

表 3-1 身体表現性障害の分類(DSM-IV-TR)

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|--|
| 身体化障害 somatization disorder                              |
| 鑑別不能型身体表現性障害 undifferentiated somatoform disorder        |
| 転換性障害 conversion disorder                                |
| 疼痛性障害 pain disorder                                      |
| 心気症 hypochondriasis                                      |
| 身体醜形障害 body dysmorphic disorder                          |
| 特定不能の身体表現性障害 somatoform disorder not otherwise specified |

[高橋三郎, 大野 裕, 染矢俊幸(訳): DSM-IV-TR 精神疾患の分類と診断の手引, 新訂版, p25, 医学書院, 2003より]

表 3-2 心気症の分類(DSM-IV-TR)

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|---|
| A. 身体症状を誤って解釈して重篤な病気に罹っていると恐怖またはとらわれ        |
| B. 適切な医学的評価/保証にもかかわらず持続的固執                  |
| C. 上記Aの確信は妄想的強固さがなく, 外見についての限られた心配に限定されていない |
| D. さまざまな領域における機能の障害                         |
| E. 6か月以上の持続                                 |
| F. 除外基準(略)                                  |

[高橋三郎, 大野 裕, 染矢俊幸(訳): DSM-IV-TR 精神疾患の分類と診断の手引, 新訂版, p191, 医学書院, 2003より]

### 3 強迫性障害と認知症

いわゆる「強迫行動」症状に関して、神経症圏の患者での症状と器質性精神障害に伴う症状では違いがあり、神経症としての強迫症状を多く見てきた精神科医は、文献などに登場する認知症や脳血管障害後の「強迫」の記述に違和感を覚える(表3-3)。強迫症状はFTDやハンチントン病、頭部外傷後遺症、脳血管障害など多くの脳器質性疾患で認められるとされている。その特徴は病識の欠如、「不安」「自我違和性」「体験の自己帰属感」の乏しさであり、前頭葉の機能低下に基づく可能性がある<sup>19)</sup>。脳器質性疾患で認められる強迫症状では、その主観的体験である強迫の「自我違和性、不合理性」と体験の「自己帰属感」が欠けている。その点が従来の強迫性障害の概念との相違である<sup>19)</sup>。

神経症圏の強迫と脳器質性のそれとは厳然と区別できそうであり、そうすべきであるようにも思える。ところが、両者は類似した基盤がある可能性がある。強迫性障害とADはグルタミン酸系神経の障害という共通の病態があることが示唆されている<sup>20)</sup>。FTDにみられる常同行為は、強迫行為とは自我異質性を有しない点で違いがあると考えられるが、実際には両者の移行もあり、前頭葉症状としてとらえることもできる<sup>21)</sup>。

このような症状面のあいまいさもあって、強迫症状と認知症との合併に関して疫学的な研究は進んでいないように見える。筆者が調べた限りでは、ADと強迫症状の関連に関する報告は症例報告レベルであった<sup>22)23)</sup>。しかし、実際の臨床場面では神経症としての強迫症状が認知症に先行することは、今回の症例のようにそれほどめずら

表 3-3 強迫性障害の分類(DSM-IV-TR)

- A. 強迫観念または強迫行為のどちらか。
- (1), (2), (3), および(4)によって定義される強迫観念：
- (1) 反復的、持続的な思考、衝動、または心像であり、それは障害の期間の一時期には、侵入的で不適切なものとして体験されており、強い不安や苦痛を引き起こす。
  - (2) その思考、衝動、または心像は、単に現実生活の問題についての過剰な心配ではない。
  - (3) その人は、この思考、衝動、または心像を無視したり抑制したり、または何か他の思考または行為によって中和しようと試みる。
  - (4) その人は、その強迫的な思考、衝動、または心像が(思考吹入の場合のように外部から強制されたものではなく)自分自身の心の産物であると認識している。
- (1)および(2)によって定義される強迫行為：
- (1) 反復行動(例：手を洗う、順番に並べる、確認する)または心の中の行為(例：祈る、数を数える、声に出さずに言葉を繰り返す)であり、その人は強迫観念に反応して、または厳密に適用しなくてはならない規則に従って、それを行うよう駆り立てられていると感じている。
  - (2) その行動や心の中の行為は、苦痛を予防したり、緩和したり、または何か恐ろしい出来事や状況を避けることを目的としている。しかし、この行動や心の中の行為は、それによって中和したり予防したりしようとしていることとは現実的関連をもっていないし、または明らかに過剰である。
- B. この障害の経過のある時点で、その人は、その強迫観念または強迫行為が過剰である、または不合理であると認識したことがある。
- 注：これは子どもには適用されない。
- C. 強迫観念または強迫行為は、強い苦痛を生じ、時間を浪費させ(1日1時間以上かかる)、またはその人の正常な毎日の生活習慣、職業(または学業)機能、または日常の社会的活動、他者との人間関係を著明に障害している。
- D. 他のI軸の障害が存在している場合、強迫観念または強迫行為の内容がそれに限定されていない(例：摂食障害が存在する場合の食物へのとらわれ、抜毛癖が存在している場合の抜毛、身体醜形障害が存在している場合の外見についての心配、物質使用障害が存在している場合の薬物へのとらわれ、心気症が存在している場合の重篤な病気にかかっているというとらわれ、性嗜好異常が存在している場合の性的な衝動または空想へのとらわれ、または大うつ病性障害が存在している場合の罪悪感の反復思考)。
- E. その障害は、物質(例：乱用薬物、投薬)または一般身体疾患の直接的な生理学的作用によるものではない。

(高橋三郎、大野裕、柴矢俊幸(訳)：DSM-IV-TR 精神疾患の分類と診断の手引、新訂版、pp 177-179、医学書院、2003より)

しいものではない。高齢者の強迫症状を診察するうえでは、AD、DLB、FTDなどの認知症の存在に配慮する必要がある。

#### 4 | その他の不安障害と認知症

不安を基盤とする症状には、上記の身体表現性障害、強迫性障害の他に、パニック障害、PTSD などがある。症例記載の中に挙げた例のようにパニック発作が初発である認知症に遭遇することは決して珍しいことではないが、パニック障害のみを対象とした認知症の合併症調査は、まだ行われていないようである。不安症状全般を対象とした研究の中にパニック発作を伴う症例が包含されているからかもしれない。パニック発作は非常に目立つ症状であり、どうしてもその症状に引きずられて診断、治療方

針を決めてしまいがちである。

しかし、高齢者では当然のことだが、狭心症などの身体疾患の鑑別をする必要があるだけでなく、問診で認知機能、生活機能についても配慮しておくことが望まれる。先に記載したように、認知機能の低下は不安を充進させやすく、それがパニック発作のような表現形態をとることは十分考えられるからである。

PTSDが認知症と共通の病態基盤を持っているとは考えにくい。しかし、症例で示したように、心的外傷となるイベントの発生が認知症の発症と時間的に近接している場合、臨床経過と症状にとらわれてストレス障害の治療のみに焦点をおいたまま時間が経過し、認知機能低下がなおざりにされてしまう危険がある。薬効や精神療法が十分な効果をもたらさない高齢者のストレス障害では、認知機能の低下が進んでいないかについても頭の隅においておくのがよいだろう。

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(服部英幸)

高齢者の在宅・施設介護における

# 性的トラブル 対応法

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タブー視されてきた介護の場での  
性的トラブル解決の指針となる本。



黎明書房

## 2 薬剤とセクシュアリティ

高齢者介護の現場で性とセクシュアリティが問題となることは稀ではない。しかしながら多くの教科書では十分に対応されておらず、授業においても十分に引き上げられることはない。しかし介護の現場では患者からセクハラを受けることも稀ではない。そのために最低限その関連の知識をもち、現場で適切に対応することは大事なことである。本節では特に薬剤とセクシュアリティの関係について総括する。

### 疾病と性的行動について

疾病の症状そのものにおいてもセクシュアリティと関係する場合がある。そもそも、パーキンソン病は性的な行動異常が観察されることがある。また、認知症の症状の1つに嫉妬妄想がある。また前頭側頭型認知症では反社会的行為が見られることがある。さらにクリューバー・ビュシー症候群においても性的な異常行動が主症状となる場合がある。

パーキンソン病の症状には大別して運動症状と非運動症状がある。非運動症状の中には、精神症状、自律神経症状などが含まれる。主要症状は以下の4つである。振戦、無動、固縮が特に3主徴として知られている。これらの神経学的症候をパーキンソニズムと呼ぶ。また、病的賭博、性欲亢進、強迫的買い物、強迫的過食、反復常同行動、薬剤の強迫的使用などのいわゆる衝動制御障害がパーキンソン病に合併することが知られるようになっている。

前頭側頭型認知症では、常識の欠如や判断力の低下により反社会的行為が見られることがあり、性的な異常行動を示すことがある。具体的には、例えば男性患者が下着をつけずに歩いたり、女性風呂に入浴しようとするなどである。

クリューバー・ビューシー症候群は純粹な扁桃體由来の症候群ではないが、扁桃體を含む関連症候群である。その症状は以下に示すように多彩である。感情の鈍麻・無関心、逆に過剰反応を示す、視覚失認、口唇傾向、例えば何でも口に入れる、食べ物でないものも食べる、時に過食を起こす。恐怖感の低下、危険なものを避けなくなる。さらに性的感覚の亢進症状がある。クリューバー・ビューシー症候群は何らかの原因で両側の扁桃體の障害を受けた時に発症すると考えられており、ヘルペス脳炎（ヘルペスビールスは側頭葉内側など大脳辺縁系を侵すことが知られている）、ピック病、戦争や交通事故などでの頭部外傷などでクリューバー・ビューシー症候群様の症状が確認されている。

## 薬剤と性機能障害について

性機能障害（インポテンス）は、勃起、射精、あるいは両者の欠陥と定義される。性的機能不全は、全身性疾患の過程（糖尿病）やそれらの治療（薬物）、性器、内分泌系の特異的疾患あるいは精神科的障害に二次的に続発する。かつては性的機能不全の男性の大多数は心理的基礎原因をもっていると考えられていた。現在は、インポテンスの男性の大多数は糖尿病などの器質性基礎疾患の要素を持っていると考えられている<sup>1)</sup>。

性欲の減退に関して、性欲やリビドー（性的衝動）の減少は、男性ホルモンすなわちテストステロンの欠乏に起因する。他の原因は、心理的要因や習慣性薬物の乱用（ヘロイン、アルコール、コカイン）などが含まれる。勃起不全と薬剤に関しては、シメチジン、スピロノラクトン、ケトラコナゾール、クロニジン、メチルドパ、ベータ遮断薬、サイアザイド利尿薬、抗コリン作動薬、抗鬱薬、鎮静薬、バルビツレート、モノアミン酸化酵素阻害薬、ベンゾジアゼピン、向精神病薬）および他の乱用薬（アルコール、メサドン、コカイン、ヘロイン）との関連が知ら



れている。射精欠如に関しては、グアネチジン、フェノキシベンザミンにより引き起こされることは知られている。

## 薬剤と性的行動について

薬剤によっては、ヒトの性的行動を変容させることがある。医療の分野ではこのことは常識ではあるが、性的行動異常を薬剤と結びつけることが容易ではなく、知識として知っておく必要がある。

### パーキンソン症状をきたしやすい薬剤

近年医学の進歩が急速で、種々の薬が作られるようになったが、薬によっては、副作用としてパーキンソン症状が出たり、あるいはパーキンソン症状を悪化させたりすることがある。

以下の薬（向精神薬、抗不安薬、精神安定剤、<sup>せいとぎい</sup>制吐剤など）は必ずパーキンソン症状が出るというのではなく、その可能性がある薬である（表3-1）。まずはこうした性的な行動や性に関連した症状が出た場合には薬剤との関連を疑う必要がある。多くの薬剤は安全と考えられており、高齢者では漫然と長期間使用されることが多いため、こうした有害事象を見逃す可能性が高い。薬剤師や医師と連携し、少しでも薬剤数を減量または中止し、有害事象の発生を未然に防ぐ必要がある。

## おわりに

高齢者自身の性格によるものがあるが、疾病そのものにより、セクシュアリティが高まることもある。

薬剤は有用性もあるが、有害事象もある。急性の有害事象はわかりやすいことが多いが、慢性の場合には把握が遅れる傾向があり、わかりにくいことも多い。そこで常に有害事象を日頃から理解し、患者の行動を十分に観察する必要がある。情報収集にはナースや介護職の他、家族の協力も得ながら、少しでも有害事象の発言を減少させることが重要であ



表 3-1 パーキンソン症状をきたしやすい薬剤

- ① フェノチアジン系
  - クロールプロマジン (コントミン, ウインタミン)
  - トリフルプロマジン (ベスプリン)
  - フルフェナジン (フルメジン, アナテンゾール)
  - トリフロペラジン (トリフロペラジン)
  - ペルフェナジン (トリオミン, PZC)
  - ペリシアジン (ニューレプチル, アパミン)
  - チオリダジン (メレリル)
- ② ブチロフェノン系
  - ハロペリドール (セレネース, ケセラン, プロトンボン, リントン)
  - ピパンペロン (プロビタン, ルバトレン)
- ③ チオキサントニン系
  - クロルプロチキセン (トラキラン, クロチキセン)
- ④ ジフェニルブチルピペリジン系
  - ピモジド (オーラップ)
- ⑤ イミノベンジル誘導体
  - カルピプラミン (デフェクトン)
  - クロカプラミン (クロフェクトン)
- ⑥ インドール誘導体
  - オキシペルチン (ホーリット)
- ⑦ 制吐剤
  - メトクロプラミド (プリンペラン, モルペラン, プロメチン)
  - フェノチアジン系 (ノバミン, トレステン, ビレチア)
- ⑧ 降圧剤
  - レセルピン (レセルピン, セルパシル)
  - アルファーメチルドーパ (アルドメット)
- ⑨ 脳循環代謝改善薬
  - フルナリジン (フルナール)
  - シンナリジン (アプラクタン)
- ⑩ その他
  - スルピリド (アビリット, ドグマチール, ミラドール)
  - チアプライド (グラマリール)
  - ドンペリドン (ナウゼリン)
  - シサプリド (アセナリン, リサモール)
  - リチウム (リチウム)

る。

また、在宅や施設介護の現場で性的トラブルが起きた場合には、事実関係を正確に把握し、冷静に対応することが求められる。適切な対応方法には正解はないが、薬剤の変更も含め、早期に発見し、予防的対応も重要であろうし、疾病やその薬剤の影響を検討する必要があるだろう。

注

- 1) 仲谷達也「性機能障害」『今日の治療指針 2010』医学書院, p.931-932

# Primary Care in Psychiatry and Brain Science

脳とこころの  
プライマリケア

2

知能の衰え

編著

池田 学

滋賀大学大学院教授

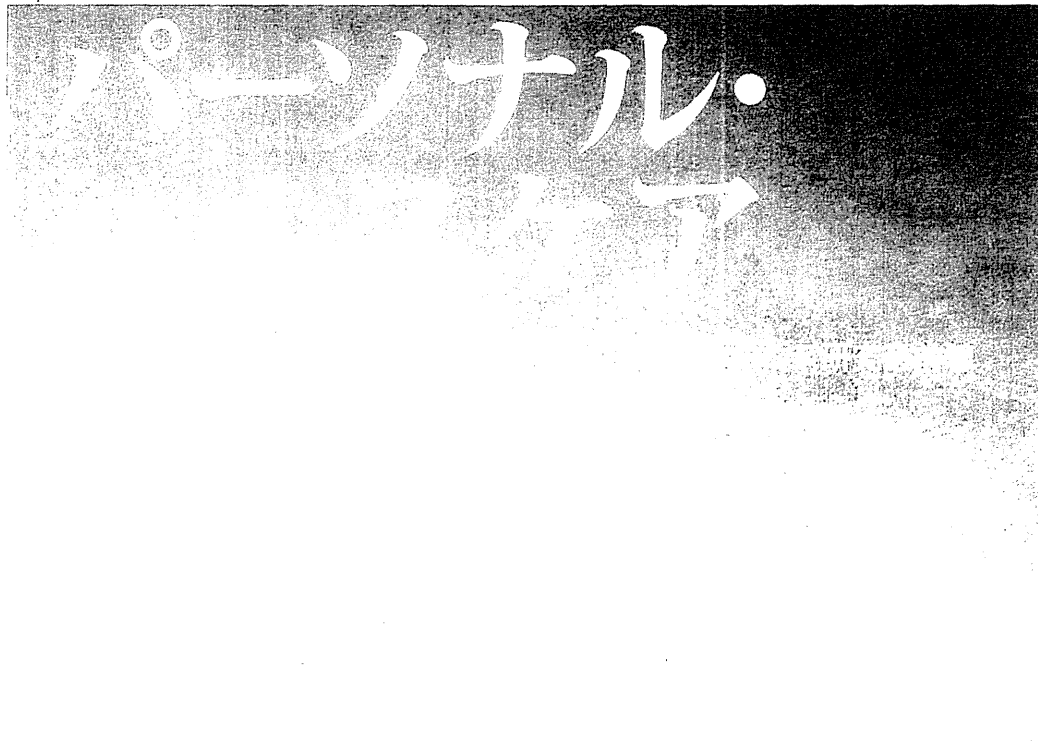
シナジー

インフォームド「コンセント」  
のための  
図説シリーズ

# 認知症の 予防と生活指導

遠藤 英俊 著

国立長寿医療研究センター内科総合診療部長



## Cerumen impaction shown by brain magnetic resonance imaging in patients with cognitive impairment

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**Aim:** Hearing loss is a risk factor for the progression of dementia. Cognitive improvement is occasionally found after removal of cerumen impaction. Because patients with dementia do not usually complain about cerumen impaction, detection methods are important. The present study aimed to investigate whether cerumen impaction is observable using brain magnetic resonance imaging.

**Methods:** Participants were six patients whose hearing level improved 15 dB or more unilaterally or bilaterally after the removal of cerumen impaction. A radiologist who was blind to the impaction side and whether magnetic resonance imaging scans were taken before or after impaction removal classified cerumen impaction as positive, negative or unclear.

**Results:** Three ears classified as impaction positive and five ears classified as impaction negative corresponded accurately to the presence or absence of cerumen impaction. Among four ears classified as unclear, two did and two did not have cerumen impaction.

**Conclusion:** Careful examination of the external ear canal on brain magnetic resonance imaging can be used to detect cerumen impaction. *Geriatr Gerontol Int* 2015; 16: 392–395.

**Keywords:** cerumen impaction, dementia, external ear canal, hearing loss, magnetic resonance imaging.

### Introduction

Among elderly patients admitted to a skilled nursing facility or undergoing evaluation for a memory disorder, hearing and mental status improved significantly after the removal of cerumen impaction. Because individuals with a cognitive disorder or dementia do not usually complain of cerumen impaction, detection is important so as to reduce hearing impairment. Visualization of the external ear with an otoscope is a basic method of detection. However, it is occasionally difficult to estimate cerumen thickness, which is positively associated with

hearing impairment. Our goal was to investigate whether brain magnetic resonance imaging (MRI) is useful for cerumen impaction detection.

To our knowledge, there have been no published reports of MRI for cerumen impaction. If this method was used to detect cerumen impaction, it might help to improve hearing and cognitive ability in cognitively impaired patients.

### Methods

#### Patients

The participants were six patients whose hearing level improved 15 dB or more unilaterally or bilaterally after the removal of cerumen impaction, from a larger study of 55 patients described previously.<sup>1</sup> The study was approved by the Committee for the Ethics of Human Research for the National Center for Geriatrics and

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**Table 1** Magnetic resonance imaging detection of cerumen impaction in patients with cognitive disorder

| Case no. | Age | Sex | Type of cerumen | MMSE | Side  | Cerumen impaction (otoscopic findings) | MRI before or after cerumen removal | Radiologist report of cerumen impaction | Hearing level before/after removal of cerumen impaction |
|----------|-----|-----|-----------------|------|-------|--|-------------------------------------|---|---|
| 1        | 86  | M   | Dry             | 19   | Right | Almost                                 | After                               | Negative                                | 48/43   |
|          |     |     |                 |      | Left  | Almost                                 | After                               | Negative                                | 63/48   |
| 2        | 80  | M   | Wet             | 27   | Right | Total                                  | Before                              | Positive                                | 64/37   |
|          |     |     |                 |      | Left  | Total                                  | Before                              | Unclear                                 | 64/38   |
| 3        | 80  | F   | Dry             | 14   | Right | Total                                  | After                               | Negative                                | 35/38   |
|          |     |     |                 |      | Left  | Total                                  | After                               | Unclear                                 | 56/38   |
| 4        | 85  | F   | Dry             | 10   | Right | Total                                  | Before                              | Positive                                | 83/59   |
|          |     |     |                 |      | Left  | Total                                  | Before                              | Unclear                                 | 53/59   |
| 5        | 74  | M   | Wet             | 24   | Right | None                                   | Before                              | Negative                                | 43/34   |
|          |     |     |                 |      | Left  | Total                                  | Before                              | Positive                                | 65/40   |
| 6        | 85  | F   | Wet             | 16   | Right | Total                                  | After                               | Negative                                | 80/51   |
|          |     |     |                 |      | Left  | Total                                  | After                               | Unclear                                 | 83/81   |

Hearing level (dB) was the average of four frequencies of 500 Hz, 1 kHz, 2 kHz and 4 kHz. In the radiologist report of cerumen impaction judged as "unclear," comments of "thin one?" or "small one?" were added. F, female; M, male; MMSE, Mini-Mental State Examination.

Gerontology. Age, sex, results of Mini-Mental State Examination, otoscopic findings, and hearing levels before and after cerumen impaction removal are shown in Table 1. Brain MRI was carried out within 1 month before ( $n = 3$ ) or after ( $n = 3$ ) cerumen impaction removal.

### MRI

Images were obtained using a 1.5-T MR scanner (MAGNETOM Avanto; Siemens Medical Solutions, Erlangen, Germany) with a 12-channel head coil. The following sequences were routinely carried out for dementia patients: transverse T1-weighted spin echo (repetition time ms/echo time ms, 485/11; flip angle, 90°; matrix, 194–230 × 256; field of view [FOV], 184–263 mm; slice thickness, 6 mm; gap, 1.5 mm); transverse T2-weighted spin echo (3800/180; flip angle, 180°; matrix, 216–256 × 256; FOV, 184–263 mm; slice thickness, 6 mm; gap, 1.5 mm); transverse fluid attenuated inversion recovery 8000/101; inversion time, 2500 ms; flip angle, 180°; matrix, 184–202 × 256; FOV, 184–263 mm; slice thickness, 6 mm; gap, 1.5 mm); coronal T1-weighted spin echo (485/11; flip angle, 80°; matrix, 194–230 × 256; FOV, 186–263 mm; slice thickness, 6 mm; gap, 1.5 mm); transverse T2\*-weighted gradient echo (500/18; flip angle, 20°; matrix, 162–192 × 256; FOV, 186–263 mm; slice thickness, 6 mm; gap, 1.5 mm); sagittal T1-weighted 3-D gradient echo (1700/3.99; inversion time, 800 ms; flip angle, 15°; matrix, 256 × 256; FOV, 230–274 mm; slice thickness,

1.25 mm; gap, 0 mm). Three-dimensional volumetric data were analyzed using an automated voxel-based morphometry method.

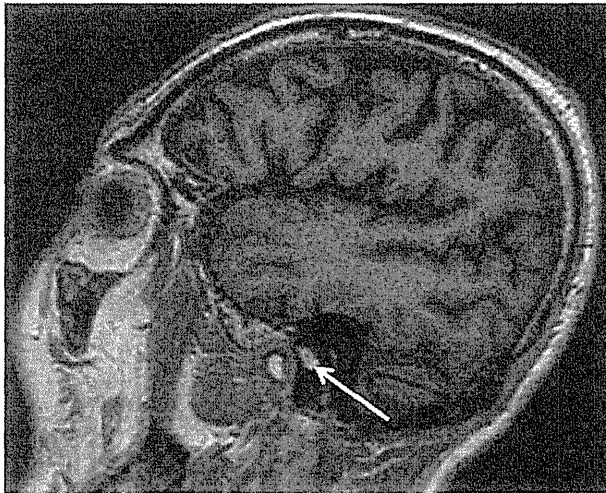
A radiologist (SN), blind to the side of cerumen impaction, to whether MRI scans were taken before or after cerumen impaction removal, and to the number of ears with cerumen impaction classified the cerumen impaction in each ear as positive, negative or unclear.

### Results

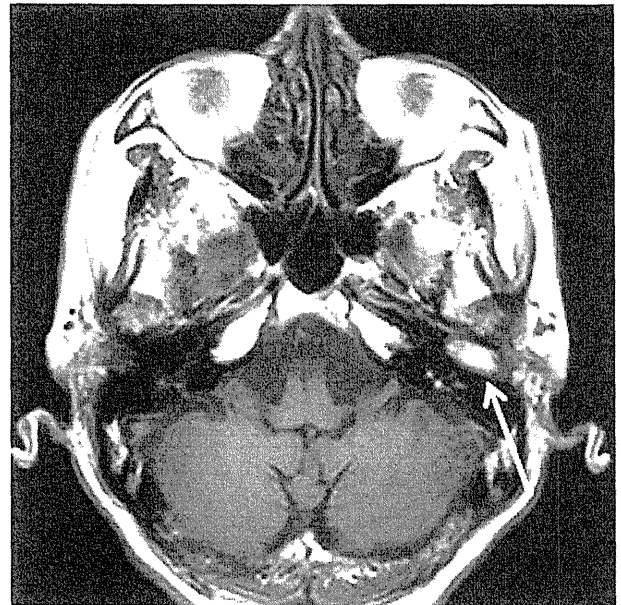
Table 1 shows the six patients from our previous study whose hearing level improved by 15 dB or more unilaterally or bilaterally after the removal of cerumen impaction. In case 2, the hearing level improved by 27 dB on the right side and 26 dB on the left side. In the other five cases, the hearing level improved more than 15 dB unilaterally. Patient ages ranged from 74 to 86 years. The average Mini-Mental State Examination score was 22. Brain MRI was taken before cerumen impaction removal in cases 2, 4 and 5, and after removal of the cerumen impaction in cases 1, 3 and 6. Five ears (both ears of case 2 and Case 4, and left ear of case 5) had cerumen impaction actually at MRI.

The radiologist's report is also shown in Table 1. When the radiologist reported the presence or absence of cerumen impaction, all reports were correct. Three ears classified by the radiologist as impaction positive and five ears classified as impaction negative corresponded accurately to the presence or absence of cerumen impaction. Of the four ears classified as

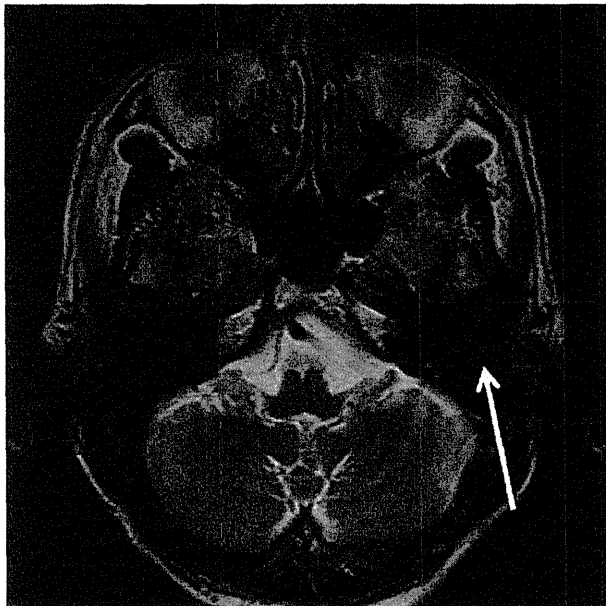




**Figure 1** A 3-D T1-weighted image with 1.5 mm thickness. Cerumen impaction is shown on the left external auditory canal (arrow), visualized as a structure with high signal intensity.



**Figure 3** A routine T1-weighted axial image with 5 mm thickness. Cerumen impaction is visualized as a high signal intensity structure similar to fat (arrow).



**Figure 2** A routine T2-weighted axial image with 5 mm thickness. Cerumen impaction is faintly visualized (arrow).

unclear, two (left ears of case 2 and case 4) had and two (left ears of case 3 and case 6) did not have cerumen impaction.

Representative images showing cerumen impaction are in Figures 1–3 (case 5 in Table 1).

## Discussion

Of the eight ears classified by the radiologist as positive or negative, all were accurately classified. If the classifi-

cations had been completely at random, the probability would have been  $1/2^8 = 0.0039$ . It appears that brain MRI was useful for identifying cerumen impaction, especially when the cerumen was large and dense.

The incidence of cerumen impaction is generally high in elderly adults.<sup>2–4</sup> Cerumen impaction is more common in patients with dementia or mental disorders who, in many cases, do not complain of hearing loss.<sup>5–7</sup> When MRI is taken for evaluation of brain in these patients, it is usually unclear whether cerumen impaction exists or not. If cerumen impaction can be recognized on brain MRI, we can specify patients with cerumen impaction and remove the cerumen impaction for them. Removal of the cerumen impaction might result in a significant improvement of cognitive function.<sup>1,6</sup> A Web of Science search that included the terms “MRI” and “dementia” revealed more than 5300 papers. There were none for a search with “MRI” and “cerumen.” The present study showed for the first time that MRI is useful for finding cerumen impaction, especially when it is large and dense. It is expected that geriatricians and radiologists pay attention to cerumen impaction at the time of MRI evaluation.

Dry and wet cerumen types differ among ethnic groups. The frequency of dry cerumen is high in Mongolian populations and low among Europeans.<sup>8,9</sup> Cerumen impaction is more common in people with wet cerumen. However, the present study showed that dry cerumen impaction could cause significant hearing loss and was visible on brain MRI.

Acoustic noise during MRI is the main source of patient discomfort and leads to verbal communication

problems, especially in children and the elderly. Recently developed silent brain MRI might soon be in wide use for patients with cognitive disorder and dementia. Silent MRI is also expected to provide high-quality images.<sup>10</sup> MRI might provide easy detection of cerumen impaction in the near future.

## Acknowledgments

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## Disclosure statement

No potential conflicts of interest were disclosed.

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ORIGINAL ARTICLE: EPIDEMIOLOGY,  
CLINICAL PRACTICE AND HEALTH

# Frontal white matter hyperintensity predicts lower urinary tract dysfunction in older adults with amnesic mild cognitive impairment and Alzheimer's disease

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**Aim:** Lower urinary tract symptoms often limit activities of daily life and impair quality of life in the elderly. The purpose of the present study was to determine whether regional white matter hyperintensity (WMH) can predict lower urinary tract symptoms in elderly with amnesic mild cognitive impairment or Alzheimer's disease.

**Methods:** The participants were 461 patients aged 65–85 years diagnosed with amnesic mild cognitive impairment or Alzheimer's disease. Patients and their caregivers were asked about symptoms of lower urinary tract symptoms (urinary difficulty, frequency and incontinence). Cognition, behavior and psychological symptoms of dementia and medication were evaluated. WMH and brain atrophy were analyzed using an automatic segmentation program. Regional WMH was evaluated in the frontal, parietal, temporal and occipital lobes.

**Results:** Patients with urinary incontinence showed significantly greater volume of WMH. WMH increased with age, especially in the frontal lobe. WMH in the frontal lobe was closely associated with urinary incontinence after adjustment for brain atrophy and classical confounding factors.

**Conclusions:** Frontal WMH was a predictive factor for urinary incontinence in older adults with amnesic mild cognitive impairment or Alzheimer's disease. Urinary incontinence in demented older adults is not an incidental event, and careful insight into regional WMH on brain magnetic resonance imaging might greatly help in diagnosing individuals with a higher risk of urinary incontinence. *Geriatr Gerontol Int* 2016; 16: 167–174.

**Keywords:** Alzheimer's disease, lower urinary tract symptoms, mild cognitive impairment, urinary incontinence, white matter hyperintensity.

## Introduction

White matter hyperintensity (WMH) is detected as hyperintense signals located in periventricular and deep subcortical areas on T2-weighted images of brain magnetic resonance imaging (MRI). WMH are composed of heterogeneous pathological changes, and are mostly related to cerebral small vessel disease.<sup>1</sup> It has been postulated that WMH are associated with cognitive dysfunction<sup>2–4</sup> and several geriatric conditions, such as lower urinary tract dysfunction,<sup>4–6</sup> gait disturbance<sup>4,7,8</sup>

and depressive symptoms.<sup>9,10</sup> Damage of nerve fibers connecting the cerebral cortex and subcortical regions or between cortical areas could cause various geriatric symptoms.

Lower urinary tract dysfunction causes lower urinary tract symptoms (LUTS), which often limit activities of daily life and impair quality of life in older adults. In addition, urinary incontinence, which is the most troublesome symptom, is one of the major reasons for increased caregivers' burden in demented older adults.<sup>11</sup> Primary lower urinary tract dysfunction including that due to prostatic hyperplasia and urinary tract infection is important in LUTS, but impaired regulation in the brain could be a potential reason in patients with dementia. Several studies have reported a correlation of WMH with LUTS in older adults.<sup>4–6</sup> However, the role of regional WMH after adjustment for brain atrophy

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and confounding factors in relation to LUTS remains uncertain. The purpose of the present study was to identify the effects of regional WMH on LUTS in older adults diagnosed with amnesic mild cognitive impairment (aMCI) or Alzheimer's disease (AD). The goals of this study were: (i) to clarify the regional progression of WMH with aging; and (ii) to determine the impact of regional WMH on LUTS after adjustment for brain atrophy and other confounding factors. The results of the present study, reported here, were that WMH increased particularly in the frontal lobe with aging, and that WMH in the frontal lobe was critical in urinary incontinence in aMCI and AD patients.

## Methods

### Participants

The study protocol was approved by the ethical review board of Japan's National Center for Geriatrics and Gerontology (NCGG). Candidate patients and their caregivers provided informed consent before participation in the study. We enrolled 461 outpatients (318 female) consecutively at their initial visit. Patients were aged 65–85 years, attended the NCGG hospital in 2010–2013 and were diagnosed with aMCI ( $n = 69$ ) or AD ( $n = 392$ ). AD was diagnosed as probable AD or possible AD based on the criteria published by the US National Institute of Neurological and Communicative Disorders and Stroke, and the Alzheimer's Disease and Related Disorders Association.<sup>12</sup> aMCI was diagnosed based on the criteria defined by Petersen *et al.*<sup>13</sup> Patients with a history of stroke or cortical lesions on MRI, severe conditions such as cardiac failure, renal disorder and liver dysfunction, or neurological disorders other than AD were excluded from the present study.

### Medical history and medication

Clinical data were obtained from NCGG Biobank, which collects biological materials of patients with clinical data for biomedical research. Information on history of hypertension, diabetes mellitus and medication were obtained from clinical charts. Participants were asked about use of medication to treat overactive bladder, benign prostatic hyperplasia, hypertension, AD, anxiety/sleeping disorders and psychological problems/depression. Hypertension and diabetes mellitus were defined as a history of disease and/or presently receiving medication.

### Evaluation of LUTS and clinical assessment

All participants underwent assessment with Comprehensive Geriatric Assessment batteries (CGA). Cognitive function was evaluated by the Mini-Mental State

Examination (MMSE). Behavior and psychological symptoms were evaluated by the Dementia Behavior Disturbance Scale (DBD). To measure obesity, body mass index (BMI) was calculated.

We examined the following LUTS: urinary difficulty, urinary frequency and urinary incontinence. Regarding LUTS, patients and their caregivers were asked the following questions: Have you experienced difficulty with urination? Have you experienced urinary frequency? Have you had urinary incontinence? Urinary difficulty and urinary frequency were assessed by CGA subitems of geriatric syndrome, and the presence and absence of urinary difficulty and urinary frequency were expressed as 0 (absence) and 1 (presence). Assessment of urinary incontinence included the DBD subitems, scored as 0–4 points (0 never, 1 infrequent, 2 sometimes, 3 frequent, 4 always). Absence of urinary incontinence was assigned 0 or 1 points, and presence was assigned 2–4 points.

### Brain MRI

MRI were obtained using 1.5T MR scanners. The images obtained during the period between 1 July 2010 and 31 December 2012 were obtained with a Siemens Avanto (Munich, Germany), and those after 1 January 2013 with a Philips Ingenia (Eindhoven, the Netherlands). The slice setting was exactly the same in the two periods; 19 slices with 6-mm thick slices and an interslice gap of 1.2 mm were obtained in parallel with the anterior commissure-posterior commissure line, covering a 135.6-mm range from the vertex down to the lower end of the pons in each session. Standard head coils (12 elements for Siemens Avanto and 16 elements for Philips Ingenia) were used for MR signal acquisition, and standard body coils were used for transmission. T2-weighted (fast spin echo sequence; repetition time [TR], 3800 ms; echo time [TE], 98 ms; echo train length [ETL], 11; field of view [FOV], 220 × 220 mm; acquisition matrix, 512 × 256; number of acquisition [NA], 1) and fluid-attenuated inversion recovery (FLAIR; FLAIR sequence, TR, 8000 ms; TE 101 ms; inversion time [TI], 2500 ms; ETL, 21; FOV, 192 × 220 mm; acquisition matrix, 256 × 202; NA, 1) images were obtained with a Siemens Avanto 1.5T MR scanner. The imaging parameters for Philips Ingenia were as follows: T2-weighted (fast spin echo sequence; TR, 3900 ms; TE, 100 ms; ETL, 13; FOV, 230 × 230 mm; acquisition matrix, 352 × 262; NA, 2) and FLAIR (FLAIR sequence; TR, 10000 ms; TE 110 ms; TI, 2600 ms; ETL, 32; FOV, 230 × 230; acquisition matrix, 224 × 164, NA, 2).

### Evaluation of WMH and brain atrophy

WMH and brain atrophy were evaluated using an automatic segmentation application (Software for Neuro-Image Processing in Experimental Research: SNIPER,

Department of Radiology, Leiden University Medical Center, Leiden, the Netherlands).<sup>14</sup> The obtained T2-weighted and FLAIR images were imported from DICOM format files and processed as follows:

1 Adaptive level processing. FLAIR images were coregistered to T2-weighted images by six-parameter rigid body transformation. Next, intracranial (IC) segmentation to extract brain tissue was applied to T2-weighted and FLAIR images using a fuzzy C-mean (FCM) clustering algorithm. To estimate gray matter, white matter (WM) and cerebrospinal fluid (CSF) components, the Montreal Neurological Institute template was used as the reference probability map.

2 Reasoning level processing. After brain stripping using a binary mask image to improve removal of the signals from subcutaneous and bone marrow tissue of the head, second level tissue segmentation to separate WMH from WM and CSF was carried out using FCM clustering. It is known that this two-level segmentation procedure is robust against the variability of MRI conditions across different MR scanners, such as image intensity range or image contrast.<sup>14</sup>

In order to improve the accuracy of WMH volumetry, manual optimization of segmentation parameters was applied using the following procedure. The five intensity parameters of the FCM algorithm to discriminate WMH and CSF were optimized to better match the anatomical brain structure by visual inspection. After manual operations to add or remove WMH were carried out, the volume of WMH, which appeared as hyperintense areas on T2-weighted and FLAIR images, was quantified for each cluster. In order to fully include small ischemic lesions, such as lacunar infarcts, as WMH, centric low intensity areas surrounded by hyperintensity on FLAIR were appended to the area of WMH. Finally, the class of the determined WM was assigned according to a built-in atlas.<sup>15</sup> To avoid misclassification of WMH, we repeated analysis in 23 out of 461 participants (5%) to evaluate intrarater reliability (intraclass correlation coefficient was 0.96), suggesting that the method of measurement used for the present study was reliable. The brain tissue was classified into frontal, parietal, temporal and occipital lobes. WMH were automatically classified as periventricular hyperintensity (PVH) or deep white matter hyperintensity (DWMH), and their corrected volumes were calculated. To minimize the bias of brain atrophy, individual WMH, parenchyma (PAR), CSF and ventricular (VCL) were divided by IC, and the brain volume was adjusted. These indices were used to evaluate whether: (i) brain atrophy can predict the risk of LUTS; and (ii) adjustment of WMH volume by brain atrophy significantly improves evaluation of LUTS risk. The results of all this processing, the WMH volume of each cluster and the index of brain atrophy are presented in Table 1.

**Table 1** Clinical characteristics

|                                      | Mean (SD)      | %    |
|--------------------------------------|----------------|------|
| Age (years)                          | 77.2 (5.1)     |      |
| Female                               |                | 69.0 |
| Education (years)                    | 10.2 (2.5)     |      |
| Body mass index (kg/m <sup>2</sup> ) | 22.0 (3.4)     |      |
| Mini-Mental State Examination        | 19.9 (5.0)     |      |
| Dementia Behavior Disturbance Scale  | 16.3 (11.3)    |      |
| Barthel index                        | 96.5 (8.9)     |      |
| Bladder control                      | 9.1 (2.2)      |      |
| History of                           |                |      |
| Hypertension                         |                | 55.6 |
| Diabetes                             |                | 28.3 |
| Medication for                       |                |      |
| Overactive bladder                   |                | 8.9  |
| Benign prostatic hyperplasia         |                | 3.6  |
| Hypertension                         |                | 39.6 |
| Calcium channel blocker              |                | 36.2 |
| Diuretics                            |                | 8.3  |
| Alpha blocker                        |                | 1.6  |
| Alzheimer's disease                  |                | 26.9 |
| Anxiety/sleeping disorder            |                | 21.4 |
| Psychological problem/depression     |                | 10.5 |
| MRI analysis                         |                |      |
| IC (mL)                              | 1373.9 (128.1) |      |
| PAR, mL (% of IC)                    | 1022.5 (101.4) | 74.5 |
| CSF, mL (% of IC)                    | 351.9 (60.4)   | 25.6 |
| VCL, mL (% of IC)                    | 62.2 (22.4)    | 4.5  |
| WMH total, mL (% of IC)              | 19.2 (20.1)    | 1.39 |
| Frontal lobe, mL (% of IC)           | 10.7 (10.9)    | 0.78 |
| Parietal lobe, mL (% of IC)          | 6.5 (7.9)      | 0.47 |
| Temporal lobe, mL (% of IC)          | 1.3 (1.7)      | 0.09 |
| Occipital lobe, mL (% of IC)         | 0.6 (0.8)      | 0.05 |
| Periventricular area, mL (% of IC)   | 18.1 (19.7)    | 1.31 |
| Deep subcortical areas, mL (% of IC) | 1.1 (1.3)      | 0.08 |

Data are presented as mean (SD),  $n = 461$ . CSF, cerebrospinal fluid; IC, intracranial; PAR, parenchyma; VCL, ventricular; WMH, white matter hyperintensity.

### Statistical analysis

All analyses were carried out using the Japanese version of SPSS for Windows version 19.0 (IBM Corporation, Armonk, NY, USA). WMH and brain atrophy volumes were analyzed by non-parametric tests, because these variables did not show a normal distribution.

When analyzing the significance of differences between patients with and without LUTS, Mann-Whitney  $U$ -test and  $\chi^2$ -tests were used. Progression of regional WMH with aging was analyzed by Kruskal-Wallis test. To explore independent risk factors for LUTS, total and regional WMH were entered into a logistic regression model with the following variables selected as possible confounders: age, sex, MMSE, BMI, diabetes, brain atrophy and medication (for overactive bladder, benign prostatic hyperplasia, hypertension, AD, anxiety/sleeping disorder and psychological