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Francisco Xavier de Araujo

Efeitos agudos da mobilização torácica na função autonômica e no limiar de dor à pressão de indivíduos assintomáticos: ensaio clínico randomizado.

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Orientador: Dr. Marcelo Faria Silva
Co-orientador: Dr. Rodrigo Della Méa Plentz

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RESUMO

INTRODUÇÃO: A mobilização interveterbral passiva acessória (MIVPA) é uma importante ferramenta utilizada por fisioterapeutas no manejo de diversas condições neuromusculoesqueléticas. Dentre os diversos mecanismos propostos para explicar os efeitos clínicos, tem crescido o interesse na investigação de efeitos neurofisiológicos e da influência do Sistema Nervoso Autônomo na modulação descendente da dor a partir da MIVPA. Em comparação com a região cervical e a região lombar, o número de estudos investigando os efeitos de MIVPA aplicada à coluna torácica é substancialmente menor. Estudos que observem o efeito de duas diferentes técnicas de MIVPA torácica, frequentemente utilizadas na pratica clínica, na variabilidade da frequência cardíaca (VFC) e no limiar de dor à pressão (LDP) concomitantemente não foram encontrados. O conhecimento do efeito destas abordagens nestes desfechos fornecerá relevantes informações sobre o papel neurofisiológico da MIVPA, assim como contribuirá para um processo de tomada de decisão clínica mais adequado. **OBJETIVO:** Descrever e comparar, o efeito de duas diferentes técnicas de MIVPA aplicadas à coluna torácica sobre a VFC e o LDP em indivíduos assintomáticos. **METODOLOGIA:** Um ensaio clínico randomizado, duplo cego, placebo-controlado, foi realizado. Oitenta e seis indivíduos assintomáticos foram recrutados, dos quais 60 foram incluídos e alocados randomicamente para receber uma única intervenção de MIVPA torácica póstero-anteriores com rotação em decúbito ventral (grupo PA), MIVPA torácica póstero-anterior em posição de SLUMP (grupo SLUMP), ou intervenção placebo (grupo Placebo). A VFC e o LDP em seis pontos anatômicos foram mensurados antes e imediatamente após a intervenção. ANOVA de medidas repetidas com dois fatores mistos foi realizada para verificar a interação entre tempo e grupo. ANOVA de um caminho com *post-hoc* de Bonferroni para os dados paramétricos, e Kruskal-Walis para os dados não paramétricos foram utilizados para comparação entre grupos. Teste-t pareado e teste de Wilcoxon foram realizados para analise intra-grupos, para os dados paramétricos e não paramétricos respectivamente. **RESULTADOS:** Não foram observadas diferenças estatisticamente significativas entre os grupos para qualquer parâmetro da VFC e do LDP. Na análise intra grupo se identificou um aumento estatisticamente significativo do LDP na mão ipsilateral à técnica após a intervenção do grupo SLUMP. **CONCLUSÃO:** As duas técnicas aplicadas, MIVPA torácica póstero-anterior em decúbito ventral ou em posição de *SLUMP*, não promoveram efeitos estatisticamente diferentes em relação a uma intervenção placebo, para esta amostra de participantes assintomáticos.

Palavras-chave: Mobilização vertebral; Sistema nervoso autônomo; Coluna torácica; Variabilidade da frequência cardíaca; Limiar de dor à pressão.

ABSTRACT

INTRODUCTION: Passive accessory interveterbral mobilization (PAIVM) is an important tool performed by physiotherapists in the management of several musculoskeletal conditions. Among the proposed mechanisms to explain the clinical effects, there is a growing interest in the investigation of neurophysiological effects and the influence of the autonomic nervous system in the descending pain modulation following PAIVM. In comparison with to cervical and lumbar spine, the number of studies investigating the effects of MIVPA applied to the thoracic spine is substantially lower. Studies that analyzed the effects of two different thoracic PAIVM techniques, frequently applied in clinical practice, in heart rate variability (HRV) and pressure pain threshold (PPT) concomitantly were not presented yet. The knowledge of the effects of these approaches in these outcomes provides relevant information about the PAIVM neurophysiological role, as well as contributes to a more appropriate clinical decision-making process. **OBJECTIVES:** Describe and compare the effect of two different PAIVM techniques applied to the thoracic spine in HRV and PPT in asymptomatic individuals. **METHODS:** A double-blind, placebo-controlled randomized clinical trial was conducted. Eighty six asymptomatic subjects were recruited, of which 60 were included and randomly assigned to receive a single postero-anterior thoracic PAIVM intervention in prone lying (PA group), in SLUMP position (SLUMP group), or placebo intervention (placebo group). HRV and PPT in six landmarks were measured before and immediately after the intervention. Repeated measures ANOVA with two mixed factors was performed to verify the interaction between time and group. Between groups comparison was realized with one-way ANOVA and Bonferroni *post-hoc* for parametric data, and Kruskal-Wallis test for non parametric data. Paired t-test and Wilcoxon test were performed for the intra-group analysis for parametric and non parametric data respectively. **RESULTS:** No statistically significant differences were observed between groups for any HRV parameters and PPT landmarks. Intra-group analyses revealed a significant increase in ipsilateral hand PPT after the intervention in SLUMP group. **CONCLUSION:** Both techniques applied, postero-anterior thoracic PAIVM in prone lying or in SLUMP position did not produce statistically different effects than a placebo intervention, for this sample of asymptomatic participants.

Key words: Spinal manipulative therapy; Autonomic nervous system; Thoracic spine; Heart rate variability; Pressure pain threshold.

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LISTA DE ABREVIATURAS E SIGLAS

ANS	Autonomic Nervous System
CH	Controlateral Hand
CNS	Central Nervous System
CT	Controlateral Tibialis
DP	Diastolic Pressure
HF	High Frequency
HR	Heart Rate
HRV	Heart Rate Variability
IH	Ipsilateral Hand
IT	Ipsilateral Tibialis
LDP	Limiar de Dor à Pressão
LF	Low Frequency
MIVPA	Mobilização Interveterbral Passiva Acessória
MV	Manipulação Vertebral
PA	Póstero-anterior
PAIVM	Passive Accessory Intervertebral Mobilization
PPT	Pressure Pain Threshold
RMSSD	Raiz quadrada dos quadrados das diferenças sucessivas entre intervalos RR normais (intervalos NN)
RRtrindex	RR Triangular Index
SMT	Spinal Manipulative Therapy
SNA	Sistema Nervoso Autônomo
SNC	Sistema Nervoso Central
SNP	Sistema Nervoso Parasimpático
SNS	Sistema Nervoso Simpático
SNDD	Desvio padrão de todos os intervalos RR normais
SP	Systolic Pressure
Std HR	Desvio padrão da frequência cardíaca
VCF	Variabilidade da Frequência Cardíaca
VLF	Very Low Frequency

SUMÁRIO

1 INTRODUÇÃO

A mobilização interveterbral passiva acessória (MIVPA) é uma importante ferramenta utilizada por fisioterapeutas no manejo de diversas condições musculoesqueléticas (MAITLAND et al., 2005). Evidências clínicas positivas do emprego desta técnica foram demonstradas em pacientes com dor cervical (STERLING et al., 2001; HOVING et al., 2002), dor craniocervical (LA TOUCHE et al., 2013), dor lombar (HANRAHAN et al., 2005; SHUM et al., 2013), epicondilalgia lateral (VICENZINO et al.,1996) e vertigem cervicogênica (REID et al., 2015). A utilização da MIVPA a partir da avaliação e classificação dos pacientes em subgrupos de tratamento específico parecem melhorar ainda mais o prognóstico (CHILDS et al., 2004; CLELAND et al., 2009).

Diversos mecanismos têm sido propostos para explicar tais efeitos clínicos. Dentre eles, se sugere que ocorra um efeito biomecânico direto (EVANS, 2002), baseado na teoria das comportas (MELZACK and WALL, 1965), e na ativação de vias ascendentes de modulação da dor, além do posicionamento articular mais adequado (SHUM et al., 2013). Entretanto, efeitos difusos, à distância do segmento mobilizado, e que perduram inclusive após a intervenção terapêutica não poderiam ocorrer exclusivamente pelas respostas biomecânicas. Neste sentido, tem crescido o interesse na investigação de efeitos neurofisiológicos e da influência do sistema nervoso autônomo (SNA) na modulação descendente da dor a partir da MIVPA (WRIGHT, 1995; SLUKA et al., 2001; SKYABA et al., 2004; ZUSMAN, 2004; BIALOSKY et al., 2009).

Duas revisões sistemáticas (SCHMID et al., 2008; KINGSTON et al., 2014) apontaram um efeito significativo em diferentes desfechos do SNA após MIVPA e independente do segmento mobilizado. Estes achados sugerem que estas técnicas são capazes de ativar áreas no sistema nervoso central (SNC), ativando um sistema amplo e complexo de controle descendente da dor e modulação da função autonômica. Este conceito, que ainda precisa ser mais explorado, promove um importante avanço em relação à teoria dos efeitos biomecânicos.

Em comparação com a região cervical (VICENZINO et al., 1996; STERLING et al., 2001; STERLING et al., 2010; LA TOUCHE et al, 2013;

SNODGRASS et al., 2014; REID et al., 2015) e a região lombar (GOODSELL et al., 2000; CHIRADEJNANT et al., 2003; KROUWEL et al., 2010; WILLET et al., 2010; PENTELKA et al., 2012; SHUM et al., 2013), o número de estudos investigando os efeitos de MIVPA aplicada à coluna torácica é substancialmente menor (EDMONDSTON e SINGER, 1997). Embora a prevalência de disfunções relacionadas à coluna torácica em relação às demais regiões da coluna seja menor (LINTON et al., 1998; LEBOEUF-YDE et al., 2009), em virtude da localização anatômica do gânglio simpático (de T1 a T9, responsável pelo suprimento autonômico da cabeça, tronco e membros superiores) (BOGDUK, 2002), a compreensão dos efeitos da MIVPA torácica e da capacidade destas técnicas em influenciarem o SNA é clinicamente relevante. Dois estudos (SLATER et al.,1994; JOWSEY & PERRY, 2010) observaram um aumento significativo na condutância da pele, dos membros superiores de indivíduos assintomáticos após MIVPA da coluna torácica, mas não correlacionaram estes achados com o limiar de dor à pressão (LDP) ou outras medidas relacionadas à percepção de dor, que concomitantemente com a avaliação do SNA pode fornecer informações mais conclusivas. REIS et al., (2014) observaram alterações em alguns parâmetros da variabilidade da frequência cardíaca (VFC) em mulheres fibromiálgicas submetidas à MIVPA póstero anterior (PA) torácica, mas não encontraram diferença estatisticamente significante na escala numérica de dor.

Apesar destes três estudos citados anteriormente (SLATER et al.,1994; JOWSEY & PERRY 2010; REIS et al., 2014) fornecerem importantes contribuições para esta lacuna científica, reforçando o papel da MIVPA na modulação autonômica, algumas questões ainda não foram completamente estabelecidas. Apenas o estudo de REIS et al. (2014) correlacionou uma medida do SNA com outro desfecho relacionado à dor, embora a compreensão desta correlação seja de fundamental relevância. Estudos que observem o efeito de duas diferentes técnicas de MIVPA torácica, frequentemente utilizadas na prática clínica, na VFC e no LDP concomitantemente não foram encontrados. Além disso, o entendimento dos mecanismos neurofisiológicos da MIVPA poderia ajudar na identificação de indivíduos que possam responder melhor à esta abordagem fornecendo maiores indicações quanto aos fatores

preditivos pertinentes para futuras regras de predição clínica (BIALOSKY et al., 2009).

2 REVISÃO DE LITERATURA – CONTEXTUALIZAÇÃO

2.1 MOBILIZAÇÃO INTERVERTEBRAL PASSIVA ACESSÓRIA

A terapia manipulativa vertebral engloba uma série de técnicas, como a manipulação vertebral (MV) e a mobilização intervertebral passiva acessória (MIVPA) (MAITLAND et al. 2005). O que difere entre estas abordagens é sobretudo a velocidade da força aplicada sobre o segmento selecionado. Enquanto a MV envolve um impulso de alta velocidade e pequena amplitude, a MIVPA se caracteriza por ser uma técnica de baixa velocidade e oscilações de pequena ou grande amplitude (MAITLAND et al. 2005). A escolha entre uma técnica ou outra é baseada na apresentação clínica do paciente, na experiência e preferência do fisioterapeuta e de acordo com a melhor evidencia disponível (CHIRADEJNANT et al, 2003).

Resultados conflitantes foram apresentados a respeito da melhor abordagem. IZQUIERDO-PEREZ et al. (2014), não encontraram diferença estatisticamente significativa entre MIVPA, MV e mobilização com movimento ativo na escala análoga de dor, no escore de incapacidade e na satisfação percebida em pacientes com dor cervical crônica. De forma semelhante, uma revisão sistemática incluindo 27 estudos demonstrou com moderada qualidade de evidencia que MIVPA e MV produziram resultados similares na dor, função e satisfação de pacientes com dor cervical com ou sem cefaléia ou achados radiculares (GROSS et al., 2010). Outros estudos apontam, todavia, que a MV torácica associada ou não com MV cervical é mais efetiva do que a MIVPA na redução de dor e incapacidade de pacientes com dor cervical (CLELAND et al., 2007; DUNNING et al., 2012). Porém, em virtude de alguns riscos decorrentes da MV (THOMAS et al., 2011) e dos resultados controversos quanto aos efeitos superiores desta intervenção em relação à MIVPA, esta última abordagem parece ser uma intervenção eficaz e segura.

Assim como a decisão entre uma abordagem ou outra é baseada na apresentação clínica, a escolha da dose de tratamento da MIVPA também se faz a partir das queixas do paciente e do raciocínio clínico (MAITLAND et al., 2005). Esta dose é definida por propriedades mecânicas como: força, direção de movimento, amplitude de movimento, frequência de oscilação e tempo de aplicação (MAITLAND et al., 2005; SNODGRASS et al., 2006). Embora exista

um interesse crescente a respeito do efeito de diferentes parâmetros mecânicos utilizados (MC LEAN et al., 2002; SNODGRASS et al., 2006; WILLETT et al., 2010; KROUWELL et al., 2010; PENTELKA et al., 2012; GORGOS et al., 2013; SNODGRASS et al., 2014), a dose ideal de tratamento ainda não está estabelecida (GROSS et al., 2010; SNODGRASS et al., 2014). Evidências preliminares demonstram que picos de força mais altos parecem produzir melhores efeitos clínicos em pacientes com dor cervical (SNODGRASS et al., 2014) e dor no epicôndilo lateral (MC LEAN et al. 2002) mas não parece produzir efeitos hipoalgésicos diferentes que picos de força menores ou placebo em técnicas de PIVMA lombar em indivíduos assintomáticos (KROUWEL et al., 2010). Da mesma forma, em indivíduos assintomáticos, maiores frequências de oscilação produzem efeitos significativamente maiores quando aplicados à coluna cervical (CHIU and WRIGHT, 1996), mas não parece diferir em relação à menor frequência ou placebo em técnicas aplicadas à coluna lombar (WILLET et al.,2010). Além disso, o número de séries de mobilização lombar, mas não o tempo de aplicação, parece ser determinante para a produção de efeitos hipoalgésicos em sujeitos assintomáticos (PENTELKA et al., 2012). O nível mobilizado também parece ser importante para os efeitos clínicos positivos. CHIRADEJNANT et al. (2002), demonstraram que a aplicação de MIVPA lombar no segmento identificado pelo fisioterapeuta como responsável pelos sintomas de pacientes com dor lombar produziu resultados significativamente superiores do que a mesma técnica aplicada a um segmento aleatório. O que reforça a necessidade de uma avaliação e raciocínio clínico adequados para que o processo de tomada de decisão clínica seja feito satisfatoriamente.

Independentemente dos parâmetros mecânicos utilizados e do segmento mobilizado, uma grande quantidade de evidências demonstra efeitos positivos da aplicação de MIVPA em diferentes condições clínicas. Uma recente revisão sistemática (VOOGT et al., 2014) demonstrou, com moderada qualidade de evidência, que a terapia manipulativa vertebral (incluindo MIVPA, MV e mobilização com movimento ativo) promoveu aumento do LDP imediatamente após a intervenção.

2.1.1. Mobilização Intervertebral Passiva Acessória Aplicada à Coluna Torácica

A MIVPA da coluna torácica é uma importante ferramenta de avaliação e intervenção (MAITLAND et al., 2005), apesar da negligência em relação à importância da coluna torácica em comparação com as regiões cervical e lombar (EDMONDSTON e SINGER, 1997). O reconhecimento da coluna torácica como fonte de dor local e referida, a influência da mobilidade torácica nos padrões de movimento das outras zonas da coluna - especificamente nas transições cérvico-torácica e tóraco-lombar - além da cintura escapular, e, ainda, a proximidade anatômica e possível influência das articulações costovertebrais e costotransversais com o trato simpático são alguns fatores clinicamente relevantes que reforçam o papel da adequada avaliação destes segmentos (EDMONDSTON e SINGER, 1997, MAITLAND et al., 2005).

Da mesma forma, o conceito de interdependência regional suporta o envolvimento da coluna torácica em condições clínicas do quadrante superior (WAINNER et. al, 2007; SUEKI et al., 2011), assim como a intervenção aplicada a estes segmentos para o manejo de problemas em locais adjacentes como dor cervical (CLELAND et al., 2005; LAU et al., 2011; MÉNDEZ et al., 2014) e síndrome do impacto do ombro (MUTH et al., 2012; HAIK et al., 2014). Inclusive, regras de predição clínica foram desenvolvidas para identificar pacientes com dor cervical (CLELAND et al., 2007), síndrome do impacto do ombro e tendinose do manguito rotador (MINTKEN et al., 2010), que se beneficiariam de terapia manipulativa vertebral aplicada à coluna torácica.

Dentre as diferentes abordagens de MIVPA torácica, algumas técnicas já foram estudadas em ensaios com diversos desenhos metodológicos, e parecem promover efeitos positivos em indivíduos assintomáticos (SLATER et al., 1994; CLELAND et al., 2002; JOWSEY e PERRY, 2010; MC GREGOR et al., 2014), em um paciente com síndrome de dor regional complexa tipo I (CLELAND e MC RAE, 2002), e em uma amostra de mulheres fibromiálgicas (REIS et al., 2014). Uma das possíveis intervenções, a MIVPA póstero-anterior em rotação, é aplicada com o paciente em decúbito ventral, com os membros superiores estendidos ao longo do corpo, enquanto o fisioterapeuta apoia a mão direita entre a coluna e a escápula direita do paciente, e a mão esquerda entre a coluna e a escápula esquerda do paciente. O contato é feito através

das eminências hipotenares próximo ao osso pisiforme, e a mobilização oscilatória é feita em três direções: póstero-anterior, céfalo-caudal e látero-lateral. A mobilização oscilatória desta forma tem o objetivo de promover deslizamentos localizados nas articulações intervertebrais, costotransversais e costovertebrais (MAITLAND et al., 2005). JOWSEY e PERRY (2010) observaram aumento significativo da atividade simpática nas mãos, através da mensuração da condutância da pele, após esta intervenção ser aplicada no segmento T4 em indivíduos assintomáticos, comparando à uma mobilização placebo.

Outra técnica de MIVPA torácica, a mobilização póstero-anterior unilateral em posição de SLUMP simpático (SLATER et al., 1994), é uma intervenção desenvolvida a partir do teste de SLUMP original (MAITLAND, 1985), com o objetivo de mobilizar seletivamente o tronco simpático torácico (CLELAND e MC RAE, 2002). Nesta intervenção o paciente é posicionado sentado, com os membros inferiores estendidos, membros superiores estendidos atrás da coluna. O paciente é conduzido para uma flexão de toda a coluna, flexão lateral e rotação da coluna torácica e flexão lateral da coluna cervical para o mesmo lado. Nesta posição, o fisioterapeuta aplica a mobilização unilateral do lado oposto à flexão e rotação torácica, com a eminência hipotenar sobre as articulações costovertebrais (SLATER et al., 1994).

SLATER et al., (1994), demonstraram aumento significativo do fluxo simpático para membros superiores de indivíduos assintomáticos, a partir da mensuração da condutância da pele, após a aplicação desta técnica. CLELAND e MC RAE (2002), em um estudo de caso de um paciente com síndrome de dor complexa regional tipo I, apresentaram benefícios clínicos após MIVPA torácica em posição de SLUMP. Os autores sugerem que esta abordagem, a partir da mobilização diretamente sobre o tronco simpático, pode ser uma alternativa para o manejo desta condição clínica que envolve o desequilíbrio autonômico.

2.2 SISTEMA NERVOSO AUTÔNOMO

O SNA compreende uma rede neural que funciona de forma inconsciente e controla automaticamente um número de ações fisiológicas através de consecutivos *feedbacks* positivos e negativos para manter a homeostase (COHEN et al., 2000). Esta rede regula a função de diferentes órgãos e glândulas, incluindo o coração, por meio de estimulações antagônicas do sistema nervoso simpático (SNS) e do sistema nervoso parassimpático (SNP) (DINAS et al., 2013).

Dentre outras funções, o SNA é responsável pelo controle do sistema cardiovascular, a partir de terminações simpáticas para o miocárdio, e parassimpáticas para o nó sinusal, miocárdio atrial e nódulo atrioventricular (VANDERLEI et al., 2009). A influência do SNA sobre o coração é dependente de informações de barorreceptores, quimiorreceptores, receptores atriais, receptores ventriculares, alterações no sistema respiratório, sistema vasomotor, sistema renina-angiotensina e do sistema termorregulador (VANDERLEI et al., 2009). O SNS age para aumentar a frequência cardíaca e desempenha um papel essencial na regulação cardiovascular na saúde e na doença. Por outro lado, o SNP atua de modo a diminuir a frequência cardíaca. Com base neste mecanismo, o ritmo da frequência cardíaca e a força de contração do músculo cardíaco são uma consequência das influências opostas exercidas pelo SNS e SNP (DINAS et al., 2013).

Além desta função reguladora do sistema cardiovascular, o desequilíbrio do SNA parece ter uma relação muito próxima com condições clínicas que envolvem dor crônica, como fibromialgia (COHEN et al., 2000; MARTINEZ-LAVIN et al., 2000; CASTRO-SANCHES et al., 2010; REIS et al., 2014), síndrome de dor regional complexa (CLELAND e MC RAE, 2002) e capsulite adesiva (WIFFEN, 2002).

Da mesma forma, a disfunção do SNA parece ter um papel no desenvolvimento de sensibilização central (NIJS et al., 2010; WOOLF, 2011). Definida como um aumento da capacidade de resposta dos neurônios centrais para a entrada de receptores unimodais e polimodais, a sensibilização central é frequentemente observada em diversas desordens de dor musculoesquelética crônica como artrite reumatóide, dor lombar crônica, dor temporomandibular,

síndrome de dor miofascial, desordens associadas ao *wiplash,* entre outras *(*NIJS et al., 2010*).* Nestes casos, os mecanismos descendentes inibitórios de dor parecem estar reduzidos, em contrapartida, os mecanismos facilitatórios descendentes e ascendentes elevados, o que resulta no aumento da transmissão nociceptiva (NIJS et al., 2011). Este quadro, somado à questões biopsicossociais torna o manejo destes pacientes muito mais complexo.

Assim como o desequilíbrio autonômico parece fazer parte de processos de cronificação da dor, o benefício clínico observado após intervenção com técnicas de terapia manipulativa vertebral, tem sido explicado em parte pela ativação do SNA e de vias de modulação da dor descendente (BIALOSKY et al., 2009). Uma grande quantidade de estudos sugere que efeitos neurofisiológicos, com o envolvimento do SNA, desempenham um importante papel na modulação da dor (CHIU e WRIGHT, 1996; STERLING et al., 2001; PICKAR, 2002; PAUNGMALI et al., 2003; ZUSMAN, 2004; JOWSEY e PERRY, 2010; LA TOUCHE et al., 2013). De acordo com estes estudos, a terapia manipulativa vertebral seria capaz de ativar áreas do SNC produzindo uma resposta múltipla, semelhantes aos achados encontrados através da estimulação da substância cinzenta periaquedutal dorsal em estudos experimentais com animais (LOVICK, 1991). Uma recente revisão sistemática apontou efeitos de excitação do SNS após MIVPA em todos os estudos incluídos, em diferentes desfechos analisados, independente do segmento mobilizado (KINGSTON et al., 2014). Portanto, a terapia manipulativa vertebral poderia promover um estímulo adequado para os sistemas descendentes inibitórios de dor. Este conceito vai muito além do modelo biomecânico simplista que defende a necessidade de estimulação específica de uma determinada articulação (SCHMID et al., 2008).

2.2.1 Variabilidade da Frequência Cardíaca

A avaliação do equilíbrio autonômico é fundamental para a compreensão das repercussões que a disfunção do SNA pode causar no quadro clínico de pacientes, assim como a mensuração da função autonômica antes e após alguma intervenção pode fornecer importantes esclarecimentos acerca do efeito destas abordagens. Visto que uma peculiaridade do SNA é sua

variabilidade instantânea e contínua, qualquer forma de medição estática sanguínea ou de catabólitos urinários não reflete adequadamente o comportamento dinâmico do sistema (MARTINEZ-LAVIN et al., 2000). Dentre as diferentes formas de mensuração indireta dinâmica da atividade do SNA a condutância da pele, temperatura da pele, pressão arterial, frequência cardíaca e frequência respiratória são frequentemente utilizadas (VICENZINO et al., 1998a; VICENZINO et al., 1998b; STERLING et al., 2001; JOWSEY e PERRY, 2010; LA TOUCHE et al., 2013)

Uma outra medida para avaliar o desempenho do SNA, é a análise da VFC. Esta técnica baseia-se no fato de que a frequência cardíaca não é fixa, mas varia constantemente e de forma aleatória (MARTINEZ-LAVIN et al., 2000). Mudanças na frequência cardíaca são normais e esperadas, de modo que indicam a capacidade do coração de responder a vários estímulos fisiológicos e ambientais, dentre eles, respiração, exercício físico, estresse mental, alterações hemodinâmicas e metabólicas, sono e ortostatismo (VANDERELI et al., 2009). Inclusive durante o repouso a frequência cardíaca varia ciclicamente (KLEIGER et al., 2005).

A VFC descreve as oscilações dos intervalos entre batimentos cardíacos consecutivos (intervalos RR), que estão relacionados com as influências do SNA sobre o nódulo sinusal, sendo uma medida não invasiva que pode ser usada para identificar fenômenos relacionados com o SNA em indivíduos saudáveis, atletas ou pacientes (VANDERELI et al., 2009). A mensuração da VFC pode ser feita através de eletrocardiograma tradicional. Entretanto, outra forma de medida é a partir de um cardiofrequencímetro portátil, um dispositivo simples, sensível, confiável e mais custo-efetivo (KINGSLEY et al., 2005; GAMELIN et al., 2006; PORTO et al., 2008).

Para a análise da VFC, os índices obtidos por métodos lineares, pelo domínio do tempo e da frequência, além de métodos não-lineares podem ser usados (TASK FORCE, 1996). Na análise pelo domínio do tempo, os intervalos entre as ondas R normais adjacentes (intervalos NN) são medidos durante o período de gravação. Uma diversidade de variáveis estatísticas podem ser calculadas a partir dos intervalos diretamente e outras podem ser derivadas a partir das diferenças entre os intervalos (KLEIGER et al., 2005).

As variáveis simples de domínio de tempo que podem ser calculados incluem o intervalo médio RR (*mean* RR), a frequência cardíaca média (*mean* HR), além do desvio padrão da frequência cardíaca (Std HR). Outros parâmetros obtidos pela análise do domínio do tempo comumente utilizados são: SDNN, o desvio padrão de todos os intervalos RR normais (NN) durante um período; RMSSD, é a raiz quadrada dos quadrados das diferenças sucessivas entre intervalos NN, essencialmente, a variação média de intervalo entre os batimentos. Outra possibilidade para processar intervalos RR no domínio do tempo é a partir de métodos geométricos, sendo o índice triangular (Poincaré plot) a mais conhecida (VANDERLEI et al., 2009). O índice triangular RR é o integral da distribuição de densidade (isto é, o número de intervalos NN) dividido pelo valor máximo da distribuição de densidade (TASK FORCE, 1996).

Na análise da VFC pelo domínio da frequência três, principais componentes espectrais são distinguidos em um espectro calculado a partir de gravações de curto prazo (2 a 5 minutos): a) componente de alta frequência (HF) variando 0,15-0,4Hz, o que corresponde à modulação respiratória e é um indicador do desempenho do nervo vago para o coração; b) componente de baixa frequência (LF), variando entre 0,04 e 0,15Hz, que é devido à ação conjunta dos componentes vagal e simpático sobre o coração, com predominância do simpático; c) componentes de muito baixa frequência (VLF) < 0-04Hz, índices menos utilizados cuja explicação fisiológica não está bem estabelecida e parece estar relacionado com o sistema renina-angiotensina-aldosterona, termorregulação e ao tônus vasomotor periférico (TASK FORCE, 1996; VANDELREI et al., 2009). Além disso, é possível calcular a relação LF/HF, que reflete as variações absolutas e relativas entre os componentes simpático e parassimpático do SNA, caracterizando o balanço simpato-vagal no coração (TASK FORCE, 1996; VANDERLEI et al., 2009).

A análise do Poincaré plot pode ser realizada de um modo qualitativo (visual), por avaliação da figura formada pela dispersão de seus pontos, que é útil para mostrar o grau de complexidade dos intervalos RR, ou quantitativa, por ajuste da elipse da figura formada, a partir do qual três índices podem ser obtidos: SD1, SD2 e relação SD1 / SD2. SD1 representa a dispersão dos pontos perpendiculares para a linha de identidade e parece ser um índice de

registro instantâneo da variabilidade batimento a batimento; o SD2 representa a dispersão dos pontos ao longo da linha de identidade e representa a VFC em registros de longo prazo (VANDERLEI et al., 2009)

Informações limitadas sobre o efeito de diferentes técnicas de terapia manipulativa vertebral sobre a VFC estão disponíveis, e não foi estabelecido um consenso sobre a capacidade destas técnicas em influenciar este desfecho. Índices de VFC pelo domínio do tempo e pelo domínio da frequência não foram alterados após a aplicação de técnicas de liberação miofascial em pacientes com cefaléia tensional crônica (TORO-VELASCO et al., 2009). A aplicação de MIVPA torácica em pacientes com fibromialgia aumentou significativamente o RMSSD (a raiz quadrada dos quadrados das diferenças sucessivas entre intervalos NN) porém não provocou diferenças significativas nos índices pelo domínio da frequência (REIS et al., 2014). BUDGELL e POLUS (2006), apontaram um aumento significativo da LF e razão LF/HF após MV da coluna torácica de indivíduos assintomáticos. Os diferentes resultados observados, as distintas amostras, os métodos de pesquisa divergentes (tempo de coleta e tempo de repouso), além das diversas intervenções aplicadas (manipulação vertebral, mobilização vertebral e liberação miofascial), impedem conclusões definitivas sobre o efeito de terapia manipulativa vertebral sobre a VFC, assim como a relação da VFC com o LDP.

2.3. LIMIAR DE DOR À PRESSÃO

A medição da dor é um componente importante da prática clínica, podendo ser útil como desfecho a ser avaliado ao longo do tempo ou como uma medida prognóstica que possa prever resultados futuros (WALTON et al., 2011). Além disso, a mensuração da dor é o desfecho primário na maioria dos estudos de intervenção músculo-esquelética (YLINEN et al., 2007). A abordagem mais comum para a mensuração da dor é através de auto-relato, a partir de escala análoga visual ou escalas numéricas de avaliação da dor. Embora a intensidade da dor auto-relatada seja importante, características psicológicas e sociais, bem como a expectativa do paciente, podem dificultar a interpretação das respostas (WALTON et al., 2011).

Neste sentido, uma medida cegada ao paciente que tem recebido atenção crescente devido ao custo, segurança e facilidade de utilização é a avaliação do LDP (WALTON et al., 2014). O LDP é definido como o menor estímulo em que o indivíduo percebe como doloroso. Este parâmetro é mensurado através do algômetro, um instrumento confiável e reprodutível para quantificar dor e sensibilidade (KEATING et al., 2001; CHESTERTON et al., 2007; YLINEN et al., 2007; WALTON et al., 2011). O algômetro registra a força (em quilogramas por centímetro quadrado) que é aplicada aos tecidos através de um pequeno cabeçote de borracha. A força registrada é a quantidade de pressão que causa desconforto ou dor (NUSSBAUM & DOWNES, 1998). Apesar de ser um instrumento operador-dependente, existem protocolos padronizados que podem evitar a influência da capacidade do operador (WALTON et al., 2014). Pesquisas anteriores indicam que mesmo avaliadores novatos podem realizar de forma confiável medições de LDP (WALTON et al., 2011).

A comparação de valores de LDP pode ser utilizada como ferramenta diagnóstica, assim como medida de desfecho de intervenções terapêuticas (VICENZINO et al., 1996, KEATING et al., 2001, VOOGT et al., 2014). Da mesma forma, a mensuração do LDP pode fornecer informações sobre o prognóstico, especialmente no caso de hiperalgesia generalizada (STERLING et al., 2005).

Como descrito anteriormente, embora evidências demonstrem o efeito hipoalgésico das técnicas de terapia manipulativa vertebral, não existe um consenso para explicar os mecanismos destes efeitos observados. Revisões sistemáticas sugerem que estas técnicas são capazes de ativar o SNA (SCHMID et al., 2008; KINGSTON et al., 2014) e ensaios clínicos observaram efeitos simultâneos de hipoalgesia e excitação simpática após MIVPA cervical (STERLING et al., 2001; LA TOUCHE et al., 2013). Contudo, o volume de informações sobre estes efeitos após MIVPA torácica é bastante limitado. Além do mais, até o nosso conhecimento, nenhum estudo prévio mensurou concomitantemente o LDP e a VFC antes e após MIVPA torácica. O conhecimento do efeito desta abordagem nestes desfechos fornecerá

relevantes informações sobre o papel neurofisiológico da MIVPA, assim como contribuirá para um processo de tomada de decisão clinica mais adequado.

Desta forma, o presente estudo tem como objetivo principal descrever e comparar, a partir de um ensaio clinico randomizado, o efeito de três diferentes técnicas de MIVPA aplicadas à coluna torácica (PA, SLUMP e Placebo) sobre a VFC e LDP em indivíduos assintomáticos. E, secundariamente, verificar se o efeito observado no LDP ocorre localmente (apenas no segmento mobilizado) ou de maneira sistêmica (em pontos remotos ao segmento mobilizado).

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4 ARTIGO

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Autonomic Function and Pressure Pain Threshold Following Thoracic Mobilization in Asymptomatic Subjects: a Randomized Controlled Trial

Francisco Xavier de Araujo, PT[1,2]
Rodrigo Della Mea Plentz, PT, DSc[1,2]
Marcelo Faria Silva, PT, DSc[1,2]

1 Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA), Porto Alegre, RS, Brasil.
2 Programa de Pós Graduação em Ciências da Reabilitação

Clinical Trials Registration Number: NCT02164123.

Address correspondence to Marcelo Faria Silva, Rua Sarmento Leite, 245, Porto Alegre – RS – Brasil, CEP:90050-170, UFCSPA/Physical Therapy Department.
E-mail:franciscoxaraujo@gmail.com

Autonomic Function and Pressure Pain Threshold Following Thoracic Mobilization in Asymptomatic Subjects: a Randomized Controlled Trial

The authors certify that they have no affiliations with or financial involvement in any organization or entity with a direct financial interest in the subject matter or materials discussed in the article.

ABSTRACT

Study Design: Randomized clinical trial.

Objective: To compare the effect of two different passive accessory intervertebral mobilization (PAIVM) techniques applied to the thoracic spine on heart rate variability (HRV) and pressure pain threshold (PPT) in asymptomatic individuals.

Background: Among the proposed mechanisms to explain the clinical effects following PAIVM, there is a growing interest in the investigation of neurophysiological effects and the influence of the autonomic nervous system in the descending pain modulation. There is no established consensus regarding the autonomic nervous system and PPT responses following thoracic PAIVM.

Methods: Sixty healthy asymptomatic subjects, aged between 18 and 40 years old were randomized to receive one single session of posterior-to-anterior (PA) rotatory thoracic PAIVM (PA group), unilateral thoracic PA in SLUMP position (SLUMP group) or placebo intervention (Placebo group). HRV and PPT at six landmarks were measured before and immediately after the intervention. Between groups comparison in each time-point was performed with one-way ANOVA with Bonferroni *post-hoc* or Kruskal-Walis test. Paired *t*-test or Wilcoxon test were applied to verify within-group differences.

Results: There were no statistically significant differences between groups for HRV and PPT measures. Within-groups comparison demonstrated higher PPT on ipsilateral hand after thoracic PAIVM in SLUMP position.

Conclusion: A passive accessory intervertebral thoracic mobilization in prone lying and in SLUMP position did not produce different effects than a placebo

technique in pressure pain threshold and heart rate variability in asymptomatic subjects after a single intervention.

Level of evidence: Therapy, level 1b-. *J Orthop Sports Phys Ther*

Key words: spinal manipulation, spinal mobilization, autonomic nervous system, sympathetic nervous system.

INTRODUCTION

In the last decades, much has been discussed in respect of the capacity of spinal manipulative therapy (SMT) in influencing autonomic nervous system (ANS) function[1,54]. SMT encompasses a broad range of techniques, including high velocity low amplitude manipulation and passive accessory intervertebral mobilizations (PAIVM)[25]. After a classical biomechanical paradigm[12], a large amount of evidence has shifted the role of SMT reporting the neurophysiological aspects of such techniques[1,33 38,39,41,54,56].

The ANS seems to be closely related to pain modulation,[1,54] as well as, the ANS dysfunction could, at least in part, play a role in the development of central sensitization[29,53] and other chronic pain conditions[3,7,51]. Experimental animal studies suggest that the stimulation of the dorsal periaqueductal gray matter produces concurrently hypoalgesia and sympathoexcitation[24,39]. Indeed, several authors have shown SMT as a way of to activate descending pain inhibitory systems[1,16,22,28,38,43,45,46,47,54]. However, despite the large amount of evidence, its quality seems to be low or very low.

The effects of thoracic PAIVM on SNS in asymptomatic participants were investigated by Slater et al.[40] and Jowsey and Perry[16]. Both studies demonstrated a side-specific significant increase on upper limbs skin conductance. However, none of the studies measured pressure pain threshold (PPT) or other pain related-measures simultaneously with ANS assessment. More recently, thoracic PAIVM applied in a sample of women with fibromyalgia demonstrated no effects on numeric pain scale, but noticed significant improvement in ANS activity measured by heart rate variability (HRV)[37]. Nonetheless, healthy women composed the control group of such study and the

numeric pain scale was measured uniquely on the patients group, which precludes an adequate comparison.

These aforementioned studies[16,37,40] reinforces the current concept that PAIVM influences ANS activity. Notwithstanding, to our knowledge no study has evaluated the effects of thoracic PAIVM on HRV and PPT concomitantly. Moreover, the comparison of two frequently performed PAIVM techniques might provide relevant insights on the neurophysiologic effects of such techniques. Hence, the present study aims to compare the effect of two different PAIVM techniques applied to the thoracic spine on HRV and PPT in asymptomatic individuals.

METHODS

Study Design

A double-blind placebo-controlled randomized clinical trial was conducted in accordance with the CONSORT statement[23] and was prospectively registered in ClinicalTrials.gov (registration number: NCT02164123).

Participants

Healthy asymptomatic subjects, aged between 18 and 40 years old were invited to participate in this study. Participants were recruited through online advertisements. Potential participants answered an online questionnaire to determine eligibility. They should be asymptomatic, SMT naive, sedentary, and body mass index ranging from 18.5 and 30 kg/m^2 to be included. Exclusion criteria were spinal pain, history of trauma or surgery to the spine, upper and lower limbs. Alcoholics, smokers, patients suffering from arterial hypertension,

diabetes, hyper or hypothyroidism or other clinical condition that might affect autonomic function including systemic and autoimmune disorders were also excluded. This trial was approved by Universidade Federal de Ciências da Saúde de Porto Alegre Ethics Committee in accordance with *Helsinki* convention, and all participants gave written informed consent prior to commencing the study.

Research Procedures

Data collection was conducted in a silent, temperature-controlled environment (22±2°), with relative humidity of 50 to 60%. All sessions took place between 5 p.m. and 8 p.m, to avoid circadian rhythm-induced variations[20]. Participants were assigned to one of the three experimental groups: (i) posterior-to-anterior (PA) rotatory PAIVM (PA group); (ii) unilateral PA in SLUMP position (SLUMP group); and (iii) placebo intervention (Placebo group) by a blinded research assistant through a computerized-based schedule. Allocation concealment was ensured by the use of opaque and sealed envelopes. The outcome evaluator was blinded to group assignment, and both the participant and therapist were blinded to the outcome assessment. The research design flow diagram and participants is illustrated in Figure 1.

Insert Figure 1 around here

Participants received recommendations about dietary intake, such as to avoid consume caffeine in the day of procedure and to have a light meal at least two hours prior the test. They were also advised to not exercise heavily during the 24h before data collection. Individuals either presenting with any

inflammatory condition or taking anti-inflammatory drugs on the day of the evaluation were excluded.

The experimental procedures were conducted by a physiotherapist post-graduated in neuromusculoskeletal manual therapy with seven years of clinical experience. The experimental conditions (i.e. PA, SLUMP and Placebo) consisted of three sets of one minute of mobilization and one minute rest between sets, as described previously[16,21,31,42,43,52].

In the PA group, subjects were comfortably positioned in prone lying, with both arms extended alongside the body. Then, a grade III rotatory PA PAIVM, with both therapist's hands adjacent to either side of the T4 vertebral segment was applied[16,25] (Figure 2a). In the SLUMP group, participants were conducted into slump long sitting position, with both arms relaxed behind the spine, lateral trunk flexion, trunk rotation and cervical lateral flexion to the same side. Then, a grade III unilateral PA PAIVM on T4 costovertebral joint of the opposite side of the trunk inclination was performed[7,40] (Figure 2b). This technique, also denominated as slump long sitting with sympathetic emphasis, was described by Slater et al. (1994)[40] adapting the original Slump Test[26], and has the objective to selective mobilize the sympathetic trunk[8]. In both intervention groups, PAIVM was performed at a frequency of 2Hz, which has been demonstrated to be effective to increase sympathetic outflow to the upper limbs[6]. A digital metronome was used to provide auditory feedback to the treating therapist to ensure adequate rate delivery. The metronome was connected to an earphone in order to avoid any influences of the sound on patients' perception. Placebo group was designed to mimic PA group intervention: participants adopted the same position, and the therapist applied

the same manual contact, however no oscillation was performed. In order to assess the side-specific effects, the side of technique application was randomized by the same researcher assistant who randomized the group assignment.

Insert Figure 2 around here

Outcomes Measurements

HRV was measured through the Polar heart rate monitor (Polar® RS800CX, Finland), an accurate, reliable and feasible device[14,18,34]. It captures variations in beat-to-beat RR intervals, at a sampling frequency of 1000Hz, by means of electrodes attached to a receptor belt fastened to the lower third of the sternum, providing real-time transmission to a wrist receiver unit where data were stored. These recordings were collected with the individuals comfortably positioned in supine lying, during 15 minutes before and after intervention. Subjects were instructed to breathe spontaneously, and have their respiratory frequency monitored to ensure eupneic condition.

Data were transferred to a computer, and processed with the Polar Pro Trainer 5 Software. Data analysis was performed according to the Task Force of European Society of Pacing and Eletrophysiology[15], using the Kubios HRV Analysis Software (MATLAB, version 2 beta, Kuopio, Finland). Only series with more than 256 RR intervals were included. The first five minutes of recording were ignored. Among the last 10 minutes of measurement, the five minutes sample with the most homogeneous signal was selected through visual inspection by a researcher blinded to group assignment.

HRV was analyzed thorough linear methods, in time and frequency domains, and by non-linear models (Poincare *plot*)[20,36]. In the time domain, the mean RR interval (mean RR), standard deviation of RR intervals (SDNN), mean heart rate (mean HR), heart rate standard deviation (std HR), square root of the mean of the sum of the squares of differences between adjacent NN intervals (RMSSD) and RR triangular index (RRtrindex) were evaluated. The frequency domain was analyzed by the auto regression spectrum model. Among these indexes were assessed the low frequency (LF) and high frequency (HF) bands, both with normalized units, as well as the ratio LF/HF. For non-linear analysis, Poincare plot measures SD1 and SD2 were observed. Autonomic control, measured throughout LF e HF/LF was considered the primary outcome.

PPT, which was defined as the least stimulus at which a subject perceive as painful[13], was measured with a handheld digital algometer (Wagner FDX-10, Wagner Instruments, Greenwich, CT), with a 1-cm2 round rubber tit, and pressure was applied at a rate of approximately 1kg/s, perpendicular to the skin surface. This measurement is has been shown to be reliable to quantify pain and tenderness[4,17,35,50,55].

Measurements were made before and after the intervention, immediately after the HRV assessment. With the participants comfortably seated, PPT of six landmarks were collected: C7 and T4 spinous process, first interossei dorsal bilaterally and muscle belly of tibialis anterior bilaterally. Since the side of technique application was also randomized, the PPT on first interossei dorsal was defined as ipsilateral hand (IH) and controlateral hand (CH). Likewise, PPT on tibialis anterior was named as ipsilateral tibialis (IT) and controlateral tibialis (CT). A mean of three measurements in each point, with 30 seconds of interval

between each reading was calculated. Before each intervention, all landmarks were marked with a water-soluble pen to enhance reliability during the entire protocol. The upper and lower limbs landmarks were selected in order to assess the widespread effects of PAIVM, and because normative data are available [4,50,52]. PPT measurements were performed by the same evaluator, which was blinded to group assignment, and practiced the rate of force application until an approximately constant rate of force application was achieved. Participants were instructed to say “pain” as soon as the threshold was reached. At this moment, the pressure was released and the displayed value (Kg/cm^2) was recorded. Before the testing procedure, participants were familiarized with algometer measurement with one set of three PPT practice trials on the left forearm. Algometer was calibrated prior to commencing the study.

Statistical Analysis

Sample-size calculations with 80% power and an alpha of .05 indicated that 55 participants, divided on the three groups, were needed to detect a significant difference of 20% on LF.

Shapiro-wilk test was applied to verify the normality of the data. Descriptive statistics with mean and standard deviation were calculated for normally distributed data, whereas median and interquartile range for non-parametric data. For PPT, percentage changes from baseline were also calculated. Logarithmic corrections were applied when necessary. For parametric data, repeated measures analysis of variance with two mixed factors, time (before and after intervention) as within-subject factor, and group (PA PAIVM, SLUMP PAIVM and Placebo) as between-subject factor was used

to determine the interactions between these two factors. Time-by-group interaction was tested for the following variables (that were met the normality conditions): PPT on all six landmarks; mean HR, mean RR, STD HR and RR_triang_index, for the time-domain analysis; LF reflecting the frequency-domain analysis. When interactions between the two factors were not reached, One-way ANOVA was used to compare the three groups in each time-point with Bonferroni *post-hoc*. Paired *t*-test was applied to verify within-group differences. For the non parametric data, between-groups differences were calculated with the Kruskal-Walis test, whereas within-group comparison was made through the Wilcoxon test. A *p* value of .05 was adopted as statistical significant. SPSS Version 20.0 (IBM Corporation, Armonk, NY) was utilized for data analysis.

RESULTS

Between July and December 2014, 86 volunteers responded to the recruitment advertisements and were screened for eligibility. From this sample, 60 subjects were enrolled, three subjects were lost, resulting in 57 individuals analyzed (Figure 1). There were no significant differences between groups in baseline characteristics (Table 1). There was no drop-out, as well as, no adverse effects observed during data collection period. 79% of the subjects did not identify correctly the group assignment.

Insert Table 1 around here

Heart Rate Variability

There were no significant group*time interactions for any parameter.

Time-domain

There were no statistically significant differences between groups in mean HR, std HR, mean RR, RRtrindex, SDNN and RMSSD either before or after intervention. As well as, no statistically significant differences within groups between baseline and post conditions (Table 2).

Insert Table 2 around here

Frequency-domain

There were no statistically significant changes in between groups and within groups' comparisons for LF, HF and LF/HF ratio between baseline and post intervention (Table 3).

Insert Table 3 around here

Non-linear

For the non-linear analysis, there was also no difference between groups for SD1 and SD2 (Table 4). Furthermore, no statistically significant changes occurred on the within-group analysis.

Insert Table 4 around here

Pressure Pain Threshold

There were no statistically significant time-by-group interaction for any PPT parameter, however there was a trend in HI (p=0.063) and TI PPTs (p=0.052). Regarding PPTs at individual landmarks, one-way ANOVA did not revealed statistical significant difference between groups in baseline and after intervention (Table 5). Paired t-test within-group analysis revealed a statistical significant IH PPT increase after the intervention in SLUMP PAIVM group (p=0.034), as well as a trend to significance in CH PPT (p=0,061) (Table 5).

Insert Table 5 around here

In regard of the percentage changes of PPT (Figure 3), it was observed an overall increase in all landmarks, except in C7 PPT, that decreased in all groups. The Placebo group demonstrated lower percentages of increasing, in comparison to the two intervention groups. Furthermore, the greatest percentages of change were observed in the SLUMP PAIVM group, that reached 12,8%, 11,9%, 9,10% and 7,84% on IH, IT, CH and CT respectively. More pronounced effects were observed on widespread points, than locally at T4 spinous process.

Insert Figure 3 around here

DISCUSSION

The primary aim of this trial was to compare the effect in HRV and PPT of two different PAIVM techniques applied to the thoracic spine in asymptomatic individuals. The main findings evinced that HRV variables, as well as PPT on six different landmarks, were not different between groups receiving either a PA

rotatory thoracic PAIVM, a PA PAIVM in SLUMP position or a Placebo intervention. Nonetheless, in the intra-group analysis, our results showed that the SLUMP PAIVM group produced a significant increase on IH PPT.

To our knowledge, this is the first study to investigate the effects of these two techniques, frequently performed on clinical practice, on such outcomes. HRV it is an important measure of autonomic function, since reflects the activity of the sympathetic and vagal components of the ANS, providing consistent information on either sympathetic or vagal activity[15]. Notwithstanding, the assessment of this outcome is less frequent than others ANS outcomes, like skin conductance, skin temperature and blood pressure, on SMT research. In the other hand, although PPT is a common and reliable tool to objectively quantify pain[50] avoiding the possible expectation effects of a numeric pain scale, a lower amount of studies were realized assessing PPT after thoracic PAIVM, and generally investigating solely the effects of such intervention on cervical spine clinical outcomes[9,10,11,27]. The findings of this study contributes with the growing body of evidence regarding the neurophysiological effects of thoracic PAIVM on HRV and PPT.

Time-domain HRV

Accordingly with the recommendations of measurement[15], time-domain analysis are ideal for long-term recordings. Thus, the time of recordings used in our study might not be enough to observe significant changes. Similarly, one study observed no effects on HRV time-domain indexes after myofascial release techniques or placebo intervention in patients with chronic tension-type headache[44]. Contrasting with these findings, Reis et al.[37] demonstrated a

significant increase of RMSSD after a PA thoracic PAIVM in a sample of women with fibromyalgia, a fact that did not occur in the control group. Although the fibromyalgia group presented also significant lower RMSSD values in the baseline. Both studies performed short-term HRV recordings of five[44] and 10 minutes[37]. However, the sample of these studies consisted of symptomatic subjects, which prevents an adequate comparison with our results.

Frequency-domain

HF band is known to be related to the parasympathetic nervous system efferent activity, while the LF component seems to be related to the SNS modulation[15,20,36]. Our hypothesis was to observe an increment in LF band, a diminished HF component, as well as an increase in the balance LF/HF after the thoracic PAIVM in comparison to Placebo group, reflecting a sympathoexcitation. Equivalently to our findings, Reis et al.[37] observed no significant changes in frequency-domain indexes (LF, HF and LF/HF) after thoracic PAIVM in both symptomatic and healthy controls subjects. Divergent effects, such as increase of LF and LF/HF indexes, were observed when thoracic high velocity low amplitude manipulation was performed instead of PAIVM[2]. These conflicting results might suggest that the mechanical properties are important to produce the ANS effects, since both techniques were applied on thoracic spine. Moreover, as a change in LF/HF ratio depends on variations of both the numerator and the denominator values. Thus, the increasing in LF band should be higher than the increasing in HF band. The 15 minutes of recordings, may have been excessive and favor the reduction of RR intervals, as well as a predominance of parasympathetic activity. Budgell and Polus[2], in

addition to perform a high velocity low amplitude manipulation technique, performed only five minutes of recordings. This combination of high velocity technique, with lower rest interval could be responsible for the increasing in LF/HF balance in such study.

A large amount of studies have assessed other ANS outcomes, and support a current concept of sympathoexcitation following SMT, irrespective of segment mobilized[6,16,22,28,31,32,40,43,45,47,48]. A recent systematic review[19] reported a consistent increase of sympathetic activity in all included studies. As none of the eight included studies evaluated HRV, comparisons cannot be made properly. However, it is possible that differences in this measure are more difficult to be detected than others, such as skin conductance or respiratory rate.

Pressure Pain Threshold

There were no significant differences between groups on six landmarks mean PPT in the present study. However, within-group analysis demonstrated a statistical significant IH PPT increase in SLUMP PAIVM group. Furthermore, in regard of the PPT percentage of change, SLUMP PAIVM group presented higher increments than the other groups. Among the other landmarks, no significant change was observed. Similarly, several previous researches have reported no difference in PPT between groups following PAIVM techniques[21,42,43,52]. Willet et al.[52] and Krowuel et al.[21] did not found differences in lumbar PPT in asymptomatic subjects following PAIVM with different rates and forces of application respectively. Similarly, Snodgrass et al.[42] reported no difference between groups in cervical PPT following PAIVM with high or low

mobilization forces and a detuned laser placebo in a sample of neck patients. In addition, Sterling et al.[43] presented no PPT differences between a cervical lateral glide PAIVM and an only manual contact placebo in patients suffering of chronic whiplash associated disorders.

Conversely, an amount of evidence demonstrated hypoalgesic effects following several SMT techniques. Voogt et al.[49], in a systematic review that included studies presenting different SMT approaches, such PAIVM, high velocity low amplitude manipulations and also mobilization with movement techniques, reported moderate evidence that SMT increases PPT immediately after the intervention. The controversial between these results might be explained by the different mechanical properties of the techniques, since an optimal treatment dose is not established yet[42]. Preliminary evidence suggests that at least four sets of mobilization are required in order to induce significant hypoalgesia[30], although most of the cited studies performed solely three mobilization sets. Moreover, subject expectation could be play a role in our trial results, as our sample was composed of SMT naïve subjects, and the three interventions were presented as genuine.

In the current study, PPT effects were more pronounced on distant landmarks, such as IH, and CH that presented a trend to significance, in comparison with T4, where the technique was applied. Similarly, McGregor et al.[27] reported statistically higher PPT at a remote site following thoracic transverse PAIVM in neck pain patients. Widespread effects were also observed after PAIVM in other regions than thoracic spine. Cervical PAIVM increased PPT on elbow joint and remote lower limb site[43,46], lumbar PAIVM seems to produce increased widespread PPT in asymptomatic subjects

although without difference between different rates[52] or force magnitudes[21]. Although no ANS effects were observed in our results, it is interesting to observe that the PPT effects occurred more pronounced on widespread landmarks. This could be explained by the activation of neurophysiological effects following SMT[19,38], since solely mechanical responses could not explain such effects on sites distant to the mobilizes segment, nonetheless, the HRV might not be so sensible to detect this changes occurring on periphery.

Other studies have reported effects on upper limbs after thoracic PAIVM performing the same techniques utilized in the present study. SLUMP PAIVM and PA rotator PAIVM were applied by Slater et al.[40] and Jowsey and Perry[16] respectively, and demonstrated a significant increase in upper limb skin conductance. Interestingly, both studies observed more pronounced side-specific effects. In order to better understand such effects, in our trial, the side of technique application was randomized, and the PPT was defined as ipsilateral or controlateral to the side of therapist application. Although a trend to significance was observed on CH, only PPT in the therapist side (IH) presented significant higher PPT. These effects might be occurred through the sympathetic outflow to the upper limbs, and this sympathoexcitation seems to be side-specific.

Limitations

As only a single intervention was performed in a sample of asymptomatic individuals, the results of this study should be interpreted with caution. Moreover, the outcomes were assessed immediately after the technique, and more long-term effects cannot be attributed. In addition, the mobilized segment,

rate of oscillation, and time of application were selected a priori, whereas in clinical practice therapists determines the level to be treated and the technique parameters based on clinical reasoning. Different results might be observed if the therapist had been allowed to select the better segment[5], as well as the properties of technique.

Implications for Future Research

Future studies should address patient samples, with long-term follow-up, over multiple treatment sessions and different mechanical properties of mobilization. Previous research has compared the effects of thoracic PAIVM and high velocity low amplitude thrust manipulation on clinical outcomes[10,11]. Besides these outcomes, studies should also compare the effects of such techniques on ANS outcomes and pain related measures, to enhance better comprehension of the neurophysiological role of clinical improvements.

CONCLUSION

The current study demonstrated that a PA rotatory and a SLUMP PAIVMs did not produce different effects than a placebo technique in PPT and HRV in asymptomatic subjects after a single intervention, although statistically significant increase IH PPT was observed following the SLUMP PAIVM technique.

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Table 1. Participant demographic characteristics at baseline.

Characteristic	PA Group (n = 18)	SLUMP Group (n= 19)	Placebo Group (n =20)	*p* value
Gender (female), n (%)	13 (72)	12 (63)	14 (70)	0.907
Age (y)	22.6 ± (4.1)	22.3 ± (2.5)	23.1 ± (5.1)	0.812
Weight (Kg)	62.7 ± (12.2)	64.9 ± (7.5)	65.1 ± (13.4)	0.776
Height (m)	1.7 ± (0.1)	1.7 ± (0.1)	1.7 ± (0.1)	0.261
Body mass index (Kg/m^2)	22.6 ± (2.6)	22.6 ± (1.9)	22.3 ± (2.8)	0.872
Systolic pressure (mmHg)	118.3 ± (10.4)	120.0 ± (9.9)	121.8 ± (12.2)	0.601
Diastolic pressure (mmHg)	74.2 ± (8.5)	73.0 ± (7.4)	70.2 ± (6.5)	0.213

Data are presented in mean ± (SD)

Table 2. Within-group and between-group differences for time domain heart rate variability indices data at baseline and post intervention.

		PA (n= 18)	SLUMP (n= 19)	Placebo (n= 20)	*p* value
Mean HR †	Baseline	75.95 ± (8.57)	72.65 ± (8.17)	73.03 ± (10.39)	0.49
	Post	71.22 ± (9.94)	71.84 ± (7.52)	71.39 ± (9.83)	0.97
STD HR †	Baseline	5.16 ± (2.22)	4.85 ± (1.95)	4.80 ± (1.47)	0.82
	Post	5.76 ± (1.83)	5.09 ± (1.83)	4.45 ± (1.70)	0.08
Mean RR †	Baseline	804.66 ± (97.39)	841.06 ± (99.08)	843.07 ± (120.51)	0.47
	Post	865.62 ± (128.86)	849.44 ± (93.11)	860.52 ± (125.21)	0.91
SDNN §	Baseline	47.6 ± [31.42;77.85]	52.20 ± [41.00;73.60]	50.30 ± [36.92;75.22]	0.918
	Post	68.25 ± [49.97.77.60]	65.40 ± [39.40;78.60]	52.20 ± [40.35;63.77]	0.184
RMSSD §	Baseline	33.95 ± [23.92;71.82]	42.30 ± [25.20;59.70]	41.40 ± [26.77;65.95]	0.943
	Post	51.90 ± [37.20;73.12]	48.00 ± [31.80;59.80]	38.75 ± [30.65;54.90]	0.371
RRtrindex †	Baseline	11.75 ± (4.17)	12.85 ± (4.98)	12.74 ± (4.60)	0.72
	Post	14.14 ± (3.72)	13.80 ± (5.72)	11.11 ± (3.96)	0.08

† *Parametric data are presented in mean* **±** *(SD). One-way ANOVA and Bonferroni post hoc test for between-group comparison. Paired-Samples T Test for within-group comparison.*

§ *Non parametric data are presented in median* **±** *[interquartile range]. Kruskal-Wallis Test for between-group comparison. Wilcoxon Test for within-group comparison.*

Abbreviations: MEAN HR, mean heart rate; STD HR, heart rate standard deviation; RRtrindex, RR triangular index; SDNN, standard deviation of RR intervals; RMSSD, square root of the mean of the sum of the squares of differences between adjacent NN intervals; PA, PA group; SLUMP, SLUMP group; Placebo, Placebo group.

Table 3. Within-group and between-group differences for frequency domain heart rate variability indices data at baseline and post intervention.

		PA (n= 18)	SLUMP (n= 19)	Placebo (n= 20)	*p* value
HF §	Baseline	52.25 ± [38.67;61.62]	38.20 ± [35.90;53.20]	50,10 ± [35.37;57.90]	0.386
	Post	44.55 ± [32.97;57.92]	43.80 ± [32.10;66.40]	40,75 ± [35.60;50.12]	0.680
LF †	Baseline	50.63 ± (17.60)	56.42 ± (16.96)	52.88 ± (14.81)	0.56
	Post	53.05 ± (15.53)	53.59 ± (18.99)	58.57 ± (15.23)	0.52
LF/HF §	Baseline	0.90 ± [0.61;1.57]	1.61 ± [0.88;1.78]	0.99 ± [0.72;1.81]	0.392
	Post	1.24 ± [0.72;2.03]	1.28 ± [0.65;2.11]	1.57 ± [0.99;1.97]	0.524

† Parametric data are presented in mean ± (SD). One-way ANOVA and Bonferroni post hoc test for between-group comparison. Paired-Samples T Test for within-group comparison.
§ Non parametric data are presented in median ± [interquartile range]. Kruskal-Wallis Test for between-group comparison. Wilcoxon Test for within-group comparison.
Abbreviations: HF High frequency; LF, Low frequency; PA, PA group; SLUMP, SLUMP group; Placebo, Placebo group.

Table 4. Within-group and between-group differences for non-linear heart rate variability indices data at baseline and post intervention.

		PA (n= 18)	SLUMP (n= 19)	Placebo (n= 20)	*p* value
SD1	Baseline	24.05 ± [16.97;50.85]	29.90 ± [17.80;42.30]	29.30 ± [18.95;46.70]	0.368
	Post	36.80 ± [26.32;51.80]	34.00 ± [22.50;42.40]	27.45 ± [21.75;38.90]	0.633
SD2	Baseline	61.85 ± [41.28;97.95]	65.10 ± [54.80;93.20]	62.55 ± [49.20;96.33]	0.142
	Post	88.70 ± [66.90;99.13]	82.50 ± [50.70;93.60]	66.90 ± [47.00;82.55]	0.398

Data are presented in median ± [interquartile range]. Kruskal-Wallis Test for between-group comparison. Wilcoxon Test for within-group comparison.
Abbreviations: PA, PA group; SLUMP, SLUMP group; Placebo, Placebo group.

Table 5. Within-group and between-group differences for pressure pain threshold (Kg/cm^2) values at baseline and post intervention.

		PA (n= 18)	SLUMP (n= 19)	Placebo (n= 20)	*p* value
C7	Baseline	8.60±(2.26)	9.26±(2.42)	9.42±(2.54)	0.552
	Post	8.78±(2.30)	9.78±(2.30)	9.59±(2.50)	0.406
T4	Baseline	6.01±(1.93)	7.31±(2.51)	7.59±(2.86)	0.158
	Post	6.17±(1.88)	7.46±(2.19)	7.40±(2.25)	0.166
IH	Baseline	5.36±(1.65)	5.01±(1.72)	6.04±(1.94)	0.190
	Post	5.37±(1.90)	5.50± (1.79) *	5.80±(1.86)	0.764
CH	Baseline	5.50±(1.92)	5.27±(1.89)	6.23±(1.97)	0.277
	Post	5.78±(2.08)	5.69±(2.03)	6.22±(1.87)	0.672
IT	Baseline	8.69±(2.32)	9.39±(2.62)	9.22±(2.71)	0.691
	Post	8.34±(2.41)	10.11±(2.37)	9.59±(2.50)	0.085
CT	Baseline	8.60±(2.26)	9.26±(2.42)	9.42±(2.54)	0.552
	Post	8.78±(2.30)	9.78±(2.30)	9.59±(2.50)	0.406

Data are presented in mean ± (SD). One-way ANOVA and Bonferroni post hoc test for between-group comparison. Paired-Samples T Test for within-group comparison.
Abbreviations: C7, seventh cervical vertebra; T4, fourth thoracic vertebra; IH, interossei dorsal ipsilateral to therapist application force; CH, interossei dorsal contralateral to therapist application force; IT, tibial tuberosity ipsilateral to therapist application force; CT, tibial tuberosity contralateral to therapist application force.
**within-group statistically significant difference ($p \leq 0.05$) between baseline and post conditions.*

Figure 1. Flow diagram of participants throughout the study. *Some participants had more than one reason for exclusion.

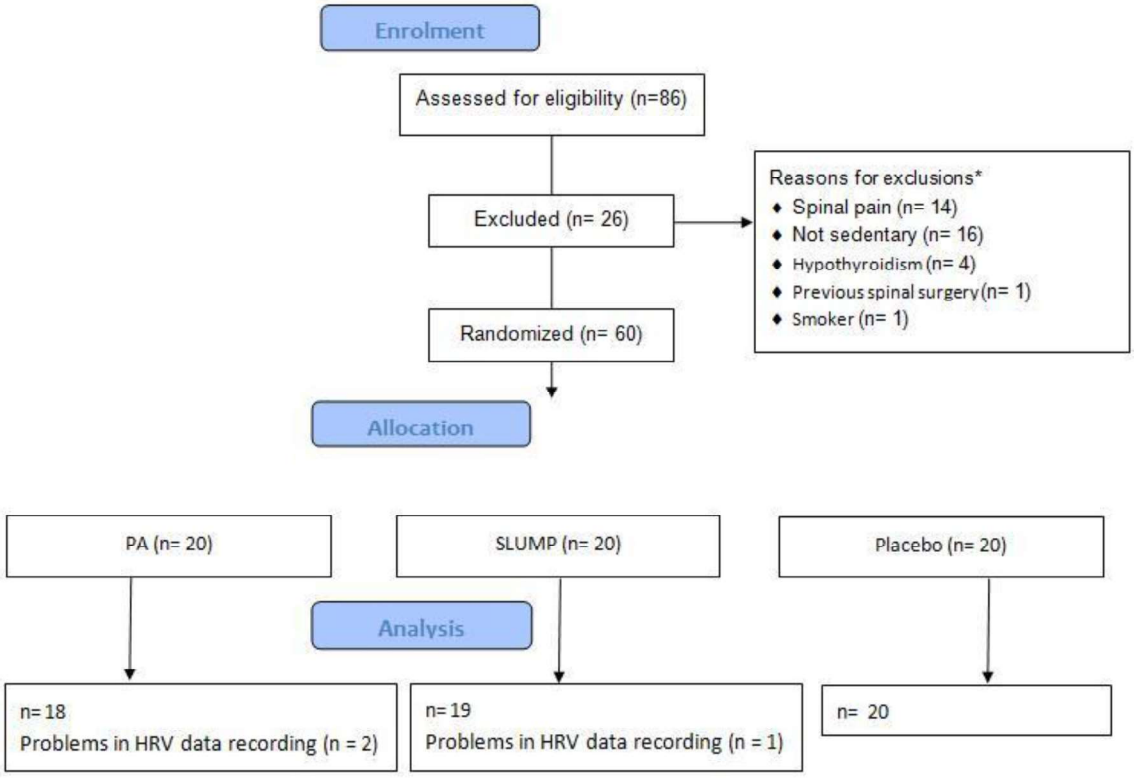
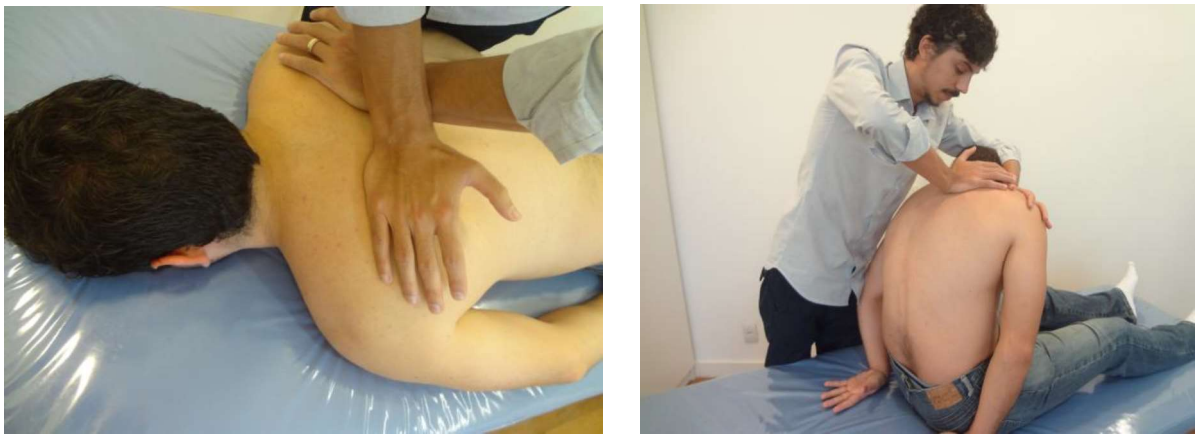
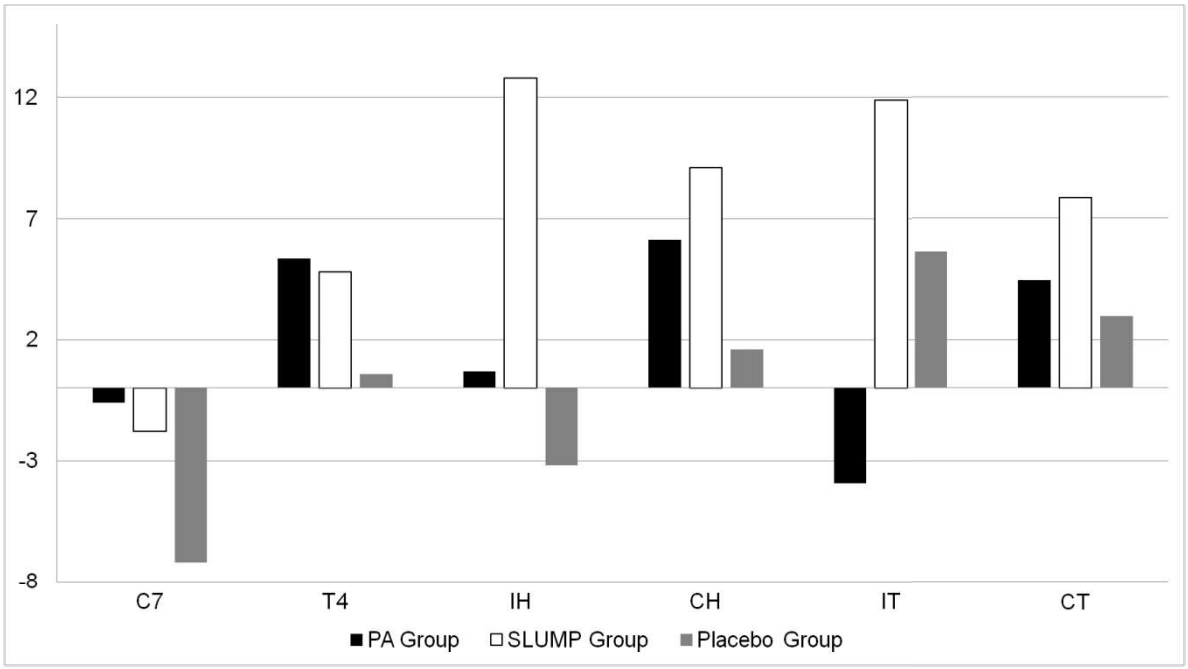


Figure 2. Ilustration of PA rotator PAIVM (a) and unilateral PA in Slump position (b).



(a) **(b)**

Figure 3. Mean PPT Percentage Changes (%)



Abbreviations: C7, seventh cervical vertebra; T4, fourth thoracic vertebra; IH, interossei dorsal ipsilateral to therapist application force; CH, interossei dorsal contralateral to therapist application force; IT, tibial tuberosity ipsilateral to therapist application force; CT, tibial tuberosity contralateral to therapist application force.

6 CONCLUSÃO GERAL

A MIVPA, independentemente do tipo de abordagem, nesta amostra de sujeitos assintomáticos, não foi capaz de promover efeitos estatisticamente significativos em nenhum parâmetro da VFC e no LDP superiores ao grupo Placebo. Na análise intra-grupo, entretanto, a técnica de MIVPA torácica PA em posição de SLUMP promoveu um aumento estatisticamente significativo no LDP na mão ipsilateral à aplicação da técnica, demonstrando um efeito à distância do segmento mobilizado.

Mais ensaios clínicos desta natureza, com rigor metodológico adequado, envolvendo sujeitos sintomáticos, são necessários para esclarecer a capacidade destas técnicas em influenciar a função autonômica e o LDP. Da mesma forma, outros desfechos do SNA, além de outras técnicas de terapia manipulativa vertebral devem ser estudadas para a maior compreensão dos efeitos neurofisiológicos, e da capacidade de modulação da dor destas abordagens.

ANEXOS

ANEXO A - PARECER CEP

UNIVERSIDADE FEDERAL DE CIÊNCIAS DA SAÚDE DE PORTO ALEGRE

Continuação do Parecer: 688.705

Objetivo da Pesquisa:

Objetivo Primário:

Descrever e comparar a influência de duas técnicas de terapia manual aplicadas à T4 no controle autonômico e no limiar de dor à pressão nos membros superiores em sujeitos assintomáticos.

Objetivo Secundário:

Verificar, dentre as técnicas utilizadas, qual apresenta maior efeito sobre o controle autonômico e o limiar de dor à pressão nos membros superiores.

Verificar a existência de correlação entre as alterações no controle autonômico e limiar de dor à pressão.

Verificar a reprodutibilidade do protocolo em dois momentos distintos. Descrever se o estado de ansiedade dos indivíduos interfere nos resultados obtidos .

Avaliação dos Riscos e Benefícios:

Riscos:

Um possível desconforto poderá ser sentido, mas isso tende a ser minimizado com instruções simples de autocuidado.

Benefícios:

O participante será beneficiado ao realizar uma avaliação fisioterapêutica. Além da sensação de bem estar causado pelas mobilizações vertebrais.

Comentários e Considerações sobre a Pesquisa:

Projeto já aprovado no CEP da UFCSPA.

Foi solicitada a prorrogação do prazo de encerramento do estudo para agosto de 2015.

Considerações sobre os Termos de apresentação obrigatória:

todos adequados

Recomendações:

aprovar

Conclusões ou Pendências e Lista de Inadequações:

não há inadequações

Situação do Parecer:

Aprovado

Necessita Apreciação da CONEP:

Não

UNIVERSIDADE FEDERAL DE CIÊNCIAS DA SAÚDE DE PORTO ALEGRE

Continuação do Parecer: 688.705

Considerações Finais a critério do CEP:

Emenda aprovada.

Término do projeto 08/2015.

PORTO ALEGRE, 16 de Junho de 2014

Assinado por:
José Geraldo Vernet Taborda
(Coordenador)

ANEXO B

Normas de formatação do periódico *Journal of Orthopaedic and Sports Physical Therapy (JOSPT)*

General Requirements

All manuscripts must meet the following basic requirements to be eligible for review by *JOSPT*®.

- Written in English
- Include a cover letter
- Present findings or data that have not been previously published either in print or electronic (online) format or widely disclosed in a form other than published abstracts of oral presentations at scientific conferences and meetings
- Undergoing exclusive review by *JOSPT*
- Address scientific, clinical, or professional issues relevant to musculoskeletal or sports-related physical therapy practice
- Written in accordance with the recommendations found in the ***Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication***by the International Committee of Medical Journal Editors, April 2010 (http://www.icmje.org/urm_main.html and http://www.icmje.org/urm_full.pdf)
- Formatted according to AMA style guidelines (*American Medical Association Manual of Style, 9th Edition*)

Submissions that do not meet the above essential requirements will be returned to the author without review. For additional guidance, please review *JOSPT*'s **Author and Reviewer Tools**.

NOTE: In the peer-review process, *JOSPT* reviewers are unaware of the author's identity and institutional afiliation. Associate editors are not blinded to author identity and vice versa.

Protection Of Human Subjects

The name of the Institutional Review Board that approved the research protocol involving human subjects must be included on the title page and in the Methods section. The Methods section must also contain a statement that informed consent was obtained and that the rights of the subjects were protected.

It is mandatory that clinical trials initiated on or after January 1, 2013 be prospectively registered in a public trials registry. In these cases, authors should provide the name of the registry and the registration number on the title page. For clinical trials initiated prior to January 1, 2013, prospective clinical trial registration is desirable but not mandatory.

When required by the appropriate Institutional Review Board, case reports should include either a statement that each subject was informed that data concerning the case would be submitted for publication or a statement indicating approval by the Board. In all cases, patient confidentiality must be protected.

Use Of Animals

Manuscripts with experimental results in animals must include a statement on the title page and in the Methods section that an animal utilization study committee approved the study.

Use Of Cadavers

When applicable, manuscripts with experimental results on cadavers must include a statement on the title page and in the Methods section that a relevant utilization study committee approved the study.

Preparing Your NEW Manuscript

All manuscripts submitted to *JOSPT* should be double-spaced and have 2.54-cm (1-in) margins on all sides of the page. Pages should be consecutively numbered, starting with the title page. Pages should be continuously line numbered, with line numbers starting at 1 on the abstract. The font should be 12-point Arial, Times New Roman, or Courier. All measurements in the manuscript should be presented in SI units, except for angular measures, which should be presented in degrees rather than radians.

The manuscript should be arranged as follows:

Title Page (separate page)

- Title of manuscript
- Names of each author with their highest academic credential (ie, PhD), or most relevant professional designation (eg, PT), or both (eg, PT, PhD). Limit credentials to these 2 items only
- Institution, city, state/province, country for each author
- Statement of the sources of grant support (if any)
- Statement of Institutional Review Board approval of the study protocol
- Name of the public trials registry and the registration number
- Corresponding author's name, address, and e-mail address

Anonymous Title Page (separate page)

- Title of manuscript
- Statement of financial disclosure and conflict of interest (see item 6 of the **Author Agreement and Publication Rights Form**)
- Acknowledgements (on a separate page)

Abstract (see also Manuscript Categories)

- **Structured Abstract:** *Research reports (including systematic literature reviews) and brief reports*require an abstract containing a maximum of 250 words, divided into 6 sections with the following headings in this order: Study Design, Objectives, Background, Methods, Results, Conclusion. Abstracts for *case reports* should have 5 sections with the following headings and order: Study Design, Background, Case Description, Outcomes, and Discussion. Abstracts for *resident's case problems* should have 4 sections with the following headings and order: Study Design, Background, Diagnosis, and Discussion.
- **Unstructured Abstract:** *Clinical commentaries and narrative literature reviews* require an abstract (called synopsis) that is not structured and that contains a maximum of 250 words.
- **All abstracts should include, where appropriate, a line item called "Level of Evidence,"** which indicates the study type and level of evidence, according to the classification system listed at theOxford Centre for Evidence-based Medicine website (http://www.cebm.net). This final line in the abstract should be in the following format example: "Level of Evidence: Therapy, level 2a." When the study does not fit any of the study type and level of evidence descriptors included in the above classification system, this line may be omitted. A list of suggested study design names and the Oxford Center for Evidence-Based Medicine levels of evidence table are provided for reference**here**.
- **All abstracts should end with a Key Words section,** containing 3 to 5 key words that do not appear in the manuscript title.

Text

- *Research reports, systematic literature reviews, and brief reports* require the body of the manuscript to be divided into 5 sections: Introduction, Methods, Results, Discussion, and Conclusion.
- *Case reports* require the body of the manuscript to be divided into 4 sections: Background, Case Description, Outcomes, and Discussion.
- *Resident's case problems* require the body of the manuscript to be divided into 3 sections: Background, Diagnosis, and Discussion.
- *Clinical commentaries and narrative literature reviews* do not have specific mandatory subdivisions or sections.

For all of these manuscript categories except brief reports, the text should be less than 4,000 words and be supplemented by a reasonable number of figures and tables. Brief reports should be less than 2,000 words (excluding no more than 20 references) and have no more than 4 tables or figures.

Key Points

The brief Key Points section of the manuscript is needed for *research reports only, including systematic literature reviews*. Key Points should be provided at the end of the text, prior to the references. These points should be written in user-friendly language, consist of brief sentences, and summarize the most important information related to the findings, implications, and caution directly resulting from the work. These 3 subheading should be used:

- **Findings:** One or 2 statements on what the study adds to current knowledge.
- **Implications:** A statement on how the results impact clinical practice or research on this topic.
- **Caution:** A statement on the most important limitations of the study, especially external validity (what may prevent wide utilization of the results).

References

- References should be numbered consecutively in alphabetical order, according to author last name and initials, title, and year. Where the first-author names are identical, references with 1 author precede those with mutiple authors. Where all the author names are identical, the title is the next ordering component, followed by the year.
- All references in the References section must be cited in the text.
- References must be cited in the text by using the reference number in superscript at the end of the sentence or the referenced portion of the sentence. The reference goes after the author's name when the author's name is listed (eg, Davies[1]). If there are only 2 authors in the reference, then the text should include both authors (eg, Davies and Ellenbecker[1]). If the reference has more than 2 authors, the text should include "et al" after the first author's name (eg, Davies et al[1]).
- In the Reference section, when a reference has 7 or more authors, list the first 3 authors, followed by "et al."
- References must include only material that is retrievable through standard literature searches. References to papers accepted but not published or published ahead of print should be designated "in press" or use the PubMed/MEDLINE [Epub ahead of print] status until an updated citation is available. Doctoral and master's theses are considered published material. Information from manuscripts not yet accepted for publication and personal communications will not be accepted. The use of abstracts and proceedings should be avoided unless they are very recent and the sole source of the information.
- Abbreviations for the journals in references must conform to those of the National Library of Medicine in Index Medicus (http://www.ncbi.nlm.nih.gov/journals).
- References that have CrossRef Digital Object Identifiers (doi) should include them at the end of the citation.
- References must be verified by the author(s) against the original documents.

Reference style and punctuation should conform to the examples that follow:

Journals

Wilson T. The measurement of patellar alignment in patellofemoral pain syndrome: are we confusing assumptions with evidence? *J Orthop Sports Phys Ther* 2007;37(6):330-341. http://dx.doi.org/10.2519/jospt.2007.2281

Books
Portney LG, Watkins MP. *Foundations of Clinical Research: Applications to Practice.* 3rd ed. Upper Saddle River, NJ: Prentice Hall Health; 2009.

Organization as Author and Publisher
US Food and Drug Administration. Guidance for industry: patient-reported outcome measures: use in medical product development to support labeling claims. Rockville, MD: FDA; 2006.

Chapter in a Book
Jones MA, Rivett DA. Introduction to clinical reasoning. In: Jones MA, Rivett DA, eds. *Clinical Reasoning for Manual Therapists.* Edinburgh, UK: Butterworth-Heinemann; 2004:3-24.

Master's or Doctoral Thesis
Langshaw M. *Cervical Spine Mobilisation: The Effect of Experience and Subject on Dose* [thesis]. NSW, Australia: The University of Sydney; 2001.

Published Abstract of a Paper Presented at a Conference
Chen YJ, Powers CM. The dynamic Q-angle: a comparison of persons with and without patellofemoral pain [abstract]. Proceedings of the North American Congress on Biomechanics. Ann Arbor, MI: 2008.

Universal Resource Locator (URL)
NFHS Associations. 2007-2008 National Federation of State High School Associations Participation Survey. Available at: http://www.nfhs.org. Accessed May 17, 2010.

Paper Presented at a Symposium
Nelson-Wong E, Gregory DE, Winter DA, Callaghan JP. Postural control strategies during prolonged standing: is there a relationship with low back discomfort? American Society of Biomechanics Annual Conference. Palo Alto, CA: American Society of Biomechanics; 2007.

Preparing Your Tables And Figures

Tables

- Each table must be self-contained and provide standalone information independent of the text.
- See *AMA Manual of Style* (9th ed.), section 2.13, to organize and format tables.
- Table titles should list the table number in uppercase bold (eg, "**TABLE1.**"), followed by a period, then the title of the table in sentence case.
- Abbreviations used in each table must be spelled out below the table.
- Footnotes must be listed below the table, after the abbreviations, in order of occurrence in the table (left to right, row to row). According to AMA style, footnotes are cited with the following superscript symbols in this order: *, †, ‡, §, ||, ¶, #, **, ††, ‡‡. Where these symbols are unavailable, superscript numbers may be used.
- All tables must be referred to somewhere in the text.
- All tables go after the reference list.

Figures

- Figure captions should list the figure number in uppercase bold (eg, "**FIGURE 1.**") followed by a period, and continue with the text of the caption in sentence case.
- All abbreviations appearing in the figures should be defined in the caption for each respective figure, and abbreviations appearing only in the figure caption must be defined at first use.
- Digital figures must be at least 350 dots per inch (dpi).
- Charts and graphs generated from spreadsheet programs must accompany, or allow access to, the data.
- Photographs must be in JPEG file format (JPG) and graphic art in GIF file format and at a resolution of at least 350 dpi.
- All figures must be referred to in the text.
- Each view (eg, A, B, C) within the figure must be defined in the figure caption.

- Color figures and graphics are welcome.
- All figures go after the tables at the end of the manuscript.

ANEXO C

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	38
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	40
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	42-43
	2b	Specific objectives or hypotheses	43
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	43
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	N/A
Participants	4a	Eligibility criteria for participants	43-44
	4b	Settings and locations where the data were collected	43-44
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	45-46
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	46-48
	6b	Any changes to trial outcomes after the trial commenced, with reasons	N/A
Sample size	7a	How sample size was determined	48
	7b	When applicable, explanation of any interim analyses and stopping guidelines	N/A
Randomisation:			
Sequence	8a	Method used to generate the random	44

generation		allocation sequence	
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	44
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	44
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	44
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	44
	11b	If relevant, description of the similarity of interventions	45-46
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	48-49
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	N/A
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	71
	13b	For each group, losses and exclusions after randomisation, together with reasons	71
Recruitment	14a	Dates defining the periods of recruitment and follow-up	49
	14b	Why the trial ended or was stopped	N/A
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	67
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	71

Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	68-70
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	N/A
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	N/A
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	N/A
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	58
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	52-57
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	52-57
Other information			
Registration	23	Registration number and name of trial registry	43
Protocol	24	Where the full trial protocol can be accessed, if available	N/A
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	N/A

APENDICE A

LETTER TO THE EDITOR-IN-CHIEF

Letters to the Editor are reviewed and selected for publication based on the relevance, importance, appropriateness, and timeliness of the topic. Please see the instructions to authors in the Journal or at www.jospt.org for further information, including submission guidelines.
J Orthop Sports Phys Ther 2015;45(1):46-48. doi:10.2519/jospt.2015.0201

AUTONOMIC EFFECTS AFTER ANTERIOR-TO-POSTERIOR CERVICAL MOBILIZATION

We read with great interest and would like to congratulate Yung et al[18] for their very interesting study titled "Blood Pressure and Heart Rate Response to Posteriorly Directed Pressure Applied to the Cervical Spine in Young, Pain-Free Individuals: A Randomized, Repeated-Measures, Double-Blind, Placebo-Controlled Study," published in the August 2014 issue of *JOSPT*. This study contributes to the knowledge of the effects of joint mobilization techniques, especially those applied on the spine, on autonomic nervous system modulation. The trial demonstrated a statistically significant drop in heart rate (HR) after an anterior-to-posterior (AP) cervical mobilization that did not occur in the placebo group. In addition, there was a statistically significant reduction in systolic blood pressure (BP) for both the intervention and placebo groups. However, due to the divergent results between this article and a recently published systematic review,[4] we would like to add to the discussion.

Due to the anatomical proximity between the stellate ganglion and cervical spine region, it appears to be relevant to explore autonomic repercussions induced by AP cervical mobilization. Anecdotal evidence suggests that this technique may emerge as an alternative in the management of clinical conditions involving unilateral symptoms of the superior quadrant[9] through sympathetic nervous system activation and subsequent hypoalgesic effects.[4] However, previous studies with a similar purpose to that of the study by Yung et al[18] observed statistically significant increases in HR and BP following cervical mobilization.[4,17] Other articles even showed concurrent effects of sympathetic excitation and an increase of pressure pain threshold after applying different techniques of spinal mobilization.[1,14] These findings are in contrast to the data published by Yung et al[18] and suggest that the excitation of the sympathetic nervous system may be part of a descending pain-modulation system.

The autonomic nervous system contributes to homeostasis by adjusting the convergence and interaction of a large number of organic and environmental stimuli. It reacts with a broad spectrum of systemic responses that aim to preserve body functions. This implies that many factors can influence autonomic modulation. Thus, rigorous methodological procedures are paramount when investigating how this system is affected by external factors. The conflicting results obtained by Yung et al[18] compared to those of other studies[4,13,16,17] might have occurred as a consequence of different procedures adopted among studies. For example, in the trial by Yung et al,[18] it is unclear whether individuals who were obese, smoked, consumed alcohol, or had systemic disorders such as diabetes were enrolled. Substantial autonomic changes have already been described for these populations.[2,10,12,15] Moreover, the level of physical activity of the participants was not reported. Sedentary individuals usually demonstrate significantly higher sympathetic activity than their physically active counterparts.[11,15] Therefore, characteristics of participants enrolled in the study might have influenced the findings. The circadian rhythm can cause significant changes in HR[3]; the type, volume, and composition of food intake can influence autonomic modulation[1]; and respiratory rate has a direct effect on HR.[2] We believe that the authors[18] should have considered the influence of the period of the day of data collection, food intake, and respiratory rate.

Considering one of the main outcomes of the study (HR), we would like to suggest an alternative parameter to assess autonomic nervous system behavior. Heart rate variability (HRV) is a noninvasive marker with good validity and reliability[11] that reflects the activity of the sympathetic and vagal components of the autonomic nervous system.[15] It provides more consistent information on either sympathetic or vagal activity. The interest in HRV as a measure of autonomic function, therefore, lies in its clinical importance, because reduced HRV is a powerful and independent predictor of an adverse prognosis in patients with heart disease and in the general population.[5,15] Among indirect assessment methods of autonomic nervous system activity, HRV appears to be the most affordable and allows recording of data during interventions.

Overall, we would like to emphasize the importance of either a wider description of the Methods section or more controlled procedures for future studies. It would make the investigation easier to reproduce and enhance the internal consistency. Moreover, we believe that incorporating HRV assessments in studies of this nature could yield interesting insights on the neurophysiological effects of joint mobilization techniques on the autonomic nervous system.

Francisco Xavier de Araujo, PT
Fabricio Edler Macagnan, PT, DSc
Rodrigo Della Méa Plentz, PT, DSc
Marcelo Faria Silva, PT, DSc
Physical Therapy Department
Universidade Federal de Ciências da Saúde de Porto Alegre
Porto Alegre, Brasil

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RESPONSE

We are pleased our Brazilian colleagues find our article[1] interesting and appreciate the opportunity to respond to their letter to the editor. First and foremost, the evidence for the effectiveness of AP cervical mobilization is not anecdotal, as claimed by Mr Araujo and colleagues, who cited the study by La Touche et al,[2] which demonstrated that it is effective in patients with head/neck pain. Another study showed that AP mobilizations achieve the best outcome and/or most efficiently attain analogous effectiveness when compared with 3 other common joint mobilization techniques.[3]

While growing evidence suggests that sympathoexcitatory response is one mechanism explaining why manual therapy may affect pain, the various interactions between the sympathetic nervous system and pain are still not fully characterized.[4] For example, preoperative blockage of the (sympathetic) stellate ganglion can reduce postoperative pain and the need for tramadol.[5] When compared to a nonpainful control condition, experimental acute pain increased HR and mean arterial BP (signs of stress-related sympathoexcitatory response) in young, healthy participants.[6]

If acute pain can induce sympathoexcitatory response and if blockage of the sympathetic nervous system can reduce pain, then it may be reasonable to speculate that sympathoinhibitory response may reduce pain. Although not cited in our article, manual techniques such as soft tissue mobilization, spinal manipulative therapy,[4,7] and 2-Hz transcutaneous electrical nerve stimulation have been shown to reduce pain via this sympathoinhibitory mechanism. The 1.5-Hz frequency of our AP mobilization technique, applied near the stellate ganglion, is analogous in frequency to the 2-Hz transcutaneous electrical nerve stimulation, which has been shown to reduce systolic BP (sympathoinhibitory response) via an enhanced BP-related hypoalgesia from the endogenous opioid response.[8]

Moreover, a recent study using transcutaneous electrical nerve stimulation to stimulate the stellate ganglion showed a reduction in post–coronary artery bypass graft surgery pain, reduced mean arterial pressure (suggesting sympathoinhibitory effects), reduced opiate requirements, and increased circulating beta endorphins.[9] Due to the proximity of the stellate ganglion to the AP mobilization site, it is possible that the AP mobilization might have stimulated the stellate ganglion, resulting in sympathoinhibitory cardiovascular response.

All studies cited by Mr Araujo and colleagues applied continuous joint mobilization, lasting anywhere from 30 to 120 seconds, for 3 sets, which is approximately 2 to 6 times the total duration of treatment employed in our study. Specifically, in our study, AP oscillations were performed for 10 seconds on and 10 seconds off, repeated over 5 cycles. This is perhaps one reason why our results differed from those of other studies.

LETTER TO THE EDITOR-IN-CHIEF (CONTINUED)

The work by La Touche et al[9] perhaps approximates our AP technique the closest. Their sham group had a decreased HR response that was similar to that of our placebo group. Although their experimental group's HR and respiratory rate went up within session 1, those findings appear to not be statistically significant, whereas our study yielded a statistically significant reduction in HR and systolic BP.

A careful reading of the description of our sample reveals that the body mass index averaged 23.6 kg/m^2, which is not obese, as defined by the World Health Organization criteria. All the participants in our study were healthy, did not consume alcohol the day of the study, were not smokers, and did not have diabetes.

The concern regarding the influence of the period of the day of data collection (circadian rhythm) would only be pertinent if the data had been collected from more than 1 session. In our study, the subjects were tested during a single session, which lasted approximately 30 minutes and included 2 baseline measurements that have high reliability. It is noteworthy that, similar to our study, all studies cited by Mr Araujo and colleagues did not address food intake, and though respiratory rate was not investigated in our study, HR and BP may be utilized as proxies for sympathetic activity.[5] In addition, even though La Touche et al[9] measured respiratory rate, they did not utilize BP as an indicator of sympathetic nervous system activity.

While the suggestion of using HRV is well intended, none of the references cited by Mr Araujo and colleagues used this methodology. Therefore, with the exception of the total procedural dosage duration, our study used similar methodologies, including inclusion and exclusion criteria, to those previously reported by those references. Reproducing our results should not be difficult, as our study was pragmatic in design and the equipment used is available in every physical therapy practice. Our original manuscript had a more thorough description of the methods, but only limited procedural details could be included within the Brief Report category.

In summary, performing AP mobilizations caused sympathoinhibitory effects. Although contrary to what is popularly accepted in manual therapy, our findings are consistent with published results reported by Knutson,[7] Delaney et al,[3] Campbell and Ditto,[1] and Cipriano et al.[2] Our disparate outcomes (results derived following comparable methods employed in applicable references mentioned by Mr Araujo and colleagues) suggest that there may be different mechanisms underlying the cardiovascular effects of various manual techniques and/or various dosage regimens.

Emmanuel Yung, PT, DPT, MA, OCS, FAAOMPT
Doctor of Physical Therapy Program
Sacred Heart University
Fairfield, CT

Michael Wong, PT, DPT, OCS, FAAOMPT
Doctor of Physical Therapy Program
Azusa Pacific University
Azusa, CA

Haddie Williams, DPT, ATC
Intermountain Physical Therapy
Salt Lake City, UT

Kyle Mache, DPT
Avail Physical Therapy
Chico, CA

The authors certify that they have no affiliations with or financial involvement in any organization or entity with a direct financial interest in the subject matter or materials discussed in this article.

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APENDICE B

Elsevier Editorial System(tm) for Journal of Manipulative and Physiological Therapeutics

Manuscript Draft

Manuscript Number: JMPT-D-15-00007

Title: Autonomic Effects of Spinal Manipulative Therapy: Systematic Review of Randomized Controlled Trials

Article Type: Literature Review

Keywords: Autonomic nervous system; Spinal manipulation; Systematic review

Corresponding Author: Mr. Francisco Xavier de Araujo,

Corresponding Author's Institution: Universidade Federal de Ciencias da Saude de Porto Alegre

First Author: Francisco Xavier de Araujo

Order of Authors: Francisco Xavier de Araujo; Rodrigo Della Méa Plentz, PT, DSc; Giovanni E Ferreira, PT; Rodrigo F Angellos, PT; Fábio F Stieven, PT, MSc; Marcelo F Silva, PT, DSc

ABSTRACT

Objectives: To systematically review the effects of SMT on autonomic nervous system outcomes, in both symptomatic and healthy populations. Secondarily, to assess the quality of evidence for the most prevalent outcomes with the GRADE approach.

Methods: PubMed, Cochrane Library, PEDro, Web of Science and EMBASE were searched from the inception until March 2014. Randomized controlled trials involving spinal manipulative therapy such as mobilization and manipulation that reported at least one outcome related to the autonomic nervous system, with placebo, control groups or other interventions as comparators, with both healthy and symptomatic samples were included.

Physiotherapy Evidence Database scale and the GRADE approach were used to assess risk of bias and quality of evidence, respectively.

Results: Eighteen trials were included in this systematic review. SMT, regardless of type (manipulation or mobilization) and treated region (cervical, thoracic or lumbar spine), influenced the autonomic nervous system. The overall quality of evidence for all analyzed outcomes ranged from low to very low-quality.

Conclusions: There is an amount of evidence that points towards autonomic nervous system effects after SMT. However the low quality of this evidence precludes a definitive conclusion of such effects. Based on current evidence there is a high level of uncertainty regarding the true effect estimates of SMT on ANS outcomes.

APENDICE C

Elsevier Editorial System(tm) for Manual Therapy
Manuscript Draft

Manuscript Number: YMATH-D-15-00035

Title: Short-term effects of different rates of thoracic mobilization on pressure pain thresholds in asymptomatic individuals: a randomized crossover trial

Article Type: Original Article

Keywords: Spinal manipulative therapy; Thoracic spine; Treatment dose; Pressure pain threshold

Corresponding Author: Mr. Francisco Xavier de Araujo,

Corresponding Author's Institution: Universidade Federal de Ciencias da Saude de Porto Alegre

First Author: Francisco Xavier de Araujo

Order of Authors: Francisco Xavier de Araujo; Maurício S Schell, PT student; Giovanni E Ferreira, PT; Mariana D Valentina, PT student; Alexandre S Pinho, Physical Educator, MSc; Rodrigo D Plentz, PT, DSc; Marcelo F Silva, PT, DSc

Abstract: Background: Passive accessory intervertebral mobilizations (PAIVM) are widely used by physiotherapists in the management of neuromusculoskeletal disorders. A large amount of evidence has shown that such techniques can reduce the sensitivity to painful stimuli in healthy and symptomatic individuals. Although there is a growing interest in determining the optimal dose of treatment, little is known about the effects of different rates of thoracic PAIVM on local and widespread pressure pain threshold (PPT).
Objectives: The primary aim of this study was to determine whether different rates of thoracic mobilization could produce hypoalgesic effects in asymptomatic subjects. Secondarily, this paper sought to investigate if such effects manifest in a local or widespread manner.
Design: Randomized cross-over trial.
Method: 20 asymptomatic participants were enrolled to three experimental conditions on three separate occasions in a random order. A posteroanterior rotatory thoracic PAIVM was performed at 2Hz, 0.5Hz and only manual contact placebo. PPT was measured before, immediately after and after 15 minutes follow-up at six different landmarks.
Results: The results demonstrated that a 2Hz thoracic PAIVM produced a between group significant hypoalgesic effect superior to 0.5Hz and placebo groups at T4 spinous process. Furthermore both intervention groups demonstrated intra-group significant increase in PPT at local and widespread sites.
Conclusions: This study suggest that in asymptomatic subjects, the rate of thoracic PAIVM could modulate PPT, with the 2Hz groups being superior to 0.5Hz or placebo. Moreover, the hypoalgesic effects occurred both local and widespread, and both immediately and after a 15 minutes follow-up.