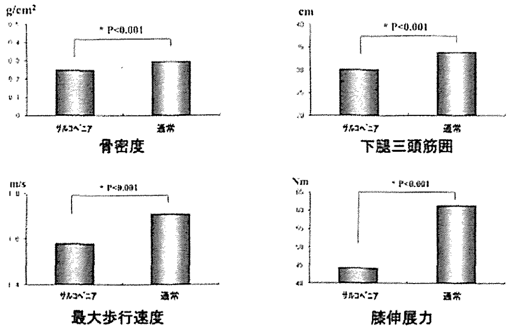
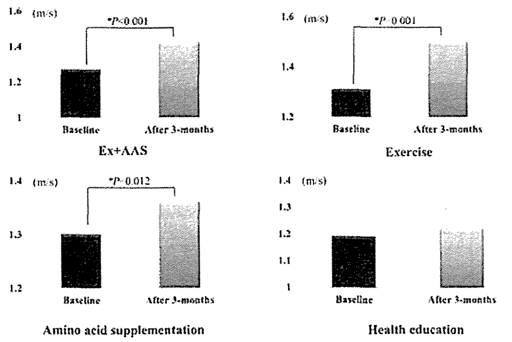


骨密度　下腿三頭筋囲　最大歩行速度　膝伸展力

図７　サルコペニア判定者と通常者の測定値の比較

健康教育の４つのグループに分けて、３か月間介入を行った。なお、アミノ酸の場合はロイシンが42%パーセント含まれる錠剤一日３gを２回補充して一日６グラム補充する介入をした。その結果、図８に示したように、歩行速度はアミノ酸の補充だけでも、運動のみでも、運動＋アミノ酸も有意に改善されることが認められた。しかし、足の筋肉量と下肢筋力については、アミノ酸だけ補充をすると筋肉の量は有意ではないものの増加傾向を示し、運動の場合は有意に改善していることが認められた。また下肢筋力は、アミノ酸補充だけでは足筋肉量は増えても変化がない結果を示した。運動グループの場合は、筋肉の量が増えても力は改善しないことが認められた。運動と栄養の介入（運動＋栄養）によって、筋力は有意に改善されるという結果が得られた（図９）。また、サルコペニアは、筋肉の量の減少と身体機能低下という複合的な概念の定義である。実際に下肢筋肉量と膝伸展力の増加あるいは足筋力と歩行速度の有意な増加は、運動＋アミノ酸のみであり、アミノ酸補充あるいは運動だけでは有意な改善がなく、複合的に支援したときに有意に改善された。よって、サルコペニアを改善するためには運動と栄養の組み合わせによる複合的支援が有効であることが強く示唆された。



Ex+AAS　Exercise　Amino acid supplementation　Health education

図８　Comparison of usual walking speed between exercise and amino acid groups.

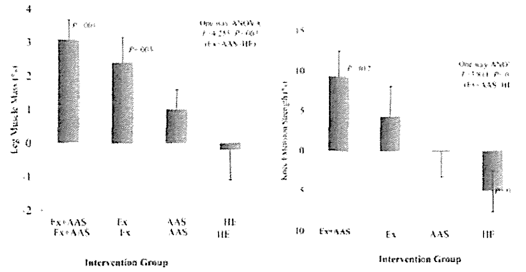


図９　Mean(±SE) changes in leg muscle mas
and knee extension strength after exercis
(Ex), amino-acid supplementation (AAS)
both (Ex+AAS), or health education (HE)
Bars indicate the average changes fro
baseline to after the 3-month interventions.
(Kim H, Suzuki T, et al. JAGS 60: 16-23, 2012)

４．転倒・骨折予防のための支援

転倒の危険因子には、身体機能と非常に強くかかわっている（表４）。転倒は、歩行中に60%発生し、特に大腿骨頸部骨折は要介護状態あるいは寝たきりに繋がりやすく場合によっては死亡原因にもなる。高齢者にとって最も深刻な大腿骨頸部骨折の引き金の90%は転倒であり、特に横に転ぶことが大きなリスクファクタ

表４　転倒危険因子の相対的危険度

危険因子	相対危険度
筋力の虚弱	4.4
転倒歴	3.0
歩行障害	2.9
バランス障害	2.9
補助器具の使用	2.6
視力障害	2.5
関節炎	2.4
ADL障害	2.3
うつ病	2.2
認知機能障害	1.8
年齢80歳以上	1.7

(AGS., JAGS, 2001)

ーになっており、身体づくりの中でも特に横に転びにくい体づくりが必要である。もう一つは、歩くときの「つまずき」が転倒の40%を占めていることに着目すべきである（図10）。転倒予防のための体づくりのポイントは歩行機能の向上とつまずき改善である。つまり、大腿四頭筋、下腿三頭筋、腸腰筋、大腿筋膜張筋、縫工筋等々の下肢筋を鍛えて歩行能力の改善を、前脛骨筋を鍛えてすり足改善を図ることが必要である。これらに重点を置いた運動を支援することによって、転倒率は、約20%軽減させることができると多くの研究で指摘されている（図11）。

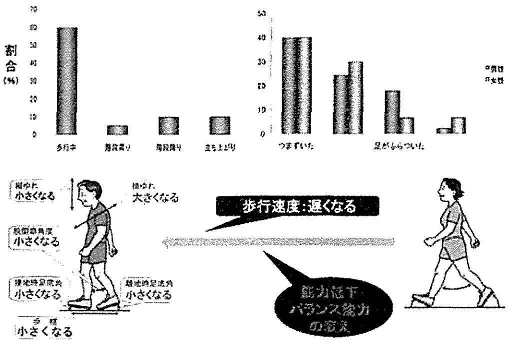


図10　転倒時の動作

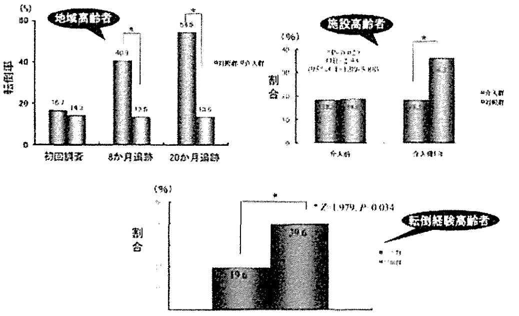


図11　介入後追跡期間中の転倒率の推移

5．尿失禁予防への支援

尿失禁は高齢者に多く（図12）、社会生活に種々の影響を及ぼす。尿失禁予防としてはこれまでに骨盤底筋運動が主流であったが、肥満が尿失禁のリスクファクターであることにも注目すべきである。すなわち、今までは骨盤底筋だけ鍛えるのが尿失禁予防の主流であったが、腹部過剰脂肪は骨盤底筋に過負荷を与える要因として、骨盤底筋を緩める原因であることを考慮すべきである（図13）。著者ら（2007）は、腹圧性尿失禁者に対して骨盤底筋運動プラス、腹部脂肪減少運動を組み合わせる介入を行った。その結果、対象の54.5%が完治した（図14）。さらに、尿失禁が完治することは、外出を控える者は運動指導前44.8%が指導後13.8%に減り、近所付き合い・知人友人との付き合いに支障がある者は運動指導前34.5%が指導後10.3%に減り、社会活動の復活に繋がることが示唆された（図15）。

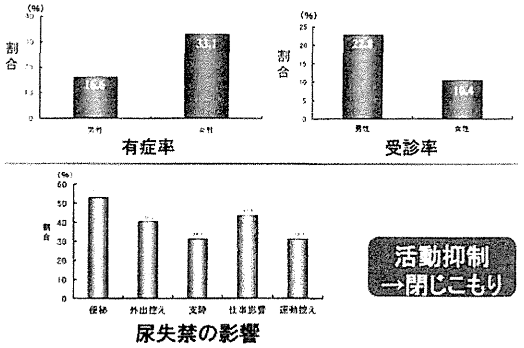
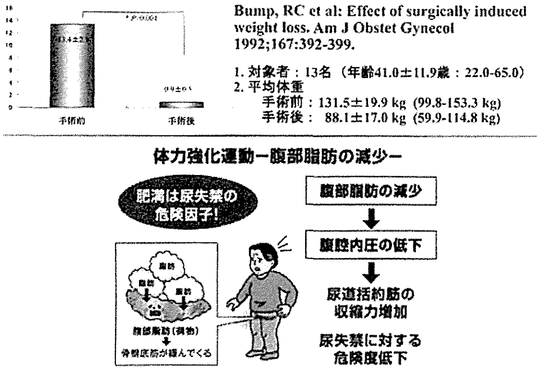


図12　地域高齢者の尿失禁の有症率と受診率



Bump, RC et al: Effect of surgically induced weight loss. Am J Obstet Gynecol 1992;167:392-399.

1. 対象者：13名（年齢41.0±11.9歳：22.0-65.0）
2. 平均体重
   手術前：131.5±19.9 kg（99.8-153.3 kg）
   手術後：88.1±17.0 kg（59.9-114.8 kg）

図13　尿失禁改善と肥満の改善との関連性

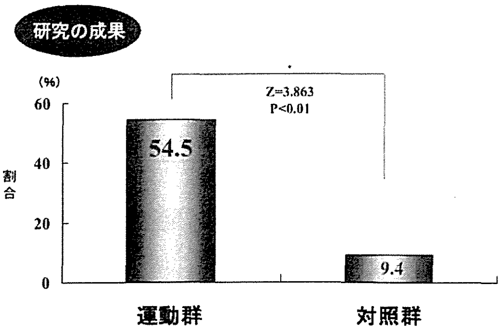


図14　3ヶ月間の運動指導による尿失禁完治率
Kim H, et al., JAGS: 2007.

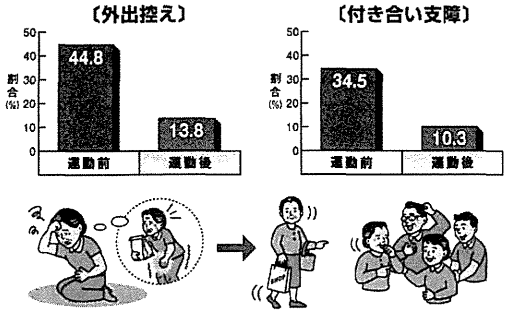


図15　運動指導後の外出控え・付き合い支障の変化

6．まとめ

体育研究者や指導者が虚弱高齢者に支援するとき、健康な期間、できればdisabilityの期間を短くする支援が必要である。なかでも支援の中心になっているのは運動であるが、運動＋栄養運動、運動＋他の要因を取り入れた方が、より効果的になると思っている。

プロフィール　金 憲経（Kim Hunkyung）
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慶北大学校（韓国）卒業、筑波大学大学院体育科学研究科修了　博士（体育科学）
研究等：虚弱高齢者の生活機能の改善を目指す介入、高齢者の転倒予防を目指す介入、介護予防を目的とした虚弱高齢者の尿失禁改善、等など

特集 **運動と老化防止**

老化防止・介護予防に効果的な運動

—とくにサルコペニア予防の視点から—

キム　ホンギョン
金　憲経
東京都健康長寿医療センター研究所研究副部長

【略歴】 1994年：筑波大学大学院修了、1996年：筑波大学専任講師、1998年：東京都老人総合研究所疫学部門主任研究員、2009年より現職
【専門分野】 虚弱高齢者健康づくり、運動処方、介護予防。とくに高齢者の転倒・骨折予防、尿失禁改善、膝痛改善、筋肉減少症改善、虚弱予防のための包括的指導。博士（体育科学）

はじめに

中年期を過ぎると身体を構成しているさまざまな組織の機能が変化した結果、環境変化への適応能力の低下ないしは機能喪失が徐々に増してくる。その背景には、筋肉を始めとする複数の臓器・器官の機能低下が内在的に進行し、身体の総合力が弱まり、自立した生活が困難になる要因を多分に併せ持っていることが挙げられる。

高齢者における複数の臓器・器官の機能低下は、歩行障害、転倒・骨折、失禁、閉じこもり、認知機能障害、うつ、痛み、睡眠障害等々の老年症候群と呼ばれる徴候発症を招く引き金にもなる。また、日常生活上は何の支障がないように見えても、各臓器の予備能力が低下しているため生体恒常性機構が崩れやすく、身体的・心理的ストレス対処能力の低下を招きかねない。

老化が進み多様な機能障害を有する人口を減らし、健康寿命を延ばすためには機能障害を起こす可能性の高いハイリスク高齢者を早期に発見し、迅速に対処することが老化防止・介護予防に有効な取り組みと考える。本章では、老化防止・介護予防に効果的な多岐の取り組みの中で、「効果的な運動」について簡単に紹介する。

筋肉量の減少と関連する要因

骨格筋量の減少には、加齢、慢性疾患、骨格筋の不使用、栄養不良などの要因が関わっているが、そのメカニズムの完全解明までには至っていない。老化の過程において、骨格筋量の減少に伴う筋力や身体機能の低下予防のためには、さまざまな要因の中で、可変因子を見出し、その因子の改善に焦点を当てた支援が有効である。可変因子として注目されているのは、骨格筋の不使用と栄養不良である1)。

骨格筋の不使用を解消するためには、運動が勧められ、とくに、漸増負荷レジスタンス運動（progressive resistance strength training）は、筋肉量や筋力の増大に効果的であることが多くの研究で実証されている2)、3)。

次は、栄養である。筋肉を構成する筋タンパク質は合成と分解を常に繰り返し、そのバランスによって筋量は一定に保たれている。高齢になるとさまざまな要因によって筋タンパク質の量が徐々に減少する。つまり、筋タンパク質の分解量が合成量を上回るか、合成速度が低下するかによって骨格筋量は減少していく。しかし、筋タンパク質の合成を促進するか分解を抑制することができれば、骨格筋量の減少を抑え、有効な対策と考えられる。高齢者でも、必須アミノ酸の摂取は筋タンパク質合成を促進し、必須アミノ酸の中でもロイシン高含量の必須アミノ酸の摂取がより効果的であると多くの研究で検証している4)。

運動、栄養補充による筋肉量や筋力の変化

高齢者に対するレジスタンス運動については、LBM増大、筋力向上の両面から検討されている。2011年Petersonらが行った49介入研究のmeta-analysis結果によれば、介入後にLBMの1.1kg（95％ CI＝0.9-1.2kg, P<0.001）増大効果を認め、50歳以上で運動せずに座位生活を続けた時に年間0.18kgの減少と比較した場合、レジスタンス運動がLBM増大に及ぼす影響は非常に大きいと指摘している2)。

一方、レジスタンス運動が筋力向上に及ぼす影響は部位によって異なり、leg press（32介入研究）31.63kg（95％

CI = 27.59-35.67kg, $P<0.001$）、chest press（36介入研究）9.83kg（95% CI = 8.42-11.24kg, $P<0.001$）、knee extension（28介入研究）12.08kg（95% CI = 10.44-13.72kg, $P<0.001$）といずれの部位でも顕著な向上効果が観察されている[5]。このように、先行研究の多くは、レジスタンス運動は筋肉量のみならず筋力増大に効果的であると報告している。

しかし、ここで注意深く観察すべき点は、先行研究で採用している運動の量である。上昇効果を認めている先行研究はいずれも高強度（higher intensity training）、多量の運動（higher-volume intervention）である。つまり強い運動を多量指導すれば効果は上昇するが、低強度負荷のレジスタンス運動の指導では筋量上昇、筋力向上効果は見込めないと指摘している。健常高齢者に対する筋肉量や筋力増大を目指す運動であれば、先行研究の考え方は受け入れるべきであろう。しかし、骨格筋量の減少に伴う筋力の衰え、歩行機能の低下といった状態のサルコペニアあるいは要介護状態の虚弱高齢者に対して高強度、多量の運動量を採用し、筋肉量や筋力の上昇効果のみに焦点を当てた場合、「介入の副作用（adverse effect）」は生じないのか、についての論議が必要と考える。

一方、Taaffeは[6]、サルコペニア改善のためには中程度（moderate intensity）のレジスタンス運動でも十分効果が期待できると提案していることから、今後、中低強度負荷のレジスタンス運動がサルコペニア高齢者の筋肉量や筋力に及ぼす影響について一層の研究成果に期待を寄せる。

次は、栄養である。さまざまな栄養成分の中で、必須アミノ酸補充が筋肉量や筋力に及ぼす影響について検討した先行研究によれば、Borsheimらは[7]、ロイシン35.88%配合必須アミノ酸11gを16週間補充した後、LBMや筋力、歩行機能の変化を調べた。LBMは12週で1.14 ± 0.36kgの有意な増大、下肢筋力は16週で22.2 ± 6.1%増加、通常歩行速度の有意な改善効果（ベースライン = 1.26 ± 0.05m/s、16週 = 1.34 ± 0.05m/s、$P = 0.002$）を検証している。しかし、Dillonらロイシン18.6%、リジン15.5%配合の必須アミノ酸7.5gを一日2回補充する試験を3カ月間実施した。その結果によれば、アミノ酸補充によってLBMは事前（43.5 ± 2.8kg）より事後（45.2 ± 3.0kg）で有意に増加しているが、筋力の変化は統計学的に有意ではなかったと報告している[8]。

これらの結果より、必須アミノ酸補充による筋肉量の上昇効果については概ね一致しているが、筋力の向上については必ずしも一致せず、研究者によって異なる結果を報告している。これらの結果を踏まえて、Drummondらは運動＋アミノ酸補充によって、上昇効果が期待できると指摘し[9]、今後一層の検証が必要であると強調している。

運動＋栄養による筋肉量や筋力の変化

（1）運動と炭水化物栄養補充の効果

1994年Fiataroneらは[1]、70歳以上の施設長期入所者100人を運動群25人、運動＋栄養群25人、栄養群24人、対照群26人に分け、運動と栄養補充の効果を調べている。運動群には週3回、1回当たり45分の筋力強化運動を10週間指導し、栄養補充は240ml（組成：炭水化物60.0%、脂肪23.0%、大豆タンパク質17.0%）の飲料を毎日1回摂取する指導を10週間行った。

その結果、運動群で筋力113.0 ± 8.0%増加（非運動群3.0 ± 9.0%増加、$P<0.001$）、歩行速度11.8 ± 3.8%改善（非運動群1.0 ± 3.8%増加、$P = 0.02$）、階段昇りパワー28.4 ± 6.6%向上（非運動群3.6 ± 6.7%向上、$P = 0.01$）、大腿筋面積2.7 ± 1.8%上昇（非運動群1.8 ± 2.0%減少、$P = 0.11$）であった。

このように、虚弱高齢者の身体機能の改善のためには運動を中心とした複合指導が有効であり、栄養補充のみでは不十分であると指摘している。

（2）運動と必須アミノ酸補充の効果

①サルコペニア高齢者の特徴

筆者は、大都市部在住75歳以上の後期高齢女性1,399名に「SMI = 6.42kg/m2以下」で「膝伸展力 = 1.01Nm/kg以下」あるいは「歩行速度 = 1.22m/sec以下」、「BMI22.0以下」で「膝伸展力 = 1.01Nm/kg以下」あるいは「歩行速度 = 1.22m/sec以下」のサルコペニア選定基準を適用し、該当者304名（21.7%）を抽出した[10]。

サルコペニア該当者304名と非該当者1,095名を比較し、その特徴を調べた。その結果によれば、サルコペニア高齢者は正常者に比べて、年齢が高く、下腿三頭筋周囲、BMI、筋肉量は有意に低値を、健康度自己評価で健康だと回答した者の割合、定期的な運動習慣を持っている者の割合は低かった。既往歴においては、高血圧症、高脂血症は正常群より低い割合を示したが、骨粗鬆症の既往はサルコペニア群38.2%、正常群30.7%、60歳以降の骨折歴はサルコペニア群28.6%、正常群22.9%、過去1年間の転倒率はサルコペニア群26.5%、正常群16.4%といずれの項目においてもサルコペニア群が有意に高い割合を示した（図1）。

以上のことから、サルコペニア高齢者は、転倒のみならず骨粗鬆症に伴う骨折危険性が高いことが示唆され、その予防策の早期確立が重要なポイントであることが強く示唆

された。

②運動＋栄養補充指導の実際とその効果

地域在住サルコペニア高齢者に対する運動、栄養補充による効果を調べるために、サルコペニアと認定された304名を事前に設けた選定基準に基づき、介入参加者155名、不参加者149名に分けた。介入参加者155名を無作為化比較試験により運動＋栄養群38名、運動群39名、栄養群39名、対照群39名に分け、3か月間の指導を行った。

指導前後における四肢の骨格筋量は運動群（事前13.90 ± 1.06kg、事後14.19 ± 1.33kg）、栄養群（事前12.86 ± 0.99kg、事後13.03 ± 1.10kg）、運動＋栄養群（事前13.25 ± 1.35kg、事後13.59 ± 1.53kg）の3群で有意な増加が観察され、サルコペニア高齢者の骨格筋量は運動のみならず栄養補充によって増える可能性が強く示唆された（Figure 3）。

通常歩行速度は運動群（事前1.31 ± 0.24m/s、事後1.50 ± 0.23m/s）、栄養群（事前1.30 ± 0.18m/s、事後1.36 ± 0.18m/s）、運動＋栄養群（事前1.27 ± 0.25m/s、事後1.43 ± 0.29m/s）の3群で有意な増加が観察された。

膝伸展力は運動＋栄養群（事前1.15 ± 0.27Nm/kg、事後1.23 ± 0.29Nm/kg）のみで有意な向上が認められた（図2）10)。

老化予防・介護予防効果的な運動の実際

サルコペニア予防の観点から効果的な運動を考える場合、考慮すべき点は運動強度、運動頻度、運動時間、運動期間、運動種類である。

対象者の体力・健康レベルが低く個人差が大きい点を考慮し、運動は週2回以上、1回当たり40～60分間、筋力強化と歩行機能の改善を目的とした運動が有効であり、自覚的運動強度の12～14レベル（ややきつく感じる程度）の運動強度が最適であろう。

運動種目は、椅子体操、レジスタンス運動（ゴムバンド：黄色、赤色使用、Ankle-weight：錘0.50kg、0.75kg、1.00kg、1.50kg使用）、歩行・バランス訓練であり、推奨運動項目は次の通りである（図3）。

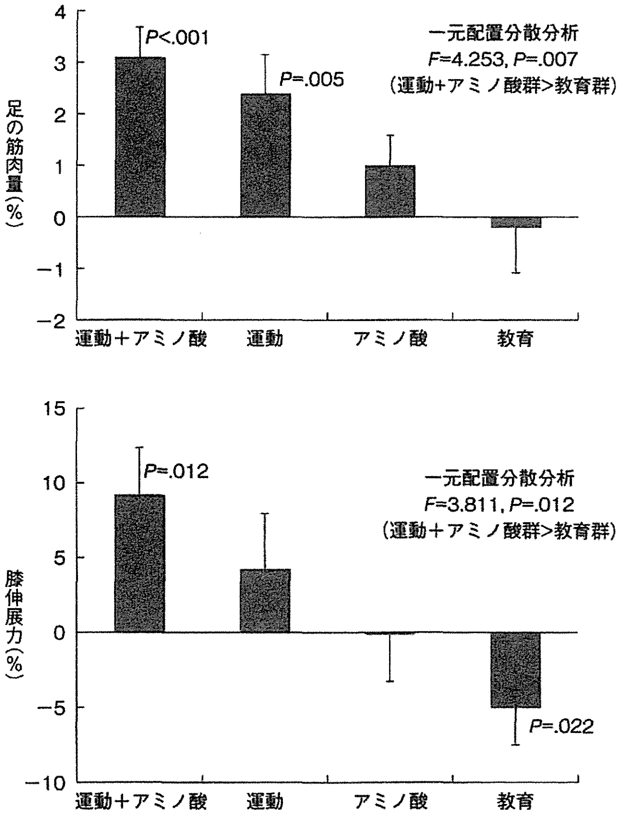
(1) 椅子体操（座位）：つま先上げ下げ、踵上げ下げ、両足上げ膝伸ばし、片足上げ胸寄せなど。

(2) 椅子体操（立位：椅子の背もたれに手を付けて行う）：踵上げ下げ、踵上げ膝曲げ、片足体重かけ、軽スクワットなど。

(3) バンド体操（黄色あるいは赤使用）：水平開き、腰伸ばし、膝開き閉じ、片足上げ胸寄せなど。

(4) アンクルウェイト体操（各自の体力レベルに合わせた錘調整）：片膝伸ばし、両膝伸ばし、片足上げ胸寄せ、両足上げ胸寄せ、両足上げ開き閉じなど。

図2　介入後における足の筋肉量と膝伸展力の変化の群間比較



（文献13より改変）

図1　サルコペニア群と正常群の比較

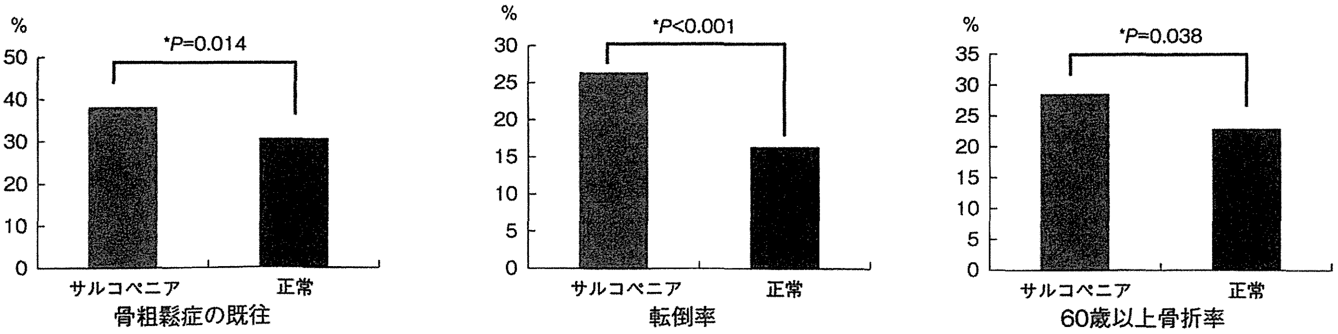
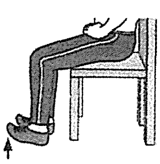
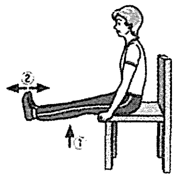


図3　虚弱高齢者における介護予防のための運動の実際

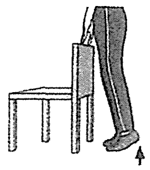
1. 筋力アップ



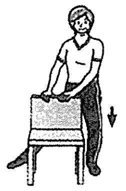
(1)爪先・踵上げ・下げ
- 椅子に腰掛け両足を揃える
- 踵を軸に爪先を上げた後、下ろす
- この動作を繰り返すことによって、前頚骨筋が強化され、すり足が改善される



(2)両足上げ・膝伸ばし
- 椅子に浅く腰掛ける
- 両足を上げ(①)、足首を手前に曲げ、踵で押し出す感じで、ゆっくり膝を伸ばす
- 足首を伸ばした後、手前に曲げて、再び伸ばした後、膝を曲げ、足を下ろす動作を繰り返すことによって(②)、太股の筋が強化される
- 慣れてきたら、両足を少し高く上げると、太ももにより強い力をかけることができる

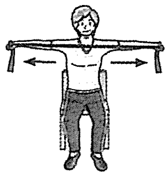


(3) 踵上げ・下げ
- 椅子に軽く手をつけ、両足を揃えて立つ
- 爪先を軸に踵をゆっくり上げた後、下ろす動作を繰り返すことによって、爪先とふくらはぎが強化され、歩行能力が改善される
- 踵を上げるときも静かに、下ろすときも静かに行う

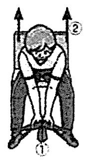


(4)片足体重かけ
- 椅子に軽く手をつけ、足を広く開き、膝を曲げる
- 片足の太ももに体重を移し、3秒くらい止めた後、反対側の足に体重を移し、太ももに体重をしっかりかける
- 腰の高さをそのまま維持しながら体重を移す

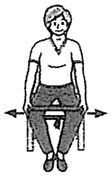
2. バンド体操



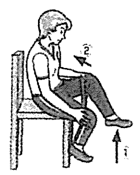
(1)水平開き
- 椅子に浅く腰掛け、手首と肘を伸ばして胸の前でバンドを肩幅くらいに握る
- 息を吐きながら、ゆっくり左右に引いた後、ゆっくり戻す動作を繰り返すことによって、上腕筋と大胸筋が強化される
- 戻す時にはゴムの力を感じながら、ゆっくり戻す



(2)腰伸ばし
- バンドの端を結び輪を作り、足の土踏まずにかけ、両手で握る(①)
- 肘は伸ばしたまま、背中をゆっくり伸ばしながら上体を起こし3～5秒保持し(②)、ゆっくり元に戻す動作を繰りかえすことによって、広背筋や脊柱起立筋が強化される



(3)膝開き・閉じ
- 椅子に浅く腰掛け、2重の輪にしたバンドを膝の上まで通し、バンドが外れないように指で軽く押さえる
- 足首は合わせたまま、両膝をゆっくり開いて3～5秒保持した後、ゆっくり閉じる動作を繰り返すことによって、中殿筋が強化される



(4)片膝上げ・胸寄せ
- バンドを膝にかけ、背中を背もたれに付けずに座る
- 片足を上げ(①)、股を胸の方へ引き寄せた後(②)、緩める動作を3回反復した後、足を下ろし、反対側も同様の動作を行う
- この動作を繰り返すことによって、腸腰筋と腹筋が強化される
- 寄せるときに、足に力を入れずに行う

おわりに

加齢に伴う筋肉量の減少は下肢部位が最も顕著であり、筋量減少に伴う筋力の衰えあるいは身体機能の低下（サルコペニア）は身体的障害、転倒・骨折率の上昇と強く関連している。サルコペニアと関連する要因は種々で複雑であるが、全メカニズムの完全解明までには至っていない現況である。しかし、身体の不使用と栄養不良は筋肉量の減少と密接に関わり、可変要因として注目されている。骨格筋の不使用を解消するためには、漸増負荷レジスタンス運動が勧められ、その実践によって筋肉量や筋力の増大効果は認められている。

一方、ロイシン高配合の必須アミノ酸の補充によって、高齢者の筋肉量の増大は認められているが、アミノ酸補充のみではサルコペニア高齢者の体力改善には不十分であるとの指摘も散見される。

結論的に、運動にロイシン高配合の必須アミノ酸を補充する包括的指導が、サルコペニア高齢者の骨格筋量の増大、筋力上昇、歩行機能の向上により効果的であることが実証されたので、老化防止・介護予防のためには運動と栄養の組み合わせを推奨する。

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Glucose Uptake During Exercise in Skeletal Muscles Evaluated by Positron Emission Tomography

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1. Introduction

Traditionally, *in vivo* skeletal muscle function has been investigated with noninvasive techniques such as magnetic resonance (MR) imaging that can characterize the motion and mechanics of contracting skeletal muscle (Axel & Dougherty, 1989; Drace & Pelc, 1994; Pipe et al., 1991). Other techniques include kinetic analyses to examine muscle activity during walking and electromyography (EMG) to evaluate muscle activity as amplitude-based algorithms. However, these techniques are limited because MR cannot be used to measure the metabolic activity of skeletal muscle, and kinetic analyses cannot measure isolated synergistic muscular activities or provide information on the etiology of the metabolic cost of exercise. Moreover, EMG quantification requires normalization of EMG amplitude to the EMG amplitude of maximal voluntary contractions, which some elderly are unable to achieve (Stevens et al., 2003). In addition, surface EMG is inappropriate for evaluating the activities of deep muscles such as the gluteus minimus.

Recently, the use of positron emission tomography (PET) and [^{18}F]fluorodeoxyglucose (FDG) has emerged as a more satisfactory method for investigating cumulative muscle activity during exercise and providing images of the spatial distribution of skeletal muscle metabolism (Fujimoto et al., 2000; Kemppainen et al., 2002; Oi et al., 2003; Shimada et al., 2007; Tashiro et al., 1999). FDG PET analysis is a metabolic imaging modality that involves the detection of intracellular FDG-6-P using gamma ray emission (Phelps et al., 1979). FDG is a glucose analog that is taken up by glucose using cells from the circulation through glucose transporters 1-4. FDG enters the glycolysis pathway and is phosphorylated into FDG-6-phosphate by hexokinase (Sokoloff et al., 1977). Intracellular FDG-6-P accumulates as it is a poor substrate for glucose-phosphate isomerase which converts glucose to fructose, and it therefore escapes dephosphorylation (Bessell & Thomas, 1973). FDG can be used to assess cumulative muscle activity over an extended period of time because the half-life of ^{18}F is relatively long (109.8 min) compared with that of other positron-emitting tracers; however, transient measurements are impossible.

FDG PET is useful for comparing task-specific muscle activity because FDG uptake is closely correlated with exercise intensity (Fujimoto et al., 2003; Kemppainen et al., 2002; Pappas et al., 2001). Results of regression analyses between normalized biceps FDG uptake and the number of repetitions of elbow flexion performed with 2 and 10 lb weights showed statistically significant positive correlations for both the 2 lb and 10 lb weights. The ratio of the slopes of the regression lines for the 10 lb and 2 lb weights was 4.94, indicating an almost fivefold difference between the external forces produced by the elbow flexors for these two loads (Pappas et al., 2001).

In this chapter, we review the findings of previous studies to demonstrate the importance of FDG PET for exercise studies and the development of rehabilitation programs for the elderly.

2. Glucose uptake in skeletal muscles during walking

2.1 Characteristics of gait function in older adults

Healthy elderly people exhibit decreased muscle mass, strength, and power production compared with healthy young people (Gallagher et al., 1997; Klitgaard et al., 1990; Larsson et al., 1979; Lynch et al., 1999; Metter et al., 1997; Porter et al., 1997; Poulin et al., 1992; Thelen et al., 1996). These decreases result in a slower gait speed, shorter step length, shorter swing phase and less range of motion at the hip, knee, and ankle joints during walking (Crowinshield et al., 1978; Elble et al., 1991; Finley et al., 1969; Hageman & Blanke, 1986; Judge et al., 1993, 1996; Kerrigan et al., 1998; Murray et al., 1969; Ostrosky et al., 1994; Winter et al., 1990). Reduced gait function in older people is associated with a decreased ability to undertake the activities of daily living (Brach & VanSwearingen, 2002; Guralnik et al., 2000).

Kinesiological studies show that older adults perform locomotor tasks nearer their maximal torque-producing capabilities than young adults. This greater effort is associated with increased neural drive to the muscles responsible for walking and enhanced coactivation of opposing muscles (Hortobagyi & DeVita, 2000; Hortobagyi et al., 2003). In addition, increased age is associated with a redistribution of joint torques and power as older adults use their hip extensors more and their knee extensors and ankle plantar flexors less when walking than the young. Data suggests that healthy older adults produce 279% more work at the hip, 39% less work at the knee, and 29% less work at the ankle compared with healthy young adults during gait (DeVita & Hortobagyi, 2000). The localized increase in muscular activation in the elderly during sustained walking may cause decreased physical activity, not because of generalized exhaustion, but due to the onset of fatigue in particular muscles. Therefore, localized muscle energy expenditure is more important than global expenditure when considering control of movement in older people (O'Dwyer & Neilson, 2000). The older adults also exposed gait instability due to enhanced coactivation of opposing muscles during walking.

2.2 Differences in glucose metabolism between young and older adults during walking

Shimada et al. (2009b) compared the differences between the glucose uptakes of skeletal muscles during walking in young and older adults using FDG PET. In this study, 10 healthy young and older men walked on a treadmill for 50 min. Walking speed was maintained at 4.0 km/hr for younger subjects and between 1.86 and 3.54 km/h as achievable limits for older subjects. FDG (360 MBq) was injected 30 min after the start of walking. PET scans of the crista iliaca-planta region were conducted in six overlapping bed positions using a 7-min emission time per position and simultaneous attenuation correction. Glucose metabolism in the regions of interest (ROIs) was evaluated from the standardized uptake value (SUV) for FDG defined as follows:

$$SUV = C/D/w \tag{1}$$

where C (Bq/ml) represents the concentration of radioactivity in the tissue, D (Bq) is the injected dose, and w is body mass (Sadato et al., 1998).

SUV was significantly increased in the semitendinosus, biceps femoris, iliacus, gluteus minimus, gluteus medius, and gluteus maximus muscles of older adults. FDG uptake ratios of older adults to young adults were 3.02 in the semitendinosus, 3.19 in the biceps femoris, 1.66 in the iliacus, 1.64 in the gluteus minimus, 3.68 in the gluteus medius, and 3.05 in the gluteus maximus muscles (Shimada et al., 2009b). The data indicate there was inefficient activity of these muscles during walking in the older adults. Figure 1 shows representative FDG PET images in a young and an older adult.

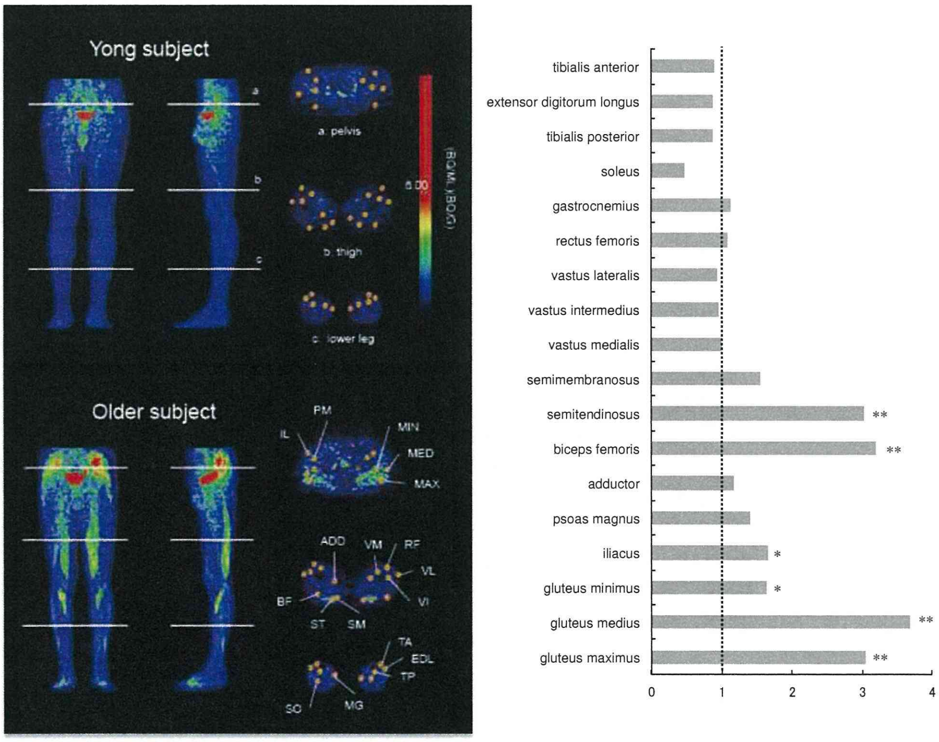

Fig. 1. FDG PET images taken after walking in a young and older subject.

Left panel: Projection and sectional images. The yellow circles indicate the following regions of interest: Section a (pelvis): 30 mm above the femoral head PM, psoas magnus; IL, iliacus; MIN, gluteus minimus; MED, gluteus medius; MAX, gluteus maximus. Section b (tight): 50% of the distance from the femoral head to the knee joint RF, rectus femoris; VL, vastus lateralis; VI, vastus intermedius; VM, vastus medialis; SM, semimembranosus; ST, semitendinosus; BF, biceps femoris; AD, hip adductor. Section c (lower leg): 30% of the distance from the knee joint to the external malleolus TA, tibialis anterior; EDL, extensor digitorum longus; TP, tibialis posterior; SO, soleus; MG, medial gastrocnemius. The red color at the center of the pelvis resulted from the accumulation of FDG in the bladder. Right panel: Graph showing FDG uptake ratios of older adults to young adults. Significant difference: $*P < 0.05$ and $**P < 0.01$.

During walking, the hamstrings are most active from the period just before to just after heel contact. Before heel contact, the hamstrings decelerate knee extension to prepare for the placement of the foot on the ground. The hamstrings are active during the initial 10% of the stance phase in walking to assist with hip extension and to provide stability to the knee through coactivation. Strong activation of the gluteus maximus allows the hip to extend and prevents forward jackknifing of the torso at heel contact. The gluteus maximus remains active from heel contact to mid stance to support the weight of the body and produce hip extension. The iliacus becomes active before toe off to decelerate hip extension. Concentric muscle activation follows eccentric muscle activation to bring the hip into flexion just before toe off and during transition into initial swing. The gluteus medius and minimus, the primary hip abductors, are most active during single-limb support to stabilize the pelvis in the frontal plane (Neumann, 2002).

A previous study showed that hip, knee, and ankle joint muscles produce 44, 5, and 51% and 16, 11, and 73% of the total extensor work during the stance phase in older and younger adults, respectively (DeVita & Hortobagyi, 2000). These data suggest that older adults perform similar amounts of work at the hip and ankle, but young adults perform the majority of work at the ankle (DeVita & Hortobagyi, 2000). In addition, coactivation time of the thigh muscles is higher in older people than in young people, and there is a linear correlation between the coactivation time and the metabolic cost during walking (Mian et al., 2006). The redistribution of joint power during walking in older adults increases glucose metabolism in the hip extensors (gluteus maximus, hamstrings) and coactivation increases glucose metabolism of the hamstrings.

The hip joint is stabilized by the gluteus medius in the initial phase of the gait cycle and by the gluteus minimus during the mid- and late-phases (Gottschalk et al., 1989). However, the degree of activation of the gluteus minimus muscle during walking is unclear because activities of deep muscles such as the iliacus and gluteus minimus cannot be evaluated by EMG. By contrast, FDG PET can measure the activity of deep muscles. FDG PET analyses showed glucose metabolism in the gluteus minimus during walking in young adults was 2.1 times higher than that at rest and higher than that of the gluteus maximus, gluteus medius, and thigh muscles (Oi et al., 2003).

3. Oxygen consumption and FDG uptake in skeletal muscles during exercise

3.1 Physical activity and oxygen consumption in older adults

Many studies have shown that there is an association between restricted outdoor activities and the deterioration of physical function in healthy and frail older people (Bruce & McNamara, 1992; Clarfield & Bergman, 1991; Fujita et al., 2006; Ganguli et al., 1996; Kono &

Kanagawa, 2001; Kono et al., 2004). A two-year prospective study in initially able-bodied older individuals showed an association between a low frequency of baseline outdoor activity and incident disability (Fujita et al., 2006). In older individuals who went outdoors once a week or less, the adjusted risks of incident mobility impairment (odds ratio = 4.02) and disability in instrumental activities of daily living (odds ratio = 2.65) were significantly higher compared with an active group who went outside once a day or more. Outdoor activity may be restricted in individuals who have difficulty walking for extended periods (Simonsick et al., 2005).

Muscle activity during exercise results in a mechanical energy cost, which is reflected by whole body metabolic cost. During physical activity, there is relatively greater muscle activity and increased levels of coactivation of opposing muscles in older people (Hortobagyi & DeVita, 2000; Hortobagyi et al., 2003). Furthermore, oxygen consumption (VO_2), which provides an index of walking efficiency, is greater in older adults even when there are no gait impairments (Malatesta et al., 2003; Martin et al., 1992; McCann & Adams, 2002; Waters et al., 1988). These data suggest that older adults may have difficulties in performing the activities of daily living as they have to work at a higher level of effort relative to their maximum capability (Hortobagyi et al., 2003).

3.2 Muscular activity and oxygen consumption

Unlike other techniques, FDG PET allows the observation of continuous activities such as extended walking and can measure cumulative muscle metabolism during unrestricted physical activities. Furthermore, FDG uptake closely correlates with exercise intensity in healthy adults and can be used to compare task-specific muscle activity (Fujimoto et al., 2003; Kemppainen et al., 2002; Pappas et al., 2001).

3.3 Relationship between FDG uptakes and VO_2

Few studies have investigated the relative contribution of different muscle groups to whole body energy consumption during walking. In one study, 10 community-dwelling older women participated in FDG PET and VO_2 analyses during exercise on separate days within one week (Shimada et al., 2010). VO_2 during walking was determined using an automated open-circuit gas analysis system (Cosmed K4b^2, Rome, Italy). The gas analyzers were calibrated immediately before each test using ambient air comprising certified standard gases at 15.94% oxygen and 4.97% carbon dioxide (Sumitomo Seika Chemicals Co., Ltd., Osaka, Japan). The subjects walked for 12 min at a comfortable speed on a circular 16 m indoor course and breath-by-breath data were obtained from the gas analyzers during walking, which was stored in the analyzer's memory. The mean VO_2 values from the 3rd to the 12th min were used to assess constant whole body energy metabolism (McArdle et al., 1997). All SUV values were adjusted for the distance walked during the 50 min FDG PET trial as:

$$\text{Adjusted SUV} = x / a \qquad (2)$$

where x represents the measured SUV, and a represents the walking distance in km.

The left and right panels show representative projection images of FDG PET uptake taken after walking. The scatterplot shows correlations between VO_2 and adjusted SUV for different muscle groups.

The VO_2 during walking was significantly and positively correlated with the adjusted SUV in the biceps femoris, gluteus minimus, gluteus medius, and the pelvis muscle group (Fig. 2; Shimada et al., 2010). This shows that these muscle groups contribute to the increase in VO_2 during walking in older adults. Evidence suggests the hamstrings, including biceps femoris, are most active from a period just before to just after heel contact during walking (Neumann, 2002). Furthermore, older adults display higher levels of antagonist coactivation during gross locomotor tasks (Hortobagyi & DeVita, 2000; Mian et al., 2006). Indeed, there is greater antagonist thigh muscle coactivation during walking in older men than young men and a linear relationship between muscle coactivation and whole body metabolic cost of walking (Mian et al., 2006).

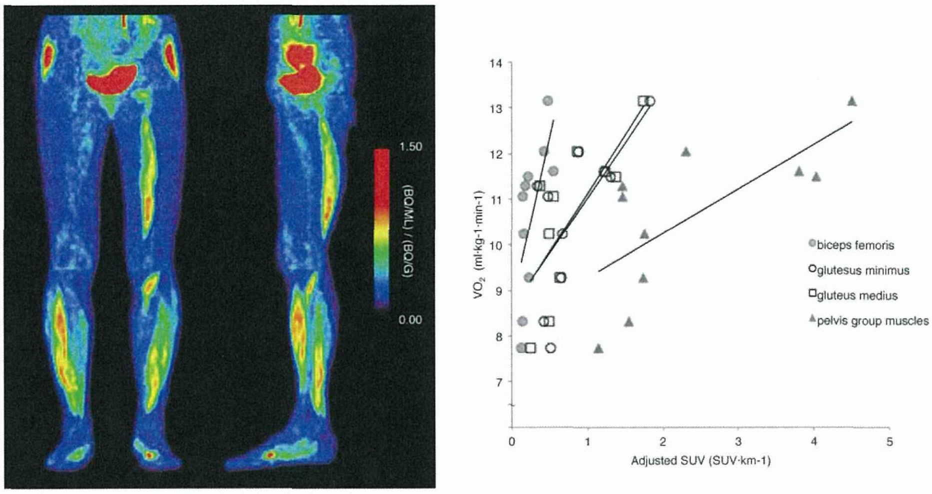

Fig. 2. Relationship between glucose uptake and VO_2 in older subjects.

Gait endurance contributes to the ability to perform the activities of daily living; however, information describing the fatiguing effect of daily activities on gait is limited. Previous studies indicate there is a relationship between muscle fatigue and physical function (Gribble & Hertel, 2004a,b; Helbostad et al.,2007; Kavanagh et al., 2006) as there are changes in gait step width, mediolateral trunk acceleration amplitude, step-length variability, and trunk acceleration variability in the vertical direction following physical fatigue induced by an atypical daily activity (i.e., sit-to-stand task), even in the absence of a change in gait speed (Helbostad et al.,2007). These gait variables are related to the incidence of falling in older people (Hausdroff et al., 2001; Maki, 1997; Mbourou et al, 2003).

The primary hip abductors, the gluteus medius and minimus, stabilize the pelvis in the frontal plane and are important for single-limb support (Neumann, 2002). During walking, the body is unstable for most of the stride cycle as its center of mass is outside the base of support 80% of the time (Winter, 1991). During walking in older people, mediolateral stability is generally reduced resulting in greater activation of the hip abductors compared with the young (Dean et al., 2007). Reduced mediolateral stability in older people can lead to an increased step width to avoid falling while walking at a preferred speed; a wider step width increases both mechanical work and metabolic energy expenditure (Donelan et al., 2001). A previous study showed older subjects selected a narrower step width when walking at a preferred speed on a treadmill with external lateral stabilization, and the energy cost with lateral stabilization was reduced in a zero step width condition i.e., tandem-like walking, compared with without stabilization (Dean et al., 2007). These findings are supported by observations of a significant relationship between the adjusted SUV in the hip abductors and VO_2.

A previous study showed that FDG uptakes by the biceps femoris, semitendinosus, iliacus, gluteus minimus, gluteus medius, and gluteus maximus muscles were significantly increased in older adults compared with young subjects (Shimada et al. 2009b). However, lower leg muscles such as tibialis anterior, tibialis posterior, and soleus had a ratio of less than one. These results suggest that the excess muscle activity of the larger thigh muscles contributes to the increase in VO_2 during walking in older adults.

Moreover, subjects with proportionally greater activity in their hip muscles had a higher VO_2 while walking compared with those with proportionally lower hip muscle activity. There may be a redistribution of muscle activity with aging; studies show increased work by the hip musculature in older adults is associated with decreased work by the musculature of the more distal joints (e.g. reduced power in plantar flexor) in both healthy older adults (DeVita & Hortobagyi, 2000; Judge et al., 1996) and older adults with a lower extremity disability (McGibbon & Krebs, 2002; McGibbon et al., 2001). FDG PET findings provide further evidence describing increased output by the hip musculature and introduce new information indicating that this increased output increases VO_2 in older adults during walking.

4. Evaluation of a walking aid using FDG PET

4.1 Importance of walking aids in older adults

Physical function is associated with the ability to perform the activities necessary for independent living without substantial risk of injury (Guralnik & Simonsick, 1993). Evidence suggests that impaired gaits in the elderly strongly affect their ability to perform daily activities (Brach & VanSwearingen, 2002; Guralnik et al., 2000); therefore, evaluation of gaits is an essential part of geriatric health and intervention programs. Kinesiological and epidemiological studies have shown that changes in gait scores such as decreased walking speed and stride length are associated with advanced age (Elble et al.,1991; Judge et al., 1996; Murray et al., 1969; Nagasaki et al., 1996; Nigg et al., 1994; Ostrosky et al., 1994; Winter et al., 1990). The age-related change in gait is characterized by a reduction in ankle power output during the terminal stance phase probably due to an age-related impairment in the power-generating capacity of the ankle which limits walking speed and stride length (McGibbon, 2003). In addition, the metabolic cost of walking is greater for the elderly than for young adults, even when there are no gait impairments (Malatesta et al., 2003; Martin et al., 1992; McCann & Adams, 2002; Waters et al., 1988). The increased metabolic cost of walking can impair the activity and quality of life of elderly people as a decrease in physical activity rapidly degrades physical and psychological functions (Backmand et al., 2006; Young et al., 1995).

There are many interventions that improve gait performance in non-disabled and disabled elderly people. Almost all these interventions include exercise programs to improve muscle strength or balance (Gillespie et al., 2003; Latham et al., 2003). Endurance in elderly people can also be improved by assisted devices such as canes or braces which affect gait speeds, stride lengths, and stability (Alexander, 1996; Joyce & Kirby, 1991; Kuan et al., 1999; Roomi et al., 1998; Van Hook et al., 2003). Shimada et al. developed an automated stride assistance system (Shimada et al., 2009a) (SAS) (Honda R & D Co. Ltd., Wako, Japan) (Figure 3), which uses robotic engineering to control walk ratios (stride length/cadence) and add supporting power to the thigh during walking. The SAS weighs 3.5 kg and it was developed to teach walking efficiency and improve gait endurance in elderly people with age-related short stride length. However, the SAS is limited because it supports movement of the hip joint during walking, which can lead to deterioration of muscle activity in the lower extremities during long-term intervention studies or practical applications.

Fig. 3. Stride assistance system that can control walk ratios (stride length/cadence) and support the thigh during walking.

4.2 Muscular metabolism during walking using a robotic stride assistance system

FDG PET has been used to evaluate muscular activity during exercise with a stride assistance system (Shimada et al., 2007, 2008). In this research, 10 healthy younger men (mean age, 24.1 years) and 7 healthy older men (mean age, 76.0 years) completed FDG PET measurements twice after walking with and without the SAS. The sequence of the experiments was randomized to negate the confounding effect of prior experience of walking on a treadmill. Subjects were asked to walk for 50 min at 4.0 km/h on a treadmill (MAT-5500; Fukuda Denshi Co. Ltd., Tokyo, Japan). All young subjects walked at the target speed of 4.0 km/h. The speed of the treadmill was adjusted to 2.89–3.82 km/h without the SAS and 3.03–4.03 km/h with the SAS for the older subjects who could walk at a constant speed.

Figure 4 shows representative FDG PET images taken in young and older subjects after walking with or without the SAS. Glucose utilization in the lower-extremity muscles was evident after walking. In young subjects, walking with the SAS significantly increased FDG uptakes by the tibialis posterior and the medial gastrocnemius compared with walking without it (Shimada et al., 2007). FDG uptake ratios (SUV after walking with the SAS: SUV after walking without the SAS) of the tibialis posterior and medial gastrocnemius were 2.13 and 2.36, respectively. Walking with the SAS did not have significant effects on any other muscles. In older adults, there were no significant differences between the SUVs with and without the SAS in all lower-extremity muscles. However, walking speeds (mean walking speed without SAS, 3.46 km/h; mean walking speed with SAS, 3.56 km/h) and stride lengths (mean stride length without SAS, 54.9 cm, mean stride length with SAS, 58.2 cm) were

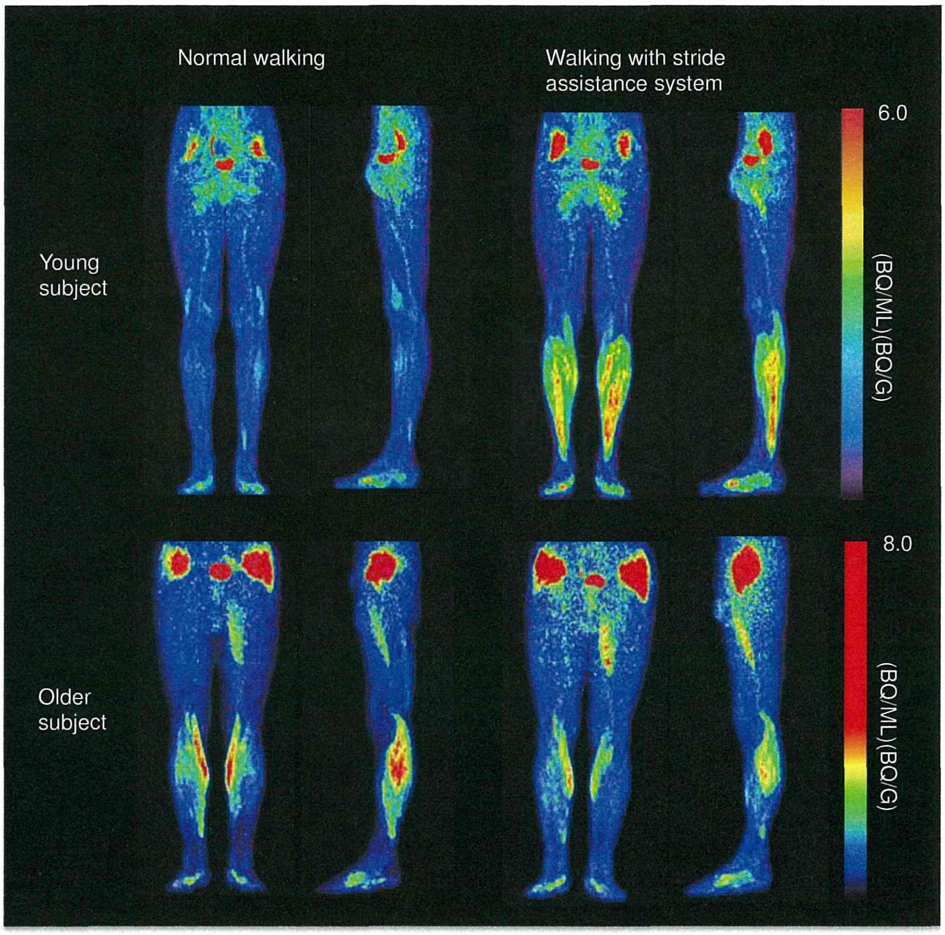

Fig. 4. FDG PET images taken after walking without or with the SAS.
The left and right panels show projection images taken after walking without or with the SAS, respectively.

significantly increased when walking on the treadmill with the SAS in the older subjects. These results suggest that the SAS can facilitate efficient walking patterns irrespective of muscle activity. The SAS may have provided assistance to the thigh and increased the torque of the hip of the older subjects resulting in improved walking scores. Therefore, stride length and walking speed increased without activating lower-extremity muscle activity.

5. Evaluation of exercise intervention using FDG PET

5.1 Effects of exercise in older adults

Older people enjoy walking exercise because it is familiar and more convenient than many other sports and recreational activities (Morris & Hardman, 1997; Mutrie & Hannah, 2004). Intervention studies show that strength or endurance training in older people can improve measures of gait such as walking speed (Binder et al., 2004; Brown & Holloszy, 1993; Buchner et al., 1997a; Ettinger et al., 1997; Judge et al., 1993). Endurance training also improves physical fitness, particularly cardiovascular fitness, as well as cognitive functions (van Uffelen et al., 2008). The development of targeted exercise programs may be facilitated by exercise intervention studies that allow a better understanding of the effects of muscle activity during walking. However, results from previous intervention studies investigating the effects of strength or endurance training on walking speed and gait are inconclusive (Buchner et al., 1997b; Ettinger et al., 1997). Walking is a near-perfect exercise for healthy and frail older people (Morris & Hardman, 1997); therefore, if walking induces walking-specific adaptations, interventions involving walking may be an efficient and appropriate means of improving walking function in older people (Shimada et al., 2003). However, knowledge of the effects of walking exercise on the physical performance of older people is limited. Most walking exercise interventions are prescribed in combination with exercises aimed at increasing muscle strength, neuromuscular coordination, and balance (Morris et al., 1999), and physical performance is not always assessed in intervention studies (Ebrahim et al., 1997).

5.2 Comparison of FDG uptakes in skeletal muscles before and after intervention

The functionality of walking may be improved by increasing the stride length of older people, which in turn may result in benefits such as improved walking efficiency. These benefits may supersede those derived from improved aerobic fitness alone. Shimada et al. (2009a) assessed the effects of a walking program for the elderly using the SAS. Fifteen subjects participated in a three-month walking program of two 90-min supervised sessions per week using the SAS. For FDG PET analysis, subjects walked for 50 min at a comfortable speed on a circular indoor walking track without the SAS. Figure 5 shows representative FDG PET images taken before and after the exercise intervention (Shimada et al., 2009a). FDG uptakes by the gluteus minimus, gluteus medius, and rectus femoris were significantly lower after the intervention than before, although walking speed during FDG PET measurements increased after the intervention. In contrast, the medial gastrocnemius and soleus (the lower distal muscles) showed higher FDG uptakes after the intervention than before, although the difference was not statistically significant.

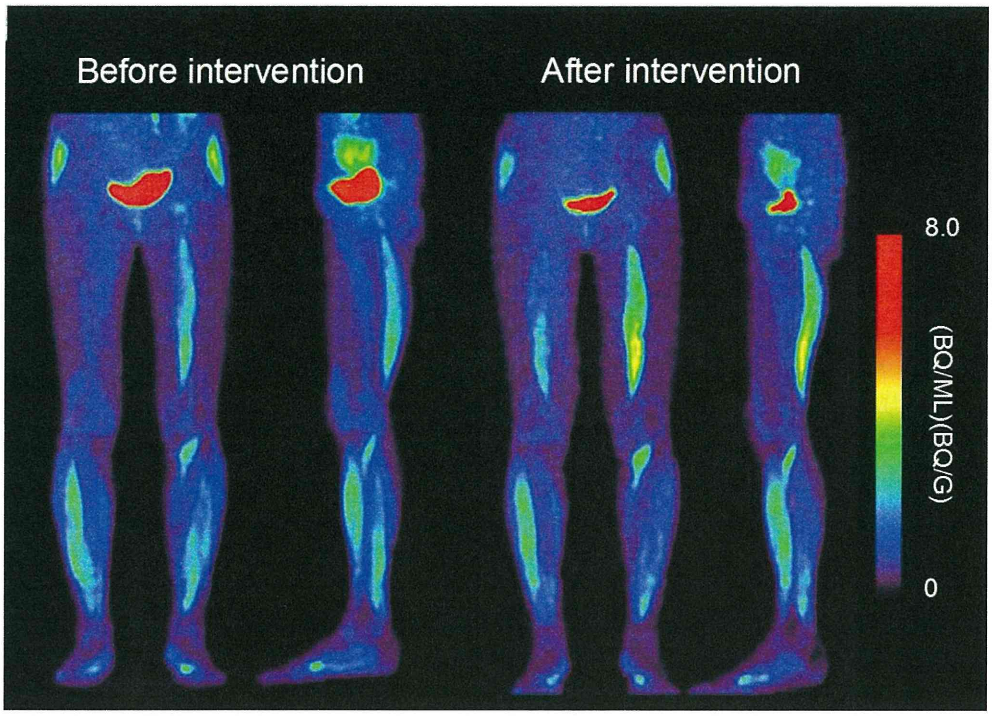

Fig. 5. FDG PET images of an older woman before and after the intervention.
The left and right panels show before and after intervention images, respectively. FDG uptakes by the gluteus minimus, gluteus medius, rectus femoris and pelvic muscles after the intervention were significantly lower than before.

The gluteus medius and gluteus minimus are the two primary hip abductors. They are most active during the first 40% of the gait cycle and they stabilize the pelvis in the frontal plane (Neumann, 2002). It is possible that the activity of the hip abductors decreases to improve mediolateral stability during long-distance walking. Further studies must be carried out using kinematic and kinetic analyses to fully understand the mechanisms involved in the change in cumulative muscle activity during prolonged walking.

Previous data indicate that the activity of hip-related muscles and hamstrings is greater than that of other lower extremity muscles in elderly people during walking. Shimada et al. 2009a found a significant decrease in the activity of the pelvic muscles (iliacus and gluteus muscles) during intervention with the SAS. However, the intervention did not increase FDG uptake of the soleus and gastrocnemius muscles, suggesting that the walking intervention improved the efficiency of muscle activity but did not redistribute muscular effort. This indicates that a walking intervention with the SAS has potential to increase walking endurance in the elderly. Indeed, the distance walked in 50 min after the intervention (median, 3579.0 m) was greater than that before the intervention (median, 3051.0 m); however, this difference was not statistically significant.

The quadriceps femoris controls knee flexion and acts as a shock absorber after heel contact; it then supports the weight of the body in mid-stance. The rectus femoris differs from that of other knee extensors as it is a hip flexor and its activity increases immediately after the toe-off phase (Neumann, 2002). A previous study showed that antagonist thigh muscle coactivation (e.g., activation of the vastus medialis, vastus lateralis, and biceps femoris) is 31% greater in older than in younger adults, and coactivation is moderately correlated with the metabolic cost of walking (Mian et al., 2006). The SAS automatically lends horizontal force to the thigh to facilitate an optimal walk ratio and may teach elderly people to use their muscles more efficiently. The consecutive stimuli provided by the SAS may help elderly people adopt an efficient walking pattern.

6. Functional FDG PET imaging as evaluating of frailty

Frail elderly people are particularly vulnerable for developing disabilities (Boyd et al., 2005; Gill et al., 2004; Hardy et al., 2005) and are at an increased risk for falls, disabilities, hospitalization, institutionalization and death, compared with their age-matched non-frail counterparts (Espinoza & Walston, 2005). Disability is closely related to medical spending; therefore, prevention of disability can lead to reduced health care costs (Cutler, 2001). Physical frailty indicators include mobility, strength, endurance, nutrition, physical inactivity, balance, and motor processing (Ferrucci et al., 2004). Gait disorder is a particularly important indicator of frailty and an independent predictor of disability. The findings of research using FDG PET has revealed a cycle of gait disorder (Figure 6).

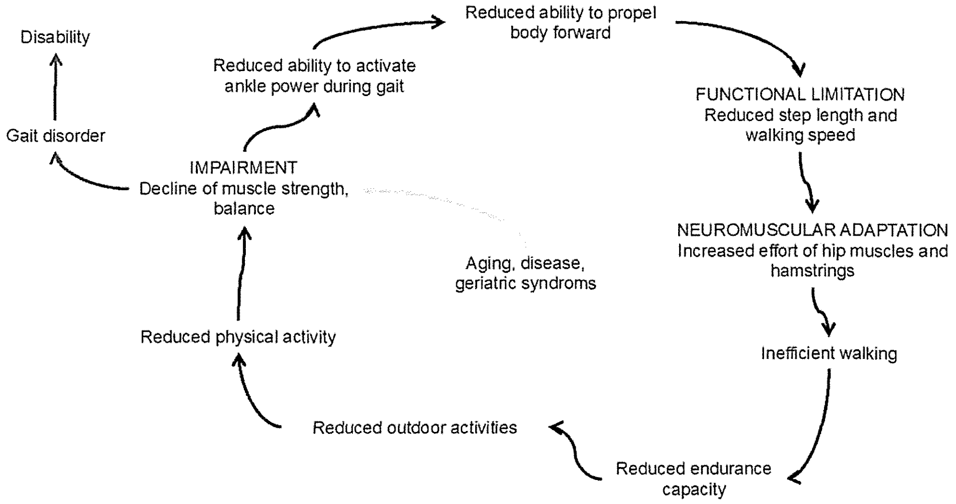

Fig. 6. Schematic diagram of the incidence of gait disorder in older adults.

Aging results in impaired muscle strength and balance, which reduces the ability to activate the ankle plantar muscles during gait and propel the body forward. These impairments manifest as functional limitations including reduced step length and walking speed, which are compensated for by neuromuscular adaptations such as increased effort of the hip muscles and hamstrings. Walking becomes inefficient and there is reduced endurance capacity. This leads to decreased involvement in outdoor activities and therefore physical activity, which worsens the impaired muscle strength and balance. Ultimately, the cycle can lead to gait disorder and disability.

7. Conclusions

FDG PET has proved useful for understanding the ability of older adults to perform physical activities. Because FDG uptake is closely correlated with exercise intensity, it can be used for comparing task-specific muscle activity. FDG PET and VO_2 analyses indicate that older adults may have difficulties in performing the activities of daily living as they have to work at a higher level of effort relative to their maximum capability due to a redistribution of muscle activity with aging. Automated exercise intervention, such as the automated stride assistance system (SAS), may help slow the cycle of events that ultimately can lead to gait disorder and disability. FDG PET evaluation of glucose metabolism in the muscles of the elderly following intervention with the automated SAS indicates that the SAS has the potential to increase walking endurance. We suggest that FDG PET is a useful method to evaluate the effects of interventions and therefore develop rehabilitation programs.

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