する方法としての有用である可能性が示唆されたといえる。

Ｅ．結論

地域在住高齢者を対象に、超音波によって測定された踵骨骨量（SOS）による介護予防事業における二次予防事業対象者のリスク評価を検証した結果、特に高齢女性においては、低骨量になるほど二次予防事業対象者に該当する危険性が高くなることが示された。一方で、高齢男性は、踵骨骨量（SOS）による二次予防事業対象者のリスク評価はあまり適してはいなかった。

Ｆ．研究発表

1．論文発表

Kojima N, Kim H, Saito K, Yoshida H, Yoshida Y, Hirano H, Obuchi S, Shimada H, Suzuki T. Association of knee-extension strength with instrumental activities of daily living in community-dwelling older adults. Geriatr Gerontol Int, (in press).

Kim H, Suzuki T, Saito K, Yoshida H, Kojima N, Kim M, Sudo M, Yamashiro Y, Tokimitsu I. Effects of exercise and tea catechins on muscle mass, strength and walking ability in community-dwelling elderly Japanese sarcopenic women: A randomized controlled trial. Geriatr Gerontol Int, 13: 458-465, 2013.

Yoshida Y, Iwasa H, Kumagai S, Suzuki T, Yoshida H. Limited functional health literacy, health information sources, and health behavior among community-dwelling older adults in Japan. ISRN Geriatrics, (in press).

Yoshimura N, Akune T, Fujiwara S, Shimizu Y, Yoshida H, Omori G, Sudo A, Nishiwaki Y, Yoshida M, Shimokata H, Suzuki T, Muraki S, Oka H, Nakamura K. Prevalence of knee pain, lumbar pain and its coexistence in Japanese men and women: The Longitudinal Cohorts of Motor System Organ (LOCOMO) study. J Bone Miner Metab, (in press).

金憲経, 鈴木隆雄, 吉田英世, 島田裕之, 山城由華吏, 須藤元喜, 仁木佳文. 都市部在住高齢女性の膝痛、尿失禁、転倒に関連する歩行要因. 日老医誌, 50(4), 528-535, 2013.

Iwasa H, Kai I, Yoshida Y, Suzuki T, Kim H, Yoshida H. Global cognition and 8-year survival among Japanese community-dwelling older adults. Int J Geriatr Psychiatry, 28: 841-849, 2013.

Kim H, Suzuki T, Saito K, Kim M, Kojima N, Ishizaki T, Yamashiro Y, Hosoi E, Yoshida H. Effectiveness of exercise with or without thermal therapy for community-dwelling elderly Japanese women with non-specific knee pain: A randomized controlled trial. Arch Gerontol Geriatr, 57: 352-359, 2013.

Kim H, Yoshida H, Suzuki T. Falls and

fractures in participants and excluded non-participants of a fall prevention exercise program for elderly women with a history of falls: 1-year follow-up study. Geriatr Gerontol Int, (in press).

Kim H, Yoshida H, Hu X, Saito K, Yoshida Y, Kim M, Hirano H, Kojima N, Hosoi E, Suzuki T. Association between self-reported urinary incontinence and musculoskeletal conditions in community-dwelling elderly women: A cross-sectional study. Neurourol Urodyn, (in press).

2. 学会発表

吉田英世, 金憲経, 小島成実, 吉田祐子, 齋藤京子, 金美芝, 平野浩彦, 岩佐一, 島田裕之, 鈴木隆雄. 地域在住高齢者の基礎的運動能力からみた要介護化の危険因子の検討. 第 72 回日本公衆衛生学会総会, 三重, 2013 年 10 月 23-25 日.

河合恒, 大渕修一, 光武誠吾, 吉田英世, 平野浩彦, 小島基永, 藤原佳典, 井原一成. 超音波画像による大腿前面筋エコー強度と運動器の機能低下リスクとの関係. 第 48 回日本理学療法学術大会, 愛知, 2013 年 5 月 24-26 日.

G. 知的財産権の出願・登録状況（予定を含む）

1. 特許取得

なし

2. 実用新案登録

なし

3. その他

なし

表1-1　二次予防事業対象者(性・年齢階級別)

	男性					女性				
年齢階級	対象者(+)		対象者(-)		計	対象者(+)		対象者(-)		計
65～69歳	13	14.8%	75	85.2%	88	22	18.5%	97	81.5%	119
70～74歳	15	15.2%	84	84.8%	99	30	22.2%	105	77.8%	135
75～79歳	16	21.1%	60	78.9%	76	35	29.9%	82	70.1%	117
80～86歳	17	27.4%	45	72.6%	62	14	31.1%	31	68.9%	45
全体	61	18.8%	264	81.2%	325	101	24.3%	315	75.7%	416

表1-2　運動器該当者(性・年齢階級別)

	男性					女性				
年齢階級	該当者(+)		該当者(-)		計	該当者(+)		該当者(-)		計
65～69歳	4	4.5%	84	95.5%	88	4	3.4%	115	96.6%	119
70～74歳	6	6.1%	93	93.9%	99	14	10.4%	121	89.6%	135
75～79歳	8	10.4%	69	89.6%	77	20	16.9%	98	83.1%	118
80～86歳	10	16.4%	51	83.6%	61	8	17.8%	37	82.2%	45
全体	28	8.6%	297	91.4%	325	46	11.0%	371	89.0%	417

表1-3　栄養該当者(性・年齢階級別)

	男性					女性				
年齢階級	該当者(+)		該当者(-)		計	該当者(+)		該当者(-)		計
65～69歳	0	0.0%	88	100.0%	88	2	1.7%	117	98.3%	119
70～74歳	1	1.0%	97	99.0%	98	3	2.2%	132	97.8%	135
75～79歳	0	0.0%	77	100.0%	77	2	1.7%	116	98.3%	118
80～86歳	1	1.6%	61	98.4%	62	2	4.4%	43	95.6%	45
全体	2	0.6%	323	99.4%	325	9	2.2%	408	97.8%	417

表1-4　口腔機能該当者(性・年齢階級別)

	男性					女性				
年齢階級	該当者(+)		該当者(-)		計	該当者(+)		該当者(-)		計
65～69歳	11	12.5%	77	87.5%	88	16	13.4%	103	86.6%	119
70～74歳	8	8.1%	91	91.9%	99	18	13.3%	117	86.7%	135
75～79歳	12	15.8%	64	84.2%	76	20	17.1%	97	82.9%	117
80～86歳	11	17.7%	51	82.3%	62	8	17.8%	37	82.2%	45
全体	42	12.9%	283	87.1%	325	62	14.9%	354	85.1%	416

表2－1　骨量4分位別の二次予防事業対象者数（男性）

男性	二次予防事業								
骨量（SOS）	対象者（+）		対象者（-）		計	オッズ比	95%信頼区間		有意確率
Q1；　～1471	19	23.8%	61	76.3%	80	1.69	（ 0.73	～ 3.91 ）	0.22
Q2；1472～1487	16	19.3%	67	80.7%	83	1.37	（ 0.59	～ 3.21 ）	0.47
Q3；1488～1509	15	19.5%	62	80.5%	77	1.62	（ 0.69	～ 3.81 ）	0.27
Q4；1510～	11	13.1%	73	86.9%	84	0.00			
全体	61	18.8%	263	81.2%	324	※年齢調整済　オッズ比			

表2－2　骨量4分位別の運動器（該当）者数（男性）

男性	運動器（3項目以上該当）								
骨量（SOS）	該当（+）		該当（-）		計	オッズ比	95%信頼区間		有意確率
Q1；　～1471	10	12.5%	70	87.5%	80	2.84	（ 0.74	～ 11.01 ）	0.13
Q2；1472～1487	8	9.5%	76	90.5%	84	2.25	（ 0.56	～ 8.97 ）	0.25
Q3；1488～1509	7	9.2%	69	90.8%	76	2.88	（ 0.71	～ 11.71 ）	0.14
Q4；1510～	3	3.6%	81	96.4%	84	1.00	（	～ ）	
全体	28	8.6%	296	91.4%	324	※年齢調整済　オッズ比			

表2－3　骨量4分位別の栄養（該当）者数（男性）

男性	栄養（2項目該当）								
骨量（SOS）	該当（+）		該当（-）		計	オッズ比	95%信頼区間		有意確率
Q1；　～1471	1	1.3%	79	98.8%	80	-	（ -	～ - ）	-
Q2；1472～1487	0	0.0%	83	100.0%	83	-	（ -	～ - ）	-
Q3；1488～1509	1	1.3%	76	98.7%	77	-	（ -	～ - ）	-
Q4；1510～	0	0.0%	84	100.0%	84	-	（ -	～ - ）	-
全体	2	0.6%	322	99.4%	324	※年齢調整済　オッズ比			

表2－4　骨量4分位別の口腔機能（該当）者数（男性）

男性	口腔機能（2項目以上該当）								
骨量（SOS）	該当（+）		該当（-）		計	オッズ比	95%信頼区間		有意確率
Q1；　～1471	14	17.5%	66	82.5%	80	1.35	（ 0.55	～ 3.33 ）	0.51
Q2；1472～1487	9	10.8%	74	89.2%	83	0.81	（ 0.31	～ 2.13 ）	0.66
Q3；1488～1509	9	11.7%	68	88.3%	77	0.98	（ 0.37	～ 2.56 ）	0.96
Q4；1510～	10	11.9%	74	88.1%	84	1.00			
全体	42	13.0%	282	87.0%	324	※年齢調整済　オッズ比			

表2－1　骨量4分位別の二次予防事業対象者数（男性）

男性	二次予防事業								
骨量（SOS）	対象者（+）		対象者（-）		計	オッズ比	95%信頼区間		有意確率
Q1；　～1471	19	23.8%	61	76.3%	80	1.69	（ 0.73	～ 3.91 ）	0.22
Q2；1472～1487	16	19.3%	67	80.7%	83	1.37	（ 0.59	～ 3.21 ）	0.47
Q3；1488～1509	15	19.5%	62	80.5%	77	1.62	（ 0.69	～ 3.81 ）	0.27
Q4；1510～	11	13.1%	73	86.9%	84	0.00			
全体	61	18.8%	263	81.2%	324	※年齢調整済　オッズ比			

表2－2　骨量4分位別の運動器（該当）者数（男性）

男性	運動器（3項目以上該当）								
骨量（SOS）	該当（+）		該当（-）		計	オッズ比	95%信頼区間		有意確率
Q1；　～1471	10	12.5%	70	87.5%	80	2.84	（ 0.74	～ 11.01 ）	0.13
Q2；1472～1487	8	9.5%	76	90.5%	84	2.25	（ 0.56	～ 8.97 ）	0.25
Q3；1488～1509	7	9.2%	69	90.8%	76	2.88	（ 0.71	～ 11.71 ）	0.14
Q4；1510～	3	3.6%	81	96.4%	84	1.00	（	～ ）	
全体	28	8.6%	296	91.4%	324	※年齢調整済　オッズ比			

表2－3　骨量4分位別の栄養（該当）者数（男性）

男性	栄養（2項目該当）								
骨量（SOS）	該当（+）		該当（-）		計	オッズ比	95%信頼区間		有意確率
Q1；　～1471	1	1.3%	79	98.8%	80	-	（ -	～ - ）	-
Q2；1472～1487	0	0.0%	83	100.0%	83	-	（ -	～ - ）	-
Q3；1488～1509	1	1.3%	76	98.7%	77	-	（ -	～ - ）	-
Q4；1510～	0	0.0%	84	100.0%	84	-	（ -	～ - ）	-
全体	2	0.6%	322	99.4%	324	※年齢調整済　オッズ比			

表2－4　骨量4分位別の口腔機能（該当）者数（男性）

男性	口腔機能（2項目以上該当）								
骨量（SOS）	該当（+）		該当（-）		計	オッズ比	95%信頼区間		有意確率
Q1；　～1471	14	17.5%	66	82.5%	80	1.35	（ 0.55	～ 3.33 ）	0.51
Q2；1472～1487	9	10.8%	74	89.2%	83	0.81	（ 0.31	～ 2.13 ）	0.66
Q3；1488～1509	9	11.7%	68	88.3%	77	0.98	（ 0.37	～ 2.56 ）	0.96
Q4；1510～	10	11.9%	74	88.1%	84	1.00			
全体	42	13.0%	282	87.0%	324	※年齢調整済　オッズ比			

厚生労働科学研究費補助金（長寿科学総合研究事業）

分担研究報告書

地域在住後期サルコペニア高齢者の特徴及び要介護状態について

分担研究者　金　憲経
東京都健康長寿医療センター研究所　研究副部長

研究要旨　地域在住後期高齢者におけるサルコペニア有症率は35.6%（サルコペニア 26.5%、重症サルコペニア 9.1%）であった。重症サルコペニアはサルコペニアより転倒（サルコペニア OR=2.38、95%CI=1.41-4.01、重症サルコペニア OR=4.09、95%CI=2.04-8.23）、変形性膝関節症（サルコペニア OR=1.01、95%CI=0.65-1.58、重症サルコペニア OR=2.67、95%CI=1.42-5.02）、IADL障害（サルコペニア OR=2.49、95%CI=0.79-7.87、重症サルコペニア OR=11.32、95%CI=3.72-34.40）の危険性が高いことを確認した。介護認定者の分布は、正常群（要支援 83.9%、要介護 16.1%）、サルコペニア群（要支援 75.8%、要介護 24.2%）、重症サルコペニア群（要支援 62.5%、要介護 37.5%）と重症サルコペニア群で要介護認定率が高いことから、重症サルコペニア予防策の確立が介護予防において今後の重要な課題といえる。

A．研究目的

地域在住後期サルコペニア高齢者における老年症候群の有症状況、体力の特徴、要介護状態について検討した。

B．研究方法

平成24年度大都市部在住高齢女性575人を対象に包括的検診を実施し、身長、体重、血圧、聞き取り調査（健康度自己評価、過去1年間の転倒、転倒恐怖感、骨折歴、外出頻度、生活機能、運動習慣、社会活動、痛み、既往歴等）体力（筋力、歩行機能、バランス能力）、身体組成（DXA法による体脂肪率、筋肉量、骨密度）、血液成分（アルブミン、コレステロール、クレアチニン、HbA1c、ヘモグロビン等）のデータを収集した。

サルコペニアの選定基準：①骨格筋量減少、②筋力低下、③歩行速度低下を用いて、サルコペニア（骨格筋量減少+筋力低下あるいは骨格筋量減少+歩行速度低下）、重症サルコペニア（骨格筋量減少+筋力低下+歩行速度低下）に分類した。

（倫理面への配慮）

本研究のプロトコルは東京都健康長寿医療センター倫理委員会の承諾を得た。また、健診参加者には個別に調査目的、調査内容、個人情報の管理、調査結果の活用、結果のフィードバックなどについて詳細に説明し、調査への参加を自ら選択するように説明すると共に自筆の承諾書を得た上で実施した。

C．研究結果

サルコペニア有症率は 35.6%（サルコペニア 26.5%、重症サルコペニア 9.1%）であった。正常群、サルコペニア群、重症サルコペニア群を比較したところ、重症サルコペニア群は筋量が少なく、下腿三頭筋囲が細く、握力や膝伸展力の衰え、歩行速度の低下が確認された。正常群を基準としたときのサルコペニア、重症サルコペニアの転倒（サルコペニア OR=2.38、95%CI=1.41-4.01、重症サルコペニア OR=4.09、95%CI=2.04-8.23）、変形性膝関節症（サルコペニア OR=1.01、95%CI=0.65-1.58、重症サルコペニア OR=2.67、95%CI=1.42-5.02）、IADL 障害（サルコペニア OR=2.49、95%CI=0.79-7.87、重症サルコペニア OR=11.32、95%CI=3.72-34.40）のオッズ比を検討したところ、サルコペニアより重症サルコペニアの OR が高かった。

さらに、正常群とサルコペニア群における要介護申請の有無について、申請有は正常群 15.0%、サルコペニア群 32.2%（χ^2=20.24、P<0.001）とサルコペニア群で有意に高かった。申請後の要介護認定率は正常群 87.5%、サルコペニア群 98.3%（χ2=4.95、P=0.026）であった。介護認定者の分布は、正常群（要支援 83.9%、要介護 16.1%）、サルコペニア群（要支援 75.8%、要介護 24.2%）、重症サルコペニア群（要支援 62.5%、要介護 37.5%）と重症サルコペニア群で要介護認定率が高かった。

D．考察

今日まで、骨格筋量の減少に伴う筋力や歩行機能の低下を指す sarcopenia に焦点を当てた研究は数多く報告され、高齢者の健康長寿に様々な影響を及ぼすことが指摘されている。さらに、European Working Group on Sarcopenia in Older People はサルコペニアの概念的段階を presarcopenia、sarcopenia、severe sarcopenia に分けて検討することを提案しているが、sarcopenia と severe sarcopenia の特徴や要介護状態について検討した研究は見当たらないのが現状である。

これらの背景を踏まえて、骨格筋量減少に伴う筋力の衰え、歩行速度の低下の段階をサルコペニアと重症サルコペニアに分けて検討したところ、転倒の危険性はサルコペニア OR=2.38、重症サルコペニア OR=4.09 と重症サルコペニアで高かった。一方、変形性膝関節症は重症サルコペニアで OR=2.67、IADL 障害は重症サルコペニアで OR=11.32 と有意に上昇していた。これらの結果より、重症サルコペニアで老年症候群の危険性が上昇することが確認された。

さらに、要介護認定率は重症サルコペニア群で 37.5%と高いことから、介護予防の観点から重症サルコペニア改善策の確立は大変重要であることが強く示唆された。

E．結論

地域在住後期高齢者におけるサルコペニア有症率は 35.6%（サルコペニア 26.5%、重症サルコペニア 9.1%）であった。重症サルコペニアはサルコペニアより転倒、変形性膝関節症、IADL 障害の危険性が高く、要介護認定率も高いことから、重症サルコペニア予防策の確立が、介護予防において今後の重要な課題といえる。

F．研究発表

1．論文発表

Kim H, Suzuki T, Saito K, Yoshida H, Kojima N, Kim M, Sudo M, Yamashiro Y, Tokimitsu I.

Effects of exercise and tea catechins on muscle mass, strength and walking ability in community-dwelling elderly Japanese sarcopenic women: A randomized controlled trial. Geriatr Gerontol Int, 13: 458-465, 2013.

Kim M, Kim H. Accuracy of segmental multi-frequency bioelectrical impedance analysis for whole-body and appendicular fat mass and lean soft tissue mass in frail women aged 75 years and older. Eur J Clin Nutr, 67: 395-400, 2013.

Sakurai R, Fujiwara Y, Saito K, Fukuya T, Kim MJ, Yasunaga M, Kim H, Ogawa K, Tanaka C, Tsunoda N, Muraki E, Suzuki K, Shinkai S, Watanabe S. Effects of a comprehensive intervention program including hot bathing, on overweight adults: A randomized controlled trial. Geriatr Gerontol Int, 13: 638-645, 2013.

金憲経, 鈴木隆雄, 吉田英世, 島田裕之, 山城由華吏, 須藤元喜, 仁木佳文: 都市部在住高齢女性の膝痛, 尿失禁, 転倒に関連する歩行要因. 日老医誌, 50: 528-535, 2013.

Iwasa H, Kai I, Yoshida Y, Suzuki T, Kim H, Yoshida H. Global cognition and 8-year survival among Japanese community-dwelling older adults. Int J Geriatr Psychiatry, 28: 841-849, 2013.

須藤元喜, 山城由華吏, 上野加奈子, 金憲経. シート式圧力センサーを用いて計測した歩容左右差による年齢推定. 日生理人類会誌, 18: 125-132, 2013.

金憲経. サルコペニア予防と健康増進. Geriatr Med, 51: 937-940, 2013.

Kim H, Suzuki T, Saito K, Kim M, Kojima N, Ishizaki T, Yamashiro Y, Hosoi E, Yoshida H. Effectiveness of exercise with or without thermal therapy for community-dwelling elderly Japanese women with non-specific knee pain: A randomized controlled trial. Arch Gerontol Geriatr, 57: 352-359, 2013.

金憲経. サルコペニアに対する運動・栄養による介入効果. 医学のあゆみ, 248: 747-752, 2014.

Kim H, Yoshida H, Suzuki T. Falls and fractures in participants and excluded non-participants of a fall prevention exercise program for elderly women with a history of falls: 1-year follow-up study. Geriatr Gerontol Int, (in press).

Kim H, Yoshida H, Hu X, Saito K, Yoshida Y, Kim M, Hirano H, Kojima N, Hosoi E, Suzuki T. Association between self-reported urinary incontinence and musculoskeletal conditions in community-dwelling elderly women: A cross-sectional study. Neurourol Urodyn, (in press).

2. 学会発表

Kim H, Suzuki T, Saito K, Kojima N, Kim M, Yoshida Y, Hirano H, Yoshida H. Exercise and thermal therapy for community-dwelling Japanese elderly women with chronic knee pain: A randomized controlled trial. 2012 American Geriatrics Society Annual Scientific Meeting, Seattle, WA, USA, 5.2-5, 2012.

Kim MJ, Kim H, Kojima N. Exploring Physical Activity Patterns on Body Composition Phenotypes of Sarcopenia and Obesity in Older Adults. The 59th annual meeting of American College of Sports Medicine, San Francisco, 5.28-6.2, 2012.

金憲経. サルコペニア・虚弱への介入研究. 第54回日本老年医学会学術集会・総会, 東京, 6.28-30, 2012.

金憲経. 転倒予防と膝痛予防. 第155回日本体力医学会関東地方会, 横浜, 7.7, 2012.

金憲経. 高齢者の元気長寿支援—廃用症候群の早期予防の視点から—. 第60回日本教育医学会記念大会, 茨城, 8.25-26, 2012.

Kim H. Intervention for chronic knee pain in community-dwelling elderly Japanese women. The 4th Asian International Seminar for Geriatrics and Gerontology, Tokyo, Japan, 9.14, 2012.

Kim H. State of research on and tasks of public health organizations for the health of the elderly. International Symposium for Public Health, Seoul, Korea, 10.1, 2012.

Kim H, Yoshida H, Hu X, Saito K, Yoshida Y, Kim M, Kojima N, Hirano H, Suzuki T. Association between urinary incontinence and pain in community-dwelling elderly women. 42nd Annual Meeting of the International Continence Society, Beijing, China, 10.15-19, 2012.

金憲経, 小島成実, 金美芝, 山城由華吏, 須藤元喜, 吉田英世, 齋藤京子, 吉田祐子, 平野浩彦, 鈴木隆雄. 膝痛高齢者を対象に実施した運動及び温熱療法の効果検証（1）—体力に及ぼす影響—. 第71回日本公衆衛生学会総会, 山口, 10.24-26, 2012.

小島成実, 金憲経, 金美芝, 山城由華吏, 須藤元喜. 膝痛高齢者を対象に実施した運動及び温熱療法の効果検証（2）—ＪＫＯＭによる評価—. 第71回日本公衆衛生学会総会, 山口, 10.24-26, 2012.

須藤元喜, 山城由華吏, 小島成実, 金美芝, 金憲経. 膝痛高齢者を対象に実施した運動及び温熱療法の効果検証（2）—歩行解析を中心に—. 第71回日本公衆衛生学会総会, 山口, 10.24-26, 2012.

G. 知的財産権の出願・登録状況

（予定を含む。）

1. 特許取得

   なし

2. 実用新案登録

   なし

3. その他

   なし

研究成果の刊行に関する一覧表

書籍

著者氏名	論文タイトル名	書籍全体の編集者名	書　籍　名	出版社名	出版地	出版年	ページ
原田敦	ヒッププロテクターの使用評価状況	井上剛伸	ヒトの運動機能と移動のための次世代技術開発	エヌ・ティー・エス	東京	2014	69-72
松井康素,原田敦	関節疾患、ロコモティブシンドローム	日本老年医学会	老年医学　系統講義テキスト	日本老年医学会	東京	2013	245-249
島田裕之	Part-6 その他の介入法: 運動	葛谷雅文,雨海照祥	栄養・運動で予防するサルコペニア	医歯薬出版株式会社	東京	2013	134-139
島田裕之	サルコペニアの診断—Q.8 サルコペニアの診断基準はありますか	関根里恵,小川純人	サルコペニア 24 のポイント～高齢者への適切なアプローチをめざして～	フジメディカル出版	大阪	2013	42-46
金憲経	サルコペニアの診断—Q.10 診断のための臨床症候について教えてください	関根里恵,小川純人	サルコペニア 24 のポイント～高齢者への適切なあブローチをめざして～	フジメディカル出版	大阪	2013	52-56
Kim H	Behavioral therapy for urinary incontinence	Eric Chung	Urinary Incontinence: Causes, Epidemiology	Nova Science Publishers Inc	New York	2013	71-88

雑誌

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Shimada H, Ishii K, Ishiwata K, Oda K, Suzukawa M, Makizako H, Doi T, Suzuki T	Gait adaptability and brain activity during unaccustomed treadmill walking in healthy elderly females	Gait Posture	38	203-208	2013
Shimada H, Makizako H, Doi T, Yoshida D, Tsutsumimoto K, Anan Y, Uemura K, Ito T, Lee S, Park H, Suzuki T	Combined prevalence of frailty and mild cognitive impairment in a population of elderly Japanese people	JAMDA	14	518-524	2013
Shimada H, Suzuki T, Suzukawa M, Makizako H, Doi T, Yoshida D, Tsutsumimoto T, Anan Y, Uemura K, Ito T, Lee S, Park H	Performance-based assessments and demand for personal care in older Japanese people	BMJ Open	3	e002424	2013
Yoshida D, Suzuki T, Shimada H, Park H, Makizako H, Doi T, Anan Y, Tsutsumimoto K, Uemura K, Ito T, Lee S	Using two different algorithms to determine the prevalence of sarcopenia	Geriatr Gerontol Int	14(Suppl.1)	46–51	2014
Yoshida D, Shimada H, Park H, Anan Y, Ito T, Harada A, Suzuki T	Development of an equation for estimating appendicular skeletal muscle mass in Japanese older adults using bioelectrical impedance analysis	Geriatr Gerontol Int			in press
Kojima N, Kim H, Saito K, Yoshida H, Yoshida Y, Hirano H, Obuchi S, Shimada H, Suzuki T	Association of knee-extension strength with instrumental activities of daily living in community-dwelling older adults	Geriatr Gerontol Int			in press
Yoshimatsu T, Yoshida D, Shimada H, Komatsu T, Harada A, Suzuki T	Relation between near-infrared spectroscopy and subcutaneous fat and muscle thickness measured by ultrasonography in Japanese community-dwelling elderly	Geriatr Gerontol Int	13	351-357	2013

Kim H, Suzuki T, Saito K, Yoshida H, Kojima N, Kim M, Sudo M, Yamashiro Y, Tokimitsu I	Effects of exercise and tea catechins on muscle mass, strength and walking ability in community-dwelling elderly Japanese sarcopenic women: A randomized controlled trial	Geriatr Gerontol Int	13	458-465	2013
Yoshida Y, Iwasa H, Kumagai S, Suzuki T, Yoshida H	Limited Functional health literacy, health information sources, and health behavior among community-dwelling older adults in Japan	ISRN Geriatrics			in press
Yoshimura N, Akune T, Fujiwara S, Shimizu Y, Yoshida H, Omori G, Sudo A, Nishiwaki Y, Yoshida M, Shimokata H, Suzuki T, Muraki S, Oka H, Nakamura K	Prevalence of knee pain, lumbar pain and its coexistence in Japanese men and women: The Longitudinal Cohorts of Motor System Organ (LOCOMO) study	J Bone Miner Metab			in press
曽根稔雅, 中谷直樹, 遠又靖丈, 相田潤, 大久保一郎, 大原里子, 大渕修一, 杉山みち子, 安村誠司, 鈴木隆雄, 辻一郎	介護予防サービス利用者における生活機能の予後予測及び効果的な運動器の機能向上プログラムの実施内容に対する評価	日衛誌	68	11-21	2013
Ito S, Harada A, Kasai T, Sakai Y, Takemura M, Matsui Y, Hida T, Ishiguro N	Use of alfacalcidol in osteoporotic patients with low muscle mass may increase muscle mass: An investigation using a patient database	Geriatr Gerontol Int	14(Suppl.1)	122-128	2014
Nishiyama KK, Ito M, Harada A, Boyd SK	Classification of women with and without hip fracture based on quantitative computed tomography and finite element analysis	Osteoporos Int	25(2)	619-626	2014
Matsui Y, Takemura M, Harada A, Ando F, Shimokata H	Effects of knee extensor muscle strength on the incidence of osteopenia and osteoporosis after six years	J Bone Miner Metab			in press

Matsui Y, Fujita R, Harada A, Sakurai T, Nemoto T, Noda N, Toba K	The association of grip strength and related indices with independence of activities of daily living in the elderly, investigated by a newly-developed grip strength measuring device	Geriatr Gerontol Int	14(Suppl.2)	77-86	2014
Matsui Y, Fujita R, Harada A, Sakurai T, Nemoto T, Noda N, Toba K	A new grip-strength measuring device for detailed evaluation of muscle contraction among the elderly	Journal of Frailty & Aging			in press
Hida T, Harada A, Imagama S, Ishiguro N	Managing sarcopenia and its related-fractures to improve quality of life in geriatric populations	Aging and Disease			in press
Hida T, Ishiguro N, Shimokata H, Sakai Y, Matsui Y, Takemura M, Terabe Y, Harada A	High prevalence of sarcopenia and reduced leg muscle mass in Japanese patients immediately after a hip fracture	Geriatr Gerontol Int	13(2)	413-420	2013
Tauchi R, Imagama S, Inoh H, Yukawa Y, Kanemura T, Sato K, Matsubara Y, Harada A, Hachiya Y, Kamiya M, Yoshihara H, Ito Z, Ando K, Ishiguro N	Risk factors for a poor outcome following surgical treatment of cervical spondylotic amyotrophy: a multicenter study	Eur Spine J	22(1)	156-161	2013
Matsui Y, Takemura M, Harada A, Ando F, Shimokata H	Utility of "loco-check," self-checklist for "Locomotive Syndrome" as a tool for estimating the physical dysfunction of elderly people	Health	5(12A)	97-102	2013
原田敦	サルコペニアとロコモティブシンドローム	医学のあゆみ	248(9)	703-709	2014
飛田哲朗, 原田敦	サルコペニアの診断法～高齢者の転倒・骨折予防を目的として～	CLINICAL CALCIUM	23(5)	707-712	2013
原田敦	サルコペニアの診断	腎と骨代謝	26(2)	119-125	2013
原田敦	医療面接・身体診察	日本臨床	71	211-216	2013

原田敦	片足立ち訓練やスクワット訓練による筋力強化が有効　サルコペニアの実態	Medical Tribune	46(23)	24	2013
原田敦, 若尾典充, 根本哲也	大腿骨近位部の骨構造と骨強度－加齢変化と治療による変化－	CLINICAL CALCIUM	23(7)	943-950	2013
原田敦	サルコペニアの概念と現状ならびに診断について	ANTI-AGING MEDICINE	9(4)	18-21	2013
原田敦	知る、診る、防ぐ！ロコモティブシンドローム 虚弱	関節外科	32(10)	1129-1133	2013
Hashidate H, Shimada H, Shiomi T, Shibata M, Sawada K, Sasamoto N	Measuring indoor life-space mobility at home in frail older adults with difficulty to perform outdoor activities	Geriatr Phys Ther	36	109-114	2013
稲葉康子, 大渕修一, 新井 武志, 柴喜崇, 岡浩一朗, 渡辺修一郎, 木村憲, 長澤弘	地域在住高齢者に対する運動介入が1年後の運動行動に与える影響　ランダム化比較試験	日老会誌	50(6)	788-796	2013
金憲経, 鈴木隆雄, 吉田英世, 島田裕之, 山城由華吏, 須藤元喜, 仁木佳文	都市部在住高齢女性の膝痛、尿失禁、転倒に関連する歩行要因	日老医誌	50(4)	528-535	2013
Kim M, Kim H	Accuracy of segmental multi-frequency bioelectrical impedance analysis for whole-body and appendicular fat mass and lean soft tissue mass in frail women aged 75 years and older	Eur J Clin Nutr	67	395-400	2013
Sakurai R, Fujiwara Y, Saito K, Fukuya T, Kim MJ, Yasunaga M, Kim H, Ogawa K, Tanaka C, Tsunoda N, Muraki E, Suzuki K, Shinkai S, Watanabe S	Effects of a comprehensive intervention program including hot bathing, on overweight adults: A randomized controlled trial	Geriatr Gerontol Int	13	638-645	2013

Iwasa H, Kai I, Yoshida Y, Suzuki T, Kim H, Yoshida H	Global cognition and 8-year survival among Japanese community- dwelling older adults	Int J Geriatr Psychiatry	28	841-849	2013
須藤元喜, 山城由華吏, 上野加奈子, 金憲経	シート式圧力センサーを用いて計測した歩容左右差による年齢推定	日生理人類会誌	18	125-132	2013
金憲経	サルコペニア予防と健康増進	Geriatr Med	51	937-940	2013
Kim H, Suzuki T, Saito K, Kim M, Kojima N, Ishizaki T, Yamashiro Y, Hosoi E, Yoshida H	Effectiveness of exercise with or without thermal therapy for community-dwelling elderly Japanese women with non-specific knee pain: A randomized controlled trial	Arch Gerontol Geriatr	57	352-359	2013
金憲経	サルコペニアに対する運動・栄養による介入効果	医学のあゆみ	248	747-752	2013
Kim H, Yoshida H, Suzuki T	Falls and fractures in participants and excluded non-participants of a fall prevention exercise program for elderly women with a history of falls: 1-year follow-up study	Geriatr Gerontol Int			in press
Kim H, Yoshida H, Hu X, Saito K, Yoshida Y, Kim M, Hirano H, Kojima N, Hosoi E, Suzuki T	Association between self-reported urinary incontinence and musculoskeletal conditions in community-dwelling elderly women: A cross-sectional study	Neurourol Urodyn			in press

G Model
GAIPOS-3763; No. of Pages 6
ARTICLE IN PRESS

Gait & Posture xxx (2012) xxx–xxx

Contents lists available at SciVerse ScienceDirect

Gait & Posture

journal homepage: www.elsevier.com/locate/gaitpost

Gait adaptability and brain activity during unaccustomed treadmill walking in healthy elderly females

Hiroyuki Shimada [a,*], Kenji Ishii [b], Kiichi Ishiwata [b], Keiichi Oda [b], Megumi Suzukawa [c], Hyuma Makizako [a], Takehiko Doi [a], Takao Suzuki [d]

[a] Section for Health Promotion, Department for Research and Development to Support Independent Life of Elderly, Center for Gerontology and Social Science, National Center for Geriatrics and Gerontology, Japan
[b] Research Team for Neuroimaging, Tokyo Metropolitan Institute of Gerontology, Japan
[c] Faculty of Health Science, Department of Rehabilitation, Course of Physical Therapy, University of Human Arts and Science, Japan
[d] Research Center, National Center for Geriatrics and Gerontology, Japan

ARTICLE INFO

Article history:
Received 8 February 2012
Received in revised form 19 July 2012
Accepted 10 November 2012

Keywords:
Treadmill walking
FDG-PET
Primary sensorimotor area
Prefrontal area
Hippocampus

ABSTRACT

This study evaluated brain activity during unaccustomed treadmill walking using positron emission tomography (PET) and [^{18}F]fluorodeoxyglucose. Twenty-four healthy elderly females (75–82 years) participated in this study. Two PET scans were performed after 25 min of rest and after walking for 25 min at 2.0 km/h on a treadmill. Participants were divided into low and high step-length variability groups according to the median coefficient of variation in step length during treadmill walking. We compared the regional changes in brain glucose metabolism between the two groups. The most prominent relative activations during treadmill walking compared to rest in both groups were found in the primary sensorimotor areas, occipital lobe, and anterior and posterior lobe of the cerebellum. The high step-length variability group showed significant relative deactivations in the frontal lobe and the inferior temporal gyrus during treadmill walking. There was a significant relative activation of the primary sensorimotor area in the low step-length variability group compared to the high step-length variability group ($P = 0.022$). Compared to the low step-length variability group, the high step-length variability group exhibited a greater relative deactivation in the white matter of the middle and superior temporal gyrus ($P = 0.032$) and hippocampus ($P = 0.034$) during treadmill walking compared to resting. These results suggest that activation of the primary sensorimotor area, prefrontal area, and temporal lobe, especially the hippocampus, is associated with gait adaptability during unaccustomed treadmill walking.

1. Introduction

Increased gait instability and inconsistency from one step to the next are common in many elderly adults [1,2]. Gait variability, such as the coefficient of variation (CV) in step length [1,2], is a quantifiable feature of walking that is altered in clinical situations, such as falling, frailty, and gait disorders in neurodegenerative diseases [3–5]. The increase in gait instability observed in elderly adults without apparent neurological disease is multifactorial. Age-associated changes may contribute to gait instability, including reduced range of motion, decreased aerobic capacity and muscle function, and impaired balance [6,7]. However, the relationship between gait instability and brain function has not been studied in detail.

Gait is a complex sensorimotor action that is based on automated and reflexive spinal programs that are under the control of several distinct supraspinal centers located in the brainstem, basal ganglia, cerebellum, and cerebral cortex. Several imaging techniques have been developed to identify activation patterns during walking. These include the measurement of glucose metabolism during actual walking using positron emission tomography (PET) with [^{18}F]fluorodeoxyglucose (FDG) [8–10] and single-photon emission tomography (SPECT) with technetium-99m hexamethylpropylene amine oxime or ^{99m}Tc-ethyl cysteinate dimer to measure fixed regional cerebral blood flow [11–13].

Previous PET and SPECT studies revealed that gait disturbance in Parkinson's disease may be associated with underactivity in the medial motor area and cerebellar hemispheres and overactivity in the cerebellar vermis [8,10–12] Recently, it was reported that elderly adults with gait disturbance, secondary to age-related white matter changes, exhibited underactivation

* Corresponding author at: Section for Health Promotion, Department of Health and Medical Care, Center for Development of Advanced Medicine for Dementia, National Center for Geriatrics and Gerontology, 35 Gengo, Morioka-machi, Obu, Aichi 474-8511, Japan. Tel.: +81 562 44 5651x5254; fax: +81 562 46 8294.
E-mail address: shimada@ncgg.go.jp (H. Shimada).

0966-6362/$ – see front matter © 2012 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.gaitpost.2012.11.008

of the supplementary motor area, thalamus, and basal ganglia compared to elderly adults without gait disturbance [13].

Treadmills are commonly used for gait analysis in clinical and research settings [14]. Treadmill walking, in theory, is mechanically equivalent to overground walking [15,16]. In reality, however, walking on a treadmill can initially be an unfamiliar experience [16,17]. Unimpaired younger adults required 4–6 min to familiarize themselves with the treadmill [14,17]. However, complete familiarization with treadmill in a 15-min single session was not attained in elderly adults [18]. Therefore, a treadmill walking task may be used to investigate the process of adaptation to an unfamiliar environment during walking.

The purpose of the study was, first, to compare the relative brain activation and/or deactivation during treadmill walking compared to resting condition and, second, to determine whether gait adaptability measured as gait variability could be explained through differences of brain activation and/or deactivation in response to an unaccustomed treadmill walk in the elderly adults.

2. Materials and methods

Two hundred and seventy-four females were selected from our database of elderly volunteers (n = 1289). Inclusion criteria were: age ≥ 75 years, no history of neurological or psychiatric disorders, cardiovascular disease, hypertension, heart failure, diabetes mellitus, head trauma, drug or alcohol abuse, or severe pain. Of the initial 274 females, 106 completed cognitive and physical performance tests including preferred walking speed. Sixty-nine females were excluded because of low cognitive function (Mini Mental State Examination score < 27 points), multiple medications, drug allergy, and gait disturbance (gait freezing, wide-based gait, or remarkable body sway during gait). Magnetic resonance imaging (MRI) with T1-weighted contrast was performed in 37 females using a 1.5-T Sigma Horizon scanner (GE, Milwaukee, WI, USA). Thirteen females were excluded based on MRI exclusion criteria (cerebrovascular lesions or high cortical atrophy). The remaining 24 females participated in the study (mean age, 78.0 ± 2.3 years; range, 75–82 years).

Participants were fully informed of the purpose and potential risks of the experiments, including radiation dose, and provided written, informed consent. The Ethics Committee of the Tokyo Metropolitan Institute of Gerontology approved the study protocol.

Brain glucose uptake in the rest and treadmill walking conditions was assessed on separate days (within two weeks, at least two days apart). Each condition consisted of three phases: preparation, rest or treadmill walking, and a PET scan. Total time of the FDG–PET measurement was about 85 min in each condition. The preparation period was 40 min in duration, after which the participants either rested for 35 min or walked for 25 min on a treadmill. A 6 min FDG–PET scan was performed subsequently.

During the preparation period, a catheter for injection of FDG was inserted into a vein of the left forearm. FDG (180 MBq) was injected intravenously at the onset of rest and treadmill walking. For the resting condition, participants lay supine with their eyes closed for 35 min. For the treadmill walking condition, participants walked on a treadmill (PW-21; Hitachi, Tokyo, Japan) for 25 min at 2.0 km/h while holding the handrails, to avoid falling during walking and to provide a uniform visual environment. The participants then rested on a bed with their eyes closed for 10 min.

A step counter with an infrared ray device (m-Stride ST-1100; S & ME, Tokyo, Japan) recorded walking speed, cadence, and step length during the treadmill walking period to evaluate temporal changes in gait characteristics. The step counter was placed on side-rail of a treadmill to measure belt speed (cm/s) of the treadmill and step time (s) during treadmill walking using infrared ray. The step length (cm) and cadence (steps/min) were calculated as follows.

$$\text{Step length} = \text{Belt speed} \times \text{Step time}. \quad (1)$$

$$\text{Cadence} = 60/\text{Step time}. \quad (2)$$

Step length was measured for 1 min at 0, 5, 10, 15, 20, and the 24th–25th min. We used 200 steps for the analysis of step length and cadence, 50 steps from each 1 min period starting at the 10th–11th min, 15th–16th min, 20th–21st min, 24th–25th min of treadmill walking. Five minutes following the rest or walking periods, PET scans were performed using a Headtome-V (SET 2400W, Shimadzu, Kyoto, Japan) in the three-dimensional (3D) mode. This 6 min emission scan therefore occurred 40 min after the intravenous injection of FDG. The scan produced images that had the following parameters: matrix size, 96 × 96 × 50; and voxel size, 2 mm × 2 mm × 3.125 mm. The attenuation was corrected via a transmission scan using a $^{68}Ga/^{68}Ge$ source.

The images were reconstructed using a filtered back projection algorithm with a second-order low-pass filter with a cutoff frequency of 1.25 cycles/cm. Corrections were applied for dead time and detector non-uniformity. Image processing and data analysis were performed using statistical parametric mapping (SPM8 software, Wellcome Department of Cognitive Neurology, Institute of Neurology, Queen Square, London, UK) implemented on MATLAB (MathWorks, Natick, MA, USA). The tasks performed using SPM8 were MRI/PET coregistration, spatial normalization, spatial smoothing, MRI segmentation, normalization, and SPM analysis. Anatomical brain MR images were spatially normalized into the Montreal Neurological Institute (MNI, McGill University, Montreal, Canada) standard template using an affine transformation (12 parameters for rigid transformations) [19]. The parameters were applied to the coregistered FDG–PET images. Therefore, all stereotactic coordinates given in this paper refer to the MNI coordinate system. Subsequently, the spatially normalized images were blurred with a Gaussian filter (FWHM 12 mm) to increase signal-to-noise ratio. All scans were analyzed after normalization to the white matter. The normalization prior to voxel-based statistics was performed using an anatomical mask in MNI space. This normalization was used for all participants to remove the effects of differences in the overall counts. The pixel values were normalized by scaling the activity in each pixel in proportion to the global activity. This ensured that the variance related to the substantially different global activity between high- and low-dose images was stabilized. In this process, the mean global activity of each scan was adjusted to 50. Planned comparisons between the rest and exercise conditions were performed using t statistics for each voxel. These analyses generated statistical parametric maps of the t statistic (SPM {t}), which were subsequently converted to unit normal distribution (SPM {Z}). The estimated final spatial resolution was 19 mm × 21 mm × 18 mm.

The standard deviation for the CV, the ratio of the standard deviation to the mean, in step length during the treadmill walk was large in our sample (mean 7.2 ± 6.0%). However, there was a bimodal distribution around the median value for the CV for step length and it was therefore appropriate to use the median step length for CV as the cut-point dividing the females into low step-length variability (LSV) and high step-length variability (HSV) groups. Student's t test was used to compare age and gait variables between the LSV and HSV groups during treadmill walking. The significance threshold was set at $P < 0.05$. SPSS version 19 (Chicago, IL, USA) was used for statistical analyses.

The locations of relatively activated and deactivated brain areas were identified and listed according to stereotaxic coordinates and visual inspection of the structural MRI provided by SPM8. Significant relative increase (walk > rest) and decrease (rest > walk) in cerebral glucose uptake during the gait condition compared with the rest condition were explored for each group separately. Both relative increases and decreases in glucose metabolism were calculated and considered significant at $P < 0.05$, and were corrected for multiple comparisons using a familywise error (FWE) method [20].

A region of interest (ROI) analysis was used to assess activated and deactivated brain areas during treadmill walking between the HSV and LSV groups, which were interpreted as the relative difference in gait-induced glucose uptake changes between groups. The ROIs were determined on visually apparent regions of relative activation (walk > rest) and deactivation (rest > walk) images for all participants. Glucose metabolism in the ROIs was measured based on the standardized uptake value (SUV), which was defined as follows.

$$\text{SUV} = C/D/w, \quad (3)$$

where C represents the radioactive concentration in the tissue (Bq/mL), D represents the injected dose (Bq), and w represents body mass (g) [21]. FDG dose was adjusted to body weight. Student's t test was used to compare the SUV between the LSV and HSV groups. The significance threshold was set at $P < 0.05$ during between-group comparisons in specific regions. The ROI analysis was performed using the Dr. View software (AJS, Tokyo, Japan). The anatomical designations used to the Talairach Client and MRI atlas of human white matter [22].

3. Results

There was no difference in age between the LSV and the HSV groups (77.4 ± 2.3 versus 78.7 ± 2.2 years; P = 0.19) or the following treadmill variables: walking speed (34.7 ± 0.4 versus 34.4 ± 0.5 m/min; P = 0.26), cadence (101.4 ± 15.1 versus 96.0 ± 15.7 steps/min; P = 0.39), and step length (34.9 ± 5.2 versus 37.4 ± 6.4 cm; P = 0.31). The HSV group had a higher step length CV compared to the LSV group (2.7 ± 0.8 versus 11.8 ± 5.5; $P < 0.001$).

The most prominent relative activations during treadmill walking in the LSV group were found in the primary sensorimotor areas (Broadman area (BA) 3 and 4), occipital lobe (BA 17, 18, and 19), and anterior and posterior lobe of the cerebellum compared with the resting condition (Table 1, Fig. 1A). The LSV group did not

Please cite this article in press as: Shimada H, et al. Gait adaptability and brain activity during unaccustomed treadmill walking in healthy elderly females. Gait Posture (2012), http://dx.doi.org/10.1016/j.gaitpost.2012.11.008

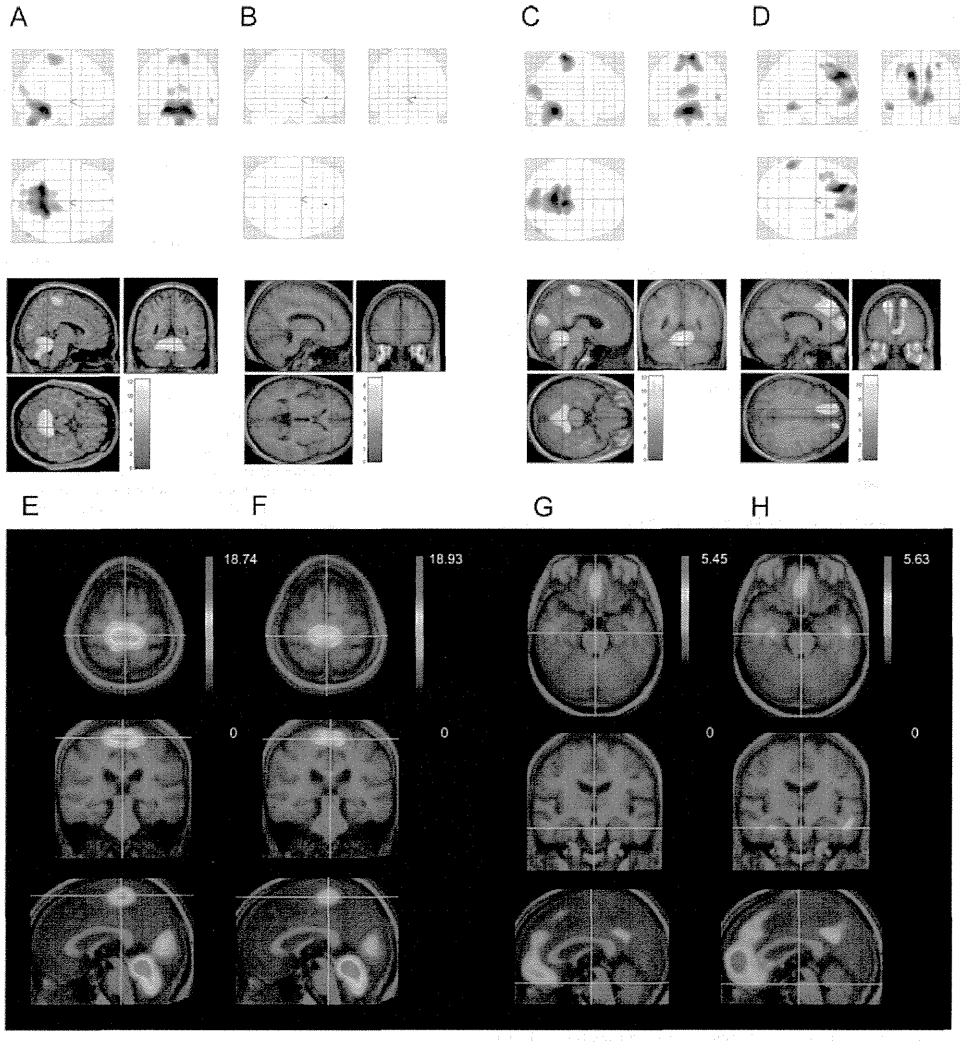

Fig. 1. FDG–PET activations and deactivations during treadmill walking in the LSV and HSV groups. During treadmill walking in the LSV group, activations (A) were prominent in the primary motor areas, visual cortical areas and anterior and posterior lobe of cerebellar. Slight deactivation (B) was found in the right sub-gyral. In the HSV group, activations (C) were prominent in the primary motor areas, visual cortical areas and anterior and posterior lobe of cerebellar. Deactivations (D) were found in the supplementary motor areas (superior and medial frontal cortex, dorsolateral prefrontal cortex). The primary sensorimotor cortex was activated more during treadmill walking versus the resting condition, in the LSV group (E) compared to the HSV group (F). Hippocampus and temporal lobe were deactivated more for treadmill walking versus the resting condition, in the HSV (H) group compared to the LSV group (G).

exhibit prominent relative deactivation during treadmill walking compared with the resting condition (Table 1, Fig. 1B)

The HSV group exhibited marked relative activation in the primary sensorimotor areas (BA 3 and 4), occipital lobe (BA 17, 18, and 19), and anterior and posterior lobe of the cerebellum during treadmill walking compared with the resting condition (Table 2, Fig. 1C). However, the HSV group showed relative deactivation in some regions during treadmill walking. The most prominent relative deactivations during treadmill walking were found in the frontal lobe, including the dorsolateral prefrontal cortex (BA 9 and 46), supplementary motor area (BA 6 and 8), and inferior temporal gyrus (Table 2, Fig. 1D).

Lower panels of Fig. 1 show FDG images of relative activations and deactivations during treadmill walking compared with the resting condition in the participants of the LSV and HSV groups. The SUV uptakes of the relatively activated and deactivated regions are shown in Table 3. The primary sensorimotor areas (BA 3 and 4), occipital lobe (BA 17, 18, and 19), and cerebellum (especially the vermis) were activated during treadmill walking. Relative deactivation of FDG was observed in the orbitofrontal cortex (BA 11), superior frontal gyrus (BA 10), dorsolateral prefrontal cortex (BA 9 and 46), supplementary motor area (BA 6 and 8), middle and superior temporal gyrus white matter, posterior cingulate cortex (BA 31), pons, and hippocampus in all participants. A detailed comparison of the relative activations and deactivations using ROI analysis revealed a more prominent activation of the primary sensorimotor area in the LSV group (Table 3, Fig. 1E) compared with the HSV group (Table 3, Fig. 1F) ($P = 0.02$). The HSV group

Please cite this article in press as: Shimada H, et al. Gait adaptability and brain activity during unaccustomed treadmill walking in healthy elderly females. Gait Posture (2012), http://dx.doi.org/10.1016/j.gaitpost.2012.11.008

Table 1
FDG activations and deactivations during treadmill walking in the low step-length variability group.

(a) FDG activation during treadmill walking in the low step-length variability group (vs. resting condition)

Cerebral hemispheres	BA	Cluster	Z	T	p	x	y	z
Left cerebellum, anterior lobe, culmen		5196	6.57	12.26	<0.001	−20	−52	−16
Right cerebellum, anterior lobe, culmen			6.46	11.75	<0.001	12	−46	−16
Right cerebellum, posterior lobe, inferior semi-lunar lobule			5.83	9.4	<0.001	4	−68	−38
Right cerebrum, frontal lobe, precentral gyrus		936	5.44	8.22	0.001	10	−30	66
Left cerebrum, parietal lobe, postcentral gyrus	3		4.84	6.69	0.014	−10	−32	66
Right cerebrum, occipital lobe, inferior occipital gyrus	19	39	5.17	7.48	0.004	56	−72	−2
Right cerebellum, posterior lobe		57	4.89	6.8	0.011	20	−50	−58
Left cerebrum, occipital lobe, superior occipital gyrus, cuneus	17	130	4.82	6.63	0.015	−14	−78	12
Right cerebrum, occipital lobe, cuneus	18	147	4.68	6.31	0.027	8	−84	16
Left cerebellum, posterior lobe		4	4.64	6.24	0.03	−24	−84	−46
Left cerebellum, posterior lobe		23	4.63	6.21	0.032	−20	−52	−56
Right cerebrum, occipital lobe, middle or lateral occipital gyrus	19	1	4.54	6.02	0.045	28	−86	38

(b) FDG deactivation during treadmill walking in the low step-length variability group (vs. resting condition)

Cerebral hemispheres	BA	Cluster	Z	T	p	x	y	z
Right cerebrum, frontal lobe, genu of the corpus callosum		5	4.82	6.64	0.015	12	40	0

(Table 3, Fig. 1H) showed relative deactivation in the middle and superior temporal gyrus white matter ($P = 0.03$) and hippocampus ($P = 0.03$) during treadmill walking compared with resting than did the LSV group (Table 3, Fig. 1G). There were no significant differences in occipital lobe, cerebellum, frontal lobe, posterior cingulate cortex, and pons between groups.

4. Discussion

This study examined changes in whole brain glucose metabolism using FDG-PET during rest and unaccustomed treadmill walking in healthy elderly females, classified as either low or high step-length variability walkers. The main findings of the study were that females with high step-length variability showed relative deactivations in the supplementary motor areas and dorsolateral prefrontal cortex compared to rest and that females with low step-length variability exhibited greater relative activations in the primary motor area during treadmill walking compared to the HSV group. The HSV group showed greater relative deactivations in the temporal lobe, especially in the hippocampus, during treadmill walking compared with the LSV group.

Hanakawa [23] proposed a hypothesis regarding the neural mechanisms that control human bipedal gait. This author postulated that multiple channels from the basal ganglia–thalamocortical system and basal ganglia–brainstem system are involved in the regulation of the central pattern generator (CPG) in the spinal cord (Fig. 2). In the present study, the most prominent relative activations during treadmill walking were found in the primary sensorimotor areas, occipital lobe, and cerebellar areas for both groups. The primary motor area projects to the spinal cord through the corticospinal tract, and it is believed that the primary motor area is involved in the precise control of limb movement during walking. The coordination of limb and trunk movements to adjust for a shift in the center of gravity associated with locomotion may be one of the primary functions of the cerebellum in gait control. Previous neuroimaging experiments have shown that the cerebellar vermis and the anteromedial part of the cerebellar hemispheres are bilaterally activated during walking in healthy individuals [9,11,12]. The cerebellum is able to make immediate alterations in ongoing movement patterns [24]. It functions as a real-time sensory processing device and modulates motor responses in a reactive or feedback manner based on sensory perturbations [25].

Our findings also suggest that the cerebellum plays an important role in gait adaptation to unfamiliar environments, such as walking on a treadmill. The occipital lobe, including the

Table 2
FDG activations and deactivations during treadmill walking in the high step-length variability group.

(a) FDG activation during treadmill walking in the high step-length variability group (vs. resting condition)

Cerebral hemispheres	BA	Cluster	Z	T	p	x	y	z
Right cerebellum, anterior lobe, culmen		3715	6.54	12.12	<0.001	0	−50	−18
Right cerebrum, parietal lobe, postcentral gyrus	6	1878	6.37	11.38	<0.001	8	−32	72
Left cerebrum, parietal lobe, postcentral gyrus	3		5.75	9.16	<0.001	−10	−34	72
Left cerebrum, parietal lobe, postcentral gyrus white matter			5.4	8.09	0.001	−14	−28	54
Right cerebrum, occipital lobe, cuneus		1402	5.52	8.46	0.001	2	−84	18
Left cerebrum, occipital lobe, cuneus			5.47	8.29	0.001	−6	−82	14
Right cerebrum, occipital lobe, middle or lateral occipital gyrus		60	5.06	7.2	0.005	52	−78	4
Left cerebellum, posterior lobe		40	4.74	6.45	0.017	−22	−46	−52
Right cerebellum, posterior lobe		7	4.67	6.3	0.022	36	−84	−40
Right cerebrum, occipital lobe, middle or lateral occipital gyrus	17	3	4.52	5.99	0.039	26	−100	−12

(b) FDG deactivation during treadmill walking in the high step-length variability group (vs. resting condition)

Cerebral hemispheres	BA	Cluster	Z	T	p	x	y	z
Left cerebrum, frontal lobe, superior frontal gyrus		5131	6.31	11.14	<0.001	−18	46	40
Right cerebrum, frontal lobe, superior frontal gyrus white matter			5.74	9.13	<0.001	10	60	6
Right cerebrum, frontal lobe, superior frontal gyrus	8		5.7	8.98	<0.001	12	54	40
Left cerebrum, temporal lobe, inferior temporal gyrus		397	5.62	8.74	<0.001	−52	−44	−14
Right cerebrum, frontal lobe, middle frontal gyrus	6	113	5.38	8.04	0.001	30	22	58

Please cite this article in press as: Shimada H, et al. Gait adaptability and brain activity during unaccustomed treadmill walking in healthy elderly females. Gait Posture (2012), http://dx.doi.org/10.1016/j.gaitpost.2012.11.008

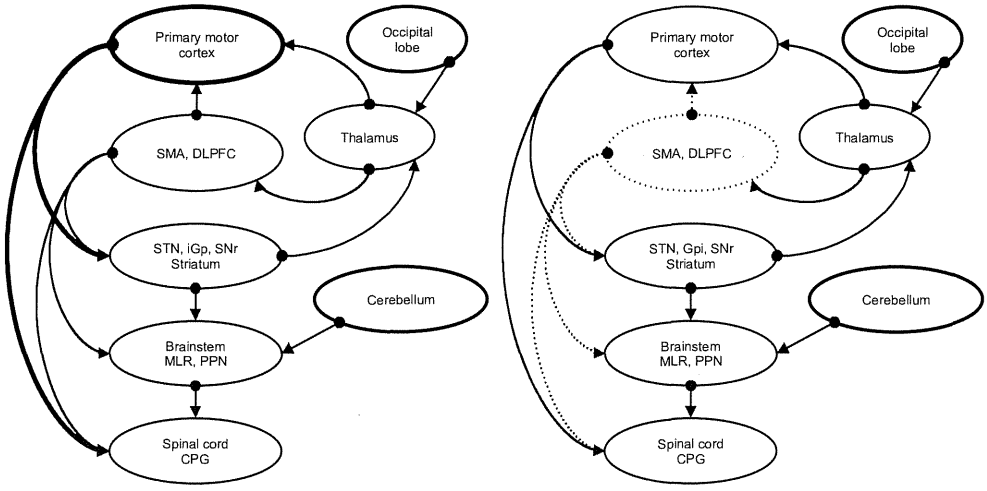

Fig. 2. Differences in neural mechanisms controlling treadmill walking in LSV compared to HSV individuals. Multiple channels from the 'basal ganglia–thalamo-cortical system' and 'basal ganglia–brainstem system' are both involved in regulating the central pattern generator (CPG) in the spinal cord. The primary motor cortex and non-primary motor areas such as supplementary motor areas constitute multiple parallel circuits with the basal ganglia counterparts. (a) Left panel displays our hypothesized neural network for the LSV group. The projections from M1 increased during walking to adapt to the unaccustomed environment (treadmill walking). (b) Right panel displays our hypothesized neural network for the HSV group. The HSV group deactivated FDG uptakes in SMA during treadmill walking and the deactivations may lead to dysfunction of 'basal ganglia–thalamo-cortical system' and 'basal ganglia–brainstem system'. *Abbreviations:* STN, subthalamic nucleus; iGP, internal segment of globus pallidus; SNr, substantia nigra pars reticulata; MLR, midbrain locomotor region; PPN, pedunculopontine nucleus.

cuneus (BA 17) and precuneus (BA 7/31), is believed to play a role in visuomotor coordination. The areas which showed relative activation were compatible with those reported in a previous activation study using FDG–PET [10]. In addition, online visual feedback was the requisite for locomotor adaptation [26] and was thought to override internal model predictions of control during locomotion [27]. Our study further supports the hypothesis that locomotor adaptation requires neuronal activation in the region related to visuomotor coordination.

In the HSV group, relative deactivations in FDG uptake were observed over a broad area of the prefrontal cortex, including the supplementary motor area and the dorsolateral prefrontal cortex. Cortical locomotor commands originating from the premotor and supplementary motor cortices are conveyed to the brainstem locomotor centers via the basal ganglia. The structure of the dorsolateral prefrontal cortex is important for selecting and planning voluntary movements [28] or simulating motor actions [29]. The relative deactivation of the supplementary motor area and dorsolateral prefrontal cortex may be associated with the finding that the participants in the HSV group might have found it difficult to adapt to an unfamiliar environment, i.e., treadmill walking.

Detailed group comparison revealed that the LSV group had a more prominent relative activation in the primary sensorimotor area compared to the HSV group and that the HSV group exhibited relative deactivation in the hippocampus compared to the LSV group during treadmill walking. The relative activation of the primary motor area may improve projection to the basal ganglia and to the CPG in the spinal cord, thus facilitating the strengthening of the basal ganglia–thalamocortical system during walking (Fig. 2). Regarding relative deactivation in the hippocampus, Zimmerman et al. (2009) found that increased variability in step length was associated with poorer hippocampal metabolism in elderly individuals. The authors suggested

Table 3
A region of interest analysis based on the standardized uptake value as the relative difference in gait-induced glucose uptake changes between groups.

	LSV group Mean (SD)	HSV group Mean (SD)	*p* value
Walk>Rest			
Primary sensorimotor area (BA 3, 4)	13.56 (3.01)	10.93 (2.16)	0.02
Occipital lobe (BA 17, 18, 19)	11.42 (4.29)	9.25 (3.55)	0.19
Cerebellum (vermis, anterior and posterior lobe)	17.18 (4.85)	17.36 (4.07)	0.92
Rest>Walk			
Orbitofrontal cortex (BA 11)	3.85 (3.18)	3.67 (2.94)	0.89
Superior frontal gyrus (BA 10)	4.16 (2.54)	4.76 (2.83)	0.59
Dorsolateral prefrontal cortex (BA 9, 46)	3.16 (2.09)	4.45 (2.25)	0.16
Supplementary motor area (BA 6, 8)	3.79 (1.74)	4.12 (1.83)	0.65
Middle and superior temporal gyrus white matter	1.85 (1.45)	3.07 (1.15)	0.03
Posterior cingulate cortex (BA 31)	3.01 (2.16)	3.67 (3.58)	0.59
Pons	2.40 (1.89)	1.84 (0.94)	0.37
Hippocampus	1.24 (1.31)	2.44 (1.29)	0.03

LSV: high step-length variability; HSV: low step-length variability.

Please cite this article in press as: Shimada H, et al. Gait adaptability and brain activity during unaccustomed treadmill walking in healthy elderly females. Gait Posture (2012), http://dx.doi.org/10.1016/j.gaitpost.2012.11.008