

原著

老健における脳活性化リハビリテーションの有効性に関する RCT 研究：集団リハで認知症重症度改善と主観的 QOL 保持

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要 旨

【目的】 老健における認知症リハのあり方を検討する。

【方法】 老健入所者 23 名（内認知症の疑い 11 名）を対象に無作為化比較試験を実施した。介入群には週 1 回、3 ヶ月間、脳活性化リハの 5 原則に基づく集団リハを実施した。評価指標には、CDR-SB、MOSES、QOL-AD、MMSE、HDS-R、TMT-A を用いた。

【結果】 介入群と対照群間で CDR-SB ($F=5.972$, $p=0.027$) と QOL-AD ($F=4.911$, $p=0.043$) に有意な交互作用を認め、介入群では認知症の全般的重症

度が有意に改善し ($p=0.039$)、主観的 QOL の維持・改善傾向を認めた。

【結論】 老健のリハは個別リハが基準とされているが、脳活性化リハの 5 原則に基づく集団リハでも、認知症重症度が低減し、主観的 QOL が維持・改善する可能性が示された。

Key words: 認知症, 老健, リハビリテーション, quality of life, 無作為化比較試験

1. はじめに

介護老人保健施設（老健）は在宅復帰のための中間施設として位置づけられ、在宅復帰へむけた積極的なリハビリテーション（リハ）が実施されてきた。近年、認知症高齢者数の増加に伴い、老健利用者のうち認知症者や身体障害に認知症を合併する者が増加している。そのため平成 18 年より「認知症短期集中リハビリテーション実施加算（認知症リハ加算）」が算定可能となった。この加算は「軽度認知症の入所者に対して、在宅復帰に向けた生活機能の回復を目的に実施される短期集中的な個別リハ」と規定され、入所後 3 ヶ月以内の対象者に対して、1 回 20 分以上の個別リハを実施した場合に、週 3 回まで算定できる。具体的なリハプログラムとして、作業療法、学習、運動療法、回想法、現実見当識練習、記憶トレーニング、芸術療法等が、個人の残存

Effect of the Brain-activation rehabilitation in a Geriatric Health Service Facility, Roken: Group rehabilitation improved severity of dementia and maintained subjective quality of life in the RCT study

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能力と嗜好に合わせて提供される。その効果として、認知機能、認知症の行動・心理症状 (behavioral and psychological symptoms of dementia; BPSD)、ADL、意欲、社会活動等の維持・改善の可能性が示されている (Toba et al., 2013; 東, 2013)。平成 21 年からは算定単位数の増額、対象範囲が重度認知症へ、算定可能施設が通所リハ、介護療養型医療施設へ拡大され、算定数が大きく増加している。一方で、算定要件が個別リハとなっているが、アルツハイマー型認知症では、小グループで、仲間同士のコミュニケーションや助け合いを引き出し、楽しい雰囲気で行うことが有効とされ (山口, 2010)、実際、対象者に合わせて個別と集団リハを使い分けているとの調査結果も示されており (田中ら, 2014)、個別・集団リハ双方で算定可能となることが望まれている。また算定期間が入所後 3 ヶ月以内と限定されているため、算定期間終了後、リハの回数が減ると、介入前の状態に戻ってしまう (内野ら, 2012)。

上記のように認知症の非薬物療法の重要性の高まりとともに、実証研究に基づくエビデンスの検証の必要性が指摘されている (「認知症疾患治療ガイドライン」作成合同委員会, 2010)。しかし、非薬物療法は介入技法や内容 (例えば RO の中に回想の要素が含まれるなど)、介入時間・頻度・期間、場所、介入者の力量、対照群の介入内容などの条件を客観的に統制することが難しいため、薬物療法と同様の方法で、エビデンスを構築することは困難との指摘がある。我々は、個々の技法のエビデンスを示すよりも、介入の原則を設定し、その原則の有効性を示す研究を重ねることで、エビデンスを示しやすくなると考え、脳活性化リハの 5 原則を提唱した (山口, 2010)。脳活性化リハの 5 原則は ① 快、② 褒め合う、③ 双方向コミュニケーション、④ 役割、⑤ 失敗を防ぐ支援であり、認知機能を改善させることだけが目的ではなく、認知症があっても生活障害を軽減し、残存能力を最大限発揮し、豊かな生活を送ること (QOL の向上) を目的としている。この 5 原則を守るため、対象者の好きな事、得意なことを取り入れ、残存能力が発揮しやすいよう、様々な技法を織り交ぜて、リハを実施する。我々は、脳

活性化リハの 5 原則に基づいた認知症リハ加算の個別プログラムが、認知機能、意欲の向上、BPSD や抑うつ等の低減に有効であることを既に示した (関根ら, 2013)。今回は、老健入所者に対する集団リハの効果 randomized controlled trial (RCT) で検証した。

2. 方法と対象

2.1 対象

介護老人保健施設 A の一般棟 (定員 40 名) の入所者のうち、ケアスタッフと作業療法士が協議の上、① 著しい麻痺・失語症を有さない、② その場のコミュニケーションが可能、③ 集団活動や簡単な作業等に参加可能、④ 改訂長谷川式簡易知能評価スケール (Hasegawa's dementia scale for revised; HDS-R) (加藤ら, 1991) が 8 点以上、の 4 条件で 26 名を選出した。そのうち介入が始まるまでに 3 名が退所し、残った 23 名 (男性 5 名、女性 18 名、平均年齢 84.0 ± 7.7 歳) を対象とした。対象者の clinical dementia rating (CDR) (Hughes et al., 1982) の内訳は CDR 0 が 5 名 (21.7%) (平均 HDS-R 21.3 ± 4.6 点)、CDR 0.5 が 7 名 (30.4%) (平均 HDS-R 17.7 ± 4.5 点)、CDR 1 が 6 名 (26.1%) (平均 HDS-R 18.0 ± 7.0 点)、CDR 2 & 3 が 5 名 (21.7%) (平均 HDS-R 12.8 ± 3.0 点) であった。対象者のうち認知症の診断があったのは 2 名のみであった。また、認知症リハ加算の算定者はいなかった。

2.2 研究デザイン・割り付け

非盲検化・並行群間 RCT とし、初期評価の HDS-R 得点に基づき、18 点以上・未満の層別ブロック無作為割り付けにて介入群 12 名と対照群 11 名に研究者が割り付けた (Fig. 1)。

2.3 介入

週 1 回、1 回 60 分のセッションを 3 ヶ月間 (全 12 回) 実施した。セッションは対象者 12 名とスタッフ 2-3 名のグループで実施した。介入スタッフのリーダーは脳活性化リハに精通し、複数の施設等で実践経験を積んだ研究者 (理学療法士) が毎回担当した。施設の全ケアスタッフ (看護師・介護士) を

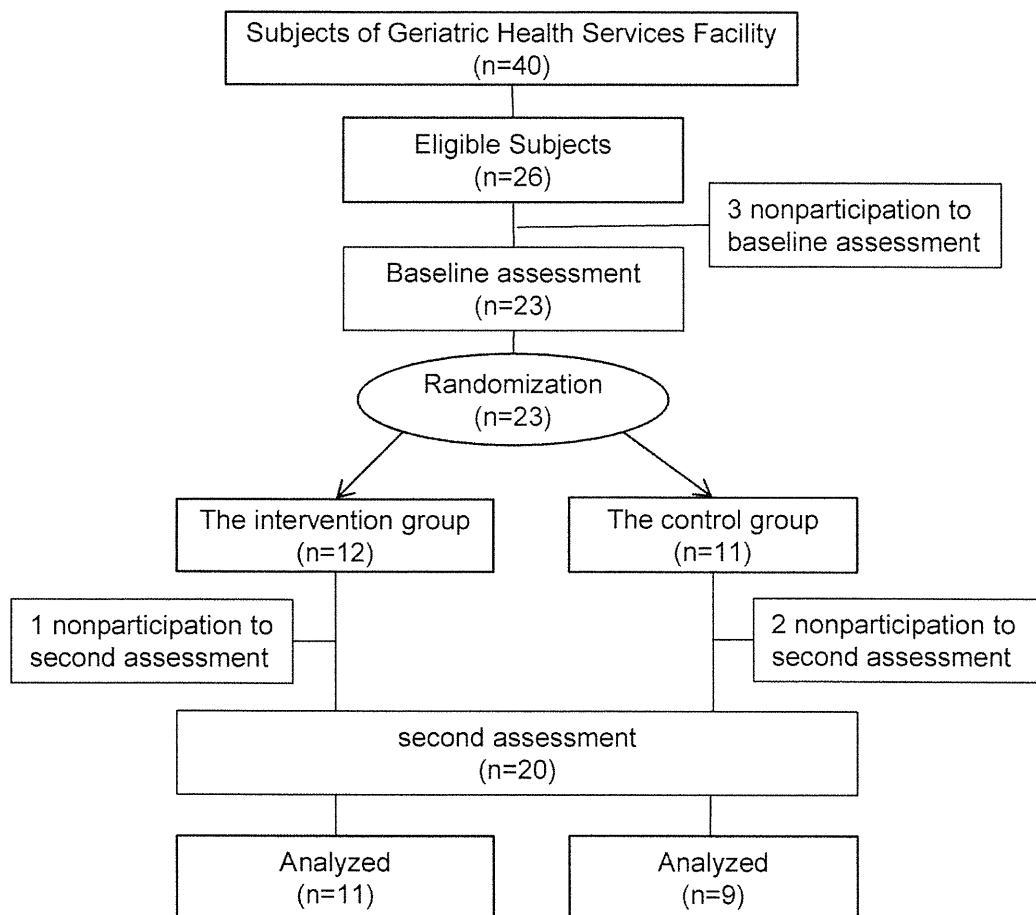


Fig. 1. subject flow diagram

対象に 60 分×2 回の脳活性化リハや回想法，認知症高齢者との接し方，コ・リーダーの役割等に関する研修を実施し，受講したケアスタッフが勤務の都合に合わせて交代でコ・リーダーとして参加した。

セッション内容は，最初の 10 分を導入として現実見当識練習を，次の 40 分を主活動として作業回想法を行い，最後の 10 分を振り返りとした。セッションは脳活性化リハの 5 原則に基づいて実施され，セッションのテーマや実施方法の選定に関しては，事前に各対象者に約 1 時間の生活歴等の聞き取りと認知・身体機能の評価を実施し，多くの対象者の生活歴に共通し，関心のありそうな事柄や，特技に関係するテーマを選定した（脳活性化リハの原則 1：快刺激）（Appendix 1 参照）。また実施にあたっては，現在の対象者の能力で回答したり，実施できないような内容とし，失敗しないようさりげなく支援し

た（原則 5：失敗を防ぐ支援）。主活動の作業回想法では対象者が体験してきた家事（洗濯板を用いた洗濯，お釜で米を炊く，農作業），手仕事（雑巾縫い，縄ない），遊び等をテーマに，馴染みのある懐かしい道具を用い，スタッフに対して作業の仕方を指導するように進めた（原則 4：役割）。スタッフはセッションの中で対象者を褒めるよう心がけ（原則 2：褒め合う），また対象者同士の会話が弾むよう，対象者の発言を他の対象者につないだ（原則 3：双方向コミュニケーション）。本セッションは，現実見当識練習や回想を通じた認知機能の活性化と，ぬか漬け作りや，うどんを打ち食べる等の作業を通じた，味覚・嗅覚・触覚など五感の刺激，身体活動を含む複合的なプログラムとなっている（Yamagami et al., 2012）。対象者のモチベーションを高めるため，和紙で作成した招待状とスタンプカードを配布し，毎

回の振り返りの際、一人ずつ感想を述べてもらい、参加に対する感謝の拍手とともにスタンプを押した。介入の質を保つため、介入後に、スタッフは Bender 観察記録表（野村，1998）を用い、対象者一人一人の介入中の様子を点数化し、次回以降の参加態度が向上するよう座席やコ・リーダーの配置や対応を検討した（Appendix 2 参照）。

介入群、対照群とも通常のケアやリハは継続された。

2.4 評価項目

primary outcome は生活障害の低減と QOL の向上とし、生活障害を sum of boxes in CDR (CDR-SB) (Berg et al., 1988) と multidimensional observation scale for elderly subjects (MOSES) (Helmes et al., 1987) で、QOL を quality of life-Alzheimer's disease (QOL-AD) 日本語版 (Logsdon et al., 1999; Matsui et al., 2006) を用いて評価した。CDR は世界的に用いられている、介護者による観察式の認知症の重症度尺度であり、CDR-SB は「記憶」、「見当識」、「判断力と問題解決」、「地域社会活動」、「家庭生活及び趣味・関心」、「介護状況」の 6 項目の合計値で 0-18 点の範囲を示し、値が小さいほど全般的な生活障害が軽いことを示す。MOSES は介護者による多元観察尺度であり、「セルフケア」、「失見当」、「抑うつ」、「イライラ・怒り」、「引きこもり」の 5 つの下位項目から構成され、各項目 8 設問、計 40 設問で構成される。各設問を「正常」1 点から「重度障害」4 点の 4 段階で評価し、40-160 点の範囲を示す。値が小さいほど、生活障害が軽いことを示し、比較的細かい変化を評価できる。QOL-AD は 13 項目から構成され、各項目を「よくない」1 点から「非常に良い」4 点の 4 段階で評価し、13-52 点の範囲を示し、値が高いほど QOL が高い。介護者へのアンケートによる客観的 QOL と本人への面接による主観的 QOL 双方が評価できる。なお認知症高齢者本人に対する主観的 QOL の聞き取りは mini-mental state examination (MMSE) (Folstein et al., 1975) が 10 点以上であれば、回答に支障ないとされており、本研究対象者は全員 MMSE 10 点以上であった。また本尺度は元々アルツハイマー型認知症患者の QOL 評価尺度

として開発されたが、アルツハイマー型認知症以外の認知症患者、認知症の診断がついていない認知障害者 (Xie et al., 2012)、健常から軽度認知障害 (Teng et al., 2012) 等を対象とした研究でも用いられている。

secondary outcome は認知機能の維持・向上とし、HDS-R, MMSE, trail making test A (TMT-A) (Reitan, 1958) を実施した。TMT-A は 1 から 25 ままでランダムに並べられた数字をなるべく早く線で結ぶよう指示し、費やした時間 (秒) を測定した。

本研究で用いた評価尺度は信頼性、妥当性が確認されている。生活障害の評価と客観的 QOL はケアスタッフが、主観的 QOL と認知機能評価は研究者が実施し、介入前後で同一の評価者が実施した。その他の基本情報として認知症以外の疾患の有無、移動能力、抗認知症・抗精神病薬の服薬状況、介護度等を情報収集した。

2.5 分析手法

統計解析は SPSS Statistic version 20 (IBM) を用いた。介入群と対照群のベースライン時の基本情報の差に関しては Mann-Whitney U test もしくは Fisher's exact test を用いて分析した。各群の介入前後の評価尺度の変化の分析は、年齢と性別を共変量とした反復測定の変異分析 (Repeated measures analysis of covariance; ANCOVA) を行い、有意差を認めた項目に関して Post hoc 検定として Bonferroni 法を実施した。また CDR の下位項目に関して、介入前後の値の変化で改善、維持、悪化の 3 群に分け、介入群と対照群でどの群が多かったか Fisher's exact test を用いて分析した。

2.6 倫理的配慮

本研究は高崎健康福祉大学研究倫理審査委員会の承認を得て実施された (第 2201 号)。施設責任者に研究の説明を行い、同意を得た上で、職員に対して説明会を開催し、同意を得た。また対象者とその家族に対して書面にて説明し、同意を得た。また介入期間終了後、対照群に対しても同様の介入を提供した。

3. 結果

3.1 ベースライン時の状態と介入参加率

ベースライン時の基本情報に関して、介入群と対照群で有意差を認める項目はなかった (Table 1)。介入期間中に介入群 1 名、対照群 2 名が退所となり、最終評価が可能であった、介入群 11 名、対照群 9 名を分析対象とした。介入への参加率は 97.7% と高く、拒否や副作用等による脱落もなかった。

3.2 各評価尺度の変化 (Table 2)

反復測定の共分散分析の結果、生活障害に関しては CDR-SB で有意な交互作用を認め ($F(1, 19) = 5.972, p = 0.027$)、Post hoc 検定の結果、介入群で初

期 7.4 ± 4.2 点から最終 6.3 ± 4.6 点と有意に改善した ($p = 0.039$) のに対して、対照群では有意な変化を認めなかった (介入前・後とも群間に有意差無し)。また CDR の下位項目では「介護状況」の項目が介入群 11 名中 6 名で改善したのに対して、対照群 9 名中改善者無しと、介入群で改善者が有意に多かった ($p = 0.007$)。MOSES の合計点は有意な交互作用を認めなかった ($F(1, 19) = 2.403, p = 0.141$)。しかし、下位項目の「抑うつ」で交互作用が有意な傾向を認め ($F(1, 19) = 4.337, p = 0.054$)、Post hoc 検定の結果、対照群が初期 9.1 ± 1.5 点から最終 10.6 ± 3.1 点と悪化傾向を示した ($p = 0.050$) のに対して介入群では有意な変化を認めなかった。

QOL は QOL-AD (主観) に有意な交互作用を認

Table 1. Demographics of the study participants (n=23)

Group	Intervention (n=12)	Control (n=11)	p
Age, years	84.3±5.8	83.7±9.6	0.875
Gender			
Male	2 (16.7)	3 (27.3)	0.455
Female	10 (83.3)	8 (72.7)	
CDR			
0 (normal)	2 (16.7)	3 (27.3)	0.675
0.5 (questionable)	4 (33.3)	3 (27.3)	
1 (mild)	2 (16.7)	4 (36.4)	
2 (moderate)	2 (16.7)	0 (0.00)	
3 (severe)	2 (16.7)	1 (9.1)	
Disease			
Cerebrovascular disease	5 (41.7)	5 (45.5)	1.000
Orthopedic disease	4 (33.3)	3 (27.3)	
Other	3 (25.0)	3 (27.3)	
Mobility			
Walking aids	1 (8.3)	2 (18.2)	0.466
Wheelchair	11 (91.7)	9 (81.8)	
Donepezil prescribed	0 (0.00)	0 (0.00)	—
Anti-psychotics prescribed	2 (16.7)	3 (27.3)	0.455
Nursing care level			
1	2 (16.7)	1 (9.1)	0.870
2	4 (33.3)	2 (18.2)	
3	3 (25.0)	2 (18.2)	
4	3 (25.0)	4 (36.4)	
5	0 (0.00)	1 (9.1)	

Values are means±SD or numbers with percentages in parentheses. Mann-Whitney U test or Fisher's exact test were used. CDR : clinical dementia rating

Table 2. Change in outcome measures for intervention (n=11) and control groups (n=9)

Outcome variable	Time period		interaction		Post Hoc
	Before test Mean (SD)	After test Mean (SD)	F	p	p
CDR-SB					
Intervention	7.36 (4.2)	6.3 (4.6)	5.972	0.027*	0.039*
Control	4.7 (4.0)	5.3 (4.7)			0.198
MOSES total					
Intervention	71.9 (15.4)	72.2 (18.1)	2.403	0.141	0.826
Control	65.6 (17.4)	69.0 (17.6)			0.071
MOSES self-care					
Intervention	19.6 (5.1)	19.7 (5.9)	0.605	0.448	0.957
Control	20.2 (5.6)	20.9 (5.8)			0.322
MOSES disorientation					
Intervention	14.6 (5.2)	15.8 (6.8)	0.557	0.466	0.232
Control	13.4 (7.3)	13.3 (7.4)			0.931
MOSES depression					
Intervention	10.0 (3.5)	9.6 (2.7)	4.337	0.054	0.416
Control	9.1 (1.5)	10.6 (3.1)			0.050
MOSES irritability					
Intervention	9.6 (2.4)	9.7 (2.0)	1.436	0.248	0.617
Control	8.6 (1.3)	9.2 (1.7)			0.051
MOSES withdrawal					
Intervention	18.2 (7.5)	17.3 (7.3)	3.111	0.097	0.169
Control	14.2 (7.0)	15.0 (7.3)			0.274
QOL-AD (subjective)					
Intervention	32.4 (8.3)	34.1 (8.3)	4.911	0.043*	0.272
Control	32.0 (6.9)	29.4 (5.4)			0.060
QOL-AD (objective)					
Intervention	31.3 (4.3)	26.6 (6.2)	2.310	0.148	0.015
Control	31.2 (4.4)	30.6 (2.9)			0.721
HDS-R					
Intervention	17.3 (6.4)	16.3 (7.7)	0.572	0.461	0.380
Control	15.9 (5.5)	16.8 (7.7)			0.838
MMSE					
Intervention	19.4 (5.4)	19.1 (6.2)	0.004	0.949	0.762
Control	18.4 (5.9)	18.3 (6.9)			0.707
TMT-A (second)					
Intervention	246 (138)	180 (120)	4.259	0.063	0.072
Control	198 (108)	228 (138)			0.221

Repeated measures ANCOVA with the covariates of age and sex was used, and post hoc analysis with Bonferroni correction was conducted. CDR-SB : the sum of boxes in clinical dementia rating, MOSES : multidimensional observation scale for elderly subjects, QOL-AD : quality of life- Alzheimer's disease, HDS-R : Hasegawa's dementia scale for revised, MMSE : mini-mental state examination, TMT-A : trail making test A. * $p < 0.05$.

め ($F(1, 19) = 4.911, p = 0.043$), Post hoc 検定の結果、対照群で初期 32.0 ± 6.9 点から最終 29.4 ± 5.4 点と低下傾向を示した ($p = 0.060$) に対して、介入群では

初期 32.4 ± 8.3 点から最終 34.1 ± 8.3 点と有意ではないが上昇した ($p = 0.272$)。QOL-AD (客観) は有意な交互作用を認めなかった ($F(1, 19) = 2.310, p =$

0.148).

認知機能テストではTMT-Aのみ交互作用が有意な傾向を認め ($F(1, 19)=4.259, p=0.063$), Post hoc 検定の結果, 介入群で初期 246 ± 138 秒が, 最終 180 ± 120 秒と早くなる傾向を示した ($p=0.072$) のに対して, 対照群では有意な変化を認めなかった. HDS-R ($F(1, 19)=0.572, p=0.461$), MMSE ($F(1, 19)=0.004, p=0.949$) は有意な交互作用を認めなかった.

4. 考 察

老健入所者を対象に脳活性化リハの5原則に基づいた集団リハを実施し, その効果をRCTにて検証した. 老健のリハ対象者の8割以上が認知症を有するとされ, そのうち4割は診断名がついていなかったとの報告がある(田中ら, 2014). 本研究対象者のうち診断がなかった者の中にもCDRと認知機能テストの結果から軽度認知障害や軽度認知症者が多く含まれていたと考えた. 本介入の結果, 認知症の全般的な重症度のみ有意な交互作用を認め, 介入群で有意に改善した. しかし主観的QOLに有意な交互作用を認め, 介入群で維持, 対照群で低下傾向を, 注意力は有意な交互作用の傾向を認め, 介入群で改善傾向を認めたが, 有意な改善を示すには至らなかった.

認知症の全般的な重症度の改善に関しては, 我々はグループホームの利用者に対して本研究と同様の介入を行い, その効果を報告している(Yamagami et al., 2012). QOLの改善に関して, Cooperら(2012)は, meta-analysisを行い, 施設入所の認知症高齢者のQOLの改善には集団で実施する認知刺激療法が有効であると報告している. またSpectorら(2003)は, MMSEが平均14.4点の認知症高齢者201名を対象に, 現実見当識練習, ゲーム, 回想, 感覚刺激等を組み合わせた認知刺激療法を集団にて実施し, その効果をRCTにて検証した結果, 主観的QOLと認知機能の改善を報告している. 以上より, 今回の我々の介入は認知症高齢者のQOL改善に妥当な方法であったと考えられた. しかし, 本研究で主観的

QOLに有意な交互作用を認め, 介入群で維持, 対照群で低下傾向を示したが有意差を示すに至らなかった. その原因として対象者数の不足が考えられた. 本研究の必要症例数は, 効果量0.25, 有意水準0.05, 検出力0.8とした場合, 66例であり, 対象者数は不十分である. しかし本邦では多施設共同研究の実施環境が十分に整っておらず, 本研究は1施設での研究に留まった.

Lawrenceら(2012)は, 介護施設に入所する認知症高齢者に対してQOLの改善に有効な心理社会的介入方法を明らかにする目的で, 質的研究のmeta-synthesisを実施し, 効果的な心理社会的介入の要素として, 介入により認知症高齢者が①「他者との交流」, ②「意味のある寄与」, ③「回想」することあげている. また心理社会的介入を効果的に実施する条件として, ④「認知症高齢者を励まし自信を持ってもらうこと」, ⑤「対象者の好みと能力にあった内容を臨機応変に提供すること」をあげている. ①「他者との交流」は脳活性化リハの「原則3: 双方向コミュニケーション」, ②「意味のある寄与」は「原則4: 役割」, ④「励まし自信を持ってもらう」は「原則2: 褒め合う」, ⑤「好みと能力にあった内容を臨機応変に提供」は「原則1: 快」, 「原則5: 失敗を防ぐ支援」に該当する. 以上より脳活性化リハの5原則は, Lawrenceらの示した効果的な心理社会的介入の要素や条件を満たしており, 認知症のリハの原則として妥当であると考えた.

Haslamら(2010)は, 施設入所高齢者を対象にRCTにて集団回想法群, 個別回想法群, 集団対照群(ゲーム)の3群の効果を比較した結果, それぞれの群に特異的な効果が得られたことから, 介入内容や集団・個別介入を使い分ける必要性を指摘している. また, 特に集団回想法群で記憶が, 集団対照群でwell-beingの改善を認めたことから, 健康やQOLの維持・改善には集団での社会交流を含むプログラムが有効である可能性を示している. 老健における認知症リハ加算は, 算定期間が入所後3ヵ月以内と限定されているため, 算定期間終了後, リハの回数が減ると, 介入前の状態に戻ってしまうとの課題が示されている. 内野ら(2012)は算定期間終

了後、算定期間中に効果のあった方法に類似するクラブ活動等への参加を促すことで、介入効果を維持できる可能性を指摘している。そのため、個別の認知症リハ加算終了後は、軽度認知障害から軽度認知症者であれば脳活性化リハの 5 原則に基づく集団リハを行うことで、認知症リハ加算算定期間終了後も、機能の維持・向上につながると期待される。

本研究の限界として、すでに述べたように対象者数が不足している。今後、対象者数・施設を増やして効果を検証したい。またさらにエビデンスレベルを高めるためには、介入実施と評価者を分け、盲検化して効果を検証する必要もある。

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Effect of the Brain-activation rehabilitation in a Geriatric Health Service Facility, *Roken* : Group rehabilitation improved severity of dementia and maintained subjective quality of life in the RCT study

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[Purpose] We aimed to prove the effective way of rehabilitation in a Geriatric Health Service Facility, *Roken*.

[Subjects and Methods] We carried out a randomized controlled trial that was not blinded. Twenty three elderly participants (mean age : 84.0 years) in a Geriatric Health Services Facility were selected according to inclusion criteria. In intervention group ($n=12$), group sessions were for 1 h, once a week, for 12 weeks, and based on the 5 principles of Brain-activating rehabilitation : pleasant atmosphere, praising, communication, social role, and supportive care. The control group ($n=11$) had no additional treatment. Outcome measures consisted of three observation scales (CDR-SB, MOSES and QOL-AD), and three cognitive test (HDS-R, MMSE and TMT-A).

[Results] Repeated measure ANCOVA with covariates of age and sex showed a significant interaction for total score of CDR-SB ($F=5.972, p=0.027$) and QOL-AD ($F=4.911, p=0.043$). In the intervention group, overall severity was significantly improved ($p=0.039$), and subjective QOL was maintained. In the control group, subjective QOL tended to worsen. Other outcome measures didn't show a significant interaction.

[Conclusion] Rehabilitation in a group, based on the 5 principles of Brain-activating rehabilitation, was effective to improve overall dementia severity and maintain QOL in the Geriatric Health Services Facility.

Key words : dementia, Geriatric Health Service Facility, rehabilitation, quality of life, randomized controlled trial

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Appendix 1

脳活性化リハの各セッションのテーマと使用道具と具体的な内容

回	テーマ	使用道具	具体的な内容
1回	自己紹介	日本地図	自己紹介とふるさと自慢
2回	昔の遊び	お手玉, おはじき, 剣玉, 竹馬等	得意だった遊びの実演
3回	学校の思い出	教科書, 教育勅語	得意科目の紹介, 音読・計算・唱歌
4回	洗濯	鹽, 洗濯板, 洗濯石けん	洗濯の実演と指導
5回	養蚕	蚕, 桑, 機織り機	蚕の育て方の指導
6回	手作りおやつ	麦こうせん, 蒸かしいも, 蒸かし器	おやつのおいしさの紹介, 試食
7回	漬け物作り	米ぬか, 野菜, 瓶	ぬか漬け作りの実演と指導, 試食
8回	冬の暮らし	あんか, 火鉢, 槽こたつ	各道具の使用法の紹介
9回	炊飯	釜, 火吹き竹, 鑿筋削り	お米の研ぎ方, 炊き方等の実演と指導
10回	針仕事	針, 糸, 裁縫箱	雑巾縫いの実演と指導
11回	台所仕事	すり鉢, すりこぎ, 割烹着	ごま和え作りの実演と指導, 試食
12回	うどん打ち	こね鉢, 麺棒, のし台	うどん打ちの実演と指導, 試食

すべての回で実演・紹介を通じて回想を促すと共に、スタッフに実施方法を指導してもらおうよう進めた。

Appendix 2

Bender 観察記録表

参加者氏名： _____

セッション	1	2	3	4	5	6	7	8	9	10	11	12
日付												
1. グループへの参加意欲												
3: 自主的に参加	+	+	+	+	+	+	+	+	+	+	+	+
2: 確認が必要	+	+	+	+	+	+	+	+	+	+	+	+
1: 説得が必要	+	+	+	+	+	+	+	+	+	+	+	+
0: 参加拒否	+	+	+	+	+	+	+	+	+	+	+	+
2. 記憶												
3: 的確な回想	+	+	+	+	+	+	+	+	+	+	+	+
2: 刺激なしでも相当な回想	+	+	+	+	+	+	+	+	+	+	+	+
1: 不的確な回想	+	+	+	+	+	+	+	+	+	+	+	+
0: 回想なし	+	+	+	+	+	+	+	+	+	+	+	+
3. 対人コミュニケーション												
3: 適切な社会的応答	+	+	+	+	+	+	+	+	+	+	+	+
2: 他の参加者にも応答	+	+	+	+	+	+	+	+	+	+	+	+
1: 尋ねられれば応答	+	+	+	+	+	+	+	+	+	+	+	+
0: 無反応, 遮断, 妨害	+	+	+	+	+	+	+	+	+	+	+	+
4. 積極性 (言語・非言語)												
3: 刺激なしでも積極的に参加	+	+	+	+	+	+	+	+	+	+	+	+
2: 刺激によって積極的に参加	+	+	+	+	+	+	+	+	+	+	+	+
1: 多少あり	+	+	+	+	+	+	+	+	+	+	+	+
0: まったくなし	+	+	+	+	+	+	+	+	+	+	+	+
5. 喜び・楽しみ												
3: 一貫して楽しんでいる	+	+	+	+	+	+	+	+	+	+	+	+
2: 大部分楽しんでいる	+	+	+	+	+	+	+	+	+	+	+	+
1: 時折楽しんでいる	+	+	+	+	+	+	+	+	+	+	+	+
0: まったく楽しんでいない	+	+	+	+	+	+	+	+	+	+	+	+

野村豊子 (1998) 回想法とライフレビュー, 120-121, 中央法規出版, 東京より一部改変して引用
 各回のセッション終了後, リーダーとコ・リーダーで話し合って採点する。経過が確認できる。採点の際は、採点のみでなく、参加中の様子で気になった点等を話し合い、同時に次回以降の対応も検討する。

ORIGINAL ARTICLE

The impact of subjective memory complaints on quality of life in community-dwelling older adults

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Key words: depression, mild cognitive impairment (MCI), quality of life (QOL), self-efficacy, subjective memory complaints.

INTRODUCTION

Even though many elderly people complain about diminishing memory function, not much attention has been given to the impact of memory complaints on quality of life (QOL).¹ Because enhancing QOL is

regarded as one of the principal goals of management for all stages of dementia and its prodromal stages,^{2,3} we investigated the impact of memory complaints on QOL in individuals with mild cognitive impairment (MCI) and in those without objective cognitive deficit.

Abstract

Purpose: The aim of this study was to evaluate the impact of memory complaints on quality of life (QOL) in elderly community dwellers with or without mild cognitive impairment (MCI).

Methods: Participants included 120 normal controls (NC) and 37 with MCI aged 65 and over. QOL was measured using the Japanese version of Satisfaction in Daily Life, and memory complaints were measured using a questionnaire consisting of four items. The relevance of QOL was evaluated with psychological factors of personality traits, sense of self-efficacy, depressive mood, self-evaluation of daily functioning, range of social activities (Life-Space Assessment), social network size, and cognitive functions including memory. The predictors of QOL were analyzed by multiple linear regression analysis.

Results: QOL was not significantly different between the NC and MCI groups. In both groups, QOL was positively correlated with self-efficacy, daily functioning, social network size, Life-Space Assessment, and the personality traits of extraversion and agreeableness; QOL was negatively correlated with memory complaints, depressive mood, and the personality trait of neuroticism. In regression analysis, memory complaints were a negative predictor of QOL in the MCI group, but not in the NC group. The partial correlation coefficient between QOL and memory complaints was -0.623 ($P < 0.05$), after scores of depressive mood and self-efficacy were controlled. Depressive mood was a common negative predictor in both groups. Positive predictors were Life-Space Assessment in the NC group and sense of self-efficacy in the MCI group.

Conclusions: Memory complaints exerted a negative impact on self-rated QOL in the MCI group, whereas a negative correlation was weak in the NC group. Memory training has been widely practised in individuals with MCI to prevent the development of dementia. However, such approaches inevitably identify their memory deficits and could aggravate their awareness of memory decline. Thus, it is critical to give sufficient consideration not to reduce QOL in the intervention for those with MCI.

As QOL is a multidimensional concept, socio-psychological factors, including depressive mood,^{4,5} personality traits,⁶ self-evaluation of remaining function for independent living, sense of self-efficacy, and social relationships, were taken into account as possible predictors of QOL.⁷

METHOD

Participants

Participants were recruited from community dwellers in Takasaki City, Japan; they agreed to participate in a 3-month programme for prevention of mental decline conducted by local municipalities between April 2010 and July 2010. Participants were required to be aged 65 and over.

Participants were screened using a questionnaire regarding cognitive status. Under the Preventive Long-Term Care Program in Japan, individuals at high risk for cognitive decline have been identified by a questionnaire. The municipalities were required by law to mail the questionnaire to inhabitants aged 65 and older. The questionnaire consists of 25 self-completed items including three items concerning mental decline: (i) Have others indicated that you may have memory problems (e.g. others saying that you often ask the same things repeatedly)?; (ii) Do you need to look up commonly used telephone numbers?; and (iii) Do you sometimes fail to remember the date? The dwellers were required to answer whether these incidents had occurred. The questionnaire was self-completed; thus, those lacking fluency in written or spoken Japanese were excluded. A total of 2387 residents answered yes to at least one of the three items in the four areas of Takasaki City, and 153 of them attended an orientation meeting. Also, at a community centre for the elderly, we recruited and obtained an additional 13 applicants. Written informed consent was obtained from 162 subjects. (Four subjects withdrew.) At the assessment, each subject completed the Mini-Mental State Examination (MMSE) and a medical interview by a specialist in dementia medicine. During the interview, five subjects were excluded who met the International Classification of Diseases 10 research criteria for the diagnosis of dementia.

We analyzed subjects who were diagnosed as suffering from MCI ($n = 37$) and controls with normal cognitive abilities (NC) ($n = 120$). MCI was diagnosed by a physician who specialized in dementia based on criteria from a report by the International Working

Group on Mild Cognitive Impairment.⁸ The questionnaire was completed at the baseline assessment of the intervention.⁹

This research was carried out in compliance with the Helsinki Declaration. The Ethics Board of Gunma University School of Health Sciences (Maebashi, Japan) approved all procedures (No. 21–47).

Measurement

Quality of life

QOL was measured using a self-rated questionnaire, the Japanese version of the Satisfaction in Daily Life (SDL).¹⁰ The SDL is a simple measurement of 11 items: physical health, mental health, self-care, gait, housework, house facilities, partner and family relationships, hobby and leisure activities, social interaction, economic state and social security, and job satisfaction (including part-time or voluntary work and housekeeping jobs). Each item was rated on a scale of 1 to 5, with 'dissatisfied' rated as 1 and 'satisfied' rated as 5. Thus, the lowest total score could be 11 and the highest score could be 55. The mean \pm SD SDL score was 44.2 ± 7.3 in individuals aged 60–69 years and 42.1 ± 8.7 in those aged 70–79 years.

Memory complaints

Memory complaints were assessed using the Questionnaire for Subjective Memory Complaint (Q-SMC),¹¹ which consisted of four questions: (i) Are there times when you are unable to remember what date it is even if you see a calendar?; (ii) Are there times when you forget where you placed your wallet or keys?; (iii) Are there times when you read something you had scheduled in your calendar or diary and are unable to recall what you had planned?; and (iv) Are there times when you are unable to remember what you heard 5 min ago? Each item was evaluated on a scale of 0 to 3, with 0 being 'never' and 3 being 'always'. The mean \pm SD Q-SMC score was 5.59 ± 1.61 in individuals aged 74.1 ± 5.8 years ($n = 95$).¹¹

Psychological factors

(1) *Depressive mood.* Depressive state was evaluated using the Japanese version of the Geriatric Depression Scale (GDS).¹² GDS is a 15-item, self-rated assessment that screens for depression in elderly populations. Scores of 0–4 indicate a lack of depressive tendency, 5–9 indicate a mild depressive tendency, and 10–15 indicate a severe depressive tendency.

(2) **Sense of self-efficacy.** Sense of self-efficacy was measured using the Japanese version of the General Self-Efficacy Scale (SE).¹³ General self-efficacy is the belief in one's competence to cope with variable stressful or challenging demands, whereas specific self-efficacy is restricted to a specific demand. SE is designed to assess optimistic self-belief to cope with a variety of difficult demands in life. The mean \pm SD SE was 77.30 ± 14.13 in men aged 65–74 years, 75.68 ± 13.96 in women aged 65–74 years, 71.86 ± 15.24 in men aged 75 years and over, and 72.37 ± 14.87 in women aged 75 and over.¹⁴

(3) **Personality traits.** Personality traits were assessed using the Big Five scale of personality traits.¹⁵ The Big Five factors are extraversion, neuroticism, openness to experience, conscientiousness, and agreeableness. As the personality traits have sociocultural implication, we used the scale that was developed and validated in Japan.

Functional capacity for independent living

Functional capacity for independent living was assessed by the Tokyo Metropolitan Institute of Gerontology Index of Competence (TMIG-IC), which was designed to measure higher-level functional capacities in community-dwelling elderly residents who could not be adequately assessed by existing basic or instrumental activities of daily living scales.^{16,17} TMIG-IC consists of 13 items on three subscales: instrumental self-maintenance, intellectual activity, and social role. The mean \pm SD TMIG-IC was 10.8 ± 3.0 in individuals with a mean age of 72.5 years ($n = 1809$).¹⁸

Social factors

(1) **Social network size.** Social network size was assessed using the Japanese version of the abbreviated Lubben Social Network Scale,¹⁹ which evaluates the size of a social network that is attributable to family ties and a parallel set attributable to friendship ties. The scores range from 0 to 30, and higher scores indicate larger social networks. In Japanese samples, the mean \pm SD Lubben Social Network Scale score was 16.2 ± 5.1 in individuals aged 67.0 ± 6.8 years ($n = 232$).²⁰

(2) **Range of activity.** The Life-Space Assessment (LSA) assessed a subject's range of activities based on how far and how often a person moves to each of the defined levels and any assistance needed to get to each level. LSA can assess the full range of mobility,

ranging from mobility dependent on assistance from another person and limited to the room where a person sleeps daily, to travel out of the person's town independently during the month preceding the assessment.²¹ The mean \pm SD LSA was 91.6 ± 13.8 in individuals aged 74.0 ± 5.5 years ($n = 321$).²²

Cognitive function

Cognitive function was measured by MMSE, and two subtests of the 5-Cog test were analyzed in the present study:²³ memory test (category-cued delayed recall test consisting of 32 words in eight categories) and executive function test (dual-task test requiring alternating attention). The mean \pm SD scores in cognitively normal subjects (age range: 65–80 years; $n = 800$) were 12.0 ± 5.8 on the memory test and 20.1 ± 9.1 on the executive function test.

Physical factors

Aged individuals generally suffer from multiple diseases in various stages. Thus, it is difficult to obtain comprehensive information from a health questionnaire. Therefore, we did not include physical factors as variables. Instead, we established inclusion criteria, and participants were limited to those who could live independently in the community.

Analysis

We compared the SDL scores between the NC and MCI groups using a two-sample *t*-test. Pearson's correlation coefficients were obtained between the social-psychological-cognitive factors and the SDL score for each of the two groups. The factors with significant coefficients were entered in a stepwise manner into the multiple linear regression model as independent variables, with the SDL score as the dependent variable. Then, we obtained the partial correlation coefficient between the SDL score and each of the variables within the final model of multiple regression. The data were analyzed using the Japanese version of SPSS for Windows version 19.0 (IBM, Armonk, New York, USA) and level of statistical significance was set as $P < 0.05$.

RESULTS

Characteristics of subjects

Table 1 contains descriptive statistics for participants and the outcome variables. SDL scores were 44.3 ± 5.6 in the NC group and 44.2 ± 7.1 in the MCI group,

Table 1 Demographic data and correlation with quality of life (QOL)

Stage	NC (<i>n</i> = 120) (Men/women) (30/90)		MCI (<i>n</i> = 37) (Men/women) (17/20)		NC vs MCI <i>P</i> -value [‡]
	Mean ± SD	<i>r</i> [†]	Mean ± SD	<i>r</i> [†]	
Gender					
QOL (SDL) [§]	44.3 ± 5.6		44.2 ± 7.1		0.926
Age	71.9 ± 4.1	-0.183*	73.1 ± 4.4	0.261	0.127
Years of education	11.9 ± 2.2	-0.019	11.5 ± 3.0	0.067	0.372
Memory complaints (Q-SMC) [§]	6.3 ± 1.7	-0.211*	6.9 ± 2.2	-0.653***	0.082
Psychological factors					
Depressive mood (GDS) [§]	3.3 ± 3.0	-0.715***	4.1 ± 3.4	-0.550***	0.141
Self-efficacy (SE) [§]	76.7 ± 12.1	0.489***	74.0 ± 12.1	0.623***	0.245
Personality traits (Big Five) [§]					
Extraversion	51.0 ± 9.5	0.425***	51.1 ± 7.3	0.372*	0.946
Neuroticism	48.8 ± 9.4	-0.332***	49.8 ± 9.3	-0.439**	0.581
Intellect	48.5 ± 8.7	0.186*	49.7 ± 9.1	0.027	0.474
Conscientiousness	53.4 ± 8.3	0.099	49.9 ± 7.8	0.495**	<0.05
Agreeableness	56.2 ± 8.2	0.185*	53.0 ± 5.6	0.622***	<0.05
Cognitive function					
MMSE	28.4 ± 1.5	-0.082	25.7 ± 1.9	0.135	<0.001
Memory test	15.2 ± 4.5	0.038	8.8 ± 3.5	0.222	<0.001
Executive function test	21.9 ± 6.4	-0.055	14.7 ± 7.2	0.026	<0.001
Functional capacity					
TMIG-IC	12.0 ± 1.4	0.278**	11.7 ± 1.6	0.380*	0.302
Social factors					
Lubben social network size	16.8 ± 6.0	0.431***	16.5 ± 5.5	0.597***	0.810
Life-space assessment (LSA) [§]	90.8 ± 19.7	0.366***	96.3 ± 17.4	0.370*	0.128

P* < 0.05, *P* < 0.001, ****P* < 0.001. [†]Correlation coefficients with SDL, level of significance. [‡]Comparison between scores of NC and MCI by two sample *t*-test. [§]Related test appears in parentheses. GDS, the Japanese version of Geriatric Depression Scale; LSA, Life-Space Assessment; Lubben, the Japanese version of the abbreviated Lubben Social Network Scale; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination; NC, normal controls; Q-SMC, the Questionnaire for Subjective Memory Complaint; SDL, Satisfaction in Daily Life; SE, the Japanese version of the General Self-Efficacy scale; TMIG-IC, Tokyo Metropolitan Institute of Gerontology Index of Competence.

and were not significantly different between the NC and MCI groups (*P* = 0.926).

Possible QOL predictors

The factors showing significant correlation with SDL scores were similar in the NC and MCI groups, with the exception of personality traits (Table 1). There were positive correlations between SDL scores and self-evaluation scores of remaining function (i.e. sense of self-efficacy and daily functioning (TMIG-IC)), social factors of social network size (Lubben Social Network Scale), and range of activity (LSA). A negative correlation was observed between SDL scores and both scores related to memory complaints (Q-SMC) and depressive mood (GDS).

No significant correlation was observed between SDL scores and either cognitive scores (MMSE, memory test and executive function test) or years of education (Table 1).

There was also no correlation between memory complaints (Q-SMC) and MMSE (NC: *r* = -0.082; MCI:

r = 0.135), memory function (NC: *r* = 0.038; MCI: *r* = 0.222), or executive function (NC: *r* = -0.055; MCI: *r* = 0.026). The gender difference on the SDL was not significant in either the NC or MCI group.

QOL predictors after controlling for other factors

There were several independent variables in the final models of the stepwise multiple regression analyses for the NC and MCI groups. Memory complaint (Q-SMC) was a negative predictor in the MCI group. The positive predictors were range of activity (LSA) in the NC group and sense of self-efficacy (SE) in the MCI group. Depressive mood (GDS) was a common negative predictor in both groups (Table 2). The partial correlation coefficient between the SDL and Q-SMC scores in the MCI group was -0.62 (*P* < 0.001), when the SE and GDS scores were controlled. In the same way, the coefficient between the SDL and GDS scores was -0.51 (*P* < 0.01) after the SE and Q-SMC scores were controlled. The coefficient between the SDL and SE scores was -0.37 (*P* < 0.05) after the GDS and

Table 2 Regression models of factors predicting QOL score

A. NC group					
Predictors	Unstandardized		Standardized β	<i>t</i> -value	<i>P</i> -value
	β	SD			
(Constant)	43.912	2.190		20.051	<0.001
GDS	-1.251	0.133	-0.662	-9.389	<0.001
LSA	0.051	0.021	0.168	2.380	<0.05
B. MCI group					
Predictors	Unstandardized		Standardized β	<i>t</i> -value	<i>P</i> -value
	β	SD			
(Constant)	45.557	6.728		6.771	<0.001
Q-SMC	-1.439	0.319	-0.490	-4.506	<0.001
GDS	-0.757	0.225	-0.374	-3.369	<0.01
SE	0.156	0.070	0.268	2.233	<0.05

GDS, the Japanese version of Geriatric Depression Scale; LSA, Life-Space Assessment; MCI, mild cognitive impairment; NC, normal controls; Q-SMC, the Questionnaire for Subjective Memory Complaint; SE, the Japanese version of the General Self-Efficacy scale.

Q-SMC scores were controlled. In the NC group, the partial correlation coefficient between the QOL and GDS scores was -0.67 ($P < 0.001$) after the LSA scores were controlled, whereas the coefficient between the QOL and LSA scores was not significant ($r = 0.17$) after the GDS scores were controlled.

DISCUSSION

Memory complaints had a negative impact on self-rated QOL in the MCI group, whereas a negative correlation was weak in the NC group. The QOL scores did not significantly correlate with the memory test in either the MCI or NC group. In multiple linear regression analysis, subjective memory complaint was found to be a negative predictor of QOL. This was further confirmed by partial correlation analysis. The QOL scores were significantly correlated with the scores of subjective memory complaints after the scores of self-efficacy and depressive mood were controlled.

These results suggest that those with MCI consider their awareness of memory decline seriously enough to affect their QOL. When self-awareness of memory decline is considered, it should be taken into account whether one can evaluate one's own memory function properly. Deterioration of self-awareness of memory decline is characteristic of patients with Alzheimer's disease and other types of dementia. Individuals with dementia tend to overestimate their capacity and ignore their deficits,²⁴ whereas those with MCI retain the ability to estimate their own memory function in

most cases.²⁵ Consequently, those with MCI may recognize that their own memory decline is more severe than age-related decline, and they are all the more afflicted with fear of developing dementia.

Depressive state was a negative predictor in the MCI group. It is well established that QOL is intrinsically related to depressive mood,²⁶⁻²⁸ which is also highly associated with the personality trait of neuroticism among elderly individuals.^{29,30}

With regard to positive predictors, sense of self-efficacy was shown to be a positive predictor of self-rated QOL in the MCI group. A higher sense of self-efficacy was reported as a positive predictor of QOL in demented individuals.³¹ As autonomy becomes limited among those with MCI, they are confronted by limits in their social lives. Thus, a higher sense of self-efficacy would contribute to higher life satisfaction.

For those with MCI, an approach that aims to improve memory function could soothe the fear of memory decline, and cognitive stimulation, including memory training, has been widely practised in individuals with MCI to prevent the development of dementia. However, it should be noted that such approaches inevitably identify what those with MCI are incapable of doing and could aggravate their awareness of memory decline. The fear of developing dementia and the realization of their memory deficits can devastate the self-confidence of those with MCI and worsen their depressive tendency. Indeed, adverse effects of cognitive training, such as frustration, anxiety, depression, and reduced self-esteem, have been reported,^{32,33} and the consensus statement of the American Association for Geriatric Psychiatry warned of the potentially harmful effects of cognitive training.³⁴ Thus, cognitive training should be conducted with full attention to the mental state of the individual, so as to avoid exacerbating his or her depressive state or damaging his or her sense of self-efficacy for the improvement of QOL.

Limitations

With regard to limitations, the questionnaires used in the study, including QOL, depressive mood, and personality assessments, were self-rated, and it is necessary to confirm the results using a more objective evaluation of QOL. Additionally, those in the NC group in this study subjectively perceived cognitive decline, although they showed no objective cognitive decline.

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The authors have no conflicts of interest to report.

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ORIGINAL ARTICLE

CSF levels of A β 1-38/A β 1-40/A β 1-42 and ^{11}C PiB-PET studies in three clinical variants of primary progressive aphasia and Alzheimer's disease

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Abstract

Primary progressive aphasia (PPA) is a cognitive syndrome characterized by progressive and isolated language impairments due to neurodegenerative diseases. Recently, an international group of experts published a Consensus Classification of the three PPA clinical variants (naPPA, svPPA and lvPPA). We analyzed 24 patients with PPA by cognitive functions, neuroimaging (MRI, $^{99\text{mTc}}$ ECD-SPECT, ^{11}C PiB-PET and FDG-PET) and cerebrospinal fluid (CSF) analysis (ptau-181, A β 1-42, A β 1-40 and A β 1-38), to elucidate relationships between neuroimaging studies and biochemical findings in the three PPA clinical variants. Cognitive and speech functions were measured by mini-mental state examination and standard language test of aphasia. The patients with lvPPA showed significant decreases in CSF A β 1-42 and ratios of A β 1-42/A β 1-40 and A β 1-42/A β 1-38, and significant increases in CSF ptau-181 and ratios of ptau-181/A β 1-42 and ptau-181/A β 1-38; these findings were similar to those of patients with Alzheimer's disease (AD). We observed a higher frequency of the ApoE ϵ 4 allele in the lvPPA patients relative to the two other PPA variants. In ^{11}C PiB-PET of lvPPA patients, PiB positive findings were detected in cortices of frontal, temporal and parietal lobes and the posterior cingulate, where massive A β may accumulate due to AD. Our results of AD-CSF markers including A β 1-38 and ^{11}C PiB-PET in the lvPPA patients demonstrate a common pathological mechanism with the occurrence of AD.

Abbreviations: A β : β amyloid β protein; AD: Alzheimer's disease; AOO: age of onset; AOS: apraxia of speech; Apo E: apolipoprotein E; ^{11}C PiB-PET: ^{11}C Pittsburgh compound B-positron emission tomography; ^{11}C PBB3-PET: ^{11}C Pyridinyl-Butadienyl-Benzothiazole-positron emission tomography; CSF: cerebrospinal fluid; ELISA: enzyme-linked immunosorbent assay; EOSAD: early-onset sporadic AD; FDG-PET: ^{18}F -fluorodeoxy glucose-positron emission tomography; FTD: frontotemporal dementia; FTLD: frontotemporal lobar degeneration; ^{123}I IMP-SPECT: N-isopropyl-p-(iodine-123)-iodoamphetamine; LOSAD: late-onset sporadic AD; lvPPA: logopenic variant PPA; MMSE: mini-mental state examination; naPPA: non-fluent/agrammatic variant PPA; ND: non-demented subject; PCA: posterior cortical atrophy; PPA: primary progressive aphasia; ptau: phosphorylated tau; S.D.: standard deviation; SLTA: Standard Language Test of Aphasia; svPPA: semantic variant PPA; $^{99\text{mTc}}$ -ECD SPECT: $^{99\text{mTc}}$ -ethyl cysteinate dimer single photon emission computerized tomography.

Introduction

Primary progressive aphasia (PPA) is a cognitive syndrome characterized by a progressive and initially isolated language

impairment caused by a neurodegenerative disease [1]. The non-fluent/agrammatic variant of PPA (naPPA) is characterized by agrammatism and/or motor speech articulatory errors due to an apraxia of speech (AOS), in which impairment of sentence comprehension for difficult syntactic constructions may also be present [2,3]. The core features of the semantic variant of PPA (svPPA) are impaired confrontation naming and single-word comprehension [4], while object knowledge

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