≪高齢者と地域医療≫ 認知症の地域連携 ——三鷹市・武蔵野市認知症医療連携の現状

長谷川 浩　神崎恒一*

要旨

- 増え続ける認知症患者に対し，認知症専門医療機関のみでは対応が不可能であり，地域の医療機関をはじめとする地域連携が必要である．
- 認知症患者を診るためには，専門医療機関とかかりつけ医との医療連携が必要であるほか，認知機能の低下自体が生活に障害をきたすという疾患の性質上，在宅で患者の生活を支える部門，すなわち地域包括支援センターや在宅介護支援センターなど，介護，福祉，その他の行政部門が深くかかわる必要がある．
- 認知症の地域連携を促進するツールとして情報交換シートを作り出した．

認知症患者の現状○

さまざまなデータ・根拠があり正確に算出することはむずかしいが，現在，認知症高齢者は日本全国で240万人を越えるといわれている．杏林大学医学部付属病院は東京都三鷹市(人口18万人，高齢化率19%)にあるが，日本全国での65歳以上の高齢者での認知症有病率8.5%という統計値を用いた場合，三鷹市だけで現在3,000人近い認知症高齢者がいると推計される．これに軽度認知障害を加え，しかも近隣の市，区を併せると，数万人の高齢者が認知症の精査もしくは治療の対象ということになる．これは脂質異常症の患者数とほぼ同じである．これだけの数の認知症もしくはその疑いのある患者を地域でみていくためには，認知症専門医療機関のみでは到底不可能であり，地域の医療機関をはじめとする地域連携が必要である．

地域連携とその必要性○

認知症患者を診るためには，専門医療機関とかかりつけ医との医療連携が必要であるほか，認知機能の低下自体が生活に障害をきたすという疾患の性質上，在宅で患者の生活を支える部門，すなわち，地域包括支援センターや在宅介護支援センターなど，介護，福祉，その他の行政部門が深くかかわる必要がある．しかしながら，在宅支援部門(ケアマネジャーなど)は認知症の疑いのある高齢者に対して，医療機関を受診させる具体的な手立てを有していないことが多い．一方，病院や診療所は介護保険の申請に始まり，ホームヘルプやデイサービスなど，地域資源の利用を進めるための知識や方法をもたないことが多い．地域包括支援センターにいくよう患者さんや家族に指示はするが，この指示だけでは患者さんや家族は具体的

* H. Hasegawa(講師)，K. Kozaki(教授)：杏林大学医学部高齢医学．

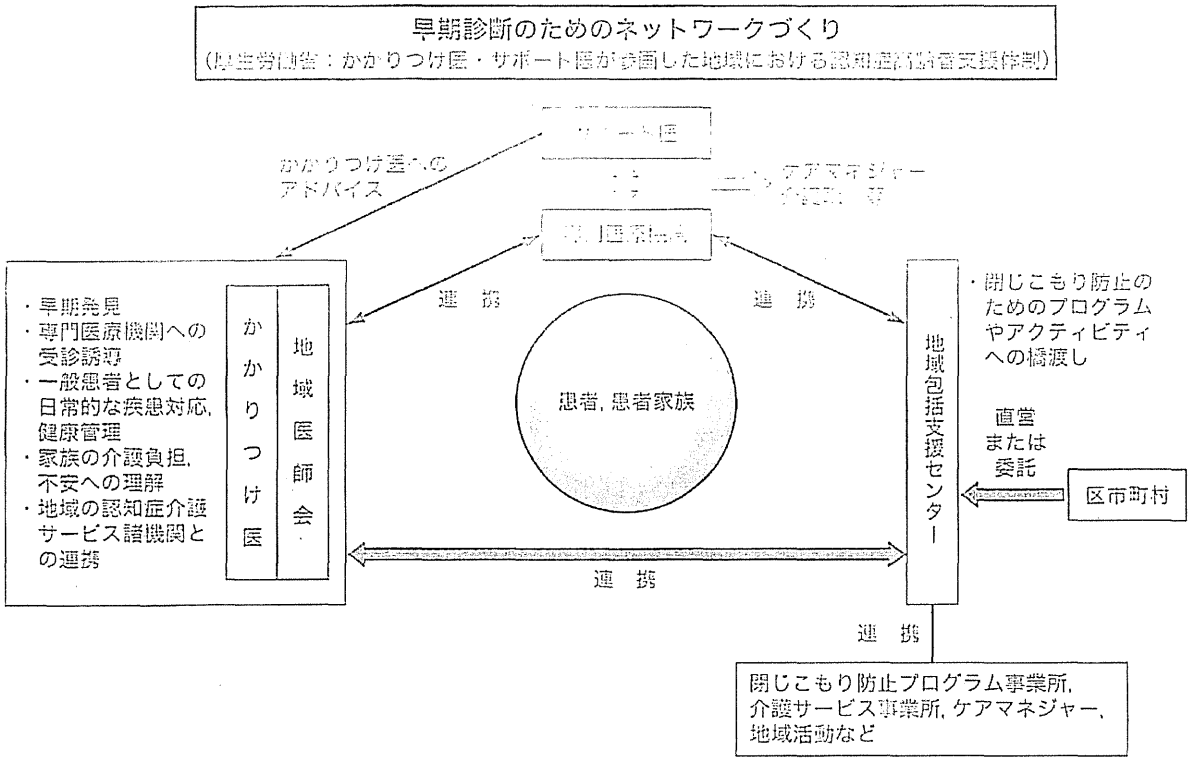

Fig. 1. 国の地域ネットワーク構想

Table 1. 三鷹・武蔵野認知症連携ワーキンググループ

三鷹市	行政	三鷹市健康福祉部高齢者支援課 5 名
	地域包括支援センター	地域包括支援センター(主任ケアマネジャー)4 名
	医師会	医師 2 名
	専門病院	杏林大学病院もの忘れセンター医師 2 名，認知症看護認定看護師 2 名，地域医療連携室 3 名
		吉岡リハビリテーションクリニック
		長谷川病院(精神科)
		井之頭病院
武蔵野市	行政 地域包括支援センター	健康福祉部高齢者支援課，地域包括支援センター計 6 名
	在宅介護支援センター	在宅介護支援センター 2 名
	医師会	医師 2 名
	専門病院	武蔵野赤十字病院医師，ソーシャルワーカー

協力病院：慈雲堂病院(周辺症状対応病院)

には動かないし，動けない．このように，それぞれの立場で知識不足，交流不足に基づく不便，困難を抱えている[1~3]．

三鷹・武蔵野認知症連携○

地域包括支援センター，地域の医師会，専門医

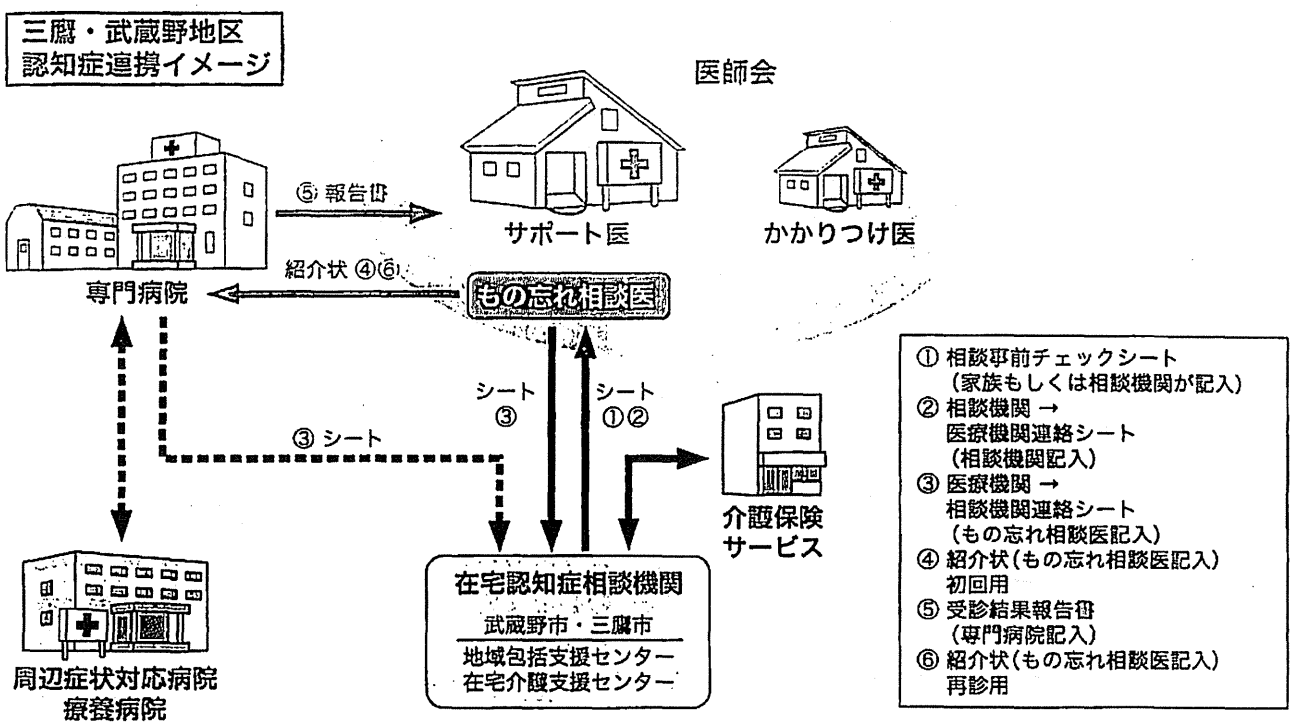

Fig. 2. 情報交換シート

療機関の三者が結びつく必要があるとの国の地域ネットワーク構想に基づいて(Fig. 1)，三鷹市と武蔵野市では(Table 1)のように，両市の 1)地域包括支援センター，在宅介護支援センター，行政，2)両医師会，3)専門病院の連携体制を構築するため，三鷹・武蔵野認知症連携ワーキンググループを組織し，2008 年より活動を開始した．当初より 2ヵ月に 1 回，連携会議を開き，具体的な課題について検討を行ってきた．その中で，完成したのが情報交換シートである(Fig. 2)．

本連携は基本的に，(Ⅰ)在宅相談機関，(Ⅱ)相談医，(Ⅲ)専門医療機関の三者間の連携である(Fig. 2)．それぞれが上記 1)～3)に対応するが，相談医はかかりつけ医の一部であり，初診であっても積極的に認知症診療にかかわることを了承した医師会所属の医師である．相談医は専門医療機関からの逆紹介を受けることもある．

情報交換シートは三者間で双方向に行う形になっている．病診連携は④～⑥のシートを用いて行う．その際，シート⑤(専門医療機関から紹介医への報告書)には認知症の経過を診るうえで必要な，日常生活自立度(基本的 ADL と手段的 ADL，JABC，Ⅰ～Ⅳ，M)，認知機能(MMSE，病期評価のための FAST)，うつ(GDS15)，生活意欲(意欲の指標)など総合的機能評価のほか，周辺症状，画像として MRI と SPECT の所見，診断名，治療方針(薬物療法と非薬物療法)，患者さん，家族への説明内容などを記載するようになっている．逆方向のシート(紹介医→専門医；④と⑥)には ADL，周辺症状，治療内容と介護の状況などを記載する．これらのシートを用いて継続的に患者の評価を行う．また，本シートで重要なのは③である．シート①②は，地域包括支援センターや在宅介護支援センターなどの在宅相談機関から，相談医や専門医に向けて，家族やケアマネジャー等が，認知症にかかわる日常生活上の問題点を記載するためのものであり，これを受けて相談医，専門医はシート③に，受診結果，本人や家族への説明，導入すべきサービス内容，今後のフォローの予定などを在宅相談機関に返す．情報が一方向に

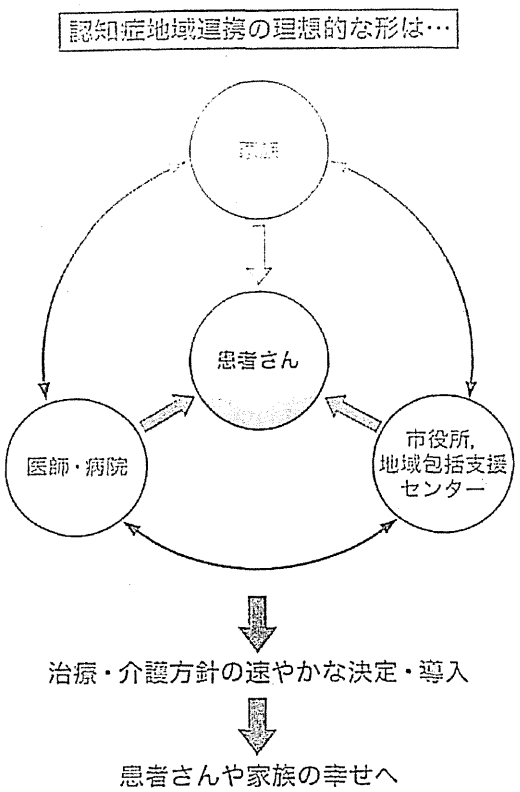

Fig. 3. 地域連携システム

ならないよう，また，情報のやりとりが継続的に行えるよう工夫している．また，シートの利用の仕方を理解する手助けとして，"シートの目的と使い方"の説明書類を添付している．

三鷹・武蔵野認知症連携の現状と課題○

2010年6月より上記シートの試験的運用を開始しており，2ヵ月に1回開催されるワーキンググループ会議で，事例発表を行い，毎回成果を確認している．また，シートはより使いやすいものに改訂を行っている．運用しながら課題をみつけ，修正していくのが本ワーキンググループのやり方である．

情報交換シートの作成以外にワーキンググループでは，医師会での認知症研修会，相談医への参加表明の確認，ケアマネジャー等を対象とした研修会，認知症サポーター養成，サポート医養成の援助などを行っている．認知症研修会では，認知症全般に関する勉強，シートの説明，事例検討などを行っている．有効な連携を築くためには，書面だけでなく顔の見える連携が重要と考えている．また，今後は市民向けの勉強会の開催も予定している．

なお，周辺症状が著しい患者さんへの対応（入所，入院が必要な場合の受け入れ先の担保），在宅相談機関でも行える認知症早期診断バッテリーの開発と普及などが当面の課題である．

さらに認知症連携に求められるもの○

認知症連携は，都市部と地方の違いなど地域により求められる内容が異なる．このためその地域の必要な要素を強化し特化した方法が必要と考えられる．

当初，患者さんや家族は，患者さんの一見おかしな言動や行動が認知症とは判断できず，どこに相談に行ってよいかわからなくなっていることが多い．大事なポイントとしては，患者さんや家族が最初に医師，市役所，地域包括支援センターのどこに相談しても，治療，介護の情報を入手することができ，地域連携システムが回り始めることが肝要である（Fig. 3）．

また，認知症の患者さんが身体疾患（肺炎，心不全など）を発症した場合，どこで診るかが速やかに決定されることも重要であり，その患者さんが退院となった場合の行き先の決定も重要（直接自宅には戻れないケースもあるため）である．これらが速やかに決定されるためにも地域に密着した認知症医療・介護連携が重要と考えられる．

文　献○

1) 武田章敬：在宅医療の制度・システム・教育：認知症地域連携ネットワーク．Geriatr Med 48：1489，2010
2) 松田　実：認知症：認知症地域連携における専門医の役割．治療 90：1166，2008
3) 弓倉　整：専門医に求められる地域連携実践講座：認知症になっても安心して暮らせる仕組みの実践・地域連携の実際：都市型の医師会が主体となった地域連携実践について．老年精医誌 17：125，2006

Geriatr Gerontol Int 2010; **10:** *280–287*

ORIGINAL ARTICLE: EPIDEMIOLOGY, CLINICAL PRACTICE AND HEALTH

Effects of dehydroepiandrosterone supplementation on cognitive function and activities of daily living in older women with mild to moderate cognitive impairment

Shizuru Yamada,[1] Masahiro Akishita,[2] Shiho Fukai,[2] Sumito Ogawa,[2] Kiyoshi Yamaguchi,[2] Jun Matsuyama,[3] Koichi Kozaki,[1] Kenji Toba[1] and Yasuyoshi Ouchi[2]

[1]Department of Geriatric Medicine, Kyorin University School of Medicine, [2]Department of Geriatric Medicine, Graduate School of Medicine, The University of Tokyo, Tokyo, and [3]Medical Corp. Shojyu-kai, Matsuyama Hospital, Gunma, Japan

Aim: There is little evidence that dehydroepiandrosterone (DHEA) has beneficial effects on physical and psychological functions in older women. We investigated the effect of DHEA supplementation on cognitive function and ADL in older women with cognitive impairment.

Methods: A total of 27 women aged 65–90 years (mean ± standard deviation, 83 ± 6) with mild to moderate cognitive impairment (Mini-Mental State Examination, MMSE; 10–28/30 points), receiving long-term care at a facility in Japan were enrolled. Twelve women were assigned to receive DHEA 25 mg/day p.o. for 6 months. The control group ($n = 15$) matched for age and cognitive function was followed without hormone replacement. Cognitive function was assessed by MMSE and Hasegawa Dementia Scale-Revised (HDS-R), and basic activities of daily living (ADL) by Barthel Index at baseline, 3 and 6 months. Plasma hormone levels including testosterone, DHEA, DHEA-sulfate and estradiol were also followed up.

Results: After 6 months, DHEA treatment significantly increased plasma testosterone, DHEA and DHEA-sulfate levels by 2–3-fold but not estradiol level compared to baseline. DHEA administration increased cognitive scores and maintained basic ADL score, while cognition and basic ADL deteriorated in the control group (6-month change in DHEA group vs control group; MMSE, +0.6 ± 3.2 vs −2.1 ± 2.2, $P < 0.05$; HDS-R, +2.8 ± 2.8 vs −0.3 ± 4.1, $P < 0.05$; Barthel Index, +3.7 ± 7.1 vs −2.7 ± 4.6, $P = 0.05$). Among the cognitive domains, DHEA treatment improved verbal fluency ($P < 0.05$).

Accepted for publication 10 March 2010.

Correspondence: Dr Masahiro Akishita MD PhD, Department of Geriatric Medicine, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan. Email: akishita-tky@umin.ac.jp

 doi: 10.1111/j.1447-0594.2010.00625.x

Conclusion: DHEA supplementation in older women with cognitive impairment may have beneficial effects on cognitive function and ADL. **Geriatr Gerontol Int 2010; 10: 280–287.**

Keywords: activities of daily living, cognitive function, dehydroepiandrosterone.

Introduction

Dehydroepiandrosterone (DHEA) and its sulfate (DHEA-S) are the most abundant circulating steroids mainly produced by the adrenal zona reticularis in both sexes.[1] Their circulating levels decline with advancing age,[1–4] and there has been growing public interest in DHEA supplementation to prevent age-associated physical and cognitive impairment. DHEA is considered a crucial precursor of human sex steroid biosynthesis, and to exert indirect androgenic and estrogenic effects following conversion into smaller amounts of testosterone and estradiol.[5,6] While this conversion contributes to a part of testosterone production in men, its role may be much more significant in postmenopausal women whose ovarian production of androgen and estrogen has waned. Importantly, postmenopausal women with intact ovaries continue to produce androgens; DHEA(-S), testosterone and androstenedione, while their production of estradiol is minimal.[7] However, the role of androgens in older women's health is not fully understood.

Clinical trials of the effects of estrogen replacement therapy on cognitive function have shown a lack of efficacy in postmenopausal women initiating hormone replacement therapy after the age of 65 years.[8,9] On the other hand, previous reports have suggested that DHEA may have neuroprotective effects, and the age-associated DHEA(-S) decline is associated with cognitive impairment in older women.[2,10–12] One longitudinal study observed lower DHEA-S levels in patients who subsequently developed Alzheimer's disease.[13] However, controlled trials with DHEA supplementation have failed to show beneficial effects on cognition in healthy middle-aged to older women.[14–16] In these studies, the participants were limited to those who did not have cognitive impairment; therefore, it is reasonable to hypothesize that DHEA supplementation may be effective in much older women with cognitive decline as well as lower DHEA levels.

Dehydroepiandrosterone deficiency is also considered to be involved in the development of physical frailty.[17] Clinical experience with DHEA supplementation in older women is limited, and the few clinical trials examining its effect on physical function and activity of daily living (ADL) have yielded inconsistent results.[18–20] Evidence is lacking for much older women in whom physical impairment becomes more apparent and is accompanied by an age-associated DHEA decline. In our previous study, plasma DHEA and DHEA-S levels, but not estradiol level, were independently related to higher basic ADL in older women aged 70–93 years with functional decline receiving long-term care.[21] We hypothesized that in older women, DHEA replacement could be effective for the age-related decline of physical as well as psychological function.

This study therefore examined the effect of relatively low-dose (25 mg daily) p.o. DHEA supplementation for 6 months on cognitive function and ADL in older women with cognitive impairment.

Methods

Subjects and study design

In this open, non-randomized controlled study, 27 women aged 65 years or older who attended a health service facility for the elderly (a facility that provides nursing care and rehabilitation services to elderly people with disability, Mahoroba-no-Sato, located in Nagano Prefecture, Japan) were enrolled. The participants were in a chronic stable condition and receiving Long-term Care Insurance service either for admission to the facility or day-care services. The principal inclusion criteria were mild to moderate cognitive decline; both Mini-Mental State Examination (MMSE)[22] and Hasegawa Dementia Scale-Revised (HDS-R)[23] scores were between 10 and 28. The subjects were diagnosed as having a mild cognitive impairment[24] or Alzheimer's disease according to the Diagnostic and Statistical Manual of Mental Disorders IV.[25] The participants had never been treated with hormone replacement therapy, and plasma DHEA-S concentration was less than 3.0 μmol/L. The exclusion criteria were history of stroke, extremely low ADL status (Barthel Index[26] <50), malnutrition (serum albumin <3.5 mg/dL), malignancy, acute inflammation (fever, white blood cell count >10 000/μL, or other signs of infection within 4 weeks before enrollment) and overt endocrine diseases, because these diseases may affect both plasma sex hormone levels and functions. None of the subjects were taking a cholinesterase inhibitor (donepezil hydrochloride) or glucocorticoid, opiate or hormone supplement.

Twelve women were assigned to receive DHEA capsule (25 mg/day, Athena Clinics International,

Honolulu, HI, USA) and 15 women were followed up without any additive medication. Medications that could influence cognitive function and plasma hormone levels were not changed during the study period. Outcome measures were cognitive function, ADL, plasma hormone levels, blood cell counts, blood chemical parameters and subjective adverse events. They were assessed at baseline, and after 3 and 6 months. The institutional review board of Mahoroba-no-Sato approved the study protocol, and all participants or their families gave written informed consent.

Hormone measurements

Blood samples were obtained from the participants in the morning after an overnight fast, and plasma hormone levels in addition to blood cell counts and blood chemical parameters were determined by a commercial laboratory (Health Sciences Research Institute, Yokohama, Japan). DHEA and DHEA-S were assayed using sensitive radioimmunoassays with minimum detection limits of 0.04 ng/mL (0.14 nmol/L) and 2.0 μg/dL (0.05 μmol/L), respectively. Total testosterone and estradiol were assayed using chemiluminescent immunoassays with minimum detection limits of 7 ng/dL (0.2 nmol/L) and 4 pg/mL (14.7 pmol/L), respectively. The intra-assay coefficients of variation for these measurements were less than 5%.

Cognitive function

Trained examiners administered two standardized cognitive function tests, MMSE[22] and HDS-R,[23] to assess multiple, diverse aspects of cognitive function at baseline and at the 3- and 6-month visits. Both scores range 0–30, with higher scores indicating better performance. HDS-R includes questions about the subject's age, orientation, immediate recall, serial subtraction of 7 s, reciting digits backward, recalling three words, recalling five objects and word fluency (generating names of vegetables). MMSE evaluates five aspects of cognition: (i) orientation; (ii) registration; (iii) attention and calculation; (iv) recall; and (v) comprehension of spoken language (naming objects, spoken language ability, following commands). MMSE, but not HDS-R, includes four performance tests: (i) three-stage command; (ii) reading and following a command; (iii) writing; and (iv) construction drawing). Based on the results of HDS-R and MMSE, we evaluated seven cognitive domains (points) as follows: (i) orientation (10); (ii) verbal memory (9); (iii) attention and calculation (5); (iv) visual memory (5); (v) spoken-language comprehension (9); (vi) verbal fluency (5); and (vii) performance (7).

Other functional parameters and anthropometric measures

Trained nurses and physical therapists visited the participants at the facility and performed the assessments. Basic ADL was assessed by Barthel Index,[26] mood by Geriatric Depression Scale (GDS, 15 items),[27] and ADL-related vitality by Vitality Index (10-point scale).[28] Higher GDS scores indicate a more marked self-reported depressive status, while higher Vitality Index scores indicate greater willingness.

Adverse events

Information regarding adverse events was obtained by questioning or examining the subjects. At each visit during the treatment period, all new complaints and symptoms were recorded. The safety of DHEA supplementation was assessed from the symptoms and by measuring blood chemical parameters including liver and kidney function, electrolyte levels and hematological parameters. Preexisting complaints or symptoms that increased in intensity or frequency during the treatment period also were examined.

Statistical analysis

Data were analyzed using SPSS statistical software ver. 17.0. Changes in outcome measures at 3 and 6 months were calculated by comparing the values at baseline with those at each measurement. Within each group, the significance of the change from baseline to 6 months was tested using paired Student's *t*-test. Repeated-measures ANOVA was used to test the statistical significance of the effects of DHEA versus control. Significance tests were two-sided, with an α-level of 0.05.

Results

Hormone changes and adverse effects

Characteristics and hormone levels at baseline according to treatment groups are shown in Table 1. There were no significant differences between the DHEA group and the control group in age, length of education, nutritional parameters, functional parameters and plasma hormone levels. DHEA supplementation was well tolerated, with high adherence, and there were no detectable adverse events and none of the subjects dropped out during the study. Measures of liver function, kidney function, electrolyte levels and hemoglobin level were not significantly altered by treatment with DHEA (data not shown). Body mass index remained unchanged in both groups.

Subjects in the DHEA group showed a significant increase from baseline to 3 and 6 months in levels of

Table 1 Participant characteristics at baseline

	DHEA	Control
No. of subjects	12	15
Age, years	82 ± 6 (69–90)	83 ± 6 (65–89)
Education, years	8 ± 2	8 ± 2
Nutritional parameters		
Body mass index, kg/m^2	22.0 ± 2.4 (18.8–26.4)	22.4 ± 3.2 (17.6–27.1)
Albumin, g/dL	4.4 ± 0.3 (3.7–4.9)	4.3 ± 3.2 (3.8–4.7)
Total cholesterol, mg/dL	227 ± 39 (166–294)	203 ± 22 (173–250)
Functional parameters		
MMSE	24.0 ± 4.2 (18–28)	23.4 ± 4.4 (14–28)
HDS-R	19.9 ± 5.8 (10–28)	21.7 ± 5.6 (10–28)
Barthel Index	89.6 ± 9.4 (55–100)	89.7 ± 6.4 (75–100)
Vitality Index	9.8 ± 0.6 (8–10)	9.9 ± 0.3 (9–10)
GDS	7.0 ± 4.4 (1–15)	7.0 ± 4.0 (1–13)
Hormones		
DHEA-S, μmol/L	1.8 ± 0.6 (0.7–2.4)	1.6 ± 0.8 (0.3–2.9)
DHEA, nmol/L	7.6 ± 4.7 (2.4–19.1)	6.6 ± 3.1 (2.1–11.5)
Testosterone, nmol/L	1.4 ± 0.4 (0.9–2.3)	1.3 ± 0.9 (0.2–3.8)
Estradiol, pmol/L	88 ± 52 (15–187)	70 ± 26 (45–115)

Values are shown as mean ± standard deviation (range). HDS-R, Hasegawa Dementia Scale-Revised; MMSE, Mini-Mental State Examination; GDS, Geriatric Depression Scale; DHEA-S, dehydroepiandrosterone sulfate; DHEA, dehydroepiandrosterone. There was no significant difference in each parameter between the groups.

circulating DHEA, DHEA-S and testosterone, with levels reaching approximately 2–3-fold higher than those at baseline, whereas the increase in estradiol level was not significant (Table 2). Subjects in the control group showed no significant change in hormone levels.

Changes in cognitive function and ADL

The changes in functional parameters in each group from baseline to 6 months are shown in Table 2. After 6 months, mean HDS-R score significantly improved in the DHEA group while it remained unchanged in the control group. Mean MMSE score significantly declined in the control group while it remained unchanged in the DHEA group. As a result, significant differences were found in these scores between the groups. DHEA treatment maintained Barthel Index score, whereas the score deteriorated significantly during 6 months in the control group, although the between-group difference at 6 months was not statistically significant. Regarding the components of Barthel Index, in the control group, the sum score of mobility deteriorated significantly after 6 months compared to baseline, while no significant change was observed in the sum score of self care (Table 3). Neither Vitality Index nor GDS changed significantly in both groups.

Table 4 shows the cognitive domain scores at baseline and at 3- and 6-month follow up. Among the seven cognitive domains, DHEA treatment improved verbal fluency ($P < 0.05$), resulting in a significant difference at 6 months between the groups. Verbal memory showed a non-significant trend towards improvement in the DHEA group. Performance test scores significantly declined over time in both groups. There were no differences between the groups in the scores of orientation, attention and calculation, visual memory and spoken-language comprehension.

Discussion

Daily administration of DHEA 25 mg for 6 months in elderly women with mild to moderate cognitive impairment improved cognitive function and maintained basic ADL, compared to the control group. Among the cognitive domains, DHEA significantly improved verbal fluency. At baseline, DHEA and DHEA-S levels were lower than those reported in healthy postmenopausal women in both groups,[2,4] and DHEA treatment increased DHEA, DHEA-S and testosterone levels by 2–3-fold to the mid-normal range for premenopausal

Table 2 Changes in hormone levels and functional parameters by treatment group

	DHEA				Control				*P*
	Baseline	3 months	6 months	0–6-month difference	Baseline	3 months	6 months	0–6-month difference	
Hormones									
DHEA-S, μmol/L	1.8 ± 0.6	4.5 ± 1.3*	5.6 ± 2.9*	3.8 ± 2.8	1.6 ± 0.8	1.8 ± 1.0	1.7 ± 0.8	−0.02 ± 0.4	<0.01
DHEA, nmol/L	7.6 ± 4.7	12.2 ± 4.8*	13.7 ± 7.7*	6.1 ± 8.2	6.6 ± 3.1	7.3 ± 3.7	7.4 ± 4.5	0.9 ± 2.8	0.04
Testosterone, nmol/L	1.4 ± 0.4	2.3 ± 0.7*	2.3 ± 0.8*	0.9 ± 0.8	1.4 ± 0.7	1.4 ± 0.7	1.6 ± 0.8	0.2 ± 0.5	<0.01
Estradiol, pmol/L	88 ± 52	92 ± 48	101 ± 37	13 ± 51	70 ± 26	68 ± 20	67 ± 42	−4.0 ± 38	0.17
Functional parameters									
MMSE	24.0 ± 4.2	24.1 ± 4.6	24.6 ± 4.3	0.6 ± 3.2	23.4 ± 4.4	23.1 ± 5.4	21.3 ± 5.0**	−2.1 ± 2.2	0.04
HDS-R	19.9 ± 5.8	20.5 ± 7.3	22.7 ± 6.3**	2.8 ± 2.8	21.7 ± 5.6	22.1 ± 5.6	21.3 ± 6.4	−0.3 ± 4.1	0.04
Barthel Index	89.6 ± 9.4	92.7 ± 6.5	93.3 ± 6.8	3.7 ± 7.1	89.7 ± 6.4	86.9 ± 7.2	87.0 ± 6.7*	−2.7 ± 4.6	0.04
Vitality Index	9.8 ± 0.6	9.7 ± 0.5	9.7 ± 0.7	−0.1 ± 1.0	9.9 ± 0.3	9.8 ± 0.5	9.7 ± 1.0	−0.3 ± 1.0	0.80
GDS	7.0 ± 4.4	6.2 ± 3.4	6.6 ± 3.7	−0.4 ± 1.7	7.0 ± 4.0	8.3 ± 3.9	7.5 ± 3.5	0.5 ± 3.3	0.60

Values are shown as mean ± standard deviation (range). *P*-values are for repeated-measure ANOVA over all three time points. DHEA, dehydroepiandrosterone; HDS-R, Hasegawa Dementia Scale-Revised; MMSE, Mini-Mental State Examination; GDS, Geriatric Depression Scale; DHEA-S, dehydroepiandrosterone sulfate; DHEA, dehydroepiandrosterone. **$P < 0.01$ compared to baseline, *$P < 0.05$ compared to baseline.

women.[2] No detectable adverse effects were observed throughout the study.

According to the previous trials, DHEA supplementation of 50 mg or more daily does not provide beneficial effects on cognition in healthy middle-aged to elderly women without cognitive impairment.[14–16] However, in a small-scale randomized double-blind placebo-controlled study, DHEA transiently improved cognition (after 3 months) in subjects with Alzheimer's disease while the improvement was not significant at 6 months.[29] Preliminary analysis of the small number of subjects in the present study suggested that DHEA treatment was no less effective in subjects with low baseline cognitive function than those with higher cognitive function (data not shown). Whether the effects of DHEA might be influenced by baseline cognitive function should be further investigated.

It is noteworthy that the 6-month effect of donepezil hydrochloride (5 or 10 mg), the only cholinesterase inhibitor used in Japan, in patients with Alzheimer's disease ranged from no change to less than 1 point improvement in MMSE score,[29–33] which is not so different from the effect of DHEA observed in the present study.

In the present study, not only the participants' cognitive function was impaired, but baseline plasma DHEA(-S) level was also low compared to that in postmenopausal or perimenopausal women.[2,4,10] Regarding DHEA-S levels, according to a report in which healthy pre- and postmenopausal women were studied, DHEA-S levels in women aged 35–44 years and 45–55 years were as follows: 4.31 ± 2.11, 3.90 (mean ± standard deviation) and 3.42 ± 2.01 μmol/L.[2] In this study, DHEA-S was measured using chemiluminescent enzyme immunometric assay; although the measurements by this method and those by radioimmunoassay have been reported to be comparable. In our study, DHEA treatment increased DHEA-S levels to the mid-normal range for premenopausal women.[2] Also, the subjects with lower baseline DHEA-S levels showed non-significant trend towards more improvement in cognitive scores (data not shown). Thus, future studies are needed to explore whether the effects of DHEA might be influenced by baseline DHEA levels.

Because the DHEA receptor has not been identified, DHEA may act after conversion to testosterone and subsequently estradiol through estrogen receptors and androgen receptors, both of which are found in the hippocampus and frontal lobes and subserve verbal memory and working memory in women.[34,35] Further, hippocampal volume and perfusion have been shown to correlate with serum DHEA-S level in demented patients.[36,37] It has also been suggested that estrogenic and androgenic derivatives of DHEA might have different effects on cognitive functions.[38] However, the mechanism by which DHEA improves cognitive

Table 3 Changes in mobility and self-care scores in Barthel Index during the study

Domains (points)	Mean ± SD Baseline	3 months	6 months	Change (0–6 months)	*P*
Mobility (55)					
DHEA	46.9 ± 9.2	48.2 ± 6.0	49.2 ± 5.2	2.3 ± 5.4	0.01
Control	47.5 ± 5.4	46.2 ± 5.5	45.0 ± 4.3*	−3.7 ± 3.9	
Self care (45)					
DHEA	42.7 ± 6.1	44.5 ± 1.5	43.1 ± 2.5	0.4 ± 6.9	0.96
Control	41.8 ± 4.2	42.5 ± 3.4	41.2 ± 4.3	0.7 ± 3.2	

Mobility is the sum score of five domains: (i) transfer (moving from a bed to a wheelchair and back); (ii) walking on a level surface; (iii) propelling a wheel chair; (iv) ascending and descending stairs; and (v) bathing and toilet use. Self care includes feeding, grooming, dressing, bowels and bladder. *P*-values are for repeated-measure ANOVA over all three time points. $^{*}P < 0.05$ compared to baseline. SD, standard deviation.

Table 4 Changes in cognitive domain scores during study

Domains (points)	Mean ± SD Baseline	3 months	6 months	Change (0–6 months)	*P*
Orientation (10)					
DHEA	8.3 ± 1.9	8.0 ± 2.7	7.5 ± 3.0	−0.1 ± 1.2	0.28
Control	8.3 ± 1.9	8.0 ± 2.8	7.5 ± 2.9	−0.7 ± 1.7	
Verbal memory (9)					
DHEA	5.7 ± 2.1	6.5 ± 2.3	6.7 ± 2.5†	1.0 ± 1.9	0.79
Control	6.5 ± 1.7	7.5 ± 1.8	7.0 ± 1.9	0.5 ± 1.7	
Attention and calculation (5)					
DHEA	2.3 ± 1.9	2.8 ± 2.0	2.7 ± 1.8	0 ± 2.3	0.79
Control	2.0 ± 1.7	1.9 ± 1.2	1.8 ± 1.5	−0.5 ± 1.4	
Visual memory (5)					
DHEA	3.6 ± 0.9	3.6 ± 1.3	3.8 ± 1.2	0.3 ± 1.1	0.91
Control	3.6 ± 1.3	3.9 ± 0.9	3.9 ± 1.0	0.5 ± 1.1	
Language comprehension (9)					
DHEA	8.5 ± 0.8	7.8 ± 2.5	8.7 ± 0.7	0.1 ± 0.3	0.12
Control	8.5 ± 0.8	8.5 ± 0.8	8.4 ± 1.1	−0.1 ± 0.9	
Verbal fluency (5)					
DHEA	2.8 ± 3.3	2.5 ± 2.0	4.3 ± 1.1*	1.5 ± 1.7	0.01
Control	3.2 ± 1.9	3.8 ± 1.6	3.3 ± 1.9	0.1 ± 2.1	
Performance (7)					
DHEA	5.7 ± 0.7	5.5 ± 0.7	4.8 ± 0.4**	−0.8 ± 0.6	0.36
Control	5.6 ± 0.6	5.1 ± 0.6	4.5 ± 0.9**	−1.1 ± 0.8	

Change refers to score change during 0–6 months for each parameter in each treatment group. *P*-values are for repeated-measure ANOVA over all three time points. DHEA, dehydroepiandrosterone. $^{*}P < 0.05$, $^{**}P < 0.01$, $^{\dagger}P < 0.1$ vs baseline. SD, standard deviation.

function is unknown. In the present study, plasma estradiol level was not significantly increased after DHEA treatment, implying that its beneficial effects on cognition might be androgen-dependent. Unfortunately, free testosterone levels were not measured, because they were considered to be undetectable in many cases in older women. In addition, sex hormone-binding globulin (SHBG) measurement was not available; however, it has been reported that DHEA 50 mg treatment for 3 months in postmenopausal women did not significantly change SHBG levels,[39] suggesting that the change in SHBG-bound hormone levels after DHEA treatment might be minimal. Given the local aromatization of androgen to estradiol in the brain, the effect of DHEA on cognition might be indirect, complex and heterogeneous. The molecular mechanism underlying the association

between DHEA and cognitive function needs to be clarified, and active forms of testosterone and estradiol should also be examined to investigate whether they would change after DHEA administration.

In our previous study, plasma DHEA and DHEA-S levels were independently related to higher basic ADL in older women aged 70–93 years with functional decline,[21] and other reports have shown a correlation between DHEA level and muscle mass, strength and physical performance.[40,41] In the present study, DHEA treatment maintained the Barthel Index score, while the score deteriorated significantly in the control group. Regarding body composition and strength, DHEA administration in postmenopausal older women aged up to 80 years did not alter body composition, physical performance or strength.[18–20] However, in one small-scale open-label trial, DHEA treatment for 4 weeks improved ADL in three out of seven patients (both men and women) with multi-infarct dementia.[42] All these studies are preliminary, and large-scale and long-term studies are required to ascertain whether DHEA could have a beneficial effect on ADL in older women.

In the present study, no effect of DHEA on depressive mood or vitality was observed, consistent with most clinical trials in older women.[15,43,44] This might be attributable to the participants' relatively low depressive status and high vitality status, namely, ceiling effects.

The limitations of our study should be acknowledged. First, this study was neither blinded nor randomized. Second, the number of participants was too small to confirm the results. Thus, results need to be confirmed by large-scale randomized trials to exclude possible selection bias. Third, considering the sensitivity and accuracy, a standard test like the Alzheimer's Disease Assessment Scale should be used in clinical trials to ascertain the effect of DHEA. Finally, our study duration was 6 months so it does not provide any information on the effects of longer-term DHEA supplementation.

In summary, this small study showed that supplementation of DHEA 25 mg for 6 months to older women with mild to moderate cognitive impairment improved cognitive scores and maintained basic ADL. The results should be confirmed in large-scale randomized trials.

Acknowledgments

This study was supported by a Health and Labor Sciences Research Grant (H17-Choju-046) from the Ministry of Health, Labor and Welfare of Japan; Grants-in-Aid for Scientific Research from the Ministry of Education, Science, Culture and Sports of Japan (20249041, 21390220); and grants from the NOVARTIS Foundation for Gerontological Research, Yamaguchi Endocrine Research Association and Mitsui Sumitomo Insurance Welfare Foundation.

References

1 Orentreich N, Brind L, Rizer R, Vogelman JH. Age changes and sex differences in serum dehydroepiandrosterone sulfate concentrations throughout adulthood. *J Clin Endocrinol Metab* 1984; 59: 551–555.
2 Davison S, Bell R, Donath S, Montalto J, Davis S. Androgen levels in adult females: changes with age, menopause and oophorectomy. *J Clin Endocrinol Metab* 2005; 90: 3847–3853.
3 Kaufman JM, Vermeulen A. The decline of androgen levels in elderly men and its clinical and therapeutic implications. *Endocr Rev* 2005; 26: 833–876.
4 Tannenbaum C, Barrett-Connor E, Laughlin GA, Platt RW. A longitudinal study of dehydroepiandrosterone sulphate (DHEAS) change in older men and women: the Rancho Bernardo Study. *Eur J Endocrinol* 2004; 151: 717–725.
5 Webb SJ, Geoghegan TE, Prough RA, Michael Miller KK. The biological actions of dehydroepiandrosterone involves multiple receptors. *Drug Metab Rev* 2006; 38: 89–116.
6 Labrie F, Luu-The V, Labrie C, Simard J. DHEA and its transformation into androgens and estrogens in peripheral target tissues: intracrinology. *Front Neuroendocrinol* 2001; 22: 185–212.
7 Arlt W. Androgen therapy in women. *Eur J Endocrinol* 2006; 154: 1–11.
8 Shumaker SA, Legault C, Rapp SR *et al.*, WHIMS Investigators. Estrogen plus progestin and the incidence of dementia and mild cognitive impairment in postmenopausal women: the Women's Health Initiative Memory Study: a randomized controlled trial. *JAMA* 2003; 289: 2651–2662.
9 Shumaker SA, Legault C, Kuller L *et al.* Women's Health Initiative Memory Study. Conjugated equine estrogens and incidence of probable dementia and mild cognitive impairment in postmenopausal women: Women's Health Initiative Memory Study. *JAMA* 2004; 291: 2947–2958.
10 Davis SR, Shah SM, McKenzie DP, Kulkarni J, Davison SL, Bell RJ. Dehydroepiandrosterone sulfate levels are associated with more favorable cognitive function in women. *J Clin Endocrinol Metab* 2008; 93: 801–808.
11 Goldman N, Glei DA. Sex differences in the relationship between DHEAS and health. *Exp Gerontol* 2007; 42: 979–987.
12 Valle'e M, Mayo W, Le Moal M. Role of pregnenolone, dehydroepiandrosterone and their sulfate esters on learning and memory in cognitive aging. *Brain Res Rev* 2001; 37: 301–312.
13 Hillen T, Lun A, Reischies FM, Borchelt M, Steinhagen-Thiessen E, Schaub RT. DHEA-S plasma levels and incidence of Alzheimer's disease. *Biol Psychiatry* 2000; 47: 161–163.
14 Kritz-Silverstein D, von Mühlen D, Laughlin GA, Bettencourt R. Effects of dehydroepiandrosterone supplementation on cognitive function and quality of life: the DHEA and Well-Ness (DAWN) Trial. *J Am Geriatr Soc* 2008; 56: 1292–1298.
15 Barnhart KT, Freeman E, Grisso JA *et al.* The effect of dehydroepiandrosterone supplementation to symptomatic perimenopausal women on serum endocrine profiles, lipid parameters, and health-related quality of life. *J Clin Endocrinol Metab* 1999; 84: 3896–3902.
16 Wolf OT, Kudielka BM, Hellhammer DH, Hellhammer J, Kirschbaum C. Opposing effects of DHEA replacement in

elderly subjects on declarative memory and attention after exposure to a laboratory stressor. *Psychoneuroendocrinology* 1998; **23**: 617–629.
17 Fried LP, Tangen CM, Walston J *et al.* Cardiovascular Health Study Collaborative Research Group. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001; **56**: M146–M156.
18 Morales AJ, Haubrich RH, Hwang JY, Asakura H, Yen SS. The effect of six months treatment with a 100 mg daily dose of dehydroepiandrosterone (DHEA) on circulating sex steroids, body composition and muscle strength in age-advanced men and women. *Clin Endocrinol (Oxf)* 1998; **49**: 421–432.
19 Percheron G, Hogrel JY, Denot-Ledunois S *et al.* Double-blind placebo-controlled trial. Effect of 1-year oral administration of dehydroepiandrosterone to 60- to 80-year-old individuals on muscle function and cross-sectional area: a double-blind placebo-controlled trial. *Arch Intern Med* 2003; **163**: 720–727.
20 Nair KS, Rizza RA, O'Brien P *et al.* DHEA in elderly women and DHEA or testosterone in elderly men. *N Engl J Med* 2006; **355**: 1647–1659.
21 Fukai S, Akishita M, Yamada S *et al.* Association of plasma sex hormone levels with functional decline in elderly men and women. *Geriatr Gerontol Int* 2009; **9**: 282–289.
22 Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiat Res* 1975; **12**: 189–198.
23 Kato S, Shimogaki M, Onodera H. Revised Hasegawa Dementia Scale (HDS-R). *Jpn J Geriatr Psychiatr* 1991; **2**: 1339–1347.
24 Winblad B, Palmer K, Kivipelto M *et al.* Mild cognitive impairment – beyond controversies, towards a consensus: report of the International Working Group on Mild Cognitive Impairment. *J Intern Med* 2004; **256**: 240–246.
25 American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 4th edn. Washington, DC: American Psychiatric Association, 1994.
26 Mahoney FI, Barthel DW. Functional evaluation: Barthel Index. *Md State Med J* 1965; **14**: 61–65.
27 Yesavage JA. Geriatric Depression Scale. *Psychopharmacol Bull* 1988; **24**: 709–711.
28 Toba K, Nakai R, Akishita M *et al.* Vitality Index as a useful tool to assess elderly with dementia. *Geriatr Gerontol Int* 2002; **2**: 23–29.
29 Wolkowitz OM, Kramer JH, Reus VI *et al.* DHEA treatment of Alzheimer's disease: a randomized, double-blind, placebo-controlled study. *Neurology* 2003; **60**: 1071–1076.
30 Winblad B, Engedal K, Soininen H *et al.* Donepezil Nordic Study Group. A 1-year, randomized, placebo-controlled study of donepezil in patients with mild to moderate AD. *Neurology* 2001; **57**: 489–495.
31 Rogers SL, Farlow MR, Doody RS, Mohs R, Friedhoff LT. A 24-week, double-blind, placebo-controlled trial of donepezil in patients with Alzheimer's disease. Donepezil Study Group [see comments]. *Neurology* 1998; **50**: 136–145.
32 Feldman H, Gauthier S, Hecker J, Vellas B, Subbiah P, Whalen E. A 24-week, randomized, double-blind study of donepezil in moderate to severe Alzheimer's disease. *Neurology* 2001; **57**: 613–620.
33 Nozawa M, Ichimiya Y, Nozawa E *et al.* Clinical effects of high oral dose of donepezil for patients with Alzheimer's disease in Japan. *Psychogeriatrics* 2009; **9**: 50–55.
34 Janowsky JS. Thinking with your gonads: testosterone and cognition. *Trends Cogn Sci* 2006; **10**: 77–82.
35 Genazzani AR, Pluchino N, Luisi S, Luisi M. Estrogen, cognition and female ageing. *Hum Reprod Update* 2007; **13**: 175–187.
36 Magri F, Terenzi F, Ricciardi T *et al.* Association between changes in adrenal secretion and cerebral morphometric correlates in normal aging and senile dementia. *Dement Geriatr Cogn Disord* 2000; **11**: 90–99.
37 Magri F, Terenzi F, Ricciardi T *et al.* Hippocampal perfusion and pituitary-adrenal axis in Alzheimer's disease. *Neuropsychobiology* 2000; **42**: 51–57.
38 Hirshman E, Merritt P, Wang CC *et al.* Evidence that androgenic and estrogenic metabolites contribute to the effects of dehydroepiandrosterone on cognition in postmenopausal women. *Horm Behav* 2004; **45**: 144–155.
39 Stomati M, Rubino S, Spinetti A *et al.* Endocrine, neuroendocrine and behavioral effects of oral dehydroepiandrosterone sulfate supplementation in postmenopausal women. *Gynecol Endocrinol* 1999; **13**: 15–25.
40 Valenti G, Denti L, Maggio M *et al.* Effect of DHEAS on skeletal muscle over the life span: the InCHIANTI study. *J Gerontol A Biol Sci Med Sci* 2004; **59**: 466–472.
41 O'Donnell AB, Travison TG, Harris SS, Tenover JL, McKinlay JB. Testosterone, dehydroepiandrosterone, and physical performance in older men: results from the Massachusetts Male Aging Study. *J Clin Endocrinol Metab* 2006; **91**: 425–431.
42 Azuma T, Nagai Y, Saito T, Funauchi M, Matsubara T, Sakoda S. The effect of dehydroepiandrosterone sulfate administration to patients with multi-infarct dementia. *J Neurol Sci* 1999; **162**: 69–73.
43 Wolf OT, Neumann O, Hellhammer DH *et al.* Effects of a two week physiological dehydroepiandrosterone substitution on cognitive performance and well-being in healthy elderly women and men. *J Clin Endocrinol Metab* 1997; **82**: 2363–2367.
44 Arlt W, Callies F, Koehler I *et al.* Dehydroepiandrosterone supplementation in healthy men with an age-related decline of dehydroepiandrosterone secretion. *J Clin Endocrinol Metab* 2001; **86**: 4686–4692.

第51回日本老年医学会学術集会記録
〈教育講演〉

高齢者の転倒予防

神崎　恒一

Key words：要介護，転倒スコア，太極拳，個別アセスメント

（日老医誌　2010；47：137-139）

高齢者の転倒と寝たきり

高齢者は屋内外，様々な場所で転倒する危険があり，地域での転倒率は20～40％と言われている．また，転倒に伴って大腿骨頸部をはじめとして骨折が生じ，これがもとで寝たきりに陥るケースが多い（図1）．統計的にも，転倒による骨折発生頻度や転倒・骨折によって要介護に至る頻度は，高齢になるほど増加することが判明している[1]．一方，転倒によって骨折やその他の重度な外傷は免れても，再度転倒するのではないかとの不安から，意欲低下や閉じこもり状態になり，やがてADLが低下し，要介護，寝たきり状態に陥る慢性的な経過をたどるケースも多い（図1）．

転倒しやすい高齢者のスクリーニング

転倒には様々な要因がかかわるが，大きく外的要因と内的要因に分けることができる．外的要因とは屋内の段差や障害物，手すりの有無，履き物など環境要因に起因する場合を指す．一方，内的要因とは1）視力，聴力障害，姿勢変化，筋力低下など加齢に伴う虚弱性変化と，2）循環器要因（起立性低血圧など），神経系要因（パーキンソン病，認知症など），筋・骨格系要因（骨粗鬆症，変形性関節症など）などの身体要因，3）薬物によるものなどを指す．転倒にかかわる要因は多岐に渡るため，一つ一つのコンポーネントを分けて評価することは難しい．外来では，問診，診察に加えて，握力や下肢の筋力検査，片足立ち持続時間，継ぎ足歩行，Up and Goテスト，重心動揺検査などを行い，筋力，バランス能，その他を総合的に評価する．しかしながら，これらの検査は機器や時間を要する難点がある．

したがって，一般高齢者の中で転倒のハイリスク者をさがすためには，より簡易な方法を用いることが望ましい．そのために考案されたのが「転倒スコア」である．転倒スコアは自己記入式調査票であり，身体機能に関連する8項目，認知，感覚器，骨運動器に関する7項目，薬の服用1項目，環境要因に関する5項目の計21項目と，過去1年間での転倒歴を問う全22項目から成っている（図2）．大河内らは転倒スコアを用いて，地域高齢者の転倒を前向きに調査し，過去の転倒と4つの質問項目を用いることによって，感度68％，特異度70％で将来の転倒を予測できることを報告している[4]．我々は，杏林大学病院もの忘れセンターの通院患者において，転倒スコアは，片足立ち持続時間，Up and Goテスト，手伸ばし試験，握力，継ぎ足歩行の各検査と有意な相関を示し，しかも将来の転倒を予測する上で，これらの検査を代用できる可能性があることを報告した[5]．転倒ハイリスク者を見出すマススクリーニングツールとして転倒スコアは有用であると期待できる．

転倒予防のストラテジー

高齢者の要介護，寝たきりを防ぐために転倒予防が重要であることは論を待たないが，予防法が十分あるわけではない．先に記したように，転倒には様々な要因がかかわり，しかもこれらは複合して転倒発生にかかわるため，単一の要因に対する介入だけでは一般に不十分である．病院に通っていない「元気な高齢者」に対する将来の虚弱予防と，施設入所中の「虚弱高齢者」とでは，当然転倒予防対策は異なるべきである．虚弱予防として有効な運動に関して，前者に対しては筋力強化訓練など比較的強度の高い運動が有効であり，後者に対しては“転倒しないよう注意しながら”バランス運動などを行うことが効果的である．太極拳はストレッチ，バランス，筋力強化の意味では最も転倒予防にむいており，半数近くまで転倒を減らすことが報告されている（表1）．その

K. Kozaki：杏林大学医学部高齢医学

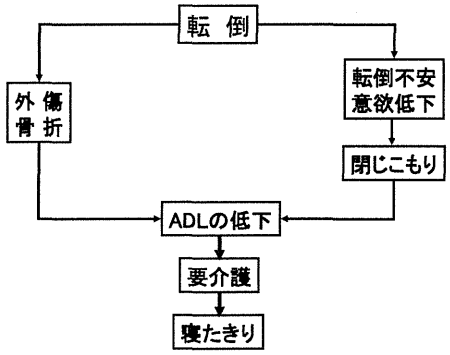

図1　転倒のもたらす影響
鈴木隆雄　老年医学 Update（文献2）より改変

過去一年に転んだことがありますか？	（はい いいえ）	
「はい」の場合、転倒回数（　回/年）		
1. つまずくことがありますか	（はい いいえ）	身体機能
2. 手すりを使わないと階段昇降ができませんか	（はい いいえ）	
3. 歩く速度が遅くなってきましたか	（はい いいえ）	
4. 横断歩道を青のうちに渡りきれますか	（はい いいえ）	
5. 1kmくらい続けて歩けますか	（はい いいえ）	
6. 片足で5秒くらい立つことができますか	（はい いいえ）	
7. 杖をつかってますか	（はい いいえ）	
8. タオルはかたく絞れますか	（はい いいえ）	
9. めまい・ふらつきがありますか	（はい いいえ）	認知 感覚器 骨運動器
10. 背中が丸くなってきましたか	（はい いいえ）	
11. 膝が痛みますか	（はい いいえ）	
12. 目が見えにくいですか	（はい いいえ）	
13. 耳が聞こえにくいですか	（はい いいえ）	
14. もの忘れが気になりますか	（はい いいえ）	
15. 転ばないかと不安になりますか	（はい いいえ）	
16. 毎日、お薬を5種類以上飲んでいますか	（はい いいえ）	
17. 家の中が暗く感じますか	（はい いいえ）	環境要因
18. 家の中によけて通るものがありますか	（はい いいえ）	
19. 家の中に段差がありますか	（はい いいえ）	
20. 階段を使わなくてはなりませんか	（はい いいえ）	
21. 生活上、急な坂道を歩きますか	（はい いいえ）	

図2　転倒スコア
文献3より

ほか，屋内環境の改善，向精神病薬等の中止，総合機能評価を用いた個別指導なども転倒予防に効果を発揮している（表1）．

医師は，転倒を誘発する可能性のある不必要と思われる薬剤を中止することが重要である．一般に，高齢者は罹患疾患数の増加とともに老年症候群の数が増加し，老年症候群の増加は処方薬剤数の増加につながる．“非特異的と思われる訴え”に対して，薬が手っ取り早く使用されがちだからである．特に，睡眠薬や安定剤，抗うつ薬，抗精神病薬などの薬剤はふらつき，転倒を誘発する薬剤である．また，錐体外路症状を起こすことが知られているメトクロプラミド（プリンペラン），ドンペリドン（ナウゼリン），シサプリド（リサモールなど），スルピリド（ドグマチールなど）などの胃薬は，長期間投与されやすいので，注意が必要である．その他，利尿薬等の各種降圧薬にも転倒誘発の危険がある．いずれの薬剤も，ふらつきのある高齢者を見たら，因果関係を疑って，一つずつ減量，中止していくよう検討する．

表1　転倒骨折予防事業の科学的成績（EBM）

予防事業の種類	研究数	対象数	危険度
家屋環境改善	1	530	0.64
筋力訓練・バランス訓練	3	566	0.80
太極拳	1	200	0.51
向精神薬中止	1	93	0.34
総合機能評価・個別指導	3	1,973	0.73
ヒッププロテクター	6	3,412	0.35

施設高齢者では朝方や，夕食前後の時間帯に転倒が発生することが多い．これは排泄や更衣，整容，食事などに際して移動が多いこと，薄暗い時間であること，注意力が散漫になりやすいこと，などが個人的要因であり，また，介護，看護職員数が少なくなることも大きな原因である．このようなアセスメントに対して，シフト制を導入し，転倒が起こりやすい時間帯に人員を増やすこと，また個別ケアプランを導入することで転倒を減らすことができることが発表されている．

ただ，いかなる手段を講じても，転倒を繰り返す高齢者は存在する．この様な場合，家族に転倒が起こる危険性を十分説明し，骨折→寝たきりの可能性があることを普段からしっかり説明しておく必要がある．そのうえで，転倒しても骨折しないようヒッププロテクター等の装具を着用してもらう．しかしながら，ヒッププロテクターは着心地の悪さのため着用率が上がらないの難点がある．

最後に

転倒は様々な要因が複雑に関連しておこるため，特定の要因を明らかにし，介入することは難しい．個別に，関連要因を抽出し，その中から介入可能な要因，特に環境改善や薬物の整理に十分注意をはらうことができれば，転倒防止への効果は大きい．その際，身近にいる配偶者，家族に注意点を具体的に指示すること，それでも転倒は起こり得ることを説明しておく必要がある．転倒予防に効果がある体操もやり方を間違えれば，転倒を誘発したり，体を痛めてADLを損なう危険もあるので，常に個人に合わせて最善の方法を選択するよう配慮すべきである．

文　献

1）厚生労働省：国民生活基礎調査，2001.
2）鈴木隆雄：転倒の疫学．老年医学 Update 2004-05（日本老年医学会雑誌編集員会編），p95-105.
3）鳥羽研二，大河内二郎，高橋　泰，松林公蔵，西永正典，山田思鶴ほか：転倒リスク予測のための「転倒スコア」

の開発と妥当性の検証．日老医誌 2005; 42: 346–352.
4) Okochi J, Toba K, Takahashi T, Matsubayashi K, Nishinaga M, Takahashi R, et al.: Simple screening test for risk of falls in the elderly. Geriatr Gerontol Int 2006; 6: 223–227.
5) Kikuchi R, Kozaki K, Iwata A, Hasegawa H, Toba K: Evaluation of risk of falls in patients at memory impairment outpatient clinic. Geriatr Gerontol Int in press.
6) 辻 一郎：介護予防に対する老年学の役割．日老医誌 2004; 41: 281–283.

Fall prevention in the elderly

Koichi Kozaki

Abstract

Causes of falling are multi-factorial. Although it is not easy to identify specific causes of falling, it is necessary to detect the significant causes of falling in each individual. In particular, use of medications and indoor hazards are important factors. We need to give instructions to families who live together with older persons how to avoid dangers of falling. Exercise has been proven to provide beneficial effects to prevent falling, however it is necessary to consider exactly what and how much exercise one should prescribe to elderly individual who are at high risk of falling. In other words, it is important to give best approach to prevent falling after considering the status of the elderly.

Key words: *Dependent elderly, Fall-predicting score, Tai-Chi exercise, Individual assessment*
(Nippon Ronen Igakkai Zasshi 2010; 47: 137–139)

Department of Geriatric Medicine, Kyorin University School of Medicine

International Psychogeriatrics (2013), 25:1, 105–110 © International Psychogeriatric Association 2012
doi:10.1017/S1041610212001482

Relative preservation of the recognition of positive facial expression "happiness" in Alzheimer disease

Yohko Maki,[1,2]* Hiroshi Yoshida,[3]* Tomoharu Yamaguchi[1,4] and Haruyasu Yamaguchi[1]

[1] *Gunma University School of Health Sciences, Gunma, Japan*
[2] *Geriatrics Research Institute and Hospital, Gunma, Japan*
[3] *Department of Social & Clinical Psychology, Hijiyama University, Hiroshima, Japan*
[4] *Department of Rehabilitation, Gunma University of Health and Welfare, Gunma, Japan*

ABSTRACT

Background: Positivity recognition bias has been reported for facial expression as well as memory and visual stimuli in aged individuals, whereas emotional facial recognition in Alzheimer disease (AD) patients is controversial, with possible involvement of confounding factors such as deficits in spatial processing of non-emotional facial features and in verbal processing to express emotions. Thus, we examined whether recognition of positive facial expressions was preserved in AD patients, by adapting a new method that eliminated the influences of these confounding factors.

Methods: Sensitivity of six basic facial expressions (happiness, sadness, surprise, anger, disgust, and fear) was evaluated in 12 outpatients with mild AD, 17 aged normal controls (ANC), and 25 young normal controls (YNC). To eliminate the factors related to non-emotional facial features, averaged faces were prepared as stimuli. To eliminate the factors related to verbal processing, the participants were required to match the images of stimulus and answer, avoiding the use of verbal labels.

Results: In recognition of happiness, there was no difference in sensitivity between YNC and ANC, and between ANC and AD patients. AD patients were less sensitive than ANC in recognition of sadness, surprise, and anger. ANC were less sensitive than YNC in recognition of surprise, anger, and disgust. Within the AD patient group, sensitivity of happiness was significantly higher than those of the other five expressions.

Conclusions: In AD patient, recognition of happiness was relatively preserved; recognition of happiness was most sensitive and was preserved against the influences of age and disease.

Key words: dementia, Alzheimer disease, emotional face recognition, positivity bias, aging, happiness, social interaction, morphing technology

Introduction

Deficits in the recognition of emotional facial expressions might lead to behavioral disturbances that often accompany Alzheimer disease (AD), and behavioral features are more distressing than cognitive deficits for caregivers of patients with AD (Donaldson *et al.*, 1998). Facial expressions are universally identified into six basic expressions: happiness, sadness, surprise, anger, disgust, and fear (Ekman *et al.*, 1971). The human face conveys non-verbal information about emotional states, the recognition of which is critical for appropriate social behavior.

In aged individuals, positivity recognition bias has been reported for facial expression (Mather and Carstensen, 2003; 2005). The positivity recognition bias was well-studied with memory; aged individuals remember a larger quantity of positive events than negative ones, and show more emotionally positive memory distortion for autobiographical information than younger adults do (Mather and Carstensen, 2005). Such positivity bias in aged individuals has been consistently reproduced in experimental settings of various recognition modalities such as emotional facial recognition and visual stimuli as well as memory (Mather and Carstensen, 2003; 2005; Kapucu *et al.*, 2008; Spaniol *et al.*, 2008). However, studies on emotional facial recognition in AD

*Equal contribution.

Correspondence should be addressed to: Haruyasu Yamaguchi, Gunma University School of Health Sciences, 3-39-15 Showa-machi, Maebashi, 371-8514 Gunma, Japan. Phone: + 81-27-220-8946; Fax: + 81-27-220-8946. Email: yamaguti@health.gunma-u.ac.jp. Received 22 May 2012; revision requested 20 Jun 2012; revised version received 30 Jul 2012; accepted 31 Jul 2012. First published online 24 August 2012.

patients have produced various results. First, it is controversial whether facial recognition itself is declined or not; some studies reported preserved ability of emotional facial recognition (Bucks *et al.*, 2004; Luzzi *et al.*, 2007; Guaita *et al.*, 2009; Yamaguchi *et al.*, 2012), whereas others reported impairments (Spoletini *et al.*, 2008; Bediou *et al.*, 2009; Drapeau *et al.*, 2009). It is also controversial whether there were differences in the recognition of various emotions. Some studies reported no difference (Bucks *et al.*, 2004; Luzzi *et al.*, 2007), whereas others reported differences, e.g. selective impairment was reported in labeling the facial expression of sadness (Hargrave *et al*, 2002), and recognition of happy facial expressions was reported to be relatively preserved in comparison with angry facial expressions (Yamaguchi *et al.*, 2012). It was also reported that the most identified emotion was happiness among seven facial expressions (six basic expressions and boredom) in the moderate and severe stage of dementia (Guaita *et al.*, 2009).

The controversy may be partly due to confounding factors. Some studies have suggested involvement of confounding factors such as deficits in spatial processing of non-emotional facial features and in verbal processing to express emotions (Cadieux *et al.*, 1997; Burnham *et al.*, 2004). The deficits shown in the experiments could be due to the decline of the spatial recognition and/or verbal processing, which were prominent in AD. Thus, in the present study, we demonstrated characteristics of emotional face recognition in AD patients, by adapting a new method that eliminated the influences of these confounding factors to reveal whether the recognition of positive expressions is relatively preserved in AD.

Methods

Participants

The participants were 12 outpatients with mild AD in Clinical Dementia Rating scale (CDR) 1, 17 aged normal control (ANC), and 25 young normal control (YNC). Participants were limited to mild AD patients to eliminate the influence of difficulties of understandings of the rules. The exclusion criteria were: prosopagnosia, psychiatric diseases, delirium, and verbal incomprehension including aphasia. Those who had weak in eyesight were also excluded; all the participants could distinguish a 2-pixel gap (0.58 mm) on a 15″ monitor screen of Landolt ring from 70 cm away. Subjects were diagnosed based on the criteria for AD by NINCDS-ADRDA (Dubois *et al.*, 2007). Scores over 7 on the Japanese version of the Short Form of the Geriatric Depression Scale (Yesavage *et al.*, 1982) were also excluded because depressive tendencies could affect facial recognition. The Ethics Board of the Gunma University School of Health Sciences approved all procedures (No. 21-26), and written informed consent was obtained from all the participants.

Stimuli

Six hundred colored face images of six basic emotional expressions (happiness, surprise, anger, sadness, fear, and disgust) were used. To eliminate confounding factors related to individual difference in non-emotional facial features and ways to express emotions, we used standardized photos of four Japanese women (one neutral and six basic expression photos for each person) in database DB99 (Advanced Telecommunications Research Institute International, Inc. Nara, Japan); facial features and expressions of non-Japanese individuals could be confounding factors for Japanese. Then we made "averaged faces", which canceled individual differences. We prepared one neutral and six emotional expression (100% expression faces) averaged faces by morphing photos of four women. For grading the ability, we prepared photos of 1%–99% intermediate expression levels of each emotion by morphing neutral and 100% expression faces with weight. In this way, the images of 600 emotional averaged faces were prepared; e.g. 38% happy image was made by morphing the 100% happy image and the neutral image with a ratio of 38–62. Each image was framed by an oval to avoid the influence of hairstyle and clothing.

Experimental setting

The experimental setting is shown in Figure 1A (stimuli were in color in the experimental setting). One of the images of intermediate expression levels was displayed on the monitor of touch panel screen in the left, and six small faces of 100% expression were displayed on the right. To eliminate the confounding factor of verbal processing, the participants were required to answer by touching the 100% face that corresponded to the expression of intermediate face. Using the choice of faces instead of verbal labels, even those who had difficulties in verbal processing could answer the question.

The sensitivity of expression was measured using staircase method. The orders of six expressions were randomized using a computer program, and the first stimulus was 100% expression faces in each expression. In each expression respectively, if the response was correct, the level of stimuli increased in the next trial (ex. 38%–35% expression face).

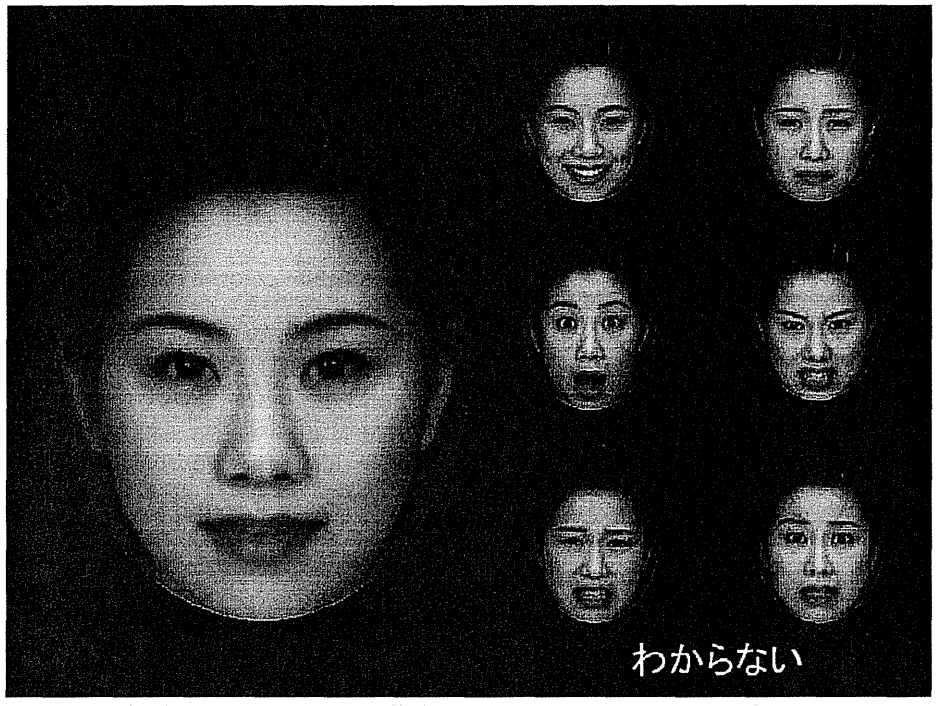

Figure 1. A stimulus shown on the monitor. On the left of the screen, 27% happy face was shown; recognition of 27% happy face corresponded to the sensitivity of 73%, which was the average sensitivity in patients with Alzheimer disease (AD). On the right, six kinds of 100% expressions were shown. The participants were required to choose and tough one of the 100% faces corresponding to the face on the left. The Japanese letters on the right bottom means to have no idea, and they could choose the option.

Alternatively if the participant made an error, the level of stimuli decreased in the subsequent trial. When the sequence was switched from ascending to descending or *vice versa*, the level was recorded as a reversal point score. The levels were changed by 15% until the first reversal point, after that, by 3%. The experiment was continued until the four reversal points were obtained. The average of the third and fourth reversal point scores was used as the sensitivity of the expression. Sensitivity was the difference calculated by subtracting expression level from 100(%); the sensitivity corresponding to 38% expression face was 62. We used the screen of a 15″ touch panel connected to a PC running C++ software based on Windows XP. Before the experimental session, a practice session was conducted. In the practice session, 100% expression images were displayed as stimuli and the participants were confirmed to be capable to match the same expression on the right, where six small faces of 100% expression were displayed as choices. The participants were also required to explain the emotion verbally to confirm that they recognized each emotion.

Statistical analysis

AD patients, ANC, and YNC were compared by using repeated-measured analysis of variance (ANOVA; 3 groups × 6 basic expressions) followed by *post hoc* testing with Bonferroni correction. According to *post hoc* analysis, significantly higher sensitivity in YNC compared with ANC was defined as age effects, and significantly higher sensitivity in ANC compared with AD patients was defined as AD effects. The data were analyzed using the Japanese version of SPSS for Windows version 19.0 (IBM Corporation, New York). Significant differences are set for two-tailed $p = 0.05$ for all analyses.

Results

The ages of the participants were 81.1±9.2 years in mild AD, 76.8±3.5 years in ANC, and 18.9±1.1 years in YNC, and there was no significant difference between age of AD patients and that of ANC by two sample *t*-test. Sensitivities of the three groups and comparisons are shown in Figure 2 and Table 1. There was a significant difference among three groups in perception of facial expressions. According to the *post hoc* analysis, both age and AD effects were observed for anger and surprise (anger: age effects $p = 0.031$, AD effects $p < 0.001$; surprise: $p < 0.001$, $p = 0.029$), whereas for happiness and fear, neither age effects nor AD effects were observed (happiness: $p = 0.138$,

Table 1. Age effects and Alzheimer disease effects

	HAPPINESS	SADNESS	SURPRISE	ANGER	DISGUST	FEAR
†YNC	86.7 ± 14.0	63.1 ± 22.9	81.1 ± 8.9	66.8 ± 15.1	55.5 ± 14.9	55.0 ± 15.3
§*YNC versus ANC*	*0.138*	*0.183*	*<0.001***	*0.031**	*<0.001***	*0.178*
††ANC	76.8 ± 16.8	48.3 ± 25.8	63.9 ± 14.3	55.0 ± 12.3	32.4 ± 19.2	43.9 ± 13.7
¶*ANC versus AD*	*1.000*	*0.048**	*0.029**	*<0.001***	*0.718*	*1.000*
AD	72.8 ± 15.8	25.3 ± 26.0	50.5 ± 18.4	23.4 ± 14.5	25.0 ± 14.6	37.3 ± 28.0

†YNC: young normal controls; ††ANC: aged normal controls; §age effects: significantly higher sensitivity of YNC in comparison with ANC; ¶AD effects: significantly higher sensitivity of ANC in comparison with AD. Both of the age and AD effects were shown by p values of intrasubject *post hoc* analysis with Bonferroni correction of 3 × 6 repeated measured ANOVA (three groups of YNC, ANC, and AD, and six expressions). *$p < 0.05$, **$p < 0.001$.

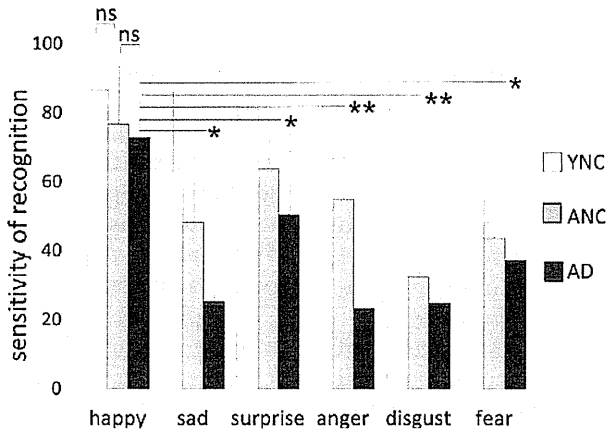

Figure 2. Results of sensitivities of the young normal controls (YNC), the aged normal controls (ANC), and the AD patients. Error bars indicate standard deviation. Regarding recognition of happy and fear faces, there was no significant difference between YNC and ANC, and ANC and AD patients. Regarding recognition of surprise and anger faces, there was significant difference between YNC and ANC, and ANC and AD patients. There was significant difference between ANC and AD in sad face recognition, and between YNC and ANC in disgust recognition. Within AD patients, sensitivity of happy face was significantly higher than that of other expressions. *$p < 0.05$, **$p < 0.001$.

$p = 1.000$; fear: $p = 0.178$, $p = 1.000$). For sadness, AD effects were observed ($p = 0.048$), whereas age effects were not ($p = 0.183$). However, for disgust, age effects were observed ($p < 0.001$), whereas AD effects were not ($p = 0.718$). Within AD patients, sensitivity of happiness was significantly higher than those of the other five expressions, and that of surprise was significantly higher than those of anger and disgust.

Discussion

This study showed that recognition of happy facial expressions was relatively preserved in AD patients. Recognition of happiness was significantly easier than recognition of five other expressions and there were no age effects or AD effects. Regarding negative expressions, age effects were observed in recognition of anger and disgust, and AD effects were observed in recognition of sadness and anger. Surprise had a neutral emotional valence and both effects were observed in surprise recognition.

The results from this study should be reliable because the task used involved a sophisticated matching task that improved on problems in previous studies to cancel confounding factors. In previous experimental settings, participants were required to match the expression of photos of different people. Thus, impairment in the matching could be a result of visuospatial dysfunctions rather than deficits in processing emotions (Ekman *et al.*, 1971). Upon misunderstanding of individual differences in facial features, the participants might fail to extract the emotional implications. The stimuli used in the present study were averaged faces with different emotional valence, where non-emotional features were shared. Thus, differences in features are directly related to emotional differences. Another merit of this matching task was to eliminate the cognitive process to convert perception to abstract verbal expression; abstract thinking and verbal recognition also decline in AD patients. The use of images of Japanese individuals for Japanese participants also eliminated irrelevant cognitive load. Social recognition, including

emotional facial expression, has sociocultural implications, and expression of facial emotions could be influenced by cultural backgrounds (Ekman *et al.*, 1987; Shioiri *et al.*, 1999).

Adding to canceling confounding factors, another advantage of this method is the precise measurement of the sensitivity by using the intermediate level of expressions. In the often used experimental settings, the participants were required to classify the photos of typical emotional faces (100% in the present study) by emotional expression. According to a meta-analysis of 17 studies on emotion recognition and aging, the average of the stimuli of one emotion was around 7. Concerning happiness recognition, the magnitude of the difference between young and aged subjects is potentially masked by a ceiling effect, with young subjects scoring 98% or better in 15 out of 17 studies (Ruffman *et al.*, 2008). Such ceiling effects could exist in the experiments comparing aged subjects and AD patients, thus more sensitive tests with subtle stimuli are desirable. In the present study, we applied 1%–99% intermediate levels of expression, which enabled precise measures of sensitivity.

After eliminating the confounding factors of deficits in spatial processing of non-emotional facial features and in verbal processing to express emotions, positivity bias in ANC was shown, in that recognition of happiness was spared in comparison with YNC. In AD patients, recognition of happiness was spared in comparison with ANC. Hargrave *et al.* (2002) reported that AD patients showed selective impairment in labeling facial expressions of sadness compared with ANC. The results were not identical, as there were differences in the methods used to eliminate the confounding factors of facial features of different people. Hargrave *et al.* (2002) tried to remove the factors by analysis. The experimental setting involved matching the emotion displayed on the reference face with one of six simultaneously presented alternatives, and all seven photographs were faces of different people. A multivariate analysis of covariance (MANCOVA) model was adapted using each subject's score on the facial identity matching task as a covariate. The advantage of the present study is eliminating the confounding factors at the experimental phase.

The mechanism of positivity recognition bias in aged individuals and AD patients remains unproven. Positivity bias in aged individuals was explained by lifetime perspective motivational changes; as the time perspective is reduced, current emotional goals associated with well-being become more important (Carstensen *et al.*, 1999). Consequently, aged individuals would tend to allocate more cognitive resources to improve emotion regulation, and their information processing was characterized by a positivity bias (Mather and Carstensen, 2005; Mather and Knight, 2005; Brassen *et al.*, 2011). Within this framework, positivity bias in facial emotional recognition could be explained by shifts in attention allocation for positive stimuli (Mather and Carstensen, 2005; Goeleven *et al.*, 2010).

Concerning such allocation of cognitive resources to emotion regulation, capacities of cognitive resources should be considered. Mather and Knight reported that aged individuals with superior cognitive abilities were more likely to exhibit positivity bias (Mather and Knight, 2005). In line with the report, the positivity bias should be reduced in AD patients with cognitive decline. However, the experiment was conducted on memory, and if the allocation occurred only in the remembering phase, and not the memorizing phase, the explanation could not be applied to facial recognition. Goeleven *et al.* (2010) suggested that increased age is associated with reduced allocation of resources to negative stimuli, and the explanation could also be true in AD patients.

The present study showed decreases of negative emotion recognition and relatively preserved positive recognition. Our results are in line with the conclusions based on the meta-analysis of Murphy and Issacowitz, which revealed an age-related decrease of negativity preference as compared to an increased positivity preference (Murphy and Isaacowitz, 2008). The above explanations are still hypotheses, and specifying the interaction between cognitive decline and emotion processing would be a valuable topic for future research.

Regarding study limitations, it is possible that recognizing happy facial expressions was easier, as this was the only positive emotion in the study. The differentiation of the four negative expressions, sadness, anger, disgust, and fear, was more difficult. Thus, the results should be confirmed in an experimental setting using stimuli with three facial expressions: happiness, a negative emotion, and a neutral expression.

This study showed that recognition of happy facial expressions was relatively preserved in AD patients; the results could be generalized to other ethnicity because emotional facial recognition is basically universal. These experimental results may be useful if they are implemented in a way to improve the daily life of AD patients. Caregivers should take advantage of cues from happy facial expressions to provide beneficial care.

Conflict of interest

None.