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Fadiga muscular periférica de membros superiores em crianças e adolescentes típicos e com espinha bífida

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Tese de Doutorado apresentada à Faculdade de Medicina de Ribeirão Preto da Universidade de São Paulo para obter o Título de Doutor em Ciências da Saúde.
Área: Fisioterapia.

Orientadora: Profa Dra Ana Claudia Mattiello-Sverzut.

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“Porque para Deus nada é impossível”

Lucas 1:37

Resumo

MARTINS, E. J**. Fadiga muscular periférica de membros superiores em crianças e adolescentes típicos e com espinha bífida.** 2023. 171f. Tese (Doutorado) – Faculdade de Medicina, Universidade de São Paulo, Ribeirão Preto, Brasil.

Introdução: Pacientes com doenças neurológicas crônicas, como a espinha bífida (EB), apresentam predomínio de alterações motoras e sensoriais nos membros inferiores, o que torna esses indivíduos mais suscetíveis ao estilo de vida sedentário, com maior predisposição para o aparecimento de doenças cardiovasculares, obesidade, fraqueza e fadiga motora. Por outro lado, nesses pacientes há aumento da exigência dos membros superiores para execução de tarefas diárias, transferências posturais e locomoção com uso de dispositivos. Logo, é importante investigar o desempenho muscular de membros superiores de crianças e adolescentes com EB, com intuito de detectar alterações e propor intervenções precoces que mantenham a independência funcional e, consequentemente previnam os riscos associados ao sedentarismo. No entanto, são escassos na literatura estudos científicos que investigaram o desempenho muscular de membros superiores, especialmente fadigabilidade, utilizando diferentes instrumentos, como dinamômetros e eletromiografia, em crianças e adolescentes com desenvolvimento típico e naquelas com doenças crônicas. Para tal investigação, os protocolos de avaliação devem monitorar o desenvolvimento de força/torque ou pressão utilizando instrumentos como dinamômetros (isocinético e de bulbo), eletromiografia de superfície (EMG) e escalas de percepção de esforço. **Objetivos:** O objetivo geral deste estudo foi avaliar o desempenho muscular, principalmente fadigabilidade motora, de membros superiores em crianças e adolescentes com desenvolvimento típico e naquelas com EB. Os objetivos específicos incluíram (a) investigar a influência da maturação sexual e sexo na fadigabilidade dos extensores do cotovelo durante contrações concêntricas voluntárias máximas repetidas em crianças e adolescentes com desenvolvimento típico (Artigo 1); (b) comparar a fadigabilidade dos flexores e extensores do cotovelo durante contrações concêntricas voluntárias máximas repetidas entre crianças e adolescentes com desenvolvimento típico e aquelas com EB (Artigo 2); (c) comparar o torque isométrico máximo, a taxa de desenvolvimento de torque - TDT (0-300 ms) dos flexores e extensores do cotovelo entre crianças e adolescentes com desenvolvimento típico e aquelas com EB (Artigo 3); (d) analisar a fadigabilidade e a influência do sexo nos músculos flexores e extensores dos dedos durante a atividade repetida de preensão palmar em crianças com desenvolvimento típico (Artigo 4); e, (e) comparar a fadigabilidade durante a atividade repetida de preensão palmar entre crianças e adolescentes com desenvolvimento típico e aquelas com EB (Artigo 5). **Métodos:** Estudo observacional transversal, aprovado pelo Comitê de Ética em Pesquisa com Seres Humanos da Faculdade de Medicina de Ribeirão Preto - USP, CAAE: 24947214.8.0000.5440; 63579916.2.0000.5440). Participaram do estudo crianças e adolescentes típicos (n=84), estudantes da cidade de Ribeirão Preto (SP) e crianças e adolescentes com EB (n=23), em acompanhamento no Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto da Universidade de São Paulo – HCFMRP/USP, de 7 a 17 anos, de ambos os sexos. Todos os participantes foram avaliados quanto a composição corporal (bioimpedância elétrica), nível de atividade física (Physical Activity Questionnaire for Older Children and Adolescent – PAQ-C/PAQ-A) e nível de maturação sexual (estágios de Tanner, 1962), e os participantes com EB foram avaliados em relação ao nível de lesão medular (achados no exame de imagem), prognóstico de deambulação (critérios estabelecidos por Schoenmakers et al., 2005) e nível de funcionalidade (The Functional Mobility Scale). Para avaliação do desempenho muscular utilizamos 3 protocolos

de avaliação: (a) contrações concêntricas máximas dos músculos flexores e extensores do cotovelo utilizando o dinamômetro isocinético - *Biodex Multjoint System* 4®, na velocidade $120^{o.s-1}$ (Artigos 1 e 2); (b) contrações isométricas explosivas e máximas dos músculos flexores e extensores do cotovelo utilizando dinamômetro isocinético (Artigo 3); e, (c) contrações concêntricas máximas dos músculos flexores dos dedos utilizando o dinamômetro de bulbo - *North Coast - NC70154* (Artigos 4 e 5). Os protocolos com contrações concêntricas compreenderam a execução 3 contrações máximas, repouso de 10 minutos, seguido de contrações cíclicas ilimitadas até o voluntário atingir queda de 50% do torque máximo e/ou relatar cansaço máximo (Children´s OMNI Scale of Perceived Exertion). O protocolo com contrações isométricas incluiu 3 contrações máximas, sustentadas por 5 segundos e repouso de 20 segundos entre cada contração. Os 3 protocolos descritos incluíram o registro EMG simultâneo dos músculos bíceps e tríceps braquial ou flexores e extensores dos dedos da mão - *Trigno™Wireless System Delsys Inc,* seguindo as recomendações do SENIAM. Foram analisadas as variáveis pico de torque (PT), pressão palmar, amplitude normalizada e frequência de potência mediana do sinal EMG provenientes dos testes anteriormente descritos. Foi realizada a análise de normalidade dos dados para direcionar a escolha dos testes estatísticos de comparação entre os grupos. Para todas as análises foi considerado um nível de significância $p \leq 0,05$. **Resultados:** Durante o teste de fadigabilidade dos extensores do cotovelo de crianças e adolescentes típicos ocorreu menor declínio do PT para o grupo pré-púbere, maior amplitude EMG para o grupo pré-púbere feminino, e maior declínio da frequência mediana para o grupo pós-pubere masculino quando comparados aos demais grupos (Artigo 1). Participantes com EB apresentaram menores valores de PT isocinético (Artigo 2), PT isométrico e TDT (Artigo 3) dos músculos do cotovelo, e menores valores de pressão palmar (Artigo 5) em comparação aos seus pares típicos. Porém, a análise do PT (normalizado para o peso corporal) durante o trabalho muscular repetitivo dos flexores do cotovelo mostrou que os participantes do EB apresentaram maior resistência à fadiga em comparação com os típicos (Artigo 2), e foram capazes de resistir à fadiga de forma semelhante aos típicos durante contrações repetidas de preensão palmar (Artigo 5); em ambos os casos não foram observadas diferenças entre os grupos para a ativação neuromuscular. **Conclusão:** Crianças e adolescentes com EB apresentaram PT (isocinético e isométrico), TDT e pressão palmar reduzidos, porém resistência à fadiga durante atividade de preensão palmar e dos músculos do cotovelo similares em comparação com seus pares típicos**.** Esses achados podem direcionar a escolha de intervenções terapêuticas para crianças e adolescentes com EB.

Palavras-chave: eletromiografia, fadiga, força muscular, isocinético, mielomeningocele.

Abstract

MARTINS, E. J**. Peripheral muscle fatigue of upper limbs in typically developing children and adolescents and those with spina bifida.** 2023. 171f. Thesis – Ribeirão Preto Medical School, University of São Paulo, Brazil.

Introduction: Patients with chronic neurological diseases, such as spina bifida (SB), have a predominance of motor and sensory disorders in the lower limbs, which makes them more susceptible to a sedentary lifestyle, with a greater predisposition to develop cardiovascular diseases, obesity, muscle weakness, and neuromuscular fatigue. However, these patients require more their upper limbs to perform daily tasks, postural transfers, and locomotion with assistive devices. Therefore, it is important to investigate the muscle performance of the upper limbs of children and adolescents with SB to detect alterations and propose early interventions that maintain functional independence and, consequently, prevent the risks associated with a sedentary lifestyle. However, few scientific studies have investigated the muscular performance of the upper limbs, especially in terms of fatigability, in typically developing children and adolescents and in those with chronic diseases. For such an investigation, evaluation protocols should monitor the development of strength/torque or pressure using instruments such as dynamometers (isokinetic and bulb) associated with the analysis of neurophysiological changes by surface electromyography (EMG) and scales of perceived effort. **Objectives:** The general objective of this study was to evaluate muscular performance, mainly motor fatigability, of the upper limbs in typically developing children and adolescents, and in those with SB. Specific objectives included (a) to investigate the influence of sexual maturation and sex on the fatigability of the elbow extensors during repeated maximal voluntary contractions in typically developing children and adolescents (Article 1); (b) to compare the fatigability of elbow flexors and extensors during repeated maximal voluntary contractions between typically developing children and adolescents and those with SB (Article 2); (c) to compare the maximum isometric torque, rate of torque development - RTD (0-300 ms) of the elbow flexors and extensors between typically developing children and adolescents and those with SB (Article 3); (d) to analyze the fatigability and the influence of sex on the flexor and extensor muscles of the fingers during the repeated handgrip activity in typically developing children (Article 4); and, (e) to compare fatigability during repeated handgrip activity between typically developing children and adolescents and those with SB (Article 5). **Methods:** Cross-sectional observational study, approved by the Ethics Committee of the Ribeirão Preto Medical School of University of São Paulo - USP, CAAE: 24947214.8.0000.5440; 63579916.2.0000.5440). The study included typically developing children and adolescents (n=84), who were students from Ribeirão Preto (SP), and children and adolescents with SB (n=23), who were followed up at Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo – HCFMRP/USP, from 7 to 17 years of age, of both sexes. All participants were assessed for body composition (electrical bioimpedance), level of physical activity (Physical Activity Questionnaire for Older Children and Adolescents, PAQ-C/PAQ-A), and level of sexual maturation (Tanner stages, 1962), and participants with SB were assessed in terms of the level of spinal cord injury (imaging records), type of locomotion (criteria established by Schoenmakers et al., 2005), and functional mobility level (Functional Mobility Scale). Three protocols were used to assess muscle performance: (a) maximum concentric contractions of the elbow flexor and extensor muscles using an isokinetic dynamometer (Biodex Multjoint System 4®, at $120^{\circ.s-1}$ (Articles 1 and 2); (b) explosive and maximal isometric contractions of the elbow flexor and extensor muscles using an isokinetic dynamometer (Article 3); and, (c) maximum concentric contractions of the finger flexor muscles using the bulb dynamometer North Coast

NC70154 (Articles 4 and 5). The protocols with concentric contractions comprised the execution of three maximum contractions, 10-min of rest, followed by unlimited cyclic contractions until the participant reached a drop of 50% of the maximum torque and/or maximum score of reported fatigue (Children's OMNI Scale of Perceived Exertion). The protocol with isometric contractions included three maximal contractions sustained for 5-sec and 20-sec of rest between each contraction. All protocols included simultaneous EMG recording of the biceps and triceps brachii muscles or finger flexors and extensors (Trigno™Wireless System Delsys Inc.), following the SENIAM recommendations. The peak torque (PT), handgrip pressure, amplitude, and median power frequency of the EMG signal from the tests described above were analyzed. Data normality analysis was performed to guide the selection of statistical tests for group comparisons. A significance level of 5% was considered for all analyses. **Results:** During the fatigue test of the elbow extensors of typically developing children and adolescents, there was a smaller decline in PT in the prepubertal group, a greater EMG amplitude in the prepubertal female group, and a greater decline in the median frequency in the postpubertal male group compared to the other groups (Article 1). Participants with SB had lower isokinetic PT (Article 2), isometric PT, and RTD (Article 3) of the elbow muscles, and lower values of handgrip pressure (Article 5) compared to their typical peers. However, the PT analysis (normalized to body weight) during repetitive muscle work of the elbow flexors showed that SB participants had a greater resistance to fatigue compared to the typical ones (Article 2) and were able to resist fatigue similar to typically developing controls during repeated handgrip contractions (Article 5); in both cases, no differences were observed between groups for neuromuscular activation. **Conclusion:** Children and adolescents with SB showed lower PT (isokinetic and isometric), RTD, and handgrip pressure; however, they had similar resistance to fatigue during repetitive elbow movements and handgrip activity compared with their typical peers. These findings may guide the choice of therapeutic intervention for children and adolescents with SB.

Keywords: electromyography, fatigue, strength, isokinetic, myelomeningocele.

SUMÁRIO

1 INTRODUÇÃO GERAL

Desempenho muscular e funcionalidade são alvo de investigação clínica e científica nos pacientes que possuem disfunções neurológicas, pois remetem às atividades de vida diária e qualidade de vida. Nestes pacientes, tais atividades tornam-se progressivamente reduzidas devido ao acometimento primário ou secundário dos sistemas nervoso e musculoesquelético (Koop and Shrader 2021). A inatividade física, que representa um acometimento secundário desse sistema, aumenta os riscos para o desenvolvimento de doenças cardiovasculares, metabólicas (incluindo obesidade), aumento do gasto energético em tarefas cotidianas e ocorrência de fadiga motora (Buffart, Roebroeck, et al. 2008; Kinne, Patrick, and Doyle 2004; Bloemen et al. 2015; Finsterer and Mahjoub 2014). No contexto pediátrico tais apontamentos não representam exceção. Portanto, ainda que a Fisioterapia aplicada à Neuropediatria tenha alcançado destaque pelo grau de aprofundamento das pesquisas que exploram aspectos do neurodesenvolvimento e aquisição de habilidades motoras para os pacientes com doenças neurológicas crônicas, durante as fases da infância e adolescência, as abordagens terapêuticas ainda guardam ressalvas quanto a eleição de modalidades de exercícios e dosagens, que devem focar no treinamento de força e potência muscular, e resistência cardiorrespiratória (Oliveira et al., 2016). Fatores como o sexo, idade, estágio de maturação sexual, grupos musculares envolvidos na tarefa e a própria doença de base tornam o desafio terapêutico ainda maior, e isto inclui aqueles pacientes que apresentam debilidades em seus membros inferiores. Portanto, é fundamental investigar o desempenho muscular de crianças e adolescentes com doenças crônicas, nas quais as estratégias de avaliação e intervenção para manutenção da qualidade de vida deverão estar focadas nos membros superiores, que são menos acometidos (e, portanto, mais utilizados) que os membros inferiores, como nos pacientes com espinha bífida (EB).

1.1 Espinha bífida

A EB é a segunda maior causa de incapacidade física na infância (Young et al. 2014). É causada pela malformação do tubo neural, que resulta em defeitos estruturais e funcionais na medula espinhal e no encéfalo (Oliveira, Jácome, and Marques 2014), especialmente no seu tipo mais grave, a EB cística ou mielomeningocele. Das alterações ocorridas na medula espinhal, podem ser identificadas alterações motoras e sensoriais em diversos níveis segmentares (Vinck et al. 2010), com predomínio de acometimento nos membros inferiores. Adicionalmente, a hipomobilidade e/ou inatividade dos pacientes com EB, aumenta o risco do

desenvolvimento de um estilo de vida sedentário, com presença de obesidade e doenças cardiovasculares (Bruinings et al. 2007; Buffart, van Berg-Emons, et al. 2008).

Baseado nas recomendações do The International Myelodysplasia Study Group (IMSG), a força muscular dos membros inferiores é usada para atribuir o nível de comprometimento neuro-segmentar e classificar funcionalmente os pacientes com EB em quatro grupos: torácico, lombar alto, lombar baixo e sacral (Hoffer et al., 1973; Wright 2001). Cada grupo apresenta características distintas, sendo possível para cada um, traçar o prognóstico do tipo de deambulação (terapêutica, domiciliar ou comunitária) e direcionar o tratamento (M. A.G.C. Schoenmakers et al. 2005). A locomoção também pode ser classificada utilizando a Escala de Mobilidade Funcional (FMS) baseada nos relatos dos pacientes com EB e seus pais a respeito da capacidade de mobilidade em casa (distância de 5 m), escola (distância de 50 m) e comunidade (distância de 500 m), e se há a necessidade do uso de dispositivos para locomoção nesses trajetos, tais como cadeira de rodas, andador, muletas ou bengalas (Davoli et al. 2021). Na maioria dos casos de EB a região da lesão medular é toracolombar, restando apenas a possibilidade de deambulação com órteses e muletas, ou uso de cadeira de rodas para locomoção (Rethlefsen et al. 2021).

Portanto, os pacientes com EB apresentam acometimento da inervação dos músculos dos membros inferiores, o que torna esses indivíduos mais suscetíveis ao estilo de vida sedentário. Por outro lado, há um aumento da exigência dos membros superiores para a execução de tarefas diárias como transferências posturais e locomoção com uso de dispositivos auxiliares. Logo, investigar aspectos relacionados ao desempenho muscular de membros superiores é de extrema importância nesta população (especialmente na infância e adolescência), com intuito de detectar alterações e propor intervenções adequadas e precoces que mantenham a independência funcional em níveis adequados e, dessa forma, previnam os riscos associados ao sedentarismo listados anteriormente.

1.2 Desempenho muscular dos pacientes com espinha bífida

Embora os pacientes com EB, em sua maioria, façam uso de vários dispositivos auxiliares na locomoção, exigindo níveis suficientes de trabalho cardiorrespiratório e de força dos músculos dos membros superiores, a revisão sistemática de Oliveira e colaboradores mostrou que 26,3-61% dos pacientes com EB têm restrição à mobilidade, apresentam menor resistência cardiorrespiratória (diminuição de 32 a 54% no pico VO2), menor força muscular de membros superiores e inferiores (redução de 58 a 90%), além de maior porcentagem de

gordura corporal (aumento de 159%) do que seus pares saudáveis (Oliveira, Jácome, and Marques 2014).

A força de preensão palmar é uma medida que representa a força muscular global e o estado de saúde em populações clínicas e saudáveis (McGrath et al. 2020; Jiang et al. 2022). A diminuição da força de preensão palmar também foi encontrada em pacientes com EB, com um valor 71,03 (23,3)% menor do que o previsto (Norrlin et al. 2003; Buffart, Roebroeck, et al. 2008), o que ainda poderia indicar disfunção neurológica relacionada a anormalidades centrais (mau funcionamento do shunt ventricular ou sintomas de malformação de Arnold Chiari) (Campbell, Vander Linden, and Palisano 2006) ou periféricas (atrofia de fibras e transição entre diferentes tipos de fibras) (Thompson 2002).

Nosso grupo de pesquisa, desde 2014, tem investigado parâmetros da função muscular e cardiopulmonar de crianças e adolescentes com EB [fomentos fornecidos pela Fapesp processos n. 2013/05936-4 (bolsa mestrado) e n. 2013/15425-7 (Auxílio Regular à Pesquisa) e CNPq processo n. 475791/2013-4 (Edital Universal)]. Entre 2014 e 2015, crianças e adolescentes não-deambuladores com EB realizaram o teste ergoespirométrico em cicloergômetro de membros superiores. Em paralelo, foi realizado teste de campo com cadeira de rodas de 12 minutos. Neste segundo teste, os participantes atingiram o esforço máximo (frequência cardíaca pico similar à obtida no teste direto), porém, a maioria não completou o percurso. Em ambos os testes de avaliação de desempenho cardiopulmonar as crianças interromperam o teste relatando alta intensidade de cansaço muscular (fadiga relatada) (Leonardi-Figueiredo et al. 2018; Tuijtelaars et al. 2019; Leonardi-Figueiredo et al. 2021). Tais estudos também demonstraram alto grau de dependência dos participantes em relação aos seus cuidadores, justificando a baixa resistência à fadiga dos músculos de membros superiores.

Em outro estudo, também do nosso grupo de pesquisa, as mesmas crianças e adolescentes com EB, usuários de cadeira de rodas (n=11) tiveram a força e torque muscular do braço comparadas com seus pares com desenvolvimento típico (n=22). A dinamometria isocinética foi utilizada para medir o pico de torque (PT) durante testes dinâmicos concêntricos ($60^{\circ.s^{-1}}$,$120^{\circ.s^{-1}}$) e isométricos dos flexores e extensores de ombro e cotovelo do membro superior dominante. O dinamômetro handheld (HHD) foi utilizado para medir a força a partir da contração isométrica voluntária máxima (CIVM) dos mesmos grupos musculares. Os participantes com EB apresentaram menores valores de PT isocinético concêntrico para extensores de ombro a $60^{\circ.s^{-1}}$ e $120^{\circ.s^{-1}}$, PT isométrico para flexores de ombro, e PT isocinético concêntrico a $60^{\circ.s^{-1}}$ e PT isométrico para flexores de cotovelo; maiores valores de PT isocinético concêntrico a $120^{\circ.s^{-1}}$ para flexores de ombro e flexores de cotovelo; e diminuição da CIVM para

os flexores do cotovelo, mas não para os extensores, em comparação com os controles quando avaliados por HHD. Portanto, os participantes com EB apresentaram níveis reduzidos de PT isocinético concêntrico de ombro e cotovelo em baixa velocidade ($60^{\circ}.s^{-1}$) e durante a contração isométrica, e maior PT isocinético concêntrico dos flexores de ombro e cotovelo em velocidade moderada ($120^{\circ}.s^{-1}$) do que os controles, possivelmente devido ao uso de cadeira de rodas manual para locomoção (Martins et al., 2019, 2022). No entanto, esses estudos avaliaram apenas cadeirantes com EB, e não mensuraram variáveis relacionadas à velocidade-torque ou fadigabilidade motora nessa população.

Sob nosso melhor conhecimento, até a presenta data, nenhum estudo avaliou a aptidão neuromotora como agilidade, ou seja, a habilidade em realizar movimentos específicos ou tarefas funcionais de forma rápida e/ou repetida dos membros superiores de pacientes com EB. Aqui também incluímos a ausência de estudos que analisaram da taxa de desenvolvimento do torque (TDT), que é derivada da curva força/torque isométrica *vs.* tempo, obtida durante contrações voluntárias rápidas, a qual está relacionada ao desempenho das tarefas funcionais e é capaz de detectar alterações agudas e crônicas na função neuromuscular (Maffiuletti et al. 2016), e já foi investigada em crianças típicas (Asai and Aoki 1996; Kochanowicz et al. 2019) e com paralisia cerebral (Moreau, Falvo, and Damiano 2012; Goudriaan et al. 2018). Além disso, a resistência à fadiga neuromuscular não foi explorada cientificamente utilizando diversos instrumentos de análise, como dinamometria e eletromuigrafia de superfície, nos pacientes com EB, comparando-os com participantes com desenvolvimento típico (Bruinings et al. 2007).

Sabe-se que fatores como idade, sexo, estatura, composição corporal e nível de atividade física devem ser considerados durante a avaliação de desempenho muscular, principalmente quando a investigação está centrada em crianças e adolescentes (Schneider, Rodrigues, and Meyer 2002; Schneider, Benetti, and Meyer 2004; Finsterer and Mahjoub 2014). No entanto, não há na literatura disponível estudos que investigaram a influência desses fatores sobre a força/torque de membros superiores de pacientes com EB.

1.3 Fadiga motora

A fadiga motora é uma resposta fisiológica ao esforço físico, mas também pode ser um sinal de incapacidade. Esta última, também conhecida como fadiga patológica, está particularmente aumentada nos pacientes com doenças neurológicas e neuromusculares (Finsterer and Mahjoub 2014; Lieke Brauers et al. 2020). A fadiga patológica primária é um sintoma que não melhora com a interrupção do esforço físico ou com o repouso (Consenso

Brasileiro de Fadiga, 2010). Por outro lado, a fadiga patológica secundária é dependente da intensidade do esforço físico e está relacionada ao desuso (Edgerton et al. 2002), devido mudanças na composição dos diferentes tipos de fibras musculares, como alteração da distribuição entre fibras oxidativas e glicolíticas e hipotrofia (Cornachione et al. 2008; Benedini-Elias et al. 2009), modificações do padrão de resposta neuromotora, do metabolismo local e da velocidade de desempenho contrátil (Roy, Baldwin, and Edgerton 1991; Edgerton et al. 2002). Logo, a fadiga pode não ser apenas um sintoma, mas também uma dimensão mensurável e quantificável, caracterizada como estado de fadigabilidade (Kluger, Krupp, and Enoka 2013; Finsterer and Mahjoub 2014).

Fadigabilidade motora descreve a incapacidade de sustentar a força de contração durante o movimento rítmico e forçado, devido a mecanismos centrais ou periféricos (O'Leary et al. 2016). Os mecanismos centrais (fadiga central) incluem déficit na taxa de recrutamento de unidades motoras em decorrência da falha do sistema nervoso em manter os potenciais de ação, e os mecanismos periféricos (fadiga periférica) caracterizam-se pela depleção dos substratos, acúmulo local de metabólitos (como o aumento da concentração do lactato), diminuição da força contrátil do músculo resultante do desuso e/ou de alterações nos mecanismos relacionados com a transmissão do potencial de ação para o músculo na junção neuromuscular (Abd-Elfattah, Abdelazeim, and Elshennawy 2015; O'Leary et al. 2016).

A avaliação objetiva da fadigabilidade motora está centrada no protocolo do estudo, que deve ser dependente de esforços físicos. Os protocolos de avaliação de fadigabilidade devem monitorar queda significativa no desenvolvimento de força durante contrações voluntárias isométricas ou concêntricas, máximas ou submáximas. No caso da avaliação de fadigabilidade a partir de contrações dinâmicas máximas, ao longo das sucessivas contrações, a força progressivamente diminui, até que o indivíduo já não é capaz de produzir a força necessária devido aos mecanismos supracitados, centrais e/ou periféricos. Portanto, além da força é importante que seja monitorada outra variável relacionada ao processo, de forma a confirmar alterações neurofisiológicas e/ou metabólicas teciduais e locais. Instrumentos tais como, dinamômetros, eletromiografia de superfície (EMG), escalas de percepção de esforço e marcadores biológicos (Vøllestad 1997; Palacios et al. 2015) podem ser úteis para confirmar o evento. Dessa forma, a fadigabilidade motora pode ser avaliada de maneira objetiva (sinal a ser medido) ou de maneira subjetiva por meio de escalas ou questionários de percepção (medidas de auto relato) durante ou após um teste de esforço físico.

O dinamômetro isocinético é um instrumento padrão-ouro para avaliação do desempenho muscular que permite estabelecer parâmetros como tipo de contração e velocidade

do movimento e oferece como variáveis-resposta: pico de torque, trabalho, potência (El Mhandi and Bethoux 2013; Dvir 1995) e índice de fadiga (Eken et al. 2013), dentre outros. Por intermédio da manutenção de contrações voluntárias isométricas ou da repetitividade de contrações voluntárias isocinéticas, utilizando o equipamento isocinético, também é possível avaliar fadigabilidade muscular. Deste modo, é possível verificar a ocorrência de fadiga quando ocorre declínio do torque no decorrer do tempo (Back et al. 2008). A fadigabilidade muscular avaliada por meio do dinamômetro isocinético em crianças, adolescentes e adultos foi estudada principalmente nos membros inferiores (Pincivero, Gandaio, and Ito 2003; Dipla et al. 2009; Eken et al. 2013) e durante contrações musculares isométricas devido homogeneidade dos dados e a facilidade para interpretação dos resultados.

Outro dinamômetro que pode ser utilizado para avaliar desempenho muscular, mas referente à atividade de preensão palmar, é o dinamômetro de bulbo (North Coast®). Considerando os apontamentos levantados nos itens anteriores, as respostas de pressão palmar poderiam refletir o desempenho dos demais grupos musculares dos membros superiores?

O dinamômetro bulbo é um instrumento prático, de fácil manuseio e financeiramente mais acessível quando comparado ao dinamômetro Jamar (considerado padrão ouro para este tipo de análise) (Lustosa et al. 2020), embora o primeiro seja utilizado para mensurar pressão palmar e o segundo para avaliar força de preensão. Além disso, estão disponíveis na literatura dados normativos da preensão palmar isométrica, utilizando o dinamômetro bulbo, de crianças típicas brasileiras de 6 a 13 anos (de Souza et al. 2014). Alguns estudos avaliaram força e fadigabilidade durante a preensão palmar (Wind et al. 2010; A. C. D. C. Ferreira et al. 2011) em contrações isométricas sustentadas por 10 segundos (Xu et al. 2015) e 30 segundos (Brauers et al., 2017) em crianças e adolescentes típicos. No entanto, apesar das tarefas funcionais realizadas diariamente envolverem principalmente contrações dinâmicas, nenhum estudo avaliou a fadigabilidade durante a atividade de preensão palmar durante contrações voluntárias máximas repetidas em crianças e adolescentes.

Simultaneamente ao estudo dinamométrico, com a finalidade de complementar o entendimento da fadigabilidade motora, a análise neuromuscular pode ser realizada por meio do estudo do sinal eletromiográfico (EMG), de forma não-invasiva, durante contrações isométricas ou dinâmicas. Assim, variáveis como amplitude e frequência mediana do sinal eletromiográfico têm sido reconhecidas como úteis no estudo da fadigabilidade muscular (Vigotsky et al. 2018; Hussain et al. 2018). Durante o esforço físico, à medida que a fadigabilidade progride, ocorre decréscimo na força muscular voluntária máxima, diminuição do número de unidades motoras ativas, da velocidade de condução das fibras musculares e da

taxa de disparo das unidades motoras. Esses efeitos provocam o aumento da taxa de disparo e o recrutamento progressivo de unidades motoras adicionais ao longo do tempo, o que reflete no aumento da amplitude e diminuição da frequência mediana (ou média) dos sinais EMG, sendo que a persistência do esforço físico leva a uma eventual falha da contração muscular (Merletti and Farina 2016; McCrary, Ackermann, and Halaki 2018; Hussain et al. 2018). A análise da ativação neuromuscular tem importância clínica, pois estudos mostraram que frequência mediana do sinal EMG aumenta durante o exercício em pessoas treinadas, diminuindo a ocorrência de fadiga (Ganter et al. 2007; Hussain et al. 2018).

As escalas de avaliação de percepção subjetiva de esforço físico são consideradas indicadores válidos e confiáveis (American College of Sports Medicine, 2003), e são amplamente aplicadas na população pediátrica (Martins et al., 2014). Muitos estudos envolvendo a população pediátrica usaram escalas de classificação de percepção de esforço físico desenvolvidas para uso em adultos, porém essas escalas desenvolvidas para adultos podem apresentar limitações metodológicas e semânticas quando aplicadas às crianças e adolescentes. A Children´s OMNI Scale of Perceived Exertion (OMNI) foi desenvolvida devido ao interesse em medir a percepção de esforço físico em crianças e adolescentes e pode ser aplicada em indivíduos de ambos os sexos de origens multirraciais. A escala OMNI contém descritores pictóricos e verbais posicionados ao longo de uma faixa de resposta numérica de 0 a 10. O "significado do esforço" de cada descritor pictórico está em consonância com seu descritor verbal correspondente (Robertson et al. 2000; 2005; Utter et al. 2002).

Com base nos resultados de estudos prévios que mostraram que pacientes com EB apresentam menor força e torque dos músculos dos membros superiores quando comparados aos seus pares típicos (Buffart, Roebroeck, et al., 2008; Buffart, van Berg-Emons, et al., 2008; Danielsson et al., 2008; Martins et al., 2022; Norrlin et al., 2003; Oliveira et al., 2014), levantamos a hipótese de que crianças e adolescentes com EB demonstrariam menor produção de força máxima (a partir de contrações isométricas e isocinéticas), menor TDT, capacidade de resistência atenuada manifestada por respostas de fadiga mais rápidas (ou seja, fadigabilidade aumentada), bem como redução da ativação neuromuscular durante as contrações máximas dos flexores e extensores do cotovelo e dos dedos da mão quando comparados aos seus pares típicos da mesma faixa etária.

Portanto, o objetivo geral do estudo foi avaliar e comparar a força e torque, TDT e fadigabilidade de músculos do membro superior em crianças e adolescentes com desenvolvimento típico e naquelas com EB. Para tanto, utilizamos 3 protocolos de avaliação: (a) contrações concêntricas dos músculos flexores e extensores do cotovelo utilizando o

dinamômetro isocinético, na velocidade $120^{o.s-1}$; (b) contrações isométricas dos músculos flexores e extensores do cotovelo utilizando dinamômetro isocinético; e, (c) contrações concêntricas dos músculos flexores (e extensores) dos dedos utilizando o dinamômetro de bulbo. Todos os protocolos descritos incluíram o registro simultâneo por EMG dos músculos bíceps e tríceps braquial ou flexores e extensores dos dedos da mão.

Os objetivos específicos foram:

- investigar a influência da maturação sexual e sexo na fadigabilidade dos músculos extensores do cotovelo durante contrações voluntárias máximas repetitivas, em velocidade moderada (120^{os-1}), em crianças e adolescentes com desenvolvimento típico. Além disso, avaliar a ativação neuromuscular (usando EMG de superfície) do tríceps braquial durante o mesmo protocolo de teste de fadigabilidade (Artigo 1);
- comparar a produção de torque dos músculos flexores e extensores do cotovelo durante o teste de fadigabilidade entre crianças e adolescentes com EB e seus pares com desenvolvimento típico da mesma faixa etária. Simultaneamente, avaliar a ativação neuromuscular dos músculos bíceps e tríceps braquial, envolvendo o registro e análise da amplitude EMG e frequência de potência mediana (Artigo 2);
- investigar o torque isométrico máximo, a TDT (na fase inicial do aumento da força muscular em relação ao início da contração, ou seja, 0-300 ms) e ativação neuromuscular nos flexores e extensores do cotovelo de crianças e adolescentes com EB versus crianças e adolescentes com desenvolvimento típico da mesma faixa etária, considerando o tipo de locomoção (deambulador versus não-deambulador) dos participantes com EB (Artigo 3);
- analisar o desenvolvimento da fadigabilidade motora e a influência do sexo na atividade de preensão palmar com contrações repetidas em crianças com desenvolvimento típico (Artigo 4);
- comparar o desenvolvimento de fadigabilidade motora de preensão palmar por meio de contrações repetidas e ativação muscular (usando EMG de superfície) entre crianças com EB e crianças com desenvolvimento típico (Artigo 5).

Portanto, a presente tese de doutorado consiste em uma coletânea de artigos sobre o tema “Desempenho muscular, especialmente a fadigabilidade motora (ou periférica), de membros superiores em crianças e adolescentes com desenvolvimento típico e aquelas com espinha bífida”. Os resultados apresentados nos capítulos 2 e 3 estão relacionados aos objetivos específicos descritos acima, respectivamente.

2 DESEMPENHO MUSCULAR AVALIADO PELO DINAMÔMETRO ISOCINÉTICO

2.1 Artigo 1 – Nova versão em elaboração

Influence of sexual maturation and sex differences in children and adolescents: motor fatigue of the elbow extensors

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Abstract

Aims: This study investigated differences between maturation and sex on motor fatigue of the elbow extensors in typical children and adolescents. **Methods:** Thirty-seven participants (both sexes) were separated into prepubertal (PrPU), pubertal (PU) and post-pubertal (PoPU) groups, following the Tanner stages. All the participants performed the isokinetic evaluation of elbow movements at $120^{\circ}.s^{-1}$ included a fatigue test to elicit a decrease of at least 50% of baseline peak torque (PT). Simultaneously the electromyographic activity of the triceps brachii muscle was recorded, and the EMG amplitude (EMG Amp) and median frequency (mF) were obtained. The estimated values between the decile from PT, EMG Amp and mF curves and time-to-fatigue were compared according to the puberty stages and sexes, using a mixed-effect linear regression model. **Results:** Pubertal comparison demonstrated PT decline rate for PrPU<PU and PrPU<PoPU, for both sexes; EMG Amp uphill rate for female PrPU>PU and female PrPU>PoPU, and mF decline rate for male PoPU>PrPU. Comparison between the sexes showed the highest EMG Amp uphill rate for female PrPU and male PoPU, and the lowest time-to-fatigue for male PoPU. **Conclusion:** Sexual maturation should be considered in the evaluation and training related to elbow extensor motor fatigue in the pediatric population.

Keywords: fatigability, isokinetic, electromyography, triceps brachii, pediatrics

1. Introduction

The triceps brachii muscle is the primary muscle group responsible for elbow extension movement (EEX). It is capable of generating dynamic torques of great magnitude during concentric or eccentric contractions at moderate to high speeds, as in the functional movements of the arms performed in the horizontal direction, in the act of pushing objects forward, swimming (Figueiredo et al. 2013), playing tennis (Brink-Elfegoun et al. 2014) and propulsion of a wheelchair (Jonkers et al. 2004; Redhead and Mandy 2015), or in movements with more vertical trajectories, such as reaching or catching objects from the top or throwing a ball (Uzun et al. 2012).

Like most arm muscles, the triceps brachii is phasic, composed mainly of fast type II fibres (60–68% type II fibres), which have less resistance to fatigue (Gejl et al. 2017; Johnson et al. 1973). Motor fatigue can be a factor that limits the performance of daily

functional tasks and high sports performance, both in healthy individuals and in those with chronic diseases and motor disabilities. Therefore, characterising motor fatigue allows optimisation of motor performance through the prescription and monitoring of exercise (Turbanski 2010; Uzun et al. 2012). Hussain et al. summarised the vast literature describing fatigue assessment protocols for the triceps brachii in adults using different equipment, such as electromyography and isokinetic dynamometry (Hussain et al. 2018). However, similar information is lacking for children and adolescents.

Motor fatigue refers to a decrease in physical performance, associated with an increase in the perceived effort necessary to exert the desired force and inability to produce contraction force during rhythmic and forced movements (O'Leary et al. 2016). Several factors, such as age (Ratel, Duché, and Williams 2006), sex (Hunter 2016), body composition (Garcia-Vicencio et al. 2015) and sexual maturation (Tonson et al. 2010) might affect the manifestation of fatigue. Most studies have evaluated muscle performance and the differences between maturation levels and sexes during the fatigue process in lower limb muscle groups, especially knee extensors, and have compared male children or adolescents to adults (Dipla et al. 2009). These studies showed that children are more resistant to fatigue compared to adults because children have lower initial peak torque (PT) values, less dependence on glycolytic metabolism, better acid-base regulation and a higher PCR re-synthesis. However, these studies reported no significant effect of sex on fatigue (Croix et al. 2009; Dipla et al. 2009). Therefore, upper limb muscle group performance and the comparison between sexual maturation and sex differences await scientific clarification regarding fatigue.

Muscle fatigue can be assessed in an objective and non-invasive manner using isokinetic dynamometry and surface electromyography (sEMG). By repeating voluntary contractions, and using moderate and high speeds (Cavalcante et al. 2016; Gentil et al. 2017), the decline in torque and sEMG (i.e. fatigue) can be measured over time (Back et al. 2008). The isokinetic fatigue assessment protocols were developed at different speeds and with a pre-established number of repetitions of the movements (Cavalcante et al. 2016; Gentil et al. 2017). Evaluations that limit the repetitions of the fatigue test or time-to-fatigue typically do not consider each individual's characteristics, such as the proportion of different types of muscle fibre, behaviour of the activation of motor units or the physiological cross-sectional area of the muscle. Ultimately, this raises the question of whether a study a single group achieves the same level of fatigue in all participants. In

this sense, no consensus has been reached regarding the best test protocol for inducing fatigue during dynamic contractions in the upper limb muscles. However, the sEMG can aggregate information about the neuromotor responses of the muscle under investigation, allowing measurement of the degree and duration of muscle activity, the occurrence of fatigue (A. de S. Ferreira, Guimarrães, and Silva 2010). The characteristics of the neural adaptation from the infant to the adult phase can be verified by analysing the sEMG signal in the time and frequency domains, based on changes in the electromyographic signal amplitude (EMG Amp) and median frequency (mF) variables. Studies that evaluated fatigue using isometric contractions have concluded that an increase occurs in the EMG Amp due to an increase in the firing of the motor units and a reduction in the mF. This is because the motor units fire more synchronously (central fatigue) and decrease the conduction speed of the motor units (peripheral fatigue) (Masuda et al. 1999; Uzun et al. 2012), which can be confirmed, for example, by electrostimulation or magnetic stimulation on the nerve, for measurements of evoked muscle contractions and voluntary activation. Even so, knowledge is sparse regarding the behaviour of the sEMG variables during muscle fatigue induced by dynamic contractions.

The primary purpose of the present study was to investigate maturation and sex differences on neuromuscular fatigue of the elbow extensors in typical children and adolescents. The overall goal was to explore the possibility of screening the human developmental process.

2. Methods

2.1 Participants

In this cross-sectional study, 37 typical individuals between 7 and 16 years of age were divided into six groups, according to their Tanner stages of puberty (Tanner 1962) and sex, as pre-pubertal (PrPU = 11, male: 6), pubertal (PU=16, male: 7) and post-pubertal (PoPU=10, male: 5). The participants were recruited from a regular school in Ribeirão Preto's city (SP, Brazil). The exclusion criteria were: a) presence of orthopaedic, cardiopulmonary and neurological morbidities; b) recent upper limb fracture less than one year previously; and c) no understanding of the evaluator's commands. All participants were assessed for body mass (kg) and height (cm).

A questionnaire with figures, based on the characteristics of genital development and pubic hair, was used to classify puberty stages proposed by Tanner (Tanner 1962)

and adapted by Taylor and collaborators (S. J. C. Taylor et al. 2001). This self-determined questionnaire was applied in a private environment and in the presence of those responsible for the participants. The researchers were previously trained to apply this questionnaire by an expert pediatric doctor to ensure the provision of direct and accurate information. The physical activity level was assessed by the Physical Activity Questionnaire for Older Children – PAQ-C and Adolescents – PAQ-A (Guedes and Guedes 2015). All participants and their guardians signed a permission and consent form, respectively. The Research Ethics Committee of the Ribeirão Preto Medical School, University of São Paulo, Brazil, approved this study (Protocol number 68338917.1.0000.5440).

2.2 Isokinetic protocol

The evaluation was performed using an isokinetic dynamometer (Biodex Mult Joint System 4®, Biodex Medical Systems, Inc., New York, USA) calibrated according to the manufacturer's instructions. After completing a warm-up using an arm cycle ergometer without load for three minutes, the participants sat on the dynamometer chair with a back angle set at 90°, stabilised with belts on the chest and pelvis following previous published studies (Back et al. 2008; E. J. Martins et al. 2019). Only the preferential arm (preferred for writing and drawing) was evaluated. Before data collection began, the participants were familiarised with the equipment use by performing a total of one submaximal and two maximal contractions.

Initially, the PT of the EEX was obtained using an average of five dynamic and consecutive concentric contractions for elbow movements, at a velocity of $120^{\circ}.s^{-1}$. This phase of the isokinetic evaluation was called the baseline. Ten minutes after the baseline assessment, corresponding to the rest interval, the protocol to induce motor fatigue was executed at a velocity of $120^{\circ}.s^{-1}$ and the participants performed maximum consecutive isokinetic concentric contractions for elbow flexion and extension until task failure, which was determined when the participant had values below 50% of the PT obtained at baseline in at least three consecutive contractions. When this drop in the PT occurred, an audible signal was emitted and the fatigue test was ended. The emission of the audible signal and the end of the fatigue test were programmed using a routine developed in a MatLab® software (version R2015a, MathWorks Inc., NetWorks, MA, USA). The PT values from the baseline test were obtained from the reports of the isokinetic equipment

and were used as the "cut-off value" to complete the fatigue test, again using a MatLab® routine. During the tests, the participants were verbally encouraged to perform their maximum torque. We recorded the duration of the test (in seconds).

2.3 Surface electromyography

The electromyographic activity of the elbow extensor muscles was recorded during the isokinetic test, using a Trigno™ Wireless® electromyography system (Delsys Inc., Boston, USA) at a sampling frequency of 1200 Hz and with an ordinary modulation rejection rate greater than 80dB. The electromyographic signals were digitised using a 16-bit A/D plate synchronised to the isokinetic dynamometer. All skin preparation and electrode placement procedures were performed according to the Surface Electromyography for the Non-Invasive Assessment of Muscles project (Biomedical Health and Research Program (BIOMED II) of the European Union. 2006). The electromyographic signal of the triceps brachii muscle (long head) was acquired with an electrode in the middle of the line between the posterior ridge of the acromion and the olecranon and two fingers medially to this line. We recorded the EMG amplitude (EMG Amp) in microvolts (μV) and median frequency (mF) sEMG in Hertz (Hz).

2.4 Effort perception scale

The perception of physical effort was assessed before and after the fatigue test using the Borg CR-10 scale (Borg 1982).

2.5 Data processing and analysis

A custom-made MatLab® routine was used to analyse the PT, EMG Amp and mF. All sEMG signals were filtered with a 4th order Butterworth Bandpass filter between 20 and 500 Hz and zero phase delay. The signal was rectified and smoothed by a linear envelope with an 8 Hz low-pass filter for each contraction. Because the number of contractions differed among the participants, we used data from the first repetition, and we divided the fatigue test into ten deciles and analysed the first contraction of each decile. For example, if one participant performed 60 movements, then repetitions 1, 6, 12, 18, 24, 30, 36, 42, 48, 54 and 60 were selected for analysis. The data obtained from the isokinetic and sEMG protocol at baseline (mean PT and maximum EMG Amp) were used as reference values to normalise the data from the fatigue test. Subsequently, we created

curves for PT, EMG Amp and mF using the mean decile values according to groups. Individual “curves" for PT and mF described a decline rate for EEX, while EMG Amp described the uphill rate for the same muscle group.

2.6 Statistical analysis

Normality (Gaussian distribution) of the present data was checked with the Shapiro-Wilk test. The anthropometric characteristics of the participants were presented using descriptive statistics (mean and standard deviation). The estimate between the decile values of the curves from PT, EMG Amp and mF and time-to-fatigue were identified and compared between the stages of puberty and sexes. These analyses were performed using a linear regression model with mixed effects, which included a random effect that correlated the various measures of each individual. These models allow for a comparison between the least squared means of the groups with corresponding 95% confidence intervals (95% CI). A 95% CI that does not include 0 suggests evidence of difference (similar to $p<0.05$). The assumption of linearity between the relationships was verified graphically, and the residual normality was determined using normal probability plots. A single regression model was performed for each outcome (PT, EMG Amp and mF). In each one we considered two factors (variable and group), as well as the interaction between them: sex and level of maturity. Data were presented as estimate values and 95% confidence intervals for each increment of 1 decile. The regression model was calculated using the SAS version 9.4 program, and the significance level was set at 5%.

3. Results

3.1 Participants

Table 1 shows the anthropometric measurements, levels of physical activity, mean PT obtained at baseline test, time-to-fatigue and effort perception scores after the fatigue test obtained by Borg CR-10 scale. Of the 37 participants, 97.3% presented right-side preference and 62.1% were moderately active (18.9% active, 18.9% sedentary). At the baseline test, the highest values for the mean PT for EEX were observed in the male PoPU. The mean time-to-fatigue ranged between 52.8 s and 95.7 s for the male and female PoPU groups, respectively. All groups reached a score of 0 and ≥7 on the Borg CR-10 scale before and after the fatigue test, respectively (Table 1).

Please, insert Table 1 about here

3.2 Peak torque, EMG amplitude and median frequency curves during the isokinetic fatiguing test protocol

Figures 1 and 2 show the curves for PT, EMG Amp and mF created by considering each decile of the concentric isokinetic fatigue test at a velocity of $120^{\circ}.s^{-1}$. The mean PT showed a significant decline in rate for all pubertal stages and sexes ($p<0.01$) (Figures 1 and 2). Muscle activation showed a significant uphill rate of the mean EMG Amp for the female PrPU and PoPU ($p<0.05$) (Figure 2). For mF, we observed a significant decline rate in male PoPU ($p<0.05$) (Figure 1) and in female PrPU, PU and PoPU ($p<0.05$) (Figure 2).

Please, insert Figures 1 and 2 about here

3.3 Sexual maturation and sex differences in the peak torque, EMG amplitude and median frequency

Table 2 shows the pubertal-associated comparisons. For both sexes, a significantly higher PT decline rate was found in PU compared with PrPU and in PoPU compared with PrPU (PrPU vs. PU; PrPU vs. PoPU, $p<0.05$). Regarding muscle activation, EMG Amp showed a higher uphill rate in PrPU and PU than in PoPU for females (PrPU vs. PU; PrPU vs. PoPU; PU vs. PoPU, $p<0.05$). The mF showed a higher decline rate in PoPU compared with PrPU in males (PrPU vs. PoPU, $p<0.05$) (Table 2). Sex-associated comparisons during a maximal isokinetic fatigue protocol demonstrated significant differences only in EMG Amp, with a higher uphill rate for female than for male PrPU (M vs. F, $p<0.05$) and for male than for female PoPU (M vs. F, $p<0.05$) (Table 3).

Please, insert Tables 2 and 3 about here

3.4 Time-to-fatigue

The test duration did not significantly differ among the pubertal stage groups for either males or females ($p>0.05$). One exception was a lower duration of the test in male than in female PoPU ($p<0.05$) (Table 4).

Please, insert Table 4 about here

4. Discussion

This study investigated the influence of sexual maturation and sex in the motor fatigability of the EEX muscles in typical children and adolescents. The results demonstrated that: 1) sexual maturation influenced the fatigue of the EEX movement for both sexes as PrPU demonstrated a lower PT decline compared to the other groups; 2) sexual maturation significantly affected the female PrPU muscle activation rate of the EEX compared to the other groups; 3) a greater sexual maturation significantly affected the neuromuscular activation of the EEX during fatigue, shifting the power spectrum towards lower frequencies in the male PoPU compared to PrPU; and 4) the male PoPU participants reached fatigue more rapidly than the other groups.

Comparison between the deciles for all pubertal stages and sexes demonstrated a significant decline in the mean PT with this concentric isokinetic fatigue test. This result was expected, since it follows the fatigue principle from which the test protocol used in the present study was developed. Although we found the expected decline in the mean PT for all puberty stages and sexes, the EMG data did not show a similar pattern for all groups. Female PrPU and PoPU showed a significant increase in the mean EMG Amp, it may demonstrate an increase in the recruitment of motor units to preserve the level of tension after decreasing strength and the occurrence of fatigue during successive contractions. The same result was observed by Masuda et al. (1999) and by Dias da Silva et al. (2006) who also reported an increase in the EMG Amp from the beginning to the end of the dynamic exercise of the knee extensors (Masuda et al. 1999; Dias da Silva and Gonçalves 2006). We also observed a significant decline in the mF for all female groups and for the male PoPU, which could reflect a change in muscle pH and a consequent decrease in the electrical potential speed in the sarcolemma (Masuda et al. 1999; Uzun et al. 2012).

Regarding sexual maturation, the differences observed for EEX in males indicated that PrPU had a lower decline in the PT than the other groups. No difference in the EMG Amp was observed between groups, and a significantly larger decline in mF was observed in PoPU compared to PrPU. According to Dipla et al. (2009) and Eken et al. (2013) the lower fatigability coincides with the smaller muscle mass and lower maximum voluntary torque at baseline in the PrPU groups (Dipla et al. 2009; Eken et al. 2013). In parallel,

considering the principle of size recruitment of motor units, previous studies have demonstrated that the children presented higher activation of motor unit type I, with preferential use for oxidative metabolism, representing the lowest fatigability (Croix et al. 2009; Ratel, Duché, and Williams 2006). The literature also indicated that children are less dependent on glycolytic metabolism and have less neuromuscular activation, better acid-base regulation and a higher re-synthesis rate of PCr (Falk et al. 2009; Ratel, Duché, and Williams 2006). All this information corroborates with our results, including our data for EMG Amp, when the motor units fired in a similar way for all the male groups. The more significant decline in mF in PoPU compared to PrPU can be related to the decrease in the conduction speed of the active motor units in the male PoPU. This raises some physiological points, such as higher fatigability of the PoPU due to higher proportions of type II fibres and the small motor units, higher glycolytic enzyme activity or metabolism rate (Glenmark et al. 1994; Russ and Kent-Braun 2003), higher accumulation of metabolites (Kent-Braun et al. 2002) and a decrease in the pH (Russ and Kent-Braun 2003). The male PoPU also showed significantly shorter time-to-fatigue compared to the women of the same group.

For the female participants, although they presented the same response of the PT as the male groups, the EMG Amp demonstrated a large increase for younger groups (PrPU and PU) compared to PoPU. The explanation could be related to the immaturity of the neuromotor system and deficits in neuromuscular coordination during childhood and adolescence, as evidenced by the differences in the rate of torque development from childhood to adulthood (Ikegawa and Tsunoda 1995). The significant uphill of the mean EMG Amp in the PrPU and PU would consequently occur as a way to preserve the contractile response by increasing the activity of the motor units (Dias da Silva and Gonçalves 2006; Masuda et al. 1999). On the other hand, there are also more recent studies showing that PrPU, in general, are not able to fully recruit their muscle fibers (in particular type II motor units) and that this deficit tends to decrease with puberty (Dotan et al. 2012; Martin et al. 2015; Chalchat et al. 2019). No difference in the mF was observed between the female groups, and no differences were observed in the time-to-fatigue.

Comparison between the sexes showed no difference in the decline of the PT and mF between male and female groups. Several studies have compared isometric and isokinetic strength and torque in healthy boys and girls, and in athletes and non-athletes,

and have demonstrated that sexual maturity influences the PT more intensely than the sex (Schneider, Rodrigues, and Meyer 2002; Schneider, Benetti, and Meyer 2004). Sex was an important covariate only for EMG Amp during the fatigue test, with female PrPu showing a significantly larger increase than males and male PoPU showing a significantly larger uphill than females. The higher motor recruitment observed in male PoPu can be explained by the higher proportion of type II fibres and the smaller size of their motor units (Ratel, Duché, and Williams 2006). It also explains the shorter time to reach muscle fatigue.

The higher neuromuscular activation obtained in female PrPU can be related to the lower cross-sectional muscle area in females than in males (Deighan et al. 2006), corroborating the PT baseline results, where PT was lower in females than in males. According to Hunter (2016), contractile mechanisms are mainly responsible for the differences between the sexes in muscle fatigue for dynamic tasks (Hunter 2016). These data might suggest that boys and girls respond differently to training and rehabilitation that involve rehabilitation exercises targeted to improve resistance to fatigue.

As limitations we point out that the groups had participants with different physical activity levels, according to PAQC-A. This instrument is not very accurate; therefore, in the future, a study with accelerometric analysis could explore the physical activity impact on fatigue responses. Furthermore, despite some studies have demonstrated the importance of applying allometric scaling to remove the confounding influence of body size on muscular performance in youth at different stages of maturation (Jaric, Radosavljevic-Jaric, and Johansson 2002; Jaric 2003; 2002), we chose to normalize the PT and EMG Amp from the fatigue test, using a reference value (baseline data), in order to minimalize the morphological differences and to permit the comparison between the groups.

5. Conclusion

For the dynamic fatigue protocol presented in this study, sexual maturation influenced the EEX fatigue in typical children and adolescents. When the goal is to reduce the fatigability of the EEX, the training should consist of a great number of repetitions and a lower load for male PoPU than for female PoPU. However, it can be carried out in male and female PrPu in a similar way. Therefore, the sexual maturation is an essential factor regarding the evaluation, training and therapeutic interventions related to EEX.

Declaration of Interest

The authors report no conflicts of interest.

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Table 1. Mean (standard deviation) of the anthropometric characteristics, peak torque obtained at baseline test, time-to-fatigue and effort perception score after the fatigue test.

Variables		Participants (Stages of puberty / Sexes)					
		PrPU		PU		PoPU	
		M (n= 6)	F (n= 5)	M (n= 7)	F (n= 9)	M (n= 5)	F (n= 5)
Age (years)		8.1 (0.4)	8.2 (1.1)	12.7 (1.1)	13.4 (0.7)	15.2 (1.1)	15.0 (1.0)
Preference	**R**	6	5	7	8	5	5
	L	0	0	0	1	0	0
Body mass (kg)		35.1 (9.6)	33.2 (11.2)	55.4 (6.3)	51.8 (6.7)	65.3 (10.6)	58.7 (9.2)
Height (cm)		137.0 (4.6)	132.2 (11.0)	170.1 (7.7)	163.9 (4.4)	177.9 (6.7)	164.1 (7.5)
Baseline - PT (Nm)		15.8 (4.5)	11.5 (3.5)	26.3 (6.6)	26.8 (3.3)	34.6 (9.3)	25.6 (2.9)
Test time (s)		61.3 (21.3)	79.7 (15.3)	89.2 (49.1)	66.7 (17.9)	52.8 (27.8)	95.7 (64.3)
Effort perception (after the fatigue test)†		9	10	8	7	8	7
PAQ-C/A	**ES**	0	0	0	0	0	0
	S	3	1	1	0	2	0
	MA	1	4	6	5	2	5
	A	2	0	0	4	1	0
	EA	0	0	0	0	0	0

PrPU: prepubertal; PU: pubertal; PoPU: postpubertal; M: male; F: female; R: right; L: left; PT: peak torque; †: The score of the effort perception, using the Borg CR-10 scale, before of the fatigue test was zero for all the groups; PAQ-C/A: Physical Activity Questionnaire for Older Children and Adolescents (ES: extremely sedentary; S: sedentary; MA: moderately active; A: active; EA: extremely active).

Table 2. Pubertal comparison of the estimate between the deciles values of the curves considering the sexes (95% confidence interval).

	PT (Nm.Nm^{-1})		**EMG Amp** (μV)		**mF** (Hz)	
	M	**F**	**M**	**F**	**M**	**F**
PrPU vs. PU	0.023 (0.007 - 0.038)*	0.021 (0.005 - 0.036)*	-0.002 (-0.029 - 0.026)	-0.039 (-0.069 - 0.009)*	0.420 (-0.323 - 1.163)	-0.200 (-1.003 - 0.603)
PrPU vs PoPU	0.033 (0.017 - 0.050)*	0.023 (0.006 - 0.041)*	-0.001 (-0.031 - 0.030)	-0.089 (-0.122 - 0.055)*	0.977 (0.168 - 1.789)*	0.203 (-0.694 - 1.099)
PU vs PoPU	0.011 (-0.005 - 0.027)	0.002 (-0.013 - 0.018)	0.001 (-0.029 - 0.030)	-0.050 (-0.078 - 0.022)*	0.557 (-0.226 - 1.339)	0.403 (-0.343 - 1.148)

PT: peak torque (Nm.Nm^{-1}); EMG Amp: EMG amplitude (μV); mF: median frequency (Hz); M: male; F: female; PrPU: prepubertal; PU: pubertal; PoPU: post-pubertal; vs: versus; Asterisk (*): denotes the statistical difference in the comparison between the groups when $p \leq 0.01$. The negative sign means that the group on the left obtained a higher mean value.

Table 3. Comparison between sexes of the estimate between the decile values of the curves for the fatigue test considering the different stages of puberty (95% confidence interval).

Variables	Comparisons	Stages of puberty	Estimate	95% Confidence interval	
				lower bound	upper bound
PT (Nm.Nm^{-1})	**M vs. F**	**PrPU**	0.004	-0.013	0.021
		PU	0.002	-0.012	0.016
		PoPU	-0.006	-0.024	0.011
EMG Amp (μV)	**M vs F**	**PrPu**	0.047*	0.014	0.079
		PU	0.009	-0.016	0.034
		PoPU	-0.041*	-0.073	-0.009
mF (Hz)	**M vs. F**	**PrPu**	0.738	-0.125	1.600
		PU	0.118	-0.555	0.792
		PoPU	-0.036	-0.881	0.809

PT: peak torque (Nm.Nm^{-1}); EMG Amp: EMG amplitude (μV); mF: median frequency (Hz); M = male; F = female; PrPU: prepubertal; PU: pubertal; PoPU: post-pubertal; vs: versus; Asterisk (*): denotes statistical difference in the comparison between the sexes ($p \leq 0.05$). The negative sign means that the male obtained a higher mean value than the female.

Table 4. Comparison between stages of puberty and sexes for the estimate in the time-to-fatigue.

	Sexes	Stages of puberty	Estimate	95% Confidence interval	
				lower bound	upper bound
Time-to-fatigue (s)	M	PrPU vs. PU	-27.935	-637.042	78.342
		PrPU vs. PoPU	8.443	-304.882	473.742
		PU vs. PoPU	36.378	-1.268	74.024
	F	PrPU vs. PU	129.756	-256.596	516.107
		PrPU vs. PoPU	-15.978	-591.069	271.509
		PU vs. PoPU	-289.536	-648.143	69.072
	M vs. F	PrPU	-18.415	-599.158	230.858
		PU	224.956	-99.049	54.896
		PoPU	-42.836*	-834.983	-21.737

M = male; F = female; PrPU: prepubertal; PU: pubertal; PoPU: post-pubertal; vs: versus; Asterisk (*): denotes statistical difference between the sexes ($p \leq 0.05$). The negative sign means lower values for the first variable of the comparison.

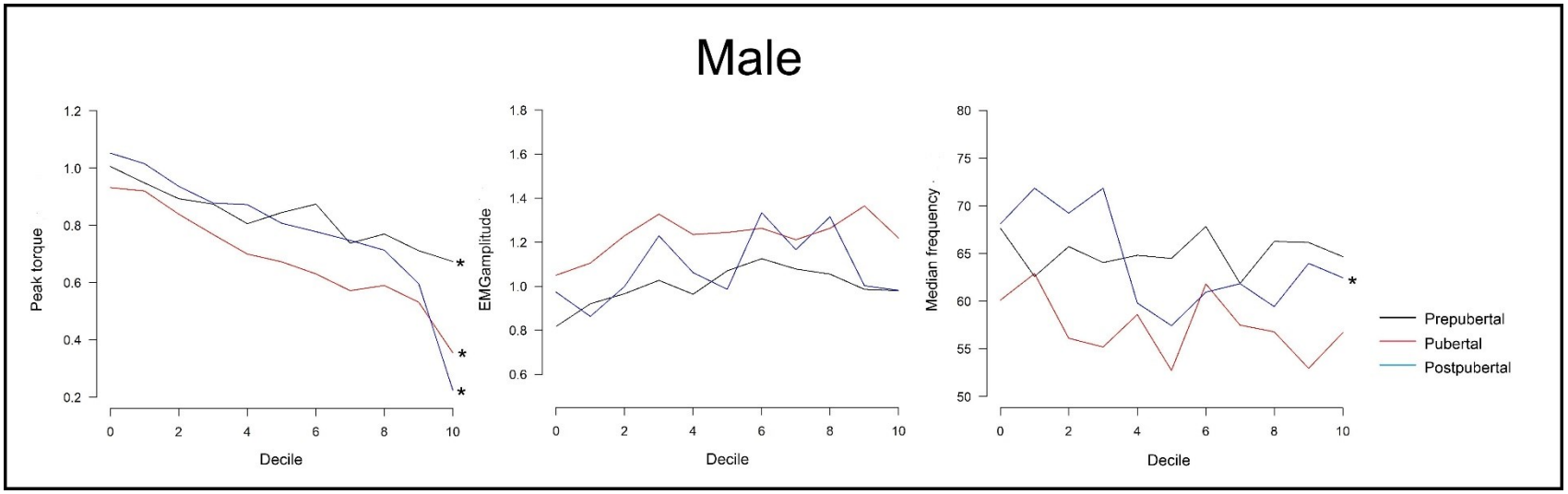

Figure 1. Muscle performance curves for peak torque ($Nm.Nm^{-1}$), EMG amplitude (μV) and median frequency (Hz) from the concentric isokinetic fatigue test of the elbow extensors, considering the different stages of male puberty. Asterisk (*): denotes statistical difference between the deciles ($p \leq 0.05$).

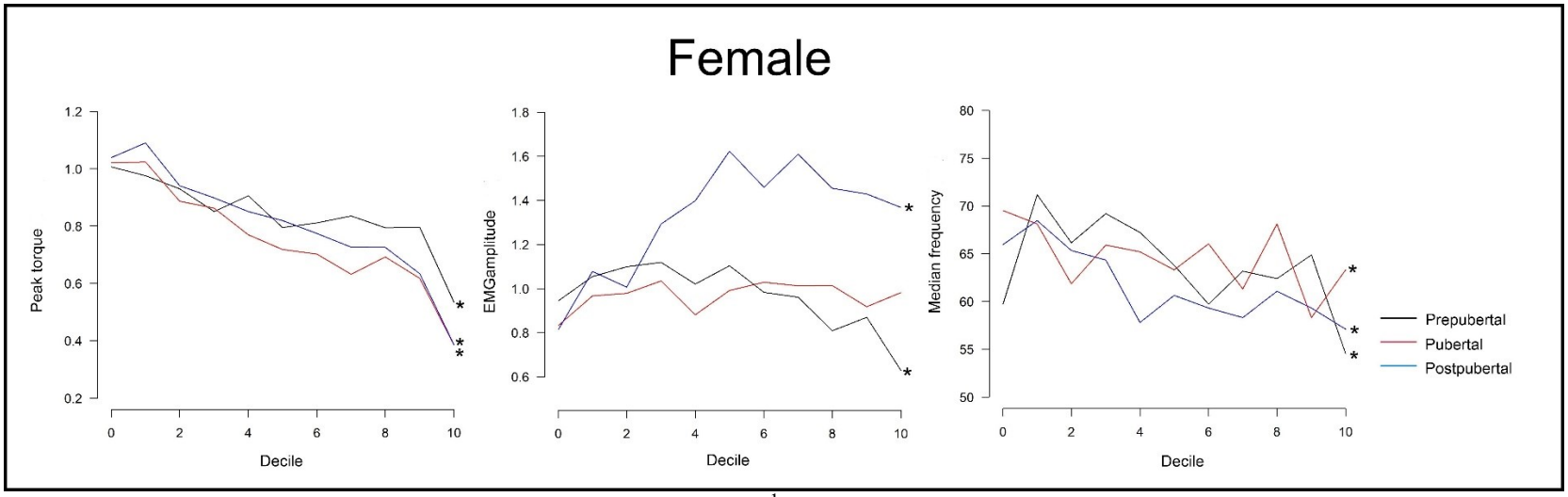

Figure 2. Muscle performance curves for peak torque ($Nm.Nm^{-1}$), EMG amplitude (μV) and median frequency (Hz) from the concentric isokinetic fatigue test of the elbow extensors, considering the different stages of female puberty. Asterisk (*): denotes statistical difference between the deciles ($p \leq 0.05$).

2.2 Artigo 2 – Submetido no jornal Physical & Occupational Therapy in Pediatrics (Março de 2023)

Repetitive voluntary contractions to evaluate motor fatigue in youth with spina bifida

Running head: Motor fatigue in spina bifida patients

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Abstract

Purpose: To assess peak torque (PT) and electromyographic (EMG) variables during repetitive muscle work to investigate the hypothesis that youth with spina bifida (SB) have lower elbow muscles strength and reduced fatigue resistance compared to their typical peers. **Methods:** Twenty-three youth with SB (SB, mean age 10.83 years) and 84 age-matched children and adolescents (Controls, mean age 12.17 years), of both sexes, performed five maximum concentric elbow flexion and extension contractions ($120^{\circ}.s^{-1}$) in an isokinetic dynamometer, to obtain maximal voluntary elbow flexor and extensor torque (MVT), which after was normalized to body weight (MVT-bw). After 10-min of rest, the participants performed a fatigue test with maximum concentric elbow muscle contractions ($120^{\circ}.s^{-1}$) until peak muscle torque (PT) dropped below 50% MVT. PT was recorded in each repetition and normalized to body weight (PT-bw) or maximum voluntary torque (PT-MVT). Simultaneously, surface-EMG activity was recorded in the biceps and triceps brachii muscles. **Results:** SB showed lower MVT-bw for elbow flexors (-24%) and extensors (-21%) than Controls. The decline in PT-bw differed between groups for elbow flexors, where SB showed lower absolute decline rates (PT-bw) than Controls, with no group differences in MVT normalized decline rates in muscle torque (PT-MVT). No statistical group differences were observed for any EMG variables (MVT normalized amplitudes, median power frequency). **Conclusion:** Contrary to our hypothesis, SB did not show signs of increased fatiguability in their elbow flexors and extensors compared to Controls. In fact, body mass normalized elbow flexor strength showed an attenuated decline rate in SB compared to Controls.

Keywords: dynamometer, electromyography, muscle fatigue, muscle strength, myelomeningocele.

1. Introduction

With an incidence of 1–10 per 1000 live births worldwide, spina bifida cystic (SB), also known as myelomeningocele, is the second most common motor disorder in children (Phillips, Burton, and Evans 2017). It occurs during gestation when the spinal column does not successfully fuse, causing defects in the bony spinal column, spinal cord, and brain, in turn causing motor, sensory and cognitive deficits, in addition to bowel, bladder and sexual dysfunctions (Dicianno et al. 2018; Copp et al. 2015). SB complexity

is related to its spinal cord level and the extent and the presence or absence of hydrocephalus and Chiari II-malformation. The loss of sensibility, muscular weakness or paralysis, and decreased efficiency of muscular function in the lower limbs typically cause moderate to severe difficulties in ambulation. Furthermore, in children with SB who are able to walk, the increased body mass, joint contractures and progressive muscle weakness developed over time may reduce the ambulation capacity, especially over long distances (Yasmeh et al. 2017).

Consequently, there is a substantial demand for the use of the upper limb muscles to perform tasks of daily living including assisted locomotion. It is essential, therefore, to assess the influence of SB on upper body muscle performance in order better understand the barriers to functional independence and societal participation in this patient group. If the goal is to prevent comorbidities and enhance an independent lifestyle, muscle function assessments and intervention efforts should start at young (child) age since adolescents with SB have an elevated risk for depressive symptoms, which may be associated with problems related to community integration, lack of independency, and social isolation (Appleton et al. 1997). Notably also, physical functioning seems to decrease already at a mean age of 40 years in persons with SB (Lidal, Lundberg Larsen, and Hoff 2021).

Strength and fatigability are essential issues in neurologically impaired patient groups. They differ significantly from healthy individuals with typical development in motor function (Kluger, Krupp, and Enoka 2013; Lieke Brauers et al. 2020; Moreau, Knight, and Olson 2016). Specifically, fatigue is a symptom of a range of conditions that compared to the general population are more frequent in neurological disorders, such as Multiple sclerosis, Parkinson’s disease, myasthenia gravis, traumatic brain injury, cerebral palsy, stroke, and congenital disabilities (Kluger, Krupp, and Enoka 2013; Lieke Brauers et al. 2020). Lidal, Larsen and Hoff (2019) evaluated self-reported physical fatigue, assessed through questionnaires, in middle-aged and older persons with SB, and reported a high prevalence of fatigue symptomatology among adults with SB (Lidal, Lundberg Larsen, and Hoff 2021). When considering functional limitations in activities of daily living, fatigue could be an important limiting factor in individuals with SB.

Motor fatigability can be defined as the decline in one or more aspects of contractile performance, i.e., agonist muscle force (torque), muscle power, limb or joint speed, or force accuracy/steadiness during sustained or repeated motor tasks (Kluger, Krupp, and Enoka 2013). Previous studies have reported differences in muscle fatigability

between subject groups with different levels of maximal muscle strength. Generally, the ability to generate higher absolute muscle force (torque) levels was associated with higher fatigability reflected by greater rate of declines in absolute or body mass normalized force, torque or power, for example, between men and women (Pincivero, Gandaio, and Ito 2003), adult and prepubertal males (Paraschos et al. 2007) or children with cerebral palsy and typically development children (Moreau et al. 2008; 2009; Eken et al. 2013). Conversely, the possibility also exist that muscle strength levels become so low that endurance capacity (fatigue resistance) becomes negatively affected. Previous studies have reported significant reductions in strength (or torque) in the upper limbs muscles of individuals with SB compared to their healthy peers (Norrlin et al. 2003; Buffart, Roebroeck, et al. 2008; Danielsson et al. 2008; Oliveira, Jácome, and Marques 2014), and individuals who are overweight or affected by traumatic spinal cord lesion (Widman et al. 2007). However, when performing a systematic search in medical databases for studies about motor fatigue (during repetitive voluntary contractions) in individuals with SB, no previous reports were found to exist.

From a neuromuscular perspective, muscle fatigue can be monitored by surface electromyography (EMG). EMG is a non-invasive method to assess muscle fiber activation in human skeletal muscles (Yamada and Kaneko 2002). However, no study so far has evaluated upper limb muscle fatigability of children and adolescents with SB using EMG analysis.

The aim of the present study was to investigate the hypothesis that children and adolescents with SB have lower elbow muscles torque and attenuated endurance capacity manifested by an accelerated fatigue responses (i.e. increased fatigability) compared to age-matched typically developing children and adolescents. During fatigue testing, maximal muscle torque production was assessed synchronously with neuromuscular activation of the elbow flexor and extensor muscles, the latter involving EMG recording and median power frequency analysis.

2. Methods

2.1 Study design

This cross-sectional observation study was performed in the rehabilitation centre of the Ribeirão Preto Medical School. All participants and their guardians signed a permission and consent form, respectively. The study received ethical approval by the

Research Ethics Committee of the Ribeirão Preto Medical School, University of São Paulo, Brazil (Protocol number 68338917.1.0000.5440).

2.2 Participants

Two different subject groups were recruited in this study: children and adolescents with SB (SB) (n=23; convenience sample) and age-matched children and adolescents without any neuromuscular impairments (Controls; n= 84). SB group included ambulatory (n=8; five girls) and non-ambulatory (n=15; six girls; wheelchair-users) participants. Participants were between 7 and 17 years of age. Controls were recruited from public and/or private schools in Ribeirão Preto and surrounding towns. SB participants were recruited from the rehabilitation center of the Ribeirão Preto Medical School, and eligibility criteria included medical diagnosis of spina bifida and radiological images verifying spinal cord injury. Participants were excluded if they had complaints of existing arm or back pain, recent upper limb fracture less than one year previously; and inability to understand evaluator's commands.

Exclusion criteria for Controls were previous or present orthopaedic, cardiopulmonary, and neurological morbidities, while exclusion criteria for SB were presence of other morbidities that would prevent the completion of the protocol test, as well as the presence of abnormal curvatures of the spine, such as severe scoliosis, which could lead to postural instability or pain during the tests. Fifteen SB participants used a ventriculoperitoneal valve to drain off cerebrospinal fluid, however, showed absence from any clinical pyramidal signs.

2.3 Procedures

Anthropometrics and body composition measurements

All participants were assessed for body mass (kg) and height (cm). SB participants who used wheelchair were weighed on a special scale (Welmy® W200/5) and their body height was estimated by arms span width (wingspan or length between the middle finger of one hand to another). Body composition was assessed by bioelectrical impedance testing (Biodynamics® - model 450), from which body mass index, fat and lean body mass were derived.

Levels of sexual maturation, physical activity, spinal cord injury and functional mobility

The level of sexual maturation was classified as prepubertal, pubertal or post-pubertal for characterization of the sample. The participants received a questionnaire with self-explanatory figures based on the Tanner puberty index (Tanner 1962) and selected the figures that most resemble their development characteristics of the genitals, breasts, and pubic hair.

Participants physical activity levels were evaluated using the Physical Activity Questionnaire for Older Children – PAQ-C and Adolescents – PAQ-A (Guedes and Guedes 2015). The participants under ten years old were assisted by their guardians in filling in the questionnaires.

The spinal cord level in participants with spina bifida was classified as thoracic, high lumbar, low lumbar, and sacral, according to criteria established by Hoffer et al. (1973) and Schoenmakers et al. (2005). Spinal cord injury was verified in the radiographic images of the spinal cord and confirmed by motor examination of the lower limbs muscles groups.

The functional mobility level of the participants with spina bifida was assessed using The Functional Mobility Scale (FMS) (Davoli et al. 2021). The FMS rating was based on patient and parents reports of the mobility of the participants at home (5 m distance), school (50 m distance) and community (500 m distance) and included the need of devices for locomotion (wheelchair, walker, crutches, or sticks).

Isokinetic dynamometry

Muscle strength measurements were performed using an isokinetic dynamometer (Biodex Multi Joint System 4, Biodex Medical Systems Inc., New York, USA) calibrated according to the manufacturer's instructions, to record torque of the elbow flexors and extensors, respectively, in the preferred arm. After completing a warm-up for three minutes using an arm cycle ergometer without load, the participants sat on the dynamometer chair with a back angle set at 90°, stabilised with belts on the chest, pelvis, and arms. The mechanical axis of the dynamometer rotation was aligned with the lateral epicondyle of the humerus. The shoulder was positioned at 30° in the scapular plane, with 30° of abduction in the frontal plane and 0° of flexion, and with the forearm in neutral position. The participants grasped a handle fixated distally at the dynamometer lever arm (E. J. Martins et al. 2019). The specific handle position on lever arm was adjusted individually to accommodate the different lower arm lengths between subjects. To correct

for the effect of gravity, the passive mass (torque) of the lower arm was measured by the dynamometer software at an elbow joint angle of 110° (0°=full extension). Prior to data collection, all participants were familiarised with the equipment by performing a total of ten maximal contractions.

Electromyography

Bipolar (inter-electrode spacing of 10 mm) surface electromyography (EMG) (Trigno™ Wireless® electromyography system, Delsys Inc., Boston, USA) was used to record muscle activation patterns of the elbow flexors (m. biceps brachii - long and short heads) and extensors (m. triceps brachii - long head) synchronized with the torque recording in the isokinetic dynamometer. Skin preparations, electrode placement procedures and EMG recordings were performed according to SENIAM guidelines (Biomedical Health and Research Program (BIOMED II) of the European Union. 2006). Recorded EMG amplitudes (EMG Amp) were expressed in microvolts (μV) and median power frequency (EMG MPF) was derived by FFT analysis and expressed in Hertz (Hz).

Maximum voluntary torque (MVT) and fatigue testing

Initially, participants performed five reciprocally coupled maximal concentric elbow flexion and extension movements with a range of motion (ROM) of 70° at an angular velocity of $120^{\circ}.s^{-1}$ (baseline).

After ten minutes of rest, the fatigue protocol was executed, also at a velocity of $120^{\circ}.s^{-1}$ and with a range of motion between 50 and 120° of elbow flexion, where participants performed maximal reciprocal concentric elbow flexion and extension movement until reaching online peak torque values below 50% of baseline peak torque (PT) in at least three consecutive contractions (elbow flexion-extension-flexion or elbow extension-flexion-extension). When this drop in online PT occurred, an audible signal was emitted, and the fatigue test was ended. The recording and online feedback of the peak torque in each contraction (flexion or extension phase) as well as the emission of the audible signal at cessation of the fatigue test (when meeting the above criteria) were achieved using a routine programmed in MatLab® (version R2015a, MathWorks Inc., NetWorks, MA, USA). Throughout the fatigue tests, all participants were verbally encouraged to perform maximum torque production. In addition, visual online feedback of the dynamometer torque and EMG signals were provided to the participants via real-

time display on a computer screen. We recorded the duration of the test (in seconds) and the number of repetitions (elbow flexor-extensor cycles).

Perceived effort

Perceived physical effort was assessed before and after the fatigue test using the Borg CR-10 scale (Borg 1982).

2.4 Data analysis

The analyses were performed for elbow flexors and extensors separately. We selected the highest PT from the data obtained at baseline test as maximum voluntary torque (MVT) and it was normalized to bodyweight (MVT-bw).

The participants with PT values from the fatigue test below or above group mean 3 (SD) were considered outliers, and were excluded of the data analysis.

All PT values from the fatigue test were normalized to the MVT (PT-MVT) as well as to bodyweight (PT-bw). To obtain the rate of decline in PT-MVT and PT-bw, linear regression analysis was performed for PT-MVT and PT-bw as a function of time. All the PT from the fatigue test were included in the regression equation. Muscle fatigue was quantified by the slope of the regression equation for each subject (Nm/kg per second) (Pincivero, Gandaio, and Ito 2003; Eken et al. 2013).

EMG recordings of the elbow muscles were collected at a sampling frequency of 1200 Hz, with a common mode rejection ratio greater than 80 dB and offline processed using Matlab programming (Matlab, The Mathworks Inc., version R2010b, Natick, MA, USA). All EMG signals were bandpass filtered between 20 Hz and 500 Hz using 4th order zero-lag Butterworth filters. Subsequently, all signals were full-wave rectified and smoothed using a 8 Hz low-pass filter (4^{th} order zero-lag Butterworth filter). Peak EMG amplitude (EMG Amp) and median power frequency (MPF) were obtained for each contraction (separate flexion-extension cycles) of the fatigue test. The peak amplitude EMG were subsequently normalized by the peak EMG amplitude value (EMG Amp-norm) obtained from the baseline MVT test for each muscle.

As described for PT above, linear regression analysis was performed on the EMG Amp-norm and EMG MPF values obtained throughout the fatigue test, i.e., including all repetitions in the fatigue test. The slopes of the calculated regression equations for each participant were taken to indicate individual fatigue-induced changes in neuromuscular

activation (EMG Amp-norm) and EMG spectral content (EMG MPF) for the elbow flexors and extensors, separately (Eken et al. 2013).

Representative outputs of PT-bw and PT-MVT obtained for the elbow flexors during the fatigue test are shown in Figure 1 (SB participant vs. Control).

2.5 Statistical analysis

Descriptive outcome statistics were presented as group mean (SD).

Differences in anthropometrics and body composition between subject groups were statistically evaluated using a one-way ANOVA e Tukey post-test. Differences between groups were noted for covariables wingspan, lean body mass and physical activity level. Therefore, ANCOVA was performed for comparing groups and controlling covariates (wingspan, lean body mass, physical activity level). In addition, Tukey post-hoc testing was used for performing multiple comparisons between groups.

Group comparisons of MVT-bw, EMG Amp and EMG MPF measured during the isokinetic baseline test with five maximal reciprocal concentric elbow flexor-extensor cycles were carried out using a linear mixed effect model. The Tukey post-test was used for multiple comparisons between groups.

Group comparisons in the rate of fatigue development (slope) in PT-bw, PT-MVT, EMG Amp-norm and EMG MPF, time-to-fatigue/number of repetitions of the fatigue test, score of perceived effort between groups were performed using ANCOVA.

Statistical significance was set at $p < 0.05$ (2-tailed). All statistical analysis was performed using SAS Statistical Software (version 9.4; SAS Institute, Inc., Cary, NC).

3. Results

3.1 Participants

Twenty-three children and adolescents with SB and 84 typically developing children and adolescents completed baseline testing and the fatigue protocol in the isokinetic dynamometer combined with EMG recording. Torque data from the fatigue test were excluded for four SB participants and six Controls because PT continued to increase across the repetitions reflecting submaximal initial efforts, or because they were outliers (defined in the “Data analysis” section). Technical EMG recording errors prevented to include four SB participants and 12 Controls in the EMG analysis.

Characteristics of the participants are presented in Table 1. Arm span and lean body mass of SB participants were significantly lower compared to Controls ($p < 0.05$). Likewise, physical activity levels differed between groups ($p < 0.05$), with a predominance of SB participants (52.1%) classified as sedentary whereas a majority of Controls was classified as moderately active (63.2%).

Other characteristics of the SB participants, such as spinal cord injury level, hydrocephalus valve, and functional mobility levels, are presented in Supplementary Material (Table A).

Our initial statistical analysis revealed no significant difference between ambulatory and non-ambulatory SB participants for any of the variables obtained. Therefore, the present SB data comprise both ambulatory and non-ambulatory SB participants (n=23).

3.2 Maximum voluntary torque (MVT) and neuromuscular activation

As shown in Figure 2, MVT-bw obtained in SB differed significantly compared to Controls for both the elbow extensors (20.83%) and flexors (23.91%) ($p < 0.05$), with Control demonstrating the highest MVT-bw for both muscle groups.

Neuromuscular activation (EMG Amp) obtained during the isokinetic baseline test was significant lower in SB than Controls both for the elbow flexors and extensors ($p<0.01$). In contrast, EMG median power frequency did not differ between SB and Controls (Supplementary information, Table B).

3.3 Fatigability: Rate of peak torque decline and changes in muscle activation

Rate of fatigue development in the elbow muscles assessed by temporal changes in PT-bw, PT-MVT, EMG Amp-norm, and EMG MPF are presented in Table 2. Generally, no statistically significant differences were identified between groups indicating similar fatigue profiles of the elbow flexors and extensors between SB and Controls. In exception, however, SB demonstrated a slower decline rate for PT-bw during the elbow flexor fatigue test compared to Controls ($p < 0.05$).

Please insert Table 2 about here

The characteristics of the fatigue test, such as the number of repetitions and hence time-to-fatigue, as well as scores of perceived effort at completion of the test, did not differ between groups (Table 3).

Group differences in MVT-bw, EMG Amp, and EMG MPF when assessed in the isokinetic baseline test (five maximal reciprocal concentric elbow flexion-extension movements) are shown in Supplementary Material (Table B). Statistically significant differences were noted between SB and Controls for MVT-bw and EMG Amp for both muscle groups. Specifically, MVT-bw was reduced in SB compared to Controls for both the elbow extensors (-20.8%) and flexors (-23.9%) ($p < 0.05$). Likewise, neuromuscular activation (EMG Amp) obtained during the isokinetic baseline test was 45.0% and 39.0% lower in SB than Controls for the elbow flexors and extensors, respectively ($p<0.01$).

Group differences in the decline rates of PT-bw, PT-MVT, EMG Amp-norm, and EMG MPF recorded during the isokinetic fatigue test are presented in Supplementary Material (Tables C and D). The only significantly difference between groups was in the decline rate of PT-bw for elbow flexors, where SB demonstrated a slower decline rate for PT-bw during the elbow flexor fatigue test compared to Controls ($p < 0.05$).

4. Discussion

The present study investigated the hypothesis that children and adolescents with SB have lower upper arm muscle strength accompanied by increased muscle fatigability (i.e. reduced fatigue resistance) compared to age-matched non-affected children and adolescents. The temporal change in PT, EMG Amp-norm, and EMG MPF during repetitive maximal contractions at $120^{\circ}.s^{-1}$ was used to test this hypothesis. In contrast to our expectations, our analysis of repetitive muscle PT normalized to body weight showed SB participants to have increased fatigue resistance (attenuated fatigue responses) compared to age-matched controls during cyclic all-out elbow flexor contractions.

Specifically, the decline in PT-bw of the elbow flexor muscles during fatigue testing was higher in the control group than in the SB group, indicating that on an absolute scale (per kilogram of body weight), children and adolescents with SB show less muscle fatigability. In addition, the significantly stronger age-matched Control participants showed the most marked decline in PT-bw of elbow flexors, whereas no differences between groups was observed in the fatigue-induced changes in neuromuscular activation of elbow flexor muscles (EMG Amp-norm and EMG MPF). Furthermore, the absence of

difference between the groups in decline in PT-MVT (PT scaled relative to maximum voluntary contraction - MVC) confirms the hypothesis that absolute measures of muscle fatigue were linked to maximum absolute muscle strength production.

Various potential mechanisms may explain why lower muscle strength levels could induce less fatigue of the elbow flexor muscles in children and adolescents with SB: (1) difficulty in maximally recruiting their motor units due to the relatively low levels of voluntary activation, which, according to the size principle, would result in preferential recruitment of more fatigue-resistant type I muscle fibers (Elwood Henneman, George Somjen 1965); (2) SB may show a predominance of type I fibers which are more resistant to fatigue; and (3) the smaller sectional area of elbow flexor muscles produce lower intramuscular pressure levels, which can *per se* contribute to greater fatigue resistance (Maughan et al. 1986), potentially also in children and adolescents with SB compared to their healthy peers. Similar mechanisms were used to explain the relationship between lower muscle strength and low motor fatigability in children with cerebral palsy (Marbini et al. 2002; Stackhouse, Binder-Macleod, and Lee 2005; Nsenga Leunkeu et al. 2010; Moreau, Falvo, and Damiano 2012; Eken et al. 2013). To our best knowledge, however, the recruitment of motor units, type fibers proportion, and muscle size of upper limb muscles have not been investigated in children, adolescents, or adults with SB.

In contrast, no difference in the decline rate of elbow extensor PT during the fatiguing protocol was observed between children and adolescents with SB versus Controls, despite the significant difference in baseline PT between these groups (Controls > SB). The changes in EMG variables did not indicate more pronounced muscle fatigue in the Control group during the fatiguing extensor contractions compared to SB. Elbow flexor and extensor muscles are highly activated during motor activities such as postural transfer and locomotion with auxiliary devices (Slavens et al. 2009; Gagnon et al. 2009). Elevated functional demands typically stimulate morphological adaptations in the agonist muscles, sometimes accompanied by the transition of muscle fiber phenotype from type 2 fibers to more fatigue resistant type 1 fibers (Edgerton et al. 2002; Thompson 2002). Therefore, the use of assistive devices for locomotion in the present group of children and adolescents with SB may have contributed to maintain elbow flexor muscle fibers that are more resistant to fatigue.

In addition to the continuous declines in elbow flexor and extensor PT observed during the present fatigue test, electromyographic variables may indicate the presence of

physiological changes responsible for the acute manifestation of muscle fatigue. In the present study, however, no differences were observed between groups in the rate of fatigue development in elbow flexor EMG Amp-norm and MPF, indicating similarities between the two groups in the pattern of neuromuscular modulation during the muscle fatigue process. These mechanisms support the conclusion that intrinsic muscle weakness (i.e. reduced muscle CSA, or/and reduced specific tension) is the main factor contributing to the apparent attenuation in muscle fatigability in children and adolescents with SB.

The present observation of reduced elbow muscle strength (MVT-bw) in the children and adolescents with SB may be at least partly explained by the lower lean body mass of these participants compared to the present Controls. In support of this notion, previous studies have reported moderate-to-strong correlations between lean body mass and MVT of elbow and knee flexors and extensors in healthy children(Lundgren et al. 2011) as well as in children affected by injury (Tapking et al. 2018). The sedentary behavior may put children and adolescents with SB at risk of developing comorbidities in the long term, such as converging towards low lean body mass. Low physical activity levels in young individuals with SB have been reported by Van Den Berg-Emons et al. (2001), Buffart et al. (2008), and (Claridge et al. 2019). Therefore, it appears essential to monitor the physical behavior of children, adolescents and young individuals with spina bifida throughout their lifespan. Another factor that may have affected the present measurements of MVT is the lower wing span of our SB participants. The arm length directly influences the torque production since torque is defined as force multiplied by the lever arm length around a single fixed joint axis., i.e., the smaller the lever arm, the lesser the torque (Dvir 1995). Here, it is essential to highlight that the wing span was one of the variables controlled in the statistical analysis of the fatigue data. Finally, EMG Amp-norm obtained during the baseline MVC test with five reciprocal maximal concentric elbow flexion-extension cycles was significantly lower for SB than for Control, indicating lower levels of maximal volitional muscle activation in children and adolescents affected by SB compared to their non-affected peers.

No differences were observed between SB and Controls in the number of repetitions during the fatigue test, time-to-fatigue, or the score of perceived effort at cessation of the test. These results indicate no differences to exist between groups in motivational factors, which otherwise could have interfered with the ability of the person

to achieve maximum performance during the contractions or cause the individual to end the test early, especially in children (De Ste Croix, Deighan, and Armstrong 2003).

5. Study limitations

A number of limitations may be mentioned with the present study. Firstly, the present SB participants may not represent the general spina bifida population because of the relatively small sample size and inclusion of patients from a single geographic area. In our analysis it was not possible to control for factors that potentially could impact physical activity status, such as socio-economic status, access to therapy and/or parks, recreational conditions, and cognitive ability. In addition, we did not examine antagonist EMG activity during repetitive elbow flexion and extension during the isokinetic fatigue protocol. However, previous studies showed that reduced EMG activity in the antagonist hamstring muscles could explain the preservation of knee extensor torque output during dynamic fatigue testing in prepubertal compared to adult males (Paraschos et al. 2007) as well as in children with cerebral palsy compared to non-affected age matched individuals (Moreau, Knight, and Olson 2016).

6. Conclusions

The present study showed that children and adolescents with SB have reduced maximal elbow flexor and extensor strength levels, respectively, yet demonstrating a similar fatigue profile for their elbow extensors compared to their non-affected peers. Contrary to our initial hypothesis, SB showed greater fatigue resistance in their elbow flexor muscles compared to controls, potentially as a result of their lower absolute strength levels (MVT-bw). Throughout the fatigue test there were no considerable group differences in the neuromuscular activation of the biceps muscle during elbow flexion and the triceps brachii muscle during elbow extension, respectively. In this way, muscle fatigue also needs to be investigated in this population using test protocols with sustained or repetitive submaximal contractions and functional activities. Future research may also assess how neuro segmental impairments and habitual activity levels affect upper limb muscle fatigability in individuals with SB over time into adulthood.

Financial interests

The authors declare they have no financial interests.

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Table 1. Anthropometric data and levels of physical activity and sexual maturity.

Variable		Control (n=84)	SB (n=23)
Age (years)		12.17 (2.96)	10.83 (2.29)
Sex	female	43 (51.1%)	11 (47.8%)
	male	41 (48.8%)	12 (52.1%)
Preference side	right	81 (96.4%)	20 (86.9%)
	left	3 (3.5%)	3 (13.0%)
Weight (Kg)		51.6 (17.1)	46.2 (21.5)
Arm span (cm)		158.8 (19.2)	147.0 (18.2)*
BMI (kg/cm^2)		20.6 (4.0)	20.9 (6.5)
Lean mass (kg)		41.7 (12.7)	29.1 (9.4)*
Fat mass (kg)		13.6 (6.9)	15.3 (12.3)
Physical activity level (n)	active	13 (16.4%)	2 (8.7%)*
	moderately active	50 (63.2%)	9 (39.1%)*
	sedentary	16 (20.2%)	12 (52.1%)*
Sexual maturity level (n)	prepubertal	17 (20.2%)	5 (21.7%)
	pubertal	47 (55.9%)	14 (60.8%)
	post pubertal	20 (23.8%)	4 (17.3%)

Results are presented as mean (SD); SB: spina bifida group; *: $p<0.05$ compared to Control.

Table 2. Rate of fatigue development based on peak elbow flexor or extensor torque normalized to body weight (PT-bw) and peak torque normalized to maximum voluntary torque (PT-MVT) along with concurrent rate of change in normalized EMG amplitude (EMG Amp-norm) and median power frequency (EMG MPF).

Movement	**Slopes (x1000)**	**Controls**	**SB**
Elbow extensors	PT-bw (Nm/Kg sec^{-1})	-2.05 (1.35)	-1.02 (0.78)
	PT-MVT (Nm/MVC sec^{-1})	-3.99 (2.53)	-2.67 (2.18)
	EMG Amp-norm (% MVC sec^{-1})	1.71 (9.72)	-3.82 (5.37)
	EMG MPF (Hz sec^{-1})	-198.52 (151.05)	-117.03 (107.25)
Elbow flexors	PT-bw (Nm/Kg sec^{-1})	-2.46 (1.79)	-0.89 (0.91)*
	PT-MVT (Nm/MVC sec^{-1})	-4.58 (2.72)	-2.18 (1.94)
	EMG Amp-norm (% MVC sec^{-1})	0.91 (5.67)	1.87 (6.79)
	EMG MPF (Hz sec^{-1})	-128.67 (127.47)	-94.71 (63.98)

Results are presented as mean (SD); SB: spina bifida group; *: $p<0.05$ compared to Controls.

Table 3. Time to fatigue and perceived effort during fatigue testing.

Variable	Control (n=84)	SB (n=23)
number of repetitions	52 (20; 211)	63 (19; 194)
time-to-fatigue (s)	79.95 (28.64; 321.67)	120.15 (44.69; 305.46)
score of perceived effort [#]	9 (4; 10)	10 (0; 10)

Results are presented as median (minimum; maximum). There were no differences between groups. SB: participants with spina bifida; #: score of perceived effort at the end of the fatigue test.

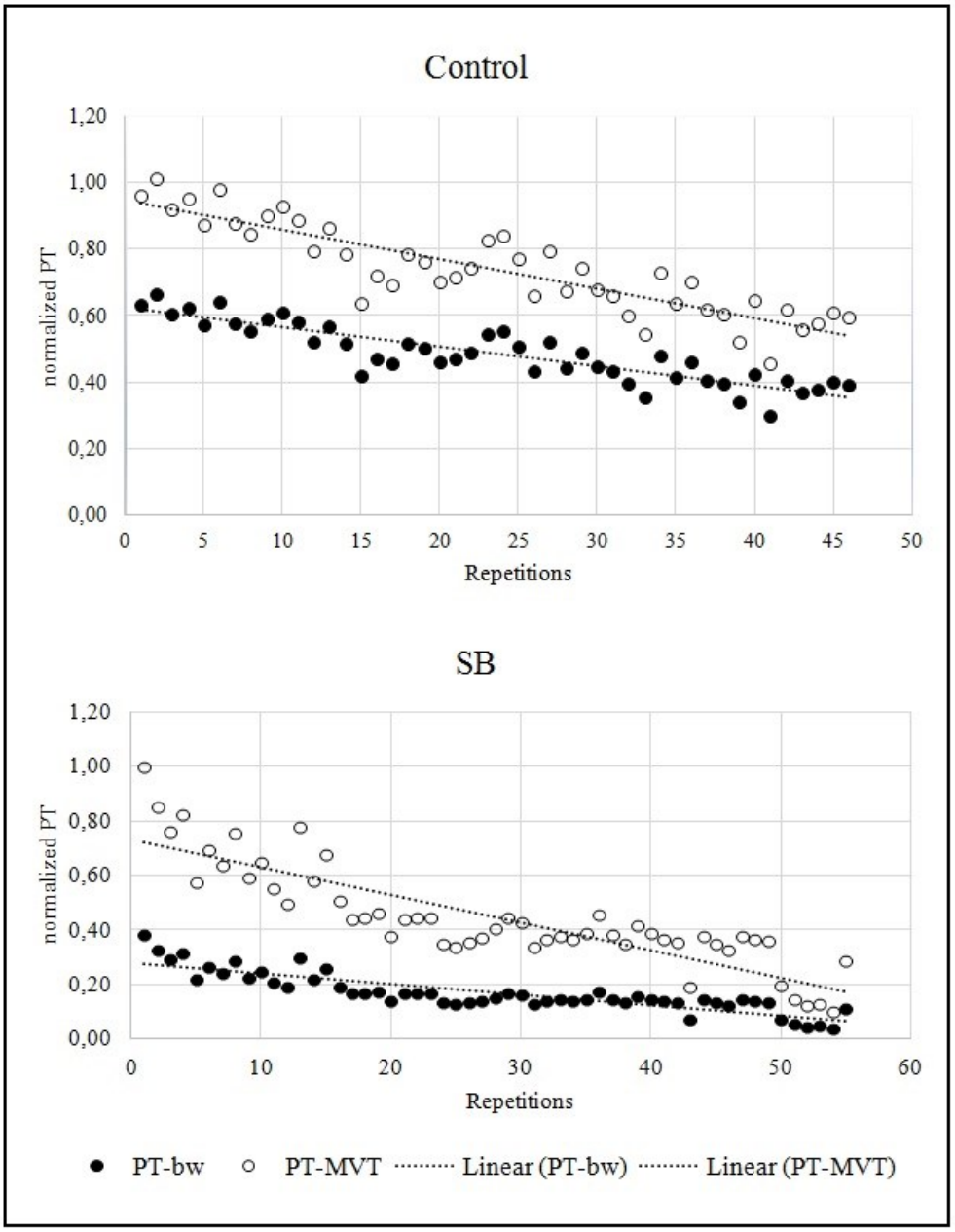

Figure 1. Decline in peak torque normalized to body weight (PT-bw) and peak torque normalized to maximum voluntary torque (PT-MVT) of the elbow flexors during fatigue test. The figure shows the data from one volunteer of the Control and one volunteer of the SB (non-ambulatory participant).

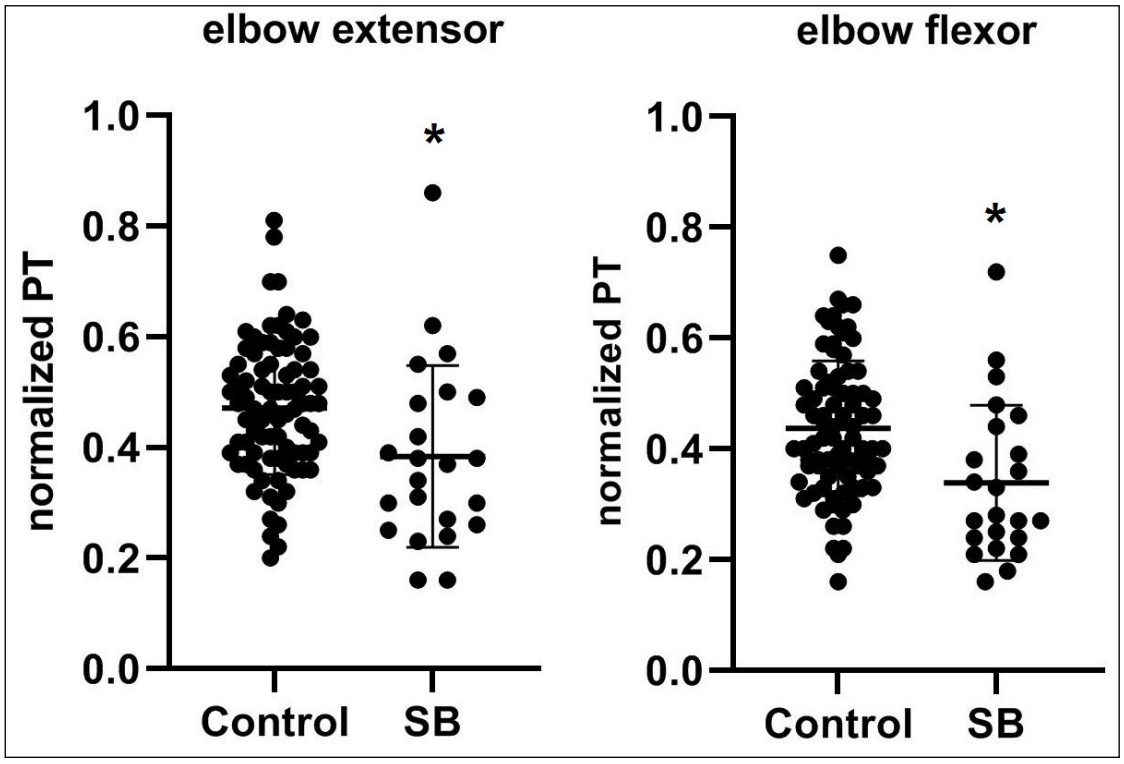

Figure 2. Mean and standard deviation of the maximum voluntary torque normalized to body weight (MVT-bw, in $Nm.Kg^{-1}$); *Different from Controls ($p<0.05$).

Supplementary Material

Table A. Characteristics of participants with spina bifida.

Variable		SB amb (n=8)	SB non-amb (n=15)
Spinal cord injury level (n)	thoracic	0 (0%)	3 (20.0%)
	high lumbar	1 (12.5%)	7 (46.6%)
	low lumbar	2 (25.0%)	3 (20.0%)
	sacral	5 (62.5%)	2 (13.3%)
Presence of the valve for hydrocephalus (n)	no	4 (50.0%)	4 (26.6%)
	yes	4 (50.0%)	11 (73.3%)
Functional mobility level (n)	5 m		
	wheelchair-user	0 (0%)	12 (80.0%)
	walker-user	0 (0%)	0 (0%)
	crutches-user	2 (25.0%)	1 (6.6%)
	sticks-user	0 (0%)	1 (6.6%)
	independent on level surfaces	3 (37.5%)	0 (0%)
	independent on all surfaces	3 (37.5%)	1 (6.6%)
	50 m		
	wheelchair-user	0 (0%)	13 (86.6%)
	walker-user	0 (0%)	1 (6.6%)
	crutches-user	2 (25.0%)	0 (0%)
	sticks-user	0 (0%)	0 (0%)
	independent on level surfaces	3 (37.5%)	0 (0%)
	independent on all surfaces	3 (37.5%)	1 (6.6%)
	500 m		
	wheelchair-user	2 (25.0%)	15 (100%)
	walker-user	0 (0%)	0 (0%)
	crutches-user	0 (0%)	0 (0%)
	sticks-user	0 (0%)	0 (0%)
	independent on level surfaces	3 (37.5%)	0 (0%)

	independent on all surfaces	3 (37.5%)	0 (0%)

SB amb: ambulatory participants with spina bifida; SB non-amb: non-ambulatory participants with spina bifida.

Table B. Comparisons between SB and Controls in maximum voluntary torque normalized to bodyweight (MVT-bw), EMG amplitude (EMG Amp) and EMG median power frequency (EMG MPF) when assessed during the isokinetic baseline test with five maximal reciprocal concentric elbow flexion-extension movements.

Movement	MVT-bw (Nm.Kg^{-1})				EMG Amp (µV)				EMG MPF (Hz)			
	Mean diference	95% CI		p Value	Mean diference	95% CI		p Value	Mean diference	95% CI		p Value
Elbow extensor	0.26	0.08	0.44	<0.01	0.44	0.14	0.74	<0.01	-1.80	-4.68	1.09	0.22
Elbow flexor	0.29	0.11	0.47	<0.01	0.61	0.23	0.99	<0.01	0.86	-4.10	5.83	0.73

*logarithmic transformation.

Table C. Comparisons between SB and Control subjects in slope of the calculated regression equation of peak torque normalized to body weight (PT-bw) and peak torque normalized to maximum voluntary torque (PT-MVT).

Movement	**Slope PT-bw (x1000; Nm/Kg sec^{-1})**				**Slope PT-MVT (x1000; Nm/MVC sec^{-1})**			
	Mean diference	**95% CI**		**p Value**	**Mean diference**	**95% CI**		**p Value**
Elbow extensor	-0.49	-1.24	0.24	0.15	-0.008	-1.51	1.49	0.84
Elbow flexor	-1.14	-2.13	-0.15	0.01*	-1.18	-2.66	0.27	0.08

Table D. Comparisons between SB and Control subjects in slope of the calculated regression equation of normalized EMG amplitude (EMG Amp-norm) and EMG median power frequency (EMG MPF).

Movement	**Slope EMG Amp-norm (x1000; % µV sec^{-1})**				**Slope EMG MPF (x1000; Hz sec^{-1})**			
	Mean diference	**95% CI**		**p Value**	**Mean diference**	**95% CI**		**p Value**
Elbow extensor	0.92	-4.81	6.65	0.64	-20.81	-124.15	82.51	0.59
Elbow flexor	-2.20	-6.96	2.54	0.30	-49.34	-133.59	34.91	0.21

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Muscle strength, rate of torque development and neuromuscular activation of the upper arm muscles in children and adolescents with spina bifida

Running head: Rate of torque development in spina bifida patients

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Abstract

Background: The use of locomotive devices requires sufficient levels of upper limb strength. Therefore, it is important to evaluate the maximal isometric torque, rate of torque development and neuromuscular activation in youth with spina bifida. The objective was to investigate these parameters in the elbow muscles of youth with spina bifida versus healthy age-matched peers. **Methods:** Forty-eight participants (8-17 years) were recruited: Spina Bifida (n=23) and non-affected Controls (n=25). Maximal isometric elbow flexor/extensor contractions were performed to assess maximal muscle strength (peak torque) and rate of torque development, along with synchronized electromyography recording in the biceps and triceps brachii muscles. **Findings:** During elbow flexor contractions, Spina Bifida showed reduced rate of torque development in the early contraction phase (0-50 ms) along with lowered relative rate of torque development in the later rate of torque development phase (0-100/200/300 ms) compared to controls. Spina Bifida showed reduced rate of torque development for the elbow extensors in the later phase of rising muscle force (0-200/300 ms) compared to controls. Lower isometric peak torque and smaller triceps brachii electromyography amplitudes (0-200/300 ms) were observed during elbow extensor contractions in Ambulatory spina bifida participants vs. controls. **Interpretation:** Although a majority of peak torque and rate of torque development parameters did not differ, significant impairments in maximal and rapid elbow muscle force characteristics were noted in Spina Bifida compared to non-affected Controls. Ambulatory and Non-ambulatory spina bifida participants demonstrated similar rate of torque development in their upper arm muscles.

Keywords: dynamometer; elbow; myelomeningocele; pediatrics; rate of force development.

1. Introduction

Spina bifida (SB) cystica also known as myelomeningocele is the most common congenital disease characterized by defect in neural tube closure and spinal cord dysplasia[1,2]. The main consequences of the SB are different levels of motor and sensory deficits in the lower limbs, bladder and bowel dysfunction and central nervous system disorders accompanied by hydrocephalus[3]. Motor dysfunction in the SB can be classified such as thoracic, high lumbar, low lumbar and sacral[4,5]. In a majority of cases, the site of

injury in the spinal cord resides at thoracic or lumbar levels, and consequently, the patients need to use orthosis and/or wheelchair assistance to enable locomotion[6]. There is an increase in the involvement of the upper limbs during the execution of daily tasks, postural transfers and overall locomotion. Therefore, the evaluation of upper limb neuromuscular capacity and mechanical muscle function is important for detecting disease-related impairments in functional capacity and to initiate relevant and early interventions supporting functional independency in the SB population.

Previous studies have reported reduced muscle strength levels in the upper limbs of patients with SB compared to their healthy counterparts[7–10] as well as compared to individuals who are overweight or affected by traumatic spinal cord lesion[11]. However, to our best knowledge, no previous studies have investigated mechanical muscle function of the upper limbs (i.e. assessed maximal contraction strength and rate of torque development - RTD) while concurrently evaluating neuromuscular function assessed by electromyography (EMG) recording in children and adolescents with SB. In the present study, neuromuscular activation was quantified as the EMG activity (mean filtered EMG amplitude) measured at maximal isometric torque production (IMVC) as well as during the RTD phase of rising muscle force (0-300 ms relative to force onset).

Rate of torque development (RTD) can be derived from the isometric torque-time curve, recorded during maximal voluntary muscle contractions, and is related to the performance of various functional tasks (e.g. walking, stair ascent and descent, postural stability[12]) while also useful for detecting acute and chronic changes in neuromuscular function[13]. Surface EMG is a useful tool for providing an estimate of the degree of muscle activation during the IMVC as well as during given time intervals from the onset of force[14–16]. The analysis of RTD and related EMG activity has previously been used to evaluate training-induced changes in neuromuscular function in different populations[14,17,18], and has also been employed in patients with chronic neural diseases such as cerebral palsy[19–21].

Given that the use of self-paced locomotive devices such as wheelchair in patients with SB may require sufficient levels of maximal upper limb strength and rapid force capacity (i.e. high RTD), there is a need for a better understanding of: (1) the differences in the magnitude of IMVC, RTD and neuromuscular activation (EMG amplitudes during IMVC and RTD, rate of EMG rise during RTD) between youth with spina bifida and their healthy peers, (2) the influence of locomotive constraints (ambulatory vs. non-

ambulatory) with SB on maximal isometric torque, RTD and agonist muscle EMG.

The aim of the present study was to investigate maximal isometric torque, contractile RTD, and neuromuscular activation (EMG activity) in the upper arm (elbow flexor and extensor) muscles of children and adolescents with SB versus healthy age-matched children and adolescents. RTD measurements were focused on the early phase of rising muscle force relative to onset of contraction (0–300 ms). Furthermore, the study compared IMVC, RTD and neuromuscular activity in SB patients with ambulatory versus non-ambulatory function.

Based on previous reports showing that patients with SB are characterized by lower strength of the upper limb muscles compared to their peers[7–10], we hypothesized that children and adolescents with SB would demonstrate lower maximal force production and RTD, respectively, as well as reduced neuromuscular activation during maximal rapid elbow extensor and flexor contractions compared to age-matched non-affected individuals.

2. Methods

The participants visited the laboratory on a single day. During this visit, participants were interviewed for their recreational physical activity habits and anthropometric variables were obtained. In sequence, the participants performed familiarization trials prior to producing for maximal and rapid voluntary muscle contractions in the dominant arm. Strength tests consisted of maximal isometric explosive-type elbow flexor and extensor contractions during which maximal muscle torque and RTD were assessed in synchronization with recordings of electromyographic (EMG) activity in the biceps brachii and triceps brachii muscles. Test sessions took about 45 minutes.

2.1 Participants

This cross-sectional study included at total of 48 study participants, dispersed into 25 healthy children and adolescents serving as controls (mean age: 11.80, SD 2.94 years) vs. 23 children and adolescents with spina bifida (SB; mean age: 11.04, SD 2.34 years). SB participants were divided into two subgroups, according to their habitual type of locomotion: ambulatory group (n=7; five girls and two boys) and non-ambulatory group (n=16; seven girls and nine boys), the latter group comprising SB participants who used manual wheelchair. All participants were between 8 to 17 years of age. The participants

of the Control group were recruited from public and/or private schools in Ribeirão Preto (SP, Brazil) and surrounding towns. SB participants were recruited from the rehabilitation centre, University of São Paulo (Ribeirão Preto, Brazil), and eligibility criteria were medical diagnosis of spina bifida and radiological images verifying spinal cord injury.

Exclusion criteria for Controls were presence of orthopaedic, cardiopulmonary and neurological morbidities, and for SB were presence of other morbidities that would prevent the completion of the test used here, and presence of abnormal curvatures of the spine, such as severe scoliosis, which could lead to postural instability or pain during the test. Combined exclusion criteria for Control and SB groups included recent upper limb fracture less than one year previously; and inability to understand evaluator's commands. Fifteen SB participants used a ventriculoperitoneal valve to drain off cerebrospinal fluid, however were absent from any clinical pyramidal signs.

All participants and their guardians signed written assent and consent forms, respectively. The study was approved by the Research Ethics Committee of Ribeirão Preto Medical School, University of São Paulo (number 68338917.1.0000.5440).

2.2 Anthropometrics and body composition measurements

All participants were assessed for body mass (kg) and height (cm). SB participants who used wheelchair were weighed on a special scale (Welmy® W200/5) and their estimated height was obtained by arms span, as it represents a proxy measure for the growth of children with SB, and shows a strong positive correlation with the conventional way of measuring body height[22]. Body composition was assessed by bioelectrical impedance testing (Biodynamics® - model 450), from which body mass index, fat and lean body mass were obtained.

2.3 Levels of sexual maturation, physical activity, spinal cord injury and functional mobility

A self-determined questionnaire with figures was used to classify puberty stages as proposed by Tanner[23] and Taylor and collaborators[24]. It was applied in a private environment and in the presence of the guardians.

Physical activity level of the participants was assessed by the Physical Activity Questionnaire for Older Children – PAQ-C and Adolescents – PAQ-A[25].

Injury level at the spinal cord was obtained from medical records in all participants

with SB, and verified by radiographic images analyzed by their doctors. Site of SB was classified as thoracic, high lumbar, low lumbar or sacral. We also assessed the functional mobility levels of participants with spina bifida using the Functional Mobility Scale (FMS)[26], and identified the need to use a device for overground locomotion (wheelchair, walker, crutches, or sticks) using 5, 50 and 500 m paths.

2.4 Maximal isometric torque (IMVC) and RTD

After completing a warm-up using an arm cycle ergometer without load for three minutes, isometric torque was measured as the maximal voluntary isometric elbow flexion and extension torque (IMVC) exerted in an isokinetic dynamometer (Biodex Mult Joint System 4®). The participants were positioned in the dynamometer chair with a back angle set at 90°, stabilized with belts on the chest, pelvis and arms. The mechanical axis of the dynamometer rotation was visually aligned with the lateral epicondyle of the humerus, and the shoulder was positioned at 30° in the scapular plane, 30° of abduction in the frontal plane, 0 of flexion and forearm in neutral position, while the elbow was positioned at 90º of flexion. Only the preferential arm (preferred for writing and drawing) was evaluated. To correct for the effect of gravity, the passive mass of the arm was measured by the dynamometer at an elbow joint angle of 110° (0°=full extension).

Prior to data collection, all participants were familiarized with the equipment and test protocol, by performing a total of three maximal contractions for each group muscle. Participants were verbally encouraged to contract as fast and hard as possible. Visual feedback was provided to the participants based on real-time display of the dynamometer force output on a computer screen.

To measure isometric peak torques of the elbow flexors and extensors, participants performed three maximal contractions, each sustained for five seconds followed by pause intervals of 20 seconds, and performed in an alternating manner (always starting with elbow extensors).

The exerted muscle torque signal was collected using a 2000 Hz sampling frequency via an external A/D conversion board, which was synchronized using a Matlab® routine (version 7.14.0, MathWorksInc., Natick, MA, USA). The trial with the highest maximal voluntary muscle torque was selected for further analyses[14].

Contractile RTD was derived as the average tangential slope of the torque-time curve (i.e., Δtorque/Δtime) in the initial phase of rising muscle torque (30, 50, 100, 200,

and 300 ms relative to onset of contraction). Onset of contraction was defined as the instant where torque increased 3.5 Nm above the rising baseline level, corresponding to ~2% of the peak moment. Finally, IMVC and RTD were individually normalized to body mass.

Measurement outcomes were maximal voluntary isometric (Nm/kg), rapid muscle torque defined as RTD (Nm/s/kg), and relative RTD (%MVC/s) calculated by normalizing RTD relative to IMVC, for both the elbow flexor and extensor muscles.

2.5 EMG recording

Electromyographic (EMG) evaluation of the upper arm muscles was performed simultaneously with the isometric strength test, using a Trigno™ Wireless® electromyography system (Delsys Inc., Boston, USA) at a sampling frequency of 1,200 Hz and a common rejection ratio greater than 80 dB. EMG and dynamometer strain-gauge signals were synchronously recorded at a 2,000 Hz A/D sampling rate using an external 16-bit analog-to-digital converter. All skin preparation and electrode placement procedures were performed according to the Surface Electromyography for the Non-Invasive Assessment of Muscles (SENIAM) project[27]. For the acquisition of the electromyographic signal of the biceps brachii (long and short heads), the electrode was positioned on the line between the acromion and the cubital fossa, 1/3 of the cubital fossa. For the triceps brachii (long head), the electrode was positioned in the middle of the line between the posterior ridge of the acromion and the olecranon and two fingers medially to this line. During later off-line analysis, EMG signals were digitally high-pass filtered using a fourth-order, zero-lag Butterworth filter with a 5-Hz cutoff frequency, followed by a moving symmetrical root-mean-square (RMS) filter with a time constant of 50 ms[14].

All EMG parameters were obtained from the trial with the highest maximal peak torque, and normalized by the maximal (i.e. peak) EMG amplitude recorded in the participant during his/her IMVC tests. EMG variables included: (1) peak EMG amplitude attained during the MVC; (2) integrated and amplitude average EMG activity (iEMG) in 30, 50, 100, 200, and 300 ms relative to onset of EMG integration (defined below); and (3) rate of EMG rise (RER), calculated as the slope of the filtered EMG–time curve (ΔEMG /Δtime) also in time intervals of 30, 50, 75, and 100 ms relative to the onset of EMG integration. Onset of EMG integration was initiated 50 ms before the individual onset of contraction, to account for the electromechanical delay [14]. EMG parameters were

analyzed for the biceps and triceps brachii, during all IMVC tests.

2.6 Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics v. 28.0 (Chicago, Illinois). Descriptive outcome statistics were presented as group means ± SD. Normality (Gaussian distribution) of the present data was checked with the Shapiro-Wilk test. We also verified the equality of variances by the Levene's test. Maximum isometric torque, absolute RTD, relative RTD, and EMG activity incl. RER were compared between subject groups (Control, Spina Bifida (SB), SB Ambulatory, and SB Non-ambulatory) using student t-testing for independent samples, with statistical significance level set at $p \leq 0.05$ (two-tailed). Cohen's d was used to estimating the effect sizes by the pooled standard deviation.

3. Results

Twenty-five typical volunteers and 23 youth with spina bifida participated in the study. Excessive noise in the EMG data of four typical volunteers and five participants with spina bifida made it impossible to analyze the recorded EMG signals, and data from these participants were excluded in the overall EMG analysis.

3.1 Descriptive characteristics

Anthropometric sample characteristics are presented in Table 1. The statistical analysis showed no differences in age (p=0.33), gender (p=0.58), preference side (p=0.13), weight (p=0.36), body mass index (p=0.92), height (p=0.53), and fat mass (p=0.47) between groups. Participants showed a higher preference for the right side compared to left side of the body in the Control (96%) and Spina Bifida (82.6%) groups. Spina bifida and Non-ambulatory groups showed lower lean mass than Control (p=0.03 and p=0.02, respectively).

A majority of participants were in the pubertal stage (64% Controls, 61% SB). Physical activity was classified for the majority of participants as moderately active in Controls (60%) and sedentary in Spina Bifida (56.5%), with a difference between groups (p=0.04).

Most of the non-ambulatory SB participants had a valve for the treatment of hydrocephalus (75%). The spinal cord injury level for the Spina Bifida group was: 21.7%

thoracic, 34.8% high lumbar, 26.1% lower lumbar, and 17.4% sacral. The score on the functional mobility scale (FMS) showed that 43% of the participants of the Ambulatory group used crutches, or they were able to walk independently without devices on all surfaces on paths of 5 and 50 m; and 43% continue to walk independently without devices on all surfaces on a path of 500 m. Conversely, 81, 87.5 and 100% of the participants in the Non-ambulatory group needed a wheelchair to perform distances of 5, 50 and 500 m, respectively.

3.2 Maximal isometric muscle strength and RTD

Mean values in maximal voluntary torque, absolute RTD and relative RTD recorded during elbow flexor and extensor MVC testing are presented in Table 2. Ambulatory SB participants demonstrated lower maximum isometric torque of the elbow extensor muscles compared to Controls (p=0.008; Cohen's d: 1.22). Mean values in maximal voluntary torque are presented in Supplementary Material (Figure A).

For the elbow flexor muscles, SB participants (collapsed) and Controls showed similar absolute RTD characteristics, except at 0-50 ms where SB participants had lower RTD compared to Controls (p=0.01; Cohen's d: 0.72), which was also observed for the subgroup of Non-ambulatory SB participants (p=0.04; Cohen's d: 0.67) (Figure 1, Table 2). Relative RTD was lower in Non-ambulatory SB in time intervals of 0-100 (p=0.02; Cohen's d: 0.76), 0-200 (p=0.01; Cohen's d: 0.87) and 0-300 ms (p=0.002; Cohen's d: 1.05) compared to Controls, as well as for the entire Spina Bifida group in intervals 0-200 (p=0.03; Cohen's d: 0.62) and 0-300 ms (p=0.01; Cohen's d: 0.72) also compared to Controls (Table 2).

For the elbow extensor muscles, RTD did not differ between SB participants (collapsed) and Controls at time intervals 0-30, 0-50, 0-100 ms (Figure 2, Table 2). However, SB participants demonstrated lower late-phase RTD compared to Controls at 0-200 ms (p=0.02; Cohen's d: 0.67) and 0-300 ms (p=0.01; Cohen's d: 0.70) (Figure 2). Similarly, Non-ambulatory SB participants had lower RTD than Controls at 0-200 ms (p=0.03; Cohen's d: 0.69) and 0-300 ms (0.05; Cohen's d: 0.63) (Figure 2). An identical trend was observed for Ambulatory SB participants at 0-300 ms (p=0.05; Cohen's d: 0.91) (Figure 2). Finally, Non-ambulatory SB participants showed reduced relative RTD in time interval 0-200 ms compared to Controls (p=0.05; Cohen's d: 0.64) (Table 2).

No differences in maximal torque or RTD were observed between Ambulatory

and Non-ambulatory SB participants.

3.3 Neuromuscular activation (EMG)

No significant differences between groups were observed for the EMG signal amplitudes recorded in the biceps brachii muscle at 0-30, 50, 100, 200 and 300 ms during elbow flexor MVCs (Figure 3, Table A suppl. material).

EMG activity recorded in the agonist triceps brachii muscle during isometric elbow extensor MVC efforts were lower in Ambulatory SB than Controls during time intervals 0-200 and 0-300 ms ($p=0.01$ and $p=0.004$; Cohen's d: 0.67 and 0.87, respectively) (Figure 4, Table B suppl. material). Ambulatory SB participants (but not non-ambulatory SB participants) showed lower triceps brachii RER in the interval 0-100 ms compared to Controls ($p=0.04$; Cohen's d: 0.65) as well as in the interval 0-75 ms ($p=0.05$; Cohen's d: 0.61).

Group mean EMG signal amplitudes (EMG at MVC Torque, EMG from the onset of contraction to 30, 50, 100, 200 and 300 ms, and RER from the onset of contraction to 30, 50, 75, 100 ms) recorded during elbow flexor and extensor MVCs are presented in Supplementary Material Tables A and B, respectively.

No differences between Ambulatory and Non-ambulatory SB participants could be observed for the magnitude of neuromuscular activation (EMG amplitudes) recorded in the biceps and triceps brachii muscles at MVC torque, or from onset of EMG integration to 30, 50, 100, 200 and 300 ms, or for RER from onset of EMG integration to 30, 50, 75, 100 ms.

4. Discussion

The present study evaluated the isometric torque, RTD, and EMG of children and adolescents with SB and healthy age-matched children and adolescents during rapid isometric voluntary contractions of the elbow flexors and extensors.

As the main observation and contrary to the initial study hypotheses, maximal and rapid force characteristics did not differ between children and adolescents with SB compared to healthy age-matched individuals. Secondly, no differences in MVIC and RTD emerged between Ambulatory and Non-ambulatory SB participants. These results indicate a comparable ability between ambulatory and non-ambulatory children and adolescents affected by SB to produce maximal isometric muscle force and explosive

strength (RTD), respectively.

Compared to age-matched healthy controls, however, SB participants (ambulatory and non-ambulatory SB collapsed) demonstrated lower RTD for the elbow flexors in the early phase of rising muscle force (time interval 0-50 ms) accompanied by reduced relative RTD in the late phase of the contraction (time intervals 0-100, 0-200, and 0-300 ms), i. e. reflecting an impaired ability of SB participants to rapidly develop force independently of their peak force capacity. As such, these results supported our initial study hypothesis. Notably, no differences in biceps brachii EMG activity (neuromuscular activation) were observed between SB and controls, suggesting the observed differences in arm flexor MVC and RTD between SB and controls to mainly rely on differences in peripheral (i.e., myocellular and/or tendinous) properties, potentially involving type II myofiber atrophy and reduced tendon stiffness. Although no data exist in the literature regarding upper limb joint kinetics during manual wheelchair propulsion in patients with SB, studies in paraplegic adults have shown that the elbow extensor and flexor muscles participate intensely in the pushing and recovery phases of manual wheelchair propulsion. Thus, biceps brachii peak EMG activity corresponds to 38% of MVC and occurs very early (initial 10% cycle) in the pushing phase and again in the recovery phase (78% to 93% cycle)[28,29]. Given these relatively high levels of neuromuscular activity in biceps brachii during wheelchair propulsion, it would seem reasonable to expect an enhanced contractile performance of this muscle in SB patients who are wheelchair-users[30,31], hence explaining the present of differences in elbow flexor RTD, relative RTD and maximal force between this SB subgroup and healthy children and adolescents.

In terms of absolute RTD characteristics, Spina Bifida participants (ambulatory and non-ambulatory collapsed) presented lower RTD for the elbow extensors in time intervals 0-200 and 0-300 ms, without any differences between groups in triceps brachii EMG activity. Further, Non-ambulatory SB participants showed lower RTD for the elbow extensors in time intervals 0-200 and 0-300 ms, and reduced relative RTD in time interval 0-200 ms compared to controls. Finally, Ambulatory SB participants demonstrated reduced RTD values for the elbow extensors in time interval 0-300 ms compared to controls. Collectively, these signs of impaired RTD characteristics with SB are in agreement with our initial study hypothesis.

The sedentary lifestyle observed in all SB participants collapsed (56.5%) as well as in Non-ambulatory SB participants (50%) may have contributed to the observed

reductions in lean body mass and the worsening in upper limb mechanical muscle function discussed above. Some of the transportive barriers in Brazil, such as irregular sidewalk infrastructure, higher ambient temperatures, and general lack of adapted public transportation, could likely lead to a greater dependency on their parents and/or caregivers, for instance during wheelchair propulsion activities, in turn resulting in reduced physical fitness in children and adolescents affected by SB.

To our best knowledge this study is the first to evaluate maximal muscle strength along with rapid force capacity (RTD) of the elbow extensors and flexors in SB children and adolescents. Schoenmakers et al. (2009) also evaluated various measures of muscle strength in ambulatory SB children (with lumbosacral spinal cord injury lesion). They reported reduced isometric strength in selected upper and lower extremity muscles (shoulder abductors, wrist extensors, hip and knee flexors, hip abductors, hip and knee extensors, dorsal ankle flexors, and grip strength), using manual muscle testing and hand-held dynamometry[32].

The present Ambulatory SB participants demonstrated weaker elbow extensor muscles than their non-affected peers (-28%), probably as a result of their lower level of physical activity (assessed by PAQ-C/A), as supported by a tendency ($p=0.06$) of higher fat mass. Notably, this group had no major need to use auxiliary equipment for locomotion (refrained from use in 57% of Ambulatory SB participants), which would otherwise have required the development of more strength in the upper limb muscle groups. Further, Ambulatory SB participants who needed to use crutches for locomotion (43%), were probably not frequently exposed to walking activities. Also, of importance for habitual physical activity levels, a majority (86%) of Ambulatory SB participants had lumbar or sacral spinal cord injury lesions. Although a lumbar levels of spinal cord injury lesion still make walking possible, it may be highly difficult to ambulate for longer distances (>500 m). Consequently, about a half of adult SB patients with sacral involvement are no longer community ambulators[33], due to increased body mass, muscle weakness and development of joint contractures, which are common problems in this population and even more so with advancing age[34,35]. Claridge et al. evaluated the active and sedentary time of 35 SB children (Hoffer classification distribution: community [n=28], household [n=3], non-functional [n=3], and non-ambulatory [n=1]) using ActiGraph or Actiheart activity monitors. They observed that SB children spent more sedentary time (mean [SD] 49.5 min/h [5.78]) and less time with moderate to vigorous

physical activities (mean [SD] 2.33 min/h [1.61]) compared with their healthy age-matched counterparts (mean [SD] 41.0 min/h [5.76] and 5.46 min/h [2.13])[35].

In contrast to the above notion, ambulatory SB demonstrated lower RTD for elbow extensors in the later phase of rising muscle force (time interval 0-300 ms), and attenuated RER in the intervals 0-75 and 0-100 ms during elbow extensor MVCs accompanied by lower EMG activity of the triceps brachii in the time intervals 0-200 and 0-300 ms when compared to healthy controls. In this case, the differences observed in the triceps brachii EMG activity support the differences found in RTD during the later phase of rising elbow extensor muscle force when performing rapid MVC efforts. Consequently, neural adaptations arising from the sedentary lifestyle (i.e. reduced MU recruitment and/or rate coding) including absence of strength training[36], may have been contributing to the present reductions in RTD observed in ambulatory SB participants.

Importantly, the reduced ability of the present SB patients to express rapid force generation could not be explained by a lower maximal force production (MVC) as this was similar between the groups (SB vs. CT; Non-ambulatory vs. CT; Ambulatory vs. Non-ambulatory). Further, in Ambulatory SB patients reduced RTD was observed for the elbow extensors compared to controls even when RTD was normalized to MVC torque (relative RTD), indicating an impaired ability to express rapid force generation capacity in qualitative terms.

Although the ability to produce rapid force depends predominantly on the magnitude of muscle activation at the onset of contraction[13,37,38], which in general, was lower or similar in SB participants compared to controls, there is still the contribution of the intrinsic speed-related properties of the muscle ifself[13]. Muscle factors such as fiber type composition are critical determinants of rapid muscle force capacity (RTD), resulting from the rate of tension development being faster in type II than type I fibers[39]. Knowledge about the proportion of different fiber types could be essential to discriminate inter-individual and inter-muscular differences in RTD[40] however, the fiber types distribution in elbow muscles in SB children and adolescents currently remains unknown.

As a limitation of the study, there was a small sample size of Ambulatory SB participants. Further, no data were obtained to quantify daily time of walking or wheelchair propulsion in Ambulatory and Non-ambulatory SB participants, respectively.

The present analysis of relative RTD (RTD/MVC) revealed that maximal isometric force production was not the main factor determining the lower RTD capacity

observed in SB patients. Thus, in this population, it appears relevant to investigate neuronal and muscular mechanisms that could selectively influence rapid force production, such as MU discharge rates, muscle fiber proportions and tendon stiffness. Additionally, more general knowledge is needed to understand the inter-individual variability in the capacity to produce maximal voluntary activation during rapid muscle contractions in children and adolescents affected by chronic neuromuscular diseases.

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Conflict of interest statement

The authors declare that there are no conflicts of interest.

Author contributions

EJM: Conceptualization, Methodology, Investigation, Formal analysis, Data curation, Writing- Original draft preparation and Writing- Reviewing and Editing.

ACMS: Conceptualization, Methodology, Formal analysis, Data curation, Writing- Original draft preparation, Writing- Reviewing and Editing, Supervision and Funding acquisition.

CSBF: Methodology, Investigation.

TWL: Methodology, Investigation, Formal analysis and Data curation.

PAA: Methodology, Formal analysis, Data curation, Writing- Original draft preparation, Writing- Reviewing and Editing, and Supervision.

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Table 1. Anthropometric data.

		Control n=25	**Spina bifida (all participants) n=23**	**Spina bifida (ambulatory) n=7**	**Spina bifida (non-ambulatory) n=16**
Age (years)		11.8 ± 2.9	11.0 ± 2.3	12.0 ± 2.2	10.6 ± 2.3
Gender (number of participants)	Male	14	11	2	9
	Female	11	12	5	7
Preference side	Right	24	19	6	13
	Left	1	4	1	3
Body mass (kg)		51.5 ± 18.3	46.3 ± 21.5	51.2 ± 19.1	44.1 ± 22.7
Height (cm)		153.2 ± 15.1	NA	NA	NA
Wingspan (cm)		155.8 ± 16.8	147.0 ± 18.1	152.2 ± 17.8	144.8 ± 18.4
BMI (kg/m^2)		21.1 ± 4.5	21.0 ± 6.7	21.5 ± 4.8	20.8 ± 7.6
Fat mass (kg)		13.3 ± 8.4	15.7 ± 12.7	22.5 ± 14.6	13.1 ± 11.3
Lean mass (kg)		37.2 ± 13.2	29.1 ± 9.5*	32.5 ± 8.1	27.8 ± 10.0*
Physical activity level (number of participants)	Extremely sedentary	0	0	0	0
	Sedentary	6	13*	5	8

	Moderately active	15	8	1	7
	Active	4	2	1	1
	Extremely active	0	0	0	0
Sexual maturation level (number of participants)	Prepubertal	3	3	1	2
	Pubertal	16	14	6	8
	Postpubertal	6	6	0	6

NA: not applicable; *: $p<0.05$ compared to Control. Results are presented as mean ± SD.

Table 2. Maximal voluntary torque, rate of torque development and relative rate of torque development obtained from the onset of force to 30, 50, 100, 200 and 300 ms into the phase of rising muscle force during isometric elbow MVCs (0 ms = onset of force).

	Groups			**Subgroups**			
	Control n=25	**Spina bifida (all participants) n=23**	**Mean Difference (95% CI)[#]**	**Spina bifida (ambulatory) n=7**	**Mean Difference (95% CI)[##]**	**Spina bifida (non-ambulatory) n=16**	**Mean Difference (95% CI)[###]**
Elbow flexor MVCs							
MVC Torque (Nm/kg)	0.34 ± 0.11	0.35 ± 0.20	-0.01 (-0.11; 0.07)	0.34 ± 0.25	-0.00 (-0.14; 0.13)	0.36 ± 0.18	-0.02 (-0.12; 0.07)
RTD 0-30 ms (Nm/s/kg)	0.28 ± 0.07	0.26 ± 0.13	0.02 (-0.03; 0.09)	0.24 ± 0.09	0.04 (-0.02; 0.11)	0.26 ± 0.15	0.01 (-0.05; 0.09)
RTD 0-50 ms (Nm/s/kg)	0.56 ± 0.32	0.35 ± 0.24*	0.21 (0.04; 0.38)	0.34 ± 0.19	0.22 (-0.04; 0.49)	0.36 ± 0.26*	0.20 (0.00; 0.40)
RTD 0-100 ms (Nm/s/kg)	0.71 ± 0.36	0.55 ± 0.50	0.16 (-0.09; 0.41)	0.60 ± 0.40	0.11 (-0.21; 0.44)	0.53 ± 0.54	0.18 (-0.10; 0.47)
RTD 0-200 ms (Nm/s/kg)	1.12 ± 0.57	0.84 ± 0.74	0.27 (-0.10; 0.66)	0.96 ± 0.53	0.15 (-0.33; 0.64)	0.78 ± 0.82	0.33 (-0.10; 0.77)

RTD 0-300 ms (Nm/s/kg)	1.02 ± 0.42	0.77 ± 0.60	0.25 (-0.05. 0.55)	0.87 ± 0.47	0.15 (-0.23; 0.53)	0.72 ± 0.66	0.29 (-0.04; 0.63)
Relative RTD 0-30 ms (%MVC/s)	87.7 ± 24.7	80.1 ± 28.4	7.61 (-8.00; 23.23)	80.5 ± 28.6	7.19 (-15.23; 29.63)	79.9 ± 29.3	7.79 (-9.57; 25.16)
Relative RTD 0-50 ms (%MVC/s)	121.7 ± 43.1	105.4 ± 55.9	16.29 (-12.94; 45.53)	109.9 ± 73.2	11.79 (-32.85; 56.44)	103.4 ± 49.2	18.26 (-11.53; 48.05)
Relative RTD 0-100 ms (%MVC/s)	217.0 ± 107.7	156.7 ± 121.8	60.26 (-7.2; 127.74	194.7 ± 180.6	22.29 (-88.65; 133.24)	140.1 ± 88.1*	76.87 (11.27; 142.47)
Relative RTD 0-200 ms (%MVC/s)	343.2 ± 178.9	233.7 ± 173.3*	109.51 (5.95; 213.06)	316.2 ± 212.9	26.97 (-136.82; 190.76)	197.6 ± 146.2*	145.62 (36.66; 254.57)
Relative RTD 0-300 ms (%MVC/s)	311.7 ± 129.2	213.6 ± 141.1*	98.09 (18.68; 177.50)	284.1 ± 182.7	27.58 (-97.09; 152.26)	182.8 ± 111.8*	128.94 (48.84; 209.05)
Elbow extensor MVCs							
MVC Torque (Nm/kg)	0.60 ± 0.12	0.53 ± 0.27	0.06 (-0.06; 0.18)	0.43 ± 0.16*	0.16 (0.04; 0.28)	0.58 ± 0.30	0.02 (-0.12; 0.16)
RTD 0-30 ms	0.36 ± 0.15	0.31 ± 0.19	0.04 (-0.05;	0.27 ± 0.18	0.09 (-0.04;	0.33 ± 0.20	0.02 (-0.08;

(Nm/s/kg)			0.14)		0.23)	0.13)
RTD 0-50 ms			0.08 (-0.12;		0.09 (-0.22;	0.08 (-0.13;
(Nm/s/kg)	0.56 ± 0.33	0.47 ± 0.39	0.29)	0.47 ± 0.46	0.40)	0.48 ± 0.37 0.30)
RTD 0-100 ms			0.22 (-0.19;		0.13 (-0.53;	0.26 (-0.15;
(Nm/s/kg)	1.02 ± 0.63	0.79 ± 0.80	0.64)	0.89 ± 1.11	0.79)	0.75 ± 0.66 0.68)
RTD 0-200 ms			.43 (.05; 0.81)		0.43 (-.15;	0.43 (0.02;
(Nm/s/kg)	1.30 ± 0.63	0.86 ± 0.65*		0.87 ± 0.80	1.02)	0.86 ± 0.61* 0.84)
RTD 0-300 ms			0.35 (0.06;		0.43 (0.01;	0.31 (-.00;
(Nm/s/kg)	1.16 ± 0.46	0.80 ± 0.53*	0.63)	0.72 ± 0.54*	0.85)	0.84 ± 0.53* 0.63)
Relative RTD 0-30 ms			-4.00 (-20.89;		-8.45 (-34.11;	-2.05 (-18.94;
(%MVC/s)	60.0 ± 23.8	64.0 ± 32.3	12.88)	68.4 ± 42.9	17.19)	62.0 ± 28.0 14.83)
Relative RTD 0-50 ms			-4.04 (-40.96;		-25.06 (-	5.14 (-30.35;
(%MVC/s)	92.4 ± 53.0	96.4 ± 69.9	32.87)	117.5 ± 98.4	83.00; 32.87)	87.2 ± 54.8 40.64)
			4.00 (-67.30;		-49.79 (-	27.54 (-34.43;
Relative RTD 0-100 ms			75.32)		160.84;	89.52)
(%MVC/s)	164.1 ± 86.3	160.1 ± 142.6		213.9 ± 215.1	61.25)	136.6 ± 104.1
			32.47 (-29.89;		-10.73 (-	51.37 (-0.99;
Relative RTD 0-200 ms			94.84)		108.35;	103.74)
(%MVC/s)	211.4 ± 70.2	178.9 ± 130.7		222.1 ± 196.8	86.87)	160.0 ± 91.1*

Relative RTD 0-300 ms (%MVC/s)	189.3 ± 48.8	166.6 ± 97.1	22.68 (-23.02; 68.40)	183.9 ± 135.6	5.44 (-61.99; 72.89)	159.1 ± 79.3	30.23 (-11.32; 71.79)

MVC: Maximal voluntary contraction; RTD: rate of torque development; *: $p<0.05$ compared to Control. Results are presented as mean ± SD; #: Mean Difference (95% CI) between SB (all participants) and Control; ##: Mean Difference (95% CI) between SB ambulatory participants and Control; ###: Mean Difference (95% CI) between SB non-ambulatory participants and Control.

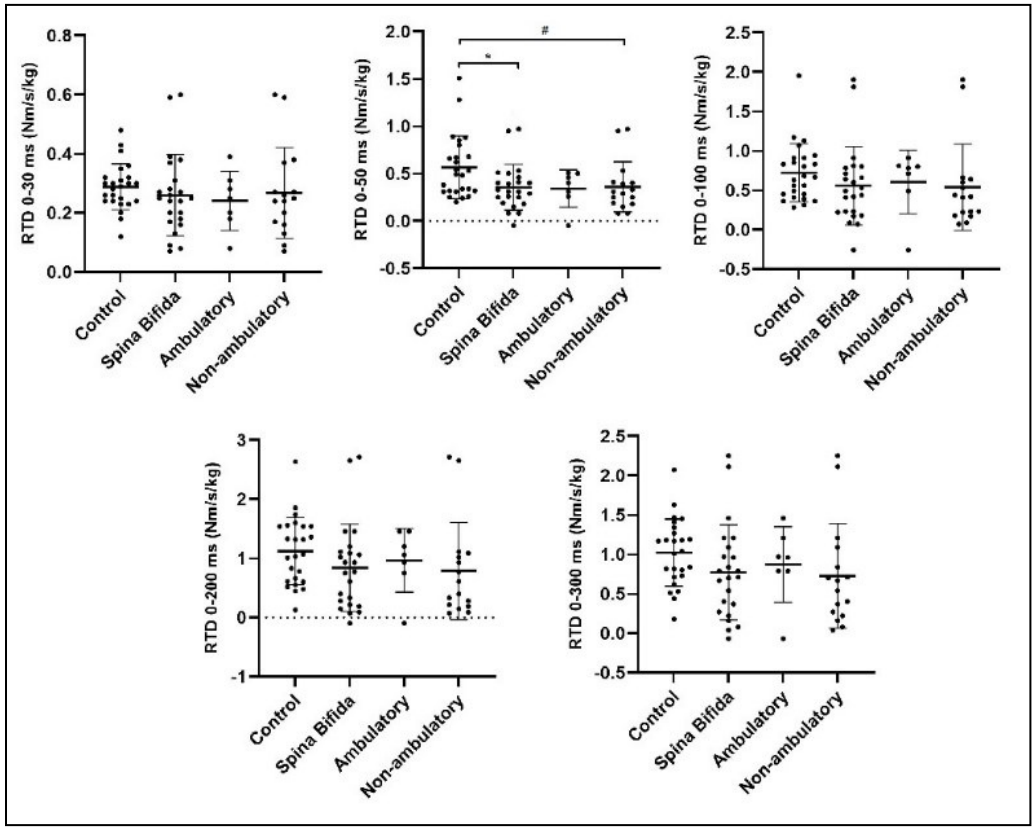

Figure 1. Rate of torque development from the onset of contraction to 30, 50, 100, 200 and 300 ms recorded during elbow flexor MVCs. Group mean ± SD. *: difference between Control and SB groups ($p<0.05$); #: difference between groups Control and Non-ambulatory SB ($p<0.05$). Filled circles indicate individual values.

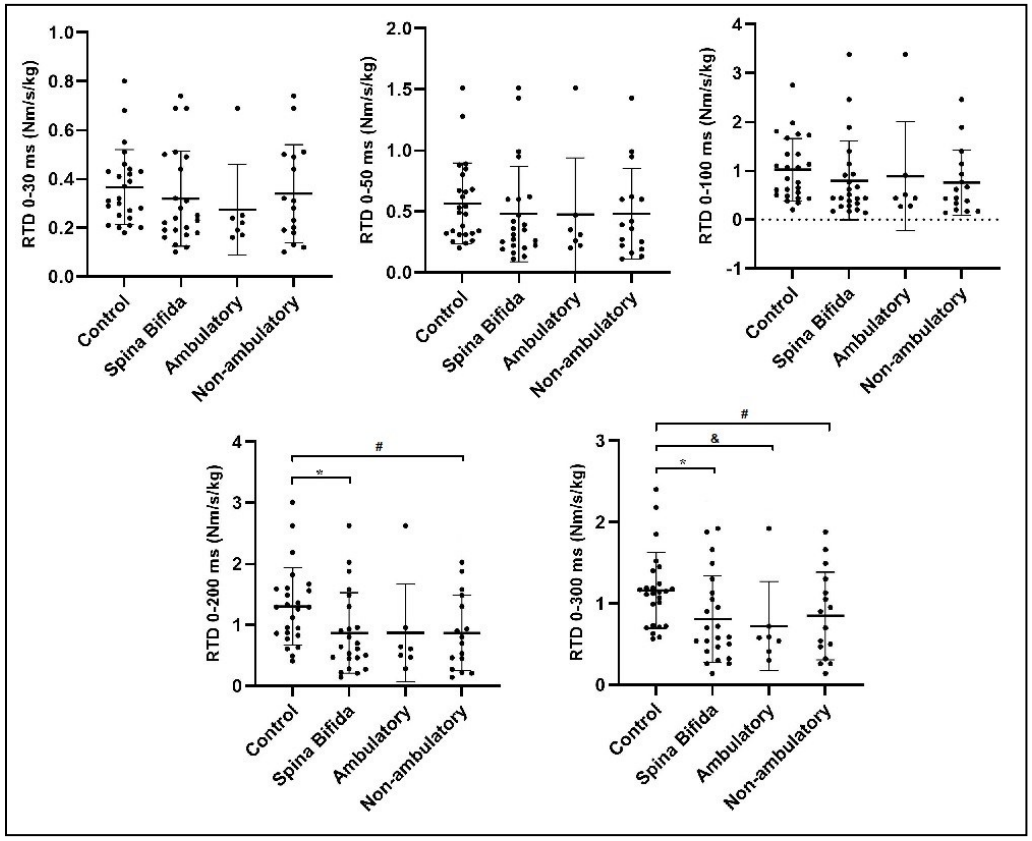

Figure 2. Rate of torque development from the onset of contraction to 30, 50, 100, 200 and 300 ms recorded during elbow extensor MVCs. Group mean ± SD. *: difference between Control and SB groups ($p<0.05$); &: difference between groups Control and Ambulatory SB ($p<0.05$); #: difference between groups Control and Non-ambulatory SB ($p<0.05$). Filled circles indicate individual values.

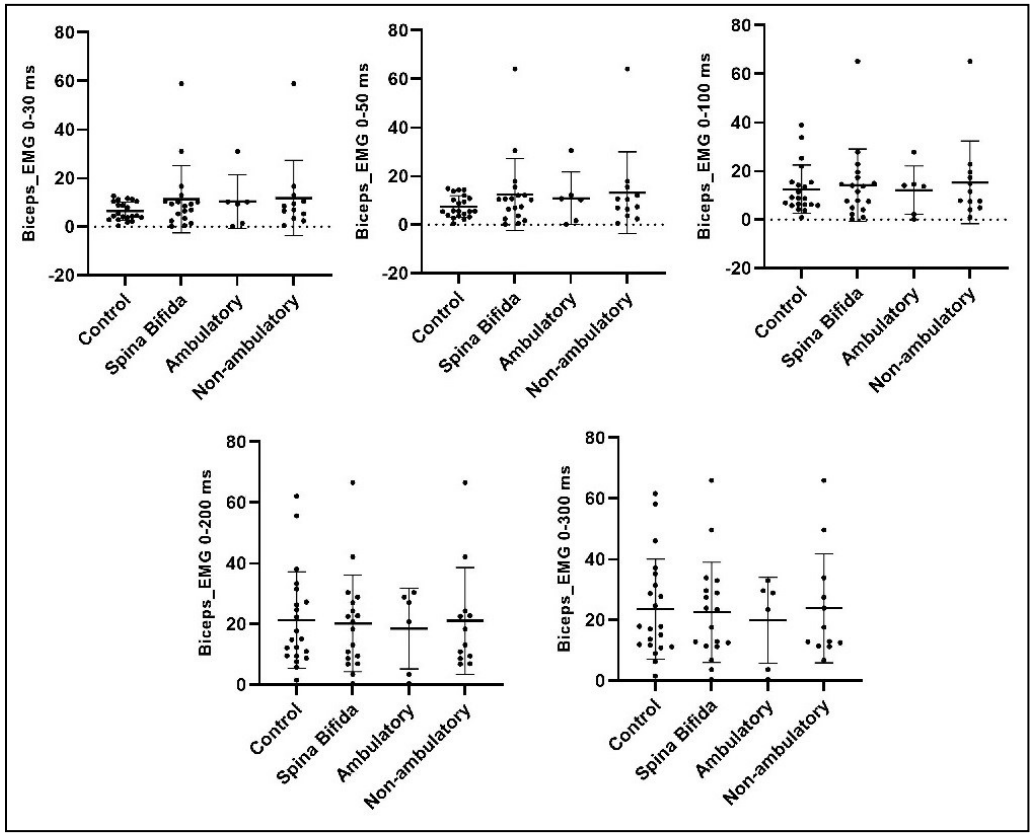

Figure 3. EMG signal amplitudes (%MVC) of the biceps brachii from the onset of contraction to 30, 50, 100, 200 and 300 ms recorded during elbow flexor MVCs. Group mean ± SD. Filled circles indicate individual values.

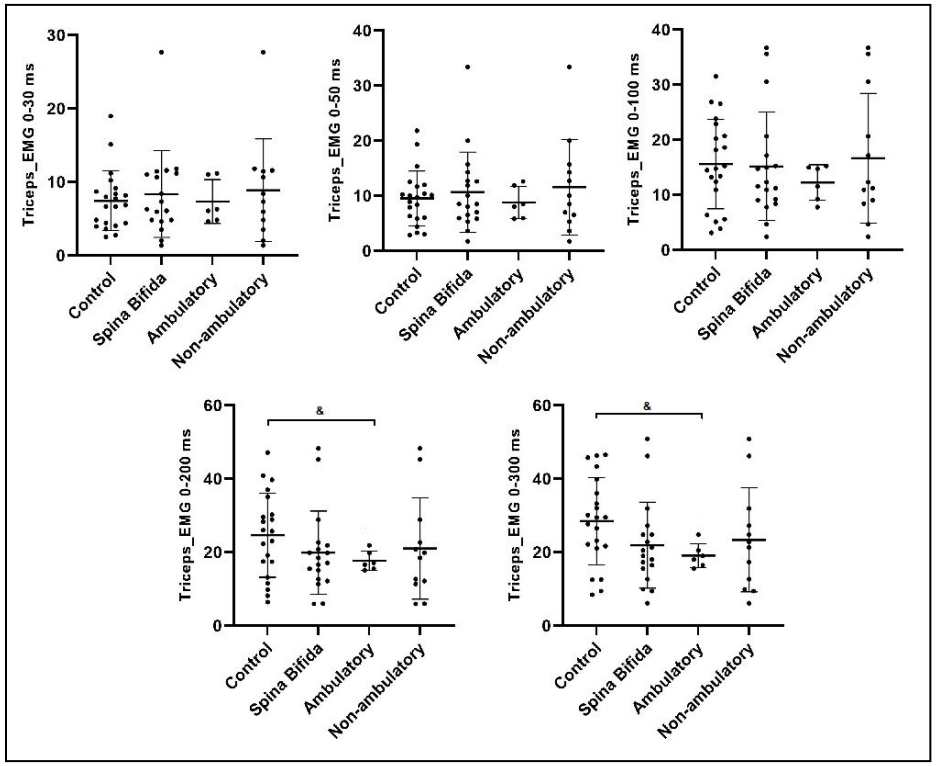

Figure 4. EMG signal amplitudes (%MVC) of the triceps brachii from the onset of contraction to 30, 50, 100, 200 and 300 ms recorded during elbow extensor MVCs.

Group mean ± SD. &: difference between groups Control and Ambulatory SB ($p<0.05$); Filled circles indicate individual values.

Supplementary Material

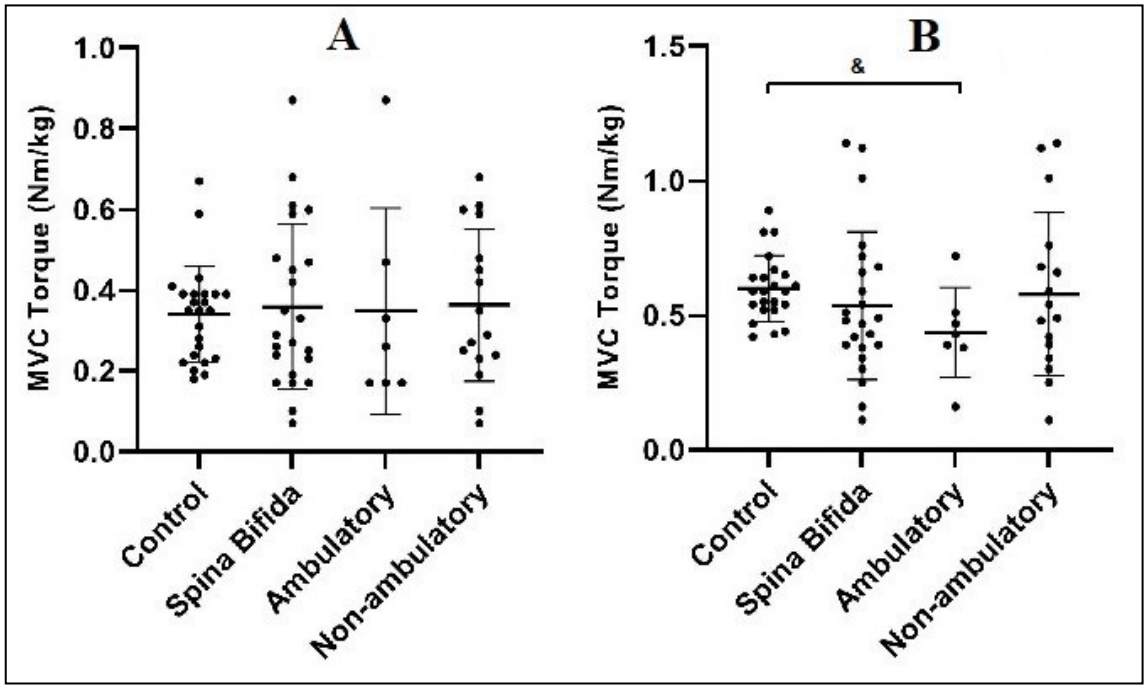

Figure A. Maximal voluntary contraction (MVC) torque expressed relative to body mass recorded during elbow flexor (A) and extensor (B) MVCs. Group mean ± SD. &: difference between groups Control and Ambulatory SB ($p<0.05$); Filled circles indicate individual values.

Table A. EMG signal amplitudes recorded during elbow flexor MVCs.

	Control	**Spina bifida (all participants)**	**Spina bifida (ambulatory)**	**Spina bifida (non-ambulatory)**
	n=21	**n=18**	**n=6**	**n=12**
EMG Biceps Brachii				
EMG at MVC Torque (%MVC)	43.5 ± 17.7	45.2 ± 25.4	33.4 ± 34.3	51.1 ± 18.6
EMG 0-30 ms (%MVC)	6.3 ± 3.8	11.3 ± 13.8	10.3 ± 11.0	11.7 ± 15.4
EMG 0-50 ms (%MVC)	7.4 ± 4.5	12.3 ± 14.8	10.8 ± 10.8	13.1 ± 16.8
EMG 0-100 ms (%MVC)	12.4 ± 9.9	14.2 ± 14.8	12.0 ± 10.0	15.3 ± 17.0
EMG 0-200 ms (%MVC)	21.2 ± 15.9	20.1 ± 15.9	18.4 ± 13.2	21.0 ± 17.5
EMG 0-300 ms (%MVC)	23.5 ± 16.5	22.4 ± 16.5	19.8 ± 14.1	23.8 ± 18.0
Biceps RER 0-30 ms (%MVC/s)	98.7 ± 99.3	112.5 ± 129.5	106.8 ± 124.2	115.4 ± 137.4
Biceps RER 0-50 ms (%MVC/s)	122.6 ± 138.7	104.5 ± 101.1	63.4 ± 86.0	125.1 ± 105.1
Biceps RER 0-75 ms (%MVC/s)	170.8 ± 201.2	81.5 ± 82.0	61.6 ± 83.8	91.5 ± 82.9
Biceps RER 0-100 ms (%MVC/s)	175.4 ± 193.6	92.4 ± 112.0	84.9 ± 94.5	96.1 ± 123.6
EMG Triceps Brachii				
EMG at MVC Torque (%MVC)	16.9 ± 12.9	15.2 ± 14.9	14.5 ± 14.8	15.6 ± 15.5

EMG 0-30 ms (%MVC)	2.9 ± 1.7	3.1 ± 2.5	2.8 ± 2.2	3.3 ± 2.7
EMG 0-50 ms (%MVC)	3.4 ± 2.1	3.5 ± 3.1	3.0 ± 2.6	3.7 ± 3.4
EMG 0-100 ms (%MVC)	4.9 ± 4.1	4.5 ± 4.9	4.1 ± 4.3	4.7 ± 5.4
EMG 0-200 ms (%MVC)	7.6 ± 7.4	7.1 ± 9.7	7.1 ± 9.3	7.0 ± 10.3
EMG 0-300 ms (%MVC)	9.0 ± 9.4	7.8 ± 10.3	8.2 ± 10.0	7.7 ± 10.9
Triceps RER 0-30 ms (%MVC/s)	30.9 ± 63.2	29.8 ± 83.1	37.1 ± 81.7	26.2 ± 87.1
Triceps RER 0-50 ms (%MVC/s)	38.9 ± 59.0	34.5 ± 75.6	30.7 ± 65.9	36.4 ± 82.8
Triceps RER 0-75 ms (%MVC/s)	50.4 ± 77.1	35.9 ± 80.6	36.8 ± 78.0	35.4 ± 85.3
Triceps RER 0-100 ms (%MVC/s)	56.0 ± 90.4	41.2 ± 89.7	40.0 ± 64.2	41.8 ± 102.7

MVC: Maximal voluntary contraction; EMG: electromyography; RER: the rate of EMG rise. Results are presented as mean ± SD.

Table B. EMG signal amplitudes recorded during elbow extensor MVCs.

	Control	**Spina bifida (all participants)**	**Spina bifida (ambulatory)**	**Spina bifida (non-ambulatory)**
	n=21	**n=18**	**n=6**	**n=12**
EMG Biceps Brachii				
EMG at MVC Torque (%MVC)	10.2 ± 6.3	9.7 ± 8.7	6.7 ± 2.7	11.2 ± 10.3
EMG 0-30 ms (%MVC)	2.8 ± 3.7	1.9 ± 1.6	2.1 ± 1.5	1.8 ± 1.7
EMG 0-50 ms (%MVC)	2.8 ± 3.5	2.0 ± 1.7	2.3 ± 1.9	1.9 ± 1.7
EMG 0-100 ms (%MVC)	3.1 ± 2.4	2.5 ± 2.2	2.9 ± 2.9	2.3 ± 1.9
EMG 0-200 ms (%MVC)	4.3 ± 2.4	4.0 ± 4.5	5.7 ± 7.0	3.2 ± 2.6
EMG 0-300 ms (%MVC)	4.8 ± 2.6	4.2 ± 4.2	5.6 ± 6.4	3.4 ± 2.8
Biceps RER 0-30 ms (%MVC/s)	2.6 ± 73.9	10.1 ± 35.7	35.0 ± 51.4	-2.3 ± 16.2
Biceps RER 0-50 ms (%MVC/s)	0.8 ± 55.5	15.1 ± 38.7	36.1 ± 60.6	4.5 ± 16.9
Biceps RER 0-75 ms (%MVC/s)	6.4 ± 56.1	15.6 ± 28.7	26.6 ± 44.7	10.1 ± 16.3
Biceps RER 0-100 ms	16.5 ± 50.9	17.7 ± 32.8	30.1 ± 54.5	11.5 ± 13.6

(%MVC/s)				
EMG Triceps Brachii				
EMG at MVC Torque (%MVC)	58.8 ± 15.4	56.2 ± 15.2	57.2 ± 15.2	55.7 ± 15.9
EMG 0-30 ms (%MVC)	7.4 ± 4.0	8.3 ± 5.9	7.3 ± 2.9	8.8 ± 7.0
EMG 0-50 ms (%MVC)	9.5 ± 4.9	10.6 ± 7.2	8.8 ± 2.8	11.5 ± 8.6
EMG 0-100 ms (%MVC)	15.6 ± 8.1	15.1 ± 9.8	12.2 ± 3.2	35.6 ± 23.4
EMG 0-200 ms (%MVC)	24.6 ± 11.4	19.9 ± 11.3	17.6 ± 2.6*	21.0 ± 13.8
EMG 0-300 ms (%MVC)	28.4 ± 11.9	21.9 ± 11.6	19.0 ± 3.3*	23.3 ± 14.1
Triceps RER 0-30 ms (%MVC/s)	170.6 ± 151.8	167.6 ± 184.4	94.6 ± 81.2	204.0 ± 212.6
Triceps RER 0-50 ms (%MVC/s)	222.2 ± 180.2	220.6 ± 211.9	139.7 ± 100.0	261.0 ± 243.9
Triceps RER 0-75 ms (%MVC/s)	217.7 ± 154.0	182.4 ± 167.0	130.3 ± 67.6	208.4 ± 196.9
Triceps RER 0-100 ms (%MVC/s)	218.2 ± 155.7	152.7 ± 140.1	125.5 ± 63.3*	166.2 ± 167.1

MVC: Maximal voluntary contraction; EMG: electromyography; RER: the rate of EMG rise; *: $p<0.05$

compared to Control. Results are presented as mean ± SD.

3 DESEMPENHO MUSCULAR AVALIADO PELO DINAMÔMETRO DE BULBO

3.1 Artigo 4 – Publicado no jornal Acta Fisiátrica

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Handgrip fatigue test using dynamic contractions in typical children

Shortened title: Fatigue using handgrip in children

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Abstract

Purpose: To verify the development of fatigue and sex-influence on the handgrip during dynamic contractions in typical children. **Methods:** Cross-section study. Fifty-eight children, distributed into two groups according to sex (30 boys), aged 8 to 12 years, of both sexes, performed successive dynamic contractions with a bulb dynamometer until they reached maximum perceived effort. The values from the first, the last contractions of the fatigue test, and the measure after 30-s of the last contraction (recovery contraction) were recorded and compared using the linear regression model with mixed effects. T-Student test was used to compare the perceived effort scores and time-to-fatigue between groups. **Results:** The handgrip values significantly decreased, and perceived effort scores significantly increased in the final measure in relation to the initial measure of the fatigue test. After the fatigue handgrip test, 30-sec of recovery was insufficient to restore the baseline handgrip values. There were no differences between the female and male groups for all variables. **Conclusion:** The handgrip fatigue test using dynamic contractions showed it efficiently induces motor and perceived fatigue in children, without differences between sexes.

Keywords: dynamometer; grip; Paediatric, fatigue, endurance.

1. Introduction

Children and teenagers have been spending increasingly more hours using electronic devices, such as smartphones, video games, tablets, and computers, either for school activities or for leisure. The excessive use of these devices has been associated with several health problems, such as headache, obesity, anxiety, stress, sleep disorders, and musculoskeletal pain and fatigue.[1,2] Recent studies have shown that both healthy children and adolescents, aged 9 to 15 years,[2] and adults, aged 18 to 24 years,[3] of both sexes, with high levels of daily smartphone use, showed decreased handgrip strength and the functional capacity of their hands during daily activities, such as opening a tight or new bottle, washing their backs, and using a knife to cut food. A possible reason for muscle pain and fatigue may be the reduced blood supply due to repetitive hand movements, compromising nutrient and oxygen absorption and metabolic exchange.[2]

Confident instruments and protocols are available in the literature for the assessment of pain[4] and strength[5] related to the upper limbs. An equipment that has been

widely used to assess handgrip pressure (HGP) is the bulb dynamometer. The bulb dynamometer is more easy-to-use, and affordable instrument compared to Jamar dynamometer[7], although the first measure grip pressure and the second is used to assess grip strength. Furthermore, normative data on handgrip isometric from Brazilian children (aged 6 to 13 years, using the bulb dynamometer North Coast - NC70154)[8] and Serbian children (aged 4 to 10 years, using the bulb dynamometer Baseline, USA) are available in the literature.[9] Contrarily, for children and adolescents, there is no gold standard protocol for assessing upper limb muscle fatigue.

Motor fatigue-assessment protocols monitored the decrease in force, or torque, during or after the development of successive isometric, concentric, or eccentric contractions.[10] Central mechanisms (such as the decreased recruitment rate of motor units) or peripheral mechanisms (such as an increased lactate concentration), decreased muscle contractile force resulting from disuse, and/or changes in mechanisms related to action potential transmission at the neuromuscular junction are responsible for the progressive reduction in strength/torque during physical efforts.[10] Variables related to the fatigue process should be monitored in order to confirm tissue and local neurophysiological and/or metabolic changes. For this purpose, instruments such as dynamometry, electromyography,[11] perceived exertion scales, and biological markers, such as lactate concentration in the blood test,[12] can be used. Some studies have assessed strength and fatigue during handgrip[13,14]in isometric contractions sustained for 10 seconds[15] and 30 seconds[16] in typical children and adolescents; however, no study has evaluated the development of handgrip fatigue using dynamic contractions. As the functional tasks performed daily mainly involve dynamic contractions, this study aimed to analyze the development of handgrip fatigue using dynamic contractions in typical children. We also investigated the sex influence and total duration of the handgrip fatigue test.

2. Methods

2.1 Study Design

This observational cross-sectional study was performed at the Ribeirão Preto Medical School, University of São Paulo, Brazil and in public and private elementary schools in the city of Ribeirão Preto, São Paulo, Brazil. The participants spontaneously accepted to participate in the research through an invitation made to them in the schools.

This research was approved by the Human Research Ethics Committee of Ribeirão Preto Medical School, reference number CAAE: 63579916.2.0000.5440. All participants and their guardians signed a permission and consent form.

2.2 Subjects

Typically developing participants were recruited from public and/or private schools in Ribeirão Preto (SP, Brazil) and surrounding towns. Participants of the study involved 62 typical children (convenience sample), aged 8 to 12 years of both sexes. The exclusion criteria included cardiopulmonary and neurological diseases, recent upper limb fracture (less than one year), and the inability to understand and perform the handgrip test. From the total sample of 62 children, 4 were excluded due to the inability to understand the test. Thus, 58 children were evaluated, of which 30 were males.

2.3 Materials and Procedure

All participants were initially submitted to a physical assessment to obtain anthropometric data (weight and height) and assess the level of physical activity by the Physical Activity Questionnaire for Older Children (PAQ-C). The PAQ-C was designed to assess children aged 8 to 13 years and comprises nine questions that measure different aspects of physical activity performed in the last seven days. The first question collects information about the frequency of weekly physical activity during free time. The next six questions are related to moderate and vigorous physical activity during specific periods of the day. The last two questions identify the level of physical activity during the week and the frequency on each specific day. The questionnaire has an extra question that identifies whether the participants were ill or unable to normally perform physical activities. Children under 10 years of age answered the questionnaire assisted by their guardians.[17]

The handgrip fatigue test was developed using a bulb dynamometer (North Coast®). The children remained in the seated posture with backrest, feet flat on the floor, upper limb with shoulder adduction and neutral rotation, elbow flexion at 90º, neutral forearm and wrist between 0 and 30º of extension, and between 0 and 15º of ulnar deviation, as recommended by The American Society of Hand Therapists.[18] Evaluation was done only for the hand of the non-preferred upper limb since, during the pilot tests,

less measure variability was observed between the dynamic repetitions of handgrip in this upper limb compared to the contralateral side.

Before the handgrip fatigue test, all the participants performed three maximal voluntary isometric contractions (MVCs) for 5-s with 20-s rest time between each one (Figure 1). To represent the HGP before the fatigue test, the mean value of these three measurements of HGP (corresponding to HGP 1, HGP 2, and HGP 3) was calculated, and we called it baseline HGP (b-HGP) (Figure 1)[8,19]. Afterward, the participants rested for 300-s. Subsequently, the handgrip fatigue test was performed using successive MVCs, with one-second intervals, standardized by a metronome. The first MVC of the fatigue test was called initial fatigue HGP (i-HGP), and the last MVC of the fatigue test was called final fatigue HGP (f-HGP) (Figure 1). The fatigue test was finished when the participant reported maximum score perceived effort using the visual analogue scale (VAS) and/or inability to synchronize the contractions with the metronome. Therefore, the time-to-fatigue was different for each participant. Finally, after 30-s of rest, one more MVC was recorded, called recovery HGP (r-HGP) (Figure 1). The participants were verbally encouraged to develop maximum contractions during the test. For analysis, the HGP values at b-HGP, i-HGP, f-HGP, and r-HGP were recorded (in psi), as well as time-to-fatigue (in seconds) and perceived effort scores before and after the fatigue test. The participants were familiarized with the bulb dynamometer previously, using five maximum isometric contractions.

2.4 Statistical Analysis

The sample's size and power were calculated using the data from a pilot test with 15 children of both sexes. We considered the difference between the means of the HGP recorded at the beginning and the end of the dynamometric test and the largest standard deviation for both female and male groups. Therefore, the estimated minimum sample size was 60 participants, comprising ten individuals in each age group (aged from 8 to 12 years), five of each sex. The statistical analysis was performed using SAS 9.2 software.

Initially, we described the data using absolute and percentage frequencies (qualitative variables) and measures such as mean, standard deviation, median, minimum, and maximum (quantitative variables). The linear regression model with mixed effects (random and fixed effects) was proposed to compare steps with more than one measure per individual. Linear mixed-effects models are used in data analysis in which responses

are grouped (more than one measure for the same individual) and where the assumption of independence between observations in the same group is not adequate.[20] We also evaluated the effect of interaction between the experimental protocol steps and sexes. These models assumed that their residues have a normal distribution with a mean of 0 and a constant variance of σ^2. For comparisons, the post-test by orthogonal contrasts was used. Therefore, we assessed whether there was a significant decrease in HGP induced by the fatigue test (i-HGP *vs.* f-HGP) and if 30 seconds of recovery is enough to restore the HGP obtained in baseline conditions (b-HGP *vs.* r-HGP). For the comparison between the perceived effort scores in the initial and final steps of the fatigue test (i-HGP *vs*. f-HGP) and the comparison between sexes on the total time of the fatigue test, we used the t-Student test (parametric test). All analysis were performed using SAS 9.2 software. For all comparisons, we adopted a significance level of 5%.

3. Results

All participants performed the protocol test. Table 1 presents data regarding the mean values (and standard deviation) for age, weight, and height. The preferred limb was the right in 92.8% and 90% of the girls and boys, respectively. The level of physical activity was sedentary to the majority for both girls and boys (Table 1). The mean value (standard deviation) of the time-to-fatigue was 107.7 (43.2) seconds for girls and 122.0 (65.0) seconds for boys, and a statistical analysis of the comparison between the sexes regarding the duration of the fatigue test showed no significant difference (p=0.33) (Table 1). The mean total time of the handgrip fatigue protocol proposed in the present study was 441.7 seconds (6.8 minutes) for girls and 456 seconds (7.6 minutes) for boys.

The initial statistical analysis showed no significant difference between the sexes for the variables analyzed, and, therefore, we will present the results considering all the participants (n=58). The mean values (standard deviation) obtained in each phase of the test protocol were at b-HGP: 5.22 (1.97); i-HGP: 4.47 (1.88); f-HGP: 0.85 (1.44); and r-HGP: 3.88 (1.57). Figure 2 shows the comparison between the HGP in different steps of the research protocol using a box plot. b-HGP was significantly higher than r-HGP (estimate difference: 1.34; 95% CI: 0.95/1.74; $p<0.01$). Also of note is that i-HGP was significantly higher than f-HGP (estimate difference: 3.62; 95% CI: 3.23/4.02; $p<0.01$), and f-HGP was significantly lower than r-HGP (estimate difference: -3.02; 95% CI: -3.41/-2.63; $p<0.01$) (Figure 2).

The analysis of the perceived effort, evaluated by VAS, indicated median values corresponding to score = 2 in the i-HGP and score = 10 in f-HGP. A comparative analysis between the test steps showed significantly higher values at the end of the test ($p<0.01$) (Table 2). Figure 3 illustrates the frequency of the scores of the perceived effort assigned in the i-HGP and f-HGP steps for males and females.

4. Discussion

The handgrip dynamometric test proposed in the present study respected an individualized performance with unlimited contractions until the participant reported maximum perceived effort. It was able to evoke motor fatigue in typical children since it was observed a significant decline in the final HGP (f-HGP) in relation to the initial HGP (i-HGP). There was no significant difference in HGP between girls and boys, so sex was not an important covariate for motor fatigue development during dynamic handgrip activity in this population. We also observed that the r-HGP values were not completely restored, indicating that 30 seconds of recovery are not enough to restore the HGP to baseline conditions.

The handgrip fatigue test induced by the bulb dynamometer showed to be feasible for clinical application because the total duration of the test was satisfactory (about 7 minutes). Additionally, it also showed to be feasible for health professionals since they prefer to use portable, practical, inexpensive, and easy-to-use equipment in their clinical rehabilitation practice. These aspects favor the measurement of handgrip clinical responses in different situations of therapeutic care. The use of the visual analogue scale corroborated the test's completion until maximum perceived effort in parallel to the monitoring of the contraction frequency by the metronome during the fatigue test. Studies that assessed handgrip fatigue using dynamic protocols with a limited number of contractions, used test protocols that consisted of 12 consecutive maximum isometric contractions of 3 seconds and a 5-second rest between repetitions.[21] Thus, the handgrip fatigue test proposed here, in addition to being able to induce fatigue, respects the individuality of the response of its participants since the number of contractions is unlimited, that is, each participant has reached fatigue in the maximum time.

De Ste Croix et al. evaluated the effect of sex and age on the development of knee flexors and extensors fatigue using an isokinetic dynamometer in children and adults.[21]The effect of sex on fatigue was not observed, but rather of age, as it was noted

that adults had more significant fatigue than children.[22] In 2002, Schneider et al. carried out a study with healthy children of both sexes and at different stages of sexual maturation.[23] They assessed muscle strength using an isokinetic dynamometer and observed that differences between sexes arise from puberty.[23] In 2004, Schneider et al. evaluated muscle strength through the isokinetic dynamometer of child athletes and verified that the differences between the sexes appear with the beginning of puberty.[24] However, the authors still concluded that sexual maturation influences muscle strength more than sex.[24] Thus, our results are in line with literature data.

Muscle fatigue, in addition to being objectively assessed, can also be monitored through scales or questionnaires of subjective perception of physical exertion (self-report measures), which are considered valid and reliable indicators. These scales are widely applied in the pediatric population,[25] especially the Children's OMNI Scale of Perceived Exertion (OMNI).[26] However, OMNI was not used in this study, as it is still in the process of being validated for Brazilian Portuguese. Therefore, we chose to use the VAS to assess perceived exertion after the fatigue test. The VAS is formatted as a numerical response range in ascending order of effort intensity (0–2: mild; 3–7: moderate; 8–10: intense) with pictorial descriptors that illustrate the face of a person experiencing various effort levels, which can help a child to adequately indicate the status of their effort/tiredness. A study that evaluated fatigue in children and adolescents with juvenile idiopathic arthritis using the VAS to measure tiredness/effort showed that the volunteers were able to safely indicate the level of fatigue.[27]

The level of physical activity of most participants was classified as sedentary. We believe that the PAQ-C cannot adequately categorize the level of physical activity of children who have good cardiorespiratory fitness. For example, a child who does physical activity regularly, that is, five days a week, rarely reports tiredness when asked about routine day-to-day activities. However, this child will be classified as sedentary or extremely sedentary by the PAQ-C. Due to this limitation, we did not relate the physical activity level classification to the fatigue data. In future studies, an alternative would be to measure the level of physical activity of children through more reliable devices, such as the accelerometer.[28]

The proposition of a new clinical assessment protocol must go through the validation process so that the degree of effectiveness of the new test in predicting the subject’s performance can be tested. The process would involve the application,

simultaneously, of two instruments that confirm the same measure, with one of these instruments already established (gold standard), and also by the process of reproducibility, to verify if the test maintains stability at different times (intra and inter-examiner analyses).[29] There is no test or protocol considered the gold standard for assessment motor fatigue in the upper limbs that it could be compared to the protocol presented in this study. One possibility would be to carry out the dynamometric assessment combined with the electromyographic analysis, since both, in a complementary way, would indicate the failure of the neuromuscular system during the fatigue process.

Activities involving handgrip are also part of a relevant clinical context in this population, involving fine and gross motor activities. Despite scientific literature presenting some studies that relate handgrip strength to muscle fatigue,[30,31] there are no strategies to evaluate the pediatric population. Therefore, future researches may investigate the interference of factors such as age, sex, sexual maturation, and body composition in resistance to fatigue in both typical participants and those with chronic diseases. In particular, in pediatric chronic diseases, this fatigue test may guide the choice of the therapy adopted for patients who report weakness and fatigue of the upper limbs, such as cerebral palsy and neuromuscular disorders. In the future, neurophysiological studies of muscle function, through the analysis of the electromyographic signal, may also help understand neuromotor response and the evolution of the diseases.[11]

This study presents limitations: a) the absence of a gold-standard fatigue visual scale for the pediatric population, translated and validated into Brazilian Portuguese; b) the level of physical activity of the participants was not related to HGP; c) handgrip pressure and fatigue in the preferred side were not assessed; d) children aged under 8 years and above12 years were not assessed; e) the validation of the handgrip fatigue test using dynamic contractions was not performed; and f) the electromyographic analysis was not performed simultaneously with the evaluation with a bulb dynamometer.

5. Conclusion

The dynamic contractions using handgrip was able to evoke fatigue in typical children and, in fact, induced a statistically significant decline in HGP associated with reporting maximum perceived effort. There was no sex-influence in the response and the time duration of the test ranged between 6 and 8 minutes. This protocol can be used in

future studies to investigate the influence of other factors, such as sexual maturation and body composition, on motor fatigue in typical children and in the investigation of motor fatigue in patients with chronic diseases.

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Declaration of interest statement

The authors have no conflicts of interest to report.

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Table 1. Physical characterization, physical activity level, and mean duration of fatigue test.

Variables		Sexes	
		F	**M**
Number of participants		28	30
Age (years)		10.0 (1.4)	9.8 (1.5)
Body weight (kg)		37.2 (11.1)	32.5 (9.5)
Height (cm)		142.8 (10.7)	138.6 (9.0)
BMI (kg/m-2)		18.0 (4.3)	16.7 (3.2)
Preference	**R**	26	27
	L	2	3
Physical activity level	**S**	24	23
	A	4	7
Time-to-fatigue (s)		107.7 (43.2)	122.0 (65.0)

Mean (standard deviation); Sex (F: female; M: male); BMI: body mass index; Preference (R: right; L: left); Physical activity level (S: sedentary; A: active).

Table 2. Comparison between the perceived effort scores obtained at initial and final steps of the fatigue test.

Steps	Median	Minimum	Maximum	p-value
i-HGP	2	0	9	<0.01*
f-HGP	10	4	10	

i-HGP: initial fatigue handgrip pressure; f-HGP: final fatigue handgrip pressure. Asterisk (*): when $p<0.01$ in the comparison of the perceived effort scores obtained at the initial and final steps of the fatigue test.

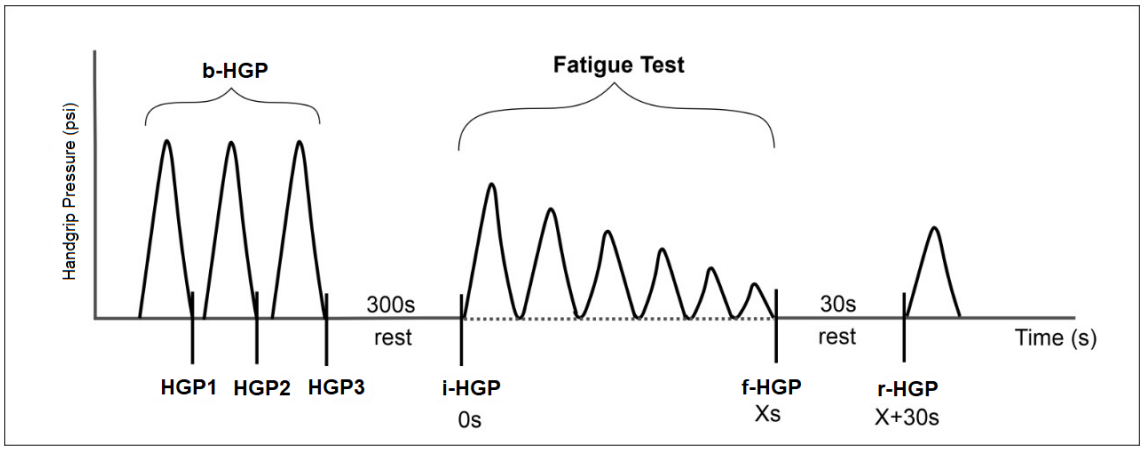

Figure 1. Schematic representation of the test protocol.

HGP1, HGP2, HGP3: handgrip pressure measured three times before the fatigue test; b-HGP: baseline handgrip pressure; i-HGP: initial fatigue handgrip pressure; f-HGP: final fatigue handgrip pressure; r-HGP: recovery handgrip pressure; s: seconds; X: unlimited fatigue test time.

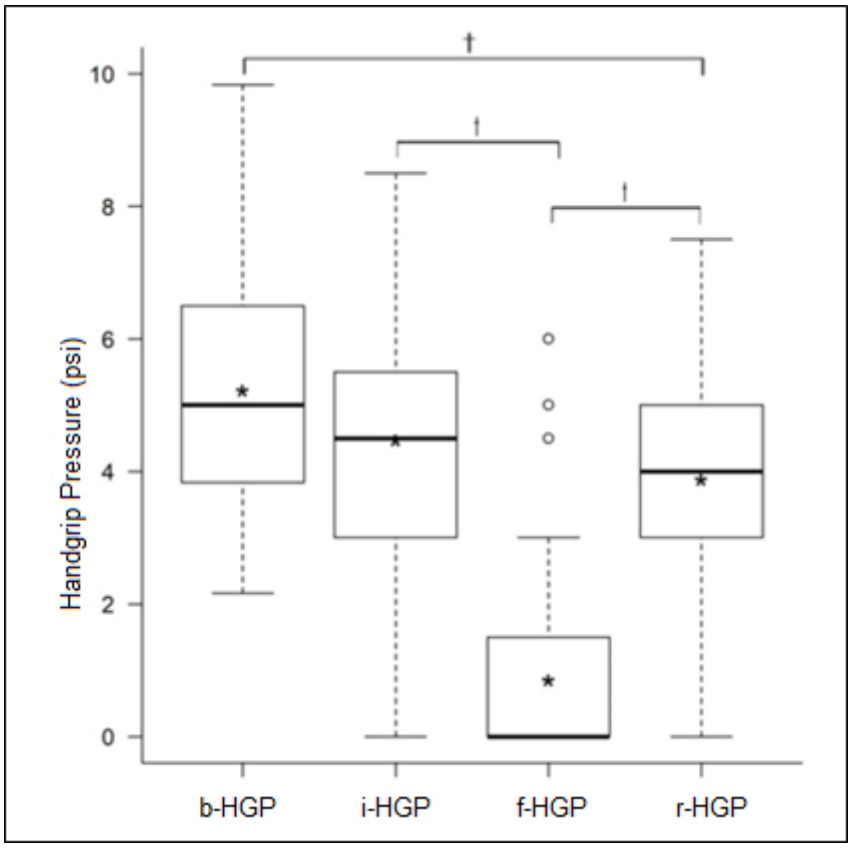

Figure 2. Caption: Handgrip pressure (in psi) for each step of the fatigue test.
b-HGP: baseline handgrip pressure (before the fatigue test); i-HGP: initial fatigue handgrip pressure; f-HGP: final fatigue handgrip pressure; r-HGP: recovery handgrip pressure; Asterisk (*): Mean; Cross (ǂ): when $p<0.01$ in the comparison between the different steps of the test protocol.

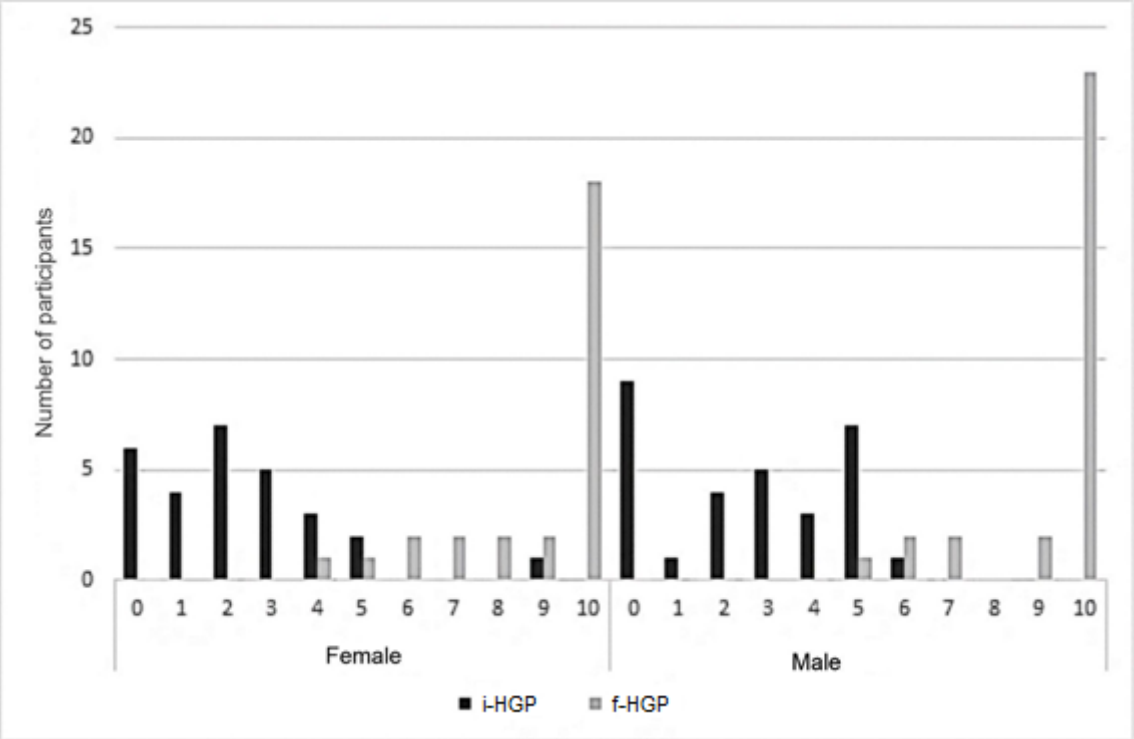

Figure 3. Caption: Frequency of the scores of perceived effort in the initial and final fatigue test for both sexes.

i-HGP: initial fatigue handgrip pressure; f-HGP: final fatigue handgrip pressure.

3.2 Artigo 5 – Submetido no jornal Developmental Neurorehabilitation

(Março de 2023)

Motor fatigue during handgrip repetitive contractions in children with spina bifida: dynamometric and electromyographic evaluation

Shortened title: Handgrip fatigue in children with spina bifida

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Abstract

Purpose: To compare handgrip pressure, fatigue resistance, and muscle activation between children with spina bifida (SB) and typically developing children. **Methods:** Sixty-eight typically developing children and 20 children with SB, aged 8 to 14 years, performed a maximal isometric handgrip test (three 5-s repetitions, with 20-s intervals) and a handgrip fatigue test (with repetitions until reaching the maximum perceived effort score) in the non-preferential hand, using a bulb dynamometer. Simultaneously, surface electromyography of the finger flexor and extensor muscles was recorded. The values from both muscular tests were compared within and between groups using multiple linear regression models. **Results:** Children with SB presented lower handgrip pressure and similar muscle fatigability compared to typically developing children, without differences between groups for muscle activation, time-to-fatigue and perceived effort. **Conclusion:** Although children with SB were weaker, they did not show signs of increased fatigue during repeated handgrip exercise contractions compared to age-matched controls.

Keywords: dynamometer; electromyography; grip; pediatric; myelomeningocele.

1. Introduction

Throughout human evolution, hand function and manual dexterity directly influence quality of life. Daily living skills, work-related functioning, and recreational activities were performed based on force and fine and sensitive movements of the hands.[1]

In individuals with spina bifida, a congenital defect in which the spinal canal is incompletely closed and associated protrusion of the spinal cord, meninges and nerve roots[2], the most common complications are paraplegia, orthopedic dysfunctions, sensitivity deficit in the lower limbs, hydrocephalus due to Arnold Chiari malformation, bladder and bowel dysfunction.[3]

About one third of patients with spina bifida who are initially community ambulators have reduced walking ability by the third decade of life, because of increased body mass, weakness and the development of joint contractures.[4] Lower values of upper and lower limb strength have been reported in individuals with spina bifida compared to healthy peers.[5,6] This set of limitations inserts the individuals with spina bifida into a sedentary lifestyle and social inactivity still in childhood.[7] A vicious cycle of disuse, weakness and

muscle fatigue worse the physical performance[8] and enlarge the loss of hand coordination and dexterity, ultimate decreasing the independence in daily activities.[9]

Decreased handgrip strength has also been found in individuals with spina bifida, with a value 71.03 (23.3)% lower than predicted.[10,11] The bulb dynamometer (North Coast – NC70154) is an easy-to-handle, affordable instrument that can be used to assess handgrip pressure[12] and the motor fatigue as well, from the decrease or failure in the ability to generate force over the time.[13] The occurrence of motor fatigue can be confirmed by analyzing the surface electromyographic signal (sEMG).[14]

Therefore, improving upper limb function is a core element of rehabilitation for patients with spina bifida interrupting the cycle of weakness, fatigue and hand incoordination. Considering that, dynamic and sustained movements are essential for daily activities, this study aimed to compare the development of handgrip motor fatigue using repetitive contractions and muscular activation (using sEMG) between children with spina bifida and typically developing children. We investigated the differences between the groups in handgrip pressure, muscular activation, perceived effort score and time-to-fatigue, all of which were recorded before and after the handgrip fatigue test (immediately, 30-s and 210-s after rest). We hypothesized that children with spina bifida would present lower values of handgrip pressure and EMG parameters, and greater reported fatigue and time-to-fatigue compared to their healthy peers.

2. Methods

2.1 Study Design

This was an observational cross-sectional study. The study was approved by the Human Research Ethics Committee of Ribeirão Preto Medical School, University of São Paulo, Brazil (reference number 63579916.2.0000.5440). All participants and their guardians signed the consent forms.

2.2 Participants

Participants of the study included 68 typically developing children (36 males); and 20 children with spina bifida (11 males, convenience sample), aged 8 to 14 years of both sexes. Typically developing children were recruited from public and/or private schools in Ribeirão Preto (SP, Brazil) and the surrounding towns. Participants with spina bifida were recruited from the rehabilitation center in the Ribeirão Preto Medical School, at the

University of São Paulo (Brazil), and the eligibility criteria were medical diagnosis of spina bifida and radiological images showing the spinal cord injury.

The non-inclusion criteria for typically developing children were the presence of orthopedic, cardiopulmonary, and neurological morbidities; for children with spina bifida the presence of other morbidities that would prevent the completion of the test used here. For both groups, recent upper limb fracture less than one year previously and no understanding of the evaluator's commands were also considered non-inclusion criteria. Fifteen SB participants used a ventriculoperitoneal valve to drain the cerebrospinal fluid; however, they did not show any clinical pyramidal signs.

2.3 Procedures

Anthropometrics and body composition measurements

All participants were initially subjected to physical assessment to obtain anthropometric data (weight and height). Body composition (lean and fat mass) was evaluated using tetrapolar bioelectrical impedance (Biodynamics 450®, São Paulo, SP, Brazil) following the manufacturer's recommendations.

Levels of sexual maturation, physical activity, spinal cord injury and functional mobility

The level of sexual maturation was classified using a questionnaire with figures and descriptions of the five puberty stages proposed by Tanner (1: prepubertal stage; 2, 3, and 4: pubertal, and 5: post-pubertal.[15] The participants answered the questionnaire in a private place and in the presence of a physical therapist and their caregivers.

The level of physical activity was assessed using the Physical Activity Questionnaire for Older Children and Adolescents (PAQ-C and PAQ-A).[16]

One experienced physical therapist performed manual muscle strength testing to determine the neuro-segmental impairment level based on recommendations by The International Myelodysplasia Study Group (IMSG).[17] In cases of asymmetric involvement, the rating for the weaker side was used. The functional mobility level of participants with spina bifida was assessed using The Functional Mobility Scale (FMS)[18].

Handgrip maximal voluntary isometric contractions and fatigue test

The handgrip test was performed using a bulb dynamometer (North Coast). All the procedures were performed according to the protocol described by Martins et al.

(2023).[19] The children remained in a seated posture with backrest, feet flat on the floor, upper limb with shoulder adduction and neutral rotation, elbow flexion at 90º, neutral forearm and wrist between 0 and 30º of extension, and between 0 and 15º of ulnar deviation, as recommended by The American Society of Hand Therapists[12,20–22]. Evaluation was performed only for the hand of the non-preferential upper limb because, during the pilot tests performed with 15 healthy children (described below), less handgrip pressure value variability was observed among the contractions in this upper limb compared to the contralateral side.

Initially, the participants were familiarized with the bulb dynamometer, performing five maximum isometric contractions. Before the handgrip fatigue test, all participants performed three maximal voluntary isometric contractions (MVICs) for 5-s with a 20-s rest time between each one (Figure 1). To represent the handgrip pressure (HGP) before the fatigue test, the mean value of these three measurements of HGP (corresponding to HGP 1, HGP 2, and HGP 3) was calculated, and we called it the baseline handgrip pressure (b-HGP) (Figure 1). Subsequently, the participants rested for 300-s. Subsequently, the handgrip fatigue test was performed using successive MVCs, with one-second intervals, standardized by a metronome. The first MVC of the fatigue test was called initial fatigue handgrip pressure (i-HGP), and the last MVC of the fatigue test was called final fatigue handgrip pressure (f-HGP) (Figure 1).

The visual analog scale (VAS) was used to classify the score of perceived effort by the participant in each minute of the fatigue test. This scale has a numerical response ranging from 0 to 10, accompanied by face drawings that represent effort intensity levels. Before performing the fatigue test, the evaluator showed the VAS to the participants and clarified possible doubts.

The fatigue test was completed when the participant reported the maximum score of perceived effort using the VAS and/or the inability to synchronize the contractions with the metronome. Therefore, the time-to-fatigue differed for each participant. After 30-s of rest, another MVC was recorded, called the post-test handgrip pressure (p-HGP) (Figure 1). Finally, 3 min after p-HGP, the pressure was measured again and referred to as recovery handgrip pressure (r-HGP). Participants were verbally encouraged to develop maximum contractions during the test. For analysis, the handgrip pressure values at b-HGP, i-HGP, f-HGP, p-HGP, and r-HGP were recorded (in psi), as well as time-to-fatigue (in seconds) and scores of perceived effort before and after the fatigue test.

Please, insert Figure 1 about here

Electromyography recording

Neuromuscular activation of muscles related to HGP was a secondary outcome recorded to confirm motor fatigability. The sEMG signals were recorded simultaneously with the dynamometric handgrip test in 22% of typically developing children (n=15) and 45% of children with spina bifida (n=9), chosen randomly and following the methodology previously described. The Trigno™ Wireless System electromyograph (Delsys Inc., Boston, MA, USA) was used, with a sampling frequency of 1200 Hz and Trigno™Wireless Sensor surface electrodes (Delsys Inc., Boston, MA, USA), with a rejection rate of common modulation greater than 80 dB. All skin preparation and electrode placement procedures were performed in accordance with the recommendations of the Surface Electromyography for the Non-Invasive Assessment of Muscles (SENIAM).[23] The electrodes were positioned over the finger flexor muscles 5 cm below the tendon of the biceps muscle, and over the finger extensor muscles 1/3 below the head of the ulna towards the olecranon.[24]

2.4 Data processing

The HGP values were normalized to body weight. The sEMG data were processed using a routine developed in a MATLAB environment (version R2015a, MathWorks Inc., NetWorks, MA, USA), and the analyzed variables were EMG amplitude (μV) and median power frequency (Hz). The EMG amplitude was normalized by the respective maximum value from the baseline test and called the normalized EMG amplitude.

2.5 Statistical analysis

Sample size and power were calculated using data from a pilot test with 15 typically developing children of both sexes. We considered the difference between the means of the HGP recorded at the beginning and end of the dynamometric test, and the largest standard deviation. Therefore, the estimated minimum sample size was 60 typically developing children. Statistical analysis was performed using the SAS 9.2 software. The spina bifida group comprised a convenience sample.

The qualitative variables (sex, sexual maturity level, physical activity level, preference for body side, and spinal cord injury level) were described as absolute frequencies and percentiles and compared between groups using the Fisher test.

The quantitative variables (age, body mass, height, BMI, lean mass, and fat mass) were presented as group median, minimum, and maximum values and compared between groups using the non-parametric Mann-Whitney test.

The intergroup comparison for time-to-fatigue was performed using ANCOVA and was controlled for sexual maturity level.

Multiple linear regression models (random and fixed effects) were used to compare other quantitative variables (HGP, normalized EMG amplitude, median power frequency, and perceived effort score) between groups. Multiple linear regression models were used in data analysis in which responses were grouped (more than one measure for the same individual), and the assumption of independence between observations in the same group was not adequate. These models assume that their residuals have a normal distribution with a mean of 0 and a constant variance σ^2. When this assumption was not observed, transformations in the variables were used. For comparison, a post-test using orthogonal contrast was used.

The comparison between groups for HGP and EMG data was controlled for the covariables sexual maturity level and fat mass, since there were significant differences between groups (Tukey test).

The analysis was performed using the SAS 9.4 software. A significance level of 5% was used.

3. Results

Anthropometric data from all participants are presented in Table 1. The spina bifida and control groups presented highest number of participants in the prepubertal and pubertal sexual maturity levels, respectively (Table 1). The spina bifida group had a significantly higher mean fat mass than the control group (+55.3%; $p<0.05$) (Table 1).

Statistical analysis showed no significant differences between the ambulatory and non-ambulatory spina bifida participants. Therefore, we presented the results from the spina bifida group considering all participants together, independent of the type of locomotion.

No differences in time-to-fatigue were observed between the groups (Table 1).

Please, insert Table 1 about here

The HGP from all moments of the test protocol is shown in Figure 2. The spina bifida group showed significantly lower values for b-HGP, i-HGP, and r-HGP compared to the control group ($p<0.05$), with decreases of 21.17, 35.34, and 25.81%, respectively. The f-HGP was significantly lower than the i-HGP in both groups ($p<0.01$). The r-HGP was significantly higher than p-HGP in both groups ($p<0.05$). The p-HGP was significantly lower compared to the b-HGP in both groups ($p<0.05$). The r-HGP was significantly higher than the b-HGP in the control group ($p<0.05$) (Figure 2).

Please, insert Figure 2 about here

The EMG data are shown in Figure 3. In both groups, the median power frequency from the finger flexor and extensor muscles was significantly lower in the f-HGP than in the i-HGP ($p<0.05$) (Figure 3). No difference was observed in EMG amplitude (NS).

Please, insert Figure 3 about here

Figure 4 presents the perceived effort scores during different moments of the test protocol for both groups. The participants in both groups reported significantly lower perceived effort scores at i-HGP and r-HGP in relation to f-HGP and p-HGP, respectively ($p<0.01$) (Figure 4).

Please, insert Figure 4 about here

The mean difference and 95% confidence interval of the HGP, EMG data, and perceived effort scores between the groups and between the different moments of the test protocol for the same group are shown in Tables A-C in the Supplementary Material.

4. Discussion

The test protocol using repetitive voluntary contractions proposed in this study produced handgrip fatigue in typically developing children and in children with spina

bifida. These findings were confirmed by the decline in the HGP and median power frequency in the finger flexor and extensor muscles during the fatigue test, and higher scores of reported fatigue by the participants of both groups at the end of the fatigue test. Moreover, the test protocol proved to be feasible to be used in a clinical setting, since the fatigue was reached in a short time (133.5s for spina bifida and 106.5s for typically developing children) and the bulb dynamometer (North Coast – NC70154) is an easy-to-handle and affordable instrument to be used in a clinical practice.

The spina bifida group presented lower values of handgrip pressure at baseline compared to controls, but they did not show differences in HGP immediately after the fatigue test (f-HGP) compared to the respective control group. In other words, they were able to resist fatigue similarly compared to healthy children during repeated contractions of handgrip exercise. These data partially agree with our hypotheses. The lower handgrip pressure values for spina bifida participants at baseline (b-HGP) and at the first contraction of the fatigue test (i-HGP) probably gives them the ability to preserve strength during the fatigue test. The relationship between maximum voluntary contraction and fatigue of knee flexor and extensor muscles in healthy children compared to adults and in children with cerebral palsy compared to healthy peers was investigated by Eken et al. (2013).[25] They found that healthy children showed less fatigability than healthy adults, and children with cerebral palsy presented lower fatigability than healthy children and adults. The authors justified these findings relating to the greater resistance to fatigue in healthy children and those with cerebral palsy, with the predominance of type I fibers (oxidative) and a lower capacity to produce muscle strength.

The present fatigue test demonstrated that the final handgrip pressure values (f-HGP) were significantly lower than the initial values (i-HGP) for both groups. These findings were in agreement with the theoretical concept of fatigue, i.e., motor fatigue is defined as the incapacity by the individual to maintain force during repetitive voluntary contractions.[26]

In addition to the decrease in handgrip pressure during the fatigue process induced by sustained or repetitive voluntary contractions in healthy individuals, changes occur in EMG signals, such as an increase in the EMG amplitude and a decrease in the EMG power frequency.[27] In the present study, both groups presented no differences in normalized EMG amplitude and significantly lower median power frequency from finger flexor and extensor muscles in f-HGP compared to i-HGP. These findings suggest that

there were no changes in the motor unit firing rate, but indicated a decrease in the amplitude and increase in the duration of action potentials, modifying the median power frequency; this neurophysiological change induced by the fatigue process was similar in healthy children and those with spina bifida.

The analysis showed that r-HGP was significantly higher than p-HGP for both groups, but compared to b-HGP was significantly higher only for the control group. Phosphocreatine resynthesis, clearance of by-products (lactate, and H+ ions), and regulation of acid-base balance are factors that influence the recovery periods[28]. These results indicate that 210-sec of rest post-fatigue test may be more effective in improving these recovery mechanisms compared to 30-sec of rest. To the best of our knowledge, this is the first study to investigate the effects of different rest intervals on the recovery of handgrip pressure post-fatigue tests in healthy children and those with spina bifida. Therefore, there are no data from previous studies on this topic (rest time to recovery strength after the handgrip fatigue test) for comparison with our data. In children, 210-s of rest may be a good recovery time between dynamic motor activities with repeated maximal grips when the goal is to reach the best baseline to start the next section of exercises or other types of activities (at home, school, or job).

For both groups, participants reported significantly higher scores of perceived effort at f-HGP and p-HGP in relation to i-HGP and r-HGP, respectively. These data confirm that the fatigue test protocol was able to induce tiredness combined with motor fatigue, and a 210-s rest was more effective in recovering handgrip strength than a 30-s.

The spina bifida group showed significantly higher fat mass values than the control group, which is similar to the results presented by Widman et al. (2007).[29] However, they used dual- energy X-ray absorptiometry (DEXA) to assess body composition in spina bifida participants aged 11 to 21 years. Although bioimpedance is a safe and useful device for evaluating children and adolescents, few studies have investigated the body composition of children with spina bifida using this device. In general, these previous studies reported that children with spina bifida showed lower lean mass and no significant differences in fat mass compared with healthy children,[30] in contrast to the results of the present study.

From a clinical point of view, the use of protocols for quantitative assessment of muscle performance (strength/pressure) and motor fatigue, using easy-to-handle instruments such as the bulb dynamometer, may help understand functional deficits

during daily living activities. In addition, it offers scientific support for the assessment of muscle performance and monitoring of therapeutic approaches in children with chronic morbidities who report upper limb fatigue during physical activities.

The limitations of this study include the failure to evaluate the reliability of the handgrip fatigue test with repetitive contractions in healthy children and those with spina bifida and the lack of inclusion of participants in other age ranges. Future studies may verify the association between HGP and anthropometric characteristics, body composition, and level of physical activity, since HGP is a measure of overall health status. Another important challenge remains in detecting changes in handgrip strength/pressure and fatigue resistance in individuals with other diseases and upper limb disabilities.

5. Conclusion

Children with spina bifida and typically developing children reached motor fatigue using a similar timeframe and reported a high intensity of effort at the end of the handgrip fatigue test with repetitive contractions to exhaustion. On the other hand, it was again confirmed that children with SB had reduced handgrip pressure compared to their peers.

Neuromuscular activation assessed by sEMG did not show any differences between groups. Since it is expected that individuals who produce less muscle strength are more resistant to motor fatigue, there is a mechanism that prevents pediatric patients with spina bifida from preserving handgrip force during fatigue testing. However, this mechanism may be investigated in future studies.

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Conflict of interest

The authors declare no conflict of interest.

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Table 1. Sample characteristics.

		Participants	
		Control (n= 68)	**Spina bífida (n= 20)**
Sex (%)	female	47.1	45.0
	male	52.9	55.0
Age (years)		10.0 (8.0; 13.0)	9.0 (8.0;14.0)
Body mass (kg)		32.0 (21.0; 64.0)	37.9 (19.3; 63.0)
Height (cm)		142.5 (125; 170)	138.5 (110.0; 164.0)
BMI (kg/m^{-2})		16.7 (11.9; 30.4)	17.9 (9.9; 31.4)
Lean mass (%)		82.8 (24.4; 96.9)	73.9 (60.8; 92.5)
Fat mass (%)		16.8 (3.1; 50.3)	26.1 (7.5; 39.2)*
Preference side (%)	right	91.1	100
	left	8.8	0
Sexual maturity level (%)	prepubertal	33.8	55.0*
	pubertal	66.1	40.0*
	post pubertal	0.0	5.0*
Physical activity level (%)	extremely sedentary	17.6	30.0
	sedentary	67.6	60.0
	moderately active	13.2	10.0
	active	1,4	0.0
Spinal cord injury level (%)	high lumbar	na	20.0
	low lumbar	na	40.0
	sacral	na	40.0
Type of locomotion (%)	ambulatory	na	65.0
	non-ambulatory	na	35.0
Time-to-fatigue (s)		106.5 (32.0; 300.0)	133.5 (60.0; 270.0)

Median (minimum; maximum); na: not applicable; *: statistical significance ($p \leq 0.05$) compared to control.

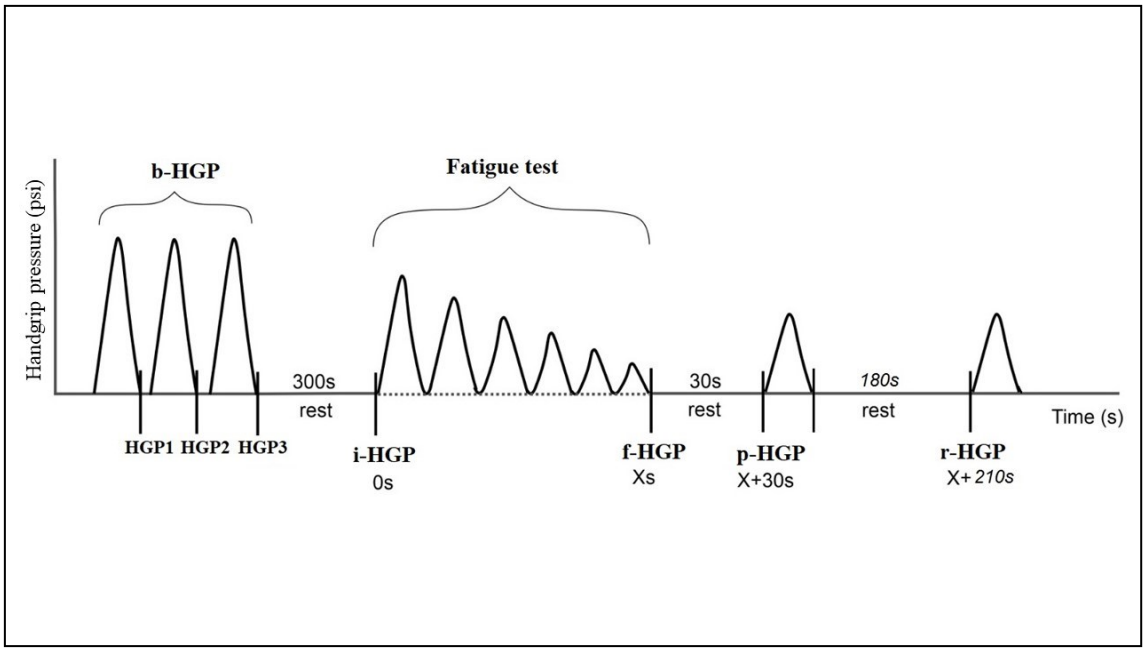

Figure 1. Schematic representation of the test protocol.

b-HGP: baseline handgrip pressure; i-HGP: initial fatigue handgrip pressure; f-HGP: final fatigue handgrip pressure; p-HGP: post-test handgrip pressure; r-HGP: recovery handgrip pressure.

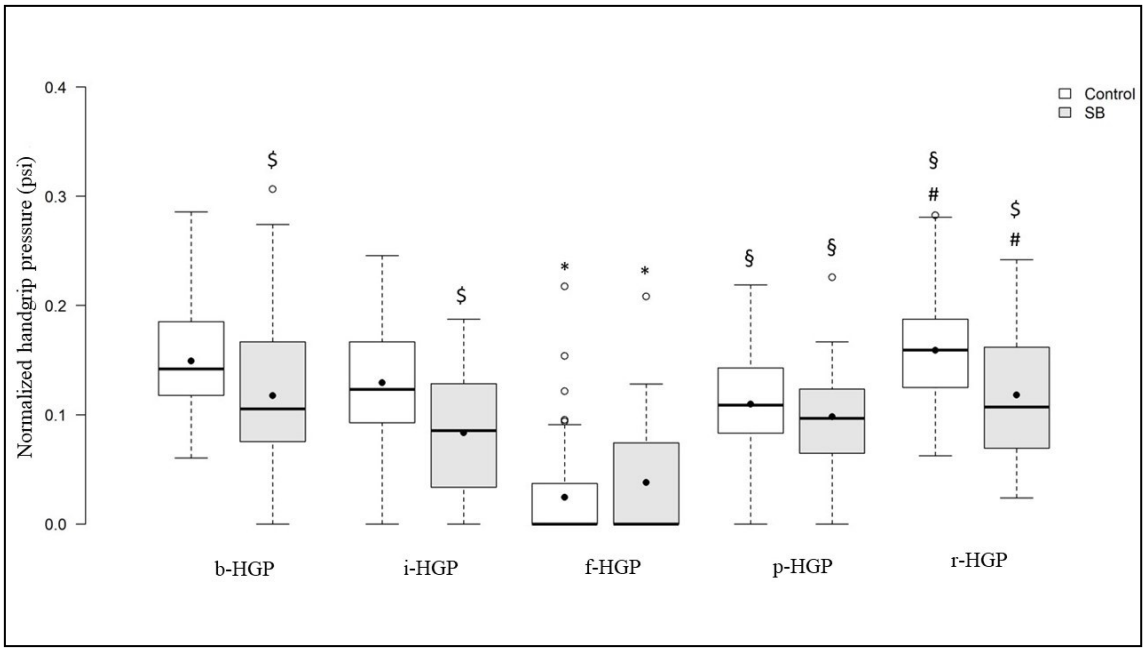

Figure 2. Normalized handgrip pressure in different phases of the test protocol.

SB: spina bifida; b-HGP: baseline handgrip pressure; i-HGP: initial fatigue handgrip pressure; f-HGP: final fatigue handgrip pressure; p-HGP: post-test handgrip pressure; r-HGP: recovery handgrip pressure; °: outliers; •: mean values; *: statistical significance ($p \leq 0.05$) compared to i-HGP; #: statistical significance ($p \leq 0.05$) compared to p-HGP; §: statistical significance ($p \leq 0.05$) compared to their respective b-HGP; $: statistical significance ($p \leq 0.05$) compared to respective control group.

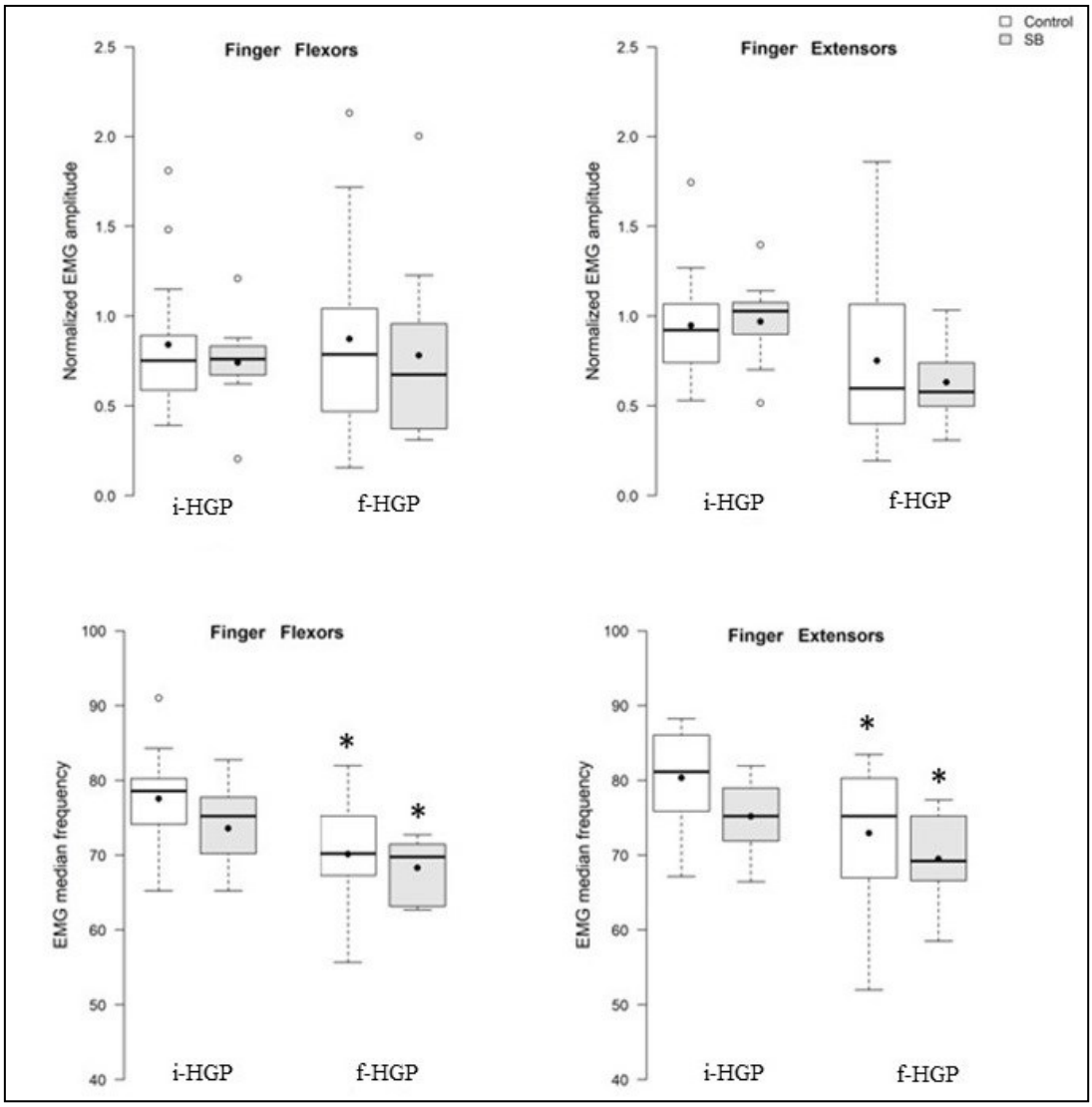

Figure 3. Normalized EMG amplitude (%MVC) and EMG median power frequency (Hz) from fingers flexor and extensor muscles during initial and final repetitions of the handgrip fatigue test.

SB: spina bifida; i-HGP: initial fatigue handgrip pressure; f-HGP: final fatigue handgrip pressure; °: outliers; •: mean values; *: statistical significance ($p \leq 0.05$) compared to i-HGP.

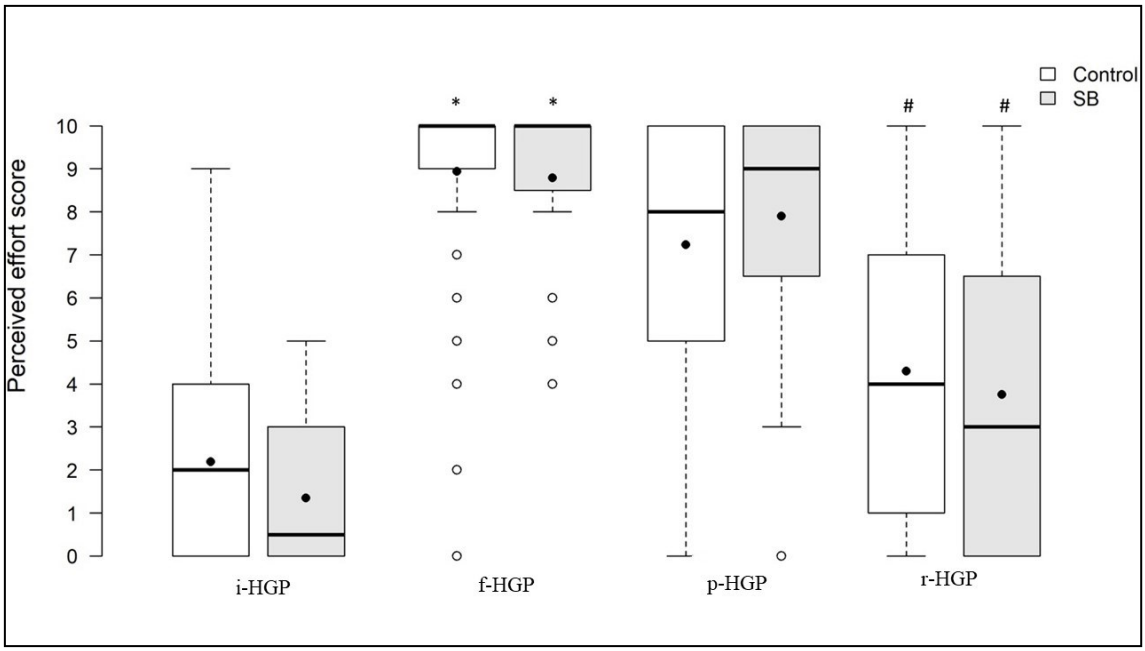

Figure 4. Perceived effort score in different phases of the test protocol.

SB: spina bifida; i-HGP: initial fatigue handgrip pressure; f-HGP: final fatigue handgrip pressure; p-HGP: post-test handgrip pressure; r-HGP: recovery handgrip pressure; °: outliers; •: mean values; *: statistical significance ($p \leq 0.05$) compared to i-HGP; #: statistical significance ($p \leq 0.05$) compared to p-HGP.

Supplementary Material

Table A. Comparison of handgrip pressure between the groups and between the moments of the test protocol for the same group.

Variable	Comparison	Mean difference	95% CI		p value
Handgrip pressure ($psi.Kg^{-1}$)	b-HGP (Control vs. SB)	0.0260	0.0017	0.0503	**0.04**
	i-HGP (Control vs. SB)	0.0400	0.0128	0.0672	**<0.01**
	f-HGP (Control vs. SB)	-0.0192	-0.0464	0.0080	0.17
	p-HGP (Control vs. SB)	0.0057	-0.0215	0.0329	0.68
	r-HGP (Control vs. SB)	0.0354	0.0082	0.0626	**0.01**
	SB (i-HGP vs. f-HGP)	0.0457	0.0272	0.0643	**<0.01**
	Control (i-HGP vs. f-HGP)	0.1049	0.0947	0.1151	**<0.01**
	SB (b-HGP vs. p-HGP)	0.0194	0.0043	0.0345	**0.01**
	Control (b-HGP vs. p-HGP)	0.0397	0.0313	0.0480	**<0.01**
	SB (b-HGP vs. r-HGP)	-0.0004	-0.0155	0.0147	0.96
	Control (b-HGP vs. r-HGP)	-0.0099	-0.0182	-0.0015	**0.02**
	SB (p-HGP vs. r-HGP)	-0.0198	-0.0383	-0.0013	**0.04**
	Control (p-HGP vs. r-HGP)	-0.0495	-0.0597	-0.0393	**<0.01**

95% CI: 95% confidence interval; SB: spina bifida; vs.: versus; b-HGP: baseline handgrip pressure; i-HGP: initial fatigue handgrip pressure; f-HGP: final fatigue handgrip pressure; p-HGP: post-test handgrip pressure; r-HGP: recovery handgrip pressure. Bold: significant statistical difference ($p \leq 0.05$).

Table B. Comparison of EMG data between groups and between the initial and final fatigue handgrip pressures for the same group.

Variable	Muscles	Comparison	Mean difference	95% CI		p value
Normalized EMG amplitude (%μV)	Fingers flexor	i-HGP (control vs. SB)	0.000010	-0.000008	0.000028	0.28
		f-HGP (control vs. SB)	0.000006	-0.000010	0.000024	0.50
		SB (i-HGP vs. f-HGP)	-0.000002	-0.000020	0.000013	0.83
		control (i-HGP vs. f-HGP)	0.000002	-0.000010	0.000014	0.73
	Fingers extensor	i-HGP (control vs. SB)	-0.062620	-0.583700	0.458400	0.81
		f-HGP (control vs. SB)	0.023290	-0.497800	0.544300	0.93
		SB (i-HGP vs. f-HGP)	0.301300	0.030960	0.571700	**0.03**
		control (i-HGP vs. f-HGP)	0.215400	0.005996	0.424900	**0.04**
EMG median frequency (Hz)	Fingers flexor	i-HGP (control vs. SB)	4.91	-0.95	10.76	0.10
		f-HGP (control vs. SB)	2.79	-3.06	8.65	0.35
		SB (i-HGP vs. f-HGP)	5.30	0.91	9.68	**0.02**
		control (i-HGP vs. f-HGP)	7.41	4.01	10.81	**<.0001**
	Finger Extensor	i-HGP (control vs. SB)	5.94	-1.84	13.73	0.13
		f-HGP (control vs. SB)	4.23	-3.55	12.02	0.28
		SB (i-HGP vs. f-HGP)	5.69	0.11	11.27	**0.05**
		control (i-HGP vs. f-HGP)	7.40	3.08	11.72	**0.00**

95% CI: 95% confidence interval; SB: spina bifida; vs.: versus; i-HGP: initial fatigue handgrip pressure; f-HGP: final fatigue handgrip pressure. Bold: significant statistical difference ($p \leq 0.05$).

Table C. Perceived effort score between groups and between moments of the fatigue test for the same group.

Variable	Comparison	Mean difference	95% CI		p value
Perceived effort score	i-HGP (control vs. SB)	0.49	-0.86	1.84	0.47
	f-HGP (control vs. SB)	-0.29	-1.67	1.08	0.67
	p-HGP (control vs. SB)	-1.00	-2.36	0.35	0.14
	r-HGP (control vs. SB)	0.22	-1.14	1.57	0.75
	SB (i-HGP vs. f-HGP)	-7.53	-9.02	-6.05	**<0.01**
	control (i-HGP vs. f-HGP)	-6.75	-7.54	-5.96	**<0.01**
	SB (p-HGP vs. r-HGP)	4.15	2.69	5.61	**<0.01**
	control (p-HGP vs. r-HGP)	2.93	2.12	3.74	**<0.01**

95% CI: 95% confidence interval; SB: spina bifida; vs.: versus; i-HGP: initial fatigue handgrip pressure; f-HGP: final fatigue handgrip pressure; p-HGP: post-test handgrip pressure; r-HGP: recovery handgrip pressure. Bold: significant statistical difference ($p \leq 0.05$).

4 SÍNTESE DOS ARTIGOS

Com a finalidade de facilitar a compreensão dos artigos que compuseram esta tese, as Tabelas A e B apresentam uma síntese dos mesmos.

Tabela A. Síntese dos artigos 1 a 3.

	Desempenho muscular avaliado pelo dinamômetro isocinético		
	Artigo 1*	**Artigo 2****	**Artigo 3*****
Desfecho primário	Investigar a influência da maturação sexual e sexo na produção de torque dos músculos extensores do cotovelo durante o teste de fadiga em crianças e adolescentes com desenvolvimento típico	Comparar a produção de torque dos músculos flexores e extensores do cotovelo durante o teste de fadiga entre crianças e adolescentes com EB e seus pares com desenvolvimento típico	Comparar o torque isométrico máximo, a TDT (na fase inicial do aumento da força 0-300 ms) dos flexores e extensores do cotovelo entre crianças e adolescentes com EB e seus pares com desenvolvimento típico, considerando o tipo de locomoção dos participantes com EB
Desfecho secundário	Investigar a influência da maturação sexual e sexo na ativação neuromuscular do músculo tríceps braquial durante o teste de fadiga	Comparar a ativação neuromuscular dos músculos bíceps e tríceps braquial durante o teste de fadiga entre crianças e adolescentes com EB e seus pares com desenvolvimento típico	Comparar a ativação neuromuscular dos músculos bíceps e tríceps braquial na fase inicial do aumento da força (0-300 ms) entre crianças e adolescentes com EB e seus pares com desenvolvimento típico

Tipo de estudo	Observacional, transversal	Observacional, transversal	Observacional, transversal
Amostra	Crianças com desenvolvimento típico: n= 37 - PrPU = 11 (masculino: 6, idade média 8,1 anos; feminino: 5, idade média 8,2 anos) - PU=16 (masculino: 7, idade média 12,7 anos; feminino: 9, idade média 13,4 anos) - PoPU=10 (masculino: 5, idade média 15, 2 anos; feminino: 5, idade média 15,0 anos)	- EB: n= 23 (8 deambuladores e 15 não-deambuladores); idade média 10,8 anos - Controles: n= 84; idade média 12,1 anos - ambos os sexos	- EB: n= 23 (7 deambuladores e 16 não-deambuladores); idade média 11,0 anos - Controles: n= 25; idade média 11,8 anos - ambos os sexos
Avaliação	Teste isocinético e EMG durante contrações voluntárias máximas repetidas ($120^{o.s-1}$)	Teste isocinético e EMG durante contrações voluntárias máximas repetidas ($120^{o.s-1}$)	Teste isométrico e EMG durante contrações voluntárias explosivas e máximas
Variáveis desfecho	PT-bw, amplitude EMG, EMG MPF, tempo e número de repetições até a fadiga, escore de esforço percebido	PT-bw, amplitude EMG, EMG MPF, tempo e número de repetições até a fadiga, escore de esforço percebido	PT-bw, TDT (0- 300ms), TDT relativo (TDT/MVT 0-300ms), amplitude EMG

Análise estatística	Modelo de regressão linear com efeitos mistos	Regressão linear simples ANCOVA - ajustada por Tukey (devido diferenças entre os grupos para envergadura, massa magra e nível de atividade física)	Teste t para amostras independentes
Principais resultados (p≤0,05)	*Comparação entre os níveis maturacionais:* Taxa de declínio do PT-bw: PrPU < PU e PrPU < PoPU, para ambos os sexos Taxa ascendente da amplitude EMG: PrPU > PU feminino e PrPU > PoPU feminino Taxa de declínio da EMG MPF: PoPU > PrPU masculino *Comparação entre os sexos:*	*PT-bw (TVM):* FLC e EXC: EB < C FLC: EB não-deamb e EB deamb <C EXC: EB não-deamb < C *Amplitude EMG:* bíceps e tríceps: EB < C bíceps e tríceps: EB não-deamb < C *EMG MPF:* tríceps: EB não-deamb > C tríceps: EB não-deamb > EB deamb *Taxa de desenvolvimento de fadiga:* PT-bw: FLC EB < C	*PT-bw (TVM):* EXC: EB deamb < C *TDT (0-50ms):* FLC: EB<C; EB não-deamb < C *TDT relativo (0-100,200,300 ms):* FLC: EB < C; EB não-deamb < C *TDT (0-200ms):* EXC: EB < C; EB não-deamb < C *TDT (0-300ms):* EXC: EB < C; EB deamb < C; EB não-deamb < C

	Maior taxa de subida da amplitude EMG para PrPU feminino e PoPU masculino, e menor tempo até a fadiga para PoPU masculino	*<u>TDT relativo (0-200ms)</u>*: EXC: EB não-deam < C *<u>Amplitude EMG (0-200; 300ms):</u>* tríceps EB deamb > C

*: artigo em elaboração/adequação; **: artigo submetido à publicação; ***: artigo publicado; EB: grupo espinha bífida; C: grupo controle (participantes com desenvolvimento típico); PrPU: grupo pré-pubere; PU: grupo púbere; PoPU: grupo pós-pubere; FLC: flexores de cotovelo; EXC: extensores de cotovelo; PT-bw: pico de torque normalizado pelo peso corporal; TVM: torque voluntário máximo; TDT: taxa de desenvolvimento de torque; EMG: eletromiografia de superfície; EMG MPF: frequência de potência mediana do sinal EMG.

Tabela B. Síntese dos artigos 4 e 5.

	Desempenho muscular avaliado pelo dinamômetro de bulbo	
	Artigo 4* **	**Artigo 5** **
Desfecho primário	Analisar o desenvolvimento de fadiga durante atividade repetitiva de preensão palmar em crianças com desenvolvimento típico	Comparar o desenvolvimento de fadiga durante atividade repetitiva de preensão palmar entre crianças com EB e crianças com desenvolvimento típico
Desfecho secundário	Investigar a influência do sexo na atividade de preensão palmar durante o teste de fadiga em crianças com desenvolvimento típico	Comparar a ativação neuromuscular dos músculos flexores e extensores de dedos durante o teste de fadiga entre crianças e adolescentes com EB e seus pares com desenvolvimento típico
Tipo de estudo	Observacional, transversal	Observacional, transversal
Amostra	Crianças com desenvolvimento típico: n=58 - F: 28 com idade média 10,0 anos - M: 30 com idade média 9,8 anos	- EB: n= 20 (13 deambuladores e 7 não-deambuladores); idade média 9,9 anos - Controles: n= 68; idade média 10,1 anos - ambos os sexos
Avaliação	Teste dinamométrico de preensão palmar durante contrações voluntárias máximas repetidas	Teste dinamométrico de preensão palmar e EMG durante contrações voluntárias máximas repetidas
Variáveis desfecho	Valores de pressão palmar (HGP), tempo e número de repetições até a fadiga, escore de esforço percebido	Valores de pressão palmar (HGP), amplitude EMG, EMG MPF, tempo e número de repetições até a fadiga, escore de esforço percebido

Análise estatística	Modelo de regressão linear com efeitos mistos	ANCOVA - ajustadas por Tukey (devido diferenças entre os grupos para nível de maturação sexual e massa gorda)
Principais resultados (p≤0,05)	b-HGP > r-HGP i-HGP > f-HGP f-HGP < r-HGP	b-HGS: EB<C <u>*Para EB e controle:*</u> i-HGS > f-HGS b-HGS > p-HGS r-HGS > p-HGS <u>*Para controle:*</u> r-HGS > b-HGS C > EB: i-HGS e r-HGS <u>*Para EB deamb e EB não-deamb:*</u> i-HGS > f-HGS C > EB deamb: i-HGS e r-HGS <u>*Amplitude EMG:*</u> sem diferenças para C vs EB

		Para EB deamb: f-HGS < i-HGS (extensores) *EMG MPF:* Para EB e controle: f-HGS < i-HGS (flexores e extensores) *Para EB deamb:* p-HGS > r-HGS (extensores) C > EB e EB não-deamb: p-HGS (flexores)

*: artigo em elaboração/adequação; **: artigo submetido à publicação; ***: artigo publicado; EB: grupo espinha bífida; C: grupo controle; EMG: eletromiografia de superfície; EMG MPF: frequência mediana do sinal EMG; b-HGP: baseline handgrip pressure; i-HGP: initial handgrip pressure in the fatigue test; f-HGP: final handgrip pressure in the fatigue test; p-HGP: post-test handgrip pressure after fatigue test (30-sec of rest); r-HGP: recovery handgrip pressure after fatigue test (3-min of rest).

5 INTERSECÇÃO ENTRE OS ARTIGOS E RELEVÂNCIA CLÍNICA

Este projeto investigou, em crianças e adolescentes com desenvolvimento típico, a influência da maturação sexual e do sexo na produção de torque, fadigabilidade motora e ativação neuromuscular (pela EMG de superfície) dos músculos extensores de cotovelo durante contrações máximas repetidas a $120^{\circ}.s^{-1}$, utilizando o dinamômetro isocinético (Artigo 1) e, a influência do sexo na produção de força e na fadigabilidade motora dos músculos flexores e extensores de dedos durante contrações máximas repetidas usando o dinamômetro de bulbo (Artigo 4). Os mesmos protocolos foram utilizados para investigar a hipótese de que crianças e adolescentes com EB têm força reduzida, acompanhada de aumento da fadigabilidade dos músculos do cotovelo (Artigo 2) e diminuição da pressão palmar (Artigo 5) quando comparados com crianças e adolescentes com desenvolvimento típico, de mesma faixa etária. Adicionalmente, um terceiro protocolo composto por contrações voluntárias isométricas máximas e rápidas dos músculos do cotovelo foi utilizado para investigar diferenças no torque isométrico, TDT e ativação neuromuscular entre crianças e adolescentes com EB e seus pares típicos (Artigo 3).

A literatura contém um elevado número de estudos que investigaram a força e fadigabilidade motora dos músculos dos membros inferiores, principalmente por meio de contrações isométricas, em jovens e adultos saudáveis ou com doenças neurológicas crônicas (Dipla et al., 2009; Eken et al., 2013; Pincivero et al., 2003). Mesmo em protocolos de testes dinâmicos de fadiga, as avaliações de estudos anteriores empregaram um número limitado de contrações/repetições/tempo até a fadiga, que pode não ser sensível às respostas neuromusculares individuais dos participantes. Portanto, do ponto de vista metodológico, foi necessário desenvolver novos protocolos de teste de fadiga que atendessem tal critério. Os protocolos de avaliação com uso do dinamômetro isocinético (instrumento padrão-ouro) e dinamômetro de bulbo (equipamento portátil, prático e barato) propostos no presente estudo respeitaram a execução individualizada do teste de fadiga com contrações dinâmicas ilimitadas até que o participante atingisse pelo menos 50% de diminuição do PT (para o teste realizado no dinamômetro isocinético) e/ou relatasse esforço máximo percebido. Ambos os protocolos foram capazes de induzir fadiga, pois ao final do teste foi observado um declínio significativo do PT e nos valores de pressão palmar e aumento da sensação de cansaço (esforço relatado) em relação aos valores iniciais, tanto nos participantes típicos (Artigos 1 e 4) quanto naqueles com EB

(Artigos 2 e 5), sem diferenças entre os grupos para tempo de duração dos testes ou número de repetições/contrações musculares.

Os achados do Artigo 1 mostraram que a maturação sexual influenciou a produção de torque e a ativação neuromuscular durante o teste de fadiga dos músculos extensores do cotovelo de crianças e adolescentes típicos de ambos os sexos (menor declínio do PT para o grupo pré-púbere; maior amplitude EMG para o grupo pré-púbere feminino; e maior declínio da frequência mediana para o grupo pós-pubere masculino quando comparados aos demais grupos).

Os resultados do Artigo 4 mostraram que o sexo não foi uma covariável importante para o desenvolvimento da fadigabilidade motora durante a atividade dinâmica de preensão palmar em crianças típicas, pois não houve diferença significativa nos valores de pressão palmar entre meninas e meninos. É importante ressaltar que nesse estudo avaliamos apenas crianças típicas entre 8 e 12 anos, e, portanto, a maturação sexual não foi considerada nas análises.

Nossos resultados novamente confirmaram os achados descritos em estudos prévios (Buffart et al., 2008; Martins et al., 2019, 2022; Norrlin et al., 2003; Oliveira et al., 2014) os quais mostraram que pacientes com EB apresentam valores reduzidos de torque voluntário máximo isocinético (Artigo 2) e isométrico (Artigo 3 – para extensores do cotovelo em participantes deambuladores com EB), e de pressão palmar (Artigo 5) em relação aos seus pares típicos. É esperado que indivíduos que produzam menos força muscular sejam mais resistentes à fadiga (Eken et al., 2013; Moreau et al., 2008, 2009; Paraschos et al., 2007; Pincivero et al., 2003), porém, em contraste com nossas hipóteses, a análise do PT normalizado para o peso corporal durante o trabalho muscular repetitivo mostrou que os participantes do EB apresentaram maior resistência à fadiga em comparação com os controles da mesma faixa etária, durante contrações cíclicas repetidas dos flexores do cotovelo (Artigo 2), e também foram capazes de resistir à fadiga de forma semelhante às crianças e adolescentes típicos durante contrações repetidas de preensão palmar (Artigo 5); em ambos os casos a EMG não mostrou diferenças importantes entre os grupos EB e controle para a ativação neuromuscular.

No entanto, déficits significativos nas características de produção de força muscular máxima e rápida dos músculos do cotovelo (ou seja, na TDT) foram observados nos participantes com EB em comparação com seus pares com desenvolvimento típico (Artigo 3), sem relação com a produção de força isométrica máxima, esta última revelada

pela análise do TDT relativo (TDT/CVM). Logo, é importante investigar outros potenciais mecanismos neuronais e musculares que possam influenciar a produção rápida de força na população com EB, por exemplo pela análise da taxa de disparo das unidades motoras, e quantificação da proporção de fibras musculares e rigidez tendínea.

Surpreendentemente, não foram identificadas diferenças significativas entre participantes EB deambuladores e não-deambuladores para todas as variáveis analisadas nos Artigos 2, 3 e 5, indicando que as diferenças encontradas no desempenho dos músculos de membros superiores entre pacientes com EB e seus pares típicos são possivelmente decorrentes mais do estilo de vida sedentário (Claridge et al., 2019) do que pelo uso diário de dispositivos auxiliares de locomoção.

O conjunto de dados apresentados nessa tese sugere que: (1) o nível de maturação sexual deve ser considerado quando o foco de investigação é a fadigabilidade motora dos músculos de membros superiores na população pediátrica com desenvolvimento típico; (2) os planos de tratamento terapêuticos e desportivos para pacientes pediátricos com EB devem contemplar o treinamento de força muscular de músculos dos membros superiores; (3) a fadigabilidade e a produção rápida de força e torque dos músculos dos membros superiores de crianças e adolescentes com EB requer investigação de fatores relacionados à fadiga central, como o impulso descendente nos motoneurônios por meio da estimulação magnética transcraniana (EMT) ou a atividade do córtex motor pela e ressonância magnética (Taylor et al., 2016); e periférica, como por exemplo a identificação do volume e proporção de fibras musculares por ultrassonografia.

A relevância clínica deste estudo está centrada na problemática dos relatos clínicos de fraqueza e cansaço muscular nos membros superiores de pacientes com EB frente à exposição de curtos esforços físicos, e ao comprometimento funcional (especialmente nas tarefas de transferências posturais e locomoção com uso de dispositivos auxiliares), as quais repercutem na qualidade de vida individual dos pacientes e de seus cuidadores. Portanto, os dados gerados por este estudo esclareceram aspectos sobre a função muscular de membros superiores de crianças com desenvolvimento típico e com EB, os quais poderão direcionar a investigação de força e resistência à fadiga, e a criação de protocolos de treinamento e intervenções terapêuticas para aquisição de habilidades neuromotoras com foco no desenvolvimento de força e hipertrofia muscular e também na potência muscular.

6 DIRECIONAMENTO PARA PESQUISAS FUTURAS

Apesar do conhecimento a respeito de fadiga muscular ter expandido nos últimos anos, ainda encontramos desafios com relação ao uso da melhor terminologia, como e quais variáveis mensurar e como analisar e interpretar os resultados. Adicionalmente, embora tenhamos desenvolvido protocolos para mensurar a fadigabilidade motora em crianças e adolescentes com desenvolvimento típico e aquelas com EB, o conhecimento científico sobre testes de fadiga aplicados nos músculos dos membros superiores na população pediátrica ainda é pequeno.

Deste modo, afim de se interpretar adequadamente os efeitos do exercício máximo nessa população, a análise cinemática e de respostas fisiológicas durante os testes com contrações voluntárias máximas poderia ser explorada, incluindo o uso de equipamentos os quais podem ser facilmente usados na prática clínica e não requerem sistemas de análise difíceis, como os dinamômetros portáteis. No futuro, seria muito interessante combinar os resultados dessas pesquisas e desenvolver critérios objetivos para testes de esforço máximo de membros superiores em crianças, especialmente para aquelas com deficiências motoras.

Apesar da dinamometria isocinética ser considerada a ferramenta padrão ouro para avaliar a função mecânica muscular e que fornece medições confiáveis, válidas e sensíveis da força muscular máxima (Van Meeteren et al., 2002), ela é uma metodologia cara que requer profissionais treinados para realizar as medições. Portanto, a dinamometria portátil (dinamômetro de bulbo) tem sido considerada uma ferramenta alternativa de avaliação de baixo custo para uso clínico. Novos estudos poderiam investigar a linearidade (associação) entre a avaliação da força e fadigabilidade muscular usando dinamometria isocinética versus dinamometria com bulbo em crianças e adolescentes com desenvolvimento típico e com doenças crônicas.

Pesquisas futuras também poderiam investigar possíveis melhoras na força e resistência à fadiga de músculos de membros superiores após programa de treinamento de força ou treinamento de habilidades em cadeiras de rodas. Além disso, elas poderiam estimar mudanças mínimas importantes detectadas pelos testes de fadiga motora apresentados no presente projeto para que mudanças clinicamente importantes possam ser identificadas na avaliação de crianças e adolescentes com ou sem doenças ou morbidades.

Pesquisas futuras do tipo longitudinal poderiam prover evidências sobre a associação entre a fadigabilidade muscular e fatores como idade, sexo, maturação sexual, composição corporal e níveis de mobilidade e de atividade física. Infelizmente, não conseguimos realizar tal análise devido ao tamanho amostral do grupo de participantes com EB ser relativamente pequeno, especialmente o subgrupo de pacientes com EB deambuladores.

7 CONSIDERAÇÕES FINAIS

O presente estudo investigou os membros superiores como segmentos-chave para a reabilitação de crianças e adolescentes com EB e também investigou a resposta dos típicos, como parametrização. Nosso foco foi identificar as diferenças de força, pressão e fadigabilidade motora, por meio de testes realizados com um instrumento padrão-ouro e outro de uso clínico, entre crianças e adolescentes com desenvolvimento típico de diferentes níveis maturacionais e sexos, e também entre crianças e adolescentes com uma morbidade crônica, a EB.

Crianças e adolescentes com EB apresentaram PT e pressão palmar reduzidos, e respostas de fadiga semelhantes (resistência à fadiga) durante o trabalho repetitivo dos músculos flexores e extensores do cotovelo e atividade de pressão palmar em comparação com seus pares com desenvolvimento típico. As descobertas deste estudo são novas e parecem altamente relevantes para a área da Fisioterapia aplicada à Neuropediatria, a qual tem sua ação focada em procedimentos de avaliação e intervenção terapêutica relacionadas ao desenvolvimento de habilidades neuromotoras.

Os protocolos de teste apresentados neste estudo podem ser utilizados por clínicos e pesquisadores para fins de avaliação antes e depois de intervenções terapêuticas, identificando mudanças na função muscular em crianças e adolescentes com desenvolvimento típico e naquelas com EB.

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