

と呼ばれ、APL作用を加えることでガラントミンの長期使用時の有用性の高さの根拠となる仮説である。つまりガラントミンは、他のコリンエステラーゼ阻害薬よりも長期に効果を示すことが報告されている。さらにアミロイドの蓄積に対する毒性を緩和する作用も報告されている。

主な有害事象は嘔気等の消化器症状である。ガラントミンの投与に当たっては、低用量から導入し、患者の状態を観察しながらゆっくりと増量することで忍容性を高め、治療を継続することが可能である。

## 2. リバスタグミン

リバスタグミンはコリンエステラーゼ阻害薬として、長期に投与した場合の有効性の報告もあり、またDAD (disability assessment for dementia) 尺度によるIADLスコアの改善効果もみられる(図2)ため、認知症の早期または軽症に使用するとよい可能性がある。

またパッチ剤の有用性として、1日1回貼付の簡便な投与方法で効果を示す。さらに食事の有無および食事時間に配慮する必要がなく、他の併用薬剤の服薬時間によって投与タイミングを制約する必要がない。介護者等が視覚的に容易に貼付状況(貼付の有無、投与量等)を確認

できるため、薬剤アドヒアランスの向上が期待できる。

## 3. メマンチン

メマンチンはコリンエステラーゼ阻害薬と全く違った作用機序で認知機能障害の進行を抑制することが確かめられている。アルツハイマー病にはグルタミン酸神経系の機能異常が関与しており、グルタミン酸受容体のサブタイプであるNMDA受容体チャネルの過剰な活性化が原因の1つと考えられている。アルツハイマー病

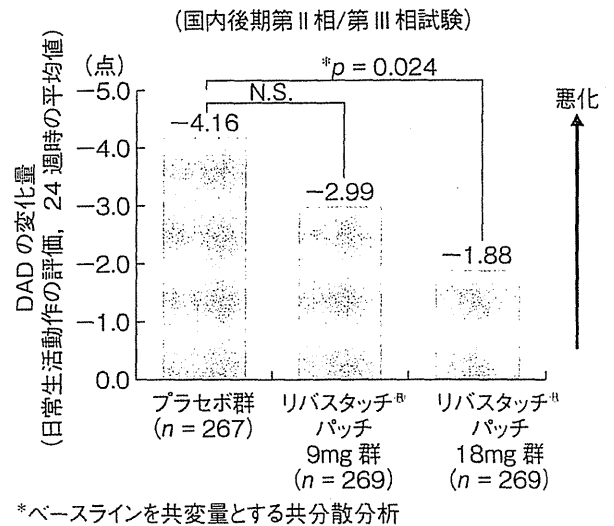
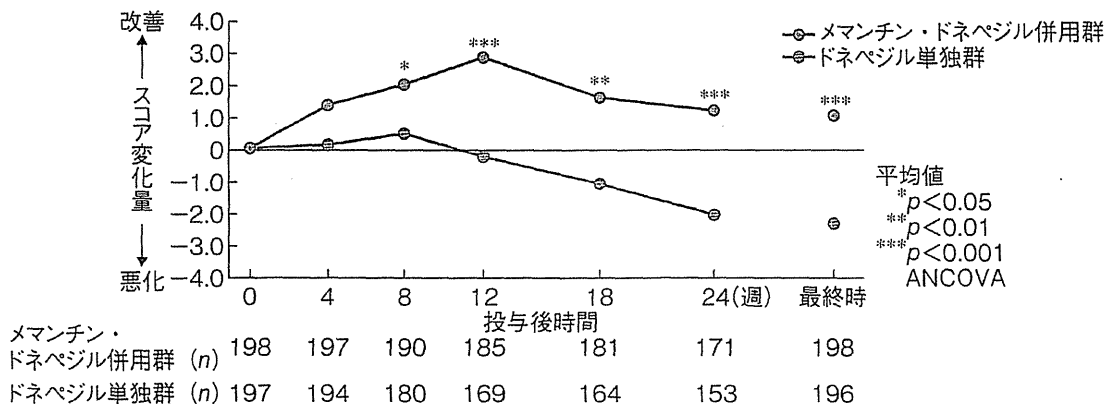


図2 IADLの改善

(小野薬品工業：承認時申請資料より引用)



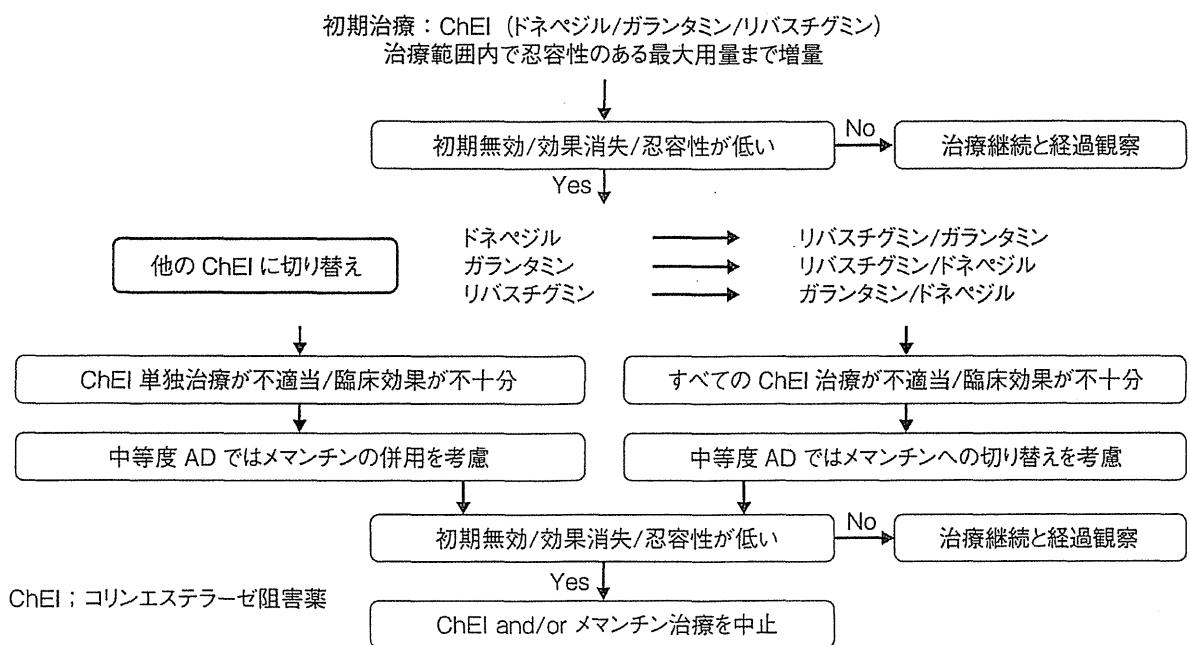
対象：80歳以上の中等度から高度のアルツハイマー病患者 403例  
 ・NINCDS-ADRDAのアルツハイマー病の診断基準を満たす  
 ・MMSE (mini-mental state examination；簡易知能検査スケール) スコア5点以上14点以下  
 ・ドネペジルの治療を6か月以上受けている  
 方法：ドネペジル (5～10mg) の治療を継続し、二重盲検下でメマンチンまたはプラセボを1日2回24週間、朝食後・昼食後に経口投与。メマンチンは5mg/日より開始し、1週間に5mgずつ増量していき、20mg/日を維持用量とした。

図3 メマンチン・ドネペジル併用によるSIB (severe impairment battery) スコア変化量の推移

(Tariot PN, et al : JAMA 2004 : 291 : 317-324 より引用)

	軽度AD	中等度AD	高度AD
メマンチン		維持用量 20mg/日 (中等度および高度)	
ドネペジル	維持用量 5mg/日 (軽度および中等度)		維持用量 10mg/日 (高度)
		維持用量 16mg/日 (軽度および中等度)	
ガランタミン		維持用量 24mg/日 (軽度および中等度) *症状に応じて 24mg までは増量可	
リバスチグミン		維持用量 18mg/日 (軽度および中等度)	

図4 日本におけるアルツハイマー病 (AD) 治療薬の治療アルゴリズム



ADMC (Alzheimer's Disease Management Council)

図5 軽度～中等度アルツハイマー病 (AD) に対する治療アルゴリズム

(Farlow MR, et al : Am J Med 2007 ; 120 : 388-397 より引用, 一部改変)

の病態時は、シナプス間隙のグルタミン酸濃度の持続的な上昇によって NMDA 受容が活性化され、細胞内への Ca イオンの流入、シナプティックノイズの発生などによって認知機能障害が引き起こされると考えられている。メマンチンは、NMDA 受容体拮抗作用により、神経細胞内への過剰な Ca イオンの流入抑制による

神経細胞保護作用と、シナプティックノイズの抑制による記憶・学習機能障害抑制作用を有するとされている。

さらにメマンチンは、コリンエステラーゼ阻害薬と併用すると、より認知機能障害の進行を遅延させることが知られている (図3)。効果は単独の場合より遅延し、3 か月後に効果のピー

クがあり、その後比較的長期に持続する可能性がある。またメマンチンを長期投与した場合には、対照群に比べ脳萎縮の程度が抑制されたとの報告もある。

#### 4. 薬剤の投与変更のポイント

ドネペジルは軽度、中等度のアルツハイマー病であれば5mgの投与を行うが、高度であれば10mgに増量する。メマンチンを併用する場合は、中等度になったら併用し、その後高度になったらドネペジルを10mgに増量する。また、ドネペジル投与中に消化器症状や易興奮などの副作用があれば、10mgを5mgへ、5mgであれば3mgへ減量する。

ガランタミンは朝夕2回の服用が特徴であるが、16mgで経過をみて、重症化するようであれば24mgへの増量を考慮する。リバスチグミンは接触性皮膚炎などの副作用がみられることがあるが、18mgまで増量し、メマンチンとの併用を検討する。一般的な治療のアルゴリズムを図4に示した。

さらに薬剤の切り替えを検討する場合には以下のアルゴリズムを参考にするとよい(図5)。すなわち、初期にはまずコリンエステラーゼ阻害薬から1剤を選択し、2~3か月ごとに効果を観察し、6か月程度みても効果が得られない場合には他の薬剤に変更する。その際には薬剤の特徴と共に、メマンチンの併用も選択肢として考慮する。興奮や攻撃性などのBPSDがある場合にはメマンチンを初期から投与することも考慮する。

薬剤の中止時期については、嚥下障害などで食事が摂れなくなったとき、介護施設に入所したとき、病状が悪化したときなど、また重度化して薬剤の効果が期待できないと判断された場合である。

### ■ BPSD の治療とケア

BPSD に関しては保険適用がとれていない薬

剤が多い。以前は抗精神病薬が用いられてきたが、最近ではリスペリドンやオランザピン、アリピプラゾールなどの非定型抗精神病薬が用いられるようになってきた。しかし米国ではこの種類の薬剤は脳卒中の発生率が高いとして、アルツハイマー病には禁忌となっている。日本では保険適用外であるが、有用性があるため、慎重に適応を判断したうえで使用されている。これらの薬剤では副作用の頻度が比較的高いため、副作用を軽減するためにも少量から投与することがポイントである。

また、漢方薬の抑肝散がよく用いられており、特にレビー小体型認知症のBPSDには有効性が高いとされている。副作用としては低カリウム血症に注意する。

メマンチンは興奮や攻撃性などのBPSDに有効であることが知られており、頻度は低いが傾眠傾向が報告されている。

BPSDをコントロールすることは、医師にとって、家族や本人の苦痛をとる意味においても重要である。

### ■ おわりに

アルツハイマー病を早期に発見し、早期に治療するに当たり、これら4剤のさらなる有用性に期待している。長期使用時の効果についても一定のエビデンスが存在しており、その有用性は確かであろう<sup>4)</sup>。しかし日本での効果の検証は、今後一定の時間を経て判断する必要がある。

新薬に対する認知症患者や家族の期待は大きいですが、効果に対する過剰な期待は問題である。

#### ..... 文 献 .....

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# 家族介護者の介護負担に関連する要因

— 要介護高齢者の介護者の介護負担を中心に —

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## 臨 牀 指 針

# 家族介護者の介護負担に関連する要因

### — 要介護高齢者の介護者の介護負担を中心に —

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#### はじめに

近年、わが国では急速に高齢化社会が進み、介護が必要な高齢者の数が急増する一方、三世帯世帯や一世帯あたりの人員数の減少が進み、家族の介護力は弱体化し、介護が必要な高齢者を介護する家族の負担は増加している。2000年4月に介護保険制度が導入され、要介護高齢者は要介護度に応じた介護サービスが受けられるようになり、2006年4月には改正介護保険法が施行され、予防重視型システムの確立や施設給付の見直し、新たなサービス体系の確立、サービスの質の確保・質の向上が図られ、在宅療養支援が強化された<sup>1)</sup>。

しかし、介護保険導入により総量としてはサービスの提供は増加しても、利用したい時に利用できないとか、公的サービスの利用に対する偏見などにより、介護保険導入後も地方では在宅で要介護高齢者を介護する家族の負担はあまり軽減されていない。

本稿では介護負担の概念を紹介するとともに、要介護高齢者を在宅で介護する家族の介護負担に影響を与える要因と介護負担軽減の社会的意義について要介護高齢者を在宅で介護する家族を中心に解説する。

#### I. 介護負担感の概念と介護負担測定のための尺度

欧米では要介護高齢者の家族介護者の負担感を測定するスケールの開発と負担感に影響を与える要因の研究がなされてきたが、最初に介護負担の概念を提唱したのは Zarit ら<sup>2)</sup>である。介護負担感には心理的負担だけでなく、身体的負担、経済

的困難なども含まれる。彼らは、認知症のある高齢者の家族介護者が受ける否定的な影響について明らかにするために介護負担尺度の開発を行い、介護負担を「親族を介護した結果、介護者が情緒的、身体的健康、社会生活および経済状態に関して被った被害の程度」と定義した。また、George ら<sup>3)</sup>は介護負担を「障害老人を介護している家族が身体的・心理的、または情緒的・経済的困難を認識している程度」と述べている。

負担感については、客観的負担感と主観的負担感とを区別する研究者もある<sup>4)5)</sup>が、自記式の質問票を用いた調査の場合、介護者自身が記入することになるので、我々は負担感を客観的負担感と主観的負担感に分けない Zarit 介護負担尺度日本語版 (Japanese version of the Zarit Caregiver Burden Interview, J-ZBI)<sup>6)7)</sup>を用いて調査を行っている。

介護負担感測定のために特別に開発された尺度のほか、Zung Self-Rating Depression Scale<sup>8)</sup>や the Center for Epidemiologic Studies Depression Scale, CES-D<sup>9)</sup>などの抑うつスコアを用いて負担感の調査を行っている研究者もいる<sup>10)</sup>。CES-D<sup>9)</sup>には逆転項目が含まれているので、回答者が調査票にきちんと回答しているかがチェックできるので、我々は J-ZBI<sup>6)7)</sup>と CES-D 日本語版<sup>11)</sup>を用いて、要介護高齢者の家族介護者の介護負担感に関する調査を行っている。我々のフィールドで行った調査では、J-ZBI と CES-D の得点は互いに良い相関関係を示しており ( $r=0.72$ ,  $p<0.001$ )<sup>12)</sup>、調査の結果は信頼できると考えられる。

J-ZBIに加えて CES-D を用いて調査を行っているもう一つの理由は介護者の抑うつの割合を一般住民と比較することで、要介護高齢者を在宅で

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表 1 介護負担の関連要因 (著者作成)

- |   |                                                                                                 |
|---|-------------------------------------------------------------------------------------------------|
| ① | 要介護高齢者の特徴                                                                                       |
|   | a. 認知症に伴う問題行動                                                                                   |
|   | b. 男性                                                                                           |
|   | c. 日常生活動作 (ADL) の障害<br>(認知症がない場合は ADL 障害の程度が高度のほうが介護負担は大きく、認知症がある場合には ADL 障害の程度が軽度のほうが介護負担は大きい) |
| ② | 介護者の特性                                                                                          |
|   | a. 配偶者<br>(高齢で自身の健康に不安がある)                                                                      |
|   | b. 高齢                                                                                           |
|   | c. 体調が悪い                                                                                        |
|   | d. 通院中の病気がある                                                                                    |
| ③ | 介護状況                                                                                            |
|   | a. 介護時間が長い                                                                                      |
|   | b. 独りでの外出ができない                                                                                  |
|   | c. 副介護者がいない                                                                                     |
|   | d. 家族・親族の協力がいない                                                                                 |
| ④ | その他                                                                                             |
|   | a. 公的サービスを利用しにくい                                                                                |
|   | b. 経済的な負担が大きい                                                                                   |
|   | c. サービスの利用に対する偏見                                                                                |
|   | d. 市町村による介護者への支援*                                                                               |
|   | e. 社会的支援ネットワークの存在*                                                                              |

無印は介護負担を増加させる要因、

\*は介護負担を減少させる要因

介護する家族の介護負担の社会的インパクトを測定することができるからである。

## II. 介護負担に影響を与える要因 (表 1)

介護保険導入以前から我々が複数の地域で行ってきた要介護高齢者の主介護者の介護負担感に関する調査を紹介する。

### 1. 要介護高齢者の特徴

要介護高齢者の特性では、認知症に伴う問題行動がある要介護高齢者<sup>13)</sup>や男性<sup>12)14)</sup>を介護している介護者の介護負担は高かった。日常生活動作の自立は認知症がある場合、無関係か<sup>12)14)-16)</sup>、むしろ低下しているほうが、介護負担は低かった<sup>13)</sup>。一方、荒井ら<sup>18)</sup>は脳卒中患者の介護者を調査し、日常生活動作と介護負担が負の相関関係を示したと報告し、川本ら<sup>10)</sup>は離床できることは介護負担を低下させると報告しているが、認知症がある場合には寝たきりのほうが、徘徊や暴力行為などの心配をしなくてすむので、このような結果になったのではないかと考えられる。男性を介護している者の介護負担が高いのは男性を介護するのに体力がいることや問題行動を伴う場合、制御するのが大変であるからではないかと考えられる。荒井ら<sup>18)</sup>は脳卒中患者の介護者の介護負担を調査し、

男性患者を介護する者の介護負担は高かったと報告している。

### 2. 介護者の特性

介護者の特性では、配偶者<sup>14)</sup>、体調が悪いこと<sup>12)14)15)</sup>、介護者自身の病気で医療機関にかかっていること<sup>13)14)</sup>が高い介護負担と関連していた。多くの場合、配偶者は要介護高齢者の妻である場合が多く、介護者自身も高齢であり、体調に不安があり、自身の病気で医療機関にかかっているのではないかと考えられる。川本ら<sup>10)</sup>は介護者が女性で自身の健康状態が悪い者は介護負担が高いと報告している。介護者が妻である場合、体調が悪くても無理をして、介護を継続している場合も考えられるので、ショートステイを利用させるなど、介護者の負担を軽減させるように指導することも必要である。

### 3. 介護状況

介護状況では、介護時間が長いこと<sup>14)15)17)</sup>、要介護高齢者を伴わない独りでの外出ができないこと<sup>12)</sup>が高い介護負担と関連していた。荒井ら<sup>18)</sup>の脳卒中患者の介護者の介護負担の報告でも、介護時間の長いことや患者から目が離せない時間が長いことは高い介護負担と関連しており、介護者に介護から開放される時間を与えることは介護負担の軽減につながると考えられる。

### 4. その他

公的サービス (フォーマルなサービス)<sup>[脚注1]</sup>の利用<sup>19)</sup>や社会的支援ネットワークは介護負担を軽減させると報告されている<sup>10)20)</sup>が、我々の調査では介護負担の高い者は低い者に比べ、サービスの利用は変わらない<sup>12)-14)</sup>か、サービスの種類によっては多く利用していた<sup>15)</sup>。これらの調査は横断研究であるので、因果の関係ははっきりしない。上記に示した理由により、介護者の負担が多いため介護のニーズが高く、その結果として、多くのサービスを利用していたとも考えられる。

介護負担の高い介護者は低い介護者に比べ、経済的に負担が大きいと感じる者が多く<sup>15)</sup>、サービスの利用に関して近所の目が気になる者が多く<sup>14)</sup>、介護保険の利用金額は少なかった<sup>14)</sup>。これらの介護負担の高い家族介護者は金銭的負担や近所の目を気にすることで、必要とされる介護サービスよりも低い基準でしかサービスを利用していないた

[脚注1] 介護保険利用のサービスだけではなく、市町村などの行政が提供する保健福祉サービスも公的サービスである。

表 2 精神科訪問看護と一般訪問看護利用者の比較 (文献25)

介護者	精神科 訪問看護利用者 (n=39)	一般 訪問看護利用者 (n=37)	p-値
男性	10(25.6)	9(24.3)	n. s.
年齢(歳)	52.8±26.9	64.5±12.4	<0.05
高齢者(65歳以上)	16(41.0)	18(48.6)	n. s.
持病あり	21(53.8)	21(56.8)	n. s.
訪問看護利用者との関係			
配偶者	11(28.2)	21(56.8)	<0.05
実子/義理の子	5(12.8)	13(35.1)	<0.01
親	17(43.6)	3(8.1)	<0.01
J-ZBI	21.8±13.9	32.3±19.7	<0.01
CES-D	12.0±7.3	15.2±8.6	n. s.
うつ状態(CES-D=16以上)	12(30.8)	19(51.4)	n. s.
訪問看護サービス利用者			
男性	12(30.7)	19(51.4)	n. s.
年齢(歳)	50.1±17.2	69.4±23.5	<0.01
Barthel index	91.9±16.8	49.6±40.1	<0.01
要介護度4/5	1(2.6)	10(27.0)	<0.05
認知症	4(10.3)	9(24.3)	n. s.
統合失調症	23(59.0)	0(0)	<0.01
介護状況			
身体介護時間(時間/日)	0.8±1.5	6.5±7.7	<0.01
見守り時間(時間/日)	4.4±5.0	9.8±9.7	<0.05
介護期間(ヵ月)	97.5±87.2	57.7±80.4	n. s.
副介護者あり	10(25.6)	19(51.4)	n. s.
一人で外出できる	28(71.8)	24(64.9)	n. s.
訪問看護を利用	39(100)	37(100)	n. s.
ホームヘルパーを利用	12(30.7)	12(32.4)	n. s.
デイケアを利用	25(64.1)	15(40.5)	<0.05
ショートステイを利用	1(2.6)	8(21.6)	<0.05

データは平均±標準偏差または人数(%)

めに、介護負担の軽減ができていないと考えられる。

また、慢性閉塞性肺疾患患者の介護者の調査<sup>21)</sup>では高負担の介護者は低負担の介護者と比べ、経済的負担が高い者が多く、多くのサービスの利用を希望しているにもかかわらず、実際のサービスの利用に差は認めなかった<sup>21)</sup>。経済的負担のためにサービスの利用を控えている可能性も否定できない。

介護負担の軽減のためには、公的サービスの利用に対する偏見をなくすとともに、インフォーマルなサービスを活用するなど、介護者の経済的負担にも配慮したサポートが必要であろう。

### Ⅲ. 介護負担の社会的インパクト

我々が福岡県の複数の地域で行った要介護高

齢者とその介護者の調査では、各地域により、高い介護負担との関連要因は微妙に異なっていたが、その一因としては各地域や時代の社会サービスの整備状況、利用可能なインフォーマルサービスの違い、要介護高齢者や介護者の違いが考えられる<sup>22)</sup>。しかし、いずれの調査でも介護者の約半数(46.6%~56.1%)が抑うつ状態(CES-Dの得点16点以上)であり、一般住民のうつ病の割合(1~5%)と比べてきわめて高く、介護者の負担を軽減するための対策が必要と考えられた<sup>22)</sup>。

福岡県M町で訪問看護サービスを利用する要介護高齢者の家族介護者の調査の場合<sup>23)</sup>、介護者の約半数が抑うつ状態にあり、抑うつの割合は介護保険の導入後5年を経過してもあまり改善されていない<sup>23)</sup>。

介護者の抑うつは介護の中断の危険因子であ

る<sup>24)</sup>。介護者への支援も要介護高齢者の入院・入所を予防する介護予防である。介護放棄などの虐待を防ぐ意味からも、保健師などの市町村の保健福祉関係者は在宅で介護を継続している高齢者の家庭を訪問するなど、積極的に家族とかがわっていく必要があろう。

#### IV. 精神科訪問看護と一般訪問看護利用者の比較 (表2)

精神科病院の訪問看護を受けている患者の介護者の場合、家族の負担は一般の訪問介護サービスを受けている要介護高齢者よりもJ-ZBIの点数は低かった<sup>25)</sup>。精神科病院の訪問看護を受けている患者は一般の訪問看護サービス利用者よりも若く、日常生活動作の自立度が高く、認知症の割合が少なかった(統合失調症が59%)。また、介護者の年齢も精神科訪問看護の利用者のほうが若かった。介護状況をみると、身体介護や見守りの時間が少なく、デイケア利用者の割合が高く、ショートステイ利用者の割合が少なかった。デイケアを利用することで、介護から解放される時間が多く取れることが、精神科訪問看護利用者の介護者の負担が少ないことの一因と考えられた。

#### お わ り に

家族は共に生きていくために相互に働きかけ、お互いのセルフケアを補う機能を持っている<sup>26)</sup>。これが、家族のセルフケア機能である。在宅医療の現場では家族は患者のセルフケア不足を補うケア提供者であると同時に、看護職からのケアの受け手でもある<sup>27)</sup>。看護職には個人と家族のセルフケア機能を最大限に発揮するように支援することが求められている<sup>26)</sup>。

在宅医療の大きな特徴は主治医のほか、訪問看護師、薬剤師、理学療法士、介護福祉士などのチームアプローチである<sup>27)</sup>。在宅医療は看護やケアの領域の部分が非常に多く、訪問看護(看護・医療処置・リハビリテーションを含む)との連携は不可欠であり、在宅医療における訪問看護師の役割は決して小さなものではない。

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## Original Study

## Priorities of Health Care Outcomes for the Elderly

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## A B S T R A C T

## Keyword:

Geriatrics  
quality of care  
health care policy

**Objectives:** Physicians are uncertain about what medical services should be provided to older and/or disabled patients. Better understanding of health outcome prioritization among health care providers and recipients may help the process of decision- and policy-making. For this purpose, surveys were conducted on priorities of health care outcomes for the elderly.

**Design:** Survey research.

**Setting:** Four groups of health care providers and four groups of health care recipients.

**Participants:** A total of 2512 health care providers and 4277 recipients.

**Measurements:** Questionnaires were sent to more than 8000 health care providers and more than 9000 health care recipients: geriatricians, physicians who commonly see older patients or work in long term care facilities, staff members and participants in adult day care, patients in outpatient geriatric clinics, family members of patients with dementia, and community-dwelling older adults. The questionnaire asked the subjects to rank 12 measures of health care outcomes.

**Results:** The mean response rate was 49%. All health care provider groups considered "improvement of quality of life" the most important. In contrast, in health care recipient groups, "effective treatment of illness," "improvement of physical function," and "reduction of carer burden" were given high priority, whereas "improvement of quality of life" was perceived as less important. All the groups, including health care providers and recipients, ranked "reduction of mortality" the least important, followed by "avoiding institutional care." Stratification analysis showed that the results did not differ by sex, nursing care level, or the existence of relatives who required nursing care, whereas age slightly influenced the order of high-ranked measures.

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**Conclusion:** Priorities of health care services and their differences between providers and recipients should be taken into account in the health care of older patients and the design of health care policies and research. Copyright © 2013 – American Medical Directors Association, Inc.

Japanese society has been rapidly aging owing to long life expectancy and a low birth rate.<sup>1</sup> People older than 65 comprised 23.8% of the population in 2012, which is expected to rise to 31.8% in 2030<sup>2</sup> and will be by far the highest in the world. Japanese physicians have been exposed to a high load of older patients, and management of older patients remains a major challenge. There are several reasons for this difficulty. Evidence is still largely lacking for older patients, especially for those older than 75 years, who account for 11.8% of the Japanese population.<sup>2,3</sup> Older patients are likely to have multimorbidities, or co-occurrence of two or more chronic conditions,<sup>4</sup> but application of disease-specific guidelines to older patients with multimorbidities may result in polypharmacy, an increased risk of adverse drug reactions, and poor outcomes.<sup>5,6</sup> At the same time, however, older patients are at increased risk of underuse of necessary medication, for fear of polypharmacy or complications.<sup>7,8</sup>

In an attempt to help optimize prescribing for older patients, investigators have devised numerous tools to guide clinicians, such as lists of indicated, beneficial medication or medication with high potential for harm.<sup>9,10</sup> Although these tools are helpful in reducing exposure of older patients to inappropriate medication and risk of adverse drug events,<sup>11</sup> they do not provide more general considerations, such as when or how to discontinue potentially inappropriate medications, how to balance risks and benefits of unlisted medication, or how to manage medication in special circumstances, such as palliative and hospice care where symptom control is of higher priority. Therefore, the process of determining the medication regimen is inevitably subjective and individualized, taking into account patients' cognitive, physical, and social function, remaining life expectancy, and the goals of care.

Unfortunately, few studies have examined the priorities of health care perceived by health care providers and recipients in geriatric medicine. One small study conducted in England more than 15 years ago showed that geriatricians and patients similarly gave high priority to reducing disability and improving quality of care, and low priority to reducing mortality.<sup>12</sup> However, the serious question of whether there may be a gap in priorities of health care between health care providers and recipients has been raised.<sup>13,14</sup>

Better understanding of health outcome prioritization among health care providers and recipients in geriatric medicine is necessary

to help physicians, older patients, and their family members discuss the goals of care and to assist health policy makers in effectively using resources to address the needs of older patients. In this study, we aimed to obtain a comprehensive picture of the views of groups with an important stake in geriatric health care services (geriatricians, physicians who commonly see older patients or work in long term care facilities, staff members and participants in adult day care, patients in outpatient geriatric clinics, family members of patients with dementia, and community-dwelling older adults) on the relative priorities of different outcome measures that are relevant to geriatric clinical practice and health care policy.

## Methods

Between September 2010 and October 2011, surveys were conducted in the following eight groups:

- (1) All geriatricians (approximately 1500) board certified by the Japan Geriatrics Society
- (2) A total of 5000 physicians randomly selected from the list of board-certified physicians in five subspecialties (two internal medicine subspecialties, two surgical subspecialties, and one other) with high exposure to older patients
- (3) Physicians working in 800 long term care facilities that were randomly chosen from the nationwide list of long term care facilities
- (4) Staff members working in adult day care at 400 randomly chosen long term care facilities as mentioned previously
- (5) Participants in adult day care at the same 400 long term care facilities as mentioned previously
- (6) Patients in geriatric outpatient clinics at five university teaching hospitals (the University of Tokyo, Kyorin University, Nagoya University, Kyoto University, and Tohoku University)
- (7) Family members of patients with dementia who had been seen in geriatric outpatient clinics at four university teaching hospitals (Tohoku University was excluded because of the Tohoku Earthquake at the time of this survey)
- (8) A total of 6000 community-dwelling, functionally independent (ie, not requiring nursing care provided by long term care

**Table 1**  
Survey Methods and Number of Valid Answers in 8 Groups

Groups	Time of Survey	Survey Methods	No. of Questionnaires Sent	No. (%) of Valid Answers*
<b>Health care providers</b>				
Geriatricians	2010, Sep	By post	1500	619 (41)
Physicians in 5 subspecialties	2011, Oct	By post	5000	1305 (26)
Physicians in long term care facilities	2011, Oct	By post	800	384 (48)
Adult day care staff	2010, Sep	By post for each facility	400 facilities (2 per facility)	204†
<b>Health care recipients</b>				
Adult day care participants	2010, Sep	By post for each facility	400 facilities (5–10 per facility)	795†
Patients in geriatric outpatient clinics	2010, Sep	Distributed by physicians and returned by post	950	512 (55)
Family members of patients with dementia	2011, Oct	Distributed by physicians and returned by post	542	333 (61)
Community-dwelling older adults	2010, Sep	By post	6000	2637 (44)

\*Responses with missing items or invalid answers were excluded.

†For adult day care staff members and participants, questionnaires were sent to each facility by post, where 2 staff members and 5 to 10 participants were offered the questionnaire; 123 facilities (31%) returned the completed questionnaires.

insurance) older adults randomly drawn from the community registers of two target areas (Kashiwa, Chiba Prefecture, a city close to Tokyo, and Sabae, Fukui Prefecture, a provincial city), from which men and women, 65 to 74 years and older than 75 years, were equally selected

Postal questionnaires were sent to all groups of physicians and community-dwelling old adults. For adult day care staff members and participants, questionnaires were sent to each facility, where two staff members and 5 to 10 participants were offered the questionnaire, to be completed on a voluntary basis. The completed questionnaires were gathered at each facility and then returned to us. Patients and family members of patients with dementia received the questionnaires from their physicians (Table 1).

The questionnaire asked about the relative priorities of 12 health care measures that were derived from a literature review and a previous Internet-based survey conducted by the National Center for Geriatrics and Gerontology in 2009 (in Japanese; <http://www.ncgg.go.jp/pdf/itaku/21hokoku/20si-3.pdf>). Each item was expressed as several words so as to help health care recipients understand the meaning. The respondents were asked to rank the measures in order of priority from 1 (most importance) to 12 (least important). To facilitate ranking the outcomes in order, they were prompted to choose and rank the three most important outcomes, then the three least important outcomes, and last, the six middle outcomes. Ties, or the same ranks, were not allowed.

To examine whether variation in the question wording could affect the results, we devised another version of the questionnaire with different wording for four items and sent that version to a randomly selected subset of participants; however, the results were almost identical (data not shown). We also tested whether the order of health care measures that appeared in the questionnaire would affect the results in a random subset of participants, but the responses to the reverse order questionnaire were similar to those of the original version (data not shown). Therefore, we analyzed the responses from different versions (wording and order) together.

The following information was also collected using the questionnaire: age and sex for all participants; specialty (internal medicine, surgery, psychiatry, or others) and years of experience for physicians; qualification and years of experience for adult day care staff; nursing care level (level of required nursing care: relatively independent, limited impairment, needing extensive help, or severely dependent) for adult day care participants; nursing care level and the existence of relatives who required nursing care for patients in geriatric outpatient clinics; nursing care level, morbid conditions, and the existence of relatives who required nursing care for community-dwelling older adults.

The study protocol was approved by the Ethics Committee of the Graduate School of Medicine, The University of Tokyo. Ethical approval for the surveys on patients in geriatric outpatient clinics and family members of patients with dementia was also obtained from the participating institutions.

**Results**

The mean response rate for the eight groups was 49%, which varied from 28% for board-certified physicians to 68% for family members of patients with dementia (Table 1). The analytic sample included a total of 2512 health care providers and 4277 recipients.

Tables 2 and 3 show the relative priorities of 12 measures of health care services from the highest importance to the lowest, with mean and 95% CI, perceived by health care providers and recipients, respectively.

All physician groups considered “improvement of quality of life” the most important, and the low mean value for this item across physician

**Table 2**  
Health Care Providers' Priorities for Health Care Outcome

Rank Order	Geriatricians (n = 619)		Physicians from 5 Relevant Subspecialties (n = 1305)		Physicians in Long Term Care Facilities (n = 384)		Adult Day Care Staff (n = 204)	
	Outcome	Mean 95% CI	Outcome	Mean 95% CI	Outcome	Mean 95% CI	Outcome	Mean 95% CI
1	Improvement of quality of life	2.62 2.45–2.80	Improvement of quality of life	3.09 2.96–3.22	Improvement of quality of life	2.88 2.62–3.14	Improvement of quality of life	4.29 3.88–4.71
2	Patient satisfaction with care	4.37 4.15–4.58	Patient satisfaction with care	4.34 4.19–4.49	Patient satisfaction with care	4.60 4.32–4.88	Maintaining a high level of activity	4.35 3.96–4.73
3	Effective treatment of illness	4.80 4.53–5.07	Maintaining a high level of activity	4.64 4.48–4.80	Improvement of physical function	4.68 4.39–4.97	Reduction of carer burden	4.80 4.42–5.17
4	Maintaining a high level of activity	4.92 4.69–5.15	Improvement of physical function	5.25 5.08–5.42	Maintaining a high level of activity	4.73 4.43–5.03	Resolution of assessed problems	5.15 4.74–5.55
5	Improvement of physical function	4.94 4.71–5.18	Effective treatment of illness	5.32 5.13–5.52	Improvement of mental health	5.50 5.29–5.71	Improvement of mental health	5.26 4.86–5.65
6	Improvement of mental health	6.04 5.87–6.20	Reduction of carer burden	5.93 5.79–6.07	Resolution of assessed problems	5.77 5.51–6.04	Patient satisfaction with care	5.43 5.03–5.83
7	Resolution of assessed problems	6.39 6.17–6.61	Resolution of assessed problems	6.12 5.97–6.27	Reduction of carer burden	6.10 5.84–6.37	Improvement of physical function	5.83 5.42–6.25
8	Reduction of carer burden	6.45 6.27–6.64	Improvement of mental health	6.39 6.26–6.52	Effective treatment of illness	6.22 5.87–6.57	Improvement of social functioning	7.17 6.79–7.55
9	Efficient use of resources	7.83 7.67–8.00	Efficient use of resources	7.50 7.37–7.62	Efficient use of resources	8.15 7.95–8.35	Effective treatment of illness	7.41 6.95–7.87
10	Improvement of social functioning	8.80 8.62–8.98	Improvement of social functioning	8.69 8.56–8.82	Improvement of social functioning	8.20 7.95–8.44	Efficient use of resources	7.43 7.04–7.81
11	Avoiding institutional care	10.28 10.15–10.42	Avoiding institutional care	10.24 10.14–10.34	Avoiding institutional care	10.31 10.13–10.50	Avoiding institutional care	9.97 9.71–10.23
12	Reduction of mortality	10.56 10.37–10.76	Reduction of mortality	10.49 10.36–10.62	Reduction of mortality	10.85 10.67–11.04	Reduction of mortality	10.92 10.66–11.17

CI, confidence interval.

**Table 3**  
Health Care Recipients' Priorities for Health Care Outcome

Rank Order	Community-Dwelling Older Adults (n = 2637)		Family Members of Patients With Dementia (n = 333)		Patients in Geriatric Outpatient Clinics (n = 512)		Adult Day Care Participants (n = 795)	
	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI
1	4.23	4.11–4.36	3.04	2.76–3.32	2.79	2.58–3.00	3.64	3.42–3.86
2	4.56	4.44–4.67	4.49	4.19–4.78	4.06	3.84–4.29	4.33	4.11–4.55
3	5.24	5.13–5.36	5.11	4.76–5.45	5.46	5.19–5.73	5.40	5.18–5.63
4	5.88	5.76–5.99	5.29	4.98–5.61	5.52	5.28–5.77	6.08	5.86–6.30
5	5.91	5.76–6.05	5.53	5.24–5.82	5.81	5.58–6.04	6.12	5.88–6.37
6	6.26	6.15–6.36	5.80	5.48–6.13	5.97	5.66–6.28	6.38	6.17–6.58
7	6.36	6.23–6.49	5.98	5.69–6.27	6.17	5.93–6.42	6.44	6.24–6.64
8	6.81	6.70–6.92	6.01	5.70–6.31	6.72	6.47–6.96	6.45	6.26–6.65
9	6.91	6.81–7.02	7.49	7.21–7.76	7.46	7.24–7.69	6.57	6.36–6.77
10	7.44	7.32–7.56	9.17	8.90–9.45	8.42	8.18–8.65	8.22	8.03–8.42
11	8.43	8.31–8.56	9.86	9.60–10.12	9.39	9.16–9.62	8.61	8.41–8.81
12	9.98	9.87–10.08	10.23	9.99–10.48	10.22	10.00–10.44	9.75	9.55–9.95

CI, confidence interval.

groups indicated physicians' strong preference for this item. All the physician groups also considered "patient satisfaction," "maintaining a high level of activity," and "improvement of physical function" important after "improvement of quality of life," with some variation in the order of their preferences. Geriatricians ranked "effective treatment of illness" the third most important, in contrast to the other two physician groups that ranked this item lower. Adult day care staff ranked "improvement of quality of life" and "maintaining a high level of activity" first and second, respectively, but placed "reduction of carer burden" the third most important, unlike physicians.

With regard to the receiving side of health care, "effective treatment of illness," "improvement of physical function," and "reduction of carer burden" were given high priority, whereas "improvement of quality of life" tended to be perceived as less important.

All the groups, including both health care providers and recipients, ranked "reduction of mortality" the least important, followed by "avoiding institutional care," "improvement of social functioning," and "efficient use of resources," except for the adult day care staff who ranked "improvement of social functioning" higher than "effective treatment of illness."

Stratification analysis demonstrated that the results from physicians were not influenced by sex (male vs female, data not shown); however, physicians older than 60 years tended to rank "effective treatment of illness" and "improvement of physical function" higher compared with younger physicians, who appeared to prioritize "patient satisfaction" and "maintaining a high level of activity." Physicians with more than 30 years' experience, most of whom were older than 60 years, showed a similar tendency, prioritizing "effective treatment of illness" and "improvement of physical function." The results from adult day care staff were identical across groups stratified by age, years of experience, and qualification (data not shown).

The results from the health care recipients did not differ by nursing care level (relatively independent vs limited impairment or higher, or limited impairment vs needing extensive help or higher) for adult day care participants and patients in geriatric outpatient clinics, the existence of relatives who required nursing care (present vs absent) for patients in geriatric outpatient clinics, study site for patients in geriatric outpatient clinics and community-dwelling older adults, or sex for all health care recipient groups (data not shown). Although stratification by age showed that the three measures given highest priority were the same across the age groups (65 to 74 vs older than 75) in community-dwelling older adults, the younger group ranked "reduction of carer burden" first, whereas the older group ranked "effective treatment of illness" first (data not shown).

## Discussion

This study is, to our knowledge, the largest survey ever conducted to describe health outcome prioritization in geriatric medicine. We aimed to obtain a comprehensive picture of the views of those involved in decision-making processes in geriatric medicine and compare views between health care providers and recipients. We chose four groups each from providers and recipients that are considered relevant to our purpose. The mean response rate was close to 50%, which was good for a large-scale postal survey and ensured the representative nature of our respondents.

This survey demonstrated that there may be an important gap in health outcome prioritization between health care providers and recipients in geriatric medicine. All health care provider groups, notably physicians, expressed a strong preference for improvement in quality of life (QOL) as a priority of care, whereas health care recipients gave the highest priority to effective treatment of diseases and tended to put lower importance on QOL. In the context of clinical medicine, QOL is often used as a nonspecific, all-encompassing term to describe

nonmortality outcomes averaged over multiple domains (ie, physical, social, and psychological functioning and well-being). Consideration of QOL is essential for the selection of a treatment option, particularly when conditions are noncurative and chronic.<sup>15</sup> Therefore, it is not surprising that physicians who regularly see older patients with multiple chronic conditions consider QOL the most important health care outcome. On the other hand, the term QOL may not be familiar to many health care recipients, and we cannot exclude the possibility that QOL might be confused with other terms, such as standard of living.

Most health care recipients ranked effective treatment of diseases as the most important, suggesting that patients are concerned about their own particular symptoms rather than nonspecific QOL, arguing for efforts to examine the symptoms most concerning to patients. The high importance of effective treatment of diseases ascribed by health care recipients, but not physicians, also implies the significance of the often-neglected aspect of inappropriate prescribing in older adults: underuse of medication likely to be beneficial to older adults. Increased evidence has suggested that failure to prescribe indicated, beneficial medication is common in older adults,<sup>7,8,16</sup> and recent attempts to provide an explicit list of appropriate, indicated medication for older adults are justified.<sup>10</sup>

Interestingly, views on patient satisfaction were also different. All physician groups ranked patient satisfaction as the second top priority, whereas health care recipients considered this to be less important. This tendency has been demonstrated in a prior small study in England more than 15 years ago.<sup>12</sup> Recently, patient satisfaction has been increasingly used to measure health care qualities and compare health plans or physicians.<sup>17</sup> However, our finding may argue against the value of patient satisfaction as a performance measure in geriatric medicine, especially in light of recent evidence suggesting that higher patient satisfaction is accomplished at the sacrifice of increased use of health care resources and may not be directly associated with technical quality of care or improved outcome.<sup>17,18</sup>

We observed agreement on several items between health care providers and recipients. The importance of physical and mental function, such as maintaining activity or improving physical function, was expressed by both health care providers and recipients. This finding was consistent with prior studies in older adults with multiple chronic conditions<sup>12,19</sup> or terminal conditions,<sup>20,21</sup> suggesting that physical and mental function should be an essential factor to consider as a health care outcome in various care settings for older patients.

Reduction in mortality was given the lowest priority by all the groups in health care providers and recipients alike. This view is similar to that observed in previous studies.<sup>12,19</sup> This finding supports the contention that treatment interventions should be assessed in terms of reduced morbidity and improved QOL in addition to reduced mortality.

In this survey, respondents' characteristics, except age, had limited influence on their views on health outcome prioritization within each group. Geriatricians older than 60 years and community-dwelling adults older than 75 years gave higher priority to effective treatment of diseases compared with their younger counterparts. This suggests that health outcome priorities may not be stable, and can change as respondents age or differ from generation to generation. The cross-sectional design of our survey prevented us from separating the age effect from the secular trend, and further studies will be required to examine the time- or setting-dependent variability of health outcome prioritization.

This study has several limitations. First, although the average response rate was high for a postal survey, it was lower in physician groups than in health care recipient groups (26% to 48% vs 44% to 61%, Table 1). Thus, selection bias cannot be excluded. Second, it was not sure that health care recipients, particularly adult day care participants, correctly understood the study terminology. Third, some of the

items used in the survey were not mutually exclusive. Nevertheless, a similar trend in priorities of outcome measures according to either side of health care providers or recipients suggests that the overall results were not significantly affected by these limitations.

## Conclusion

We demonstrated that there was significant agreement and disagreement of health outcome prioritization between health care providers and recipients in geriatric medicine. Health care providers and recipients agreed on high priority for function and low priority for reduction in mortality, but there was obvious disagreement in how they perceived QOL, treatment effect, and patient satisfaction as goals of care. Such disagreement necessitates better communication between providers and recipients to reach goals of care that are mutually understandable and tailored to meet patients' specific needs. The low importance of reduction in mortality and patient satisfaction ascribed by health care recipients may question the value of these outcomes as a way to assess treatment interventions and quality of care. We propose that the priorities of health care outcomes and their differences between providers and recipients demonstrated in this study should be taken into account in the health care of older patients and the design of health care policies and research.

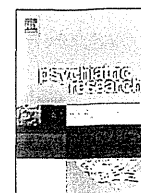
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## The high frequency of periodic limb movements in patients with Lewy body dementia

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### ABSTRACT

**Background:** Although dementia with Lewy bodies (DLB) is the second most common form of neurodegenerative dementia after Alzheimer's disease (AD), the clinical diagnosis is frequently difficult. Because both REM sleep behavior disorders and Parkinson's disease also have alpha-synucleinopathy similar to DLB, and show an increase in periodic limb movements (PLM), we evaluated the association between DLB and PLM, which may serve as an additional information to differentiate AD and DLB.

**Methods:** Overnight polysomnographic recordings were performed for the inpatients in our hospital who were suspected to have dementia. The quality of sleep, oxygen-desaturation index and periodic limb movements were compared among the patients clinically diagnosed with DLB, AD or as having no dementia.

**Results:** Nine DLB patients, twelve AD patients and ten non-demented patients were enrolled in the study. The number of PLM during sleep per hour of total sleep time (PLMS index) was significantly higher in the DLB patients than the AD patients or the non-demented patients. No significant differences were found between the AD patients and the non-demented patients. To differentiate DLB from AD, a PLMS index of more than 15.0 had a sensitivity of 88.9% and a specificity of 83.3%.

**Conclusions:** The DLB patients exhibited a higher PLMS index than the AD patients, and this index could be clinically useful for the diagnostic differentiation of DLB from AD.

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### 1. Introduction

Dementia with Lewy bodies (DLB) is the second most common form of neurodegenerative dementia after Alzheimer's disease (AD), affecting 15–25% of elderly demented patients (McKeith et al., 1996). DLB is characterized by intracytoplasmic inclusions called Lewy bodies, which consist of filamentous protein granules composed of alpha-synuclein and ubiquitin. Although the pathological diagnosis of DLB can be made based on the observation of Lewy body deposit throughout the cortex and subcortical regions, this is not generally possible except during autopsy.

The clinical diagnostic criteria for DLB were first published in 1996 (McKeith et al., 1996), and were modified in 2005 (McKeith et al., 2005). The central or core symptoms in DLB are progressive cognitive decline, recurrent visual hallucinations, spontaneous features of parkinsonism, and fluctuating cognition. These diagnostic

criteria require a clinical evaluation by a trained neurologist and include few objective markers. Although Single Photon Emission Computed Tomography (SPECT) and <sup>123</sup>I-metaiodobenzylguanidine (MIBG) myocardial scintigraphy are useful in the differential diagnosis of DLB (Lobotesis et al., 2001; Colloby et al., 2002; Yoshita et al., 2001; Hanyu et al., 2006), these examinations are too expensive to be generally utilized.

DLB is frequently complicated with REM sleep behavior disorder (RBD) (McKeith et al., 2005; Boeve et al., 2001, 2003, 2007; Gagnon et al., 2006), which is characterized by an increase in periodic limb movements (PLM) (Fantini et al., 2002). Some reports have also indicated that there is an increase of PLM in patients with Parkinson's disease (PD) (Wetter et al., 2000; Lavault et al., 2009). In addition, both RBD and PD are alpha-synucleinopathies, similar to DLB.

The pathophysiology of PLM is not well understood. In addition to RBD and PD, some studies have also shown that advancing age is associated with PLM (Coleman et al., 1981; Ancoli-Israel et al., 1991). Furthermore, Rose et al. have suggested that there is an increase of PLM in severely demented patients (Rose et al., 2011).

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However, these hypotheses have not yet been systematically studied, and no controlled data have been published to date.

We hypothesized that the patients with DLB would exhibit a higher frequency of PLM compared to the demented patients with AD, and evaluated the usefulness of PLM measurement as a novel tool for the differential diagnosis of dementia. As a result, we observed that patients with DLB exhibited a significantly higher PLMS index compared to patients with AD.

## 2. Methods

### 2.1. Subjects

The study population was comprised of the consecutive inpatients of the Department of Geriatric Medicine at the University of Tokyo Hospital, who were admitted for the evaluation of progressive cognitive impairment. The patients underwent neuropsychological assessments, including the Mini-Mental State Examination (MMSE), Frontal Assessment Battery and Clock Draw Test. They also underwent blood tests and neuroimaging tests, such as Magnetic Resonance Imaging (MRI) and SPECT. The diagnosis was made at a consensus conference of physicians and neurologists, based on the clinical diagnostic criteria for DLB proposed by McKeith et al. in 2005 (McKeith et al., 2005), and the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's disease and Related Disorders Association (NINCDS-ADRDA) (McKhann et al., 1984). The patients with probable DLB and possible DLB were included in the DLB group. The non-demented group comprised the patients who did not fit the criteria for dementia in the medical and neurological examinations. Patients with cognitive impairments other than AD or DLB (e.g., normal pressure hydrocephalus, vascular dementia) were excluded from the study.

From November 2010 to September 2011, 43 patients were enrolled in this study. We excluded the 4 patients whose recorded total sleep time was less than two hours. In addition, we excluded five patients who were taking antipsychotics, antidepressants, levodopa, dopamine-agonists and clonazepam, for those drugs could have some effect on the PLM.

The study was approved by the institutional review board of the Graduate School of Medicine, University of Tokyo, and written informed consent was obtained from all participants before the study.

### 2.2. Polysomnography

The patients underwent overnight polysomnographic recordings in the inpatient ward. Thirty of the 31 patients underwent polysomnography at least three days after admission. The remaining patient, who was in the non-demented group, underwent polysomnography on an adaptation night. The recordings included two electroencephalogram (EEG) leads (C3–A2 and O2–A1), an electrooculogram (EOG) and submental electromyogram (EMG). Nasal and oral thermistor channels, arterial oxygen saturation (finger oximetry) and an EMG of both anterior tibialis muscles were also monitored (Somnotrac Pro, CareFusion, USA). All sleep recordings were scored visually by an experienced rater according to the standard criteria (Iber et al., 2007).

PLM were scored during sleep in accordance with international scoring rules (Zucconi et al., 2006). PLM were defined as four or more consecutive leg movements, which lasted 0.5–10 s, the interval of which was 5–90 s. Leg movements following apneas or hypopneas were excluded. Respiratory events were scored according to AASM guidelines (Iber et al., 2007). Sleep apneas were defined as complete cessation of airflow >10 s. Hypopneas

were defined as a reduction  $\geq 50\%$  in airflow plus  $\geq 3\%$  drop in SpO<sub>2</sub> and/or a micro arousal. The apneas-hypopneas index (AHI) was calculated as the number of apneas and hypopneas per sleep hour. In some patients who removed the airflow sensor, oxygen desaturation of 3% or more was substituted to exclude the leg movements associated with breathing disorders and to calculate the AHI. Sleep efficiency, which was defined as the ratio of total sleep time to time in bed, was also calculated.

The number of PLM during sleep per hour of total sleep time (the PLMS index), the apneas-hypopneas index and the number of occasions of oxygen desaturation of 3% or more per hour of total sleep time (3%ODI) were calculated.

The patients who had REM sleep without atonia on polysomnography and had a history of harmful behaviors in sleep were diagnosed with RBD according to the diagnostic criteria (Iber et al., 2007).

### 2.3. Statistical analysis

The distribution of data was examined using the Shapiro–Wilk test. If data were normally distributed, a one way analysis of variance with Games–Howell post-hoc tests were applied for group comparisons. If the data deviated significantly from normality, the Kruskal–Wallis test was used, followed by evaluation with the Mann–Whitney *U* test for multiple comparisons, with the *p* values being corrected according to the Bonferroni method. The  $\chi^2$  test was used to compare categorical variables, such as gender and the number of RBD patients.

The diagnostic cutoff points for the PLMS index to discriminate between DLB and AD were estimated for each outcome by maximizing the Youden index. The discrimination ability was assessed by the area under the curve (AUC). Using this threshold, the sensitivity and specificity were calculated.

All of the statistical analyses were performed using the SPSS software program (version 19.0, SPSS inc., Chicago). Statistical significance was defined as *p* values < 0.05.

## 3. Results

### 3.1. Patients

Nine patients with DLB, twelve patients with AD and ten non-demented patients were enrolled in the study. Among the nine patients in the DLB group, five patients had probable DLB and four patients had possible DLB. The diagnoses in the four possible DLB patients were all supported by the typical findings in SPECT; generalized low uptake, reduced occipital activity, and relatively preserved hippocampal blood flow. In addition, three of the four possible DLB patients underwent MIBG myocardial scintigraphy and all showed low uptake. Table 1 shows the characteristics of the subjects. The age, sex distributions, and renal function were not significantly different among the three groups. No significant difference was found between the DLB group and the AD group (*p* = 0.337) in the MMSE. The use of medications for hypertension, hyperlipidemia and diabetes mellitus were similar between the groups. Two patients in the DLB group, two patients in the AD group and no patients in the non-demented group had taken donepezil. None of the patients fit the diagnostic criteria for restless legs syndrome (Allen et al., 2003).

### 3.2. Findings of polysomnography

The sleep and respiratory measurements are shown in Table 2. There were no significant differences in the percentage of Stage N3 or the percentage of REM sleep among the three groups. As

**Table 1**  
Characteristics of DLB patients, AD patients and non-demented patients.

Characteristics	DLB patients	AD patients	Non-demented	p value
Number of subjects	n = 9	n = 12	n = 10	
Age (years)	82.9 ± 5.9	80.9 ± 6.2	79.1 ± 4.5	n.s.
Sex (men/women)	4/5	3/9	3/7	n.s.
MMSE	22.4 ± 3.5	20.3 ± 3.3	27.8 ± 2.1	<0.001*
Serum creatinine (mg/dl)	0.74 ± 0.27	0.74 ± 0.22	0.67 ± 0.15	n.s.
Hypertension	3 (33.3)	4 (25.0)	5 (50.0)	n.s.
Hyperlipidemia	1 (11.1)	1 (8.3)	1 (10.0)	n.s.
Diabetes mellitus	1 (11.1)	1 (8.3)	3 (30.0)	n.s.

Values expressed as mean ± standard deviation or number (%). \* = one way analysis of variance with Games-Howell post-hoc tests: DLB vs AD  $p = 0.337$ , DLB vs non-demented  $p = 0.005$ , AD vs non-demented  $p < 0.001$ . AD = Alzheimer's disease; DLB = Dementia with Lewy bodies; MMSE = Mini-mental State Examination; n.s. = not significant.

expected, the prevalence of RBD was significantly higher in the DLB group compared to the AD group or the non-demented group ( $p = 0.004$ ). The AHI and 3%ODI was slightly higher in the AD group compared to the DLB group and the non-demented group, but the difference was not statistically significant.

The observed PLMS indices are shown in Fig. 1. The patients in the DLB group had a significantly higher PLMS index compared to the patients in the AD group and those in the non-demented group. No significant differences in the PLMS index were found between the AD group and the non-demented group. The PLMS indices of the four DLB patients with RBD were 27.8, 147.8, 43.7 and 149.3, respectively. After the exclusion of these four DLB patients with RBD, there was also a statistically significant difference in the PLMS index between the patients with DLB and AD ( $p = 0.025$ ). To discriminate DLB patients from AD patients using the PLMS index, the most favorable diagnostic threshold was found to be 8.0 (AUC = 0.926). This threshold had a sensitivity of 100% and a specificity of 75.0%. A PLMS index of more than 15.0 had a sensitivity of 88.9% and a specificity of 83.3%.

#### 4. Discussion

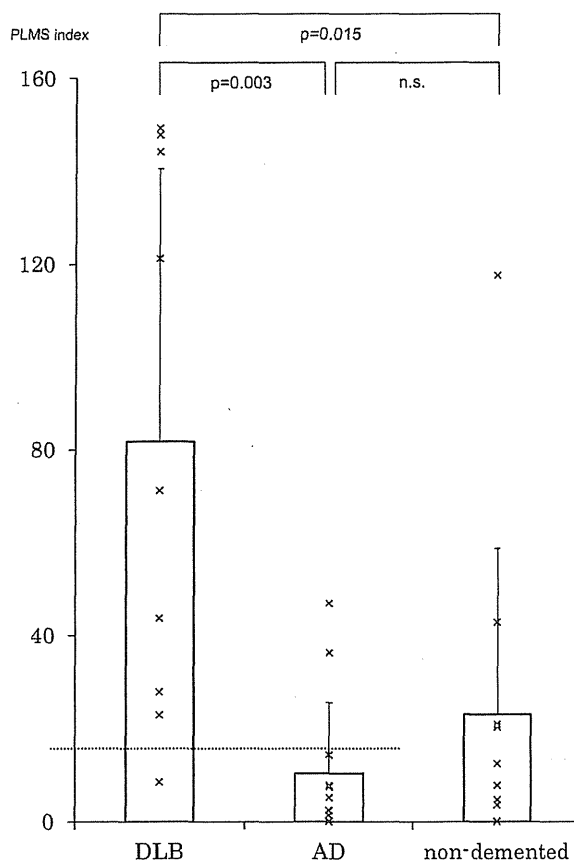
In this study, we first observed that patients with DLB exhibited a significantly higher PLMS index compared to patients with AD.

Although the pathophysiology of PLM is not well understood, a decrease in dopaminergic activity is reported to be associated with PLM (Wetter et al., 2000; Desseilles et al., 2008; Staedt et al., 1995; Hening et al., 2004). Because abnormalities of the

**Table 2**  
Sleep measures and respiratory measures of DLB patients, AD patients and non-demented patients.

Polysomnography	DLB patients	AD patients	Non-demented	p value
Total sleep time (min)	283.3 ± 105.8	360.3 ± 89.1	341.8 ± 70.5	n.s.
Stage N1 (%TST)	40.6 ± 12.6	29.9 ± 13.4	29.6 ± 16.5	n.s.
Stage N2 (%TST)	41.0 ± 9.4	50.5 ± 9.5	47.8 ± 12.8	n.s.
Stage N3 (%TST)	3.6 ± 4.9	6.5 ± 4.8	7.4 ± 6.1	n.s.
REM (%TST)	14.8 ± 10.2	13.1 ± 7.8	15.3 ± 8.4	n.s.
Sleep efficiency (%)	75.5 ± 14.3	76.3 ± 8.6	76.5 ± 12.5	n.s.
Sleep onset latency (min)	25.9 ± 23.9	22.2 ± 25.8	21.8 ± 16.5	n.s.
Wake time (min)	96.8 ± 74.4	112.2 ± 44.1	104.1 ± 53.0	n.s.
AHI	11.1 ± 10.5	15.0 ± 12.8	13.8 ± 14.8	n.s.
3%ODI	11.0 ± 11.1	15.2 ± 14.6	13.4 ± 14.3	n.s.
RBD (No. of patients)	4	0	0	0.004*

Values expressed as (mean ± standard deviation). \* = Significant differences with the  $\chi^2$  test ( $p = 0.004$ ). AD = Alzheimer's disease; DLB = Dementia with Lewy bodies; TST = Total sleep time; REM = Rapid eye movement; AHI = apnea hypopnea index; ODI = oxygen desaturation index; RBD = REM sleep behavior disorder; n.s. = not significant.



**Fig. 1.** Individual values for the periodic limb movements during sleep (PLMS) index in DLB patients, AD patients and non-demented patients. The boxes indicate mean and the vertical bars represent standard deviation; DLB = 81.8 ± 58.8, AD = 10.3 ± 15.3, non-demented = 23.0 ± 35.7. Mann-Whitney *U* test for multiple comparisons with the *p* values being corrected according to the Bonferroni method; significant differences in DLB vs AD ( $p = 0.003$ ) and DLB vs Control ( $p = 0.015$ ). The dashed line indicates the diagnostic threshold of the PLMS index of 15.0 between DLB and AD. This threshold had a sensitivity of 88.9% and a specificity of 83.3%. PLMS = periodic limb movements during sleep; AD = Alzheimer's disease; DLB = dementia with Lewy bodies; n.s. = not significant.

nigrostriatal dopaminergic pathway are also present in DLB patients, they would also be expected to exhibit a high frequency of PLM as a result of the decrease in dopaminergic activity (Walker et al., 2007; Walker and Walker, 2009).

We also found a high prevalence of RBD in patients with DLB, as indicated previously (McKeith et al., 2005; Boeve et al., 2001, 2003). RBD is now recognized to be a manifestation of various alpha-synucleinopathies, including DLB (Boeve et al., 2007; Claassen et al., 2010), and is also frequently complicated with an increase in PLM (Fantini et al., 2002; Manconi et al., 2007). These findings suggest the presence of strong pathophysiological associations among the DLB, PD, RBD and PLM through a common central nervous system degenerative process.

Several studies have shown an increase in the PLM frequency with advancing age (Coleman et al., 1981; Ancoli-Israel et al., 1991). Bliwise et al. reported a mean PLMS index during sleep of 20.6 in elderly individuals (Bliwise et al., 1988), which was compatible with our findings in the non-demented group. The clinical use of the PLMS index as a biomarker has not been anticipated, perhaps because of the high frequency of PLM in the elderly. However, our findings indicated that the PLMS index of the DLB patients was still higher than that of elderly patients without dementia, and

furthermore, the distribution of the PLMS index was more clearly separated between the DLB patients and AD patients, likely because the non-specific variability of the PLM frequency would be overcome by the effects of predominantly progressing specific neurodegeneration in these patients.

In this study, we also compared the PLMS index between the AD group and non-demented group. No significant differences were found, but the PLMS index in the AD patients tended to be lower than that in the non-demented group. These findings might also be a characteristic feature of AD, otherwise it can not be ruled out whether the small sample size may account for a random bias with quite low PLMS indices in the AD group. Therefore, the relevance and phenomenology of PLMS especially in AD, but also in DLB has to be addressed in further studies.

Currently, DLB and AD are diagnosed according to their respective clinical diagnostic criteria (McKeith et al., 2005; McKhann et al., 1984), and their differentiation are frequently difficult. Our findings suggested the usefulness of the PLMS index to discriminate patients with DLB from those with AD. While the utilization of SPECT and MIBG myocardial scintigraphy are limited to well-equipped hospitals, simplified mobile device for the measurement of PLM (Sforza et al., 2005) is expected to perform the examination for more outpatients with dementia in clinical practice.

There are several limitations to the present study. First, we included the patients with possible DLB and probable DLB in the same DLB group. And we also did not make a pathological diagnosis of DLB or AD, which remains to be reported even in MIBG myocardial scintigraphy for the diagnosis of DLB. A prospective investigation on the course of the PLM index and cognitive impairment, including the eventual pathological diagnosis, should be examined in a future study. Second, the number of patients in each group was relatively small. However, our data indicate that there is a significant correlation between DLB and PLMS, and the data may provide a first hint for a difference between AD and DLB on the PLMS index. Third, the data for this study did not include objective or subjective measures of daytime sleepiness or day–night schedule. In the future study, an additional investigation involving a larger number of subjects should be performed.

In conclusion, we found that DLB patients exhibit a higher PLMS index than AD patients, and this index may be clinically useful in the diagnostic differentiation of DLB from AD.

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The funding source had no involvement in the study, design, analysis, interpretation or decision to submit this work.

#### Contributors

Shinichiro Hibi was involved in design, analysis, interpretation, and drafting of article. Yasuhiro Yamaguchi was responsible for conception, design, analysis, interpretation, and drafting of article. Yumi Umeda-Kameyama and Katsuya Iijima were involved in design. Toshimitsu Momose was involved in analysis. Hiroshi Yamamoto, Masahiro Akishita, and Yasuyoshi Ouchi were involved in design and interpretation. All authors had full access to the data and take responsibility for its integrity and the accuracy of the analysis.

#### Conflict of interest

All authors declare that they have no conflicts of interest.

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