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特集 ■ 前頭側頭葉変性症

FTLD 患者への対応

Care for the Patients with Frontotemporal Lobar Degeneration

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Abstract

In frontotemporal lobar degeneration (FTLD), which primarily involves the front of the brain, characteristic psychiatric symptoms and disordered behaviors, such as disinhibition and stereotypical behaviors, often appear in the foreground at the initial stages of the disease. It is therefore an extremely difficult disease to treat. However, unlike diseases such as Alzheimer's disease, which involve general dementia, there is a clear dissociation between the conserved and disordered functions; therefore, it is possible to enhance the conserved functions and simultaneously modify the disordered functions into adaptive behaviors in order to provide care and increase the quality of life (QOL). In this paper, we report the use of routinizing therapy, which is an occupational therapeutic approach, involving speech therapy for semantic dementia (SD), drug therapy for stereotypic behaviors and psychiatric symptoms of FTLD, family education, etc.

Key words : frontotemporal dementia, semantic dementia, stereotypic behavior, routinizing therapy, care

はじめに

認知症における記憶・言語・視空間認知などの機能低下は、日常生活ならびに社会生活上の障害をもたらすが、認知症に伴う精神症状や行動障害は、認知機能の低下を加速させ、より広範な生活上の障害となり、家族や介護者にとっての大きな負担となる。脳の前部部に主病巣を有する前頭側頭葉変性症 (frontotemporal lobar degeneration : FTLD) では、脱抑制や常同行動などの特徴的な精神症状や行動障害が病初期から前景に立つことが多く、そのため最も処遇の困難な疾患と考えられている¹⁾。しかもこれらの行動上の破綻は家庭での介護のみならず、入院や施設内ケアの場面においても甚だしい困難をもたらす。

しかし、Alzheimer 病のような全般性の認知機能低下をきたす疾患とは異なり、保たれる機能と障害される機能の乖離が鮮明で、保たれている機能を強化すると共に、

障害された機能である症状さえも、それを適応的な行動に変容させるといった対応で、QOL を高めるケアを実施することが可能である。

本稿では FTLD の行動特性を生かした作業療法的アプローチであるルーティン化療法や環境調整、家族教育、側頭葉に病変の主座を有し語義失語を呈する意味性認知症 (semantic dementia : SD) に対する言語療法、FTLD の常同行動や精神症状に対する薬物療法について、自験例に基づき報告する¹⁾。

I. 症状を利用したケア^{2,3,4)}

多様な前方症状がみられる FTLD 患者の主にデイケアや入院における作業療法を用いたケアについて、特有の前方症状の利用、保たれている機能の活用、環境設定の3点から考える。

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1. 前方症状の利用

1) 被影響性の亢進の利用

被影響性の亢進という症状は活動の開始や導入、気分の切り替えに有効である。立ち去り行動が目立つ症例であっても、同時に被影響性も亢進している場合が多く、作業活動の導入時や作業活動の途中で立ち去り行動の防止策として利用可能である。

FTLDの立ち去り行動を軽減させるためには、視覚的に理解しやすいことが重要で、導入の際にすぐ取り掛かれるように目の前に道具などを準備しておく。これは、道具へうまく注意を向けさせると、作業開始への導入が不要となるからである。また、作業活動の途中で立ち去り行動がみられたときは、道具を手渡したり、道具をみせて声をかけたりして、再びその道具に注意喚起を促すことで、作業の継続が可能となる。

言語指示や強引な誘導を行うと理解困難から拒絶反応を示し、逆に立ち去り行動を誘発してしまう。作業活動の材料や道具にうまく注意を引きつけ、亢進した被影響性を利用して自然な形で作業の継続を促すアプローチが有効と考えられる。

進行期に自発性の低下が目立ってくると、食事時、食物をずっと咀嚼し続け嚥下しないまま口腔内に溜め込んでしまうようになる。促さなければ昼食の最後の一口が夕食時にまで口腔内に残ってしまうこともある。咀嚼や嚥下機能に問題はないため保続と自発性低下による症状と考えられるが、こういった症状が目立ってくると食事に時間や介助を要し、それが患者の興奮や抵抗につながったり、長時間口腔内に食物が残るため誤嚥性肺炎や齲歯のリスクにもなる。

被影響性を利用して、コップに水分を少量ずつ継ぎ足し、口元にもっていけば飲水行為と共に食物を嚥下し、食事がスムーズに進む。食事の最後にも同様にすれば、食物が長時間口腔内に残ることを防ぐことが可能な場合もある。

2) 常同行動・保続の利用

なんらかの常同行動は初期から中期のFTLD患者においてほぼ全例にみられる²¹⁾。例えば、常同的周遊の途中にみられる無銭飲食や万引きのような社会生活上で問題となる行動がみられることも多い。そのようなときには短期入院や毎日型のデイケアの利用によって、それらの行動を断ち切り、そこで新たに形成される常同行動をより適応的な習慣に変容させることが重要である⁹⁾。

また、習慣化させようとする一連の行動が定着するような工夫も必要である。作業活動を習慣として定着させるには、活動内容についての段階付けが必要である。立

ち去り行動が激しいときには、落ち着いて作業ができず仕上がりが増えたりミスも出現しやすい。そのような状況下でスタッフからの指示や介助を受けると、余計に手を止め立ち去る頻度が高くなる。したがって最初は自由度が低く失敗が少なく、しかもそれほど労力をかけずに仕上がる作業が適している。

工程が理解できて作業に興味を示すようになり、立ち去り行動が軽減した段階で、少しずつ活動の枠を拡げ本人の趣味や保たれている手続記憶を利用した自由度の高い作業活動へと段階づけを行うことが望ましい。編物やカラオケなど本人の趣味を常同行動に組み入れた場合は、その習慣化はいつそう容易であり、本人の受け入れもよく、その行動に没頭する間の行動障害は減少し、家族の負担も軽減する。われわれはこれをルーティン化療法と名付け、多くのFTLD患者で実践し、効果をあげている⁶⁾。

3) 転導性の亢進・維持困難の利用

本来であれば立ち去り行動の原因ともなる症状であるが、易怒性が亢進し、急に興奮がみられたとき、あるいは作業活動を嫌がり拒否的になり始めたとき、活動中に盗食などの行動障害が起こったときには、スタッフが馴染みの歌を歌いかけたり、別の興味ある活動を促す。つまり、その場とは関連のない新奇な刺激を与えると、転導性が亢進しているため、興奮の原因となっている対象から、比較的容易に注意をそらせることが可能になる場合もある。

2. 保たれている機能の活用

1) エピソード記憶の活用

Alzheimer病と異なり、エピソード記憶が保たれていることはさまざまなケアを行ううえで有利である。担当の看護・介護スタッフや作業療法士を決め、一貫して同じ患者を受け持ちケアすることや、ケアや活動の場所を固定すれば、立ち去り行動や考え不精が目立つ例でも、馴染みの関係をつくるのが十分に可能である。記憶力が良好な初期から中期であれば、固定されたデイケアプログラムを覚えることも容易で、場所やスタッフに対する馴染みの関係が短期間に形成できる。

2) 手続記憶の活用⁷⁾

患者の職業歴、教育歴や趣味などから発症前に獲得されていたと考えられる手続記憶を探り出し、これを積極的に取り入れた作業を選択することで、導入時の患者のストレスを緩和でき、その遂行はいつそう容易となる。また作業の常同化に伴い、新たな手続記憶が獲得された例もある。

3) 知覚・運動機能・視空間認知機能の活用

前述した前方症状のケアへの利用の前提条件となるのが、FTLD 患者における知覚・運動・視空間認知などの脳の後方部の諸機能の保存である。このような諸機能の保存がさまざまな介入を可能にする一方、さまざまなケアが FTLD 患者の脳の後方機能を活性化し QOL を維持することに働いていると考えられる。

II. 食行動異常

FTLD 患者では初期から、甘いもの、味付けの濃い料理への嗜好の変化、大食、決まった少数の食品や料理に固執する常同的な食行動が目立つことが多い⁹⁾。FTLD の診断がついたときには、糖尿病を発症している例も多く、糖尿病性昏睡に至った例もあるため注意が必要である。

甘いコーヒー牛乳を1日数リットル飲んだり、アイスクリームを1日十数個食べるといったことが、常同行動として定着しているときは、前述のように短期の入院やショートステイによってコーヒー牛乳やアイスクリームから物理的に切り離すことも必要である。入院後それらのものが目に入らなければ、執拗にそれらのものを要求することはめったにみられない。その間に家庭環境を整え、退院・退所後は、目につく所にそれらの甘いものを置かない工夫も必要である。

進行期になると、口唇傾向がさらに強まる。盗食が目立ってきたり、食べ物でなくても目の前にあるものをなんでも口に入れたりするようになる。そのためこの時期には、異食や窒息には特に注意が必要である。

Alzheimer 病患者が異食する物は色味が鮮やかで、一見食べ物に見間違えやすい物が多いが、FTLD 患者が異食する物はオムツやウェットティッシュ、ストローの外袋、石鹸などさまざまである。異食を防止するために、必要以上に隔離や身体拘束時間が増加することを防ぐために、病棟や施設ではオムツ交換に使用する用具の管理や、食膳の取り扱いなどに工夫が必要である。

また、症状が進行し十分に咀嚼せず、次々と口に食事を詰め込むようになってきたときには、嚥下に問題がない場合でも、食事内容をより柔らかいものや刻み食に変更し、窒息を防ぐ必要がある。

III. 環境設定

1. 症状に配慮した環境設定

FTLD 患者の作業活動を妨げる最も大きな要因は立

ち去り行動にあると考えられる。そのため立ち去り行動の起こりにくい環境設定が大切である。被影響性の亢進、転導性の亢進がみられる FTLD 患者では、些細な物音でも作業が中断し、立ち去り行動につながる。立ち去り行動が顕著な症例では、作業の導入時にほかからの刺激ができるだけ少ない環境を設定し、その作業に没頭できるように工夫したほうが、活動を定着させやすい。

例えば、部屋のドアから聞こえる物音や他患者がドアノブを回す音などにも反応し、注意が途切れ作業が中断し、立ち去り行動に至る。そのため、ドアに近い場所で作業を行うときにはドア側にケアスタッフが座り、外部からの刺激を遮断するだけでも、立ち去り行動は明らかに減少する。加えて頻回の立ち去りや作業の中断にタイミングよく対応する必要性を考慮すると、導入時は集団活動よりも個別の対応が望ましい。立ち去り行動が著しい場合には、段階的に立ち去り行動を軽減させることが必要な場合もある。

施設や病棟では部屋のドアが開いているとその刺激につられて、他患者の部屋に入り、そのベッドで臥床してしまうため、他患者とトラブルになることもある。そのような場合、部屋のドアを閉めておく（施錠するのではなく）だけで他患者の部屋へ入室する頻度は明らかに減少し、トラブルを防ぐこともできる⁹⁾。

2. グループホームケア

藤沢ら¹⁰⁾は FTLD 患者に対して、グループホームにおいて、患者の過去の生活習慣を反映した家庭的環境を提供し、生活者としての個性を尊重した個人中心のケアを実践している。入所者には料理、食事、お茶の時間、散歩、買い物といった、日常生活に当たり前の活動を勧めている。それによって、向精神薬の減量が可能になり、不安、抑うつ、無関心、易刺激性、異常行動が改善したと報告している。

IV. SD に対するケア

SD の呈する進行性の失語症状に対して、言語のリハビリテーションが試みられている。いずれも1年以上にわたって、意味的なカテゴリーが共通の語を線画などと組み合わせて、再学習ないし新たに学習させることを試みている。Graham ら^{11,12)}はカテゴリー別語産生課題を用いて、既に患者が自ら試みていた方略（カテゴリー別の多数のカラー線画とその名称でページが構成されている The Oxford English Picture Dictionary の名称部分を隠して各線画を呼称する練習）を援用して、リハビリ

テーションを行った。

われわれも伊藤ら¹³⁾の90単語指示呼称課題や地図を用いて、線画や県名・国名などの呼称と指示の訓練を行った。結果は訓練した語に関しては完全に呼称できるようになったものの、実際の生活における同種の対象物の呼称への般化(課題間般化)や同じカテゴリーに属する非訓練語への項目間般化はみられなかった。

再学習した語に関しても、Grahamら^{11,12)}の症例では辞書で学習した順番で語産生がみられ、われわれの症例でも疾患の進行に伴って線画の配置の順番でしか呼称できなくなった。また、Grahamら^{11,12)}の症例は十分な病識を有していたので、毎日の訓練によって、失語症を認識して抑うつ状態を呈した。

さらにわれわれは他の2症例に対して訓練前に呼称が可能であった語に限定して訓練を継続したが、病期の進行に伴って呼称可能な語は減少した。減少速度は明らかに遅くなった印象はあるものの、対照群との比較がなく、今後の検討が必要である。2例とも訓練前から脱抑制的な行動がみられ始めていたが、訓練開始後は、1日数時間自ら訓練に没頭するため精神的にも落ち着くというquality of life (QOL) 面での間接的効果は認められた。

現在もわれわれは数例のSD患者に対して、同様に伊藤ら¹³⁾の90単語指示呼称課題を用いて、在宅での訓練を継続して行っている。そのうちごく初期から言語訓練を開始することが可能であった1例を紹介する¹⁴⁻¹⁶⁾。

症例は訓練開始当時57歳であり、言語面で典型的な語義失語症状を呈するほかは、全般的な認知機能検査の成績は良好で、視空間認知の機能もよく保たれていた。頭部MRIで左側頭葉前方部に限局性の萎縮を認めた。

まず、毎日家庭で行う課題として、90単語課題の1カテゴリー(10単語)から線画の呼称・指示・書字の訓練を開始し、2週間後の受診時に学習された語の評価を行い、新たなカテゴリーを追加していった。隔週で10語ずつ段階的に学習語を漸増していったが、本例は毎日積極的に課題に取り組み18週後の時点では呼称・指示・書字ともにほぼ完全に習熟した。さらに、学習語の提示順序に依存した呼称や書字を行っていないかを点検するために、受診の際に自宅での学習時と異なる順序で評価を行った。訓練を継続し、毎回自宅学習時と異なる配置でカテゴリーを混合させた線画の提示に対しても、高い正答率を維持することができた。

また、書字では訓練開始時は平仮名のみの表記であったが、次第に漢字や片仮名の使用が増加し、病前には書くことがなかったと思われる複雑な漢字の使用が認められた。加えて、訓練開始後、自宅訓練時に自ら辞書を引

くという新たな習慣も形成されるようになった。本症例からはSDの初期例では言語訓練によって語彙の再獲得の可能性が示唆される。1日数時間の自宅での言語訓練は毎日の生活の中に常同行動として組み込まれた。そのため会社を退職後通所するようになったデイケアにも、当初は自ら言語訓練課題を持参し、自主的に個人活動時間に訓練を行うことができた。

症状は徐々に進行したものの、同時期から通院中のほぼ同じ重症度であったSD患者と比較して、自宅でもデイケアの場面でもFTLD特有の行動障害は少なく、介護負担の軽減という側面でも間接的な効果を認めた。

V. FTLD に対する薬物療法

FTLD患者に対しては有効な薬物療法はなく、興奮や暴力、行動障害に対して抗精神病薬の投与が余儀なくされてきた。しかし、認知症患者に対して抗精神病薬を使用することは、過鎮静、錐体外路系副作用などによって、activities of daily living (ADL) の低下や認知機能の悪化をきたし得る。

最近になってSwartzら¹⁷⁾によって選択的セロトニン再取り込み阻害薬(selective serotonin reuptake inhibitor: SSRI)が前頭側頭型認知症の脱抑制、常同行動、食行動異常に効果があると報告された。この研究は、前頭側頭型認知症の剖検脳でセロトニンレセプターの結合能が低下していることに基づき行われた後方視的研究であり、種々のSSRIが使用されている¹⁸⁾。

そこでわれわれは同様にオープン試験ではあるが、FTLD16例にフルボキサミンのみを用いた精神症状、常同行動に対する治療を行い、その効果を検討した¹⁹⁾。全般的な精神症状をthe Neuropsychiatric Inventory (NPI)²⁰⁾、FTLDに特徴的な常同行動をわれわれが開発したthe Stereotypy Rating Inventory (SRI)²¹⁾を用いてフルボキサミン投与後12週間で評価を行った。

Swartzらの報告と同様に脱抑制や行動障害で明らか改善がみられた。行動障害の改善内容の大部分はSRIで詳細に評価された常同行動であった。この結果からもFTLDの常同行動や脱抑制に対するフルボキサミンの有効性が示唆された²²⁾。また、相対的セロトニン再取り込み阻害薬であるトラゾドンについても、FTLDの焦燥、興奮、抑うつ、ならびに食行動異常に対する効果が報告されている²²⁾。一方、SSRIに属するパロキセチンでは、有効性について意見が分かれており、さらに研究の蓄積が必要である。

薬物療法は前述の作業療法などの非薬物療法との組み

合わせて使用するとより有効であると思われる。

VI. 家族教育

FTLDは、Alzheimer病や血管性認知症といった一般的な認知症の介護知識に基づき熱心に介護を実践しても、それらとの症状の違いに戸惑い、家族やスタッフがケアに行き詰まることが多い。そこでわれわれはFTLDの行動障害に関する最近の報告とわれわれの研究グループが実施してきたリハビリテーションやケアの試み、さらには疫学的なデータを加えて、啓発用冊子を作成した²³⁾。

冊子の内容に沿って具体的な指導を実施すると、介護者の疾患に関する理解が著しく深まるだけでなく、訪問相談や電話相談を通じて、ケアマネージャーやケアスタッフにFTLDの行動特徴やケアのポイントを伝えることも可能になり、在宅ケアを支援することができるようになった。また、訪問相談では、個々の患者の生活環境における危険因子を把握し、介入が必要な行動障害を抽出でき、利用可能な社会環境を提示することが可能になった。

例えば多くの認知症で出現する“徘徊”は在宅介護が困難になる大きな要因であり、介護者にとってそれを見守ることは大きな負担である。しかし記憶・見当識が比較的保たれ、常同的に行われるFTLDの“周遊行動”はAlzheimer病の“徘徊”とは異なり、ほぼ毎日同じコースを周り、症状がかなり進行するまで道に迷うことはない。周遊するコースの安全が確認されていれば、介護者がその都度同伴する必要はない。このようなことを介護者に理解してもらい、家族の同伴を中止すれば介護者の精神的・身体的負担感は軽減できる。

また自発性の低下が進行してくると、入浴を嫌がり、無理に勧めると興奮がみられるようになり在宅介護が困難になることも多い。それに対し今後の必要性を家族に説明し、入浴行為に問題がない病初期から、デイケア・デイサービスでの入浴を習慣化することを勧める。それによって自発性が低下してからも入浴が常同行動として定着し続け、長期間の在宅介護が可能になる場合もある。

おわりに

Alzheimer病に比べ、FTLDにおけるケアや薬物治療は確立したものが乏しいのが現状である。しかし、これまで述べたように種々の試みが実践されており、他の認知症疾患と同様に、初期からの適正な介入を行い、経

過中に出現する精神症状やさまざまな行動障害を疾患の特徴を踏まえて理論的に対処していくことで、これらの症状に伴う重い介護負担を軽減してゆくことが可能になり、ひいては患者と介護者のQOLの向上につながると考える。

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Relationship of frontal lobe dysfunction and aberrant motor behaviors in patients with Alzheimer's disease

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ABSTRACT

Background: In order to address the neuropsychological pathogenesis of aberrant motor behaviors in Alzheimer's disease (AD), we used a cross-sectional study design to investigate the association between frontal lobe function, including executive function, and activity disturbances (wandering, purposeless activities and inappropriate activities).

Methods: Among 75 consecutive outpatients with AD, 50 subjects with a Clinical Dementia Rating (CDR) score of 1 or 2 were selected and divided into two groups based on data obtained from interviews with their caregivers: an aberrant motor behaviors (AMB) group ($n = 22$), and a non-aberrant motor behaviors (NAMB) group ($n = 28$). Aberrant motor behavior was defined according to whether the "activity disturbance" score (ranging from 0 to 9) of the Behavioral Pathology in Alzheimer Disease (Behave-AD) scale was 0 or ≥ 1 . The total and subtest scores of the Frontal Assessment Battery (FAB) were then compared between the two groups.

Results: Significant differences were found between the FAB total ($P < 0.05$) and the subtest scores (lexical fluency, conflicting instructions; $P < 0.05$) in the two groups. The FAB score was significantly associated with the activity disturbance score ($r = -0.49$; $P < 0.001$). A stepwise multiple regression analysis showed that only the FAB score significantly influenced the activity disturbance score ($P < 0.001$).

Conclusions: This finding suggested that in addition to episodic memory disturbance, frontal lobe dysfunctions might lead patients with AD to develop aberrant motor behavior.

Key words: Frontal Assessment Battery, dementia, activity disturbances, wandering, executive function

Introduction

Alzheimer's disease (AD) is a progressive neurodegenerative disorder that is mainly characterized by episodic memory disorder, visuospatial impairment, attentional impairment, and executive dysfunction (Perry *et al.*, 2000; Baudic *et al.*, 2006). During the course of this disease, aberrant motor behaviors are reportedly observed as behavioral and psychological symptoms of dementia (BPSD) (Mega *et al.*, 1996; Devanand *et al.*, 1997).

The prevalence of aberrant motor behaviors is estimated to be in the range of 14–60% among patients with AD (Mega *et al.*, 1996; Devanand

et al., 1997; Liu *et al.*, 2004; Chiu *et al.*, 2006). On the other hand, the prevalence of aberrant motor behaviors among patients with frontotemporal lobar degeneration (FTLD) has been reported to be about 60–92% (Mendez *et al.*, 1998; Liu *et al.*, 2004; Chiu *et al.*, 2006).

Murman *et al.* (2002) reported that BPSD in patients with AD significantly increases the direct costs of care. In particular, aberrant motor behaviors in patients with dementia can create a distressful burden and cause suffering among caregivers, triggering or predicting nursing home placement (Donaldson *et al.*, 1997; Shinoda-Tagawa *et al.*, 2004; Scarmeas *et al.*, 2007). Thus, research on the etiology and treatment of these disturbances in patients with AD is urgently needed.

From a neuroanatomical aspect, the manifestation of aberrant motor behaviors in patients with neurodegenerative disease is associated with the right dorsal anterior cingulate cortex (dACC) and

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left premotor cortex in voxel-based morphometry (VBM) studies using magnetic resonance imaging (MRI) (Rosen *et al.*, 2005). However, a single-photon emission computed tomography (SPECT) study indicated that AD patients with wandering had a more severe decline in regional cerebral blood flow (rCBF) in the left parietal-temporal lobe (Rolland *et al.*, 2005).

From the neuropsychological perspective, previous studies have reported that behavioral problems or aberrant behaviors, such as wandering, purposeless activity and inappropriate activities, in patients with AD were significantly correlated with a decline in the Mini-mental State Examination (MMSE) score, which reflects global cognitive function (Folstein *et al.*, 1975; Devanand *et al.*, 1997; Harwood *et al.*, 2000). Moreover, in those studies, a positive correlation between the level of activities of daily living (ADL) and the severity of the aberrant motor behaviors in patients with AD was reported (Devanand *et al.*, 1997; Harwood *et al.*, 2000). Chiu *et al.* (2004) stated that behaviors that led to AD patients getting lost and beginning to wander might be caused not only by visuospatial impairments (O'Brien *et al.*, 2001), but also by executive and attentional dysfunction when navigating in unfamiliar environments. In another study, the severity and frequency of aberrant motor behaviors in patients with AD were associated with a decline in the scores of the behavioral assessment scale reflecting frontal lobe features (Engelborghs *et al.*, 2006).

For these reasons, the association between aberrant motor behaviors and cognitive impairment remains unclear, and the relationship between frontal lobe dysfunction and aberrant motor behavior is controversial. The Frontal Assessment Battery (FAB) is an easily administered test that can be completed at bedside within 10 minutes (Dubois *et al.*, 2000; Nakaaki *et al.*, 2007). Moreover, the FAB total and subtest scores differ significantly between FTLD and AD, but the MMSE scores do not; the ability of FAB to reflect frontal lobe function was previously confirmed in two studies examining different types of degenerative diseases (Slachevsky *et al.*, 2004; Lipton *et al.*, 2005). We previously reported that the manifestation of delusional thoughts in patients with AD was associated with a reduction in the FAB scores (Nagata *et al.*, 2009), reflecting executive function. However, the manifestation of aberrant motor behaviors has not been discussed as a cognitive aspect in conjunction with frontal lobe function. In the present cross-sectional study, we investigated the relationship between frontal lobe function and aberrant motor behavior using the FAB.

Methods

Participants

Seventy-five consecutive AD patients who had been referred to the Jikei University Kashiwa Hospital outpatient clinic were enrolled in this study. All the patients were diagnosed as having probable AD based on the National Institute of Neurology and Communicative Disorder and Stroke/Alzheimer Disease and Related Disorder Association (NINCDS/ADRDA) criteria (McKhann *et al.*, 1984). All diagnoses were made after an examination of the patients' past medical history, an evaluation of physical or neurological examinations, routine blood tests, and magnetic resonance imaging (MRI) findings by a geriatric psychiatrist (one of the four authors). The exclusion criteria were a history of alcohol or other substance abuse, brain injury, major depressive or psychotic disorder, epilepsy, delirium, metabolic disorder, or treatment with acetylcholine esterase inhibitor. Neuropsychological tests (FAB and MMSE) were administered by a clinical psychologist. To determine the severity of each patient's dementia, the geriatric psychiatrists used the Clinical Dementia Rating scale (global CDR scores ranging from 0 to 3, where 0 = normal; 0.5 = questionable; 1 = mild; 2 = moderate; 3 = severe) (Hughes *et al.*, 1982) while interviewing each patient's caregiver. To recruit patients with mild- or moderate-stage AD, we selected patients (N = 50) with a global CDR score of either 1 or 2. Patients with a global CDR score of either 0.5 or 3 were excluded from this study. The patients were divided into two groups: an aberrant motor behaviors (AMB) group, and a non-aberrant motor behaviors (NAMB) group. The manifestation of aberrant motor behavior was assessed based on information obtained from a structured interview with each patient's caregiver by the same geriatric psychiatrists, and the aberrant motor behaviors were rated using the "activity disturbance" score of the Behavioral Pathology in Alzheimer's Disease (Behave-AD) scale (Reisberg *et al.*, 1987). The four geriatric psychiatrists and clinical psychologist were experienced at performing neuropsychological and behavioral examinations, and the inter-rater validity of the scales was sustained by periodic discussions and exchanges of views. This study was approved by the Ethics Committee of the Jikei University School of Medicine.

Definition of aberrant motor behaviors

To determine whether the patients had aberrant motor behaviors, we used the activity disturbance scale of the Behave-AD (total behavioral or

psychological problems scale). This scale was completed based on the results of an interview with each patient's caregiver, who was asked whether the patient had experienced any of the following aberrant motor behaviors in the previous four weeks: (1) "wandering away from home or caregivers", (2) "purposeless activity", and (3) "inappropriate activity" (Reisberg *et al.*, 1987). The severity range of each score was from 0 to 3, and the range of the total activity disturbance score was from 0 (not present) to 9 points. If the total score was ≥ 1 point, the patient was classified in the aberrant motor behaviors (AMB) group. If the total score was 0, the patient was classified in the non-aberrant motor behaviors (NAMB) group.

FAB assessment

The Japanese FAB version consists of six subtests: (1) similarities (conceptualization); (2) lexical fluency (mental flexibility); (3) motor series (programming); (4) conflicting instructions (sensitivity to interference); (5) go - no go (inhibition control); and (6) prehension behavior (environmental autonomy) (Takagi *et al.*, 2002). Each subtest was rated from 3 to 0, with the total score ranging from 18 to 0.

Statistical analysis

SPSS 16.0J for Windows (SPSS Japan Inc) was used for all statistical analyses. To compare differences between the two groups, we used a one-way ANOVA with post-hoc testing for age, education (years), duration of illness (months), the MMSE total score, the CDR Scale sum of boxes (CDR SB: ranging from 0 to 18), the FAB total score, and the FAB subtest scores. The sex ratio (female to male) was assessed using a χ^2 test. Other behavioral or psychological problems (delusion, hallucination, and anxiety score of the Behave-AD subscale) were compared between the two groups

using a one-way ANOVA with Tukey post-hoc test. Pearson correlation coefficients were used to evaluate the associations between FAB or MMSE and the activity disturbance score (ranging from 0 to 9). Finally, a stepwise multiple regression analysis was performed to examine the contribution of age, sex, education, duration of illness, FAB total score, MMSE score and CDR SB score as independent variables of the activity disturbance score. A p value <0.05 was considered statistically significant.

Results

Patient characteristics

Fifty AD patients (11 males and 39 females; average age, 78.2 ± 7.1 years; range, 59–91 years) were classified as belonging to either the AMB group ($n = 22$) or the NAMB group ($n = 28$). These two groups were not significantly different with regard to the sex ratio ($\chi^2 = 1.601$; $df = 1$; $P = 0.206$), age ($F = 1.483$; $df = 1$; $P = 0.229$), duration of illness (months) ($F = 0.421$; $df = 1$; $P = 0.405$), education (years) ($F = 0.704$; $df = 1$; $P = 0.519$), MMSE score ($F = 3.350$; $df = 1$; $P = 0.074$), or CDR SB score ($F = 3.271$; $df = 1$; $P = 0.077$). However, the FAB total scores ($F = 7.044$; $df = 1$; $P = 0.011$) were significantly different between the two groups (Table 1). The mean \pm standard deviations (SDs) of the FAB scores were 12.3 ± 3.3 (NAMB) and 9.3 ± 4.5 (AMB). The two subscores of the FAB, lexical fluency ($F = 6.390$; $df = 1$; $P = 0.015$) and conflicting instructions ($F = 5.469$; $df = 1$; $P = 0.024$), were both significantly lower in the AMB group than in the NAMB group (Table 2). The mean \pm SDs of the lexical fluency scores were 1.86 ± 1.01 (NAMB) and 1.10 ± 1.09 (AMB), while those of the conflicting instrument scores were 2.71 ± 0.53 (NAMB) and 2.10 ± 1.26 (AMB).

Table 1. Subject characteristics (mean \pm SD)

GROUP	AMB (n = 22) (MEAN \pm SD)	NAMB (n = 28) (MEAN \pm SD)	χ^2 OR F SCORE	P VALUE
Sex (male/female)	3/19	8/20	1.601	0.206
Age	79.5 ± 6.6	77.1 ± 7.3	1.483	0.229
Education (years)	10.8 ± 3.4	11.6 ± 2.5	0.421	0.519
Duration of illness (months)	28.7 ± 18.3	24.2 ± 19.3	0.704	0.405
MMSE score	18.2 ± 5.3	20.3 ± 2.8	3.35	0.074
FAB score	9.3 ± 4.5	12.3 ± 3.3	7.044	0.011*
CDR SB	8.18 ± 3.20	6.80 ± 2.17	3.271	0.077

AMB = aberrant motor behavior, NAMB = non-aberrant motor behavior; CDR SB = Clinical Dementia Rating Scale sum of boxes (ranging from 0 to 18).

* $P < 0.05$ (ANOVA with post-hoc test).

The sex ratio was analyzed using the χ^2 test.

Table 2. FAB subtest scores (mean \pm SD)

SUBTEST	AMB (n = 22) (MEAN \pm SD)	NAMB (n = 28) (MEAN \pm SD)	F SCORE	P VALUE
Similarities	1.00 \pm 0.95	1.25 \pm 1.17	0.638	0.428
Lexical fluency	1.10 \pm 1.09	1.86 \pm 1.01	6.39	0.015*
Motor series	1.57 \pm 1.25	2.04 \pm 1.17	1.785	0.188
Conflicting instructions	2.10 \pm 1.26	2.71 \pm 0.53	5.469	0.024*
Go-no go	1.14 \pm 1.24	1.61 \pm 1.10	1.922	0.172
Prehension behavior	2.38 \pm 1.02	2.82 \pm 0.48	4.044	0.05

AMB = aberrant motor behavior; NAMB = non-aberrant motor behavior.

* $P < 0.05$ (ANOVA with post-hoc test).

Table 3. Stepwise multiple regression analysis for activity disturbance scores of Behave-AD

VARIABLE	B	SE	β	t value	P VALUE
Constant	2.856	0.512		5.577	$P < 0.001$
FAB	-0.18	0.43	-0.522	-4.156	$P < 0.001$

Stepwise multiple regression analysis of FAB score, age, sex, education, duration of illness, MMSE score, and CDR sum of boxes for activity disturbance scores (N = 50).

B = partial regression coefficient; SE = standard error; β = standardized partial regression coefficient.
R = 0.522, R² = 0.273.

Other behavioral and psychological problems including delusion, hallucination and anxiety in the two groups

We also compared other behavioral and psychological problems that might have influenced the aberrant motor behaviors between the AMB group and the NAMB group. The two groups were not significantly different with regard to the delusion score ($F = 0.473$; $df = 1$; $P = 0.495$), the hallucination score ($F = 1.874$; $df = 1$; $P = 0.177$), or the anxiety score ($F = 2.016$; $df = 1$; $P = 0.162$) of the Behave-AD subscales.

Contribution of age, sex, education, duration of illness, FAB total scores, MMSE scores and CDR sum of boxes scores to the severity of aberrant motor behaviors

The FAB score was significantly correlated with the activity disturbance score ($r = -0.490$; $P < 0.001$) and the MMSE score ($r = 0.670$; $P < 0.001$). The MMSE score was also significantly correlated with the activity disturbance score ($r = -0.317$; $P < 0.001$). A stepwise regression analysis showed that the FAB score significantly affected the activity disturbance score ($P < 0.001$; R² = 0.273) (Table 3).

Subtypes of aberrant motor behaviors

Although 22 patients had experienced aberrant motor behaviors, several types overlapped in one patient. Purposeless activity (e.g. opening and closing a pocketbook, packing and unpacking clothing, repeatedly putting on and removing clothing, insistently repeating demands or questions) was the most frequently reported aberrant motor behavior (N = 15). Inappropriate activity (e.g. storing and hiding objects in inappropriate places, throwing clothing in a waste basket or putting empty plates in the oven; inappropriate sexual behaviors such as inappropriate exposure) was reported in 13 patients, while wandering was reported in three patients.

Discussion

The results indicate that the FAB total score in patients with AD was significantly related to the presence of aberrant motor behaviors. While the MMSE total score reflects global cognitive function weighted on orientation and memory function (Folstein *et al.*, 1975), the FAB has been confirmed to reflect executive function and working memory in patients with FTLD (Dubois *et al.*, 2000; Nakaaki *et al.*, 2007). Moreover, the FAB total and subtest scores significantly differ between FTLD and AD, emphasizing the validity of using the FAB to reflect frontal lobe function (Slachevsky *et al.*, 2004; Lipton *et al.*, 2005; Nakaaki *et al.*, 2007). The FAB was also shown to be a valid frontal function test in a SPECT study (Yoshida *et al.*, 2009), with a positive correlation observed between the left callosomarginal and precentral rCBF.

Some previous studies have reported that global cognitive and functional impairments in AD patients are associated with several BPSD, including aberrant motor behaviors (Mega *et al.*, 1996; Devanand *et al.*, 1997; Harwood *et al.*, 2000). Although some studies have indicated that aberrant motor behaviors are associated with cognitive or ADL decrements, only a few studies

have indicated an association between frontal lobe function and aberrant motor behavior (Swanberg *et al.*, 2004; Engelborghs *et al.*, 2006). In the present study, the activity disturbances score was significantly correlated with the MMSE score ($r = -0.317$; $P < 0.001$), but a stronger correlation ($r = -0.490$; $P < 0.001$) and association with the FAB was revealed using a statistical regression analysis. Among several aspects of neurocognitive dysfunction, we were particularly interested in the association between frontal lobe dysfunction and aberrant motor behavior from a neuropsychological aspect.

The FAB subtests (lexical fluency, conflicting instructions) were significantly lower in AD patients with aberrant motor behavior. Dubois *et al.* (2000) described that in the lexical fluency task, patients needed the ability to recall as many words as possible starting with a given letter within a limited number of seconds. Such literal fluency tasks also require self-organized retrieval from semantic memory and flexible behavioral adaptations to new situations (Dubois *et al.*, 2000). Therefore, the aberrant motor behaviors, including wandering or inappropriate activity, might be caused by an inability to react flexibly with variable stimuli in their environment. The conflicting instructions subtest resembles the Stroop test task and requires the ability to perform a contrary reaction to each of two pattern directions effectively (Dubois *et al.*, 2000). In patients with AD, in addition to memory disorders and visuospatial impairments, the lack of such self-correction in executive functions might particularly cause impairments in their ability to carry out these tasks efficiently, leading to wandering, inappropriate activity or purposeless activity resembling stereotypical behaviors as a result. Moreover, several studies have reported associations between each subtest and specific regions of frontal lobes using various neuroimaging methods. For example, functional magnetic resonance imaging (fMRI) or position emission tomography (PET) studies have reported an association between lexical fluency and the medial frontal cortex, including the anterior cingulate gyrus (Waburton *et al.*, 1996; Crosson *et al.*, 1999) and between the conflicting instructions and the right orbito-frontal and anterior cingulate cortex (Bench *et al.*, 1993). These reports partially support the results of a previous voxel-based morphometry study in patients with neurodegenerative disease and might imply an association between the anterior cingulate cortex and the aberrant motor behaviors (Rosen *et al.*, 2005).

In the present study, among the 22 AD patients (44%) with aberrant motor behaviors, only three exhibited wandering, 15 exhibited purposeless

activity, and 13 exhibited inappropriate activity. Previous studies have shown that the prevalence of aberrant motor behaviors in patients with mild- or moderate-stage AD ranges from about 12% to 67% (Mega *et al.*, 1996; Devanand *et al.*, 1997), similar to our reported data. Schonfeld *et al.* (2007) also showed that wandering in nursing homes was frequently (21%) observed in patients with severe cognitive impairments.

The present study has some limitations. First we must consider the relatively small sample size and the lack of objective measures, with only two neuropsychological assessments – the FAB and the MMSE – being performed. In particular, the subjects with wandering might have a high risk of visuospatial memory or perception impairments leading to “getting lost” (Chiu *et al.*, 2004). Secondly, the present study was limited to subjects with mild- to moderate-stage AD whose CDR scores were 1 or 2, because even though the FAB tasks can be performed without tools or instruments, the tasks do contain relatively complex question forms that include several steps. Thirdly, apraxia symptoms as focal signs of AD should be quantitatively assessed, as subjects with severe ideational apraxia cannot carry out sequences of action to achieve an intended purpose in the correct order (Zadikoff *et al.*, 2005). Fourthly, because the FAB score was significantly correlated with the MMSE score ($r = 0.670$; $P < 0.001$), we might have used two relevant neuropsychological tests. Therefore, we confirmed that the activity disturbances score was more strongly associated with the FAB score than with the MMSE score or the CDR SB using a stepwise regression analysis. Finally, this study had a cross-sectional design, and significant associations with other BPSD symptoms (delusional ideation, hallucination and anxiety) were not observed. If the clinical courses of the patients were to be pursued longitudinally, another BPSD symptom might be added, resulting in a worsening of the aberrant motor behaviors.

In spite of these limitations, the present study supported the hypothesis that frontal lobe dysfunction might be related to aberrant motor behaviors in patients with AD, supporting the results of neuroimaging studies. Moreover, these results suggest that a simple neuropsychological screening test reflecting frontal lobe function and including mainly executive function – such as the FAB – might be useful for predicting the manifestation of aberrant motor behaviors in patients with AD, providing important information regarding the selection of treatment stages that might reduce the early burden placed on caregivers.

Conflict of interest

None.

Description of authors' roles

Tomoyuki Nagata designed this study, examined the subjects, and wrote the paper. Shunichiro Shinagawa gave advice, including the analysis methods, and reviewed the manuscript. Hirohide Kada, Yusuke Ochiai and Hiroo Kasahara examined the patients with AD at the Jikei University School of Medicine, Kashiwa Hospital. Kazutaka Nukariya and Kazuhiko Nakayama reviewed and commented on the final manuscript.

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Regular Article

Correlation between a reduction in Frontal Assessment Battery scores and delusional thoughts in patients with Alzheimer's disease

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Aims: The purpose of the present study was to investigate the relationship between delusional thoughts (delusional ideation or misidentification) and frontal lobe function using the Japanese version of the Frontal Assessment Battery (FAB) bedside screening neuropsychological test in early stage Alzheimer's disease (AD) patients.

Methods: Forty-eight probable AD patients with Mini-Mental State Examination score ≥ 18 points and a clinical dementia rating score of either 0.5 or 1.0 were divided into two groups based on data obtained from interviews with their caregivers: a delusional thought group ($n = 19$) and a non-delusional thought group ($n = 29$). The FAB total and subtest scores were then compared for the two groups.

Results: Significant differences were found between the FAB total ($P < 0.01$) and subtest scores (similarities, motor series, conflicting instructions; $P < 0.05$) for the two groups. Multiple regression analysis showed that delusional thought was significantly associated with the FAB total score.

Conclusions: In addition to episodic memory disorders, a reduction in the FAB score may reflect frontal lobe dysfunctions, including executive function, in patients with AD, leading to delusional ideation.

Key words: Alzheimer's disease, delusional ideation, Frontal Assessment Battery, misidentification.

ALZHEIMER'S DISEASE (AD) is mainly characterized by episodic memory disorders, visuospatial impairments, and executive dysfunction.^{1,2} With the progression of neuropathology or cognitive decline, delusional ideation or misidentification are frequently seen as behavioral and psychological

symptoms of dementia (BPSD).³ AD with psychosis (delusional ideation or misidentification and hallucination) occurs in approximately 30–60% of patients with AD.^{4–6} Regarding the type of delusion experienced by AD patients, several studies have reported delusions of theft, persecution, infidelity, and abandonment.^{4–7} Delusional misidentifications such as believing that one's house is not one's home, that one's spouse is an imposter, and that televised images are actually present in the house have also been reported.^{4–7} Delusions in AD patients can create a distressful burden on their caregivers and can trigger or predict nursing home placement or death.^{8,9}

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Therefore, the assessment of delusions in AD patients is considered important, and some studies have investigated the incidence and risk factors for delusions in AD patients.^{10,11}

In demented patients, the manifestation of psychosis, such as delusional thought or hallucination, is considered to result from the development of executive dysfunction.¹²⁻¹⁴ Frontal lobe function involves executive function and, reportedly, is significantly correlated with the total Frontal Assessment Battery (FAB) score.¹⁵⁻¹⁷ A previous study reported that the FAB score reflects frontal lobe dysfunction, including executive dysfunction, and is an easily administered test that can be completed at the bedside within 10 min.^{15,17} The FAB screening neuropsychological test consists of six subtests involving comparatively simple tasks that do not require any tools.¹⁷ FAB scores significantly differed between patients with frontotemporal dementia and those with AD, but MMSE scores did not, therefore the validity of FAB reflected frontal lobe function, as indicated in a study of two different types of brain region degeneration.¹⁸

With regards to neuroimaging, studies using single-photon emission computed tomography have found hypoperfusion in the bilateral dorsolateral frontal cortex, right anterior cingulate gyrus, inferior-middle temporal cortices, and right posterior parietal region in AD patients with delusional thoughts or psychosis.¹⁹⁻²¹ Blackwood *et al.* reviewed and stated that the presence of 'reality distortion', which leads to persecutory delusions, was correlated with the cerebral blood flow in the left lateral prefrontal cortex, ventral striatum, superior temporal gyrus, and parahippocampal region,²² and a positron emission tomography study found hypometabolism in the right prefrontal cortex and left medial occipital region in AD patients with delusional thoughts.^{23,24} Although various disputable results have been demonstrated in such previous studies, some neuroimaging studies support a relationship between neuropsychological frontal lobe dysfunction and delusional thoughts in patients with AD.^{23,20}

The FAB has not been previously reported as a tool for performing neuropsychological evaluations in AD patients with delusional thoughts. In the present study we used the Japanese version of the FAB²⁵ to investigate the relation between the manifestation of delusional thoughts and frontal lobe dysfunction in patients with AD.

METHODS

Participants

Forty-eight consecutive Japanese subjects (16 men, 32 women; average age, 77.2 ± 7.0 years; range, 59-88 years) who had been referred to the Jikei University Kashiwa Hospital outpatient clinic were enrolled in this study. All patients were diagnosed as having probable AD based on the National Institute of Neurology and Communicative Disorder and Stroke/Alzheimer disease and Related Disorder Association (NINCDS/ADRDA) criteria;²⁶ all diagnoses were made after evaluations of the patients' past medical history, physical or neurological examinations, routine blood tests, and magnetic resonance imaging findings. To recruit patients with early stage AD, we selected patients with a clinical dementia rating (CDR) of either 0.5 or 1.0 and a Mini-Mental State Examination (MMSE) score of ≥ 18 points.²⁷ The subjects were then divided into two groups: a delusional thought (DT) group, and a non-delusional thought (NDT) group. The manifestation of delusions was assessed based on information obtained from a structured interview with each patient's caregiver, and the delusions were rated using the delusion scale of Behavioral Pathology in Alzheimer Disease (Behave-AD).²⁸ Patients were excluded if history of other neurological disease, brain injury, substance abuse, major depressive or psychotic disorder, epilepsy, delirium, metabolic disorder or treatment with acetylcholine esterase inhibitor were noted.²⁹ The present study was approved by the Ethics Committee of the Jikei University School of Medicine, and informed consent was obtained from all the subjects or their caregivers.

Assessment of delusional thought

To determine whether the patients had delusional thoughts, we utilized the delusional scale of Behave-AD (total behavioral or psychological problems scale). This scale was completed based on the results of an interview with each patient's caregiver, who was asked whether the patient had experienced any of the following delusions in the previous 4 weeks: (i) 'people are stealing things'; (ii) 'my house is not my home'; (iii) 'my spouse (or other caregiver) is an imposter'; (iv) delusion of abandonment; (v) delusion of infidelity; (vi) suspiciousness of other people; and (vii) any other delusions.

Table 1. Subject characteristics (mean \pm SD)

	DT (<i>n</i> = 19)	NDT (<i>n</i> = 29)	<i>P</i>
Sex (M/F)	8/11	12/17	n.s.
Age (years)	77.7 \pm 8.0	77.7 \pm 7.5	n.s.
Education (years)	10.4 \pm 3.0	11.6 \pm 1.8	n.s.
Duration of illness (months)	19.4 \pm 14.3	20.3 \pm 17.2	n.s.
MMSE score	22.0 \pm 2.7	23.3 \pm 2.2	n.s.
FAB score*	11.6 \pm 2.8	13.9 \pm 2.5	<0.01

*Significant difference: $P < 0.01$ (*t*-test).

Sex ratio was analyzed on χ^2 test.

DT, delusional thought; FAB, Frontal Assessment Battery; MMSE, Mini Mental State Examination; NDT, non-delusional thought.

FAB assessment

The Japanese FAB version consists of six subtests: (i) similarities (conceptualization); (ii) lexical fluency (mental flexibility); (iii) motor series (programming); (iv) conflicting instructions (sensitivity to interference); (v) go-no go (inhibition control); and (vi) prehension behavior (environmental autonomy). Each subtest is rated from 3 to 0, with the total score therefore ranging from 18 to 0.

Statistical analysis

Data were analyzed using SPSS 11.0 J for Windows (SPSS Japan Inc). Age, education (years), duration of illness (months), MMSE score, and FAB scores were compared between the two groups using unpaired independent sample *t*-tests. The sex ratio was assessed using a χ^2 test. Logistic regression analysis was conducted to examine delusional thought, with age, sex, education, duration of illness, FAB total score, and MMSE score as independent variables.

RESULT

Patient characteristics

The 48 AD patients were divided into a DT group (*n* = 19) and an NDT group (*n* = 29). These two groups were not significantly different with regard to sex, age, duration of illness (months), education (years), or MMSE scores (Table 1).

FAB total and subtest scores

The FAB total scores were significantly different between the two groups, whereas the other examined

Table 2. FAB subtest scores (mean \pm SD)

	DT	NDT	<i>P</i>
Similarities*	0.73 \pm 1.04	1.48 \pm 1.12	<0.05
Lexical fluency	1.84 \pm 0.90	2.03 \pm 0.90	n.s.
Motor series*	1.68 \pm 1.29	2.51 \pm 0.78	<0.05
Conflicting instructions*	2.47 \pm 0.70	2.90 \pm 0.409	<0.05
Go-no go	1.47 \pm 1.17	2.00 \pm 1.22	n.s.
Prehension behavior	2.84 \pm 0.38	2.82 \pm 0.54	n.s.

*Significant difference: $P < 0.05$ (*t*-test).

DT, delusional thought; FAB, Frontal Assessment Battery; NDT, non-delusional thought.

variables were not ($P < 0.01$; Table 1). The FAB total score of the DT group was 11.6 \pm 2.8 (mean \pm SD), while that in the NDT group was 13.9 \pm 2.5 (mean \pm SD). Furthermore, several FAB subtest scores (similarities, motor series, and conflicting instructions) were significantly lower in the DT group than in the NDT group ($P < 0.05$; Table 2). Logistic regression showed that the FAB scores ($P = 0.048$), but not the MMSE scores ($P = 0.507$), significantly influenced the manifestation of delusional thoughts in an independent manner (Table 3).

Subtypes of delusional thought

The subtypes of delusional thought are listed in Table 4. Although 19 patients had experienced delusional thoughts, most of the patients had experienced several types of delusional thoughts. Among the 19 patients with delusional thoughts, the 'people are stealing things' delusion (12 patients) was the most frequent delusion. 'Suspiciousness' ideation was

Table 3. Multiple logistic regression analysis: influence on delusional thoughts

Variable	OR	95% CI	<i>P</i>
Age	0.991	0.895–1.098	0.867
Sex	1.883	0.402–8.820	0.422
Education (years)	1.094	0.846–1.414	0.494
Duration of illness (months)	1.030	0.981–1.081	0.239
MMSE score	1.111	0.862–1.432	0.417
FAB score*	1.287	1.008–1.643	0.043

*Significant difference: $P < 0.05$.

CI, confidence interval; FAB, Frontal Assessment Battery; MMSE, Mini Mental State Examination; OR, odds ratio.

Table 4. Types of delusional ideation

Delusional ideation	No. patients
1. 'People are stealing things' delusion	12
2. 'One's house is not one's home' delusion	0
3. 'Spouse is an imposter' delusion	0
4. 'Delusion of abandonment'	3
5. 'Delusion of infidelity'	4
6. 'Suspiciousness' ideation	10
7. Other delusion	7

reported in 10 patients, 'delusion of infidelity' was reported in four patients, and 'delusion of abandonment' was reported in three patients. None of the patients in the present series experienced delusional misidentification: either 'one's house is not one's home' or 'spouse (or other caregiver) is an imposter'. 'Other' delusions experienced by the patients were envy delusion in four patients, hypochondriac delusion in two patients, erotomania in one patient, and TV syndrome ('images on the television are actually present in the house') in one patient.

DISCUSSION

The present results showed that the FAB total and subtest scores (Similarities, Motor series, and Conflicting instructions) were significantly lower in AD patients with delusional thoughts than in those without delusional thoughts. Dubois *et al.* reported that the FAB scores were significantly correlated with the number of criteria and the number of perseverative errors on the Wisconsin Card Sorting Test (WCST), which was established to measure executive function.¹⁷ The WCST is considered to be sensitive to executive dysfunction³⁰ and evaluates both conceptual ability and behavioral regulation.³¹

In previous studies, dementia patients with psychosis were characterized as having greater executive and visuospatial impairments in their neuropsychological functioning patterns.^{13,14} The present study showed that a decrease in the FAB score, including executive dysfunction, but not the MMSE score, was related to delusional thoughts. The MMSE has a few items of executive function but is heavily weighted toward orientation or memory items.¹⁸ Therefore, impairments in frontal lobe function, including executive function, rather than episodic memory or orientation disorder might be strongly related to the manifestation of delusional thoughts.

Of the six FAB subtests, the Similarities subtest includes the function of abstract reasoning, which can also be investigated using card-sorting tasks and proverb interpretation.¹⁷ Subjects have to conceptualize or integrate the links between some objects from the same category. In previous studies, patients with psychosis showed specific impairments on task requiring complex integration, that is, the capacity to form an overall impression by holding various fragments of information.^{31,32} Therefore, AD patients with delusional thoughts might manifest as the result of inaccurate memory with poor insight related to executive dysfunction, leading to errors in logic and comparing internal experiences with reality.^{13,23} The Motor series subtest measures the capacity to execute a sequence of actions successively in separate tasks; it resembles the 'first-palm-edge' task in Luria's motor series.¹⁷ The Conflicting instructions subtest resembles the Stroop test task and requires the capacity to perform a contrary reaction to each of two pattern directions.¹⁷ In order to carry out both tasks effectively, self-correcting or monitoring capacity that evaluates whether subject himself could perform the tasks accurately are required. Previous studies reported that alternations in self-monitoring were associated with psychosis with evidence of specificity for delusional ideation.^{31,33,34} Therefore, such impairments of self-correcting system might lead to delusion in AD patients in the present study.

Regarding the subtypes of delusional thoughts, the present study indicated that the 'people are stealing things' delusion and 'suspiciousness' ideation occurred frequently, similar to that found in previous studies.^{20,23} In contrast, typical delusional misidentification, such as 'one's house is not one's home' and 'one's spouse is an imposter', were not reported in the present study. Previous studies have reported that approximately 40–50% of delusional thoughts in patients with AD are delusional misidentifications.^{4,20,35} Lower levels of cognitive functions and lower average scores on cognitive tests, such as the MMSE, have been reported for AD patients with delusional misidentifications, compared with those with persecutory delusions.^{4,35}

The limitations of the present study included the relatively small sample size and the use of only two neuropsychological tests: the FAB and the MMSE. If simple scales or tests measuring attentional, visuospatial function, or semantic memory had also been used, significant differences might have been obtained. The present study was limited to subjects

with early stage AD whose MMSE scores were ≥ 18 points and who had a CDR of either 0.5 or 1.0 because even though the FAB tasks can be performed without tools or instruments, the tasks do contain relatively complex question forms that include several steps.

In spite of these limitations, the present study supports the hypothesis that frontal lobe dysfunction might be related to delusional ideation or misidentifications in patients with AD, supporting the results of neuropsychological and neuroimaging studies. Moreover, these results suggest that a simple neuropsychological screening test reflecting frontal lobe function and including mainly executive function – such as the FAB – might be useful for predicting the manifestation of delusional thoughts in patients with AD, providing important information regarding the selection of treatment stages that will reduce the early burden of caregivers.

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