o teu estado emocional, o ambiente em que te encontras.

5. O cérebro envia mensagens para a medula espinhal, que podem alterar a informação que aqui chega (mensagens de perigo) diminuindo-a (se achar que não há perigo ou estiver ocupado com coisas mais importantes) ou aumentando -a (se achar que há perigo);

6. Ao longo deste processo, os nervos podem adaptar-se produzindo mais canais iónicos na sua parede, aumentar o seu nível de excitação em repouso e tornar-se mais sensíveis aos estímulos de perigo.

Pontos-chave

-Numa fase inicial, a dor é boa e funciona como um sinal de alerta;
-Quando te magoas, recetores especiais transmitem mensagens de perigo para a tua medula espinhal e depois para o teu cérebro;
-O cérebro decide quando vais sentir dor, e a sua decisão é afetada por muitas coisas (exemplo: experiências/acontecimentos anteriores, estado emocional, ambiente em que te encontras)
-O cérebro controla as mensagens de perigo que sobem através da medula e pode diminuir a quantidade destas mensagens (resposta inibitória), se achar que não há perigo, ou aumentá-las se achar que há perigo.

1. A dor persistente (crónica)

Vimos que a perceção da dor pode ser diferente consoante as situações. Quantas vezes te arranhaste, magoaste os teus os teus tecidos, e não sentiste dor? E quando foste apanhar uma vacina e já sentiste dor ainda antes de te espetarem a agulha? A dor dependo muito do contexto em que te encontras e se o teu cérebro está atento ao que está a acontecer (ou, por outro lado, distraído com coisas que são mais importantes para ti). No caso da dor persistente ela está presente há mais de 3 meses (ultrapassa o tempo que o corpo necessita para recuperar de uma lesão). Como persistiu, o SN foi-se tornando cada vez mais especialista a transmiti-la e ocorreram um conjunto de alterações que tornaram os recetores mais sensíveis à transmissão das mensagens de perigo:

1. Na periferia há um aumento do número portões (canais iónicos) nos recetores especiais da dor (nociceptores) e a energia necessária para os ativar é mais baixa do que era anteriormente;

2. A transmissão da mensagem de perigo ao longo do nervo tornou-se muito mais eficaz, pois a comunicação entre neurónios, (i.e., sinapses), também se tornou mais eficaz;

3. A quantidade de informação que ascende ao cérebro, pela nossa medula espinhal (que a amplia), é maior e, portanto, o cérebro vai estar constantemente ativo, com mais áreas ativadas e a responder às mensagens de perigo que lhe chegam.

Para entenderes a tua dor agora, também **precisas entender o teu cérebro!**

O cérebro adapta-se e procura ajudar em função da ameaça. As principais mudanças no cérebro têm a ver com a ativação de mais áreas e mais substâncias químicas que ativam a dor. Isto quer dizer que o cérebro vai ser mais fácil de ativar. Por exemplo, a área da memória é ativada se tivermos um acidente desagradável numa rua, sempre que passarmos nessa rua, vamos lembrar-nos do que aconteceu e, por vezes, até estremecemos, pois foi construída **uma etiqueta no cérebro**.

As várias etiquetas formadas no cérebro criam um mapa no cérebro semelhante ao mapa da rota dos aviões, que correspondem a todas as áreas que são ativadas com uma experiência dolorosa.

Mas, não existem áreas de dor no cérebro! Quando sentes dor, a dor utiliza várias áreas no cérebro usadas pelo movimento, sensações, emoções e memória. Estas áreas começam a comunicar umas com as outras. Desenvolves um "mapa da dor". Quando todas essas áreas se ativam e tu "percorres o mapa", vais sentir dor. Com a persistência da dor, estes mapas tornam-se cada vez mais fortes e, portanto, é mais difícil de nos libertarmos deles.

A boa notícia: Quanto mais cedo tentares modificar estas etiquetas no teu cérebro, mais cedo modificas o teu comportamento, evitando que a dor persista, se espalhe e piore ao longo do tempo. Quanto mais entenderes sobre dor, mais os teus nervos se vão acalmar.

Pontos-chave

- A dor não ocorre só quando estás magoado ou em risco de te magoares! Ela pode surgir mesmo quando não existem mensagens nervosas provenientes de uma parte do corpo dolorosa. Mas, também podes ter uma lesão e não sentir dor!
- As piores lesões nem sempre resultam numa pior dor.

No caso da tua dor no pescoço, os nervos estão mais sensíveis que o normal e por isso incomodam-te com mais facilidade, sobretudo quando o movimentas. O cérebro processa o movimento como uma ameaça, percorre o mapa de dor e responde de forma mais exagerada a este estímulo com a dor. Mas agora, percebes que as mensagens de perigo que tens durante os movimentos não são um sinal de lesão ou dano nos teus tecidos! O teu pescoço pode mais sensível ou mesmo com pouca força, mas não está magoado.

3. Fatores que influenciam a dor

Infelizmente, agora sabemos que, quando um desconforto persiste por um longo período de tempo, crias mapas de dor e os teus nervos tornam-se mais "sensíveis", e os impulsos elétricos que são normais, ficam mais perto do limiar de excitação. Neste caso, podem tornar-se sensíveis a coisas estranhas como o medo, stress, ansiedade, movimento. Assim, basta um pouco de medo, stress, movimento ou pensamento negativo para elevar a atividade ao nível necessário para fazer os teus nervos se excitarem e enviarem mensagens de perigo ao cérebro!

Então o que acontece? Neste caso, os músculos podem ficar mais cansados e sensíveis, a tua respiração torna-se superficial e, portanto, menos sangue e oxigénio chega aos tecidos fazendo com que estes fiquem também mais cansados e sensíveis. Entras em modo de stress constante. Tens problemas com o sono, ficas com mais dores e, entras num ciclo vicioso que terá tendência a aumentar!

Mas, não precisas ter medo! Estes mapas podem ser alterados. Quanto mais

entenderes sobre o teu desconforto e menos medo tiveres, mais estes mapas vão perder o seu poder. Quando um mapa ficar ativo pode resultar em dor ou não, uma vez que, tu entendes mais sobre a tua dor e assim o seu significado será diferente.

Ao perceberes a tua dor, consegues diminuir o estado de alerta em que está o teu cérebro, tornar menos sensível, todo o sistema de alarme, e acalmar a tua dor!

Da próxima vez que sentires desconforto, em vez de reagires como se te aparecesse um grande leão pela frente, vais reagir como se te aparecesse um pequenino leão, pois tu já consegues perceber o porquê e não o vais deixar tomar o controlo da tua vida e das tuas atividades do dia-a-dia. Agora, será a leão a ter medo de ti e não tu a teres medo dele!

Pontos-chave

- Quando estás lesionado, o ambiente em que estás, influencia muito a quantidade de dor que experimentas, mesmo que a lesão seja exatamente a mesma;

- Se magoares um pé a limpar a casa, de certeza que essa dor te vai incomodar e vais cessar de imediato as tarefas de limpeza. Mas, se magoares o pé da mesma maneira no teu último baile de finalista, provavelmente, só vais sentir dor quando chegares a casa. Até lá, vais continuar a dançar com os teus amigos!

-A forma como nos sentimos pode influenciar as respostas que são enviadas pelos nossos neurónios descendentes (quer para diminuir a tua dor, quer para a aumentar). No caso de teres pensamentos negativos, a tua dor pode aumentar, contrariamente aos pensamentos e comportamentos positivos que podem ajudar a diminuir a resposta de dor.

4. O papel fundamental do sono

O sono pode ajudar-te a sentires-te melhor!

Dormir bem é muito importante para revigorar o organismo do desgaste ocorrido durante o dia e ajudar o corpo a combater a dor. O nosso corpo tem um sistema próprio para combater a dor, a ativação de certas zonas do cérebro e a libertação de substâncias opióides (os nossos próprios Ben-u-rons) são alguns exemplos. Contudo, quando dormimos pouco ou dormimos mal ele torna-se menos capaz de ativar essas regiões do cérebro e de produzir estas substâncias! Para além do impacto na dor, também pode afetar o teu rendimento escolar e familiar.

Estratégias para uma boa noite de sono:

Tentar dormir pelo menos 8.5 a 10h por noite (se não conseguires dormir, levanta-te e faz uma atividade relaxante, como ler ou fazer exercícios de respiração, antes de tentares dormir outra vez)
Ter um horário regular de sono tentando deitar e levantar sempre à mesma hora (não deve variar mais que 1h aos fins-de-semana ou férias)
Ter uma rotina na hora de deitar (ter uma sequência habitual de atitudes para a preparação para o sono como: banho, jantar, ida para o quarto, leitura, música calma, lanche ligeiro como um copo de leite)
Ter o ambiente do quarto sossegado e escuro, com temperatura amena (a luminosidade e o ruído dos pc's, telemóveis, consolas, televisão, atrasam a chegada do sono e podem ajudar a despertar durante a noite)
Não ter fome ao deitar (a sensação de fome perturba o adormecer)
Evitar alimentos ou bebidas com estimulantes nas horas que antecedem o sono (evitar ingerir depois da hora do lanche coca-cola e, outros refrigerantes, chá, café, assim como chocolate, que contêm cafeína)
Não ingerir líquidos excessivos ao deitar ou durante as horas noturnas (a necessidade de ir ao wc pode levar a despertares repentinos)
Evitar atividades vigorosas nas 2 horas que antecedem a hora de deitar (o exercício é muito importante, mas pode atrasar o sono)

Deves ir para a cama apenas quando tiveres sono e usá-la apenas para dormir.

Os dispositivos eletrónicos não devem estar junto de ti (sempre podes virá-los para baixo ou tapá-los para diminuir a luminosidade), os livros de estudo devem ficar na tua secretária e os problemas da vida/escolares/familiares devem ficar à entrada do teu quarto!

5. Mantém-te ativo!

Como falaste ao longo das últimas sessões, os estudos mostram que quanto mais tu entenderes sobre o teu desconforto, mais os teus nervos se vão acalmar e menos desconforto vais sentir!

É importante também que encontres estratégias que vão minimizando o desconforto, e o teu pensamento sobre ele, no dia-a-dia/rotinas (e isto não quer dizer que não tenhas de ir ao médico e que procures ajuda para o resolver quando for necessário!) mas, por exemplo, **encontrar coisas para fazer que te distraiam, que gostes de fazer,** e que não te coloquem em foco o pensamento sobre o desconforto; **continuar com as atividades e movimentos do dia-a-dia** (mesmo que mais lentamente ou com algumas restrições), pois só assim vais conseguir **enviar mensagens positivas para o cérebro** quando este prevê uma ameaça ou perigo e minimizar a informação que chega ao cérebro.

Lembra-te que com o exercício, vais ajudar a bombear mais sangue e oxigénio pelo teu corpo. Isso permitirá que teus nervos de acalmem e que fiques com menos receio e de bom humor!

Quando tiveres um desconforto, tenta sempre perceber o porquê de o estares a sentir. Às vezes ele surge apenas porque fizeste um esforço inabitual. **O importante é que tentes manter o teu dia-a-dia normal, com um estilo de vida mais ativo e não pensar muito nele.** Lembra-te que quanto maior for o foco no desconforto, mais desconforto vais sentir!

Continua a realizar os exercícios que te ensinámos aqui para o teu desconforto no pescoço, para te ajudar a prevenir que ele surja, e relê este folheto quantas vezes forem necessárias para que continues a ser tu a ter o controlo da tua dor e o grande leão não se apodere da tua vida!

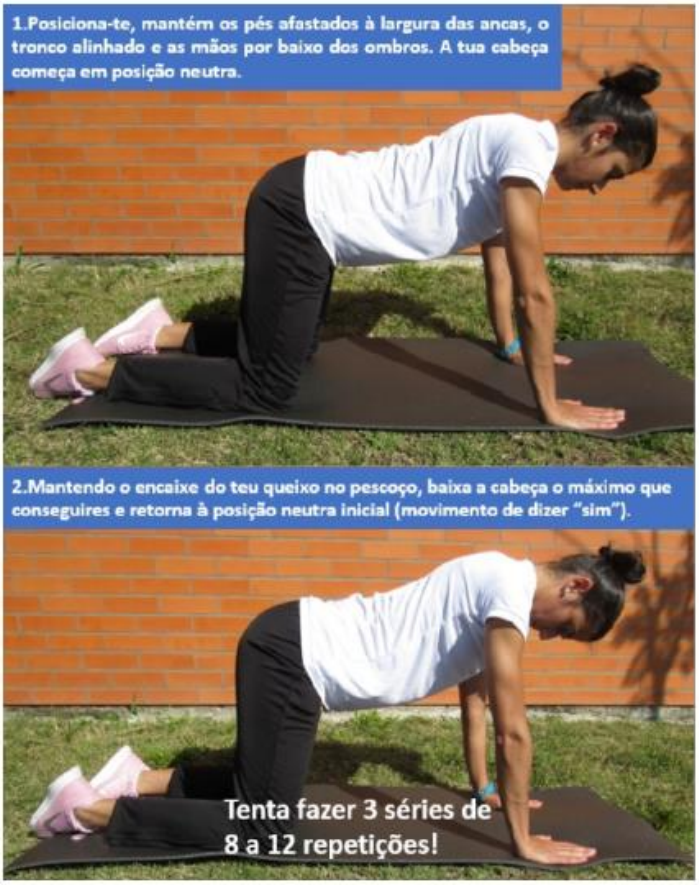
11.5. Appendix 5

Videos and pictures created for the exercise sessions of the randomized controlled trial by the research team.

Session	Video
3	https://www.youtube.com/watch?v=QLrVCGxA_E0
5	https://www.youtube.com/watch?v=gIbZbYOcyXc
6	https://www.youtube.com/watch?v=C_QrOCLM0RE
7	https://www.youtube.com/watch?v=xQETLmb1vOM
8a (exercise group)	https://www.youtube.com/watch?v=4_Tr7h8HvzI
8b (exercise plus PNE group)	https://www.youtube.com/watch?v=DrAFtMsfYqs

Other examples of exercise illustrations used

Tenta fazer 3 séries de 8 a 12 repetições! Se manter a posição por 3-5 segundos já for fácil para ti, podes aumentar o tempo de contração até chegar aos 8-10 segundos!




1.Posiciona-te, mantém os pés ligeiramente afastados à largura das ancas, o tronco inclinado a 45°, a cabeça em posição neutra e os cotovelos apoiados a 90° à altura e largura dos ombros.
2.Nesta posição, faz pequenos movimentos para juntar as tuas omoplatas, (vê a direção do movimento nas setas da figura!) aguentando a posição de junção das omoplatas, cerca de 3-5 segundos!
Tenta fazer 3 séries de 8 a 12 repetições!


Posiciona-te e alonga em cada posição, pelo menos, 20 a 30 segundos!