中高年者の脳萎縮を抑制する日常歩行量の解明
～地域からの無作為抽出者を対象とした大規模縦断研究～

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The Association between Daily Physical Activity Levels and Brain Atrophy Progression in Middle-aged and Elderly Japanese

by

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ABSTRACT

Brain structural atrophy is associated with impairment in learning function and cognitive function. The purpose of this study was to determine whether daily physical activity prevents age-related brain atrophy progression.

The subjects were 381 males and 393 females who had participated in both the baseline and follow-up examinations (mean duration, 8.2 years). Magnetic resonance imaging of the frontal and temporal lobes was performed at the time of the baseline and follow-up surveys. The number of steps of the subjects was recorded at baseline with uniaxial accelerometry sensors. Multiple logistic regression models were fit to determine the association between number of steps variables and frontal and temporal lobe atrophy progression while controlling for possible confounders.

In males, the odds ratio of frontal lobe atrophy progression was increased by 1.480 (95% confidence interval [CI], 1.007-2.175)-fold for every 3,000 decrease in the number of steps. The odds ratio of frontal lobe atrophy progression for the fifth quintile compared to the first quintile in the number of steps was 3.651 (95% CI, 1.304-10.219). There were no significant differences between frontal lobe atrophy progression and the number of steps in females. There were also no significant differences between temporal lobe atrophy progression and the number of steps in males and females.

The results indicate that physical activity is significant predictors of frontal lobe atrophy progression over an 8-year period. Promoting participation in activities may be beneficial for attenuating age-related frontal lobe atrophy and for preventing dementia.

要　旨

地域から無作為抽出された中高年者を対象に，日常歩行量が脳萎縮進行に与える影響を検討した．

対象者は「国立長寿医療研究センター・老化に関する長期縦断疫学研究」第2次調査と8年後に実施された第6次調査の両方に参加した，50～79歳の男性381名，女性393名とした．8年間における前頭葉及び側頭葉萎縮の進行状況を，MRI画像より評価した．第2次調査時における歩行量調査を基に，脳萎縮進行を防ぐ歩行量閾値について，ロジスティック回帰分析により検討した．

男性において，歩行量が3,000歩ずつ減少した際の前頭葉萎縮進行のオッズ比は1.480（95%信頼区間，1.007－2.175）であった．また歩行量を5分位とした際の，第5分位に対する第1分位の前頭葉萎縮進行のオッズ比は3.651（95%信頼区間，1.304-10.219）であった．女性では前頭葉萎縮進行と歩行量との間に関連を認めなかった．側頭葉萎縮進行は，男女ともに歩行量との関連を認めなかった．

中高年男性では，前頭葉萎縮進行を予防するために，一日あたり5,800歩以上の歩行量を維持する必要性が示唆された．

緒　言

アルツハイマー病では脳の構造的な萎縮が顕著におこり，認知機能や学習機能に障害をきたす[13]．脳萎縮は加齢によっても進行し，ヒトの脳灰白質量は20歳代から70歳代にかけて，約15%減少することが報告されている[25]．一般高齢者を対象とした6年間の追跡調査では，脳萎縮の進行状態と認知機能レベルは強い関連を示すことが報告されており[20]，脳萎縮を予防することで認知機能の低下や障害の予防に繋がる可能性が示唆されている．

近年では，有酸素運動が神経新生を促進し，脳量の増加，保持に働くことが示されている[8]．高齢者では6ヶ月間の有酸素運動トレーニングによって前頭葉，側頭葉，海馬の脳量が増加したことが報告されている[5]．また，速歩を用いた有酸素性トレーニングは海馬の萎縮を改善するなど[10]，有酸素運動による脳萎縮の予防的効果が示されている．

脳量と有酸素運動の関連性が示される一方で，日常生活における身体活動と脳量の関連については不明な点が多い．中高年者では，身体活動量と有酸素能は相関することが報告されており[1,4]，日常の身体活動量を高く保つことが脳萎縮の予防へと繋がるものと考えられる．実際に横断研究において，身体活動量と脳量は関連することが報告されているが[3,11]，日常の身体活動量と脳量及び脳萎縮との関連を検討した縦断研究は見当たらない．近年では，身体活動量の多い高齢者では加齢による認知機能低下のリスクが低いことが，縦断研究によって示されている[21]．日常身体活動による脳萎縮抑制へと繋がる知見が得られれば，身体活動が認知機能低下を抑制することを裏付ける根拠となり，認知機能低下の予防を目的とした身体活動を推奨するためのエビデンスとなると考えられる．

そこで本研究は，無作為抽出された地域在住の中高年者を対象とする約8年間の追跡データを用い，日常歩行量と加齢による脳萎縮進行の関連について検討を行い，脳萎縮進行を抑制する歩行量閾値を解明することで，認知機能低下の予防を目的とした運動処方のエビデンスを作成することを目的とした．

1．方　法

1．1　地域住民におけるデータの収集

本研究は「国立長寿医療研究センター・老化に関する長期縦断疫学研究（NILS-LSA）」の参加者のデータを用いて行われた．NILS-LSAの参加者は長寿医療研究センター周辺の，観察開始時年齢が40歳から79歳までの地域住民約2,300名であり，住民台帳から年齢・性別に層化した無作為抽出によって選定された[22]．選定された者を説明会に招き，調査の目的や方法などを十分に説明し，書面による同意を得た上で調査は実施された．またNILS-LSAは，国立長寿医療研究センター倫理委員会での研究実施の承認を受けた上で実施された．

1．2　対象者

対象者は，ベースラインとしたNILS-LSAの第2次調査（2000年4月から2002年5月まで）を完了した参加者1,545名（男性715名，女性830名）中，その約8年後に実施された第6次調査（2008年7月から2010年7月まで）にも参加した男性514名，女性566名とした．そのうち，脳萎縮の保有率と進行率が他の年代と比較して特に少ない40歳代と，参加人数の少ない80歳代は解析の対象から除外した．また，パーキンソン病既往歴，認知症既往歴，開頭手術歴を有する者についても解析の対象から除外し，最終的な解析の対象は男性381名，女性393名とした．解析対象者のうち，第2次調査時において脳萎縮がグレード4（重度）に該当する者は含まれていなかった．

1．3　頭部核磁気共鳴画像法（MRI）検査

第2次調査時とその8年後に実施された第6次調査時において，頭部MRI検査（Visart 1.5T, 東芝）を実施した．頭部MRI検査はRepetition time = 500msec，Echo time = 15msec，Slice thickness = 8mm，Slice gap = 1.5mm，Matrix = 256×256 の条件でスキャンを行い，眼窩耳孔線に対し平行となるT1強調画像14枚を得た．

各調査時において得られた頭部MRI画像を基に，前頭葉及び側頭葉についてそれぞれ，萎縮を4段階（1 無し；2 軽度；3 中等度；4 重度）に分類した（図1）[16,23]．さらに第2次調査時と第6次調査時の萎縮グレードを比較し，第6次調査時の萎縮グレードが第2次調査時のものと比較して高い群を「萎縮進行あり群」として，それ以外の場合を「萎縮進行なし群」として分類した．

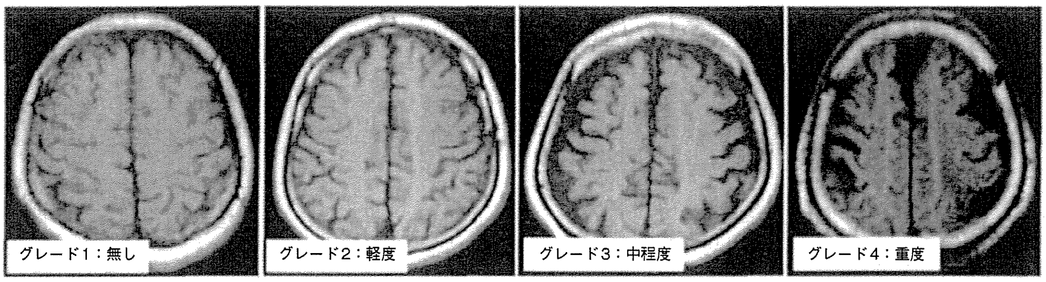

図1　脳萎縮の分類

1．4　歩行量調査

本研究では身体活動量指標として，歩行量を用いた．歩行量調査は，ベースラインに当たる第2次調査時において実施した．歩行量は，加速度計（Lifecorder, スズケン）を対象者の腰部に装着してもらうことで得た．調査期間は，旅行などの特別なイベントの無い7日間とし，入浴時及び就寝時は除外した．得られた7日間の歩行量のうち，最大値と最小値を除外した計5日間分のデータより，一日当たりの平均歩数を算出した．

1．5　対象者の特性に関する検査及び調査

第2次調査時における身長及び体重より，BMIを求めた．体脂肪率は，二重エネルギーX線吸収法による全身スキャンによって算出した（QDR-4500A, Hologic）．一日当たりのアルコール摂取量，現在の喫煙の状況，教育年数は自記式の調査票により得た．脳卒中，虚血性心疾患，糖尿病，高血圧症，脂質異常症の既往歴について，対象者に自記式の調査票への回答を求めるとともに，医師の問診による確認を行った．またNILS-LSAでは，対象者の過去2週間において使用したすべての処方薬及び市販薬について調査を行っている[22]．本研究では，血糖降下薬，降圧薬，脂質降下薬の使用者はそれぞれ，糖尿病，高血圧症，脂質異常症既往歴保有者に分類した．

1．6　統計解析

各変数のデータは，平均値 ± 標準偏差，または標準誤差で示すとともに，t検定またはχ^2検定を用い，群間における差及び分布状況についての比較を行った．対象者の年代と脳萎縮の進行の関係について，Cochran-Mantel-Haenszel検定を用いて年代上昇による増減傾向を検定した．

ベースラインから8年間の脳萎縮の進行状況と一日平均歩数の関連について，多重ロジスティック回帰分析を用いて検討した．多重ロジスティック回帰分析は，目的変数に萎縮進行の有無を，説明変数として一日平均歩数を投入し，年齢[25]，BMI[11]，教育年数[11]，脳卒中，虚血性心疾患，糖尿病，高血圧症，脂質異常症既往歴の有無[2, 7]，現在の喫煙状況[6]，アルコール摂取量で調整した[24]．一日平均歩数は，連続変数，5分位としたカテゴリー変数としてそれぞれ投入し，脳萎縮進行のオッズ比を求めた．解析はStatistical Analysis System ver. 9.3（SAS Institute Inc）を用いて行い，有意水準は5% 未満とした．

2．結　果

2．1　対象者の特性

表1に，ベースライン時における対象者の特性について男女別に示した．平均追跡期間は男女共に8.2± 0.3年であった．年齢，BMI，一日平均歩数は男女間に差を認めなかった．身長及び体重，アルコール摂取量，教育年数は，女性と比較して男性で高値を示した（各$p<0.0001$）．体脂肪率は，男性と比較して女性で高値を示した（$p<0.0001$）．脳卒中，虚血性心疾患，高血圧症の

表１　対象者の特性

	男性 (n = 381)	女性 (n = 393)	p value
追跡期間（年）	8.2 ± 0.3	8.2 ± 0.3	0.5777
年齢	60.4 ± 7.3	60.8 ± 7.6	0.5421
身長（cm）	164.7 ± 5.4	152.2 ± 5.2	< 0.0001
体重（kg）	62.5 ± 7.1	52.7 ± 7.0	< 0.0001
BMI（kg/m2）	23.0 ± 2.4	22.7 ± 2.9	0.1279
体脂肪率（%）	21.0 ± 4.0	31.3 ± 4.9	< 0.0001
アルコール摂取量（g/day）	16.6 ± 20.9	2.7 ± 6.1	< 0.0001
教育年数（年）	12.3 ± 2.7	11.4 ± 2.3	< 0.0001
一日平均歩数（/day）	7993.2 ± 2588.0	7925.6 ± 2297.1	0.7011
脳卒中既往歴（n）	14 (3.7%)	7 (1.8%)	0.105
虚血性心疾患既往歴（n）	13 (3.5%)	19 (4.8%)	0.3203
高血圧症既往歴（n）	40(10.5%)	40 (10.2%)	0.8836
脂質異常症既往歴（n）	61(16.0%)	94 (23.9%)	0.006
糖尿病既往歴（n）	32 (8.4%)	16 (4.1%)	0.0126
喫煙者（n）	102(26.8%)	27 (6.9%)	< 0.0001

平均値 ± 標準偏差　p 値は t 検定，χ^2 検定による

既往歴保有者の割合は，男女間で差を認めなかった．脂質異常症の既往歴保有者の割合は，男性と比較して女性で高かった（p=0.0060）．糖尿病既往歴保有者，喫煙者割合は，女性と比較して男性で高かった（糖尿病 p=0.0126; 喫煙者 p<0.0001）．

２．２　年代別にみた脳萎縮進行の頻度

表２に，ベースラインから８年間の前頭葉及び側頭葉における萎縮の進行状況について，性，年代別に示した．男性対象者 381 名中 55 名（14.4%），女性対象者 393 名中 35 名（8.9%）に萎縮の進行が認められ，その割合は女性と比較して男性で高かった（χ^2 検定，p = 0.0213）．また，男女とも年代上昇で前頭葉萎縮進行者の割合は増加した（p trend < 0.0001）．側頭葉では，男性対象者 381 名中 100 名（26.3%），女性対象者 393 名中 78 名（19.8%）に萎縮の進行が認められ，その割合は女性と比較して男性で高かった（χ^2 検定，p = 0.0344）．また，男女とも年代上昇で側頭葉萎縮進行者の割合は増加した（p trend < 0.0001）．

２．３　脳萎縮の進行状況と一日平均歩数

図２に，一日平均歩数について，前頭葉及び側頭葉の萎縮進行群別に示した．男性では，前頭葉の萎縮進行なし群と比較して，萎縮進行あり群では一日平均歩数が低値を示した（p = 0.0131）．一方側頭葉では，群間に差を認めなかった．また女性では前頭葉及び側頭葉ともに，一日平均歩数は群間に差を認めなかった．

表２　脳萎縮進行者の年代別分布

		前頭葉萎縮		trend p value	側頭葉萎縮		trend p value
		進行なし	進行あり		進行なし	進行あり	
男性（n）	50-59 歳	176 (95.1%)	9 (4.9%)		156 (84.3%)	29 (15.7%)	
	60-69 歳	112 (79.4%)	29 (20.6%)	< 0.0001	87 (61.7%)	54 (38.3%)	< 0.0001
	70-79 歳	38 (69.1%)	17 (30.9%)		38 (69.1%)	17 (30.9%)	
	計	326 (85.6%)	55 (14.4%)		281 (73.8%)	100 (26.3%)	
女性（n）	50-59 歳	191 (96.0%)	8 (4.0%)		188 (94.5%)	11 (5.5%)	
	60-69 歳	117 (90.0%)	13 (10.0%)	< 0.0001	92 (70.8%)	38 (29.2%)	< 0.0001
	70-79 歳	50 (78.1%)	14 (21.9%)		35 (54.7%)	29 (45.3%)	
	計	358 (91.1%)	35 (8.9%)		315 (80.2%)	78 (19.8%)	

trend p 値は Cochran–Mantel–Haenszel 検定による

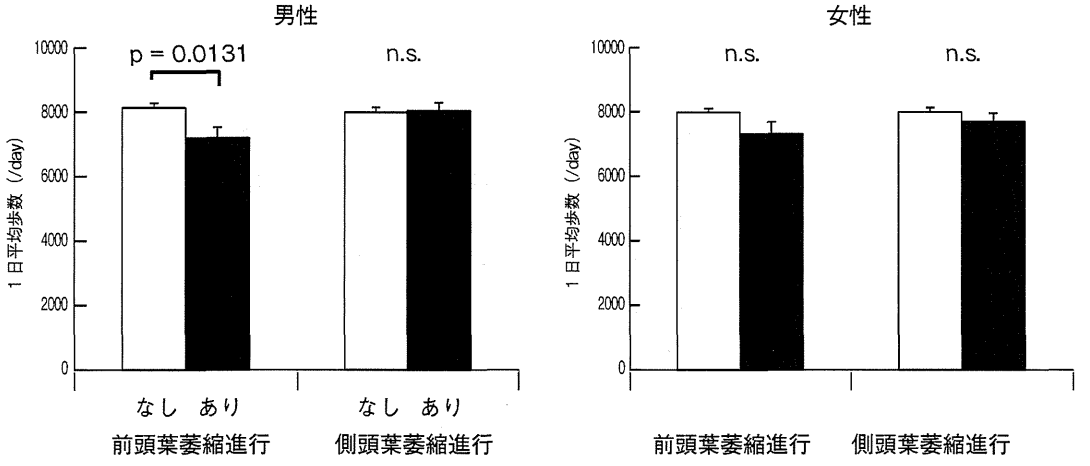

図2　一日平均歩数の比較
平均値 ± 標準誤差　p 値は t 検定による

2．4　脳萎縮進行のリスクと関連する一日平均歩数

表３及び表４に，前頭葉及び側頭葉における萎縮の進行と，一日平均歩数の関連性について検討したロジスティック回帰分析の結果を示す．男性において，８年後の前頭葉萎縮の進行と一日平均歩数との間に関連性を認めた．一日平均歩数を連続変数（マイナス 3,000 歩ごと）とした際の前頭葉萎縮進行のオッズ比は，1.480（95% 信頼区間 , 1.007 – 2.175; p=0.0460）と有意な関連を示した．また一日平均歩数を５分位とし，第５分位を基準した際の各分位の前頭葉萎縮進行のオッズ比を求めたところ，第１分位におけるオッズ比は 3.651（95% 信頼区間 , 1.304 – 10.219; p=0.0072）と有意な関連を示した．一方，側頭葉萎縮進行と一日平均歩数との間に関連を認めなかった．女性では，前頭葉及び側頭葉のいずれも，萎縮の進行と一日平均歩数との間に関連を認め

表３　男性対象者における脳萎縮進行のオッズ比

		n	前頭葉萎縮進行		側頭葉萎縮進行	
			オッズ比（95% 信頼区間）	p value	オッズ比（95% 信頼区間）	p value
1 日平均歩行量	-3000 歩ごと	381	1.480（1.007 – 2.175）	0.046	0.979（0.742 – 1.290）	0.8787
	Q1: 5736.0 歩未満	76	3.651（1.304 – 10.219）	0.0072	0.938（0.435 – 2.024）	0.6269
	Q2: 5736.0 – 6955.0 歩未満	76	1.261（0.383 – 3.863）	0.3108	1.100（0.519 – 2.330）	0.8715
	Q3: 6955.0 – 8261.4 歩未満	76	1.487（0.471 – 4.689）	0.6501	1.142（0.538 – 2.425）	0.7501
	Q4: 8261.4 – 10407.4 歩未満	76	2.403（0.819 – 7.052）	0.2874	1.123（0.528 – 2.389）	0.8039
	Q5: 10407.4 歩以上	77	1.00（基準）		1.00（基準）	

年齢，BMI，教育年数，脳卒中，虚血性心疾患，糖尿病，高血圧症，脂質異常症既往歴の有無，喫煙状況，アルコール摂取量で調整

表４　女性対象者における脳萎縮進行のオッズ比

		n	前頭葉萎縮進行		側頭葉萎縮進行	
			オッズ比（95% 信頼区間）	p value	オッズ比（95% 信頼区間）	p value
1 日平均歩行量	-3000 歩ごと	393	1.298（0.766 – 2.197）	0.3323	0.961（0.656 – 1.407）	0.8361
	Q1: 5825.2 歩未満	78	1.559（0.420 – 5.791）	0.78	0.879（0.355 – 2.178）	0.8452
	Q2: 5825.2 – 7090.0 歩未満	79	2.269（0.627 – 8.209）	0.1784	0.789（0.311 – 2.005）	0.5798
	Q3: 7090.0 – 8374.0 歩未満	78	0.826（0.181 – 3.769）	0.2578	0.825（0.317 – 2.147）	0.7003
	Q4: 8374.0 – 9910.4 歩未満	79	1.887（0.505 – 7.053）	0.426	1.206（0.489 – 2.974）	0.3522
	Q5: 9910.4 歩以上	79	1.00（基準）		1.00（基準）	

年齢，BMI，教育年数，脳卒中，虚血性心疾患，糖尿病，高血圧症，脂質異常症既往歴の有無，喫煙状況，アルコール摂取量で調整

なかった.

3. 考　察

地域から無作為に抽出された中高年者を対象とし，加齢による脳萎縮進行と関連を示す一日平均歩数について縦断解析を行った結果，男性では前頭葉萎縮進行と一日平均歩数との間に関連を認めた（表4）．一日平均歩数を連続変数とした際の前頭葉萎縮進行のリスクは，歩数が3,000歩ずつ減少するごとに約1.5倍ずつの上昇を示し，日本人の中高年男性では日常の歩行量を高く保つことで，加齢による前頭葉萎縮の進行を抑制する可能性が示唆された．さらに一日平均歩数を5分位とし，歩行量が最も多い群（10,407.4歩以上）を基準として，各分位における前頭葉萎縮進行のリスクを検討したところ，歩行量が最も少ない群（5,736.0歩未満）では前頭葉萎縮進行のリスクが約3.7倍高いことが示された．このことから，男性では前頭葉萎縮の進行を予防する日常の歩行量の最少閾値が，約5,800歩付近に存在している可能性が考えられた．一般に歩行量は加齢に伴い減少することが知られている．日本人男性の一日平均歩数は，50歳代が7,772歩，60歳代が6,949歩，70歳以上が4,707歩と報告されており[17]，70歳以降の男性では前頭葉萎縮の進行リスクが他の年代と比較して特に高いことが推察される．従って日本人の中高年男性では，一日の歩数を概ね5,800歩以上に保つこと，また特に70歳以降において歩行量を増やすことが，加齢による前頭葉の萎縮進行の予防において重要である可能性が示唆された．

対照的に，女性では加齢による前頭葉萎縮進行と日常の歩行量の間に関連を認めなかった（表4）．一般的に，男性は女性と比較して脳萎縮の頻度は高い[25]．そして実際に本研究においても，男性では前頭葉萎縮進行の頻度が女性と比較して高く（表2），身体活動の効果が男性でより明確化したことが考えられる．また，テストステロンやエストロゲンなどの性ホルモンについても，脳量に影響を及ぼす因子であることが報告されており[8, 15]，身体活動に対する脳の可塑性には性差が存在する可能性も考えられる．

本研究はヒトを対象とし，脳萎縮の進行についてMRI画像を基に評価した非侵襲的研究であることから，身体活動が前頭葉萎縮進行を抑制したメカニズムを明らかにすることはできない．マウスの脳ではアミロイドβの蓄積量と活動量との間に関連が認められることが報告されており[14]，身体活動が高いことでアミロイドβの蓄積が抑制された可能性が考えられる．また，身体活動により神経細胞の増殖や生存に不可欠とされる成長因子の発現量が変動した可能性もある[26]．

運動が脳量に与える効果は，前頭葉に限らず，側頭葉や頭頂葉，海馬など多くの脳領域に及ぶことが報告されている[3,5,11]．興味深いことに，本研究では前頭葉と側頭葉を脳萎縮進行の評価の対象としたが，高い身体活動量との関連は前頭葉に限られている．脳における神経新生を促す要因として，脳血流量の増加が指摘されている[19]．そして身体運動は脳血流量を変動させるが，その変動様式は運動の種類や強度により異なるとされる[12, 18]．本研究は加速度計を用いて得た歩数を身体活動レベルの指標としており，身体活動の種類や強度などは考慮されていない．今後は，身体活動の種類や強度などの影響を考慮した上で，さらなる検討を行う必要があると思われる．

4. まとめ

本研究は地域から無作為に抽出された50歳から79歳までの男女774名を対象に，日常歩行量と加齢による脳萎縮進行の関連について，縦断的に検討した．その結果，男性において日常の

歩行量を高く保つことが，前頭葉萎縮進行を抑制することが示された．また5,800歩が，前頭葉萎縮の進行を抑制する一日当たりの歩行量閾値として示され，認知機能低下の予防に繋がる身体活動量の目標値の一つとなる可能性が示唆された．

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文　献

1）青山友子，浅香明子，金子香織，石島寿道，河野寛，坂本静男，田畑泉，樋口満．中高年男性における心肺体力と身体活動の量およびその強度との関係．体力科学．59: 191-198（2010）

2）Bruehl H., Wolf O.T., Sweat V., Tirsi A., Richardson S., Convit A., Modifiers of cognitive function and brain structure in middle-aged and elderly individuals with type 2 diabetes mellitus. *Brain Res*., 1280: 1896-194（2009）

3）Bugg J.M., Head D., Exercise moderates age-related atrophy of the medial temporal lobe. *Neurobiol Aging*., 32: 506-514（2011）

4）Cao Z.B., Miyatake N., Higuchi M., et al., Prediction of VO2max with daily step counts for Japanese adult women. *Eur. J. Appl. Physiol*., 105: 289-296（2009）

5）Colcombe S.J., Erickson K.I., Scalf P.E., et al., Aerobic exercise training increases brain volume in aging humans. *J. Gerontol. A Biol. Sci. Med. Sci.*, 61: 1166-1170（2006）

6）Debette S., Seshadri S., Beiser A., et al., Midlife vascular risk factor exposure accelerates structural brain aging and cognitive decline. *Neurology.*, 77: 461-468（2011）

7）Enzinger C., Fazekas F., Matthews P.M., et al., Risk factors for progression of brain atrophy in aging: six-year follow-up of normal subjects. *Neurology*., 64: 1704-1711（2005）

8）Erickson K.I., Colcombe S.J., Raz N, et al., Selective sparing of brain tissue in postmenopausal women receiving hormone replacement therapy. *Neurobiol Aging*., 26: 1205-1213（2005）

9）Erickson K.I., Kramer A.F., Aerobic exercise effects on cognitive and neural plasticity in older adults. *Br. J. Sports Med*., 43: 22-24（2009）

10）Erickson K.I., Voss M.W., Prakash R.S., et al., Exercise training increases size of hippocampus and improves memory. *Proc. Natl. Acad. Sci. USA*., 108: 3017-3022（2011）

11）Ho A.J., Raji C.A., Becker J.T., et al., The effects of physical activity, education, and body mass index on the aging brain. *Hum. Brain Mapp*., 32: 1371-1382（2011）

12）Ide K., Horn A., Secher N.H., Cerebral metabolic response to submaximal exercise. *J. Appl. Physiol*., 87: 1604-1608（1999）

13）Killiany R.J., Gomez-Isla T., Moss M., et al., Use of structural magnetic resonance imaging to predict who will get Alzheimer's disease. *Ann. Neurol*., 47: 430-439（2000）

14）Lazarov O., Robinson J., Tang Y.P., et al., Environmental enrichment reduces Abeta levels and amyloid deposition in transgenic mice. *Cell*., 120: 701-713（2005）

15）Lessov-Schlaggar C.N., Reed T., Swan G.E., et al., Association of sex steroid hormones with brain morphology and cognition in healthy elderly men. *Neurology*., 22: 1591-1596（2005）

16）Manolio T.A., Kronmal R.A., Burke G.L., et al., Magnetic resonance abnormalities and cardiovascular disease in older adults. The Cardiovascular Health Study. *Stroke*., 25: 318-327（1994）

17）厚生労働省．平成21年度国民健康・栄養調査結果．（2010）

18）Nielsen H.B., Boushel R., Madsen P., Secher N.H., Cerebral desaturation during exercise reversed by O2 supplementation. *Am. J. Physiol*., 277: H1045-1052（1999）

19）Pereira A.C., Huddleston D.E., Brickman A.M., et al., An in vivo correlate of exercise-induced neurogenesis in the adult dentate gyrus. *Proc. Natl. Acad. Sci. USA*., 104: 5638-5643（2007）

20）Rusinek H., De Santi S., Frid D., et al., Regional brain atrophy rate predicts future cognitive decline:

6-year longitudinal MR imaging study of normal aging. *Radiology.*, 229: 691-696 (2003)

21) Sattler C., Erickson K.I., Toro P., et al., Physical fitness as a protective factor for cognitive impairment in a prospective population-based study in Germany. *J. Alzheimers Dis.*, 26: 709-718 (2011)

22) Shimokata H., Ando F., Niino N., A new comprehensive study on aging the National Institute for Longevity Sciences, Longitudinal Study of Aging (NILS-LSA). *J. Epidemiol.*, 10: S1-9 (2000)

23) Shimokata H., Ando F., Fukukawa Y., et al., Klotho gene promoter polymorphism and cognitive impairment. *Geriatrics & Gerontology International.*, 6: 136-141 (2006)

24) Taki Y., Kinomura S., Sato K., et al., Both global gray matter volume and regional gray matter volume negatively correlate with lifetime alcohol intake in non-alcohol-dependent Japanese men: a volumetric analysis and a voxel-based morphometry. *Alcohol Clin. Exp. Res.*, 30: 1045-1050 (2006)

25) Taki Y., Kinomura S., Sato K., et al., A longitudinal study of gray matter volume decline with age and modifying factors. *Neurobiol. Aging.*, 32: 907-915 (2011)

26) Thoenen H., Neurotrophins and neuronal plasticity. *Science.*, 270: 593-598 (1995)

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Does high educational level protect against intellectual decline in older adults?: A 10-year longitudinal study[1]

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Abstract: This study examined the relation between educational level and intellectual change in Japanese older adults. Participants (age = 65–79 years, n = 593) comprised the first-wave participants of the National Institute for Longevity Sciences-Longitudinal Study of Aging (NILS-LSA). They were followed for 10 years and were tested six times. Educational levels were divided into two groups (low-educated or high-educated), and intellectual changes for the 10 years were assessed using the Japanese Wechsler Adult Intelligence Scale-Revised Short Forms (JWAIS-R-SF); subtests included Information, Similarities, Picture Completion, and Digit Symbol. General linear mixed-model analyses revealed that education had not affected 10-year changes of the Information, Similarities, and Picture Completion subtest scores. In contrast, education was significantly associated with a change in the Digit Symbol subtest score; individuals with higher levels of education showed greater decline than those with less education, although they had higher ability at every time point. These findings suggest that higher education does not protect against intellectual decline in late life, although it is associated with long-term individual differences in intelligence.

Key words: intelligence, education, older adults, longitudinal study.

Many studies have suggested that early-life educational level is associated with better intellectual abilities in late life (e.g., Kaufman & Lichtenberger, 2006; Schaie, 2005; Wechsler, 1981). However, recent articles based on longitudinal data have shown conflicting results with respect to the relation between educational level and intellectual changes in old age. Some longitudinal studies have reported that educational attainment moderates intellectual decline in samples of older adults (e.g., Alvarado, Zunzunequi, Del Ser, & Beland, 2002; Arbuckle, Maag, Pushkar, & Chaikelson, 1998; Evans, Beckett, Albert, Hebert, Scherr, Funkenstein, & Taylor, 1993; Farmer, Kittner, Rae, Bartko, & Regier, 1995; Koster, Penninx, Bosma, Kempen, Newman, Rubin, Satterfield, Atkinson, Ayonayon, Rosano, Yaffe, Harris, Rooks, Van Eijk, & Kritchevsky, 2005; Lee, Kawachi, Berkman, & Grodstein, 2003; Lyketsos, Chen, & Anthony, 1999). However, others disagree with these findings, suggesting

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that higher education does not protect against intellectual decline (e.g., Seeman, Huang, Bretsky, Crimmins, Launer, & Guralnik, 2005; Tucker-Drob, Johnson, & Jones, 2009; Van Dijk, Van Gerven, Van Boxtel, Van der Elst, & Jolles, 2008; Wilson, Hebert, Scherr, Barnes, Mendes de Leon, & Evans, 2009; Zahodne, Glymour, Sparks, Bontempo, Dixon, Macdonald, & Manly, 2011), or that relations between education and intellectual change appear to differ by intellectual domain (e.g., Alley, Suthers, & Crimmins, 2007; Anstey & Christensen, 2000; Anstey, Hofer, & Luszcz, 2003).

From the perspective of the *cognitive reserve* hypothesis, it is noteworthy that previous longitudinal studies have reported the mixed results described above. The hypothesis of cognitive reserve asserts that older individuals with greater experiential resources exhibit better cognitive functioning and are able to tolerate brain pathology before displaying clinical symptoms (Scarmeas & Stern, 2004; Stern, 2002). Stern (2002) postulated that high cognitive reserve may allow individuals to cope more successfully with age-related brain changes, and that one of the most well-established proxy measures of cognitive reserve capacity in the elderly was educational attainment, which is thought to reflect more effective use of brain networks or cognitive paradigms.

Two competing cognitive reserve models could offer insight into the effect of education on the rate of cognitive change (Stern, 2002; Van Dijk et al., 2008). First, if high education was found to slow the rate of cognitive decline, this finding would support an *active* cognitive reserve hypothesis. In this case, individuals with higher education would be hypothesized to process tasks more efficiently. Further, because they make more efficient use of brain networks, the same amount of organic cognitive damage would result in a smaller decline in cognitive function relative to those with less education. Second and alternately, if educational level does not relate to the rate of cognitive change, this would support a *passive* cognitive reserve hypothesis. If aging individuals begin to lose cognitive function from a common cause, such as normal aging brains, people with higher education would change at a rate similar to the total population, but would continue to perform at a higher level at any age because of greater baseline brain reserve. These theories of *active* and *passive* cognitive reserve processes are often evaluated with respect to the implications for *moderation* versus *stability* (Salthouse, 2003; Tucker-Drob et al., 2009) or *differential-preservation* versus *preserved-differentiation* (Bielak, Anstey, Christensen, & Windsor, 2012; Salthouse, 2006).

Inconsistencies in previous longitudinal studies may be due to some methodological differences among the studies. For example, studies differed in the number of consecutive assessments, or the measures of intellectual abilities used.

In terms of the number of assessments, some studies (e.g., Alvarado et al., 2002; Arbuckle et al., 1998; Evans et al., 1993; Farmer et al., 1995; Koster et al., 2005; Lee et al., 2003; Lyketsos et al., 1999) examined intellectual change by calculating a difference between only two test occasions and then used traditional regression analysis or repeated measures analysis of variance techniques. However, ideally, to estimate a true change, intellectual ability should be assessed at multiple time points rather than using a simple difference in two test administrations (Alley et al., 2007; Wilson et al., 2009). The use of three or more assessments of longitudinal intellectual aging can reduce measurement error (Winkens, Schouten, Van Breukelen, & Berger, 2006) as well as avoid the regression toward the mean phenomenon (Dufouil, Fuhrer, Dartigues, & Alpérovitch, 1996; Zahodne et al., 2011). Moreover, the use of three or more assessments makes possible the use of more sophisticated analytic techniques, such as multilevel modeling or general linear mixed modeling (Laird & Ware, 1982; Morrell, Brant, & Ferrucci, 2009; Verbeke & Molenberghs, 1997).

A second methodological difference concerns which domain of intellectual ability was being measured; it remains possible that education may have different effects on the changes in different intellectual domains. For example,

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in their review of the literature, Anstey and Christensen (2000) found that education appears to be more predictive for crystallized ability, but less predictive for fluid ability or processing speed. Similarly, Wilson et al. (2009) pointed out that their results were based on overall global cognition, so they could not establish whether education was related to decline in some intellectual domains but not others. Additionally, some studies (e.g., Evans et al., 1993; Farmer et al., 1995; Lee et al., 2003) have used mental status measures that assess the most basic level of cognitive abilities (e.g., the Mini Mental State Examination; Folstein, Folstein, McHugh, Practical, & Patients, 1975). Such basic level measures may be insensitive to change among well-educated older adults due to ceiling effects that prevent detection of changes within the upper levels of functioning, resulting in spurious relations between initial performance and change (Tucker-Drob et al., 2009). Thus, multiple and more sensitive assessments that reflect greater variability in intellectual functions might better address educational differences in future research.

The present study

The purpose of the present study was to determine whether educational level is associated with the rate of intellectual change in community-dwelling older Japanese. The important characteristics of this study included the following: (a) the participants were followed for 10 years, tested six times, and general linear mixed models were used to analyze the data; and (b) to measure intelligence in late life, we used neuropsychological tests to cover the multiple intellectual abilities of the adults: the Japanese Wechsler Adult Intelligence Scales-Revised Short Forms (JWAIS-R-SF; Kobayashi, Fujita, Maekawa, & Dairoku, 1993). The JWAIS-R-SF includes four standardized subtests (Information, Similarities, Picture Completion, and Digit Symbol). To our knowledge, this may be the first study that approaches the effect of educational levels on intellectual changes for Japanese older adults.

Methods

Participants

The data for the present study were collected as a part of the National Institute for Longevity Sciences-Longitudinal Study of Aging (NILS-LSA; Shimokata, Ando, & Niino, 2000). The NILS-LSA is a population-based prospective cohort study of aging and age-related diseases. The participants were sex- and age-stratified random samples of Japanese community-dwelling adults aged from 40 to 79 years at baseline (Wave1: 1997–2000). This baseline sample consisted of 2267 participants who were followed up every 2 years (Wave2: 2000–2002, Wave3: 2002–2004, Wave4: 2004–2006, Wave5: 2006–2008, Wave6: 2008–2010). Informed consent was obtained from each participant at the beginning of the study.

We selected an initial sample of individuals who were aged 65 years or older at baseline ($n = 816$). We excluded individuals who: (a) provided data only at baseline ($n = 210$) because longitudinal analyses required a minimum of two valid scores per individual, (b) had a history of dementia at baseline ($n = 1$), or (c) had missing data on all dependent variables at baseline or on the independent variables ($n = 12$). Based on these criteria, the data from 593 individuals were included at baseline. Mean age at baseline was 70.96 years ($SD = 3.90$ years, age range = 65–79 years), with 46.54% of the sample being women.

Measures

Intelligence. The Wechsler Adult Intelligence Scale (WAIS) is one of the most popular tools for assessing intelligence (Wechsler, 1944). In this study, intelligence was assessed using the JWAIS-R-SF (Kobayashi et al., 1993). The trained testers (clinical psychologists or psychology graduate students) administered the test to each participant one on one. The JWAIS-R-SF consists of the following four subtests: Information, Similarities, Picture Completion, and Digit Symbol.

1. Information: Participants were asked general knowledge questions covering people, places, and events (29 items, possible range 0–29). This subtest measured the fund of factual knowledge.
2. Similarities: Participants were asked to tell what way two things are alike (14 items, possible range 0–28). This subtest measured logical abstract reasoning.
3. Picture Completion: Participants were asked to spot the missing element in a series of drawings (21 items, possible range 0–21). This subtest measured the long-term visual memory and the ability to differentiate essential from inessential details.
4. Digit Symbol: Participants were asked to write down the symbol that corresponded to a given number (as many as they could in 90 s, possible range 0–93). This subtest measured processing speed and visual-motor coordination.

Educational levels. Participants self-reported their level of education on a scale with four options (1 = *elementary school or junior high school*, 2 = *high school or junior high school under the former Japanese educational system*, 3 = *higher vocational school or junior college*, and 4 = *college or graduate college*). The baseline sample reported 47.39% ($n = 281$) elementary school or junior high school, 35.92% ($n = 213$) high school or junior high school under the former Japanese educational system, 10.96% ($n = 65$) higher vocational school or junior college graduates, and 5.73% ($n = 34$) college or graduate college graduates. Given this distribution, we divided educational levels into two groups: the low-educated group (level = 1) and the high-educated group (levels = 2–4).

Covariates. At baseline assessment, marital status (0 = unmarried, 1 = married), occupation (0 = inoccupation, 1 = having occupation), smoking (0 = nonsmoker, 1 = smoker) and past and present illness (stroke, hypertension, heart disease, and diabetes: 0 = none, 1 = having past or present illness) were examined using questionnaires.

Results

Statistical analyses were performed using the SAS System version 9.1.3. A *p*-value of <0.05 was considered statistically significant.

Sample characteristics

Table 1 presents the baseline sample characteristics by level of education. There were no significant differences in age, sex, and other covariates by educational levels. All baseline intelligence scores in the high-educated group were significantly greater than in the low-educated group (all *p*s < .001).

In addition, compared with the excluded group ($n = 210$), which provided data only at baseline, this study sample showed higher scores on all intelligence measures (Information, 10.30 vs. 13.13, $t(793) = 6.47, p < .001$; Similarities, 8.73 vs. 11.17, $t(792) = 5.41$, $p < .001$; Picture Completion, 7.40 vs. 9.74, $t(794) = 7.87$, $p < .001$; Digit Symbol, 34.17 vs. 39.62, $t(792) = 6.49, p < .001$). However, there were no significant differences between the level of education, $\chi^2(3) = 4.24$, *ns*.

Participation in follow up

There was an average of 4.18 repeated measurements per participant (range 2–6). The mean duration of follow up from baseline to final assessment for each participant was 6.80 years (range 1.92–11.21 years). Information about follow-up participation is summarized in Table 2. The participation rates in Wave5 and Wave6 in the high-educated group were significantly higher than in the low-educated group (Wave5, $\chi^2(1) = 4.53$, $p = .033$; Wave6, $\chi^2(1) = 5.39, p = .020$). However, there were no significant differences between the level of education and the participation rate in other follow-up measures (Wave2, $\chi^2(1) = .50$, *ns*; Wave3, $\chi^2(1) = .04$, *ns*; Wave4, $\chi^2(1) = .46$, *ns*).

Educational levels and intellectual change

General linear mixed models were used to evaluate the effects of the level of education on the rate of intellectual change over time. We obtained fixed effects (i.e., average effects for the group of educational levels) and random

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Table 1 Descriptive statistics of baseline sample by level of education

Variable	High-educated ($n = 312$)	Low-educated ($n = 281$)	t/χ^2 *test*	
Age at baseline, mean (*SD*)	70.70 (3.96)	71.26 (3.82)	$t(591) = 1.75$	*ns*
Sex, women, *n* (%)	138 (44.23)	138 (49.11)	$\chi^2(1) = 1.41$	*ns*
Marital status, married, *n* (%)	253 (81.09)	216 (76.87)	$\chi^2(1) = 1.59$	*ns*
Occupation, having occupation, *n* (%)	86 (27.56)	79 (28.11)	$\chi^2(1) = 0.02$	*ns*
Smoking, smoker, *n* (%)	57 (18.27)	49 (17.44)	$\chi^2(1) = 0.07$	*ns*
Past and present illness, *n* (%)				
Stroke	17 (5.45)	15 (5.34)	$\chi^2(1) = 0.00$	*ns*
Hypertension	130 (41.67)	101 (35.94)	$\chi^2(1) = 2.04$	*ns*
Heart disease	66 (21.15)	47 (16.73)	$\chi^2(1) = 1.88$	*ns*
Diabetes	36 (11.54)	34 (12.10)	$\chi^2(1) = 0.04$	*ns*
Intelligence at baseline, mean (*SD*)				
Information	15.32 (5.66)	10.70 (4.21)	$t(591) = 11.17$	***
Similarities	13.36 (5.27)	8.73 (4.70)	$t(590) = 11.23$	***
Picture Completion	10.51 (3.41)	8.88 (3.73)	$t(591) = 5.57$	***
Digit Symbol	44.09 (10.16)	34.61 (8.32)	$t(589) = 12.32$	***

Note. The final sample consisted of 593 participants who had at least two visits. Data were missing as follows: Similarities, $n = 1$; Digit Symbol, $n = 2$.
***$p < .001$. *ns* = not significant.

Table 2 Follow-up participation information

	Participants, *n* (high-educated/low-educated)	Follow-up years from baseline, mean (*SD*)
Baseline	593 (312/281)	0.00
Wave2	566 (296/270)	2.05 (0.11)
Wave3	443 (232/211)	4.08 (0.18)
Wave4	363 (195/168)	6.20 (0.25)
Wave5	289 (165/124)	8.28 (0.28)
Wave6	223 (131/92)	10.27 (0.28)

Note. The final sample consisted of 593 participants who had at least two visits.

effects (i.e., individual deviation from the fixed effects) to model individual intellectual change. That is, intellectual change was assumed to follow the mean path of the group, except for person-specific random effects that cause the initial individual level of functioning to be higher or lower and the rate of change to be faster or slower. In addition, general linear mixed models can handle missing data more appropriately than traditional models (e.g., general linear models), so they can use all available data during follow up. Moreover, the correlation between the repeated measures is properly accounted for through the variance-covariance structure of the random effects. A general linear mixed model was chosen for the analysis of intellectual change in some recent studies (e.g., Alfaro-Acha, Snih, Raji, Kuo, Markides, & Ottenbacher, 2006; Crane, Gruhl, Erosheva, Gibbons, McCurry, Rhoads, Nguyen, Arani, Masaki, & White, 2010; Ganguli, Du, Dodge, Ratcliff, & Chang, 2006; Nishita, Tange, Tomida, Ando, & Shimokata, 2012a; Van Dijk et al., 2008; Wilson, Beckett, Barnes, Schneider, Bach, Evans, & Bennett, 2002). Further information on the application of general linear mixed models to repeated measures data is published elsewhere (e.g., Laird & Ware, 1982; Morrell et al., 2009; Verbeke & Molenberghs, 1997).

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Table 3 Educational levels and 10-year change in intelligence as estimated from linear mixed effects models

Intelligence scale	Model terms	Parameter estimate	*SE*	*p*-value
Information	Education	4.44	0.39	***
	Time	–0.09	0.03	**
	Education × time	–0.02	0.04	*ns*
Similarities	Education	4.36	0.38	***
	Time	–0.09	0.04	*
	Education × time	0.00	0.04	*ns*
Picture completion	Education	1.37	0.26	***
	Time	0.10	0.03	***
	Education × time	–0.04	0.03	*ns*
Digit symbol	Education	8.66	0.71	***
	Time	–0.27	0.06	***
	Education × time	–0.22	0.07	**

Note. Higher scores indicate better performance. Possible score for the Information is 0–29; Similarities 0–28; Picture Completion 0–21; Digit Symbol 0–93. Time = years since baseline; Education = 0 (low level education: reference) or 1 (high level education). In addition to the terms shown in the table, each model included terms to control for the fixed effects of age at baseline, sex, marital status, occupation, smoking, each past and present illness and practice effect were included as covariates, and the random effects of the intercept (baseline performance) and slope (change over time).

***$p < .001$.

**$p < .01$.

*$p < .05$. *ns* = not significant.

The model used in the current study included fixed terms for the Intercept (baseline performance for an individual with value zero on all predictors), Education (0 = low-educated group, 1 = high-educated group), Time (time in years since baseline), and an Education × Time interaction term. Age (at baseline), sex (0 = men, 1 = women), marital status (0 = unmarried, 1 = married), occupation (0 = inoccupation, 1 = having occupation), smoking (0 = nonsmoker, 1 = smoker) and each past and present illness (0 = none, 1 = having past or present illness) were included as covariates. In addition to controlling for practice effects, we added indicators of prior exposure to the tests. To do this, we followed the procedure described by Alley et al. (2007) to account for the effects of repeated test exposures, by assigning the respondents a 0 for baseline participation and then 1 at each subsequent administration of tests for intellectual assessment. Moreover, random effects of intercept (baseline performance) and slope (change over time) were calculated using an unstructured covariance matrix. The term of primary interest for this study was the Education × Time interaction, which reflects whether the high- or low-educational groups differ in the rate of change in intellectual performance over time. Table 3 shows the general linear mixed models estimates for each intelligence score as a function of educational levels over a 10-year period. Figure 1 gives visual representations of intellectual changes as a function of educational levels.

The term for Education was significant for all subtests (Information, $\beta = 4.44$, $p < .001$; Similarities, $\beta = 4.36$, $p < .001$; Picture Completion, $\beta = 1.37$, $p < .001$; Digit Symbol, $\beta = 8.66$, $p < .001$). As can be seen in Figure 1, participants in the high-educated group scored better compared with those in the low-educated group on all intellectual abilities. The term for Time was also significant for all subtests (Information, $\beta = -0.09$, $p = .003$; Similarities, $\beta = -0.09$, $p = .015$; Picture Completion, $\beta = 0.10$, $p < .001$; Digit Symbols, $\beta = -0.27$, $p < .001$). As can be seen in Figure 1, scores of Information, Similarities, and Digit Symbol subtests showed a trend for a decline over time as the study progressed. In contrast, there was a significant

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improvement in performance over time on the Picture Completion subtest.

Of particular importance to the current study was the test of the Education × Time interaction, which would show whether intellectual change over time varied with educational levels. The interaction was not statistically significant for the subtests of Information, Similarities, and Picture Completion. However, on the Digit Symbol subtest score, there was significant interaction ($\beta = -0.22$, $p = .002$), indicating that the rate of change of the Digit Symbol scores was significantly related to educational level. The direction of this association indicated that there was greater decline for individuals in the high-educated group (*slope* = −0.49, $p < .001$) than in the low-educated group (*slope* = −0.28, $p < .001$).

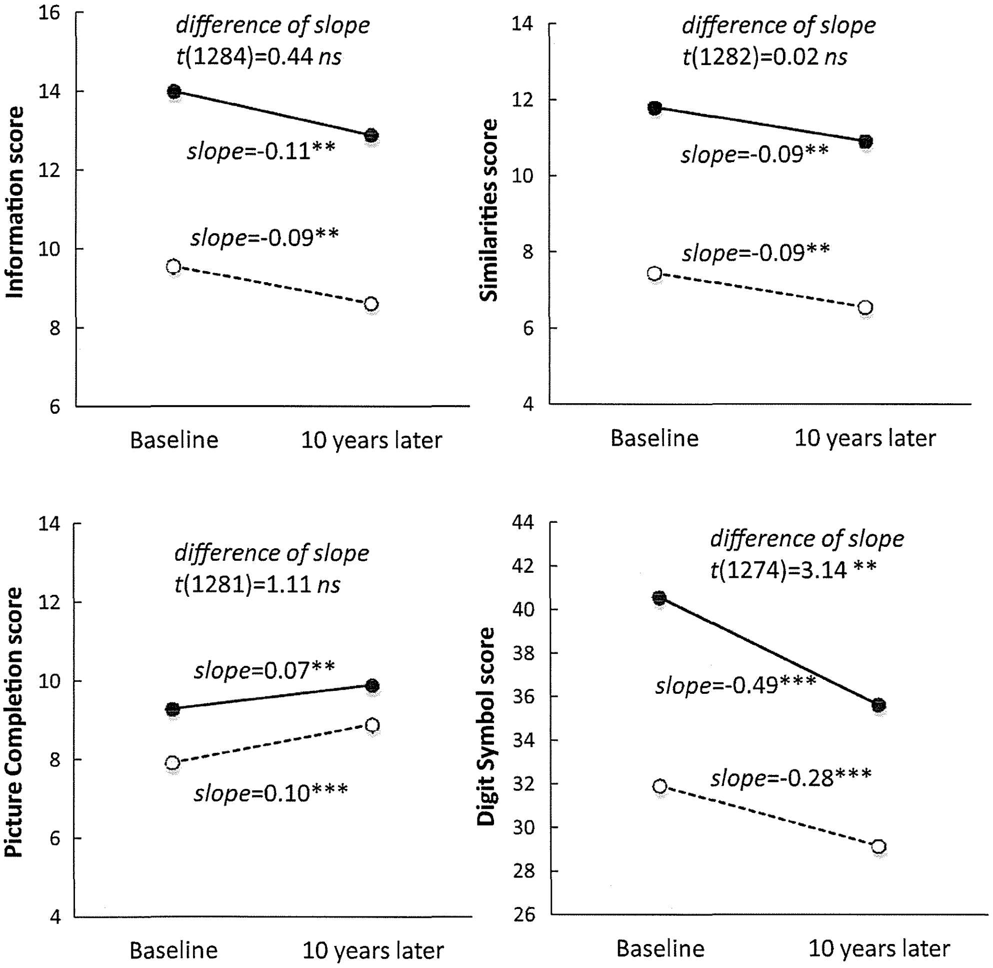

Figure 1 Model-predicted 10-year change in intelligence by education levels. (a) The solid lines are estimated for individuals with a high education level; the dashed lines are estimates for individuals with a low education level. (b) Higher scores indicate better performance. Possible score for the Information is 0–29; Similarities 0–28; Picture Completion 0–21; Digit Symbol 0–93. (c) All models controlled for age at baseline, sex, marital status, occupation, smoking, each past and present illness and practice effect. (d) ***$p < .001$, **$p < .01$, *$p < .05$, *ns* = not significant.

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Discussion

Summary and discussion of findings

The purpose of this study was to determine whether educational attainment was associated with the rate of intellectual change among a community sample of Japanese 65 years of age and over. The participants were followed for approximately 10 years and tested a maximum six times (at baseline and 2, 4, 6, 8, and 10 years after baseline).

As expected, level of education had a large cross-sectional effect on all intellectual performances. Some insist that education may improve brain function. That is, because enriched environments result in a greater number of synapses, individuals with higher education may enter old age with a greater synaptic density (Jacobs, Schall, & Scheibel, 1993). Additionally, education early in life is related to adult occupation or lifestyle, so higher education may result in greater intellectual activities in occupations or leisure pursuits throughout life (Kramer, Bherer, Colcombe, Dong, & Greenough, 2004). Thus, educational attainment early in life might have direct or indirect association with intellectual functions later in life.

In contrast, the relation between education and intellectual change differed by intellectual domain. However, on the whole, there was no statistically significant protective effect of higher education on changes in intellectual abilities over time, although education was associated with long-term individual differences in intelligence. Therefore, the *active* cognitive reserve hypothesis was *not* supported by the results of this study.

Information, similarities, and picture completion subtests. The Education × Time interaction was not statistically significant for the Information, Similarities, and Picture Completion subtests, suggesting that there were no effects of educational attainment on intellectual change over time. These findings are consistent with some recent studies that have observed no effects of education on intellectual change with aging (e.g., Seeman et al., 2005; Tucker-Drob et al., 2009; Van Dijk et al., 2008; Wilson et al., 2009; Zahodne et al., 2011). Thus, these results support a *passive* cognitive reserve hypothesis, in which individuals with higher educational attainment continue to perform at a high level compared with similarly aged individuals with less education, but change at a similar rate (Stern, 2002; Van Dijk et al., 2008).

Regardless of the educational level, the Information and Similarities subtest scores displayed a slightly declining trend with the progress of the study. These subtest scores consist of the verbal scales of the WAIS-R-SF, assessing the fund of factual knowledge and logical abstract reasoning that are reflective of crystallized intelligence (Cattell & Horn, 1978; Kaufman & Lichtenberger, 2006). Crystallized intelligence is strongly influenced by culture and experience, and is considered to remain relatively intact through adulthood. Longitudinal data from a previous study suggest that there is an increase in crystallized intelligence (measured using the "verbal meaning" test) until the age of 60 years, with little decline thereafter (Schaie & Willis, 2002). Our study sample with a baseline age of greater than 65 years was likely to show a similar intellectual decline over a 10-year period. However, the influence of education on this aging-associated change was not observed.

In contrast, the Picture Completion subtest is a performance scale in the WAIS-R-SF that measures fluid intelligence, which is more reflective of aging (Cattell & Horn, 1978). However, contrary to our expectations, trajectories of individual change showed improvements that were reflected in the Picture Completion test score, after adjusting for practice effects. The Picture Completion subtest consists of a basically simple task of finding missing parts of familiar pictures with a simple motor, or vocal output (pointing, or one-word responses). Therefore, it has been suggested that the Picture Completion subtest might be resilient to the impact of brain damage (Kaufman & Lichtenberger, 2006), and to hold up with age better than most other performance tests (Wechsler, 1944). In addition, habituation to the test situation or attrition might be important factors in the increased Picture Completion test score. It is suggested that the design of future studies should take these factors that may confound the results of longitudinal studies into consideration.

Digit symbol subtest. The digit symbol subtest measures processing speed, which is considered to be highly reflective of aging (Kaufman & Lichtenberger, 2006; Wechsler, 1944). Therefore, it is noteworthy that education in early life, which is a marker of cognitive reserve, contributed to the 10-year persistence of earlier differences in the Digit Symbol score, even after 65 years of age. Moreover, the Education × Time interaction was statistically significant for the Digit Symbol subtest. Surprisingly, individuals with higher levels of education actually experienced a greater decline in the Digit Symbol subset scores than those with less education, although they had a higher ability at every point in time.

There are two possible explanations for this finding. First, it is possible that highly educated adults might make the most of their high quality crystallized ability to supplement the declining fluid ability, or processing speed (Alley et al., 2007). As a result, when highly educated adults get to be aged 65 years or older, they eventually begin to lose their crystallized abilities (for example, measured by the Information and Similarities subtest) to draw on educational attainment, and as a result experience a faster rate of decline in processing speed than those with lower education. This phenomenon could be explained in terms of the *compensation* hypothesis, in which intact domains compensate for declines in other cognitive abilities until they, too, begin to deteriorate, leading the way for more rapid decline (Alley et al., 2007; Reuter-Lorenz & Mikels, 2006; Zahodne et al., 2011).

Second, it may be possible that the low-educated group showed a greater rate of decline in intellectual performance before age 65 years, prior to baseline. That is, for low-educated older adults, the rate of decline in processing speed could have been greater earlier in life, but slower after age 65 years. In contrast, it is possible that the high-educated group had very small or little decline in processing speed earlier in life (before age 65 years), but that their greatest rate of decline was observable after baseline. Thus, our findings may reflect a difference in the "onset of degeneration" (Alley et al., 2007) in processing speed between higher- and lower-educated older adults.

Some studies have reported that education was not related to the rate of change in processing speed (Christensen, Hofer, Mackinnon, Korten, Jorm, & Henderson, 2001; Tucker-Drob et al., 2009; Van Dijk et al., 2008). However, these previous studies had shorter durations (5–7-year periods) than our investigation (10-year period), or were restricted to the range of educational level in the samples (not enough low-education or high-education participants were included). Considering the better methods used in the present study, our results may reflect a true null finding of education on the change in processing speed; however, further studies on the matter are still needed. In order to confirm the abovementioned explanations, longer study observation periods (including age groups younger than 65 years) and the analyses of inflection points or nonlinear trajectories in processing speed will be required in future research.

Limitations and future directions

Our study has some important limitations. First, it should be noted that this study included participants who were, on the whole, at higher baseline levels of intellectual functioning. Therefore, our findings may only be relevant to healthier aging patterns among community-residing older adults. Second, the statistical models used in this study did not include several factors that may influence intelligence, such as the visual and auditory senses, or motor functions. Third, it remains possible that cognitive reserve mechanisms may act differently in intellectual domains outside of this study (e.g., episodic memory and working memory). Therefore, we must limit our conclusion to the levels and rates of change in intelligence, as measured

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using the JWAIS-R-SF (Information, Similarities, Picture Completion, and Digit Symbol). Fourth, the measure of educational attainment in this study assumes an equivalence of educational quality across persons and time. However, this is unlikely to be true. Other measures, such as literacy or acquired knowledge, may better address the quality of education as the marker of cognitive reserve. In addition, we assessed the level of educational attainment by using a categorical scale with only four options. However, it is likely that individuals with very low education (fewer than 6 years) may experience the greatest intellectual declines in late life (Lyketsos et al., 1999). Further studies are required to measure educational experience, defined as the number of years of schooling, in order to examine the possibility of steeper decline among older adults with very low educational attainment.

Additionally, differences in adult lifestyle may increase cognitive reserve by making the individual more resilient (Scarmeas, Zarahn, Anderson, Habeck, Hilton, Flynn, Marder, Bell, Sackeim, Van Heertum, Moeller, & Stern, 2003). So the relation between education in early life and intellectual change in late life may be mediated by participation in leisure activities or an occupation throughout adulthood. Moreover, there are several psychological factors that may modulate or mediate the relation between education and intelligence. For example, Nishita, Tange, Tomida, Ando, and Shimokata (2012b) suggest that the personality trait of openness to experience, highly correlated with education, influences intellectual change in later adulthood. Van Dijk et al. (2008) asserts that physical or mental health factors have important effects on intellectual change in late life, and that even higher educated individuals, who may initially have a benefit of greater cognitive reserve, are not protected against the effects of intellectual aging once they acquire certain physical or mental disease. An understanding of the precise nature and mechanisms of the relation between education in early life and intellectual change in late life invite further studies, including lifestyle and personal traits.

References

Alfaro-Acha, A., Snih, S. A., Raji, M. A., Kuo, Y. F., Markides, K. S., & Ottenbacher, K. J. (2006). Handgrip strength and cognitive decline in older Mexican Americans. *Journals of Gerontology. Series A: Biological Sciences and Medical Sciences*, **61**, 859–865.

Alley, D., Suthers, K., & Crimmins, E. (2007). Education and cognitive decline in older Americans: Results from the AHEAD sample. *Research on Aging*, **29**, 73–94.

Alvarado, B., Zunzunequi, M. V., Del Ser, T., & Beland, F. (2002). Cognitive decline is related to education and occupation in a Spanish elderly cohort. *Aging Clinical and Experimental Research*, **14**, 132–142.

Anstey, K. J., & Christensen, H. (2000). Education, activity, health, blood pressure, and apolipoprotein E as predictors of cognitive change in old age: A review. *Gerontology*, **46**, 163–177.

Anstey, K. J., Hofer, S. M., & Luszcz, M. A. (2003). A latent growth curve analysis of late-life sensory and cognitive function over 8 years: Evidence for specific and common factors underlying change. *Psychology and Aging*, **18**, 714–726.

Arbuckle, T. Y., Maag, U., Pushkar, D., & Chaikelson, J. S. (1998). Individual differences in trajectory of intellectual development over 45 years of adulthood. *Psychology and Aging*, **13**, 663–675.

Bielak, A. A. M., Anstey, K. J., Christensen, H., & Windsor, T. D. (2012). Activity engagement is related to level, but not change in cognitive ability across adulthood. *Psychology and Aging*, **27**, 219–228.

Cattell, R. B., & Horn, J. L. (1978). A check on the theory of fluid and crystallized intelligence with description of new subtest designs. *Journal of Educational Measurement*, **15**, 139–164.

Christensen, H., Hofer, S. M., Mackinnon, A. J., Korten, A. E., Jorm, A. F., & Henderson, A. S. (2001). Age is no kinder to the better educated: Absence of an association investigated using latent growth techniques in a community sample. *Psychological Medicine*, **31**, 15–28.

Crane, P. K., Gruhl, J. C., Erosheva, E. A., Gibbons, L. E., McCurry, S. M., Rhoads, K., Nguyen, V., Arani, K., Masaki, K., & White, L. (2010). Use of spoken and written Japanese did not protect Japanese-American men from cognitive decline in late life. *Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, **65**, 654–666.

Dufouil, C., Fuhrer, R., Dartigues, J. F., & Alpérovitch, A. (1996). Longitudinal analysis of

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the association between depressive symptomatology and cognitive deterioration. *American Journal of Epidemiology*, **144**, 634–641.

Evans, D. A., Beckett, L. A., Albert, M. S., Hebert, L. E., Scherr, P. A., Funkenstein, H. H., & Taylor, J. O. (1993). Level of education and change in cognitive function in a community population of older persons. *Annals of Epidemiology*, **3**, 71–77.

Farmer, M. E., Kittner, S. J., Rae, D. S., Bartko, J. J., & Regier, D. A. (1995). Education and change in cognitive function: The Epidemiologic Catchment Area Study. *Annals of Epidemiology*, **5**, 1–7.

Folstein, M. F., Folstein, S. E., McHugh, P. R., Practical, A., & Patients, O. F. (1975). "Mini-mental state": A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychosomatic Research*, **12**, 189–198.

Ganguli, M., Du, Y., Dodge, H. H., Ratcliff, G. G., & Chang, C. C. H. (2006). Depressive symptoms and cognitive decline in late life: A prospective epidemiological study. *Archives of General Psychiatry*, **63**, 153–160.

Jacobs, B. O. B., Schall, M., & Scheibel, A. B. (1993). A quantitative dendritic analysis of Wernicke's area in humans. Gender, hemispheric, and environmental factors. *Journal of Comparative Neurology*, **327**, 97–111.

Kaufman, A. S., & Lichtenberger, E. O. (2006). *Assessing adolescent and adult intelligence*. 3rd ed. Hoboken, NJ: John Wiley & Sons.

Kobayashi, S., Fujita, K., Maekawa, H., & Dairoku, H. (1993). *Japanese Wechsler Adult Intelligence Scale-Revised Short Forms*. Tokyo: Nihon Bunka KagakuSha. (In Japanese.)

Koster, A., Penninx, B. W. J. H., Bosma, H., Kempen, G. I. J. M., Newman, A. B., Rubin, S. M., Satterfield, S., Atkinson, H. H., Ayonayon, H. N., Rosano, C., Yaffe, K., Harris, T. B., Rooks, R. N., Van Eijk, J. T., & Kritchevsky, S. B. (2005). Socioeconomic differences in cognitive decline and the role of biomedical factors. *Annals of Epidemiology*, **15**, 564–571.

Kramer, A. F., Bherer, L., Colcombe, S. J., Dong, W., & Greenough, W. T. (2004). Environmental influences on cognitive and brain plasticity during aging. *Journals of Gerontology. Series A: Biological Sciences and Medical Sciences*, **59**, 940–957.

Laird, N. M., & Ware, J. H. (1982). Random-effects models for longitudinal data. *Biometrics*, **38**, 963–974.

Lee, S., Kawachi, I., Berkman, L. F., & Grodstein, F. (2003). Education, other socioeconomic indicators, and cognitive function. *American Journal of Epidemiology*, **157**, 712–720.

Lyketsos, C. G., Chen, L. S., & Anthony, J. C. (1999). Cognitive decline in adulthood: An 11.5-year follow-up of the Baltimore Epidemiologic Catchment Area Study. *American Journal of Psychiatry*, **156**, 58–65.

Morrell, C. H., Brant, L. J., & Ferrucci, L. (2009). Model choice can obscure results in longitudinal studies. *Journals of Gerontology. Series A: Biological Sciences and Medical Sciences*, **64**, 215–222.

Nishita, Y., Tange, C., Tomida, M., Ando, F., & Shimokata, H. (2012a). Do depressive symptoms cause intellectual decline among elderly?: A 8-year longitudinal study. *Japanese Journal of Gerontology*, **34**, 370–381. (In Japanese with English abstract.)

Nishita, Y., Tange, C., Tomida, M., Ando, F., & Shimokata, H. (2012b). Openness and intellectual change among Japanese middle-aged and elderly adults: A six-year longitudinal study. *Japanese Journal of Developmental Psychology*, **23**, 276–286. (In Japanese with English abstract.)

Reuter-Lorenz, P. A., & Mikels, J. A. (2006). The aging mind and brain: Implications of enduring plasticity for behavioral and cultural change. In P. B. Baltes, P. A. Reuter-Lorenz, & F. Roesler (Eds.), *Lifespan development and the brain: The perspective of biocultural co-constructivism*. Cambridge, UK: Cambridge University Press, pp. 255–276.

Salthouse, T. A. (2003). Interrelations of aging, knowledge, and cognitive performance. In U. M. Staudinger & U. E. R. Lindenberger (Eds.), *Understanding human development: Dialogues with lifespan psychology*. Norwell, MA: Kluwer Academic Publishers, pp. 265–287.

Salthouse, T. A. (2006). Mental exercise and mental aging evaluating the validity of the "Use It or Lose It" hypothesis. *Perspectives on Psychological Science*, **1**, 68–87.

Scarmeas, N., & Stern, Y. (2004). Cognitive reserve: Implications for diagnosis and prevention of Alzheimer's disease. *Current Neurology and Neuroscience Reports*, **4**, 374–380.

Scarmeas, N., Zarahn, E., Anderson, K. E., Habeck, C. G., Hilton, J., Flynn, J., Marder, K. S., Bell, K. L., Sackeim, H. A., Van Heertum, R. L., Moeller, J. R., & Stern, Y. (2003). Association of life activities with cerebral blood flow in Alzheimer disease: Implications for the cognitive reserve hypothesis. *Archives of Neurology*, **60**, 359–365.

Schaie, K. W. (2005). *Developmental influences on adult intelligence: The Seattle Longitudinal Study*. New York: Oxford University Press.

Schaie, K. W., & Willis, S. L. (2002). *Adult development and aging*. 5th ed. Upper Saddle River, NJ: Prentice Hall.

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