UNIVERSIDADE FEDERAL DE SÃO CARLOS
CENTRO DE CIÊNCIAS BIOLÓGICAS E DA SAÚDE
PROGRAMA DE PÓS-GRADUAÇÃO EM FISIOTERAPIA

ANIELLE CRISTHINE DE MEDEIROS TAKAHASHI

MODULAÇÃO AUTONÔMICA DA FREQUÊNCIA CARDÍACA E TREINO DE FORÇA EXCÊNTRICA NO PROCESSO DE ENVELHECIMENTO

SÃO CARLOS
2010

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Tese de Doutorado apresentada ao Programa de Pós Graduação em Fisioterapia da Universidade Federal de São Carlos como parte dos requisitos para obtenção do título de Doutor em Fisioterapia, área de concentração: Processos de Avaliação e Intervenção em Fisioterapia. Projeto desenvolvido com apoio da FAPESP (06/52860-0) e CAPES (PDEE/1228/08-0)

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SÃO CARLOS

2010

Ficha catalográfica elaborada pelo DePT da Biblioteca Comunitária/UFSCar

T136ma

Takahashi, Anielle Cristhine de Medeiros.
Modulação autonômica da frequência cardíaca e treino de força excêntrica no processo de envelhecimento / Anielle Cristhine de Medeiros Takahashi. -- São Carlos : UFSCar, 2010.
131 f.

Tese (Doutorado) -- Universidade Federal de São Carlos, 2010.

1. Fisioterapia. 2. Envelhecimento. 3. Sistema nervoso autônomo. 4. Variabilidade da frequência cardíaca. 5. Treinamento resistido. 6. Entropia. I. Título.

CDD: 615.82 (20ª)

MEMBROS DA BANCA EXAMINADORA PARA DEFESA DE TESE DE DOUTORADO DE **ANIELLE CRISTHINE DE MEDEIROS TAKAHASHI**, APRESENTADA AO PROGRAMA DE PÓS-GRADUAÇÃO EM FISIOTERAPIA DA UNIVERSIDADE FEDERAL DE SÃO CARLOS, EM 22 DE FEVEREIRO DE 2010.

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Dedico este trabalho a minha mãe,
Ivênia, por todo o amor, carinho, amizade, apoio,
dedicação, determinação e superação.
Você é meu exemplo de vida.
Sem você essa conquista não seria possível.

“O futuro tem muitos nomes.
Para os fracos é o inalcansável.
Para os temerosos, o desconhecido.
Para os valentes, é a oportunidade”.
(Victor Hugo)

AGRADECIMENTOS

À Deus por abençoar a minha vida, meu trabalho e iluminar meus passos nesta estrada, colocando em meu caminho pessoas especiais que me ajudaram nesta conquista.

Aos meus pais Ivênia e Mário que nunca mediram esforços para que eu concluísse esta etapa. Vocês são fundamentais na minha vida. Minha eterna gratidão e minha profunda admiração Amo vocês!

Às minhas irmãs Anne e Vanessa por todo carinho, incentivo, força, coragem e amizade. Também amo muito vocês!

À Profª. Drª. Aparecida Maria Catai que me acolheu em seu laboratório por todos estes anos (dez anos!!!). Mais que uma orientadora, uma professora e amiga que com seu conhecimento e sabedoria me ensinou, me guiou e me incentivou, sempre com muita paciência, atenção e carinho. Por seus ensinamentos, oportunidades e pela sua amizade meu eterno e imenso agradecimento.

Ao Prof. Dr. Nicola Montano por ter aberto as portas do seu laboratório para mim. Pela atenção dedicada e pelos inúmeros ensinamentos. Minha eterna gratidão.

Ao Prof. Dr. Alberto Porta pelos ensinamentos, pela disponibilidade, pela paciência e atenção. Meu profundo agradecimento.

Ao Prof. Dr. Luis Eduardo Barreto Martins, pela paciência, perseverança, ensinamentos e disponibilidade nas minhas inúmeras visitas ao seu laboratório e na sua casa.

À Bia minha irmã de coração pela amizade sincera, pelo apoio incondicional, pelas incontáveis ajudas, pelos sábios conselhos, pelas palavras de carinho e incentivo, pelas risadas e pelos inúmeros momentos compartilhados nesta caminhada.

Aos meus grandes amigos de laboratório que passaram a ser amigos para toda a vida, mais conhecidos como a Máfia da Cardio: Luciana, Daniel, Karla, Michel e Natália (Caipi). Obrigada por todos os conselhos, pelos ensinamentos, pelas risadas e gargalhadas compartilhadas e acima de tudo pela amizade que nem a distância conseguiu separar.

Ao Robison e a Ruth amigos e parceiros nesta pesquisa e sem os quais este trabalho seria impossível de ser realizado. Obrigado por tornar este caminho mais suave, por todo apoio, ajuda e amizade. Foi muito bom caminhar ao lado de pessoas como vocês.

Aos amigos do laboratório: Victor, Natália, Marlus, Poliana, Laura, Rodrigo, Renata, Camila, Luciana, Vivi, Michele, Pozzi, Mali, Valéria, Torrinha, Thomas, Patrícia. Com vocês a caminhada com certeza foi mais completa e feliz. Obrigada por todos os momentos compartilhados.

Ao meu grande amigo Thiago Luiz pelas palavras de carinho, de apoio e incentivo e pela ajuda e amizade incondicional. Minha eterna gratidão.

Aos meus amigos: Vanessa (Foca), Lúcia, Letícia, Davilene, Tatu, Neto, Renata, Paula e Camila pelo apoio e amizade.

Aos meus alunos co-orientandos de IC: Ester, Fernanda, Ana Cristina, Natália, Rafael, Marina e Victor. Com os quais aprendi muito.

À Isabela Verzola pelas avaliações clínicas cardiológica dos voluntários deste estudo.

À Profª. Drª. Ester da Silva pelo seu incentivo, ensinamentos e colaboração neste trabalho.

À Profª. Drª. Audrey Borgui-Silva pelo apoio e incentivo neste trabalho.

À Profª. Drª. Tânia Salvini pela disponibilidade quanto à utilização do dinamômetro isocinético e pelo incentivo à pesquisa.

Ao Prof. Dr. Valdo José Dias da Silva pela sua disponibilidade e contribuição no meu trabalho e em especial por ter sido a ponte para a realização do meu estágio no exterior. Minha profunda gratidão.

Aos meus amigos da Itália: Carola, Ideli, Ivani, Alberto, Roberto e em especial ao Flaminio. Sem vocês minha estadia em Milão com certeza não teria sido tão especial.

Aos colegas do Ospedale Sacco: Eleonora, Ottavia, Giorgio, Ana, Mara, Madalena, Karina, Mônica, Marta.

Aos professores do Programa de Pós Graduação em Fisioterapia da Universidade Federal de São Carlos.

Aos funcionários da secretaria da Pós, em especial a Kelly, pela paciência e ajuda constante.

Aos meus queridos voluntários, pela atenção, carinho e amizade. Sem vocês este estudo não seria possível.

Aos órgãos de fomento CAPES e FAPESP pelo suporte financeiro.

A todas as pessoas que de alguma forma contribuíram para a realização deste trabalho.

Muito obrigada!

RESUMO

O processo de envelhecimento é marcado por várias transformações fisiológicas, dentre estas se observa uma redução da força muscular. Existem recomendações para o uso do treinamento contra resistência para a população idosa com intuito de amenizar este declínio. Ainda, estudos na literatura referem que a contração do tipo excêntrica seria a mais adequada para indivíduos idosos, uma vez que gera menor sobrecarga cardiovascular no momento da realização da contração. No entanto, não está claro o efeito crônico de um treinamento de força excêntrica (TFE) sobre a modulação autonômica da frequência cardíaca (FC). Assim o *primeiro estudo* teve como objetivo investigar se o TFE modifica a FC e variabilidade da frequência cardíaca (VFC) durante contrações voluntárias isométricas submáximas (CVIS). Participaram deste estudo 17 voluntários que foram alocados em dois grupos: grupo treinamento (9 homens, 62 ± 2 anos) e grupo controle (8 homens, 64 ± 4 anos). Os resultados obtidos indicam que apesar deste tipo de treinamento melhorar a força excêntrica, este não causou adaptações suficientes para promover alterações no controle autonômico da FC durante exercício isométrico. Outro fator importante a ser considerado é o aumento da incidência da doença cardiovascular com o envelhecimento. Somado a isso, tem sido observado que com o avanço da idade o controle autonômico da FC também sofre modificações constatadas por uma redução da VFC e mudanças na complexidade das dinâmicas fisiológicas. Diante destas considerações foi conduzido o *segundo estudo* que teve por objetivo verificar se as alterações na modulação da FC, causada pelo processo do envelhecimento, podem ser detectadas pela entropia de Shanon (ES), entropia condicional (EC) e análise simbólica (AS). Foram avaliados 23 idosos (63±3 anos) e 21 jovens (23±2 anos). Observou-se que com o processo de envelhecimento as distribuições de padrões presentes na VFC permanecem similares aos indivíduos jovens. No entanto, os padrões são mais repetitivos, reduzindo assim a complexidade. Esta redução é o resultado do aumento da presença de padrões estáveis e da diminuição de padrões altamente variáveis. Estas diferenças indicam que indivíduos idosos aparentemente saudáveis, apresentam um desequilíbrio na regulação autonômica cardíaca. Os resultados do segundo estudo indicam que as análises empregadas podem ser úteis para melhor caracterizar as alterações no controle autonômico da FC, decorrentes do avanço da idade.

Palavras-chave: Envelhecimento. Sistema nervoso autônomo. Variabilidade da frequência cardíaca. Treinamento de força. Análise não linear. Entropia.

ABSTRACT

The aging process is marked by several physiological changes, and the reduction in muscle strength is very important one. In order to minimize this force decline there are recommendations for using resistance training for elderly persons. Some studies available in the literature state that the eccentric contraction would be more suitable for the elderly, since it generates less cardiovascular overload during the exercise. However, the chronic effect of the eccentric strength training (EST) on the heart rate (HR) autonomic modulation is unclear. So, the aim of the first study was to investigate whether the EST changes HR and heart rate variability (HRV) during submaximal isometric contractions (SIC). This study included 17 volunteers who form divided into two groups: training group (9 men, 62 ± 2 years) and control group (8 men, 64 ± 4 years). The results indicate that although this type of training improves eccentric strength, the EST does not have any effect sufficient to promote changes in the autonomic control of HR during isometric exercise. Another important factor to consider is the increase in incidence of cardiovascular disease that occurs with aging. Furthermore, there are modifications of autonomic control of HR related to ageing that are detected by the reduction in HRV and changes in the complexity of physiological dynamics. Based on these considerations the aim of the second study was to verify whether changes in HR modulation, caused by the aging process, can be detected by the Shannon entropy (SE), conditional entropy (CE) and symbolic analysis (SA). In this study were evaluated 21 elderly (63 ± 3 years) and 21 young (23 ± 2 years). Elderly present distributions of patterns in HRV that are similar to young subjects. However, the patterns are more repetitive, thus reducing the complexity. This decrease of complexity comes from the increased presence of stable patterns and a decreased presence of highly variable patterns. This difference indicates that apparently healthy older subjects have a marked unbalance in autonomic regulation. The results of the second study indicate that non-linear approaches might be helpful to better characterize the changes on the autonomic control of HR in the aging process.

Keywords: Ageing. Autonomic nervous system. Heart rate variability. Strength training. Nonlinear analysis. Entropy.

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1. CONTEXTUALIZAÇÃO

1. CONTEXTUALIZAÇÃO

Nas últimas décadas, o Brasil vem passando por transformações tanto na sua estrutura populacional quanto nos seus padrões de morbi-mortalidade. Nota-se redução da taxa de fecundidade e aumento da expectativa de vida devido ao declínio da mortalidade, ocasionado por melhorias das condições sanitárias e da qualidade de vida (IBGE, 2000). No Brasil, em pouco mais de 40 anos, o número de idosos passou de três milhões em 1960, para 14 milhões em 2002, portanto um aumento de 500%, sendo que existem estimativas de que no ano de 2025 a população brasileira com mais de 60 anos alcance 34 milhões de indivíduos (IBGE, 2008).

Dessa forma, estudos que enfoquem caracterizar o processo de envelhecimento em seus diferentes aspectos são essenciais, uma vez que esta população vem aumentando de forma progressiva e bastante acelerada.

Várias são as transformações fisiológicas que ocorrem no processo de envelhecimento, sendo uma das mais marcantes a redução da força muscular (HYAT et al., 1990; MACALUSO e De VITO, 2004; WILLIAMS, HIGGINS e LEWEK, 2002). O principal fator para a diminuição da força muscular é a perda quantitativa de massa muscular, referida como sarcopenia (EVANS, 1995). A sarcopenia está associada à fragilidade e tem com conseqüências não só a diminuição da força muscular como também baixa tolerância ao exercício e redução da velocidade da marcha (WALSTON et al. 2006). A sarcopenia é uma das variáveis utilizadas para definição da Síndrome de Fragilidade, sendo altamente prevalente em idosos e conferindo maior risco para quedas, fraturas, incapacidade, dependência, hospitalização recorrente e mortalidade (WALSTON et al. 2006). Tem sido associada à atrofia das fibras musculares rápidas (tipo II a) e à substituição por tecido adiposo e fibrótico com diminuição da síntese protéica, ocasionando redução da força e eficiência muscular (MACALUSO e De VITO, 2004; WILLIAMS, HIGGINS e LEWEK, 2002). Observa-se ainda uma alteração na qualidade das fibras musculares, na efetividade neural, no controle fino do equilíbrio e na diminuição das aferências sensitivas e motoras (WALSTON et al. 2006). Estes eventos se relacionam com outras disfunções como diminuição da capacidade funcional, da taxa metabólica basal, da sensibilidade à insulina, da densidade mineral óssea e capacidade aeróbia (CIOLAC e GUIMARÃES, 2002; MACALUSO e De VITO, 2004). Esta situação acomete frequentemente o idoso, sendo considerada a principal causa do aumento da prevalência da incapacidade. A sarcopenia tem um grande impacto na capacidade funcional de um indivíduo. A diminuição da força muscular e da tolerância ao exercício leva à diminuição da capacidade das atividades de vida diária e conseqüentemente ao aumento da dependência (MACEDO, GAZZOLA e NAJAS, 2008; WALSTON et al. 2006).

Outro fator importante a ser considerado são as modificações ocorridas no sistema cardiovascular com o envelhecimento que não resultam em doenças cardíacas por si, porém comprometem a capacidade de reserva cardíaca e pode afetar o limiar de sinais e sintomas, bem como agravar o processo de uma patologia cardíaca já instalada (LAKATTA e LEVY, 2003). Pode-se observar com o avanço da idade alterações na estrutura e função das artérias (dilatação da luz da artéria, aumento da rigidez, diminuição da complacência, disfunção endotelial) (LAKATTA, 2008), bem como alterações do padrão de enchimento diastólico, aumento e alterações do colágeno no ventriculo esquerdo e aumento da prevalência e complexidade de arritmias supraventriculares e ventriculares (LAKATTA e LEVY, 2003). É claro também o aumento da incidência de doenças cardíacas com o envelhecimento (LAKATTA e LEVY, 2003). Somado a isso, tem sido observado que com o avanço da idade o controle autonômico da FC também sofre modificações constatadas por uma redução da variabilidade da freqüência cardíaca (VFC) (CATAI et al, 2002; JENSEN-URSTAD et al, 1997; LAKATTA e LEVY, 2003; LIPSITZ et al, 1990; MELO et al, 2005; PAGANI et al, 1986).

A VFC é o termo utilizado para indicar as oscilações entre freqüências cardíacas instantâneas consecutivas, ou no intervalo entre batimentos cardíacos, oscilações estas que são moduladas por vários fatores, dentre eles o principal é o sistema nervoso simpático e parassimpático no nó sinoatrial (TASK FORCE, 1996). A VFC pode ser analisada no domínio do tempo (DT), a partir de métodos estatísticos, obtendo-se índices, como o RMSSD (raiz quadrada da somatória da diferença entre os intervalos RR e seu adjacente elevada ao quadrado, dividido pelo número de intervalos RR num determinado período menos um) e o SDNN (desvio padrão dos intervalos RR) dos intervalos R-R que apresentam relação com a atuação vagal e com a variabilidade total, respectivamente, e também no domínio da freqüência (DF), que por meio da análise espectral, decompõe a VFC em componentes oscilatórios fundamentais, sendo que os principais são: a) componente de alta freqüência (AF) com faixa de variação de 0,15 a 0,4Hz, que corresponde à modulação respiratória e é um indicador da atuação do nervo vago sobre o coração; b) componente de baixa freqüência (BF), com faixa de variação entre 0,04 a 0,15Hz, que é decorrente da ação conjunta do componente vagal e simpático sobre o coração, sendo o componente simpático predominante, portanto, esta banda de freqüência tem sido utilizada como um marcador da modulação simpática atuante no coração; c) componente de muito baixa freqüência (MBF), com faixa de variação entre 0 e 0,04Hz, cuja explicação fisiológica não está bem definida e parece estar relacionada ao sistema renina-angiotensina-aldosterona, termoregulação e tônus vasomotor periférico. (TASK FORCE, 1996).

Estudos relatam que o treinamento físico aeróbio de longa duração possui ações benéficas no controle autonômico da FC (CATAI et al, 2002; MELO et al, 2005; NOVAIS et al, 2004, STEIN et al 1999), no entanto, o efeito do treinamento contra resistência, aqui denominado como exercício resistido, ainda não está esclarecido. Na literatura existem recomendações para a realização deste tipo de treinamento principalmente para a população idosa (ACSM, 1998; MACALUSO e De VITO, 2004). Isto se deve aos inúmeros benefícios que este proporciona não somente no ganho de força como também na melhora da densidade mineral óssea, sensibilidade à insulina e melhora na qualidade de vida (CIOLAC e GUIMARÃES, 2002; EVANS, 1999; MACALUSO e De VITO, 2004; WILLIAMS, HIGGINS e LEWEK, 2002).

Dentre os tipos de exercícios utilizados para o treinamento resistido, a literatura refere que o exercício isocinético é a única maneira de sobrecarregar um músculo que está se contraindo dinamicamente até sua capacidade máxima em todos os pontos da amplitude de movimento (DVIR, 2002). Por sua vez, a contração excêntrica tem sido cada vez mais estudada e recomendada nos programas de treinamento contra resistência (ACSM, 2002; HATHER et al, 1991; OVEREND et al, 2000; POULIN et al, 1992). A literatura relata que esta contração é mais apropriada para idosos, pois proporciona maior ganho de força, acompanhado de maior síntese protéica, além de sua ação sobre o tecido conjuntivo e menor sobrecarga cardiovascular gerada (MACALUSO e De VITO, 2004; OVEREND et al, 2000; POULIN et al, 1992).

A menor resposta cardiovascular observada na contração excêntrica é explicada pelas características especiais da mesma, ou seja, ela ocorre durante o alongamento muscular. Portanto uma parte da força gerada é decorrente da energia potencial armazenada nos componentes elásticos do músculo, e não exclusivamente do recrutamento de fibras musculares (MEYER et al, 2003).

Dentro deste contexto, a primeira parte deste trabalho se firma na tentativa de elucidar a influência de um período de treinamento de força excêntrica dos músculos extensores e flexores do joelho, realizado em dinamômetro eletrônico, na modulação autonômica da FC avaliada por meio da resposta da FC e VFC durante um teste de função autonômica, o exercício isométrico. Os resultados deste estudo levaram a questionamentos principalmente relativos a metodologias de análise da VFC. Devido às características do sinal, durante o exercício isométrico, somente foi possível a realização da análise da VFC no domínio do tempo. Em busca de novas formas de análise da VFC foi desenvolvido o segundo estudo.

Este segundo trabalho teve como objetivo explorar novas técnicas para avaliação da modulação autonômica da FC e contou com a parceria do Prof Dr. Nicola Montano e Prof Dr. Alberto Porta, ambos da Università degli Studi di Milano/Itália. Neste estudo optou-se pelo uso de metodologia não linear ao invés das tradicionais (DT e DF), aplicada aos dados coletados no Brasil.

Os métodos tradicionais apresentam uma importante limitação, uma vez que os resultados obtidos são muito sensíveis a definição das bandas de oscilações (principalmente na definição do limite inferior da banda de BF, ou seja, geralmente 0,04 Hz, e na abrangência da banda de AF em torno da frequência respiratória). Em contrapartida, índices baseados em métodos não lineares não necessitam de qualquer definição de bandas de frequências (PORTA et al, 2007c). Outra consideração importante é que todos os índices baseados na densidade espectral de potência são úteis apenas em condições caracterizadas por alterações recíprocas da modulação simpática e parassimpática. Assim, mudanças não recíprocas da modulação neural cardíaca permanecem indeterminadas. De fato, a BF e AF expressas em unidades normalizadas e a razão BF/AF foram propostas sob a hipótese de que o aumento da modulação simpática corresponde a uma diminuição da modulação vagal equivalente. (PORTA et al, 2007c).

Assim, índices não lineares podem fornecer resultados mais estáveis e reprodutíveis e também identificar anormalidades e alterações não aparentes (HUIKURI, MAKIKALLIO e PERKIOMAKI, 2003; LIPSITZ e GOLDBERGER, 1992; MÄKIKALLIO et al, 2002). Além disso, os métodos não lineares são por si mais adequados para extrair informações relevantes relacionadas à complexidade (HUIKURI et al, 2000; HUIKURI MAKIKALLIO e PERKIOMAKI, 2003).

Dessa forma no segundo estudo foi realizada a análise da complexidade da VFC por meio do cálculo da entropia de Shannon, entropia condicional e análise simbólica para detectar as modificações causadas pelo processo de envelhecimento na modulação autonômica da FC.

Os estudos desenvolvidos são apresentados a seguir. O primeiro estudo foi publicado no periódico *European Journal of Applied Physiology* e o segundo foi submetido ao periódico *Journal of Gerontology: Medical Sciences.* Os textos originais estão apresentados nos ANEXOS A e B, respectivamente.

2. Primeiro estudo.

(Versão em português com inclusão de ilustrações)

EFEITO DO TREINAMENTO DE FORÇA EXCÊNTRICA NA FREQUÊNCIA CARDÍACA E SUA VARIABILIDADE DURANTE O EXERCÍCIO ISOMÉTRICO EM IDOSOS SAUDÁVEIS.

Takahashi ACM; Quitério RJ; Melo RC; Silva E; Catai AM. The effect of eccentric strength training on heart rate and on its variability during isometric exercise in healthy older men. **European Journal of Applied Physiology** , v. 105, n. 2, p. 315-323, 2009.

2. PRIMEIRO ESTUDO.

EFEITO DO TREINAMENTO DE FORÇA EXCÊNTRICA NA FREQUÊNCIA CARDÍACA E SUA VARIABILIDADE DURANTE O EXERCÍCIO ISOMÉTRICO EM IDOSOS SAUDÁVEIS.

2.1 RESUMO:

O objetivo deste estudo foi investigar se o treinamento de força excêntrica (TFE) modifica a frequência cardíaca (FC) e variabilidade da frequência cardíaca (VFC) durante contrações voluntárias isométricas submáximas (CVIS). O grupo treinamento (GT) (9 homens, 62 ± 2 anos) foi submetido ao TFE (12 semanas, 2 dias/semana, 2-4 séries de 8-12 repetições a 75-80% do pico de torque (PT)). O grupo controle (CG) (8 homens, 64 ± 4 anos) não realizaram o TFE. A FC e a VFC (índice RMSSD) foram avaliadas durante CVIS de extensão do joelho (15, 30 e 40% do PT). Somente o GT apresentou aumento do torque excêntrico, porém o treinamento não alterou o PT isométrico, nem o tempo de realização das CVIS. Durante as CVIS, o padrão de resposta da FC e o índice RMSSD dos intervalos RR, em ms, foram semelhantes nos dois grupos tanto nas avaliações pré e pós treinamento. Embora o TFE tenha aumentado o torque excêntrico no GT, ele não gerou mudanças na FC ou na VFC durante as CVIS.

Palavras-chave: Frequência cardíaca. Sistema nervoso autônomo. Variabilidade da frequência cardíaca. Exercícios isométricos. Treinamento de força.

2.2 INTRODUÇÃO

A variabilidade da frequência cardíaca (VFC) é uma medida não-invasiva utilizada para analisar a influência do sistema nervoso autonômico sobre o coração, fornecendo informações sobre a modulação simpática e parassimpática nas oscilações da frequência cardíaca (FC) (TASK FORCE, 1996). A VFC diminui com a idade (CATAI et al, 2002; JENSEN-URSTAD et al, 1997; LAKATTA e LEVY 2003; LIPSITZ et al, 1990; MELO et al, 2005; PAGANI et al. 1986) como consequência da redução da modulação parassimpática e predomínio da simpática (LIPSITZ et al, 1990). Este fato apresenta um importante impacto clínico no envelhecimento, uma vez que valores reduzidos de VFC podem estar associados à maior morbidade e mortalidade cardiovascular (BIGGER et al, 1992).

O treinamento aeróbio de longa duração parece melhorar a VFC em homens mais velhos e, consequentemente, poderia ser considerado como uma terapia não-farmacológica (DE MEERSMAN 1993; MELO et al, 2005; STEIN et al, 1999). Na verdade, o exercício aeróbio desempenha um papel importante na manutenção da capacidade de trabalho físico em idosos (MCGUIRE et al, 2001), mas os efeitos do envelhecimento sobre o sistema muscular só podem ser reduzidos a partir do treinamento de força (ACSM et al, 1998; EVANS 1999; FRONTERA et al, 1988; MACALUSO e DE VITO 2004; WILLIAMS, HIGGINS e LEWEK, 1995). Entre os tipos existentes de contração, a excêntrica tem sido recomendada para os programas de treinamento de força, pois leva à hipertrofia sem sobrecarregar o sistema cardiovascular (isto é, menores valores de FC, pressão arterial e consumo de oxigênio para o mesmo valor de torque na contração concêntrica) (HUGGET et al, 2004; LASTAYO et al, 1999; OVEREND et al, 2000).

Poucos estudos avaliaram os efeitos do treinamento de força sobre o controle autonômico da FC e na maioria destes não foram observadas quaisquer alterações na VFC (COOKE e CARTER 2005; FORTE et al, 2003; HEFFERNAN et al, 2007; MADDEN,LEVY STRATTIN, 2006). Por outro lado, a sobrecarga sobre o sistema cardiovascular durante o exercício excêntrico é menor do que em outros tipos de contrações (HUGGET et al, 2004; LASTAYO et al, 1999; OVEREND et al, 2000), por isso é de se esperar uma não modificação no controle autonômico da FC. No entanto, em um estudo anterior realizado em nosso laboratório (MELO et al, 2008), observou-se que o treinamento excêntrico de alta intensidade, causou um desequilíbrio autonômico, induzido por um mecanismo desconhecido, no sentido de uma predominância da modulação simpática. Por isso, seria importante esclarecer, por meio de mais estudos, se o treinamento excêntrico tem um efeito desfavorável sobre o controle autonômico da FC.

Os métodos mais comuns utilizados para análise da VFC incluem análises no domínio do tempo e da frequência. O método no domínio do tempo fornece informações sobre a magnitude das variações dos intervalos RR (iRR) em torno do valor médio de iRR. Este método é utilizado para avaliar a modulação parassimpática sobre o nó sinusal durante diferentes condições como de repouso e exercício (MALIK et al, 1996). Outro teste de função autonômica bem difundido é a avaliação da resposta da FC durante o exercício isométrico (HONLOSER e KLINGENHEBEN 1998; GALVEZ et al, 2000; MACIEL et al, 1987; MACIEL et al, 1989; IELLAMO et al, 1997; SILVA et al, 1999). A vantagem de se utilizar o exercício isométrico como teste autonômico, em vez de condições de repouso, é poder avaliar as interações entre os sistemas cardiovascular e musculoesquelético, de forma não invasiva, sendo interessante sua utilização em avaliações após um período de treinamento de força muscular.

Programas de treinamento de força excêntrica são reconhecidos como um importante componente terapêutico na melhora da força muscular, que diminui com a idade (EVANS, 1999; FRONTERA et al, 1988; MACALUSO e DE VITO 2004, WILLIAMS, HIGGINS e LEWEK, 1995). No entanto, não está claro se este tipo de treinamento de força pode trazer benefícios ou efeitos nocivos para a modulação autonômica da FC. Com base nessas considerações, optou-se analisar a resposta da FC e a VFC durante um teste de função autonômica (exercício isométrico), com intuito de avaliar se o TFE afeta o controle autonômico da FC durante as CVIS.

2.3 MÉTODOS

2.3.1 Voluntários

Trinta idosos aparentemente saudáveis (faixa etária de 60-69 anos) voluntariamente participaram deste estudo, porém apenas vinte e dois cumpriram os critérios de seleção. Dos doze participantes atribuídos ao grupo treinamento (GT), apenas nove completaram o programa de TFE, enquanto que no grupo controle (GC), apenas oito, dos dez voluntários, completaram as avaliações. Todos os voluntários foram considerados aparentemente saudáveis, com base no exame clínico e físico, bem como em testes de laboratório, que incluiu: eletrocardiograma de repouso (ECG), teste de esforço máximo realizado por um médico, radiografia de tórax, hemograma completo, exame de urina e testes bioquímicos (glicose, ácido úrico, creatinina, uréia, colesterol total e frações e triglicérides). Os critérios de exclusão consistiram: presença de hipertensão arterial, diabetes mellitus, doença pulmonar obstrutiva crônica, lesões neurológicas, cardiovasculares, respiratórias e/ou musculoesquelética. Fumantes, etilistas ou voluntários que faziam uso de qualquer tipo de medicação ou que tinham participado de um programa regular de treinamento de força no período de 6 meses anteriores ao estudo, também foram excluídos. Todos os voluntários foram informados sobre os procedimentos experimentais e assinaram um termo de consentimento livre e esclarecido. Este estudo foi aprovado pelo Comitê de Ética da Instituição.

2.3.2 Procedimentos experimentais

Todos os experimentos foram realizados em sala com temperatura ambiente controlada (22-23° C), umidade relativa do ar entre 50 e 60% e no mesmo período do dia, considerando as influências do ciclo circadiano. Foi dado um intervalo de 5 a 7 dias entre as realizações dos protocolos. Os indivíduos foram familiarizados com a sala de experimento, com os procedimentos e os equipamentos a serem utilizados. Todos os voluntários foram instruídos a evitar cafeína e bebidas alcoólicas, bem como evitar a realização de qualquer exercício moderado ou intenso na véspera do protocolo aplicado. No dia do experimento, antes do teste, os indivíduos foram entrevistados e examinados para confirmar sua condição de saúde, a ocorrência de uma noite de sono regular, e para verificar se os valores de FC e pressão arterial sistêmica estavam dentro da normalidade.

Durante o protocolo II, descrito a seguir, os sujeitos foram monitorizados na derivação MC5 para o registro da FC e dos intervalos RR. O eletrocardiograma (ECG) e a FC foram obtidos a partir de um monitor cardíaco de um canal (TC 500, ECAFIX, São Paulo, SP, Brasil) conectado a um microcomputador por meio de uma placa A/D (*National Instruments Corporation, Austin*, TX, E.U.A.). A frequência de amostragem foi de 500 Hz. Os intervalos RR (ms) foram calculados batimento a batimento, utilizando um software específico (Silva et al. 1994). Durante a gravação do ECG, a frequência respiratória foi observada e se manteve na faixa de normalidade. Além disso, para todos os protocolos de exercício (ou seja, os protocolos I, II, III e IV), que são descritos a seguir, foi realizada a medida não invasiva da pressão arterial (PA) antes e após cada esforço, usando o método auscultatório. O VO_2 máximo/pico foi determinado para assegurar que todos os voluntários possuíam a mesma classificação funcional. O VO_2 máximo/pico foi obtido por meio de um teste ergoespirométrico de carga incremental até a exaustão, em cicloergômetro (CPX-D, Medical

Graphics, St Paul, MN, E.U.A.). A exaustão foi definida pela: 1) incapacidade de manter uma velocidade em torno de 60 rpm; 2) presença de platô nas respostas do consumo de oxigênio mesmo com um aumento na carga de trabalho (VO_2 máximo), 3) FC máxima prevista para a idade e 4) razão de troca respiratória> 1,1. Dois ou mais dos critérios citados deveriam ser observados, a fim de classificar os indivíduos.

2.3.3 Protocolo experimental

2.3.3.1 Protocolo I: contração voluntária isométrica máxima (CVIM)

A CVIM de extensão do joelho da perna dominante foi testada a 60° de flexão do joelho (extensão completa = 0^o), usando um dinamômetro isocinético (*Biodex Multi Joint System III, Biodex Medical System Inc., Shirley, NY,* E.U.A.). A célula de carga foi calibrada antes de cada teste, posicionando e estabilizando o braço de alavanca paralelamente ao chão e anexando um peso conhecido. Antes do teste, os voluntários realizaram um aquecimento de 4 minutos em cicloergômetro, seguido de alongamento dos músculos quadríceps e isquiotibiais. A seguir, os voluntários foram posicionados na cadeira do dinamômetro (ângulo de encosto do banco = 90°) e foram estabilizados por cintas na pelve, tórax e coxa. O eixo de rotação do dinamômetro foi alinhado com o epicôndilo lateral do fêmur e a resistência foi posicionada distalmente acima do maléolo, permitindo dorsiflexão completa. O fator de correção da gravidade (torque adicional devido ao peso da perna e das almofadas de resistência) foi determinado em 60° de flexão de joelho com a musculatura relaxada.

Os indivíduos realizaram 3 CVIM (duração = 10 segundos), com um período de repouso de 10-15 minutos entre cada repetição. Durante a CVIM, os voluntários foram incentivados verbalmente e instruídos a: ficarem atentos ao *feedback* visual gerado pela tela do computador do dinamômetro isocinético; evitarem a contração de outros músculos; manterem a respiração espontânea para evitar a ocorrência da manobra de Valsalva, que pode ser verificada pela ausência de bradicardia após cada contração. O maior valor obtido da série foi utilizado como pico de torque isométrico (PT) (Nm). A ilustração do procedimento experimental é mostrada na figura 1.

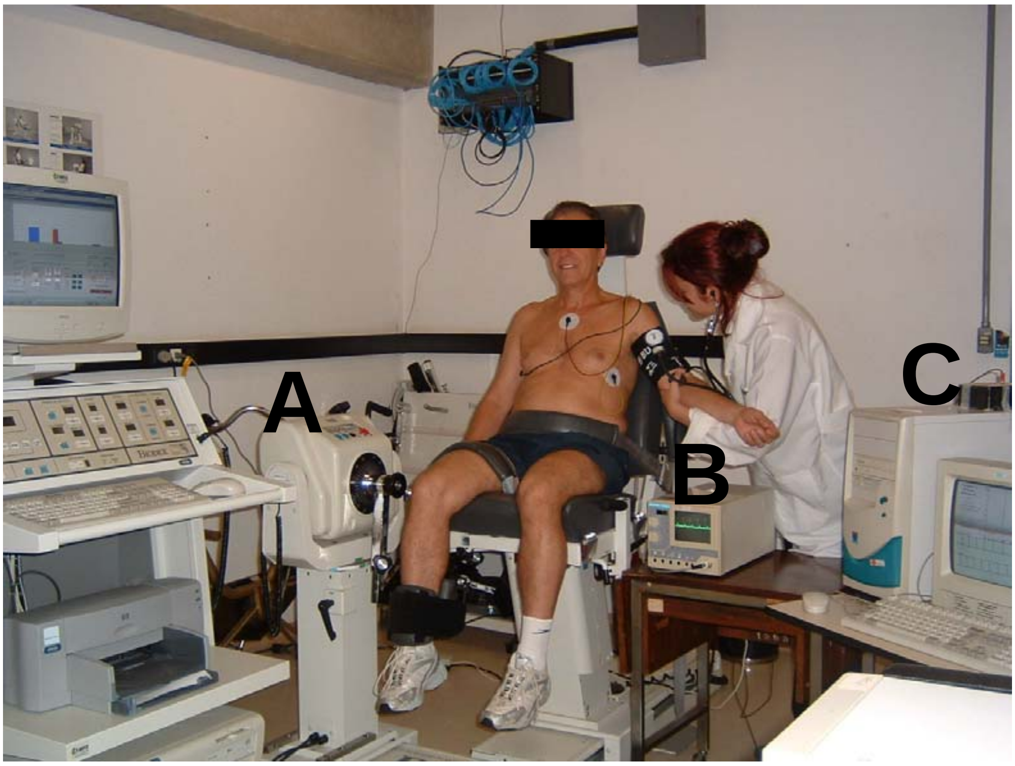


Figura 1: Ilustração do procedimento experimental: A) dinamômetro isocinético e acessórios, B) monitor cardíaco, C) sistema de captação da freqüência cardíaca, batimento a batimento.

2.3.3.2 Protocolo II: Contrações voluntárias isométricas submáximas (CVIS)

Os voluntários foram submetidos a três contrações voluntárias isométricas submáximas (CVIS) de extensão de joelho. A primeira intensidade de contração realizada foi de 15%, seguida de 30% e por último 40% do PT isométrico determinado no protocolo I. Os procedimentos relacionados com a calibração do dinamômetro isocinético, preparação dos voluntários e instruções durante o teste foram os mesmos descritos no protocolo I. As contrações submáximas foram realizadas em uma ordem fixa (isto é, 15, 30 e 40%), com 15-20 minutos de intervalo entre cada intensidade. Este período de recuperação foi elaborado para garantir que a FC e a pressão arterial retornassem aos valores basais. Além disso, esta sequência foi adotada a fim de reduzir as chances de que contrações mais intensas, realizadas anteriormente, afetassem as respostas cardiovasculares das contrações de menor intensidade (TURLEY et al, 2002).

Cada contração submáxima foi mantida por 240 segundos, ou até a exaustão, que foi confirmada pela incapacidade de manutenção do torque estipulado por mais de 5 segundos (HUNTER, CRITCHOLOW e ENOKA, 2005). A verificação da intensidade da contração foi realizada por meio da visualização do torque, em tempo real, na tela do monitor do dinamômetro (Figura 2).

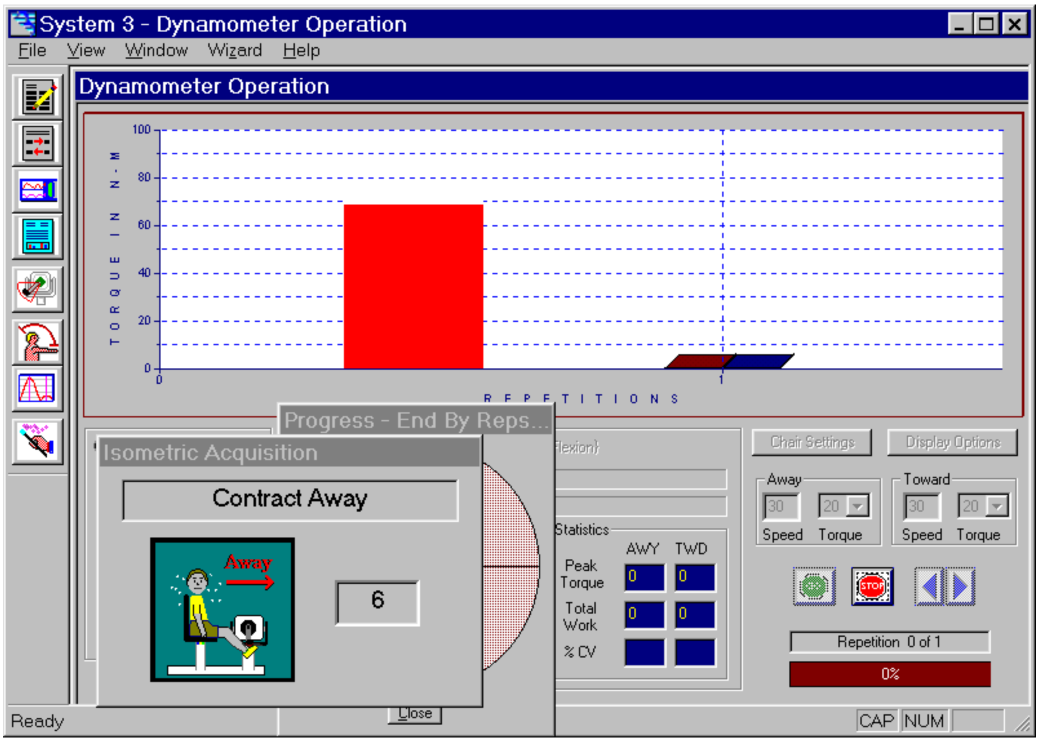


Figura 2: Ilustração da tela do monitor do dinamômetro isocinético mostrando a visualização do torque realizado por um dos voluntários em tempo real.

Neste protocolo, a FC foi registrada no repouso (60 segundos), durante a contração isométrica submáxima e nos primeiros 2 minutos de recuperação, conforme ilustrado na Figura 3.

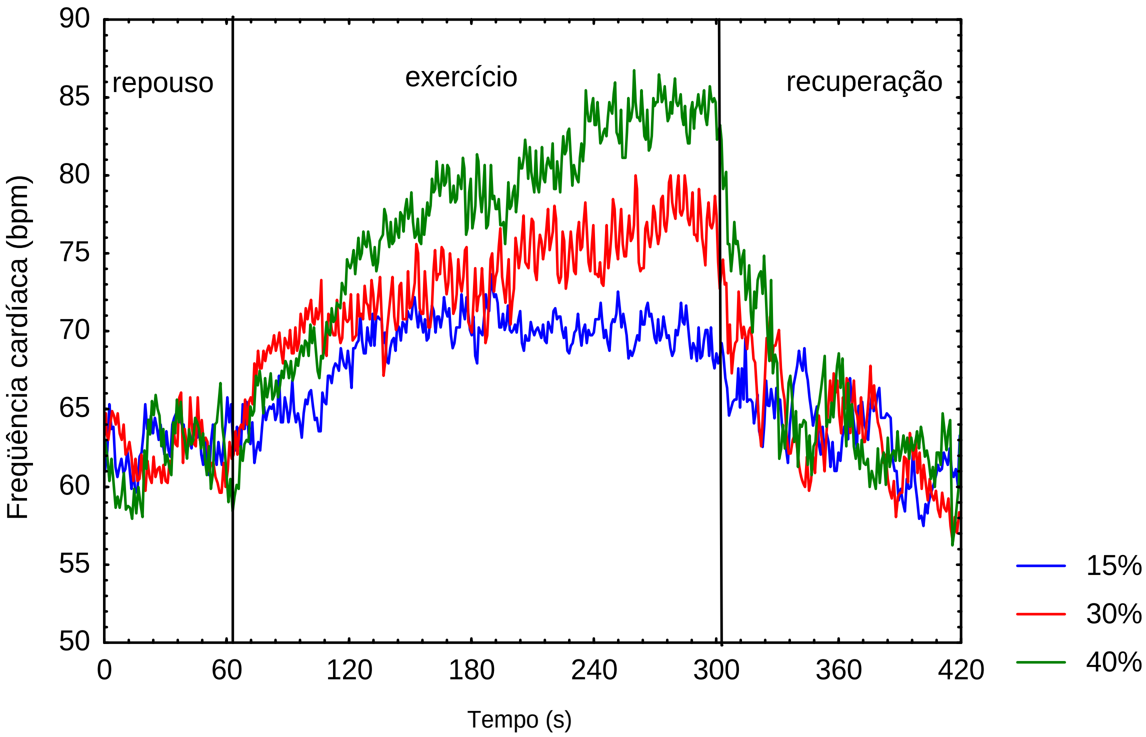


Figura 3: Freqüência cardíaca, batimento a batimento, durante o repouso pré exercício (60s), durante as contrações isométricas submáximas nas intensidades de 15%, 30% e 40% e nos 120s iniciais de recuperação, de um dos voluntários estudados.

2.3.3.3 Protocolo III: Contração voluntária excêntrica máxima

Para estimar os ganhos de força em resposta ao programa de TFE, o PT isocinético excêntrico, da extensão e flexão do joelho foi medido antes e após o período de treinamento. O PT excêntrico foi testado na velocidade de 60°/s, no arco de movimento de 90° a 30° de flexão do joelho (extensão total = 0°), usando o modo reativo (ou seja, ciclos excêntrico/excêntrico) do dinamômetro isocinético (*Biodex Multi Joint System III*, *Biodex Medical System Inc.*, *Shirley*, NY, E.U.A.). Os procedimentos relacionados com a calibração e de preparação dos voluntários foram os mesmos descritos no protocolo I. Os indivíduos realizaram três séries de cinco contrações, com um período de repouso de 120 segundos entre cada série. O maior valor obtido de todos os esforços máximos foi utilizado como PT excêntrico (Nm).

2.3.3.4 Protocolo IV: Programa de treinamento de força excêntrica

O programa constou de 2-4 séries de 8-12 repetições de flexão e extensão de joelho no modo excêntrico. O treinamento foi realizado em ambas as pernas e utilizando o mesmo dinamômetro isocinético do protocolo III. Os voluntários foram treinados 2vezes/semana, durante 12 semanas, com uma resistência de aproximadamente 70-80% do PT

(MACALUSO e DE VITO 2004, ACSM et al, 2002). Cada série foi seguida por um período de 2 minutos de repouso. O arco de movimento e a velocidade foram os mesmos utilizados na avaliação inicial (Protocolo III). O PT foi determinado no início do período de treinamento e a cada duas semanas, com objetivo de reajustar a intensidade do TFE. Cada sessão de treino começou com um aquecimento de quatro minutos em bicicleta ergométrica seguido por alongamento dos músculos quadríceps e isquiotibiais.

2.3.4 Análise de Dados

Para analisar a resposta da FC durante uma contração isométrica, foram calculadas a variação (Δ) entre a FC de repouso (60s pré contração) e a FC nos 10s, 30s, 60s, e ao final da contração (Δ10s, Δ30s, Δ60S e Δfinal, respectivamente).

A VFC foi analisada no domínio do tempo, utilizando o índice RMSSD dos iRR em ms (raiz quadrada da somatória da diferença entre o iRR e seu adjacente elevada ao quadrado, dividido pelo número de intervalos RR num determinado período menos um), que representa a modulação parassimpática sobre o nó sinusal (MALIK et al, 1996).

Para avaliar o controle autonômico da FC durante a CVIS, o índice de RMSSD foi calculado para os primeiros e últimos 30 segundos da série de iRR, em cada contração.

2.3.5 Análise Estatística

O teste t não pareado foi utilizado para comparar as características dos voluntários entre o GT e o GC. As demais variáveis foram analisadas pela ANOVA de medidas repetidas. Quando necessário, o teste de Tukey foi utilizado para a análise *post-hoc*. Os efeitos do tempo (pré *vs* pós treinamento), do grupo (GT vs GC) e interação entre estes foram avaliados para o PT excêntrico, o PT isométrico e duração da CVIS. Os efeitos do tempo, do grupo, da intensidade de contração isométrica (15% vs 30% vs 40%), do tempo de contração (10 segundos vs 30 segundos vs 60 segundo vs final da contração) e a interação entre estes efeitos foram avaliados para a Δ da FC durante o exercício isométrico. Para o índice RMSSD foram avaliados os efeitos do tempo, do grupo, da intensidade de contração, o momento da contração (primeiros 30 segundos *vs* os últimos 30 segundos) e interação entre esses efeitos. Os valores do índice RMSSD foram transformados em logaritmos naturais, pois esta variável apresentou distribuição não normal. Todos os dados foram apresentados em média ± desvio padrão e o nível de significância adotado foi $P<0,05$. As análises foram realizadas no *software Statistica for Windows* 7.0 (programa de computador manual, StatSoft, Inc., 2004).

2.4 RESULTADOS

A Tabela 1 apresenta as características dos voluntários. Não foram encontradas diferenças entre os GT e GC. O teste ergoespirométrico indicou que ambos os grupos apresentaram uma capacidade aeróbia média, de acordo com a classificação da *American Heart Association* (COOPER e STOKER, 2001).

Tabela 1: Características dos voluntários.

Características	Grupo treinamento	Grupo controle
Idade (anos)	62 ± 2	64 ± 4
Massa corporal (kg)	72,4 ± 7,6	74,5 ± 8,9
Altura (cm)	168,3 ± 5,5	167,1 ± 4,1
IMC (kg/m^2)	25,5 ± 1,8	26,6 ± 2,6
VO_2 pico ($mL.kg^{-1}.min^{-1}$)	25,93 ± 4,8	26,2 ± 4,9

Dados em média ± DP

2.4.1 Tempo de contração e torque

A Tabela 2 apresenta o PT excêntrico (flexor e extensor), o PT isométrico e a duração de cada CVIS. Não foram observadas alterações significativas no PT isométrico e no tempo de execução de cada CVIS após o TFE em ambos os grupos. No entanto, para PT excêntrico houve interação entre os efeitos tempo e grupo, ou seja, um aumento significativo na força excêntrica apenas para GT.

Tabela 2: Pico de torque excêntrico e isométrico (N.m) e duração das contrações isométricas submáximas.

	Grupo treinamento		**Grupo controle**	
	1ª avaliação	**2ª avaliação**	**1ª avaliação**	**2ª avaliação**
Pico de torque excêntrico (N.m)				
Extensor	210 ± 38	253 ± 61*	203 ± 33	215 ± 40
Flexor	118 ± 25	133 ± 27*	126 ± 20	135 ± 26
Pico de torque isométrico (N.m)	178 ± 25	195 ± 32	172 ± 27	176 ± 26
Tempo de duração da CVIS (s)				
15%	240 ± 0	240 ± 0	240 ± 0	240 ± 0
30%	204 ± 54	224± 37	189 ± 66	205 ± 56
40%	137 ± 58	146 ± 52	132± 67	152 ± 56

CVIS= contração voluntária isométrica submáxima. Dados em média ± DP, **P*< 0,05 em comparação ao pré treinamento.

2.4.2 Respostas de FC durante a contração isométrica

A Tabela 3 mostra as variações da FC do repouso para o exercício durante as CVIS para o GT e GC nas avaliações pré e pós treinamento.

Não houve efeito de grupo e tempo na ΔFC durante a CVIS, ou seja, os dois grupos tiveram respostas semelhantes nas avaliações pré e pós treinamento.

No entanto, a interação entre o nível de esforço e tempo de contração foi significativa (*P* <0,05). A ΔFC no final da contração foi significativamente diferente da ΔFC aos 10, 30 e 60 segundos para as intensidades de 30% e 40% da CVIM. Além disso, as ΔFC nos 10, 30 e 60 segundos, apresentaram significância estatística entre as intensidades 15% e 40%. Ainda a ΔFC ao término da contração foi significativamente diferente entre as intensidades de 15% e 40%, entre 15% e 30%, e entre 30% e 40% da CIVM.

Tabela 3: Variações da FC (Δ FC) do repouso para o exercício.

	Grupo treinamento		Grupo controle	
	1ª avaliação	2ª avaliação	1ª avaliação	2ª avaliação
ΔFC (bpm) - 15%CVIM				
10 s	4 ± 6†	2 ± 3†	1 ± 4†	0 ± 3†
30 s	3 ± 5†	2 ± 3†	2 ± 5†	2 ± 2†
60 s	4 ± 4†	5 ± 3†	2 ± 3†	2 ± 4†
Final da contração	5 ± 5†,‡	5 ± 4†,‡	5 ± 3†,‡	4 ± 2†,‡
ΔFC (bpm) - 30% CVIM				
10 s	6 ± 3	3 ± 3	5 ± 5	2 ± 4
30 s	7 ± 4	8 ± 7	8 ± 3	5 ± 5
60 s	11 ± 5	9 ± 6	10 ± 6	8 ± 8
Final da contração	16 ± 6*,†	17 ± 8*,†	17 ± 5*,†	17 ± 9*,†
ΔFC (bpm) - 40% CVIM				
10 s	10 ± 7	10 ± 6	8 ± 4	6 ± 6
30 s	10 ± 8	11 ± 9	12 ± 7	11 ± 4
60 s	14 ± 6	15 ± 8	14 ± 8	13 ± 8
Final da contração	25 ± 11*	26 ± 13*	28 ± 10*	31 ± 17*

Dados em média ± DP. CVIM = contração voluntária isométrica máxima; ΔFC = variação da frequência cardíaca do repouso para o exercício. * P <0,05 em comparação a ΔFC nos 10s, 30s, 60s de contração (efeito do tempo de contração). † P <0,05 em comparação a 40% (efeito da intensidade de contração). ‡ P <0,05 em comparação a 30% (efeito da intensidade de contração).

2.4.3 VFC durante as contrações isométricas submáximas

A Figura 4 apresenta os valores do índice RMSSD dos iRR em ms calculados para duas janelas pré selecionadas (ou seja, 30 segundos iniciais e 30 segundos finais da série dos intervalos RR). Foi observada interação entre os efeitos intensidade de contração e momento da contração (primeiros 30 segundos *vs* últimos 30 segundos) (P<0,05). Uma diminuição significativa no índice RMSSD foi observada durante a contração isométrica de 30% e 40% da CVIM. Além disso, o índice RMSSD dos últimos 30 segundos nas intensidades 30% e 40% foram inferiores aos 30s finais em 15%. Não foram observados efeitos de grupo, nem de tempo no índice RMSSD durante o exercício isométrico, ou seja, as respostas foram semelhantes para os dois grupos na primeira e na segunda avaliação.

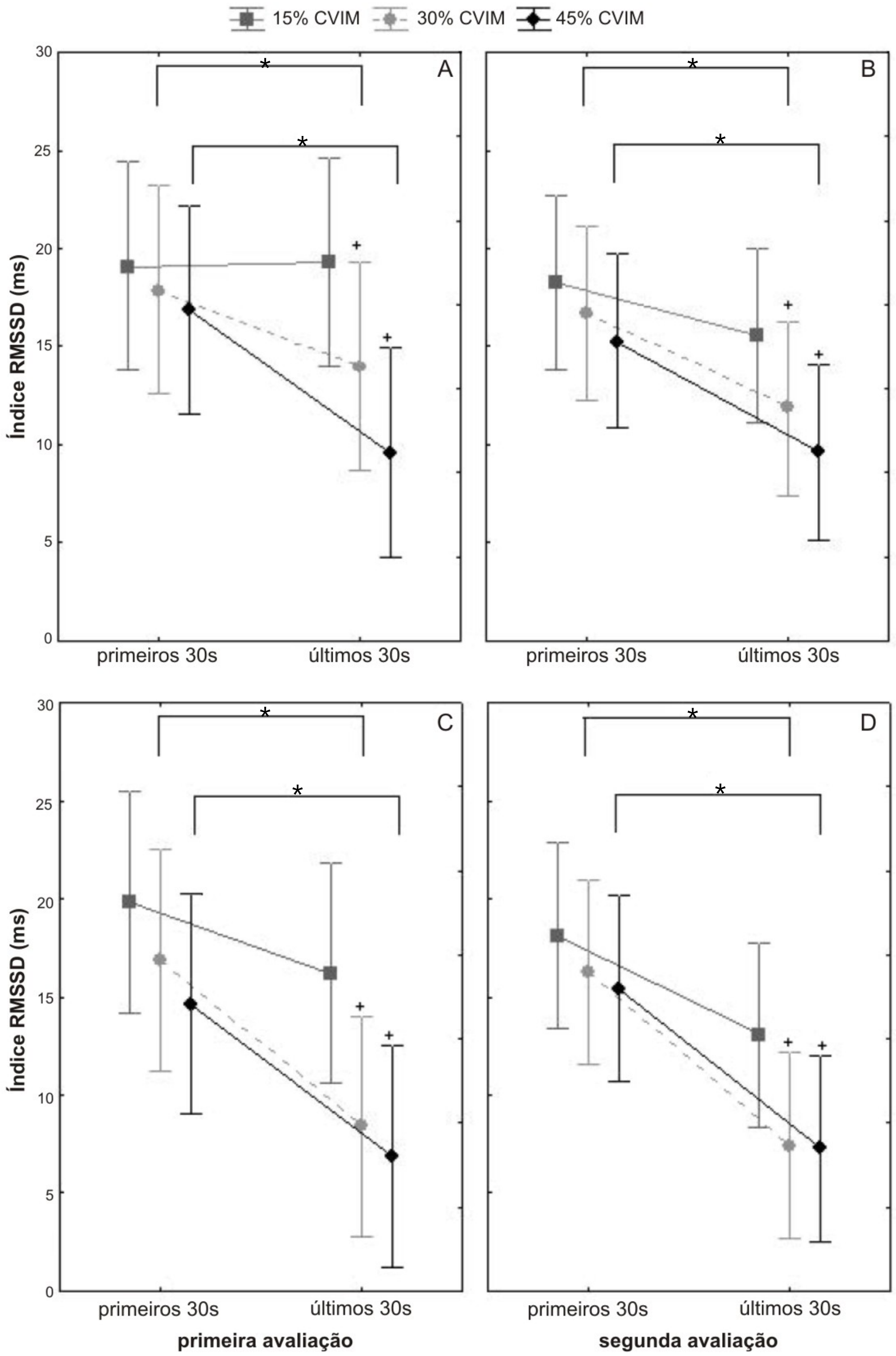


Figura 4: Índice RMSSD nos primeiros e nos últimos 30 segundos das contrações isométricas submáximas para o grupo treinamento - na primeira avaliação pré (A) e na segunda avaliação (B), e para o grupo controle - na primeira (C) e na segunda avaliação (D). CVIM = contração voluntária isométrica máxima. Dados em média ± DP. *$P<0{,}05$ em comparação com os últimos 30 segundos das contrações. $^{+}P<0{,}05$ na comparação dos últimos 30 segundos na intensidade de 15% CVIM.

2.5 DISCUSSÃO

Foi observado ganho de força após o período de treinamento somente na contração excêntrica, o que demonstra a especificidade do treinamento utilizado. Nossos dados são concordantes com Symons et al. (2005) e Paddon-Jones et al. (2001), que também relataram maiores ganhos de força no tipo de contração em que foi realizado o treinamento. Quanto ao tempo de contração isométrica submáxima, este não foi alterado com o treinamento aplicado, possivelmente devido à especificidade dos exercícios realizados (flexão e extensão do joelho de modo excêntrico). No entanto, Ray e Carrasco (2000) adotaram em seu treinamento contrações isométricas submáximas e também não observaram alterações no tempo de manutenção das contrações isométricas.

Estudos prévios com bloqueio farmacológico (MACIEL et al, 1985; MACIEL et al, 1987; MARTIN et al, 1974) relatam que o padrão de resposta da FC ao exercício isométrico é baseado em um mecanismo bifásico, que é dependente do tempo. No início da contração, a elevação rápida da FC ocorre devido à retirada vagal. Com a manutenção do exercício isométrico, uma taquicardia gradual torna-se evidente e é atribuída à modulação simpática. Este padrão de resposta da FC foi observado em nosso estudo e também por autores que não usaram bloqueio farmacológico (HUNTER, CRITCHOLOW e ENOKA 2005; IELLAMO et al, 1997; MACIEL et al. 1989, RAY e CARRASCO, 2000; SEALS 1993).

A resposta da FC ao exercício isométrico está também relacionada à intensidade da contração, sendo que a magnitude da taquicardia é dependente do nível de força executado (GALVEZ et al, 2000; MACIEL et al, 1989; SEALS 1993). Para diferentes grupos musculares, estudos na literatura apresentam um aumento significativo da FC, a partir de níveis de força superiores a 20% da contração voluntária máxima (GALVEZ et al, 2000; HUNTER et al, 2005; IELLAMO et al, 1997; MACIEL et al, 1989; RAY e CARRASCO, 2000; SEALS 1993). Nossos resultados estão de acordo com esses estudos uma vez que, baixa intensidade de contração isométrica (15% CVIM) não provocou um aumento significativo na ΔFC. Além disso, maiores percentuais de CVIM evocaram um maior aumento na FC. Na análise no decurso do tempo, as intensidades de 30% e 40% da CVIM geraram um aumento significativo na ΔFC a partir de 60 segundos até o final da contração.

O treinamento de força excêntrica não modificou a resposta da FC ao exercício isométrico. Estes resultados podem ser atribuídos à especificidade, à duração do treinamento, à massa muscular envolvida (apenas flexores e extensores de joelho), e/ou ao estímulo do treinamento, que pode não ter sido mantido por tempo suficiente durante cada sessão de exercício para influenciar esta variável (cerca de 20 minutos).

Este é o primeiro estudo em que foi enfocado o efeito do treinamento de força excêntrica na resposta da FC ao exercício isométrico realizado por idosos. Outros autores estudaram diferentes tipos de treinamento, tais como resistência aeróbia de membros inferiores (MACIEL et al, 1989) e *handgrip* (RAY e CARRASCO, 2000), mas nenhum observou o efeito do treinamento na resposta da FC durante o exercício isométrico.

Com relação à VFC, o índice RMSSD mostrou uma redução do início para o final da contração em 30% e 40% da CVIM. Adicionalmente, maiores percentuais de CIVM induziram menores valores de RMSSD nos últimos 30 segundos de contração, ou seja, houve uma redução da modulação vagal no final das contrações isométricas de maior intensidade. Iellamo et al. (1999) utilizaram a VFC (análise no domínio da frequência) para avaliar o controle autonômico durante exercício isométrico. Resumidamente, este método fornece a densidade espectral das duas principais faixas de frequência: baixa (0,04-0,15 Hz) e alta (0,15-0,4 Hz), que são representativas das modulações simpática e parassimpática, respectivamente (MALIK et al, 1996). Após esta análise, Iellamo et al. (1999) observaram uma redução significativa nas oscilações de alta frequência em unidades normalizadas e um aumento da baixa frequência na densidade espectral avaliada durante exercício isométrico de extensão do joelho na intensidade de 30% da CVIM. Estes autores sugeriram que uma redução na alta frequência refletiria uma diminuição da modulação parassimpática no nó sinusal e que um aumento na baixa freqüência indicaria uma modulação simpática aumentada. Resultados semelhantes foram observados no presente estudo: redução da modulação parassimpática, avaliada por meio do índice RMSSD, durante a CIS de 30% e 40%. O índice RMSSD é apenas uma medida para a avaliação da modulação vagal, dessa forma a partir deste não se pode fazer afirmações sobre a contribuição simpática durante o exercício isométrico. Além disso, como nossos traçados não eram estacionários, não foi possível realizar a análise no domínio da frequência, que tem como premissa um sinal estacionário para garantir a qualidade e fidedignidade do resultado (TASK FORCE, 1996).

Quanto aos efeitos do treinamento de força sobre a VFC, a maioria dos estudos existentes tem avaliado a VFC somente durante a condição de repouso (COOKE e CARTER 2005; FORTE, De VITO e FIGURA, 2003; HEFFERNAN et al, 2007; MADDEN, LEVY e Stratton, 2006; MELO et al, 2008; TAYLOR et al, 2003). Desses estudos, apenas Taylor et al. (2002) e Melo et al. (2008) relataram alterações na VFC após treinamento de força. Taylor et al. (2002) observaram um aumento nas oscilações de alta frequência de idosos hipertensos, após o treinamento de *handgrip* a 30% CVIM. No entanto, Melo et al. (2008), que avaliaram idosos saudáveis, observaram um desequilíbrio autonômico com predominância da modulação simpática na VFC após treinamento de força excêntrica.

Nossos resultados não mostraram alterações na VFC durante o exercício isométrico. Algumas possíveis explicações para estes resultados poderiam ser as mesmas citadas anteriormente para a não alteração da resposta da FC ao exercício isométrico. Adicionalmente, a VFC diminui com a idade (JENSEN-URSTAD et al, 1997; CATAI et al, 2002; MELO et al, 2005), este fato pode afetar a "treinabilidade" desta variável tornando-a menos sensível ao treinamento de força. Esta idéia também foi sugerida por Forte et al. (2003), ao avaliarem o efeito do treinamento dinâmico de resistência na VFC de mulheres idosas. No entanto, mesmo Cooke e Carter (2005) que estudaram voluntários jovens, não observaram efeito do treinamento de força sobre a VFC no domínio do tempo e da frequência.

Pelo menos duas limitações importantes devem ser enfatizadas. Primeiro, o pequeno número de indivíduos de ambos os grupos, experimental e controle, restringe a aplicação destes resultados para outras populações. Segundo, o comportamento não estacionário da série dos iRR, principalmente nas contrações de intensidade mais elevadas, não nos permitiu aplicar a análise no domínio da frequência para avaliar a VFC. Apesar de Bosquet et al (2008) sugerirem que a variação diária da VFC pode mascarar os resultados da avaliação após períodos de treinamento, procurou-se minimizar os efeitos do ciclo circadiano, realizando todos os testes no mesmo período do dia. Além disso, todas as avaliações foram realizadas em sala com temperatura e umidade do ar controladas e todos os participantes foram instruídos a evitar bebidas alcoólicas, cafeína e atividade física no dia anterior e no dia dos procedimentos experimentais. Finalmente, os sinais foram registrados e processados com base nas diretrizes de avaliação da VFC (TASK FORCE, 1996).

Neste estudo foi explorada a relação entre o efeito do treinamento de força excêntrica e a modulação autonômica da FC avaliada durante o exercício isométrico. Embora o treinamento tenha melhorado a força excêntrica, ele não modificou, positivamente ou negativamente, a resposta da FC ou da VFC (no domínio do tempo) durante o exercício isométrico submáximo. No entanto, mais estudos são necessários para avaliar outros tipos de treinamento e a utilização de outros grupos musculares, assim como a aplicação de análises não lineares da VFC durante a condição de exercício. Além disso, estudos futuros são necessários para elucidar se a combinação de treinamento de força excêntrica e exercícios aeróbios podem provocar efeitos adicionais sobre a VFC.

2.6 AGRADECIMENTOS

Os autores são gratos a Dra. Tania de Fátima Salvini, que permitiu a utilização do dinamômetro isocinético e à FAPESP (Fundação de Amparo à Pesquisa do Estado de São Paulo) pelo apoio financeiro (proc. n º. 06/52860- 0 e 05/54838-9).

3. Segundo estudo.

(Versão em português com inclusão de ilustrações)

O ENVELHECIMENTO REDUZ A COMPLEXIDADE DA VARIABILIDADE DA FREQUÊNCIA CARDÍACA AVALIADA PELA ENTROPIA CONDICIONAL E ANÁLISE SIMBÓLICA.

Takahashi ACM; Porta A; Melo RC; Quitério RJ; Silva E; Borghi-Silva A; Tobaldini E; Montano N; Catai AM. Aging reduces complexity of heart rate variability assessed by conditional entropy and symbolic analysis. Manuscrito submetido ao periódico *Journal of Gerontology: Medical Sciences.*

3. Segundo estudo

O ENVELHECIMENTO REDUZ A COMPLEXIDADE DA VARIABILIDADE DA FREQUÊNCIA CARDÍACA AVALIADA PELA ENTROPIA CONDICIONAL E ANÁLISE SIMBÓLICA.

3.1 RESUMO

Introdução: O aumento da idade na vida adulta está associado a uma redução da variabilidade total da frequência cardíaca e às mudanças na complexidade das dinâmicas fisiológicas. O objetivo deste estudo foi verificar se as alterações na modulação autonômica da frequência cardíaca, causada pelo processo do envelhecimento, podem ser detectadas pela entropia de Shanon (ES), entropia condicional (EC) e análise simbólica (AS). Métodos: As medidas de complexidade foram realizadas em 44 indivíduos saudáveis que foram alocados em dois grupos: idosos (n=23, 63±3 anos) e jovens (n= 21, 23±2 anos). Foram avaliadas ES, EC (índice de complexidade (IC) e índice de complexidade normalizado (ICN)) e AS (padrões: 0V, 1V, 2VS, 2VD) de séries temporais de curta duração (200 batimentos). As séries foram obtidas a partir do registro do eletrocardiograma (ECG) durante 15 minutos em repouso, na posição supina. As sequências caracterizadas por três batimentos cardíacos sem variações (0V) e com duas variações diferentes (2VD) refletem mudanças na modulação simpática e parassimpática, respectivamente. Para a análise estatística foi utilizado o teste t não pareado (ou Mann-Whitney quando apropriado). Resultados: A distribuição de padrões (ES) foi similar em ambos os grupos. No entanto, a regularidade foi significativamente diferente, sendo que os padrões foram mais repetitivos no grupo de idosos (redução do IC e do ICN). A quantidade dos tipos de padrões também foi diferente entre os grupos: o padrão 0V apresentou um aumento e os padrões 2VS e 2VD redução no grupo de idosos, indicando um desbalanço na regulação autonômica. Conclusão: A EC e a AS foram técnicas factíveis para detectar alterações no controle autonômico da frequência cardíaca no grupo idoso.

Palavras-Chave: Envelhecimento. Sistema nervoso autônomo. Variabilidade da frequência cardíaca. Análise não linear. Entropia.

3.2 INTRODUÇÃO

O sistema cardiovascular possui uma organização integrada, caracterizada pela interação de subsistemas, oscilações auto-sustentáveis e circuitos de retroalimentação que respondem a estímulos internos e externos, incluindo o comando central, mecanismos reflexos e controle humoral (Di RIENZO e PORTA, 2009; MALLIANI e MONTANO, 2002; PORTA et al, 2007b; PORTA et al, 2007d). O processo de envelhecimento está associado com a redução da habilidade destes subsistemas interagirem (PIKKUJÄMSÄ et al, 1999; PINCUS et al, 1995). Estas mudanças se refletem na redução da variabilidade total da frequência cardíaca (KAPLAN et al, 1991; LIPSITZ et al, 1990; PIKKUJÄMSÄ et al, 1999) e também na complexidade das dinâmicas fisiológicas (KAPLAN et al, 1991; LIPSITZ e GOLDGERGER, 1992; PIKKUJÄMSÄ et al, 1999).

Uma série de estudos sobre variabilidade da frequência cardíaca (VFC) foram baseados nas medidas tradicionais no domínio do tempo e da frequência (TASK FORCE 1996; LIPSITZ et al, 1990; MELO et a, 2008). Contudo, este tipo de análise apresenta uma importante limitação, uma vez que os resultados obtidos são muito sensíveis a definição das bandas de oscilações (principalmente na definição do limite inferior da banda de baixa frequência (BF), ou seja, geralmente 0,04 Hz, e na abrangência da banda de alta frequência (AF) em torno da frequência respiratória). Em contrapartida, índices baseados em métodos não lineares não necessitam de qualquer definição de bandas de frequências (PORTA et al, 2007c). Estes índices podem fornecer resultados mais estáveis e reprodutíveis e também identificar anormalidades e alterações não aparentes (HUIKURI, MAKIKALLIO e PERKIOMAKI, 2003; LIPSITZ et al, 1992; MÄKIKALLIO et al, 2002). Além disso, os métodos não-lineares são por si mais adequados para extrair informações relevantes relacionadas à complexidade (HUIKURI et al, 2000; HUIKURI, MAKIKALLIO e PERKIOMAKI, 2003).

Recentemente, várias abordagens foram propostas visando quantificar a complexidade. A maioria destes estudos foi baseada em índices desenvolvidos para a análise de séries temporais de longa duração e, portanto, em gravações ambulatoriais de 24 horas (HUIKURI et al, 2000; MAESTRI et al, 2007a; MÄKIKALLIO et al, 2001; PIKKUJÄMSÄ et al, 1999). Por outro lado, registros de laboratório de curta duração (<10 min) oferecem uma oportunidade única para avaliar a regulação autonômica cardiovascular em condições controladas e padronizadas (MAESTRI et al, 2007b). A avaliação da complexidade em registros de curta duração é baseada no cálculo de entropias (KAPLAN et al, 1991; PINCUS

1995, PORTA et al, 1998), na predição local não-linear (PORTA et al, 2000) e na dinâmica simbólica (GUZZETTI et al, 2005; PORTA et al, 2007c).

A complexidade é quantificada pela avaliação da quantidade de informação carreada por uma série temporal (quanto maior a informação, maior a complexidade). Comumente, a complexidade de registros curtos da VFC é avaliada com base na estimativa da entropia condicional, que analisa a quantidade de informação transportada por uma amostra da série temporal, quando amostras passadas são conhecidas (quanto menor a informação, mais regular e previsível é a série) (PORTA et al, 2007a,d). Além disso, Porta et al. (2007c) propuseram recentemente uma nova ferramenta não linear baseada na análise simbólica de sequências de 3 batimentos para distinguir a modulação cardíaca simpática e parassimpática.

No presente estudo, testamos a hipótese de que as modificações causadas pelo processo de envelhecimento na modulação autonômica da freqüência cardíaca podem ser detectadas pela entropia de Shannon, entropia condicional e análise simbólica de registros de curta duração da VFC.

3.3 MÉTODOS

3.3.1 Voluntários

Quarenta e quatro homens voluntariamente participaram desse estudo. Foram divididos em dois grupos de acordo com a faixa etária: idosos (N = 23; 63±3 anos) e jovens (N = 21; 23±2 anos). Todos os voluntários foram considerados aparentemente saudáveis, com base na história clínica, anamnese e exame físico, bem como em testes de laboratório, que incluíram eletrocardiograma (ECG) e teste de esforço máximo realizado por um cardiologista. Os critérios de exclusão foram hipertensão arterial, diabetes mellitus, doença pulmonar obstrutiva crônica, lesões neurológicas, cardiovasculares, respiratórias e/ou musculoesquelética e uso de medicamnetos. Fumantes e etilistas também foram excluídos. Todos os voluntários foram informados sobre os procedimentos experimentais e assinaram um termo de consentimento livre e esclarecido. Este estudo foi aprovado pelo Comitê de Ética da Instituição.

3.3.2. Procedimentos experimentais

Todos os experimentos foram realizados em sala com temperatura ambiente controlada (22-23°C), umidade relativa do ar entre 50 e 60% e no mesmo período do dia, considerando as influências do ciclo circadiano. Os indivíduos foram familiarizados com a sala de experimento, os procedimentos e os equipamentos a serem utilizados. Todos os voluntários foram instruídos a evitar cafeína e bebidas alcoólicas, bem como evitar a realização de qualquer exercício moderado ou intenso na véspera da aplicação do protocolo. No dia do experimento, antes do teste, os indivíduos foram entrevistados e examinados para confirmar sua condição de saúde, a ocorrência de uma noite de sono regular e para verificar se os valores de freqüência cardíaca e pressão arterial sistêmica estavam dentro da normalidade.

3.3.3 Protocolo experimental

Os indivíduos foram mantidos em repouso por 20 minutos para que a freqüência cardíaca fosse estabilizada em valores basais. Em seguida, foi realizado o registro do ECG em repouso, durante 15 minutos, na posição supina. Os voluntários foram orientados a respirar espontaneamente e a não falar durante o registro.

O ECG foi monitorizado na derivação MC5 e captado por um monitor cardíaco de um canal (TC 500, ECAFIX, São Paulo, SP, Brasil), conectado a um microcomputador por meio de uma placa A/D (*National Instruments Corporation, Austin*, TX, E.U.A.). A frequência de amostragem foi de 500 Hz. O período cardíaco foi definido como a distância temporal entre dois picos consecutivos de onda R (RR). Os intervalos RR (ms) foram avaliados batimento a batimento, utilizando um *software* específico (SILVA et al, 1994).

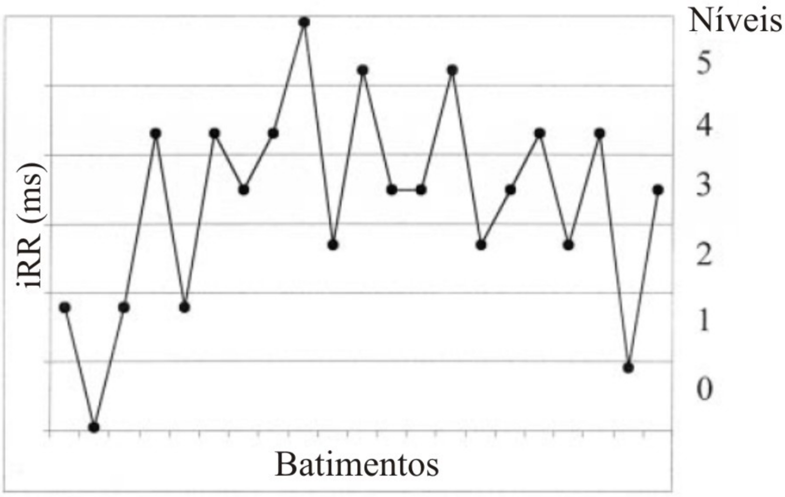
3.3.4 Análise de Dados

O comprimento da série N foi fixado em 200 batimentos. A média e a variância dos intervalos RR da série foram calculadas.

3.3.4.1 Análise simbólica

A técnica, descrita por Porta et al (2001), baseia-se 1) na transformação da série de VFC em uma seqüência de números inteiros (símbolos), 2) na construção de padrões (palavras), 3) na redução do número de padrões agrupando-os em um pequeno número de famílias, e 4) na avaliação das taxas de ocorrência dessas famílias. Uma abordagem de simplificação baseada no processo de quantização uniforme foi usada para transformar a série RR em uma seqüência de símbolos.

Resumidamente, a série foi alocada sobre ξ símbolos com resolução de (RRmax-RRmin)/ξ, onde RRmax e RRmin eram o valor máximo e o mínimo de intervalo RR da série. Após a quantização, a série de intervalos RR se tornou a sequência $RR_\xi = \{RR_\xi(i), i=1,...,N\}$ de valores inteiros variando de 0 a ξ-1. A técnica de atraso das coordenadas foi utilizada para transformar a série $RR\xi$ na sequência de padrões $RR_{\xi,L}=\{RR_{\xi,L}(i), i=L,...,N\}$ com $RR_{\xi,L}(i)=[RR_{\xi}(i), RR_{\xi}(i-1),..., RR_{\xi}(i-L + 1)]$. O número de padrões possíveis $RR_{\xi,L}(i)$ foi ξ^L. Como ξ^L aumenta rapidamente com aumento de L e ξ, ambos os parâmetros foram mantidos em baixos valores: para a aplicação em dados de registro de curta duração, a melhor escolha foi ξ=6 e L=3, e o número de padrões possíveis foi de 216. A ilustração sintética da metodologia da análise simbólica é demonstrada na Figura 5.



1 0 1 4 1 4 3 4 5 2 5 3 3 5 2 3 4 2 4 0 3 Símbolos
1 0 1
0 1 4
1 4 1
4 1 4
1 4 3
4 3 4
3 4 5
4 5 2
5 2 5
2 5 3
5 3 3
3 3 5
3 5 2
5 2 3
2 3 4
3 4 2..

Figura 5: Ilustração sintética do método da análise simbólica. Os intervalos RR (iRR) são uniformemente distribuidos em 6 níveis (de 0 a 5). Cada nível foi identificado com um símbolo (número) e foram construidos padrões com comprimento de 3 símbolos. Adaptado de Guzzetti et al, (2005) *Circulation.*

A entropia de Shannon (ES) foi calculada para fornecer uma qualificação de complexidade da distribuição dos padrões. A ES é um índice que descreve a forma da distribuição dos padrões. A ES é alta se a distribuição é plana (todos os padrões são identicamente distribuídos e a série transporta o máximo de informações). Pelo contrário, a SE é baixa se um subconjunto de padrões é mais comum, enquanto outros estão ausentes ou são pouco frequentes (por exemplo, em uma distribuição de Gauss) (PORTA et al, 2001).

Para reduzir o número de padrões sem perda de informações, foi efetuado um processo de redução de redundância. Todos os padrões foram agrupados em quatro famílias, de acordo com o número e tipos de variações de um símbolo para o próximo. As famílias foram as seguintes: 1) padrões, sem variação [0V: todos os símbolos são iguais, por exemplo, (4,4,4) ou (2,2,2); Figura 6, A e B], 2) padrões com uma variação [1V: 2 símbolos consecutivos são iguais e o símbolo restante é diferente, por exemplo, (3,4,4) ou (4,4,2); Figura 6, C e D], 3) padrões com duas variações similares [2VS: os 3 símbolos formam uma rampa ascendente ou descendente , por exemplo, (1,2,4) ou (4,3,2); Figura 6, E e F], e 4) padrões com duas variações diferentes [2VD os 3 símbolos formam um pico ou um vale, por exemplo, (2,4,2) ou (4,1,2); Figura 6, G e H]. Foram avaliados os índices de ocorrência de todas as famílias: 0V%, 1V%, 2VS% e 2VD%. O cálculo destes índices foi baseado no número de vezes que um padrão $R_{\xi=6,L=3}(i)$ pertencente a uma família específica foi encontrado em $RR_{\xi=6,L=3}$. O resultado (multiplicado por 100) foi dividido por [N-(L-1)].

Estudos com bloqueio farmacológico (GUZZETTI et al, 2005) e testes autonômicos (GUZZETTI et al, 2005; PORTA et al, 2007c) indicaram que os índices 0V% e 2VD% são capazes de avaliar as modulações simpática e parassimpática, respectivamente.

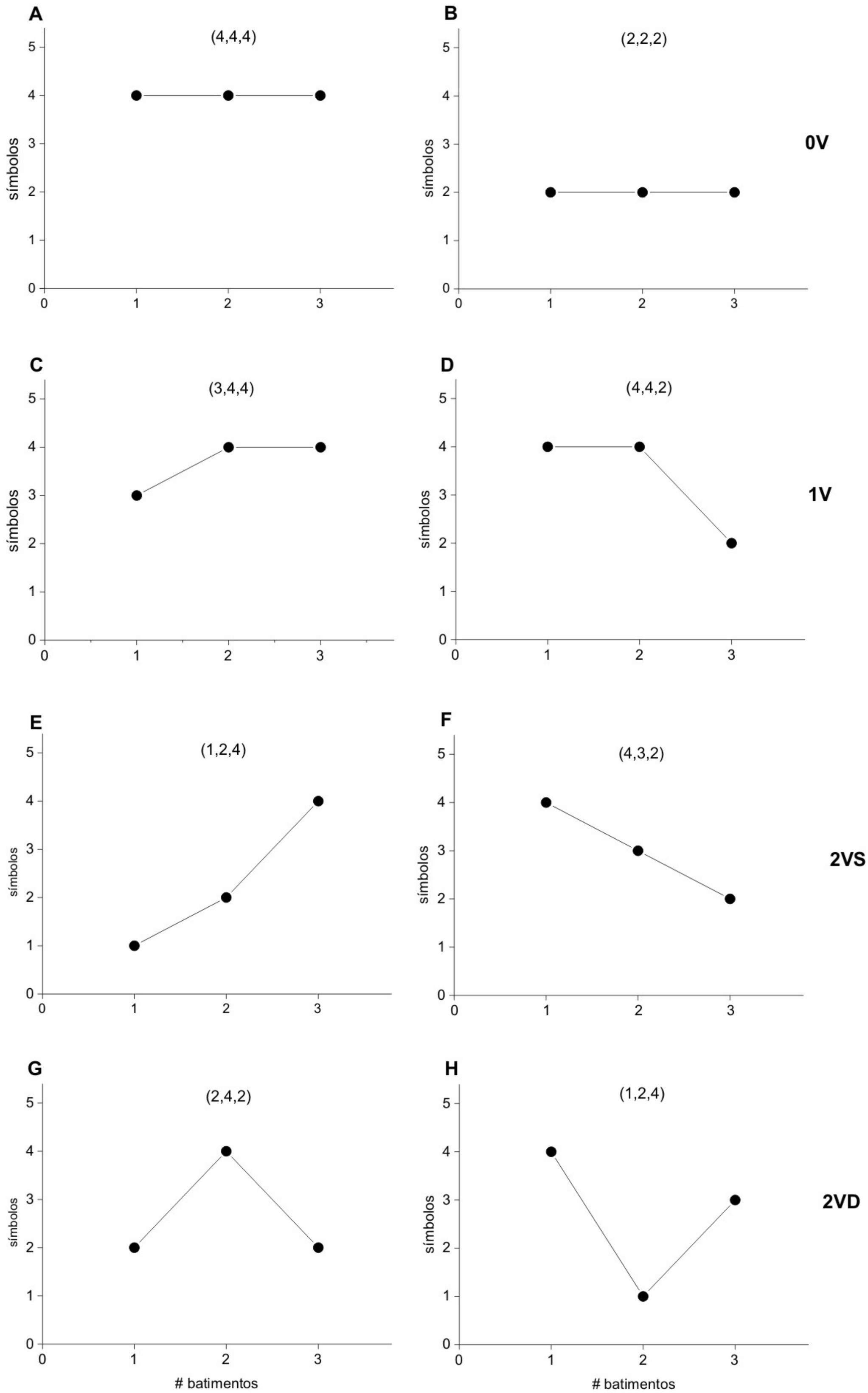


Figura 6: Representação de exemplos de padrões sem variações (0V, A e B), padrões com uma variação (1V, C e D), padrões com duas variações similares (2VS, E e F) e padrões com duas variações diferentes (2VD, G e H). Adaptado de Porta et al. (2007c) *Am J Physiol Heart Circ Physiol.*

3.3.4.2 Entropia Condicional (EC)

Esta abordagem, descrita por Porta et al (1998), explorou a entropia condicional (EC) para quantificar a informação transportada por uma nova amostra, que não pode ser obtida a partir de uma seqüência de L valores passados. Para esta técnica foi realizado o processo de quantização uniforme, conforme descrito na seção anterior "análise simbólica". A EC foi modificada para definir a EC corrigida (ECC).

Em função de L valores passados, foi demonstrado que a ECC: i) permanece constante em caso de ruído branco, ii) reduz a zero no caso de sinais totalmente previsíveis; iii) exibe um valor mínimo se padrões repetitivos são incorporados no ruído. O comprimento do padrão (L) não foi fixado *a priori*, enquanto que ξ foi fixado em seis.

Deste modo, o valor mínimo da ECC, em função de L valores passados, foi considerado como índice de complexidade (IC). Esse índice foi expresso em números naturais. Além disso, esse índice foi normalizado pela entropia de Shannon da série RR para se obter o IC normalizado (ICN), possibilitando exprimir a complexidade em unidades adimensionais. O ICN varia de 0 (informação nula) a 1 (máxima informação) (PORTA et al, 2007a). Quanto maior o IC e o ICN , maior a complexidade e menor a regularidade da série.

3.3.5 Análise Estatística

Foi utilizado o teste t não-pareado (ou o teste de Mann-Whitney quando apropriado) para a comparação das características dos indivíduos, da média e variação dos intervalos RR, dos índices simbólicos, do IC e do ICN. Os dados foram apresentados como média ± desvio padrão e o nível de significância adotado foi $P<0,05$. A análise estatística foi realizada no *software SigmaPlot* para *Windows* versão 11.0.

3.4 RESULTADOS

A Tabela 4 apresenta as características dos voluntários. A estatura e o índice de massa corpórea (IMC) foram significativamente diferentes entre os grupos ($P<0,05$).

Tabela 4: Características dos voluntários.

Características	Grupo Jovem	Grupo Idoso
Idade (anos)	23 ± 2	63 ± 3*
Massa corporal (kg)	75,3 ± 7	72,0 ± 8
Estatura (m)	1,80 ± 0,05	1,68 ± 0,05*
IMC (kg/m^2)	23 ± 2	26 ± 2*

Valores em média ± DP. IMC, índice de massa corpórea. * *P*<0,05 grupo jovem *vs* grupo idoso.

O grupo idoso apresentou menor variância dos intervalos RR, em comparação ao grupo de jovens (*P*<0,05). No entanto, a média dos intervalos RR foi similar em ambos os grupos (Tabela 5).

Os resultados da análise de complexidade estão apresentados na Tabela 5. A ES não foi influenciada pelo envelhecimento. No entanto, o IC e o ICN apresentaram menores valores no grupo idoso (*P*<0,05). A análise simbólica indicou um aumento do padrão 0V e uma redução dos padrões 2VS e 2VD no grupo de idosos em comparação com o grupo de jovens (*P* <0,05).

Tabela 5: Análise de complexidade da variabilidade da frequência cardíaca dos grupos jovem e idoso.

	Grupo Jovem	Grupo idoso
média dos RR (ms)	968 ± 124	905 ± 209
VAR (ms^2)	2743 ± 1698	1652 ± 2317*
Entropia de Shanon	3,67 ± 0,43	3,50 ± 0,30
Entropia Condicional		
IC	1,17± 0,17	1,05 ± 0,16*
ICN	0,80 ± 0,07	0,71 ± 0,10*
Análise simbólica		
0V%	16,01 ± 10,90	24,97 ± 11,32*
1V%	45,66 ± 6,78	48,53 ± 5,60
2VS%	15,03 ± 6,67	10,22 ± 4,78*
2VD%	23,31 ± 10,47	16,30 ± 8,00*

Valores em média ± DP. RR, intervalos R-R; VAR, variância; IC, índice de complexidade; ICN, índice de complexidade normalizado. * *P*<0,05 grupo jovem *vs* grupo idoso.

3.5 DISCUSSÃO

Os principais achados desse estudo foram os seguintes: 1) um aumento significativo no índice de regularidade (ou seja, diminuição do IC) no grupo idoso, enquanto que a ES permaneceu inalterada, e 2) a análise simbólica revelou aumento do padrão 0V e redução dos padrões 2VS e 2VD nos idosos.

De acordo com as definições, a ES e o IC fornecem informações diferentes (PORTA et al, 2001). A ES é uma medida da complexidade do padrão de distribuição (ou seja, o histograma de freqüência da distribuição dos padrões). A presença de picos na distribuição dos padrões (relativos aos padrões mais freqüentemente detectados) ou de vales (relativos à padrões menos freqüente ou a ausência de certos padrões) determina a diminuição da ES em relação ao seu valor máximo previsto por uma distribuição plana (PORTA et al, 2001). Por sua vez, o IC quantifica a complexidade da relação dinâmica entre um padrão e o seu subsequente (regularidade). Se a seqüência temporal dos padrões é completamente regular (ou seja, os padrões se sucedem de modo periodicamente repetitivo), o IC é zero. Em contrapartida, o valor máximo do IC é atingido quando não existe nenhuma relação entre um padrão e seu subsequente (a sequência de padrões é completamente aleatória) (PORTA et al, 2001).

Assim, o aumento significativo da regularidade (ou seja, uma diminuição do IC), não implica numa mudança na ES. De fato, observa-se que a ES permaneceu similar em ambos os grupos, demonstrando que os padrões apresentaram a mesma distribuição, porém esses padrões formaram sequências mais regulares e previsíveis no grupo de idosos, ocasionando uma redução no IC.

Adicionalmente, a ES não fornece qualquer indicação sobre os tipos de padrões detectados na série. Se duas séries são caracterizadas por diferentes padrões com distribuição idêntica, a ES é igual (PORTA et al, 2001). Assim, uma classificação de padrões (análise simbólica) é necessária para a compreensão de quais padrões estão envolvidos na geração da complexidade.

Neste estudo, os jovens e os idosos apresentaram valores similares de ES, no entanto, os tipos de padrões são diferentes. Os idosos apresentaram um aumento da taxa de ocorrência do padrão 0V e uma redução dos padrões 2VS e 2VD em comparação ao grupo de jovens. Os padrões 0V são característicos de ondas lentas (por exemplo, oscilações de baixa frequência), enquanto que os padrões 2VS e 2VD são fragmentos de ondas mais rápidas (por exemplo, oscilações de alta frequência) (PORTA et al, 2001). Estudos prévios com bloqueio farmacológico e testes autonômicos, em indivíduos saudáveis e doentes, têm relacionado os padrões simbólicos com a modulação autonômica cardíaca (GUZZETTI et al, 1995; MAESTRI et al, 2007b; PORTA et al, 2007c). O padrão 0V tem sido associado à modulação simpática enquanto o 2VD tem sido associado à modulação vagal (GUZZETTI et al, 1995; PORTA et al, 2007c). Dessa forma, os resultados do presente estudo indicam que o grupo idoso apresenta maior modulação simpática e menor modulação vagal relativa em comparação ao grupo de jovens.

As modificações dos índices de complexidade podem estar associadas a uma função deprimida do órgão, uma perda de interação entre os subsistemas, uma ação preponderante de um subsistema sobre os outros e/ou um prejuízo dos mecanismos de regulação (PIKKUJÄMSÄ et al, 1999; PINCUS et al, 1995; PORTA et al, 2009). Além disso, a complexidade da dinâmica da VFC em registros de curta duração depende da condição do sistema nervoso autonômico, ou seja, a complexidade diminui na presença de um aumento da modulação simpática (PORTA et al, 2007a). Frequentemente, essas alterações estão relacionadas a uma situação patológica, mas podem estar presentes no processo de envelhecimento como pode ser observado neste estudo. Os idosos apresentaram não só padrões mais regulares e previsíveis (IC e ICN reduzidos) como também um predomínio da modulação simpática (maior taxa de ocorrência do padrão 0V) em relação aos jovens.

No processo de envelhecimento as distribuições de padrões presentes na VFC permanecem similares aos indivíduos jovens. No entanto, os padrões são mais repetitivos, reduzindo assim a complexidade. Esta redução é o resultado do aumento da presença de padrões estáveis e da diminuição de padrões altamente variáveis. Estas diferenças indicam que indivíduos idosos aparentemente saudáveis, como os avaliados neste estudo, apresentam um desequilíbrio na regulação autonômica. As mudanças observadas nos índices de complexidade causadas pelo processo de envelhecimento são semelhantes às associadas com processos patológicos, como insuficiência cardíaca crônica (MAESTRI et al, 2007a) ou o aparecimento de arritmias graves (GUZZETTI et al, 1995).

Em conclusão, as alterações autonômicas avaliadas pela entropia condicional e análise simbólica desempenham um papel importante não só em processos patológicos, mas também no processo de envelhecimento, no qual estas análises podem ser úteis para melhor caracterizar as alterações decorrentes do avanço da idade.

3.6 FINANCIAMENTO

Este trabalho foi financiado pela Fundação de Amparo à Pesquisa do Estado de São Paulo (06/52860-0 para ACMT e 05/54838-9 para AMC), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (PDEE/1228/08-0 para ACMT).

4. CONSIDERAÇÕES FINAIS

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Os estudos apresentados fornecem informações importantes a respeito da modulação autonômica da VFC em idosos. Foi possivel detectar por meio de uma coleta simples, de curta duração e de baixo custo que indivíduos idosos aparentemente saudáveis apresentam uma redução da complexidade da VFC, indicando um desequilíbrio na regulação autonômica. A predominância da modulação simpática na VFC, concomitante com a redução da modulação vagal também é característica em diversas doenças cardiovasculares. Considerando a existência de uma associação entre o processo de envelhecimento e a ocorrência de doenças cardiovasculares, a identificação de alterações no controle autonômico é de grande importância para a busca de terapêuticas não farmacológicas que revertam ou minimizem essas modificações. Neste sentido, este trabalho procurou também elucidar o efeito do treinamento de força excêntrica na modulação autonômica da FC.

Desta forma, este trabalho contribui para a Fisioterapia de dois modos: 1) Idosos aparentemente saudáveis já apresentam modificações na modulação autonômica da FC que podem ser detectadas por uma metodologia simples e de baixo custo. Sendo assim sugerem-se intervenções da Fisioterapia para estes indivíduos. 2) Apesar do exercício resistido ser uma ferramenta largamente utilizada nos processos de intervenção na Fisioterapia e das recomendações quanto ao uso da contração excêntrica, observou-se que o treino de força excêntrica de alta intensidade, aplicado de modo isolado não foi capaz de induzir alterações benéficas no controle autonômico da FC. Os resultados obtidos indicam que apesar deste tipo de treinamento melhorar a força excêntrica, este não causou adaptações suficientes para promover alterações no controle autonômico da FC durante exercício isométrico.

Adicionalmente, o presente trabalho traz contribuições para a Gerontologia, podendo seus resultados ser aplicados na avaliação e intervenção na rede de cuidado em saúde. Especialmente em idosos pré-frágeis e fragilizados, nos quais a sarcopenia possui um papel importante nesta condição, estudos como este que se propõe a investigar formas de reversão ou amenização deste processo são de muita importância, pois poderão contribuir em políticas públicas para manutenção ou melhora das atividades funcionais e qualidade de vida destes indivíduos.

5. OUTRAS ATIVIDADES REALIZADAS DURANTE O PERÍODO DO DOUTORADO

5. OUTRAS ATIVIDADES REALIZADAS DURANTE O PERÍODO DO DOUTORADO

Durante o período de realização do Doutorado (2007-2010), foram desenvolvidas outras atividades relacionadas à participação em outros projetos de pesquisa do Laboratório de Fisioterapia Cardiovascular/NUPEF e ao doutorado sanduiche realizado na *Università degli Studi di Milano.*

5.1 Participação em outros projetos do Laboratório de Fisioterapia Cardiovascular

A participação no projeto de pesquisa “Efeitos dos exercícios isométrico e isocinético (excêntrico e concêntrico) de diferentes grupamentos musculares sobre o torque, variabilidade da frequência cardíaca e atividade eletromiográfica” resultou no artigo: *“High eccentric strength training reduces heart rate variability in healthy older men”* publicado no periódico British Journal of Sports Medicine, no qual sou co-autora. (Anexo C).

Co-orientação informal relacionada ao projeto de mestrado “Análise não linear da variabilidade da freqüência cardíaca de idosos: comparação entre gêneros”, realizado pela aluna Natália Perseguini. Este trabalho tem como objetivo avaliar se a dinâmica não linear da variabilidade da frequência cardíaca de mulheres idosas saudáveis se assemelham ou não a de homens idosos, uma vez que a menopausa traz várias modificações fisiológicas ao corpo da mulher, sendo que uma delas seria a perda do efeito cardioprotetor nesta população.

Co-orientação relacionada aos projetos de iniciação científica: 1) “Estudo do limiar de anaerobiose obtido pelo comportamento da freqüência cardíaca e de sua variabilidade em protocolos de exercício físico dinâmico descontínuo em cicloergômetro X esteira” das alunas de graduação em Fisioterapia Ester Souza de Araújo e Natália Maria Perseguini (bolsistas Pibic-CNPq-UFSCar) o qual gerou um manuscrito que foi submetido à Revista Portuguesa de Desportos. 2) “Análise da resposta da freqüência cardíaca durante exercício isocinético concêntrico de flexores e extensores do joelho” do aluno de graduação em Fisioterapia Rafael Donato Guerra, 3) “Efeito do envelhecimento e da velocidade angular na resposta da freqüência cardíaca ao exercício excêntrico” dos alunos Marina Neves e Victor Fiorelli.

Colaboração no projeto de mestrado “Efeito do treinamento muscular inspiratório na arritmia sinusal respiratória de pacientes com infarto agudo do miocárdio” desenvolvido pelo aluno Victor Ribeiro Neves, que resultou no manuscrito que está em fase final de elaboração intitulado: “Effect of exercise training on respiratory sinus arrythmia in patients with acute myocardial infarction” no qual sou co-autora.

5.2 Atividades adicionais relacionadas ao projeto de pesquisa

Parte dos dados do primeiro estudo, referentes ao efeito do treinamento de força excêntrica na atividade eletromiográfica do músculo quadríceps, foram apresentados na forma de resumo expandido no XVII Congress of the International Society of Electromyography and Kinesiology (ISEK 2008 - Niagara Falls), sob o título "Effect of eccentric strength training on median frequency and time of fatigue in different levels of isometric contraction"(Anexo D).

5.3 Atividades relacionadas ao estágio de doutorado sanduíche

No período de 1 de julho de 2008 a 31 de dezembro de 2008, foi realizado o estágio de doutorado sanduiche na Università degli Studi di Milano, que contou com a coorientação do Prof. Dr. Nicola Montano e a colaboração do Prof. Dr. Alberto Porta (Anexo E). As atividades realizadas no estágio foram:

1) aprendizado e treinamento do uso da análise espectral com o modelo autoregressivo;

2) aprendizado e treinamento na aplicação de análises não lineares: análise simbólica, entropia de Shanon e entropia condicional;

3) aplicação das análises acima mencionadas nos dados de FC relativos ao efeito do treinamento excêntrico de idosos no controle autonômico da FC (dados coletados no Brasil) e apresentação dos resultados no XIX IAGG World Congress of Gerontology and Geriatrics (2009-Paris). Os títulos dos trabalhos foram: *"The eccentric strength training increases cardiac sympathetic modulation in resting condition"* e *"Cardiac autonomic modulation during isometric exercise does not change after eccentric strength training"* (Anexo F e G).

4) Participação no projeto: efeito do treinamento respiratório no balanço simpatovagal e marcadores inflamatórios em indivíduos com depressão.

5) Participação no projeto: estudo do controle nervoso autonômico, da sensitividade baroreflexa e análise da dinâmica não linear durante o tilt gradual em sujeitos saudáveis que resultou no artigo "Characterization of the Information Transfer along the Spontaneous Baroreflex in Healthy Humans" aceito para publicação no periódico Methods of Information in Medicine, no qual sou co-autora. (Anexo H).

A participação em todas as atividades desenvolvidas contribuiu de forma significativa para a minha formação acadêmica, científica e pessoal. Destaco a fundamental importância do trabalho realizado em equipe, considerando todos os membros do Laboratório de Fisioterapia Cardiovascular/NUPEF/UFSCar, como também os pesquisadores do Laboratório de

Fisiopatologia Cardiovascular da Università degli Studi di Milano, especialmente o Prof. Dr. Nicola Montano e o Prof. Dr. Alberto Porta.

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ANEXO A

Takahashi ACM; Quitério RJ; Melo RC; Silva E; Catai AM. The effect of eccentric strength training on heart rate and on its variability during isometric exercise in healthy older men. **European Journal of Applied Physiology** , v. 105, n. 3, p. 315-323, 2009.

Eur J Appl Physiol (2009) 105:315–323
DOI 10.1007/s00421-008-0905-5

ORIGINAL ARTICLE

The effect of eccentric strength training on heart rate and on its variability during isometric exercise in healthy older men

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Accepted: 14 October 2008 / Published online: 6 November 2008

Abstract The purpose of this study was to investigate if chronic eccentric strength training (ST) affects heart rate (HR) and heart rate variability (HRV) during sub-maximal isometric voluntary contractions (SIVC). The training group (TG) (9 men, 62 ± 2) was submitted to ST (12 weeks, 2 days/week, 2–4 sets of 8–12 repetitions at 75–80% peak torque (PT). The control group (CG) (8 men, 64 ± 4) did not perform ST. The HR and the HRV (RMSSD index) were evaluated during SIVC of the knee extension (15, 30 and 40% of PT). ST increased the eccentric torque only in TG, but did not change the isometric PT and the duration of SIVC. During SIVC, the HR response pattern and the RMSSD index were similar for both groups in pre- and post-training evaluations. Although ST increased the eccentric torque in the TG, it did not generate changes in HR or HRV.

Keywords Heart rate · Autonomic nervous system · Heart rate variability · Isometric exercise · Strength training

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Introduction

Heart rate variability (HRV) is a non-invasive measure used to analyze the influence of the autonomic nervous system on the heart, providing information about both sympathetic and parasympathetic contribution in consecutive HR oscillations (Malik et al. 1996). HRV decreases with age (Catai et al. 2002; Jensen-Urstad et al. 1997; Lakatta and Levy 2003; Lipsitz et al. 1990; Melo et al. 2005; Pagani et al. 1986) as a consequence of parasympathetic reduction and sympathetic modulation predominance (Lipsitz et al. 1990). This fact has an important clinical impact on the elderly, because reduced HRV can be associated with higher cardiovascular morbidity and mortality rates (Bigger et al. 1992; Melo et al. 2005).

Long-term aerobic training seems to improve HRV in older men and, consequently, could be considered as a non-pharmacological therapy (Melo et al. 2005; Stein et al. 1999; De Meersman 1993). In fact, aerobic exercise plays an important role in the maintenance of physical working capacity in the elderly (McGuire et al. 2001), but the effects of aging on the muscular system can only be reduced by resistance training (Evans 1999; Frontera et al. 1988; Macaluso and De Vito 2004; Mazzeo et al. 1998; Williams et al. 2002). Among the existing types of contraction, the eccentric one has been recommended for strength training (ST) programs because it leads to hypertrophy without overloading the cardiovascular system [i.e., lower values of heart rate (HR), arterial pressure, and oxygen consumption for the same absolute torque output of concentric exercise] (Hugget et al. 2004; LaStayo et al. 1999; Overend et al. 2000).

Few studies have evaluated the effects of ST on HR autonomic control and most of those did not observe any changes in HRV (Cooke and Carter 2005; Forte et al. 2003;

Heffernan et al. 2007; Madden et al. 2006). On the other hand, overload on the cardiovascular system during eccentric exercise is lower than in other types of contractions (Hugget et al. 2004; LaStayo et al. 1999; Overend et al. 2000), so it is to be expected that autonomic control would not improve. However, in a previous study performed in our laboratory (Melo et al. 2008), it was observed that eccentric training caused an autonomic imbalance, induced by an unknown mechanism, towards a predominance of sympathetic modulation. Hence, we found it important to clarify, through further studies, if eccentric training has an unfavorable effect on the autonomic control of HR.

The most common methods used for HRV analysis include time and frequency domain measurements. The time domain method provides informations about the magnitude of R–R variations around the average recorded interval. The RMSSD index is often used to quantify parasympathetic modulation on the sinus node during both resting and exercise conditions (Malik et al. 1996). Another well-known test of the autonomic nervous system is the evaluation of HR response patterns during isometric contractions (Hohnloser and Klingenheben 1998; Galvez et al. 2000; Maciel et al. 1987, 1989; Iellamo et al. 1997; Silva et al. 1999). This active autonomic test has advantages over the kinds which take their measurements during rest, as interactions between the musculoskeletal and cardiovascular systems can be assessed non-invasively, for example, after ST of a specific muscle group.

Eccentric ST programs are recognized as an important therapeutical component in the improvement of muscular strength, which reduces with age (Evans 1999; Frontera et al. 1988; Macaluso and De Vito 2004; Williams et al. 2002). Nevertheless, it is not clear if this kind of ST can bring benefits or harmful effects to the autonomic modulation of the HR. Based on these considerations, we chose the HR and HRV response to an autonomic test (isometric exercise) in order to evaluate if chronic eccentric ST affects the autonomic control of HR during sub-maximal isometric voluntary contractions (SIVC).

Methods

Subjects

Thirty apparently healthy elderly men (age range 60–69 years old) volunteered to take part in this study, but only 22 of them were able to participate. Of the 12 participants assigned to the training group (TG), only nine completed the ST program, while in the control group (CG), only eight of the ten volunteers completed the evaluations. All subjects were healthy, based on clinical and physical examination, as well as on laboratory tests which included a standard electrocardiogram (ECG), a maximum exercise test conducted by a physician, a chest X-ray, a total blood count, urinalysis, and a clinical biochemical screen test (glucose, uric acid, creatinine, urea, total and fraction cholesterol, and triglycerides). Subjects that presented hypertension, diabetes, chronic obstructive pulmonary disease, neurological injuries, cardiovascular, respiratory, or musculoskeletal diseases were excluded. Smokers, habitual drinkers, and subjects who were taking any kind of medication or who had participated in a regular ST program in the 6-month period prior to the study, were also excluded. The subjects were informed about the experimental procedures and signed a formal acceptance form approved by the Ethics Committee of the Institution involved.

Experimental procedures

All subjects were evaluated during the same period of the day in order minimize differing responses due to circadian changes. The experiments were carried out in a climate-controlled room (22–23°C) with a relative air humidity of 50–60% over a 5- to 7-day interval for each protocol. Before the day of the experiment, the subjects were taken to the experimental room for familiarization with the procedures and the equipment to be used. Each subject had been instructed to avoid caffeine and alcoholic beverages as well as to avoid performing any moderate or heavy exercise on the day before the applied protocol. On the day of the experiment, before the test, the subjects were interviewed and examined to confirm their health condition, the occurrence of a regular night's sleep, and to confirm that HR and systemic blood pressure (BP) were within the normal range.

During the Protocol II, which is described below, the subjects were monitored at a CM5 lead to register the HR and the R–R intervals. The ECG and the HR were obtained from a one-channel heart monitor (TC 500, ECAFIX, São Paulo, SP, Brazil) having a sampling frequency of 500 Hz, and they were processed at a Lab.PC + analog-digital converter (National Instruments Corp., Austin, TX, USA), which is an interface between the heart monitor and a microcomputer. The signals were recorded in real time after converting them from analog to digital. The R–R intervals (ms) were calculated on a beat-to-beat basis, using specific software (Silva et al. 1994). During the ECG recording, the respiratory frequency was observed and maintained at a normal range. In addition, for all exercise protocols (i.e., Protocols I, II, III and IV), which are described below, a non-invasive BP measurement was carried out before and after each effort, using the auscultatory method. To confirm that the subjects were classified in the same functional class, VO_2 was determined during an incremental cycle ergometer exercise until exhaustion using a metabolic analyzer (CPX-D, Medical Graphics, St Paul, MN, USA). Exhaustion was defined as: (1) the inability to maintain a speed of ~60 rpm, (2) a plateau in the VO_2 uptake with an increase in work rate (VO_2 maximal), (3) the achievement of maximal HR for age and (4) a respiratory exchange ratio >1.1. Two or more of these criteria had to be met in order to classify the subjects.

Experimental protocol

Protocol I: Maximal isometric voluntary contraction

The maximal isometric voluntary contraction (MIVC) of the dominant leg knee extension was tested at 60° of knee flexion (full extension = 0°) by using an isokinetic dynamometer (Biodex Multi Joint System III, Biodex Medical System Inc., Shirley, NY, USA). The load cell was calibrated before each test by positioning and stabilizing the lever arm parallel to the floor and by hanging a confirmed weight on the load cell. Before testing, the subjects performed a 4-min light warm-up on a cycle ergometer followed by stretching of the quadriceps and hamstrings. After that, they were positioned on the dynamometer chair (seat back angle = 90°) and were stabilized by using pelvis, chest and thigh straps. The rotational axis of the dynamometer was aligned with the lateral femoral epicondyle and the resistance pad was distally positioned above the malleoli on the lower leg, still allowing full ankle dorsiflexion. The gravity correction factor (additional torque produced by the leg segment and by the resistance pad weights) was determined at about 60° below horizontal position, with the subject being in a relaxed position.

The subjects performed three MIVCs (duration = 10 s), with a resting period of 10–15 min between each repetition. During the MIVC, the subjects were motivated with loud and consistent verbal encouragement and instructed to pay attention to the visual feedback generated by the isokinetic dynamometer screen, to avoid contractions of other muscles, to keep breathing spontaneously, and to avoid the occurrence of the Valsalva maneuver, which can be checked by the absence of bradycardia after the contraction. The highest value obtained of all maximum efforts was used as the peak torque value (PT) (N.m).

Protocol II: Sub-maximal isometric voluntary contraction

The subjects were submitted to three SIVC of their knee extension. The first contraction was performed at 15%, the second at 30% and the last at 40% of the maximal isometric PT determined in Protocol I. The procedures related to the isokinetic dynamometer calibration, the subject preparation and the test instructions were the same as described above in Protocol I. The sub-maximal contractions were performed subsequently in a fixed order (i.e., 15, 30 and 40%) with a 15–20 min resting period between each level. This long recovery period was established to ensure that the HR and the BP would return to their basal values. In addition, sub-maximal contractions were performed from lowest to highest intensities in order to eliminate the chances of previously fatiguing contractions affecting cardiovascular responses.

Each sub-maximal contraction was maintained for 240 s or until exhaustion, which was confirmed when the subject was not able to keep the stipulated torque for more than 5 s (Hunter et al. 2005). In this protocol, the HR was recorded at rest (60 s), during the sub-maximal isometric contraction and the first 2 min of recovery.

Protocol III: Maximal eccentric voluntary contraction

To estimate the strength gains in response to the strength-training program (ST), the PT isokinetic eccentric (ECC) of the knee extension and flexion was measured before and after the training period. The PT eccentric knee extension and flexion of the dominant leg was tested at 60°/s, through a range of 90° to 30° knee flexion (full extension = 0°), by using the reactive mode (i.e., ECC/ECC cycles) and was measured by using an isokinetic dynamometer (Biodex Multi Joint System III, Biodex Medical System Inc., Shirley, NY, USA). The procedures related to isokinetic dynamometer calibration and to subject preparation were the same as described above in Protocol I. The subjects performed three sets of five maximal eccentric cycles, with a resting period of 120 s between each set. During the maximal effort trials, the participants were motivated with loud and consistent verbal encouragement. The highest value obtained from all maximal efforts was used as the PT value (N.m).

Protocol IV: Strength training program

The ST program consisted of 2–4 sets of bilateral knee eccentric flexion and extension on the same isokinetic dynamometer. Subjects of the TG were trained 2 days/week for 12 weeks and performed 8–12 repetitions with an approximate resistance of 70–80% PT (Macaluso and De Vito 2004; Kramer et al. 2002). Each set was followed by a 2 min resting period. The range and velocity of movement were the same as the initial evaluation (Protocol III). PT was measured at the beginning of the training period and every 2 weeks until the training period had been completed. Each training session started with a light 4-min warm-up on a cycle ergometer followed by a supervised stretching of the quadriceps and hamstring muscle groups.

Data analysis

To analyze the HR response during an isometric contraction, the variation (Δ) between the HR at rest (60 s pre-contraction) and the HR at 10, 30, 60 s as well as the ending of the contraction (Δ10, Δ30, Δ60 s and Δending of contraction, respectively), were calculated.

The HRV was analyzed by the time domain methods, using the RMSSD index (the square root of the mean sum of the squares of the difference between adjacent normal iR–R in the record divided by the number of the R–R intervals within a given time minus one), which represents the parasympathetic modulation on the sinus node (Malik et al. 1996).

To evaluate the autonomic control of HR during the sub-maximal isometric contraction, the RMSSD index was calculated for the first 30 s and for the last 30 s of the iR–R section in each contraction.

Statistical analysis

The unpaired *t* test was used to compare the subject's characteristics between TG and CG. ANOVA with repeated measures was used to analyze other variables. When appropriate, post-hoc analyses were conducted using the Tukey test. The effects of time (pre- vs. post-training evaluations), group (TG vs. CG) and interaction between both effects were evaluated for the eccentric PT, the isometric PT and the execution time of each sub-maximal isometric contraction. The effects of time, group, levels of contraction (15 vs. 30 vs. 40%), time of contractions (10 vs. 30 vs. 60 s vs. ending of contraction) and the interaction between these effects were evaluated through the ΔHR during isometric exercise. Furthermore, the effects of time, group, levels of contraction, moment of contraction (first 30 vs. last 30 s) and interaction between these effects were evaluated through the RMSSD index. The variable RMSSD was transformed to natural logarithms because its distribution was skewed. All data are presented as means ± SD and the significance level was set at $P < 0.05$. The analyses were carried out using Statistica for Windows 7.0 software (computer program manual, StatSoft, Inc. 2004).

Table 1 Subjects' characteristics

Characteristics	Training group	Control group
Age (years)	62 ± 2	64 ± 4
Weight (kg)	72.4 ± 7.6	74.5 ± 8.9
Height (cm)	168.3 ± 5.5	167.1 ± 4.1
BMI (kg/m^2)	25.5 ± 1.8	26.6 ± 2.6
VO_2 peak (mL/kg/min)	25.93 ± 4.8	26.2 ± 4.9

Data are reported as means ± SD

Results

Table 1 presents the subjects' characteristics. No differences were found between TG and CG. The oxygen uptake test showed that both groups had an "average" aerobic capacity according to the American Heart Association standards (Cooper and Stoker 2001).

Exercise duration and torque

Table 2 presents the eccentric PT (flexor and extensor), the isometric PT and the execution time of each sub-maximal isometric contraction. No significant changes in the isometric PT and in the execution time of each sub-maximal isometric contraction were observed after the ST in both groups. However, for eccentric PT an interaction between time and group effects were observed, i.e., a significant increase in eccentric force after the ST only for TG.

HR responses during the isometric contraction

Table 3 shows the HR change from rest to exercise in time course analysis during the sub-maximal isometric

Table 2 Eccentric and isometric peak torques (N.m) and duration of the submaximal isometric contractions (SIC)

	Training group		Control group	
	Pre-training	Post-training	Pre-training	Post-training
Peak eccentric torque (N.m)				
Extensor	210 ± 38	253 ± 61*	203 ± 33	215 ± 40
Flexor	118 ± 25	133 ± 27*	126 ± 20	135 ± 26
Peak isometric torque (N.m)	178 ± 25	195 ± 32	172 ± 27	176 ± 26
Execution time of SIC (s)				
15%	240 ± 0	240 ± 0	240 ± 0	240 ± 0
30%	204 ± 54	224 ± 37	189 ± 66	205 ± 56
40%	137 ± 58	146 ± 52	132 ± 67	152 ± 56

SIC sub-maximal isometric contraction

* $P < 0.05$ compared to pre-training, Data are reported as mean ± SD

Table 3 Heart rate change (ΔHR) from rest to exercise

	Training group		Control group	
	Pre-training	Post-training	Pre-training	Post-training
15% MVC − ΔHR (bpm)				
10 s	4 ± 6†	2 ± 3†	1 ± 4†	0 ± 3†
30 s	3 ± 5†	2 ± 3†	2 ± 5†	2 ± 2†
60 s	4 ± 4†	5 ± 3†	2 ± 3†	2 ± 4†
Ending of contraction	5 ± 5†,‡	5 ± 4†,‡	5 ± 3†,‡	4 ± 2†,‡
30% MVC − ΔHR (bpm)				
10 s	6 ± 3	3 ± 3	5 ± 5	2 ± 4
30 s	7 ± 4	8 ± 7	8 ± 3	5 ± 5
60 s	11 ± 5	9 ± 6	10 ± 6	8 ± 8
Ending of contraction	16 ± 6*,†	17 ± 8*,†	17 ± 5*,†	17 ± 9*,†
40% MVC − ΔHR (bpm)				
10 s	10 ± 7	10 ± 6	8 ± 4	6 ± 6
30 s	10 ± 8	11 ± 9	12 ± 7	11 ± 4
60 s	14 ± 6	15 ± 8	14 ± 8	13 ± 8
Ending of contraction	25 ± 11*	26 ± 13*	28 ± 10*	31 ± 17*

MVC maximal voluntary contraction, *ΔHR* heart rate change from rest to exercise

* $P < 0.05$ compared to ΔHR at 10, 30, 60 s of contraction (time of contraction effect)

† $P < 0.05$ compared to 40% (level of effort effect);

‡ $P < 0.05$ compared to 30% (level of effort effect)

Data are reported as mean ± SD

contractions for TG and CG in pre-training and post-training evaluations.

There were no effects for group and time on ΔHR during sub-maximal isometric contraction, i.e., the two groups had similar responses, and pre and post-training evaluations were similar. The ST did not modify the ΔHR during the sub-maximal isometric contractions.

However, the interaction between effort level and contraction time was significant ($P < 0.05$). The Δending of the contraction was different at Δ10, Δ30 and Δ60 s for 30 and 40% MIVC. Furthermore Δ10, Δ30, Δ60 s showed statistical significance between 15 and 40% and Δending of the contraction was significantly different between 15 and 40%, between 15 and 30% and between 30 and 40% MIVC.

HRV during the sub-maximal isometric contraction

The RMSSD index values were calculated on the two pre-selected windows (i.e., a 30 s duration at the beginning and ending of the R–R interval data) for each level of force, and they are presented in Fig. 1. An interaction between level and the effects of the moment of contraction (first 30 vs. last 30 s) was observed in the RMSSD index ($P < 0.05$). A significant decrease in the RMSSD index was observed during the isometric contraction for 30 and 40% MIVC. Moreover the RMSSD in the last 30 s of 30 and 40% were lower than 15% MIVC. No time or group effects were observed in the RMSSD index during the isometric exercise, i.e., responses were similar for the two groups and for the pre and post-training evaluations.

Discussion

Our study observed an increase only in eccentric force, which demonstrates the specificity of the training used. Our data are in accordance with Symons et al. (2005) and Paddon-Jones et al. (2001), who showed the greatest gains in strength generated by training that used specific muscle contraction. After the training, no change in the duration in which the sub-maximal contraction could be maintained was observed. A possible explanation for these results would be our use of contraction-specific training for the present study. However, Ray and Carrasco (2000) used a sub-maximal isometric contraction during their evaluation and training and also did not observe changes in the time that isometric contractions could be maintained.

Previous studies using pharmacological blockade (Maciel et al. 1985; Maciel et al. 1987; Martin et al. 1974) report that the pattern of the HR response to isometric exercise is based on a biphasic mechanism which is time dependent. At the beginning of the contraction, the fast elevation in HR occurs due to a vagal withdrawal. By continuing with the isometric exercise, a gradual tachycardia becomes evident and it is attributed to a sympathetic contribution. This pattern of HR response was observed in our study and also by authors who did not use a pharmacological blockade (Hunter et al. 2005; Iellamo et al. 1997; Maciel et al. 1989; Ray and Carrasco 2000; Seals 1993).

The HR response to isometric exercise is also dependent on contraction intensity. For different muscle groups, the literature has related a significant increase in HR, considering force levels above 20% of maximal voluntary contraction

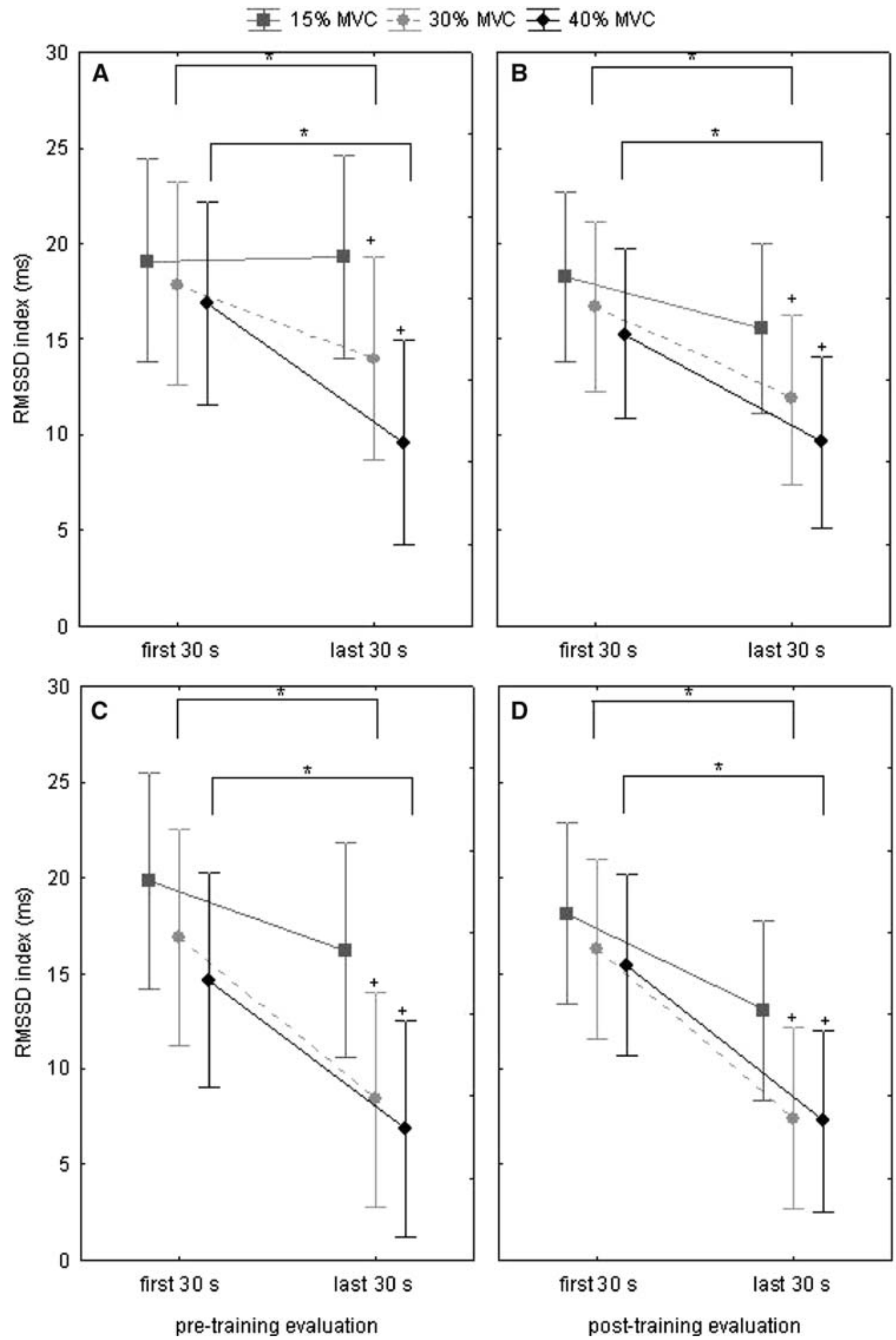

Fig. 1 RMSSD index in the first and in the last 30 s of the submaximal isometric contractions for training group in pre-training (**a**), and post-training (**b**), evaluations and for control group in pre-training (**c**), and post-training (**d**), evaluations. *MVC* maximal voluntary contraction. Data are reported as means ± SD. * $P < 0.05$ RMSSD index compared to the last 30 s of the contractions. $^{+}$ $P < 0.05$ RMSSD index compared to last 30 s of 15% MVC

(Galvez et al. 2000; Hunter et al. 2005; Iellamo et al. 1997; Maciel et al. 1989; Ray and Carrasco 2000; Seals 1993). It is also reported that the magnitude of tachycardia is directly related to the contraction intensity (Galvez et al. 2000; Maciel et al. 1989; Seals 1993). Our results are in accordance with these studies. The low level of force (15% MIVC) did not elicit a significant increase in the ΔHR. Moreover, an interaction between level of effort and time of contraction was observed. Thus, a greater % MIVC evoked a greater increase in the HR. In the time-course analysis, 30 and 40% MIVC generated a significant increase in the ΔHR from 60 s to the ending of the exercise.

Eccentric ST did not modify the HR response to isometric exercise. These results could be attributed to the specificity of the training, to the time of training, to the involved muscle mass (only flexors and extensors of knee), and/or to the training stimulus, which was not sufficiently sustained during each exercise session to influence this variable (about 20 min). Furthermore, according to what we know so far, this is the first study in which the effect of eccentric ST on the HR response to isometric exercise was evaluated in older men. Other authors have studied different types of training, such as leg endurance (Maciel et al. 1989) and handgrip (Ray and Carrasco 2000), but neither of these studies observed the effect of such training procedures on the HR response during isometric exercise.

With respect to HRV, the RMSSD during SIVC showed a decrease from the beginning to the end of contraction in 30 and 40% MIVC. In addition, a higher percentage of MIVC induced lower values of RMSSD in the last 30 s of contractions, i.e., vagal modulation reduced from the beginning to the end in higher isometric contractions. In the same way, Iellamo et al. (1999) used the HRV (frequency domain analysis) to evaluate autonomic control during isometric exercise. Briefly put, this method provides the spectral density of two main frequency ranges low (0.04–0.15 Hz) and high (0.15–0.4 Hz), which are representative of sympathetic and parasympathetic modulation, respectively (Malik et al. 1996). After this analysis, Iellamo et al. (1999) observed a significant decrease in the normalized units of high-frequency and an increase in the low-frequency when the power spectral analysis of the HRV was evaluated during isometric exercise of the knee extension at 30% MIVC. These authors suggested that a decrease in the high frequency would reflect a decrease in the parasympathetic outflow to the sinus node and that an increase in the low frequency would indicate augmented sympathetic modulation in the sinoatrial node. Similar results were observed in the present study due to the fact that the parasympathetic modulation, evaluated using the RMSSD index, was reduced during sub-maximal isometric contraction at 30 and 40% of MVC. Seeing that the RMSSD index is only a surrogate measure of vagal modulation, nothing could be affirmed about sympathetic contribution during isometric exercise. In addition, the low stability behavior of our tracings did not allow us to run the frequency domain analysis, which requires a stationary signal as a quality criterion (Malik et al. 1996).

Regarding the effects of ST on HRV, most of the extant studies have evaluated this variable only during the resting condition (Cooke and Carter 2005; Forte et al. 2003; Heffernan et al. 2007; Madden et al. 2006; Melo et al. 2008; Taylor et al. 2003). Of these studies, only Taylor et al. (2003) and Melo et al. (2008) reported changes in HRV after ST. Taylor et al. (2003) observed an increase in the high frequency after handgrip training at 30% MIVC in hypertensive older adults. Nevertheless, Melo et al. (2008), who evaluated healthy older men, noticed an autonomic imbalance towards sympathetic modulation predominance of HRV after eccentric ST.

Howbeit, we did not observe such changes in HRV during isometric exercise. Some possible explanations for these results could be the same as described previously in the unchanged HR response to isometric exercise. Moreover, the HRV decreased with age (Jensen-Urstad et al. 1997; Catai et al. 2002; Melo et al. 2005) which could have affected the “trainability” of the HRV and made it less sensitive to ST. This idea was also suggested by Forte et al. (2003) when evaluating the dynamic resistance training effect on HRV in older women. Nevertheless, neither did Cooke and Carter (2005) observe any ST effect on HRV in time and frequency domains, in spite of the fact that the subjects in their study were young.

At least two important limitations should be emphasized. First, the small number of subjects in both experimental and CGs restrains extrapolation for other populations. Second, the non-stationary behavior of our ECG signals, mainly in the higher sub-maximal intensities, did not allow us to apply frequency domain analysis. Although Bosquet et al. (2008) suggest that daily HRV variance can mask the results of training periods, we tried to minimize the effects of circadian changes on the variables, by performing all of the tests in the same period of the day and in a climate-controlled room. In addition, all participants were asked to avoid alcoholic beverages, caffeine and physical activity the day before and on the day of the experimental procedures. Finally, the signals were recorded and processed based on the Task Force guidelines (Malik et al. 1996).

In summary, the relationship between the effect of eccentric ST and autonomic modulation on the HR evaluated during isometric exercise in older men was explored in this study. Although the training improved the subjects' strength, it did not modify, positively or negatively, the HR response or the HRV (in the time domain) during sub-maximal isometric exercise. However, more studies are needed to evaluate other training stimuli, muscle mass, and non-linear analysis of HRV during exercising conditions. Furthermore, future studies are required to determine whether or not a combination of eccentric ST and aerobic exercise can provoke additional effects on HRV.

Acknowledgments The authors are grateful to Tânia de Fátima Salvini, Ph.D., for allowing the use of the isokinetic dynamometer and to FAPESP (Fundação de Amparo à Pesquisa do Estado de São Paulo) for financial support (proc. no. 06/52860-0 and 05/54838-9).

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ANEXO B

Takahashi ACM; Porta A; Melo RC; Quitério RJ; Silva E; Borghi-Silva A; Tobaldini E; Montano N; Catai AM. Aging reduces complexity of heart rate variability assessed by conditional entropy and symbolic analysis. Manuscrito submetido ao periódico *Journal of Gerontology: Medical Sciences.*

OXFORD UNIVERSITY PRESS Journal of Gerontology: Medical Sciences

AGING REDUCES COMPLEXITY OF HEART RATE VARIABILITY ASSESSED BY CONDITIONAL ENTROPY AND SYMBOLIC ANALYSIS

Journal:	*Journal of Gerontology: Medical Sciences*
Manuscript ID:	Draft
Manuscript Type:	Research Article
Date Submitted by the Author:	
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Keywords:	aging, heart rate variability, complexity, conditional entropy, symbolic analysis

AGING REDUCES COMPLEXITY OF HEART RATE VARIABILITY ASSESSED BY CONDITIONAL ENTROPY AND SYMBOLIC ANALYSIS.

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Running title: Aging and complexity of heart rate variability

Abstract

Background: The increasing age is associated with a reduction in overall heart rate variability and also changes in the complexity of physiological dynamics. The aim of this study was to verify if the alterations on autonomic modulation of heart rate caused by ageing process can be detect by Shannon entropy (SE), conditional entropy (CE) and symbolic analysis (SA). **Methods**: Complexity analysis was carried out in 44 healthy subjects divided in two groups: older (n=23, 63±3 years) and young group (n= 21, 23±2). It was analyzed SE, CE (complexity index (CI) and normalized CI (NCI)) and SA (0V, 1V, 2LV and 2ULV patterns) during short heart period series (200 cardiac beats) derived from ECG recordings during 15 minutes of rest in supine position. The sequences characterized by three heart periods with no significant variations (0V) and that with two significant unlike variations (2ULV) reflect changes in sympathetic and vagal modulation, respectively. The unpaired t-test (or Mann-Whitney rank sum test when appropriate) were used in the statistical analysis. **Results** In the aging process, the distributions of patterns (SE) remain similar to young subjects. However, the regularity was significantly different; the patterns were more repetitive in older group (a decrease of CI and NCI). The amounts of patterns types were different: 0V is increased and 2LV and 2ULV are reduced in older group. These differences indicate a marked unbalance in autonomic regulation. **Conclusions:** The CE and SA were feasible techniques to detect alteration in autonomic control of heart rate in older group.

INTRODUCTION

Cardiovascular system has an integrated organization characterized by interacting subsystems, self-sustained oscillators and feedback loops reacting to internal and external inputs including central commands, reflex mechanisms and humoral factors (1-4). Ageing process is associated with reduced ability of these subsystems to interact (5-6). These changes are reflected in a reduction in overall heart rate variability (HRV) (6-8) and also in the complexity of physiological dynamics (6-7, 9).

Most studies on HRV have been based on traditional time and frequency domain measures (8, 10-11). This type of analysis have important limitations because the results may be very sensitive to the definition of the bands (mainly to the setting of the inferior cut-off of the low frequency (LF) band, i.e., usually 0.04 Hz, and the width of the high frequency (HF) band around the respiratory rate). On the contrary, indexes based on nonlinear methods do not require any frequency band definition (12). They may provide more stable and repetitive results and uncover "hidden" abnormalities and alterations that are not otherwise apparent (9, 13-14). Moreover, nonlinear methods are inherently best suited to extract relevant information related to complexity (14-15).

Recently, several approaches have been proposed aimed to quantify the complexity. Most of these studies were based on indexes designed for the analysis of long-term time series and hence focused on 24 h ambulatory recordings (6, 15-17). On the other hand, short-term (<10 min) laboratory recordings offer the unique opportunity to assess autonomic cardiovascular regulation under controlled and standardized conditions (18). The short-term complexity has been quantified based on calculation of entropies (5, 7, 19), local nonlinear prediction (20) and symbolic dynamics (12, 21).

Complexity is measured by evaluating the amount of information carried by a time series (larger the information, greater the complexity). Usually complexity of short heart period variability series is evaluated based on estimation of the conditional entropy quantifying the amount of information that is carried by a sample of the series when past samples are known (smaller the information, more regular and predictable the series) (3, 22). Furthermore, Porta et al. (12) recently proposed a new nonlinear tool based on symbolic analysis of 3-beats sequences to distinguish sympathetic and parasympathetic cardiac modulation.

In the present study, we tested the hypothesis that the modifications caused by aging process on autonomic modulation of heart rate can be detect by Shannon entropy, conditional entropy and symbolic analysis obtained from short-term heart period variability.

METHODS

Subjects

Forty- four men volunteered took part in this study. They were divided into two groups according to age: older (N = 23; 63±2.8 years) and young (N = 21; 23±2 years). All subjects were apparently healthy, based on clinical and physical examination, as well as on laboratory tests which included a standard electrocardiogram (ECG) and a maximum exercise test conducted by a physician. Subjects that presented arterial hypertension, diabetes, chronic obstructive pulmonary disease, neurological injuries, cardiovascular, respiratory or musculoskeletal diseases were excluded. Smokers and habitual drinkers were also excluded. The subjects were informed about the experimental procedures and signed a formal acceptance form. This study was approved by the Ethics Committee of our Institution.

Experimental Procedures

All subjects were evaluated during the same period of the day in order to minimize effects due to circadian changes. The experiments were carried out in a climate-controlled room (22-23°C) with a relative air humidity of 50-60%. The day before the experiment, the subjects were taken to the experimental room for familiarization with the procedures and the equipment to be used. Each subject were instructed to avoid caffeine and alcoholic beverages as well as to avoid performing any moderate or heavy exercise on the day before the applied protocol. On the day of the experiment, before the test, the subjects were interviewed and examined to confirm their health condition, the occurrence of a regular night's sleep, and to confirm that heart rate and systemic blood pressure were within the normal range.

Experimental Protocol

Subjects were maintained at rest for 20 min for heart rate to return to control conditions. Then, 15 min of ECG recording were obtained while subjects rested quietly in the supine position. The subjects breathed spontaneously but were not allowed to talk.

ECG were monitored at a CM5 lead and was recorded from a one-channel heart monitor (TC 500, ECAFIX, São Paulo, SP, Brazil) connected to PC via an A/D board National Instruments Corp., Austin, TX, USA). Sampling frequency was 500 Hz. The heart period was approximated as the temporal distance between two consecutive R-peaks (RR). RR intervals (ms) were assessed on a beat-to-beat basis, using specific software (23).

Data Analysis

The series length N was fixed at 200 beats. The mean RR and the variance of RR series were calculated.

Symbolic analysis

The approach, which has been described by Porta et al. (24), is based on 1) transformation of heart period variability series into a sequence of integers (i.e., symbols), 2) construction of patterns (i.e., words), 3) reduction of the number of patterns by grouping them into a small number of families, and 4) evaluation of the rates of occurrence of these families. A coarse graining approach based on a uniform quantization procedure was used to transform the RR series into a sequence of symbols. Briefly, the full range of the series was spread over ξ symbols with a resolution of (RRmax-RRmin)/ξ, where RRmax and RRmin were the maximum and the minimum of the series. After quantization, the RR series became a sequence $RR_\xi = \{RR_\xi(i), i=1,...,N\}$ of integer values ranging from 0 to ξ-1. The technique of the delayed coordinates was used to transform the RR_ξ series into a sequence of patterns $RR_{\xi,L}=\{RR_{\xi,L}(i), i=L,...,N\}$ with $RR_{\xi,L}(i)=[RR_\xi(i), RR_\xi(i-1),..., RR_\xi(i-L+1)]$. The number of possible $RR_{\xi,L}(i)$ was ξ^L. Since ξ^L grew very rapidly with L and ξ, both parameters had to be small: for applications over short data sequences, the best compromise was ξ=6 and L=3, and the number of possible patterns was 216.

The Shannon entropy (SE) of the distribution of the patterns was calculated to provide a qualification of complexity of the patterns distribution. SE is an index describing the shape of the distribution of the patterns. The SE is large if the distribution is flat (all patterns are identically distributed and the series carries the maximum amount of information). On the contrary, SE is small if there is a subset of patterns more likely, while others are missing or infrequent (e.g., in a Gaussian distribution) (24).

To reduce the number of patterns without losing information, we followed a procedure of redundancy reduction. All the patterns were grouped without loss into four families, according to the number and types of variations from one symbol to the next. The pattern families were as follows: 1) patterns with no variation [0V: all the symbols are equal, e.g., (4,4,4) or (2,2,2)], 2) patterns with one variation [1V: 2 consecutive symbols are equal and the remaining symbol is different, e.g., (3,4,4) or (4,4,2)], 3) patterns with two like variations [2LV: the 3 symbols form an ascending or descending ramp, e.g., (1,2,4) or (4,3,2)], and 4) patterns with two unlike variations [2ULV: the 3 symbols form a peak or a valley, e.g.,(2,4,2) or (4,1,2)]. We evaluated the rates of occurrence of these families designated 0V%, 1V%, 2LV%, and 2ULV%. To compute these indexes, we simply count the number of times a pattern $R_{\xi=6,L=3}(i)$ belonging to a specific family was found in $RR_{\xi=6,L=3}$. The result (multiplied by 100) was divided by [N-(*L*-1)].

Studies with pharmacological blockade (21) and autonomic tests (12, 21) indicated 0V% and 2ULV% indexes capable to assess sympathetic and parasympathetic modulations, respectively.

Corrected Conditional Entropy (CCE)

This approach, described by Porta et al (19), exploited conditional entropy (CE) to measure the amount of information carried by a new sample that cannot be derived from a sequence of *L* past values. Approximation of the probabilities via sample frequencies was accomplished via a uniform quantization as reported in previous Section “Symbolic analysis”. The CE was modified to define the corrected CE (CCE). As a function of *L* past values it was shown that CCE: i) remains constant in case of white noise, ii) decreases to zero in case of fully predictable signals; iii) exhibits a minimum if repetitive patterns are embedded in noise. The pattern length L was not a priori fixed, while ξ is again fixed to six. Thus, the minimum of the CCE with respect to L past values was taken as a complexity index (CI). It was expressed in nats instead of bits because the natural logarithm was utilized. This index was normalized by the Shannon entropy of the RR series to obtain a normalized CI (NCI), thus expressing complexity in terms of dimensionless units. This index ranges from 0 (null information) to 1 (maximum information) (3). The larger both indexes, the higher complexity, the smaller regularity.

Statistical Analysis

Unpaired t-test (or Mann-Whitney rank sum test when appropriate) was used to compare the subject's characteristics, mean and variation of RR, symbolic indexes, NCI and CI. All data are presented as means ± SD and the significance level was set at $p<0.05$. The analyses were carried out using SigmaPlot for Windows Version 11.0 software.

RESULTS

Table 1 presents the subjects' characteristics. The groups presented height and BMI different ($p<0.05$).

<< Insert Table 1 >>

The older group presents lower variance of RR intervals in comparison to young group ($p<0.05$) but the mean of RR was similar in these two groups (Table 2).

<< Insert Table 2 >>

The results of complexity analysis are summarized in Table 2. The SE was not influenced by ageing. The CI and NCI were reduced in older group ($p<0.05$). The symbolic analysis indicated increase of 0V pattern and reduction of 2LV and 2ULV patterns in older group in comparison to young group ($p<0.05$).

DISCUSSION

The main findings of this study are the following: 1) a significant increase in the regularity index (a decrease of CI) in older group was observed, while SE remained unchanged; and 2) the symbolic analysis reveals differences between these groups: 0V pattern is increased and 2LV and 2ULV patterns are reduced in older group.

According to definitions, SE and CI indexes provide different informations (24). The SE is a measure of the complexity of the pattern distribution (frequency histogram of patterns distribution). The presence of peaks in the pattern distribution (relevant to patterns more frequently detected) or valleys (relevant to missing or less frequent patterns) determines the decrease of SE with respect to its maximum value provided by a flat distribution (24). The CI provides measures of the complexity of the dynamical relationship between a pattern and the next one (regularity). If the temporal sequence of the patterns is fully regular (i.e., the patterns follow each other in a repetitive periodic way), the CI is zero. On the contrary, the maximum value of the CI is found when no relationship between a pattern and the next one is found (the sequence of pattern is completely random) (24).

Thus, significant increase of regularity (i.e., a decrease of CI) does not imply a change of SE. Indeed, we observed that SE was unchanged in older subjects, thus demonstrating that patterns had the same distribution, but these patterns formed more regular and predictable sequences, thus decreasing CI.

Furthermore, SE does not provided any indication about the type of patterns detected in the series. If the dynamics of two series are characterized by different patterns with identical distribution, the SE is equal (24). Thus, a pattern classification (symbolic analysis) is necessary to understand which patterns are involved in generating the complexity.

In this study the young and older groups have similar SE values but the types of patterns are different. The older group presents an increased of 0V pattern and a reduced of 2LV and 2ULV patterns in comparison to young group.

The 0V patterns are features of slow waves (e.g., LF oscillations), while 2LV and 2ULV patterns are fragments of faster waves (e.g., HF oscillations) (24). The symbolic patterns have been related with sympathetic and vagal cardiac modulation in previous studies with pharmacological blockade and autonomic tests in healthy and disease population (12, 16, 21). The 0V pattern has been associated to sympathetic modulation while 2ULV has been associated to vagal modulation (12, 21). Thus, our results indicates that older group had an increased sympathetic and a reduced vagal cardiac modulation in comparison to young group.

A modification of complexity indexes may be associated to depressed organ function, a loss of interaction among subsystems, an overwhelming action of a subsystem over others and an impairment of regulatory mechanisms (5-6, 25). Also, complexity of the short term heart period dynamics depends on the state of the autonomic nervous system i.e., it decreases in presence of an increased sympathetic modulation (3). Frequently, these alterations are related to a pathological situation but can be present in ageing process as can be observed in this study. The older group has more regular and predictable patterns (CI and NCI reduced) and presents a predominant sympathetic modulation (higher values of 0V than young group).

In the aging process the distributions of patterns present in heart rate variability remain similar to young subjects. However, the patterns are more repetitive, thus reducing the complexity. This decrease of complexity is the result of the increased presence of stable patterns and a decreased presence of highly variable patterns. This difference indicates that apparently healthy older subjects, as evaluated in our study, have a marked unbalance in autonomic regulation. The observed changes in complexity index caused by aging process are similar to those associated with disease processes, such as chronic heart failure (16) or the onset of major arrhythmias (21).

In conclusion, autonomic alterations assessed by conditional entropy and symbolic analysis might play an important role not only in pathological condition but also in ageing process, when it might be helpful to better characterize alterations of this process.

FUNDING

This work was supported by Fundação de Amparo à Pesquisa do Estado de São Paulo (06/52860-0 to A.C.M.T. and 05/54838-9 to A.M.C.), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (PDEE/1228/08-0 to A.C.M.T.) and grant number PRIN 2007 to N.M.

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Table 1 Subjects characteristics

Characteristics	Young group	Older group
Age (years)	23 ± 2*	63 ± 3
Weight (kg)	75.3 ± 7	72.0 ± 8
Height (cm)	1.80 ± 0.05*	1.68 ± 0.05
BMI (kg/m^2)	23 ± 2*	26 ± 2

Values are expressed as mean ± SD. BMI, body mass index. * $p<0.05$ young group vs older group.

Table 2: Nonlinear analysis between young and older group.

	Young group	**Older group**
RR mean (ms)	968 ± 124	905 ± 209
VAR (ms^2)	2743 ± 1698*	1652 ± 2317
Shanon Entropy	3.67 ± 0.43	3.50 ± 0.30
Conditional entropy		
CI	1.17± 0.17*	1.05 ± 0.16
NCI	0.80 ± 0.07 *	0.71 ± 0.10
Symbolic analysis		
0V%	16.01 ± 10.90*	24.97 ± 11.32
1V%	45.66 ± 6.78	48.53 ± 5.60
2LV%	15.03 ± 6.67*	10.22 ± 4.78
2ULV%	23.31 ± 10.47*	16.30 ± 8.00

Values are expressed as mean ± SD. RR, R-R interval; VAR, variance; CI, complex index; NCI, normalized complex index. * p<0.05 young group vs older group.

ANEXO C

Melo RC; Quiterio RJ; Takahashi ACM; Silva E; Martins LEB; Catai AM. High eccentric strength training reduces heart rate variability in healthy older men. **British Journal of Sports Medicine**, v. 42, p. 59-63, 2007.

High eccentric strength training reduces heart rate variability in healthy older men

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Accepted 22 May 2007
Published Online First 11 June 2007

ABSTRACT

Background: Evaluation of non-pharmacological therapies that improve autonomic control of the heart rate in older subjects has a clinical significance, because reduced heart rate variability (HRV) can be associated with higher cardiovascular morbidity and mortality rates.

Objective: To investigate if strength training improves cardiac autonomic control in healthy older men.

Methods: The HRV of nine older healthy men (mean age 62 (2.0) years) was evaluated before and after 12 weeks of isokinetic eccentric strength training (2 days/week, 2–4 sets of 8–12 repetitions at 75–80% peak torque, involving knee flexion and extension. Electrocardiogram was continuously recorded for 15 min at rest, in supine and seated positions, before and after the strength training period. To estimate strength gains, the eccentric peak torque of the dominant leg was measured at 60°/s by the same isokinetic dynamometer.

Results: Mean systolic blood pressure decreased (123.78 (8.3) to 117.67 (10.2) mmHg, $p<0.05$) and peak torque increased (extension 210.02 (38.5) to 252.71 (60.9) N.m; flexion: 117.56 (25.1) to 132.96 (27.3) N.m, $p<0.05$) after the strength training. The frequency domain indices showed a significant training effect ($p<0.05$), since low frequency in normalised units and low frequency/high frequency ratio increased (supine, 57 (14) to 68 (14), 1.56 (0.85) to 2.35 (1.48); seated, 65 (15) to 74 (8.0), 2.48 (1.09) to 3.19 (1.31), respectively), and high frequency in normalised units decreased (supine, 43 (14) to 32 (14); seated, 35 (15) to 26 (8)) after the training period.

Conclusion: The results of the present investigation suggest that high eccentric strength training performed by healthy older men increases peak torque and reduces systolic blood pressure. However, an autonomic imbalance towards sympathetic modulation predominance was induced by an unknown mechanism.

Heart rate variability (HRV), used as a non-invasive tool to analyse the influence of the autonomic nervous system on the heart,[1] decreases with aging as a consequence of parasympathetic reduction and sympathetic modulation predominance.[2] This fact has an important clinical impact on the elderly, because reduced HRV can be associated with higher cardiovascular morbidity and mortality rates.[3]

On the other hand, long-term aerobic training seems to improve the HRV in older men[4–6] and, consequently, could be considered as a non-pharmacological cardio-protective therapy.[4] In fact, aerobic exercise plays an important role in the maintenance of physical working capacity in the elderly,[7] but the effects of aging on the muscular system (that is, the loss of muscular mass and reduction in muscle strength and power) can only be reduced by resistance training.[8] In addition to muscular function improvement, strength training appears to decrease resting blood pressure in normotensive adults[9] and in hypertensive older subjects.[10] However, the effects of resistance training on HRV remain under-investigated.

It seems reasonable that this type of exercise could have an effect on cardiac autonomic control, yet the mechanism involved is still unknown. Taylor *et al*[10] reported that handgrip isometric training, with contractions at 30% of the maximum voluntary force, was capable of reducing resting blood pressure and increasing vagal modulation in older subjects with hypertension. In contrast, other authors[11–13] did not observe any changes in HRV after resistance training.

Considering that progressive resistance training, which has been widely used to improve muscle mass and strength in the elderly,[8] could modify coronary risk factors,[14] we hypothesised that strength training would induce some changes on cardiac autonomic control, towards vagal modulation predominance. Thus, the purpose of the present study was to investigate the effects of strength training on cardiac autonomic control in healthy older men.

METHODS

Subjects

Twenty eight apparently healthy older men (age 60–69 years old) volunteered to participate in this study, but only nine of them were able to participate and/or complete the strength training. The remaining nine subjects (mean age 62 (2.0) years) were in good health based on clinical and physical examination and laboratory tests that included a standard ECG, maximum exercise test conducted by a physician, chest *x* ray, total blood count, urinalysis and clinical biochemical screen test. Subjects were excluded if they were current smokers, were taking any type of medication, or if they had participated in a regular strength training programme in the six months before initiation of the study. The subjects were informed about the experimental procedures and signed an informed consent form, approved by the ethics committee of the institution, to participate in the study. All subjects were evaluated at the same time of day in order to avoid different responses of physiological variables due to circadian changes. The experiments were carried out in a climatically controlled room at 22–23°C and relative air humidity at 50–60%, and performed on different days separated by a five-day interval. Before the day of the experiment, the subjects were taken to the experimental room for familiarisation with the procedures and the equipment to be used. Each subject had been oriented to avoid caffeinated and alcoholic beverages and to not perform moderate or heavy exercise on the day before the application of the protocols. Before beginning the test on each experimental day, the subjects were interviewed and examined to confirm their state of good health, the occurrence of a normal night's sleep, and to confirm that the control conditions (heart rate and systemic blood pressure) were within normal range.

Peak oxygen uptake (Vo_2peak)

To confirm that subjects were classified in the same functional class, Vo_2peak was determined during an incremental cycle ergometer exercise to exhaustion using a metabolic analyser (CPX-D, Medical Graphics, St Paul, MN, USA).

Heart rate variability

First, the subjects were maintained at rest for 20 min to allow the heart rate to return to control conditions. Then, 15 min of ECG data were obtained while the subjects rested quietly, breathing spontaneously, in supine and seated positions. During the experiments the subjects were monitored at the CM5 lead to register heart rate and R-R intervals (intervals between R waves on ECG). The ECG and heart rate were obtained from a one-channel heart monitor (TC 500, ECAFIX, São Paulo, SP, Brazil) and processed using an analog-digital converter Lab.PC+ (National Instruments, Co, Austin, TX, USA), which represents an interface between the heart monitor and a microcomputer. The signals were recorded in real time after analogue to digital conversion at a sampling rate of 500 Hz and the R-R intervals (ms) were calculated on a beat-to-beat basis using customised software.[15]

The HRV was analysed by the time and frequency domain methods. In the time domain, the R-R intervals were analysed by the RMSSD index, which corresponds to the square root of the mean sum of the squares of the difference between adjacent normal R-R intervals in the record divided by the number of R-R intervals within a given time minus one. Previous to the frequency domain analysis, the highest stability section RR intervals, which included at least a minimum of 5 min, were selected for HRV analysis as the criterion required for application of the spectral methods (that is, Fast Fourier Transform). Then, the power spectral components were obtained at low (0.04–0.15 Hz), and high (0.15–0.4 Hz) frequencies, in absolute units (ms^2/Hz), and the normalised units (nu) were computed by dividing the absolute power of a given low or high frequency component (ms^2/Hz) by the total power, after subtracting from it the power of the component with a frequency range between 0 and 0.03 Hz—that is, very low frequency—and then multiplying this ratio by 100. The low/high frequency ratio was also measured.[1]

Isokinetic peak torque

To estimate strength gains in response to the strength training programme, isokinetic eccentric knee extension and flexion peak torque were measured before and after training. Eccentric knee extension and flexion peak torque of the dominant leg were tested at 60°/s, through a range of 90° to 30° knee flexion and were determined using an isokinetic dynamometer (Biodex Multi Joint System III, Biodex Medical System Inc, Shirley, NY, USA). Before testing, the subjects performed a 3-min light warm-up on a cycle ergometer followed by stretching of the quadriceps and hamstring muscles. After that, they were positioned on the dynamometer's chair (seat back angle 85°) and were stabilised using pelvis, chest and thigh straps. The subjects performed three sets of five maximal eccentric cycles, with a resting period of 120 s between each set. During the maximal effort trials, they were motivated with loud and consistent verbal encouragement. The highest value obtained of all maximum efforts was used as the peak torque value (N.m).

Training programme

The strength training programme consisted of 2–4 sets of bilateral knee eccentric flexion and extension on the same isokinetic dynamometer cited above. Subjects trained for two days/week for 12 weeks and performed 8–12 repetitions with resistance equaling approximately 75–80% peak torque; each set was followed by a 2-min rest period. Peak torque was measured at the beginning of the training period and every two weeks thereafter until the training period was completed. Each training session started with a light, 3-min warm-up on a cycle ergometer followed by supervised stretching of the quadriceps and hamstring muscle groups. The non-invasive blood pressure measurement was taken before and after each exercise.

Statistical analysis

Changes in weight, body mass index (BMI), blood pressure and peak torque were assessed by t test for dependent samples. HRV indices (RMSSD, total power, low and high frequency in absolute units) were logarithmically transformed to correct the distribution skewness. The effect of strength training on HRV indices in the supine and seated positions was assessed by two-way ANOVA for repeated measures. All data are presented as mean (SD) and the level of significance was set at $p<0.05$.

RESULTS

As shown in table 1, no changes in weight, BMI, diastolic blood pressure (DBP) and mean arterial pressure (MAP) were observed after the strength training. However, systolic blood pressure (SBP) decreased after strength training (123.78 (8.3) to 117.67 (10.2) mmHg, $p<0.05$).

The oxygen uptake test showed that subjects had an "average" aerobic capacity (Vo_2peak 25.93 (4.7)) according to the American Heart Association standards.[16] The strength training increased the extension and flexion peak torque in 20% (210.02 (38.4) to 252.71 (60.95) N.m) and 13% (117.56 (25.1) to 132.96 (27.27) N.m), respectively ($p<0.05$) as shown in table 1.

Table 1 Subjects' characteristics

	Before training	After training
Age (years)	62 (2.00)	–
Height (cm)	1.69 (0.05)	–
Weight (kg)	72.52 (7.67)	73.56 (6.88)
BMI (kg/m^2)	25.43 (1.92)	25.78 (1.32)
SBP (mmHg)	123.78 (8.28)	117.67 (10.21)*
DBP (mmHg)	81.44 (6.13)	79.44 (7.16)
MAP (mmHg)	95.54 (6.73)	92.17 (7.98)
Vo_2peak (ml/kg/min)	25.93 (4.76)	–
Extension peak torque (N.m)	210.02 (38.46)	252.71 (60.95)*
Flexion peak torque (N.m)	117.56 (25.07)	132.96 (27.27)*

Data are reported as mean (SD).
DBP, diastolic blood pressure; MAP, mean arterial pressure; SBP, systolic blood pressure; Vo_2peak, peak of oxygen uptake.
*$p<0.05$.

Table 2 Pre- and post-training analysis

	Pre-training		Post-training		p Values		
	Supine	Seated	Supine	Seated	T	C	I
Time domain							
HR (bpm)	61.75 (10.6)	62.30 (11)	65.13 (8.6)	66.03 (8.6)	0.15	0.44	0.85
LogRMSSD	3.17 (0.63)	3.24 (0.61)	2.97 (0.48)	2.87 (0.38)	0.18	0.94	0.41
Frequency domain							
LogTP	7.11 (1.0)	7.07 (0.9)	7.27 (1.2)	6.70 (0.7)	0.46	0.80	0.23
LogLF	5.63 (1.2)	5.68 (1.3)	6.05 (1.1)	5.66 (0.8)	0.57	0.70	0.26
LogHF	5.34 (1.0)	4.90 (0.8)	5.39 (1.1)	4.58 (0.7)	0.18	0.74	0.37
LF (nu)	57 (14)	65 (15)	68 (14)	74 (8.0)	0.04	0.27	0.78
HF (nu)	43 (14)	35 (15)	32 (14)	26 (8.0)	0.04	0.21	0.72
LF/HF	1.56 (0.85)	2.48 (1.09)	2.35 (1.48)	3.19 (1.31)	0.03	0.17	0.83

C, condition effect (supine position vs seated position); HF, high frequency; HR, heart rate; I, interaction between training and position effects; LF, low frequency; LF/HF, low frequency/high frequency ratio; nu, normalised units; RMSSD, square root of the mean squared difference of successive R-R intervals; T, training effect (pre- vs post-training); TP, total power.
Data are reported as mean (SD).

No changes were observed in heart rate and logRMSSD for all effects studied (that is, training effect, position effect and interaction between training and position). In addition, only the frequency domain indices in normalised units and LF/HF ratio showed significant training effects ($p<0.05$), since low frequency and LF/HF increased (supine, 57 (14) to 68 (14) nu, 1.56 (0.85) to 2.35 (1.48); seated, 65 (15) to 74 (8.0) nu, 2.48 (1.09) to 3.19 (1.31), respectively), and high frequency decreased (supine, 43 (14) to 32 (14) nu; seated, 35 (15) to 26 (8) nu) after the training period. No additional effects were observed in these indices (table 2).

DISCUSSION

The present study investigated the effects of strength training on the cardiovascular variables of blood pressure and HRV indices in healthy older men. Strength training decreased the SBP and, on the other hand, increased the sympatho/vagal balance. Similar effects on HRV have not been reported before. The present results are very important as resistance training is recommended and widely used in cardiovascular rehabilitation of patients that commonly have reduced HRV.

A recent meta-analysis study reported that progressive resistance exercise decreases resting systolic and diastolic blood pressure in normotensive adults.[9] Similarly, Ray and Carrasco[17] and Taylor *et al*[10] evaluated the effects of isometric handgrip training on the cardiovascular system of normotensive young and hypertensive older adults, respectively. The first study found reduction in DBP (~5 mmHg) and MAP (~4 mmHg), while the second[10] reported a reduction in SBP (~19 mmHg) and in MAP (~11 mmHg). It is important to note that the heart rate remained unchanged in both studies. Although the present study included normotensive healthy older adults, our results are in accordance, in part, with the studies cited above. The strength training performed by our subjects reduced the SBP (~6 mmHg) without altering the DBP, MAP and heart rate.

It is well established in the literature that strength training improves muscle mass, strength and power, independent of gender and age.[18] The ACSM[18] recommends that both concentric and eccentric muscle actions must be included in strength training programmes. However, eccentric muscle action produces great force per unit of muscle size and is more neuromuscularly efficient, less metabolically demanding and more conducive to hypertrophy.[18] Additionally, studies have reported that this kind of muscle action produces less cardiovascular demand in comparison to concentric action.[19 20] Thus, the "high force, low cost" abilities of eccentric exercise are thought to be suitable for elderly subjects engaging in resistance training.[21 22] Considering the statements above, we chose to study eccentric action with the objective of increasing muscular strength without overloading the cardiovascular system.

The increase of extension and flexion peak torque, observed in the present study, were expected and in partial accordance with the literature.[23–26] However, the experimental designs used in the literature cited above made data comparison between the studies difficult, because almost all of these studies used dynamic machines to train the subjects (that is, concentric and eccentric actions) and evaluated only the concentric peak torque of knee extension.[23–25] To our knowledge, only a recent study conducted by Symons *et al*[26] compared changes in strength in response to isokinetic eccentric training to those elicited by isometric and isokinetic concentric training in older adults of both genders. After 12 weeks of strength training (three sets of 10 repetitions at 100% of knee extension peak torque), the authors observed an increase of 26% in force production for the eccentric group. Increases in peak torque were also noted in the present study, but the magnitude of knee extension peak torque gain was only 20% and lower than that observed by Symons *et al*.[26] However, these differences were expected because the intensity used in our study (75–80% of peak torque) was also lower than that used in the Symons study (100% of peak torque).

In relation to HRV, the modification observed in the present study was unexpected and is in contrast both to the beneficial changes reported for long-term aerobic training[4–6] and to the absence of modification reported for strength training.[11–13] As there are few studies in the literature relating the effect of strength training to HRV, results remain controversial. Recently, Madden *et al*[13] confirmed the hypothesis that aerobic training would have a beneficial effect on HRV while six months of whole-body strength training (three sets of 8–12 repetitions at 85% of one repetition maximum (1RM)) would have no effect in healthy older women. Similarly, Forte *et al*[11] and Cooke and Carter[12] found no modifications in the HRV indices after 16 weeks of dynamic resistance training on a cycle ergometer in healthy older women and after eight weeks of high-intensity whole-body strength training (75–80% 1RM) in young adults, respectively. In contrast, only Taylor *et al*[10] found improvement of vagal modulation after 10 weeks of isometric handgrip training (30% of the maximum voluntary contraction) in older adults with hypertension. It is important to note that in all non-trained control groups of these studies,[10 12 13] the HRV remained unchanged during the period of experimental procedures. Thus, we believe that the absence of a control group does not affect the present findings because the literature also reports that the HRV of older men and women did not modify over a 12-month control period.[5] Finally, although the differences between the experimental designs and the populations of the studies cited above made comparison with our results difficult, these facts do permit us to raise some suppositions to explain our findings.

It is possible that strength training performed at high intensity, which is necessary to bring great improvements in the muscle mass and strength, causes structural modifications in the arterial wall[27 28] and/or changes in the plasma concentration of cathecolamines.[29] It is known that during each bout of resistance exercise, arterial blood pressure achieves high values.[30] The acute intermittent elevations of arterial blood pressure, observed during strength exercise, would cause modifications in the arterial structure leading to an increase in arterial stiffness[27] and a decrease in arterial compliance[28] in young adults. In addition, intense strength training would be a strong stimulus to increase sympathetic nervous system modulation that is confirmed by increased plasma catecholamines.[29 31] As both increased arterial wall stiffness[32] and increased catecholamine levels[33] are negatively associated with cardiac vagal modulation, modifications of the autonomic control confirmed by sympathovagal imbalance would be possible within a heavy strength training programme.

However, we do not believe that the present results are associated with increased arterial wall stiffness as our strength training programme diminished the SBP, an important variable directly related to arterial wall stiffness in the elderly.[34] Moreover, a recent study[35] showed improvement of endothelial function, confirmed by the increase of NO levels (a potent vasodilator), and no modifications of central arterial stiffness in older men submitted to strength training. Thus, taking into account that HRV was modified towards sympathetic modulation predominance, increased catecholamine levels seem to be the most probable mechanism that could explain the changes presented. In fact, an elevation of basal heart rate is also an expected consequence of increased catecholamines. However, we must consider that the aging process reduces β-adrenergic responsiveness[36] and may explain the unchanged basal heart rate observed in the present study.

Additionally, there are some important limitations to this study that should be emphasised. First, there was no control group that remained sedentary during the training period. Second, endothelial function and plasma catecholamine level measurements were not performed. Therefore, our experimental design only permits us to make suppositions about the mechanisms involved in the change in HRV after a high strength training programme. It is well established that strength training produces beneficial effects on the musculoskeletal system, but its effects on cardiac autonomic modulation remain unclear. However, the present study does at least lead us to reconsider what the best resistive training prescription (that is, intensity, frequency, volume and muscle action) is for older adults, because a 12-week high strength training programme, that was performed only two days per week and localised in the leg, has produced unfavourable effects on HRV, an important indicator of cardiac health.

What is already known on this topic

- Recent studies have reported that strength training does not change heart rate variability in healthy young and older subjects.
- There are no studies in the literature that have investigated the influence of eccentric strength training on heart rate variability in healthy older subjects.

What this study adds

- Short-term eccentric strength training changes the autonomic control of heart rate towards sympathetic modulation predominance in healthy older subjects.
- These results suggest that high eccentric strength training has unfavourable effects on heart rate variability, and we should reconsider the best resistive training prescription for the elderly.

CONCLUSIONS

The results of the present investigation suggest that eccentric strength training, performed by healthy older men, increases peak torque and reduces SBP. However, it also causes an autonomic imbalance towards sympathetic modulation predominance, produced by a mechanism that is not yet identified. Therefore, further studies on the effect of eccentric exercise in different populations are needed.

Acknowledgements: The authors are grateful to the Dr T F Salvini for authorising the use of the isokinetic dynamometer. This work was funded by CAPES and FAPESP (05/54838-9).

Competing interests: None declared.

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ANEXO D

Takahashi ACM; Oliveira AO; Melo RC; Quiterio RJ; Porto PS; Catai AM. Effect of eccentric strength training on median frequency and time of fatigue in different levels of isometric contraction. In: **XVII Congress of the International Society of Electrophysiology and Kinesiology (ISEK 2008)**, 2008, Niagara Falls. XVII Congress of the International Society of Electrophysiology and Kinesiology (ISEK 2008), 2008.

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June 25th, 2008

To Whom It May Concern:

This is to certify that the study "Effect of eccentric strength training on median frequency and time of fatigue in different levels of isometric contraction", authors Anielle C. M. Takahashi, Ana Beatriz de Oliveira, Ruth C. de Melo, Robison J. Quitério, Patricia S. Porto, Aparecida M. Catai, was presented as poster at the XVII Congress of the International Society of Electrophysiology and Kinesiology (ISEK 2008).

Sincerely yours,

David A. Gabriel

David A. Gabriel, PhD,
Secretary General, ISEK2008
Email: dgabriel@Brocku.ca
(905) 688-5550, ext: 4362

EFFECT OF ECCENTRIC STRENGTH TRAINING ON MEDIAN FREQUENCY AND TIME OF FATIGUE IN DIFFERENT LEVELS OF ISOMETRIC CONTRACTION.

Anielle C. M. Takahashi[1]; Ana Beatriz de Oliveira[1]; Ruth C. Melo[1]; Robison J. Quitério[1,2]; Patrícia S. Porto[1]; Aparecida M. Catai[1]

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INTRODUCTION

The eccentric contraction has been recommended for strength training (ST) programs because, comparing it to any other contraction modes, it induces more hypertrophy (Kramer et al. 2002) and less metabolic demands (Hugget et al. 2004). The aim of this study was to evaluate the effect of eccentric strength training of knee muscles (extensors and flexors) on median frequency and time of fatigue in different levels of isometric submaximal contractions,

METHODS

The training group, TG (9 men, 62 ± 2 years old) was submitted to 12 weeks of ST for both knee muscles, extensors and flexors (2x/week, 2-4 series of 8-12 repetitions, 70-80% of eccentric peak torque). The control group, CG (8 men, 63 ± 3) did not carry out ST. Both groups were evaluated before and after the period of ST. The maximal isometric peak of torque (PT) of the dominant leg knee extension was tested at 60° of knee flexion (full extension = 0^o) by using an isokinetic dynamometer (Biodex Multi Joint System III, Biodex Medical System Inc., Shirley, NY, USA). The submaximal isometric contractions (SIC) of knee extension (15, 30 and 40% of isometric PT) were performed during 240s or until exhaustion, with a 15-20 min resting period between each level. The EMG signal during the SIC were recorded with bipolar surface electrodes (Ag/AgCl, 1-cm diameter: 20mm between electrodes) that were placed over the muscle vastus lateralis (SENIAM, 1999). Reference electrode was placed on wrist. The EMG signals were amplified (x1000), bandpass filtered (20-500Hz) and digitized at 1000 samples/s. Data analysis: the eccentric PT, the isometric PT and the duration of SIC were quantified before and after the ST period. To evaluated the muscle fatigue and EMG activity were calculated a) the median frequency over the first 30s and the last 30s of SIC. The ANOVA for repeated measures and post hoc Unequal N HSD were used for statistical analysis ($p<0.05$). For the eccentric PT, the isometric PT and the duration of SIC were evaluated the effect of ST (pre *vs* post), group (TG *vs* CG) and interaction between both effects. For the median frequency was evaluated the effect of ST (pre *vs* post training), group (TG *vs* CG), levels of contraction (15% *vs* 30% *vs* 40%), the beginning to the ending of contraction (first 30s *vs* last 30s) and interaction between these effects.

RESULTS AND DISCUSSION

As shown in table 1, no significant changes in the isometric PT and in the execution time of each sub-maximal isometric contraction were observed after the ST in both groups. However, only for TG it was possible to observe the interaction between ST and group effects, i.e. a significant increase on eccentric force, showing the specificity of the training used (Paddon-Jones et al. 2001). The table 2 shows the median frequency. For this variable it was possible to observe the effect of the beginning to the ending of contraction, i.e. for all level of effort, pre and post training, and for both groups the median frequency had a significant decrease from the first 30s to the last 30s of contraction. This result suggests that all SIC causes muscle fatigue (Merletti et al.2004). Also, we observed the interaction between ST and group effect, i.e. the TG had an increase of MF while the GC had a decrease of MF in post ST. This result suggests that ST can reduce the myoeletrical fatigue.

SUMMARY/CONCLUSIONS

Eccentric ST improves eccentric force and reduces the myoeletrical fatigue in SIC but unchanged isometric force and the time of fatigue.

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ACKNOWLEDGEMENTS

To Ph.D. Tânia de Fátima Salvini for allowing the use of isokinetic dynamometer and FAPESP (Proc.06/52860-0).

Table 1: Eccentric and isometric peak torques (PT) and time of fatigue in isometric submaximal contractions (SIC).

	Training group		Control group		p values		
	pre	**post**	**pre**	**post**	**ST**	**G**	**I**
Eccentric PT (N.m)							
Extensor	210 ± 38	253 ± 61	203 ± 33	215 ± 40	ns	0.004	0.008
Flexor	118 ± 25	133 ± 27	126 ± 20	135 ± 26	ns	0.001	0.003
Isometric PT (N.m)	178 ± 25	195 ± 32	172 ± 27	176 ± 26	ns	ns	ns
Time of fatigue in SIC (s)							
15%	240 ± 0	240 ± 0	240 ± 0	240 ± 0	ns	ns	ns
30%	203 ± 55	218 ± 50	189 ± 66	205 ± 57	ns	ns	ns
40%	136 ± 57	145 ± 56	132 ± 67	152 ± 56	ns	ns	ns

Data are reported mean ± SD. PT= peak of torque, SIC= submaximal isometric contraction, G=group effect (training *vs* control), ST=strength training effect (pre *vs* post training), I=interaction between G and T effects, ns=not significant.

Table 2: Median frequency (MF) on the first and the last 30s of contraction.

	Training group				Control group			
	pre		**post**		**pre**		**post**	
MF (Hz	**first 30s**	**last 30s**	**first 30s**	**last 30s**	**first 30s**	**last 30s**	**first 30s**	**last 30s**
15%	73 ± 9	71 ± 7	80 ± 10	77 ± 10	85 ± 11	80 ± 10	80 ± 14	74 ± 9
30%	73 ± 8	70 ± 7	79 ± 10	78 ± 12	84 ± 6	79 ± 14	78 ± 10	75 ± 12
40%	74 ± 9	69 ± 9	83 ± 10	76 ± 12	84 ± 10	75 ± 12	80 ± 10	73 ± 11

Data are reported mean ± SD.

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ANEXO E

Declaração de realização de estágio de doutorado sanduiche no período de 1 de julho de 2008 a 31 de dezembro de 2008, na Università degli Studi di Milano e descrição das atividades realizadas sob a coorientação do Prof. Dr. Nicola Montano e a colaboração do Prof. Dr. Alberto Porta. Processo: CAPES/PDEE 1228/08-0.

Coordenação de Aperfeiçoamento de Pessoal de Nível Superior
Ministério da Educação - Anexos I e II - 2º Andar
Caixa postal 365
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Brasil

CAPES

A QUEM INTERESSAR POSSA

Declaramos, para os devidos fins, que o(a) interessado(a) abaixo, foi bolsista da Capes e realizou Estágio de doutorando no Exterior, por meio do Programa de Doutorado no País com Estágio no Exterior - PDEE.

Bolsista: ANIELLE CRISTHINE DE MEDEIROS TAKAHASHI
Período da bolsa:07/2008 a 12/2008
Instituição:UNIVERSITÀ DEGLI STUDI DI MILANO
País:ITÁLIA
Área:FISIOTERAPIA E TERAPIA OCUPACIONAL.

Brasília, 7 de Abril de 2009

MARIA LUIZA DE SANTANA LOMBAS
Coordenadora-Geral de Bolsas no Exterior

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Prof. Nicola Montano

Milano, January 7, 2009

TO WHOM IT MAY CONCERN

This letter is to confirm that Dr Anielle Takahashi spent the time period from 1/07/2008 to 31/12/2008 in my lab, at the Department of Clinical Sciences, Sacco Hospital, University of Milan.

During her staying, Dr Takahashi partecipated actively to several research projects of our labs in the field of neural control of cardiovascular system.

Being exceptionally skilled in cardiovascular physiology, she was able to learn the most sophisticated linear and non-linear signal processing analysis to extract information about autonomic nervous system and cardiovascular function in control conditions and during isometric exercise. After a couple of months of study and practice, she became very active in signal processing and data interpretation.

She devoted a lot of time and effort in analyzing experiments performed in healthy human subjects undergoing an exercise training. She applied the signal analysis techniques also to other set of data consisting in patients before and after physical rehabilitation therapy.

Moreover, she performed and analyzed a series of important experiments in healthy humans, undergoing a graded tilt protocol, to evaluate the relationship between graded alterations of the autonomic nervous system and the baroreflex sensitivity and non-linear cardiac dynamics, whose preliminary data are extremely promising.

Finally she was also involved in a study on depressive subjects aimed to evaluate the effects of a breathing training on cardiac sympathovagal balance and inflammatory markers.

Working with Dr Anielle, I had the opportunity to note that she is particularly talented and well-gifted in terms of data analysis, technical skills, experimental design, protocol accomplishments. Finally, it would not be possible not to mention her extraordinary human capability of interacting with the greatest kindness and enthusiasm with everybody in the lab.

In conclusion, the staying of Dr Anielle was very fruitful for all of us and I am delighted to underline that to have the opportunity to work with Dr Anielle was a very nice human and scientific experience.

Sincerely Yours,

Prof. Nicola Montano

ANEXO F

Takahashi ACM; Melo RC; Quiterio RJ; Silva E; Tobaldini E; Porta A; Montano N; Catai AM. The eccentric strength training increases cardiac sympathetic modulation in resting condition. In: XIX IAGG World Congress of Gerontology and Geriatrics, 2009, Paris. **Journal of Nutrition, Health & Aging. Paris**: Springer, 2009.

XIX[th] IAGG World Congress of GERONTOLOGY and GERIATRICS
PARIS, 5–9 July, 2009

19th IAGG World Congress of Gerontology and Geriatrics

Paris, 5 - 9 July 2009

Société Française de Gériatrie et Gérontologie

CERTIFICATE FOR

POSTER PRESENTATION

Anielle Takahashi

We hereby certify that the above mentioned author presented the following poster:

PB6 344

THE ECCENTRIC STRENGTH TRAINING INCREASES CARDIAC SYMPATHETIC MODULATION IN RESTING CONDITION.
Ruth C Melo, Robison J Quitério, Ester Silva, Eleonora Tobaldini, Alberto Porta, Nicola Montano, Aparecida M Catai

during the 19th IAGG World Congress of Gerontology and Geriatrics, held in Paris from July 5 to 9, 2009.

Paris, July 6, 2009

The Scientific Secretariat

19th IAGG World Congress of Gerontology and Geriatrics
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participants through exercises. Bone strength and physical function were measured in all subjects before and after the program. Bone strength was assessed by a quantitative ultrasonic technique. Physical function was assessed by four tests: 10m-rapid gait time, maximum step length, 40-cm steps, and tandem gait. Differences in bone strength and physical function between groups were analyzed with unpaired t-test and analysis of covariance (ANCOVA). Partial correlations between bone density and changes in physical function were calculated after controlling for age, body mass index, and body weight in each group. The statistical package SPSS (Ver.15.0) was used for statistical analysis with 5% as the level of significance. Results: Body weight and bone strength decreased significantly ($p < 0.05$) after the program relative to values before the program in the institutionalized elderly. A significant ($p < 0.05$) negative correlation was observed between changes in body weight and changes in 10m-rapid gait time ($r=-0.452$) or bone strength ($r=-0.326$) in the institutionalized elderly. Conclusion: Decreased bone strength and physical deterioration were observed only in the institutionalized elderly. Our results suggest that the risk of fall and fracture might be higher in the institutionalized elderly compared to the community dwelling elderly. These might be prevented by improving nutrition and physical activity.

PB6 341 THE INFLUENCE OF BODY MASS INDEX (BMI) OVER THE BONE MASS IN ELDERLY WOMEN.

K. HELENA COELHO VILAÇA* (University of São Paulo, Ribeirão Preto, Brazil)
J. OLIVEIRA CARNEIRO(1), G. ARCARO DE LIMA(1), E. FERRIOLII(1), N. KILZA COSTA LIMA (1), F. JOSÉ ALBUQUERQUE DE PAULA(1), J. CESAR MORIGUTI(1) - (1) University of São Paulo (Ribeirão Preto, Brazil)

Introduction: Obesity and osteoporosis are chronic illness of high prevalence. Although not universal accepted, the obesity seems to be an osteoporosis protector agent. The aim of this study is to analyze the influence of the BMI over the bone mass in elderly women. Methods and Materials: 51 women over 65 years old were random selected to participate. The sample was divided according to the BMI classification by WHO: normal (N), overweight (OW) and obesity (OB) groups. The lumbar spine (L1-L4) and the total hip bone mineral density (BMD) were measured by the Dual-energy X-ray Absortiometry (DXA). Statistic analysis: Fisher's exact test. Results: Volunteers mean BMI was $28.4 \pm 5.7 kg/m^2$. In the N group (30%, n=15, age: 69.7±4.6) the normal BMD rates were 6.7% in the L1-L4 and 0% in the hip; osteopenia BMD rates were 60% and 80%, and the osteoporosis BMD rates were 33.3% and 20%, respectively ($P<0.01$). In the OW group (31%, n=16, age: 69.2 ±4.9) the normal rates were 25% in the L1-L4 and 50% in the hip; osteopenia rates were 37.5% and 37.5%, and osteoporosis was detected in 37.5% and 12.5%, respectively ($P<0.01$). In the OB group (39%, n=20, age: 69.8±4.4) the normal rates were 55% in the L1-L4 and 75% in the hip; osteopenia rates were 45% and 20%, and the osteoporosis was 0% and 5%, respectively ($P<0.01$). Conclusion: In this study, the elderly women with the higher BMI showed lower osteopenia and osteoporosis rates, both in the spine and the hip. These results suggest that, even in this group, the weight was a protector factor against the loss of mineral bone mass.

PB6 342 DYNAMICS AND HETEROGENEITY IN THE PROCESS OF HUMAN FRAILTY AND AGING: EVIDENCE FROM THE U.S. OLDER ADULT POPULATION

Y. YANG* (University of Chicago, Chicago, IL, United States)
L. LEE(1) - (1) University of Chicago (Chicago, IL, United States of America)

Introduction: This study investigated dynamics and heterogeneity of the frailty index (FI) conceived as a systemic indicator of biological aging in the community-dwelling older adult population in the U.S. Methods and materials: We used panel data on multiple birth cohorts from the Health and Retirement Survey 1993 – 2006 and growth curve models to estimate age trajectories of the FI and their differences by sex, race, and socioeconomic status within cohorts. Results and conclusions: The FI for cohorts born before 1942 exhibit quadratic increases with age and accelerated increases in the accumulation of health deficits. The average levels and rates of increment in the FI decrease in successive cohorts. Females, nonwhites, and individuals with low education and income exhibit greater degrees of physiological deregulation than their male, white, and high SES counterparts at any age. Patterns of sex, race, and SES differentials in rates of aging vary across cohorts. Adjusting for social behavioral factors, the analysis provides evidence for actual physiological differences in the aging process in recent cohorts of older adults, points to the need to seek biological explanations for female excess in general system damage, and reveals the inadequacy of any single mechanism for depicting the racial and SES differences in the process of physiological deterioration.

PB6 343 WHICH IS MORE EFFECTIVE AT REDUCING FALLS AND IMPROVING QUALITY OF LIFE IN OLDER FALLERS? DOMICILIARY VERSUS CENTRE-BASED REHABILITATION.

T. COMANS* (The University Of Queensland, Brisbane, Australia)
M. CURRIN(1), C. PETERS(1), S. BRAUER(1), T. HAINES(2) - (1) University of Queensland (Brisbane, Australia); (2) Monash University (Brisbane, Australia)

Aim: The Southside District Community Rehabilitation Service offers falls prevention programs to older community dwellers. This paper presents results from a RCT of the effects of two falls prevention programs on falls rates, HRQOL, activity [illegible] status and depression. Method: Data has been analysed for differences [illegible] between participants undertaking a home based rehabilitation program [illegible] undertaking a centre based rehabilitation program. Measures were taken [illegible] assessment and two follow up points – after an 8 week program and again at 6 [illegible] initial assessment. Between group analyses was conducted using generalized [illegible] equations for normally distributed data and negative binomial regression for [illegible] (e.g. falls). Results: Subjects presented with a wide range of issues in addition [illegible] including being outside normal weight range, incontinence and anxiety [illegible] Physical skills were poorer than normal for age for walking, balance, strength [illegible] times and hand function. The centre based service demonstrated significantly [illegible] in preventing falls over the home based service. Clients in the centre based arm [illegible] experienced less total falls and this group also had a greater reduction in the [illegible] of fallers after the intervention. Quality of life, timed up and go and reaction [illegible] improved in the group based intervention over the home based intervention [illegible] did not reach significance. Activity levels were similar in both groups however [illegible] scores as measured by the K-10 scale improved more in clients receiving the [illegible] service. Conclusion: This research demonstrates that delivering a similar [illegible] different settings – home based or centre based has implications for the effective[illegible] service as measured by changes in falls rates and health related quality of life. [illegible] this research shows that clients presenting with different types of co-morbidit[illegible] depression may benefit from different service delivery models.

PB6 344 THE ECCENTRIC STRENGTH TRAINING INCREASES C[illegible] SYMPATHETIC MODULATION IN RESTING CONDITION.

A. TAKAHASHI* (Universidade Federal de São Carlos, São Carlos, Brazil)
R. MELO(1), R. QUITÉRIO(2), E. SILVA(3), E. TOBALDINI(4), A. PO[illegible] MONTANO(4), A. CATAI(1) - (1) Universidade Federal de São Carlos ([illegible] Brazil); (2) UNESP (São Carlos, Brazil); (3) Universidade Metodista de Pira[illegible] Carlos, Brazil); (4) Universitá degli Studi di Milano (São Carlos, Italy)

Introduction: A decline in muscle force occurs with the aging process. The [illegible] eccentric strength training (ET) on the cardiac autonomic modulation is not clear. [illegible] and materials: The training group (TG) (9 men, 62±2 years) was submitted [illegible] (12 weeks, 2 days/week, 2-4 sets of 8-12 repetitions at 75-80% peak torque (PT) [illegible] knee flexion and extension). The control group (CG) (8 men, 64±4 years) did [illegible] the ET. The cardiac autonomic modulation was evaluated by two symbolic [illegible] percentage of sequences characterized by three heart periods with no significant [illegible] (0V%) and that with two significant unlike variations (2UV%) reflect [illegible] sympathetic and vagal modulations, respectively. Symbolic analysis was carried [illegible] heart period variability series (around 200 cardiac beats) derived from ECG [illegible] during 15 minutes of rest in supine position. The unpaired and paired t-test was [illegible] statistical analysis. Results: ET increased the eccentric torque only for TG (TG: [illegible] 253±61 and 118±25 to 133±27 N.m; CG: 203±33 to 215±40 N.m and 126±2[illegible] extensor and flexor PT respectively). There was a significant increase in 0V% [illegible] (TG: 21±10 to 32±11; CG: 28±14 to 30±7). The 2UV% declined in both [illegible] 21±11 to 15±10; CG: 17±10 to 12±5) Conclusions: ET has improved the muscle [illegible] had a negative effect on the cardiac autonomic modulation. The increase of sym[illegible] 0V% reflects a shift of the sympathovagal balance toward a sympathetic activ[illegible] fact has an important clinical impact on the elderly, because it can be associ[illegible] higher cardiovascular morbidity and mortality rates.

PB6 345 INFECTIOUS DISEASES IN HOSPITALIZED ELDERLY PATI[illegible] BEHESHTI HOSPITAL OF KASHAN-IRAN 2007

M. MOMEN HERAVI* (Kashan university of medical sciences, Kashan, Islamic [illegible] of Iran)
Z. SOLEYMANI(1), K. ESALATMANESH(2) - (1) 1 (kashan, Islamic Repub[illegible] (2) 2 (kashan, Islamic Republic of Iran)

Authors: Momen Heravi M, Soleymani Z, Esalatmanesh k Introduction: Elder[illegible] major and increasing portion of the world population. there are at increased [illegible] infection because of immunity and physiologic changes. Their mortality ,duratio[illegible] of hospitalization are more than younger patients. This study was carried out [illegible] the common infectious diseases in elderly. Materials & Methods: This descript[illegible] was performed on 200 elderly patients(≥65) who hospitalized in infectious disease [illegible] Beheshti hospital in 2007. After history taking and physical examination labor[illegible] were requested. Clinical and Para clinical findings were entered in spss and [illegible] Results: 113 (56.5%) of patients were male and 87 (43.5%)were female. 65[illegible] urban.the. The maen of age was 75.7±5.97.1.5% of them are above 90, 46% [illegible] 52.5% 65-75 year.the rate of mortality was 2.5% and the most common cause of [illegible] sepsis. The most common chief complaint and underlying disease was respirator[illegible] and hypertension 31.5%) respesctively. History of hospitalization was in [illegible] patients.) The infections included: sepsis 29 (14.5%), COPD29 (14.5%), pne[illegible] (13%), gastroentritis 25 (12.5%), UTI 21 (10.5%), viral infection 12(6%), cellul[illegible] brucellosis 8 (4%), herpes zoster 6 (3%), prostatitis 4 (3%), TB 3 (1.5%) [illegible] (1.5%), tracheobronchitis 3 (1.5%) Osteomyelitis 2 (1%), epididimoorchitis [illegible] cholecystitis 2 (1%), typhoid 1 (0.5%), non infectious 9 (4.5%) Conclusion: Seps[illegible]

ANEXO G

Takahashi ACM; Melo RC; Quiterio RJ; Silva E; Tobaldini E; Porta A; Montano N; Catai AM. Cardiac autonomic modulation during isometric exercise does not change after eccentric strength training. In: XIX IAGG World Congress of Gerontology and Geriatrics, 2009, Paris. **Journal of Nutrition, Health & Aging. Paris**: Springer, 2009.

XIXth IAGG World Congress of GERONTOLOGY and GERIATRICS
PARIS, 5-9 July, 2009

19th IAGG World Congress of Gerontology and Geriatrics

Paris, 5 - 9 July 2009

Société Française de Gériatrie et Gérontologie

CERTIFICATE FOR POSTER PRESENTATION

Anielle C M Takahashi

We hereby certify that the above mentioned author presented the following poster:

PB7 214

CARDIAC AUTONOMIC MODULATION DURING ISOMETRIC EXERCISE DOES NOT CHANGE AFTER ECCENTRIC STRENGTH TRAINING.
Ruth C Melo, Robison J Quitério, Ester Silva, Eleonora Tobaldini, Alberto Porta, Nicola Montano, Aparecida M Catai

during the 19th IAGG World Congress of Gerontology and Geriatrics, held in Paris from July 5 to 9, 2009.

Paris, July 6, 2009

The Scientific Secretariat

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[illegible] death. The potential risk of suboptimal end-of-life care for the [illegible] for the medical practice and policymakers.

[illegible] OF LIFE FOR INSTITUTIONALIZED ELDERLY PERSONS : [illegible] THE TERMINAL PHASE CARE IN LONG-TERM CARE UNITS
[illegible] Hôpital Charles Foix , Ivry sur Seine, France)
[illegible] BENTS(1), S. IKHEFOULMA(1), A. DE SAINT LEGER(1), [illegible] KEROMNES(1), C. PETIT(1), P. GAUTHIER(1), A. AZEMARD(1), [illegible] AP-HP Hôpital Ch. Foix (Ivry sur Seine, France)

[illegible] of our ongoing evaluation of our professional practice, we have [illegible] terminal phase care in the long-term care units of our hospital. [illegible] We set up a multidisciplinary workgroup that reviewed the [illegible] palliative care published by ANAES in 2002. We reviewed patient [illegible] those who died in 2008 and who were known to be in the [illegible] before death and requiring palliative care. From this group, [illegible] Each set of records (both paper based and computerized [illegible] in comparison with the audit criteria by one of the 6 teams [illegible] a paramedic and a doctor. This was done in the presence of the [illegible] The multidisciplinary meeting decisions have been recorded in [illegible] large number of cases (19/28), the records reflected a specific [illegible] approaching the end of their life. In 7/30 cases, our Palliative [illegible] assistance to the usual medical and nursing team in the care of [illegible] The administration of analgesics of the 3rd category was frequent [illegible] relatives of the dying patient was usually not discussed in the [illegible] The therapeutic or diagnostic interruption aimed at avoiding an [illegible] referred to in 17/30 of the cases. The medical and nursing [illegible] completing entire pain evaluation scores (11/30), in some cases [illegible] at all (9/21), and delivered poor mouth care (11/30). In [illegible] of the agonizing phase are seldom anticipated (4/30 for

[illegible] ELDERLY HOSPITALISED PATIENTS; ARE WE ACTING IN [illegible]
[illegible] Hospitals Bristol, Bristol, United Kingdom)
[illegible] R. FACKRELL(1) - (1) University Hospitals Bristol [illegible]

[illegible] cardiopulmonary resuscitation (CPR) services places enormous [illegible] their resources. Many healthcare systems will automatically [illegible] inpatients unless senior medical staff have documented an [illegible] CPR is inappropriate. The recently updated UK Resuscitation [illegible] healthcare staff to consider the burden of CPR as well [illegible] the patients best interests and recent published data have [illegible] are associated with poor outcome. Materials and [illegible] of 55 inpatients in a University hospital for whom the [illegible] separate intervals in 2008 and 2009 respectively. Our [illegible] survival rate and to document the clinical features and [illegible] in order to ascertain their prior likelihood of survival after [illegible] in 49 patients, 61% male. Overall survival; 2%. 90% [illegible] cardiac rhythms; pulseless electrical activity 53%, [illegible] fibrillation 12%. Monitored beds were used in 20%. Listed [illegible] included prior dependancy on carer support in 71%, chronic [illegible] COPD 26%, cancer diagnosis 24% and left ventricular [illegible] 18% respectively. Conclusions; Survival rate was [illegible] of patients were elderly and a significant proportion had [illegible] been shown to be associated with poor outcome. In [illegible] interests we need to consider a more rigorous approach in [illegible] suitable for CPR so as to permit improved care planning for [illegible]

[illegible] PALLIATIVE CARE OUTCOME MEASURES ARE SUITABLE [illegible] AGED CARE FACILITIES?
[illegible] Queensland, Brisbane, Australia)
[illegible] Care (Brisbane, Australia)

[illegible] results of a Joanna Briggs Institute systematic review [illegible] properties (reliability/validity) and feasibility of [illegible] to assess the quality of palliative care provided in [illegible] Articles were obtained from searching Medline, Cinahl, [illegible] Articles, DARE, Cochrane Reviews, TRIP and hand [illegible] journals published between 1/1/2000 and 1/9/2008. A [illegible] of which 14 were included in the final review. These [illegible] properties of ten outcome measures. This poster compares these ten outcome measures and provides recommendation for use of these in measures for clinical practice and research.

PB7 212 ARTIFICIAL NUTRITION OR HYDRATION FOR ADVANCED DEMENTIA PATIENTS. PERSPECTIVES FROM DUTCH AND AUSTRALIAN DOCTORS
H. BUITING* (Erasmus MC, Rotterdam, The Netherlands)
P. BUTOW(2), J. CLAYTON(2), J. VAN DELDEN(3), A. VAN DER HEIDE(1) - (1) Erasmus MC (Rotterdam, The Netherlands); (2) University of Sydney (Sydney, Australia); (3) University Medical Center Utrecht (Utrecht, The Netherlands)

Background It is sometimes difficult to decide about the use of artificial nutrition or hydration (ANH) for patients suffering from advanced dementia. A study in 6 European countries showed that forgoing ANH in patients nearing death is a substantial practice that, however, significantly varies between countries. Medical practitioners may thus have different ideas about the appropriateness of making decisions about ANH. We explored how Dutch and Australian doctors decide about the use of ANH for advanced dementia patients. Methods and materials We performed semi-structured interviews with 15 Dutch and 15 Australian doctors. Interviews were transcribed, coded and analysed using constant comparative analysis. Results Both Dutch and Australian doctors are hesitant to provide ANH for patients with advanced dementia, which is a progressive deteriorating disease. However, they are willing to provide ANH for a short period of time as (1) temporary treatment to overcome an acute illness, as (2) a trial of recovery potential and / or (3) to keep other persons, such as the patient's relatives, comfortable. Most Dutch doctors speak openly about withholding and withdrawing ANH as an end-of-lice decision; withdrawing ANH seems harder for them than withholding it. For Australian doctors, the difference between the two seems less relevant: they frequently do not recognize forgoing ANH as explicitly refraining from potentially life-prolonging treatment. Conclusion Dutch and Australian doctors to a great extent use similar considerations when administering ANH to patients with advanced dementia. Their decisions are largely based on medical grounds, but other factors, such as the comfort of relatives, play a role as well. Discussions about forgoing ANH seem to be more culturally determined. Open discussion may contribute to transparent and rational decision making.

PB7 213 A PILOT STUDY OF A COMMUNITY BASED YOGA INTERVENTION AMONG THE ELDERLY AND ITS EFFECTS – A QUALITATIVE STUDY
N. PATEL* (University of Texas Health Science Center San Antonio, Texas, USA, San Antonio, , United States)
S. AKKIHEBBALU(1) - (1) Kaveri Natya Yoga (San Antonio, United States of America)

Scientific evidence indicates that physical activity can extend years of active independent life, reduce disability, and improve the quality of life for older persons. Yoga is an alternative to high impact aerobic exercises that can be strenuous on the body and discouraging to the elderly. Yoga may benefit the elderly by increasing longevity; increasing cognitive and perceptual flexibility; increasing behavioral flexibility; improving mental health and sense of well-being; prevention of osteoporosis; increasing strength and improving balance and gait; and reducing falls. Also, yoga activities can be varied to suit individual needs, and the benefits of yoga may be derived from even brief periods of activity. Therefore, any elder could participate and each would benefit. Although many benefits are described, research and scientific evidence of yoga are lacking. Objectives: To identify and explore the short- and long-term outcomes of a yoga intervention Methods: Cross sectional study - yoga intervention in a senior retirement community. Pre-post intervention qualitative assessment by focus groups and key informant interviews. Group classes conducted weekly. Residents of the community, both male and female age 65 – 89 years voluntarily participated. Intervention tailored to individual functional level. 60 minutes sessions included stretching, flexibility, endurance and balance, and relaxation. Effects were evaluated at, baseline, 3 months, and 1 year. Results: Demographic measures. Other outcomes measured based on themes identified by focus group discussions and key informant interviews. Participants reported improvements in gait and stability, decreased pain, decreased falls, improved self esteem, decreased medications, improved sleep, at one year participants felt peaceful and "connected with self." Conclusion: - Intervention appealing and available to the elderly. Can be tailored to suit individual needs, may serve as a viable alternative to more strenuous physical activities. This study formed the basis for designing intervention with objective measures and stronger study design

PB7 214 CARDIAC AUTONOMIC MODULATION DURING ISOMETRIC EXERCISE DOES NOT CHANGE AFTER ECCENTRIC STRENGTH TRAINING.
A. TAKAHASHI* (Universidade Federal de São Carlos, São Carlos, Brazil)
R. MELO(1), R. QUITÉRIO(2), E. SILVA(3), E. TOBALDINI(4), A. PORTA(4), N. MONTANO(4), A. CATAI(1) - (1) Universidade Federal de São Carlos (São Carlos, Brazil); (2) UNESP (Marilia, Brazil); (3) Universidade Metodista de Piracicaba (13565905, Brazil); (4) Universitá degli Studi di Miano (Milano, Italy)

Introduction: Isometric exercise is an autonomic test that allows studying interactions between the musculoskeletal and cardiovascular systems and can be useful to evaluate strength training. The effect of eccentric strength training (ET) on the cardiac autonomic modulation is not clear. Methods and materials: Training group (TG) (9 men, 62±2 years) was submitted to ET (12 weeks, 2 days/week, 2-4 sets of 8-12 repetitions at 75-80% peak torque (PT) involving knee flexion and extension). Control group (CG) (8 men, 64±4 years) did not perform the ET. The cardiac autonomic modulation was evaluated by two symbolic indexes. The 0V% and 2UV% reflect changes in sympathetic and vagal modulations, respectively. Symbolic analysis was carried out over heart period variability series (around 200 cardiac beats) derived from ECG recordings during isometric contraction of knee extension muscle (15% of maximal voluntary contraction). The unpaired and paired t-test was used in the statistical analysis. Results: ET caused an increase on the eccentric PT only for TG (TG: 210±38 to 253±61 N.m and 118±25 to 133±27; CG: 203±33 to 215±40 N.m and 126±20 to 135±26 extensor and flexor, respectively). Isometric torque did not change for both groups (TG: 178±25 to 195±32 N.m; CG 172±27 to 176±26 N.m). The 0V% and 2UV% did not change in both groups (TG: 20±15 to 24±12 and 18±10 to 17±7, 0V% and 2V% respectively; CG: 23±10 to 17±9 and 15±5 to 19±7, 0V% and 2V% respectively). Conclusions: ET has improved only the eccentric force which can be explained by the specificity of training. The symbolic analysis has indicated that ET does not modify the cardiac autonomic control during the isometric exercise.

PB7 215 CAN MEDICATION REVIEW USING THE DRUG BURDEN INDEX IMPROVE FUNCTION IN OLDER AUSTRALIANS LIVING IN RETIREMENT VILLAGES?

D. GNJIDIC* (University of Sydney, Faculty of Medicine, Sydney, Australia)
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Introduction: The Drug Burden Index (DBI) uses the principles of dose-response and maximal effect to estimate an individual's exposure to anticholinergic and sedative medications. The association between higher DBI and impaired function has been validated in two populations of older people in the USA, and in a population of older Australian men. This study aims to assess the impact of information about DBI on prescribing in older people, and the association between change in DBI and function over 3 months. Methods: Study population includes older people living in self-care retirement villages, Sydney, Australia. Participants are randomised into intervention and control groups. The intervention involves a letter and phone call to General Practitioners, using DBI to prompt them to consider cessation or dose reduction of anticholinergic and sedative medications. Objective functional outcomes include the Short Physical Performance Battery (SPPB), maximum score 12. Results: To date, 91 (of 150) participants have been enrolled in the study (46 intervention, 45 control group). The mean age is 82.7 years. Approximately 23% are exposed to anticholinergic drugs and 22% to sedative drugs, with a mean DBI of 0.23±0.37. At baseline, after adjusting for confounders (sociodemographics, comorbidities, cognitive impairment), for every unit increase in DBI, the SPPB score decreased by 1.00 (p=0.16). The average DBI at 3 months in the 71 participants who have been followed up is 0.23±0.40. At follow up, no change in DBI was observed in 63 participants. DBI decreased in 6 (2 intervention, 4 control group), and it increased in 2 (intervention) subjects. Conclusions: On preliminary analysis, there is a non significant trend between higher DBI and poorer physical function in older Australians living in retirement villages. The intervention has not resulted in decreased DBI at 3 months.

PB7 216 A SUITABLE MODE OF RESISTANCE EXERCISE FOR COMMUNITY-DWELLING OLDER ADULTS WITH LOW MUSCULAR PERFORMANCE

R. HASEGAWA* (Seijoh University, Tokai Aichi, Japan)
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Community-dwelling older adults with low muscular performance often avoid machine-based resistance exercises from fear of their inability to do that. In this study, we evaluated the influence of pre-intervention muscular performance score (PMPS) on the outcome of a community- and home-based resistance exercise (CHRE) program among older adults. Methods: 108 older adults (46 men and 62 women, 72 +/- 5 years) participated in a 10-wk CHRE program where they performed exercises at least twice a week at home. Simultaneously, they participated a weekly exercise session (warm-up, elastic band-based resistance and cool-down exercises) at a local community center provided by instructors . Muscular performance was assessed by 30-sec arm curl test (AC) and 30-sec chair stand test (CS) before and after intervention in all participants. Participants were divided into three groups [low-score group (LS), middle-score group (MS) and high-score group (HS)] based on their PMPS. One-way ANOVA with post hoc was done to examine the differences of pre-post intervention % changes among three groups. Results: In AC, 40 participants belonged to LS (<21 reps), 30 to MS (22-23 reps) and 38 to HS (>24 reps). After CHRE program, significant differences in changes among groups were only found when LS (34 +/- 22%) was compared with MS (13 +/- 11%) and HS (16 +/- 11%). In CS, 34 participants belonged to LS (<19 reps), 35 to MS (20-21 reps) and 39 to HS (>22 reps). After CHRE program, significant differences in changes among groups were only found when LS (31 +/- 23%) was compared with MS (16 +/- 16%) and HS (16 +/- 17%). Conclusion: These results suggest that CHRE program is more effective for older [illegible] with low muscular performance, and it could be a suitable mode of resistance exercises [illegible] these people.

PB7 217 EXERCISE AND RISK OF INJURIOUS FALL IN HOME-DWELL[illegible] ELDERLY

S. IINATTINIEMI* (University of Oulu, Oulu, Finland, Oulu, Finland)
J. JOKELAINEN(1), H. LUUKINEN(1) - (1) Institute of Health Sciences, Univers[illegible] Oulu, Oulu (FI-90014 University of Oulu , Finland)

Objectives. To examine the relationship between different types of physical exercise [illegible] the risk of subsequent fall-related injury. Study Design. A prospective study of the [illegible] dwelling elderly. Methods. A population sample of home-dwelling subjects aged 85 [illegible] or older (n=512) in northern Finland participated in the study. Baseline data were [illegible] by home-nursing staff through postal questionnaires and clinical tests. Frequency and [illegible] of physical exercise – that is, walking exercise and other exercise (home exercise, [illegible] exercise, gardening, cross-country skiing, dancing, swimming, bicycling) – and falls [illegible] recorded by a nurse examiner, who telephoned the participants 8 times during a [illegible] follow-up period. Statistical analyses were based on Cox regressions and pooled [illegible] regressions. Results. The risk of injury-causing falls was reduced by other exercise [illegible] least 1 hour per week compared with corresponding non-exercise; adjusted odds [illegible] (0.19–0.72) but not by walking exercise. The risk of injury-causing falls was not [illegible] by any kind or amount of exercise taken. Female sex, a history of recent fall-related [illegible] and poor baseline near-vision acuity were the other significant predictors of injury-[illegible] falls. Conclusions. Habitual physical exercise proved to be safe and some of the [illegible] were associated with reduced risk of subsequent fall-related injury. Female sex, [illegible] causing fall in the recent past and problems with near vision increased the risk.

PB7 218 FRACTURES AFTER NURSING HOME ADMISSION: INCIDENCE [illegible] POTENTIAL CONSEQUENCES

K. RAPP* (Robert Bosch Hospital , Stuttgart, Germany)
S. LAMB(1), J. KLENK(2), A. KLEINER(2), S. HEINRICH(3), H. KÖ[illegible] T. NIKOLAUS(4), C. BECKER(5) - (1) Warwick Clinical Trials Unit, Warwick [illegible] School, University of Warwick (Coventry, United Kingdom); (2) Ins[illegible] Epidemiology, Ulm University (Ulm, Germany); (3) Health Economics Resea[illegible] Department of Psychiatry, University of Leipzig (Leipzig, Germany); (4) [illegible] Geriatric Clinic Ulm (Ulm, Germany); (5) Department of Clinical Gerontolog[illegible] Bosch-Hospital (Germany)

Introduction: Residents of nursing homes are a high risk group for fractures. The [illegible] study was to analyse fracture rates as a function of time from admission to nursing [illegible] across a range of fracture sites, gender and functional abilities. Methods: Fract[illegible] upper limb, femur, pelvis and lower leg, time to first and subsequent fractures, [illegible] and functional ability at admission were measured in 93,424 women and [illegible] 65 years and older and newly admitted to nursing homes in Bavaria between [illegible] 2006. Results: Fracture incidence was highest during the first months after [illegible] nursing homes and declined thereafter. This pattern was observed for all fract[illegible] women and men and in residents with different degrees of functional [illegible] example, fracture rates of the upper limb declined from 30.0 to 13.5/1000 person [illegible] the first nine months after admission, and for all fracture sites from 135.3 to [illegible] person-years in a corresponding time period. Conclusion: Newly admitted res[illegible] the highest fracture risk. The pattern of risk is similar across all fractures [illegible] generic causal pathway. Implementation of effective fracture and fall preven[illegible] should be a priority at the time of admission to nursing homes.

PB7 219 FALL PREVENTION PROGRAM, FOR ELDERLY IN A PORT[illegible] HOSPITAL SETTING

M. CALDEVILLA* (Escola Superior de Enfermagem do Porto, Porto, Portugal)
M. COSTA(1), M. MELO(2), J. RIBEIRO (2) - (1) Instituto Ciências Biomé[illegible] Salazar (ICBAS) (Porto, Portugal); (2) Hospital Valongo (Valongo, Portugal)

Preventing falls in hospitals or nursing homes, is today an important quality [illegible] care. In Portugal is not nursing practice the use of falls assessments tools for [illegible] nurse lead fall prevention program was developed in a Portuguese hospital. [illegible] prevention program, purposes were: Nursing education; Fall team formation [illegible] prevention protocols. With organizational support, nursing staff and a nursing [illegible] "Falls Prevention Program" started in 2008, May. With this initiative, it was [illegible] involve more than 60% of the nurses into formation and practical orientation. [illegible] nurse (FTN) approach was created. Team members included nurses and a [illegible] The FTN developed the "Falls Prevention Program", which includes: - Fall risk [illegible] of older inpatients. For this we chose de Hendrich II fall risk model; - Fall [illegible] Availability of supplies and equipments such a bed alarms, low beds, fall [illegible] (red stickers, red socks, red arm bands and bed sign) and leaflet informative [illegible] education for patient and family; - Falls reports, which includes, time, date [illegible] falls. Location, injury results and fall witnessed. Hendrich II fall risk model [illegible] cause, fall prevention kit in use and medical notice. Our fall prevention [illegible]

ANEXO H

Porta A; Catai AM; Takahashi ACM; Magagnin V; Bassani T, Tobaldini E; Montano N. Characterization of the Information Transfer along the Spontaneous Baroreflex in Healthy Humans. Manuscrito aceito para publicação no periódico **Methods of Information in Medicine.**

YAHOO! MAIL Classic

Fw: Decision on Manuscript ID ME09-02-0036.R1 - Methods of Information in Medicine Saturday, December 12, 2009 2:27 AM

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To: mcatai@ufscar.br, ninitz@yahoo.com, "tobaldini eleonora" <ele.tobaldini@gmail.com>, "Nicola Montano" <nicola.montano@unimi.it>, "Bassani Tito" <tito.bassani@libero.it>, "Magagnin Valentina" <valentina.magagnin@tin.it>

ciao

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Sent: Saturday, December 12, 2009 6:08 AM
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> Manuscript ID: ME09-02-0036.R1
> Title: Information Transfer through the Spontaneous Baroreflex in Healthy Humans
> Author(s): Porta, Alberto; Catai, Aparecida; Takahashi, Anielle; Magagnin, Valentina; Bassani, Tito; Tobaldini, Eleonora; Montano, Nicola
>
>
> 12-Dec-2009
>
>
> Dear Dr. Porta:
>
> I am glad to let you know that your revised manuscript can be accepted for publication in Methods of Information in Medicine. Your manuscript will now be sent to the publisher.
>
> Thank you for your contribution. On behalf of the Editors of Methods of Information in Medicine, we look forward to your continued contributions to the Journal.
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Information Transfer through the Spontaneous Baroreflex in Healthy Humans

Journal:	*Methods of Information in Medicine*
Manuscript ID:	ME09-02-0036.R1
Manuscript Type:	Original Article for a Special Topic
Date Submitted by the Author:	

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Keywords:	Information Transfer, Cross-Conditional Entropy, Baroreflex, Autonomic Nervous System, Cardiovascular Control

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Information Transfer through the Spontaneous Baroreflex in Healthy Humans

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Running title: Cross-conditional entropy during head-up tilt

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Summary

Objectives. This study assesses the information transfer through the spontaneous baroreflex (i.e. through the pathway linking systolic arterial pressure to heart period) during an experimental condition soliciting baroreflex (i.e. head-up tilt). **Methods.** The information transfer was calculated as the conditional entropy of heart period given systolic arterial pressure using a mutual neighbour approach and uniform quantization. The information transfer was monitored as a function of the forecasting time k. **Results.** We found that during head-up tilt the information transfer at k=0 decreased but the rate of rise of information transfer as a function of k was faster. **Conclusions.** We suggest that the characterization of the information transfer from systolic arterial pressure to heart period might complement the traditional characterization of the spontaneous baroreflex based on transfer function analysis.

Keywords: Information Transfer, Cross-Conditional Entropy, Baroreflex, Autonomic Nervous System, Cardiovascular Control.

Introduction

Baroreflex is one of the most important cardiovascular control reflex aiming at guaranteeing the homeostasis of the organism [1]. The characterization of baroreflex is based on the assessment of the baroreflex sensitivity derived as the variation of the heart period, approximated as the time interval between two consecutive R peaks on the ECG (RR interval), per unit change of systolic arterial pressure (SAP) consequent to the administration of a vasoactive drug [1].

It has been proposed that the baroreflex sensitivity could be estimated without perturbing cardiovascular regulation from the analysis of the spontaneous beat-to-beat variability of RR and SAP [2]. The analysis of the spontaneous baroreflex is limited to the assessment of parameters characterizing the transfer function between RR and SAP (i.e. gain and phase), while aspects related to information transfer between RR and SAP series along the causal direction of baroreflex (i.e. from SAP to RR) are disregarded. These aspects are very important because they allow a better characterization of the complexity of the cardiovascular control [3]. For example, if the information transfer from SAP to RR decreased (i.e. the predictability of RR given SAP was larger), it could be hypothesized a more important role of baroreflex in controlling RR dynamics. Also the assessment of the rate of rise of information transfer from SAP to RR with the forecasting time might be helpful for characterizing the complexity of the RR regulation. Indeed, it might be hypothesized that, in presence of an overwhelming regulatory mechanism as it occurs during an important baroreflex activation, the rate of rise of information transfer from SAP to RR with the forecasting time is different from that observed in presence of contemporaneous actions of multiple, weakly correlated, control mechanisms.

The aim of the study is to assess the information transfer from SAP to RR and the rise of information transfer as a function of the forecasting time using cross-conditional entropy [4] during an experimental condition known to reduce the complexity of the RR control through the important activation of the baroreflex (i.e. head-up tilt). The comparison with resting condition and uncoupled surrogates will be utilized to clarify the significance of the information transfer along baroreflex.

Methods

1. Mutual neighbour approach to the estimate of the cross-conditional entropy

Given SAP={SAP(i), i=1,…,N} and RR={RR(i), i=1,…,N}, where i is the progressive cardiac beat number, the RR and SAP series are coarse-grained according to an uniform quantization procedure: the full range of SAP and RR dynamics (i.e. the difference between the maximum and minimum value) is spread over ξ quantization bins and the values inside each bin are substituted with an integer ranging from 0 to ξ-1 coding the specific bin. Therefore, SAP and RR become quantized integer series, i.e. $SAP^{\xi}=\{SAP^{\xi}(i), i=1,\dots,N\}$ and $RR^{\xi}=\{RR^{\xi}(i), i=1,\dots,N\}$. Let us construct patterns from the quantized series using the technique of the delayed coordinates as $SAP_L^{\xi}(i)=(SAP^{\xi}(i),SAP^{\xi}(i-1), \dots, SAP^{\xi}(i-L+1))$ and $RR_L^{\xi}(i)=(RR^{\xi}(i),RR^{\xi}(i-1), \dots, RR^{\xi}(i-L+1))$. Let us be $SAP_L^{\xi}=\{SAP_L^{\xi}(i), i=1,\dots,N-L+1\}$ and $RR_L^{\xi}=\{RR_L^{\xi}(i), i=1,\dots,N-L+1\}$, the series of all patterns that can be constructed from SAP^{ξ} and RR^{ξ}. We define as neighbours of $SAP_L^{\xi}(i)$, the patterns $SAP_L^{\xi}(j)$'s in SAP_L^{ξ} such that $SAP_L^{\xi}(i)=SAP_L^{\xi}(j)$ (including $SAP_L^{\xi}(i)$) and we define as image of $SAP_L^{\xi}(i)$ the value of SAP^{ξ} occurring k steps ahead in the future (i.e. $SAP^{\xi}(i+k)$). We define as mutual neighbours of $SAP_L^{\xi}(i)$ the patterns $RR_L^{\xi}(j)$'s in RR_L^{ξ} such that their time index j coincides with the time index of the neighbours of $SAP_L^{\xi}(i)$ in SAP_L^{ξ} [5]. Given the images of the mutual neighbours of $SAP_L^{\xi}(i)$, $RR^{\xi}(j+k)$'s, the Shannon entropy (SE) of their distribution can be assessed as

$$SE(RR^{\xi}/SAP_L^{\xi}(i)) = -\sum p(RR^{\xi}(j+k)) \cdot \log(p(RR^{\xi}(j+k))) \qquad (1)$$

with $p(RR^{\xi}(j+k))=n(RR^{\xi}(j+k))/n(RR_L^{\xi}(j))$ where $n(RR^{\xi}(j+k))$ is the number of times that $RR^{\xi}(j+k)$ is detected in the set of images of mutual neighbours of $SAP_L^{\xi}(i)$ and $n(RR_L^{\xi}(j))$ is the number of mutual neighbours of $SAP_L^{\xi}(i)$. The sum is extended over all the different images of the mutual neighbours of $SAP_L^{\xi}(i)$. The cross-conditional entropy (CCE) is assessed by summing the SEs evaluated over all different $SAP_L^{\xi}(i)$'s weighted with the probability of each $SAP_L^{\xi}(i)$ as

$$CCE(RR^{\xi}/SAP_L^{\xi}) = \sum p(SAP_L^{\xi}(i)) \cdot SE(RR^{\xi}/SAP_L^{\xi}(i)) \qquad (2)$$

with $p(SAP_L^{\xi}(i))=n(SAP_L^{\xi}(i))/N-L+1$ where $n(SAP_L^{\xi}(i))$ is the number of times that $SAP_L^{\xi}(i)$ is detected in SAP_L^{ξ}. The sum is extended over all the different patterns in SAP_L^{ξ}. The CCE is a function of the embedding dimension, L, and of the forecasting time k, i.e. CCE=CCE(L,k) . The CCE for k=0, i.e CCE=CCE(L,0) is exactly the CCE defined by Porta et al in [4] according to the concept of mixed phase space constructed using one sample of RR and L-1 samples of the SAP (the current and L-2 past SAP samples). The CCE(0,k) is set equal to the SE of RR^{ξ}, i.e.

$$SE(RR^{\xi}) = -\sum p(RR^{\xi}(i)) \cdot \log(p(RR^{\xi}(i))) \qquad (3)$$

representing the amount of information carried by RR^{ξ} when SAP^{ξ} is not given with $p(RR^{\xi}(i))=n(RR^{\xi}(i))/N$ where $n(RR^{\xi}(i))$ is the number of times that $RR^{\xi}(i)$ is found in RR^{ξ}. The sum is extended over all the different values in RR^{ξ}.

2. Corrected cross-conditional entropy

As suggested by Porta et al [4], assigned k, CCE=CCE(L,k) decreases towards 0 while increasing the embedding dimension L. CCE(L,k) equals 0 when the distribution of the images of the mutual neighbours of $SAP_L^\xi(i)$ exhibits no uncertainty, thus producing $SE(RR^\xi/SAP_L^\xi(i))=0$, and this situation occurs for every $SAP_L^\xi(i)$ in SAP_L^ξ. The zero value of CCE(L,k) might be artificial and fully related to the shortness of the series: indeed, having more samples it might appear that the distribution of the images of the mutual neighbours of $SAP_L^\xi(i)$ is actually spread and CCE is different from 0. This tendency towards a decrease of CCE(L,k) follows the monotonic increase of the percentage of patterns found only once in the joint phase space $(RR^\xi(i+k),SAP_L^\xi(i))=(RR^\xi(i+k),SAP^\xi(i),SAP^\xi(i-1),\ldots, SAP^\xi(i-L+1))$, indicated as $perc(RR^\xi,SAP_L^\xi)$ with $0\leq perc(RR^\xi,SAP_L^\xi)\leq 1$ [4]. The decrease of CCE=CCE(L,k) does not depend on k but solely on L. We follow the approach set in Porta et al [4] to prevent the artificial decrease of the information carried by RR given SAP with L. We define the normalized corrected CCE (NCCCE) as

$$NCCCE(RR^\xi/SAP_L^\xi) = CCE(RR^\xi/SAP_L^\xi)/SE(RR^\xi) + perc(RR^\xi, SAP_L^\xi) \qquad (4).$$

This function decreases towards 0 only in case that RR is perfectly predictable given SAP, it remains constant when SAP is not helpful to predict RR, and it exhibits a minimum when SAP is only partially helpful to predict RR. In addition, this function is bounded between 0 and 1, where 0 indicates a full predictability of RR given SAP (null information carried by RR given SAP), while 1 indicates a perfect unpredictability (i.e. maximum information carried by RR when SAP is given). The minimum of NCCCE, labelled as $NCCCE_{min}$ in the following, is taken as a measure of information carried by RR given SAP (the larger this value, the larger the uncoupling from SAP to RR, the larger the information transfer from SAP to RR). The value of L at $NCCCE_{min}$, indicated as L_{min}, is monitored as well.

Experimental protocol and data analysis

1. Experimental protocol

We studied 19 healthy humans (aged from 21 to 48, median=30; 11 females and 8 males). We recorded surface ECG (modified lead II) and finger photopletysmographic arterial pressure (Finometer MIDI, Finapres Medical Systems, The Netherlands) at rest (R) for 7 minutes in supine position and during head-up tilt (T) at 90 degrees for 10 minutes. The study adheres to the Declaration of Helsinki on ethical principles for medical research involving human subjects. Ethical committee and review board of the "L. Sacco" Hospital approved the experimental protocol. The signals were sampled at 300 Hz. The position of the QRS complex on the ECG was fixed using parabolic interpolation. Heart period was approximated as the time distance between two consecutive QRS complexes (RR interval). The i-th SAP value was searched inside the i-th RR interval. Sequences of 256 RR and SAP values were randomly chosen inside the R and T periods and linearly detrended before any further analysis. Given this sequence length the number of quantization bins, ξ, was set to 6 [6].

2. Surrogate series

For each pair of original RR and SAP series one pair of surrogate series was constructed. The surrogate series preserved distribution and power spectrum of the original series, while phases were substituted with uniformly distributed random numbers ranging from 0 to 2π. An iteratively refined procedure was exploited [7]. It preserved exactly distribution, while the power spectrum was the best approximation of the original power spectrum according to the number of iterates (here 100). Since two independent random sequences were utilized to randomize phases of RR and SAP series, the resulting RR and SAP surrogates were uncoupled [4].

3. Statistical analysis

Wilcoxon signed rank test was utilized to check changes of sample mean and variance of RR and SAP during T. The same test was applied to the values of L_{min} when pooled together independently of k. We performed one way Friedman repeated measures analysis of variance on ranks (Dunnett's test) to compare $NCCCE_{min}$ and L_{min} derived at different forecasting time k ($1 \le k \le 8$) with $NCCCE_{min}$ and L_{min} at k=0 both at R and during T. Linear regression analysis of $NCCCE_{min}$ on k was carried out both at R and during T. The null hypothesis of slope equal to 0 (i.e. no linear relationship) was tested. In the case we found a significant linear relationship both at R and during T, the two regression lines were compared and the null hypotheses of equal slopes and equal intercepts were tested. A $p<0.05$ was considered significant in any test.

Results

Table 1 reports median (25^{th}-75^{th} percentiles) of sample mean (μ) and variance (σ^2) relevant to RR and SAP. The RR mean and variance significantly decreased during T, while SAP mean and variance significantly increased.

Figure 1 shows the box-and-whiskers plots reporting the 10^{th}, 25^{th}, 50^{th}, 75^{th} and 90^{th} percentiles of $NCCCE_{min}$ at R and during T as a function of the forecasting time k. $NCCCE_{min}$ was calculated over the original series (Figs.1a,b) and surrogates (Figs.1c,d). At R the unpredictability of RR given SAP increased as a function of the forecasting time k (Fig.1a). The same trend was observed during T (Figs.1b). $NCCCE_{min}$ became significantly different from that derived at k=0 when k was equal to or larger than 7 at R and 5 during T. When the values of L_{min} were pooled together independently of k, the median of L_{min} was 3 (min=1,max=12) at R and 3 (min=2,max=11) during T. L_{min} at R was not significantly different from L_{min} during T. L_{min} at k=0 was similar to L_{min} at k≠0 both at R and during T. $NCCCE_{min}$ at k=0 assessed over the original series was significantly smaller that that derived over surrogates both at R and during T. In addition, $NCCCE_{min}$ did not change with k when derived from surrogates both at R (Fig.1c) and during T (Fig.1d).

Linear regression analysis in the plane (k,$NCCCE_{min}$) is shown in Fig.2. A significant linear relationship of $NCCCE_{min}$ on k was found both at R (Fig.2a) and during T (Fig.2b): indeed, the slope of the linear regressions was significantly different from 0 with $p<0.05$ both at R and during T. Correlation coefficient was 0.29 at R and 0.32 during T. The slopes were positive, thus confirming that unpredictability of RR given SAP increased as a function of the forecasting time (i.e. the information transfer from SAP to RR increased with k). When assessed from surrogates, $NCCCE_{min}$ was not linearly related to k both at R (Fig.2c) and during T (Fig.2d) .

Regression lines derived from the original series at R and during T were compared. During T intercept was significantly smaller, while slope was steeper (see Fig.2 and its caption). These results indicate that the information transfer from SAP to RR was reduced during T at k=0 but the rate of rise of information transfer with k was faster.

Discussion

It is well known that T yields an important sympathetic activation as demonstrated by the significant RR decrease and an increase of the sympathetic modulation as corroborated by the significant increase of SAP variance. It is also well-known that head-up tilt produces a decrease of the baroreflex sensitivity [8].

While several studies have been focused on the assessment of the SAP-RR transfer function mainly with the aim at estimating the baroreflex sensitivity, few studies were carried out with the purpose of assessing the amount of information transferred from SAP to RR. A decrease of the information transfer from SAP to RR (i.e. a smaller unpredictability of RR given SAP) suggests a simplification of the RR regulation and a more dominant action of the baroreflex over different control mechanisms. Conversely, an increase of the information transfer (i.e. a larger unpredictability of RR given SAP) suggests a more complex regulation of RR (or a lack of regulation) and a reduced action of the baroreflex (or, possibly, an impairment of the baroreflex) in favour of different control mechanisms. We confirm that during T the information transfer from SAP to RR was reduced at k=0 (i.e. the unpredictability of RR given SAP was smaller at k=0), thus suggesting a simplification of the RR regulation during T and the important involvement of baroreflex [9].

For the first time we assessed the information transfer as a function of the forecasting time. As expected the information transfer was monotonically increased as a function of the forecasting time (i.e. the prediction made early into the future was more effective than that made far ahead). However, the rate of the rise of information transfer with the forecasting time was faster during T than that at R. Since at R multiple regulatory mechanisms are likely to be contemporaneously active and govern together the RR dynamics, while during T the RR regulation is simplified by the dominant action of baroreflex, it can be concluded that the rate of rise of information transfer through the spontaneous baroreflex is faster when baroreflex is the dominant regulatory mechanism. It is worth noting that during T the recovery of the information transfer seems incomplete ($NCCCE_{min}$ at k=8 during T remained far from 1 and below the corresponding values at R). Surrogate analysis can partially explain this finding. Indeed, when $NCCCE_{min}$ values derived from surrogates were pooled together independently of k, $NCCCE_{min}$ during T was significantly smaller than that at R, thus suggesting that the incomplete recovery of the information transfer during T is simply a bias related to the larger RR predictability observed during T [9].

Since the information transfer from SAP to RR at k=0 derived from the original series was significantly smaller than that derived from uncoupled surrogates and the information transfer from SAP to RR derived from surrogates was unrelated to k both at R and during T, we conclude that the information transfer at k=0 and the dependence of information transfer on the forecasting time typify the causal coupling from SAP to RR.

Conclusions

The characterization of the information transfer from SAP to RR as a function of the forecasting time might complement more traditional analyses of spontaneous baroreflex based on the evaluation of the gain and phase of the transfer function.

Since the proposed method is based on the assessment of the degree of unpredictability of RR given SAP, even more traditional approaches for the evaluation of unpredictability such as those based on linear and non linear causal prediction [10,11] or causal coherence [12] might be fruitfully exploited. Further studies are necessary to elucidate differences among these approaches.

Acknowledgments

The PRIN 2007WB35CW grant to A.P partially supported by the study. A.M.C. was financially supported by PDE CNPq (200717/2008-1) and A.C.M.T. by CAPES (PDEE/1228/08-0) and FAPESP (06/52860-0).

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Figure captions

Fig.1 Box-and-whiskers plots relevant to $NCCCE_{min}$ at R (a) and during T (b) as a function of the forecasting time k. Results relevant to the analysis of surrogates derived at R and during T are shown in (c) and (d) respectively. The symbol * indicates a significant difference with $p<0.05$ with respect to $NCCCE_{min}$ at $k=0$.

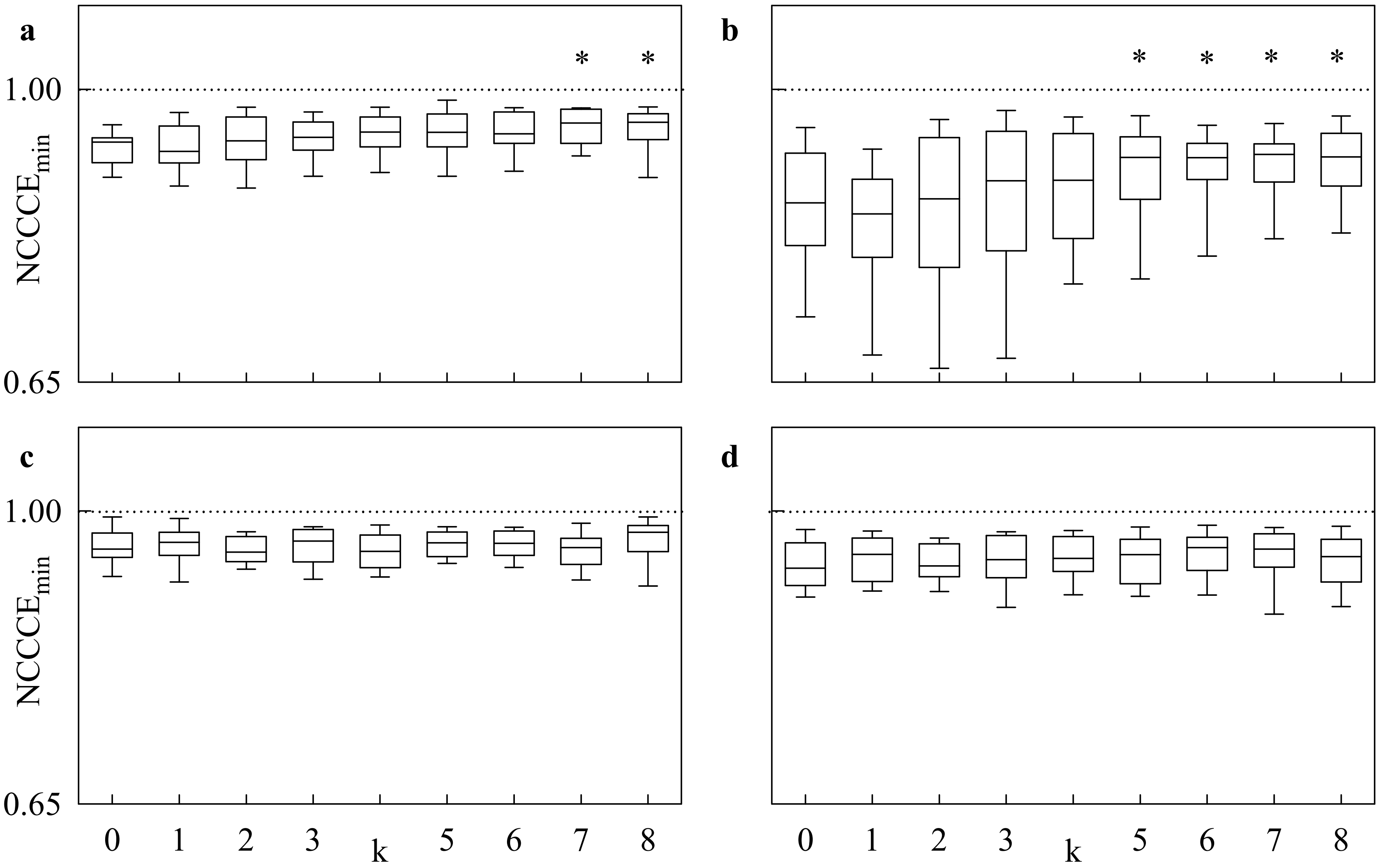
Fig.2 Individual values of $NCCCE_{min}$ are shown as a function of k. $NCCCE_{min}$ is calculated at R and during T over the original series (a and b) and surrogates (c and d). The regression line (solid line) and the 95 percent confident interval of the regression line (delimited by the dotted lines) are plotted when the regression line has slope significantly different from 0 with $p<0.05$. The two regression lines in (a) and (b) have different slopes (0.0033 and 0.0093 at R and during T) and intercepts (0.93 and 0.84 at R and during T) with $p<0.05$.

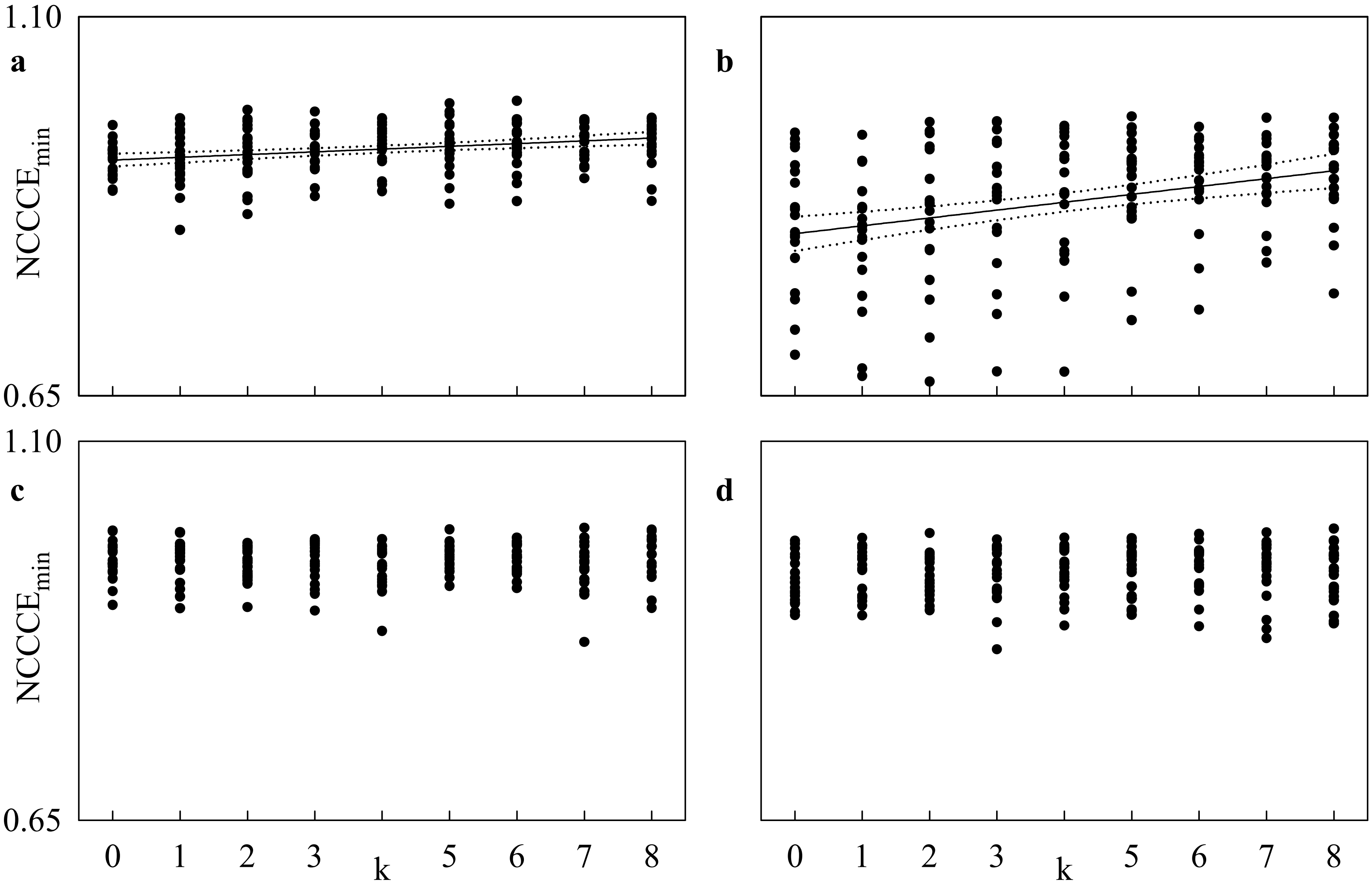
TABLE 1

MEAN AND VARIANCE OF THE RR AND SAP SERIES

	R	T
μ_{RR} [ms]	1005 (912-1060)	736 * (654-787)
σ^2_{RR} [ms^2]	3317 (2336-5435)	1800* (1336-3234)
μ_{SAP} [mmHg]	121 (117-122)	131* (125-139)
σ^2_{SAP} [mmHg^2]	16.5 (9.0-22.5)	25.3* (16.0-36.5)

Values are expressed as median (first quartile – third quartile).
μ = mean; σ^2 = variance; R = rest in supine position; T = 90° head-up tilt.
The symbol * indicates a significant difference with respect to R with $p<0.05$.


a
b
c
d
1.00
0.65
NCCCEmin
*
0
1
2
3
k
5
6
7
8


1.10
0.65
1.10
0.65
a
b
c
d
NCCCE$_{min}$
NCCCE$_{min}$
0 1 2 3 k 5 6 7 8
0 1 2 3 k 5 6 7 8

ANEXO I

Parecer do Comitê de Ética em Pesquisa da Universidade Federal de São Carlos.

UNIVERSIDADE FEDERAL DE SÃO CARLOS
PRÓ-REITORIA DE PÓS-GRADUAÇÃO E PESQUISA
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CAAE 0021.0.135.000-05

Título do Projeto: .Efeito do Treinamento de Força Excêntrica na Modulação Autonômica da Freqüência Cardíaca e nas Respostas da Eletromiografia Durante Contrações Isométricas Máximas e Submáximas

Classificação: Grupo III

Pesquisadores (as): Anielle Cristhine de Medeiros Takahashi, Profa. Dra. Aparecida Maria Catai

Parecer Nº 098/2005

1. Avaliação

O Comitê de Ética em Pesquisa em Seres Humanos da Universidade Federal de São Carlos (CEP/UFSCar) analisou o projeto de pesquisa acima identificado e considerando os pareceres do relator e do revisor DELIBEROU: O presente estudo envolverá doze indivíduos adultos, do sexo masculino, com idade entre 60 e 70 anos. A pesquisa terá por finalidade avaliar o efeito do treinamento de força nas respostas de torque, da freqüência cardíaca e do sinal eletomiográfico ao exercício isométrico durante contração máxima e da variabilidade da freqüência cardíaca e sinal eletromiográfico durante contrações sobmáximas. O pesquisador garante que testes de triagem serão supervisionados por um médico cardiologista, no laboratório de Fisioterapia Cardiovascular. Durante os exercícios, a pressão arterial e a freqüência cardíaca serão monitorizadas. Como risco potencial, os sujeitos poderão referir dor muscular após os exercícios. O Termo de consentimento está completo. Mas como em outros projetos, o pesquisador utiliza a expressão "estou ciente da importância do protocolo que serei submetido e procurarei seguir com o programa, salvo algum problema que possa surgir que me impossibilite de participar". Na seqüência o pesquisador ameniza: "No entento, tenho a liberdade de abandonar o programa, a qualquer momento, caso seja de minha vontade." Neste caso específico, entedemos que a frase acima apontada não compromete a aprovação do projeto.

2. Conclusão:

Projeto aprovado

3. Normas a serem seguidas

•O sujeito da pesquisa tem a liberdade de recusar-se a participar ou de retirar seu consentimento em qualquer fase da pesquisa, sem penalização alguma e sem prejuízo ao seu cuidado (Res. CNS 196/96 – Item IV.1.f) e deve receber uma cópia do Termo de Consentimento Livre e Esclarecido, na íntegra, por ele assinado (Item IV.2.d).

• O pesquisador deve desenvolver a pesquisa conforme delineada no protocolo aprovado e descontinuar o estudo somente após análise das razões da descontinuidade pelo CEP que o aprovou (Res. CNS Item III.3.z), aguardando seu parecer, exceto quando perceber risco ou dano não previsto ao sujeito participante ou quando constatar a superioridade de regime oferecido a um dos grupos da pesquisa (Item V.3) que requeiram ação imediata.

• O CEP deve ser informado de todos os efeitos adversos ou fatos relevantes que alterem o curso normal do estudo (Res. CNS Item V.4). É papel do pesquisador assegurar medidas imediatas adequadas frente a evento adverso grave ocorrido (mesmo que tenha sido em outro centro) e enviar notificação ao CEP e à Agência Nacional de Vigilância Sanitária – ANVISA – junto com seu posicionamento.

• Eventuais modificações ou emendas ao protocolo devem ser apresentadas ao CEP de forma clara e sucinta, identificando a parte do protocolo a ser modificada e suas justificativas. Em caso de projetos do Grupo I ou II apresentados anteriormente à ANVISA, o pesquisador ou patrocinador deve enviá-las também à mesma, junto com o parecer aprovatório do CEP, para serem juntadas ao protocolo inicial (Res. 251/97, item III.2.e).

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• Relatórios parciais e final devem ser apresentados ao CEP, inicialmente em ___/____/____ e ao término do estudo.

São Carlos, 7 de junho de 2005.

Profa. Dra. Márcia Niituma Ogata
Coordenadora do CEP/UFSCar