assumed that optical path lengths are constant across subjects and at different measurement points. Hence, evaluations using NIRS machines which cannot measure absolute values must be considered estimates. Nevertheless, Ferrari et al. [17,18] argued that this type of NIRS instrument can accurately measure changes in [oxy-Hb] and [deoxy-Hb] because the path length does not change more than 10% across channels. Second, the cortical region/channel association in our study differed depending on subject head shape, as the channels departed from Fpz (according to the international 10/20 electrode placement system for EEG) on which we set the lowest center photodiode. Thus, a perfect cortical region/channel association is not guaranteed, and even the possibility that some channels were overlying superior temporal regions in some individuals cannot be excluded. Other NIRS instruments, for instance those equipped with two channels can obtain identical cross subject anatomical positioning based on personalized arrays of probes according to the subject's head shape [4,26]. Further development of NIRS machines addressing this issue will be necessary. Finally, third, since NIRS data are thought to be affected by anxiety and personality traits [27,36] as well as by systemic response [21,10], interpersonal comparison of NIRS data is not always reliable. The potential influence of particular individual factors on NIRS data needs further investigation.

In summary, we have demonstrated that multichannel NIRS during ATMT performance is a useful tool to detect bilateral DLPFC and VLPFC activation associated with speeded and unconscious VSWM processing in a paradigm mimicking VSWM performance in daily-life activity. This activation might be associated with the central executive component of VSWM. To our knowledge this is the first study using multichannel NIRS during ATMT performance. Since working memory is considered to be one of the most impaired cognitive functions associated with brain injury and neurologic diseases [2,22], future NIRS/ATMT applications may include assessments of patients suffering from neuropsychiatric conditions to help elucidate the neural network implicated in VSWM and to better understand the pathophysiological mechanisms of various brain disorders.

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Laughter and humor as complementary and alternative medicines for dementia patients

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Abstract

Background: The number of dementia patients has increased worldwide, with an estimated 13.7 million dementia patients in the Asia Pacific region alone. This number is expected to increase to 64.6 million by the year 2050.

Discussion: As a result of advances in research, there several pharmacological therapies available for the treatment of dementia patients. However, current treatments do not suppress the disease process and cannot prevent dementia, and it will be some time before these goals are realized. In the meantime, complementary and alternative medicine (CAM) is an important aspect in the treatment of dementia patients to improve their quality of life throughout the long course of the disease. Considering the individuality of dementia patients, applicability of laughter and humor therapy is discussed. Even though there are many things that need to be elucidated regarding the mechanisms underlying the beneficial effects of laughter and humor, both may be good CAM for dementia patients if they are applied carefully and properly.

Summary: In this debate article, the physiological basis and actual application of laughter and humor in the treatment of dementia patients are presented for discussion on the applicability to dementia patients.

Background

Because of the rapidly increasing elderly population, the need for psychogeriatric services will increase in coming years. In particular, a faster aging of the population has been observed in Asian countries compared with that in Western countries. The World Health Organization has proposed that for a society to be called 'aging', the proportion of elderly citizens (aged 65 years and older) must be 7%. Once this proportion reaches 14%, a society becomes an 'aged society' [1]. It took 24 years for Japan to move from an aging society (in 1970) to an aged society (in 1994); in comparison, in most Western countries this process takes 60-120 years [1]. Korea is expected to become an aged society by 2019, only 19 years after becoming an aging society (2000).

Considerable progress has been made in psychogeriatric services as a result of increased knowledge of brain science, neuroscience, molecular genetics, brain imaging, and many other new technologies [2]. The mechanisms underlying the cognitive impairment in dementia patients are now understood because of findings from brain science and neuropsychological investigations [3,4]. Electrophysiology (e.g. electroencephalography topography, event-related potentials (ERP), and magnetoencephalography (MEG), brain imaging (e.g. magnetic resonance imaging (MRI), single photon emission computed tomography (SPECT), positron emission tomography (PET) and even newer technologies, such as near-infrared spectroscopy (NIRS) and magnetic resonance spectroscopy (MRS), are versatile tools available to confirm psychogeriatric diagnoses [5]. Furthermore, genetic information is routinely used to evaluate the risk, as well as the prognosis, of a disease and a patient's response to drug treatment [6].

Treatment of behavioral and psychological symptoms of dementia (BPSD) remains one of the most unmet needs in psychogeriatrics [7,8], with more effective pharmacological [9,10] and non-pharmacological interventions [11-13] needed. Psychogeriatrics is, however, a clinical subspecialty in which treatment should be directed towards the person as a whole. Consideration of the person and holistic care are essential, including a bio-

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psycho-socio-ethical evaluation of each patient, because the life of the elderly is so different [1]. Furthermore, psychogeriatric services can be applied to patients in the prestages of dementia, including those with mild cognitive impairment (MCI) [14,15] and subjective cognitive impairment (SCI) [16]. Dementia patients, including those with MCI and SCI, can benefit from psychogeriatric services, and the specific application of laughter and humor therapy in the treatment of these patients is discussed in the present article.

Dementia patients require individualized and life-long intervention

In 2005, it was reported that there were 13.7 million dementia patients in the Asia Pacific region alone and that this number is expected to increase to 64.6 million by the year 2050, a 4.7-fold increase in just 45 years [1]. In addition to its high prevalence, the considerable disruption to patients' daily lives, the burden to caregivers, and the long duration of the disease make dementia, especially Alzheimer's disease (AD), the most malignant disease of our time.

The symptoms of AD differ between individual patients. At the onset of dementia in some patients, certain personality traits that had been well controlled in the past become accentuated, whereas in others there is a 'loss of personality', where the uniqueness of the patient's personality is lost. Some patients show a more rapid deterioration of cognitive function, whereas others show a slower rate of cognitive decline. Some patients exhibit various types of BPSD, whereas others exhibit few abnormal behaviors [7]. Furthermore, the physical, personal, familial, economic, and social environments differ between patients. Thus, each patient should be evaluated as an individual in terms of his/her needs for intervention, taking into account previous social functioning, family structure, and the patient's living environment in order to deliver the most appropriate care. Interventions for dementia patients need to be individualized further taking into consideration the different genetic and environmental factors that are specific to each patient.

The premorbid mental capacity differs between subjects and the symptoms exhibited by dementia patients vary quite widely. Considering the difference in symptoms of dementia patients, a more individualized treatment and management program should be considered taking into account of the emotional and affective responses of each patient individually. In this respect, the possibility of using laughter and humor therapy as a complementary and alternative medicine (CAM) for the treatment of dementia patients is discussed below.

Discussion

Laughter as a CAM

Although modern medical science has enabled correct diagnoses to be made and proper treatments to be initiated for acute diseases caused by exogenous pathogenic factors, there are still numerous chronic, incurable diseases caused by endogenous factors, such as cancer, dementia, hypertension, diabetes, chronic pain etc., for which there is no effective treatment, leaving patients with these conditions to suffer. To facilitate the better management of these chronic diseases, recent attention has focused on the use of CAM, together with Oriental and traditional medicines [17]. CAM is defined by the American Cancer Society as '...supportive methods used to complement evidence-based treatment. Complementary therapies do not replace mainstream treatment and are not promoted to cure disease. Rather, they control symptoms and improve well-being and quality of life'[18]. In contrast, alternative therapies, or alternative medicine, involve non-mainstream treatments that are sometimes used by patients instead of orthodox treatments. Examples of CAM include music therapy, drama therapy, aromatherapy, animal-assisted therapy, gardening, horse riding, exercise, bathing, herbal medications, acupuncture, moxibustion, shiatsu, and yoga among others [19]. However, these therapies have not been well defined. Some are simply based on legend or belief, whereas others are traditionally applied but without any scientific basis.

It is widely accepted that a patient's emotional state will affect the course of the disease. Human emotional behavior can be either negative or positive. Negative emotional behavior is accompanied by disgust, fear, or alarm, which induces a prompt, narrowed response to the stimulus responsible for the life crisis. The 'fight-or-flight' response is the general outcome of negative emotions, in which the sympathetic autonomic nervous system is dominant. Conversely, in safe and relaxing situations, positive emotional behavior is associated with joy, play, and humor, with predominant functioning of the parasympathetic system, which induces responses of extended open behaviors that are helpful in learning new behavioral patterns. Laughter associated with a pleasant feeling is often observed under positive emotional conditions.

Laughter has a unique position in CAM. The benefits of laughter have been recognized historically. As stated by Bertrand Russell, 'Laughter is the most inexpensive and most effective wonder drug. Laughter is a universal medicine'. Laughter has been regarded as beneficial for human health for a long time, with some of the benefits

attributed to laughter including improved immunological [20] and endocrinological [21] responses and increased pain tolerance [22]. Laughter therapy, humor therapy, laughter meditation, and laughter clubs all have unique implications as group programs and as self-management techniques. For practitioners to implement credible programs and effectively teach self-management techniques, further empirical research on the physical, psychosocial, and placebo effects of laughter and humor needs to be conducted.

Physiology of laughter and smiling

Speech and laughter are unique to humans. Although there is considerable information regarding the neuronal representation of speech, little is known about the neural mechanisms of laughter. As described by Charles Darwin, laughter, which is a ubiquitous and unique maneuver of humans that results in a totally defenseless posture involving movement of such a wide area of musculature, should have some beneficial meaning in terms of the evolution of this species [23]. Laughter should mean a lot to our lives.

Newborn babies smile within the first 5 weeks after birth and laugh within the first 4 months. Some smiles are voluntary and smiling can be differentiated into 16 different expressions [24], but there is only one expression of laughter. When we smile, the mouth angles are lifted and the orbits of the eye become thin and surrounded by wrinkles as a result of the simultaneous contraction of the muscularis zygomaticus major and orbicularis oculi. In addition to these muscles, when a person is laughing a wider area of the musculature, including facial, pharyngeal, and respiratory muscles, is simultaneously contracted [24].

Laughter and smiling are usually produced as a message of good will to others. In primates, facial expressions showing bared teeth mean friendliness and primates use these expressions to transmit their sociability and the fact that they have no hostile feelings. Because some forms of smiling are voluntary and easily faked, laughter, which requires a more synergetic contraction of the wider musculature, is believed to have evolved in humans to express a secure, safe message to others.

Neural circuits of laughter and smiling

Laughter is the physiological opposite of crying and is usually an expression of happiness involving typical facial movements and contractions of the respiratory muscles [25]. Neural correlates for laughter may include the anterior cingulate gyrus, which provides emotional consciousness to an individual's experience and is partially under the control of the frontal cortex [26]. The caudal hypothalamus is also involved, acting as the center coordinating emotional changes, including laughter, whereas the temporal amygdala may provide emotional coloring to perceptions and aid in understanding humor [26,27]. Finally, the ventral pontomedullary center for laughter coordinates facial expressions, expirations, and emotional vocalization.

The expression of laughter depends on two partially independent neuronal pathways. One is the 'involuntary' system involving the amygdala, thalamic, hypothalamic and subthalamic areas, and the dorsal brain stem [27]; the other is 'voluntary' and originates in the premotor opercular areas, leading through the motor cortex and the pyramidal tract to the ventral brain stem.

The neural circuit underlying laughter may have three main brain components: (i) cognitive areas, such as sections of the frontal lobe that help a person understand the situation; (ii) a movement area (probably the supplemental motor area) that triggers muscle movements to induce a smile or laughter; and (iii) an emotional component that actuates the perception of happiness after an amusing experience, possibly facilitated by the nucleus accumbens [28].

Neural circuits of humor

Humor can be broadly defined as 'something that is, or is designed to be, comical or amusing'. More specific definitions vary, but humorous communication certainly causes increased feelings of happiness and laughter in those who respond to it, whether due to witty comments or amusing behavior.

Freud's psychodynamic viewpoint described humor as the strongest form of the defense mechanism that allows an individual to face problems and avoid negative emotion [29]. Humor is believed to be effective in distancing oneself, framing problems with perspective, and proactively managing distress [30-32].

Although physiological research on the effects of humor on the body is only just developing, there may be quantifiable health care benefits of humor. Research involving additional measurements of a sense of humor, including self-reported instruments, peer ratings, and comedy monologues, suggests that humor moderates the impact of stressful life events on mood disturbances, such as depression and anxiety, salivary immunoglobulin, and positive affect [33-35]. Similar moderating effects of humor have been identified for depression, insomnia, loneliness, and self-esteem, although not for anxiety [36-39].

Good humor makes people laugh just like pain makes people cry, but humor requires complex neural circuits. Humor is perceived at the beginning as surprise or disharmony, then the paradox is solved, and, finally, the punch line is understood in association with a pleasant feeling. The appreciation of humor requires a wide area of neural circuits covering attention, working memory,

flexible thinking, extraction of word meaning, and positive mood. Patients with lesions in the right frontal lobe have difficulty appreciating humor because of impaired integration of cognition and emotion. Different brain areas are activated by jokes/puns and comics [40]. Humor is present in any social situation, and the nature of what is perceived as amusing varies widely among individuals, societies, and cultures. Everyone enjoys laughing, but a misjudged humorous comment can cause offense, so although laughter is almost always positive, humor itself can provoke mixed emotional responses.

Classification of laughter and smiling

Laughter and smiling can be classified into one of three categories based on evolutional staging as follows: (A) that evoked by a release of tension; (B) that associated with pleasant feelings; and (C) that used for social communication (Table 1).

Laughter or smiling caused by a release of tension is the most basic biological form, and occurs spontaneously in an individual who experiences release from a strenuous tension. The purpose of laughter in this context has been hypothesized to be the release of inner energy accumulated in response to the stress [23]. Laughter to relax is important for the maintenance of mental health. Long-lasting mental tension is accompanied by a hyperaroused state of the sympathetic nervous system, which can be released by laughing [24]. From the viewpoint of mental health, laughter evoked in response to the release of tension is the most important.

The second category, laughter that is provoked or accompanied by pleasant feelings, can be further subdivided into laughter caused by: (B1) fulfillment of instinctive needs; (B2) fulfillment of expectations; (B3) a feeling of superiority; and (B4) recognition of mix-ups. As early as 5 weeks after birth, babies smile after feeding. This is the first laughter observed in human life, elicited by a fulfillment of instinctive needs. Similar laughter is observed in adults after a good meal or a good sleep. When our expectations are realized, especially after hard work and/or endeavor, we usually laugh in association with pleasant feelings, which can be amplified by colleagues sharing in our achievement, with the most explosive form of laughter then being observed. Laughter caused by a feeling of superiority is a type of scornful laughter or a cold smile that has been proposed by some researchers to be the prototype of laughter [23]. Laughter associated with disharmony and/or mismatch is caused by simple mistakes or funny happenings that cause no harm. This sort of laughter can be elicited only when the disharmony is sudden, unexpected, and the results of the misunderstanding are harmless.

Table 1: Relationship between laughter/smiling and the progression of dementia

Type of laughter/smile	Preservation in dementia	
	Early stages	Advanced stages
A1. Release from strong tension	+	+
A2. Release from weak tension	+	+
B1. Fulfillment of instinctive needs	+	+
B2. Fulfillment of expectations	+	-
B3. Feelings of superiority	+	-
B4. Feelings of disharmony	+/-	-
C1. Cooperative	-	-
C2. Defensive	-	-
C3. Aggressive	-	-
C4. Devaluating	-	-

The type of laughter and/or smiling can be classified into one of three categories: (A1,2) that evoked by a release of tension; (B1-4) that associated with pleasant feelings; and (C1-4) that used for social communication. Laughter and smiling induced by a release of tension is regarded as the most basic type and is preserved as the phylogenetically primitive type. Laughter and smiling associated with pleasant feelings has developed with the evolution of humans. Laughter and smiling as communication tools are the most sophisticated and have developed with the sociability of humans. Dementia patients lose the ability to laugh and smile as the disease progresses. Laughter and smiling as communication tools may be lost in the early stages of dementia, when the clinical symptoms of dementia appear. Of the different forms of laughter and smiling associated with pleasant feelings, those induced by disharmony may be lost in early stages of dementia because of the cognitive impairment that may limit a patient's understanding. However, laughter and smiling induced by feelings of superiority, fulfillment of expectations, and fulfillment of instinctive needs are preserved until the advanced stages of dementia. Laughter and smiling in response to a release of tension are preserved in most dementia patients.

The third category of laughter is that used as a communication tool. Facial expressions are important components of laughter and we use these expressions to transmit our intention to be friends with others. Laughing and smiling used to communicate with others can be further subdivided into laughter and smiling for cooperation, defense, aggression, and devaluation. A typical example of cooperative smiling is that used as a greeting. We usually say hello and shake hands while smiling. A defensive smile can be observed when someone is trying to conceal their inner feelings, whereas aggressive laughter can also be called scornful laughter. Everyone dislikes being laughed at and, consequently, aggressive laughter is

extremely powerful. Smiling to devalue something is often used in daily life; for example, when the train door shuts in our face, we often give a wry smile to cancel out the impact of the event.

Laughter in dementia patients

Laughter is usually provoked or accompanied by positive emotions. In clinical settings, it is always desirable for patients, their families, and staff to share relaxed and happy feelings, because patients are often under continuous strain and enormous pressure as a result of their illness. The more serious the illness, the more overwhelming the strain to the patients and their families. Dementia patients are usually under considerable strain, at least at the beginning of their illness. Patients' families are placed under even more stress because of the burden of care [41]. A positive emotion, together with laughter, may enable dementia patients to cope with their illness better, improve immune function, increase pain tolerance, and decrease the stress response. When a positive attitude is shared by patients and staff, it can have a positive effect on the emotional-affective and cognitive functioning of the patients [42,43].

Because the social life of dementia patients is impaired by their illness, they can easily feel isolated. Thus, a feeling that unites them, or provides some sort of bond, with their family and the community can be very beneficial. Dementia patients are often encouraged to participate in daily activities with other people and the positive emotions that are shared by the patients and the care staff help the patients maintain social contact.

Several psychosocial interventions are applied to dementia patients in clinical settings [44]. Examples include cognitive rehabilitation, reminiscence therapy, art therapy, drama therapy, and aerobic exercise [45]. In these activities, a positive attitude of patients is essential and it is always true that a greater effect can be expected when patients participate willingly with a positive outlook. In the case of cognitive rehabilitation, active participation is the condition under which good outcomes can be expected. If the patients are reluctant to participate in the activities, it is unlikely that the program will have any beneficial effects.

Dementia patients become anxious and irritated because they are unable to glean sufficient information from their surroundings due to their impaired cognitive functioning [46]. They are easily trapped in a state in which they feel unsafe, alarmed, and insecure, which, in turn, reduces their ability to process information from their surroundings. With even less secure information, they become more alarmed, leading to negative emotional behavior.

Dementia patients often show various types of BPSD during the course of their illness. Aggression, refusal to cooperate, negativity, and apathy are common, all of which contribute to the further isolation of these patients. In this sense, it is important to keep patients with BPSD within the community.

Because BPSD can often be the most formidable barrier to the care of dementia patients, it is highly recommended that the occurrence of BPSD is prevented. To reduce the occurrence of BPSD in dementia patients, patients should be kept in a stable and safe environment, efforts should be made to ensure good communication with the patients, and patients should be kept feeling relaxed and safe. By doing so, the patients are more likely to laugh and smile.

It is true that laughter and smiling decrease over time in most dementia patients, but it is important to note that not all forms of laughter and smiling are equally reduced. The ability to laugh for social communication is readily lost by dementia patients at the onset of their illness, concomitant with the loss of a social life and their ability to process information, but laughter in response to the release of tension is preserved until the advanced stages of the disease. When dementia patients are released from either physical or mental strain, they always smile. Laughter caused by feelings of disharmony is not usually preserved in dementia patients because of impaired cognitive functioning and because these patients are no longer able to understand the meaning of complicated situations, which means they often cannot understand the punch lines of jokes or appreciate humor.

As discussed above, laughter associated with pleasant feelings can be further subdivided into four types, fulfillment of instinctive needs, fulfillment of expectations, a feeling of superiority, and recognition of mix-ups. Most laughter associated with pleasant feelings is preserved in dementia patients, with observations indicating that these patients laugh and smile when they are exposed to pleasant stimuli. They smile when they are well fed and when they have had a good sleep. They also smile and laugh when they have attained self-set goals. Laughter associated with feelings of superiority is clearly preserved in most dementia patients; they become happy and pleasant when their superiority is recognized. Conversely, when these patients feel humiliated, they become angry and insulted.

Thus, the basic form of laughter is preserved in dementia patients, but the social form of laughter is sometimes lost in the advanced stages of the disease. It is important to ensure that dementia patients are kept in a safe and relaxed environment (and not in alarmed and tensioned),

which will make it more likely that these patients will be able to laugh and smile.

Humor in dementia patients

Humor has positive physiological and psychological effects in a variety of situations. The psychiatric literature purports humor as an effective tool in psychiatric illness and psychotherapy. Benefits of humor in business, management, education, and clinical settings are widely recognized because the right perspective facilitates problem solving both interpersonally and in a group setting. Furthermore, humor puts people at ease, promoting the expression and exchange of ideas. Not only can humor benefit patients, but the use of humor can facilitate the effective management of staff and others in the health care setting [22].

Humor is delicate and sensitive by nature. Humor can be properly appreciated when it is expressed in the right time, right place, and on the right occasion. Confidence, or trust, between the sender and receiver is an important aspect of humor. Establishing this trust is a prerequisite for the introduction of appropriately timed humor. No humor can be appreciated by patients when there is no trust between the patient and care staff. If one side is defensive or angry, he/she may find that the use of humor by the other party is offensive or insulting [47,48]. Patients may also become upset about jokes made at their expense, fearing humiliation and stigmatization [49]. The appropriateness of humor depends on the culture, education, and cognitive function of the receiver. Therefore, the use of humor must be timed wisely and it must be used carefully.

Dementia patients may be more sensitive to jokes or humor than healthy people because patients in the early stages of the disease know that they have difficulties understanding complicated things. Dementia patients with cognitive impairment have difficulty appreciating the disharmony in information sent as humor. Humor should be presented to dementia patients after close evaluation. There are no definitive rules, but humor should generally be introduced slowly; if there is no response or the response is negative, it may be a good idea to abandon all attempts to introduce humor, at least during that clinical encounter [50]. Humor can be used as a defense mechanism in an adverse setting and has obvious value for dementia patients if it is properly addressed and accepted. But the impaired cognitive function of dementia patients must be kept in mind so that humor is presented at the right time, in the right place, and on the right occasion. Everyone enjoys laughing, but a misjudged humorous comment can cause offense, so although laughter is almost always positive, humor itself can provoke mixed emotional responses.

> The other reactions--anger, depression, suppression, denial--took a little piece of me with them. Each made me feel just a little less human. Laughter made me more open to ideas, more inviting to others, and even a little stronger inside. It proved to me that, even as my body was devastated and my spirit challenged, I was still a vital human being. Scott Burton [51]

Summary

Dementia patients should be cared for taking into consideration their individual capacities, which differ from patient to patient. Most laughter and smiling is preserved in dementia patients until the end of the clinical course, even though laughter and smiling as a means of communication is lost during the early stages of the disease. Laughter and smiling associated with pleasant feelings, with the exception of laughing in response to feelings of disharmony, and laughter induced by the release of tension can be used in the treatment of dementia patients. The use of humor, covering issues of the fulfillment of instinctive needs and expectations, as well as feelings of superiority (Table 1), can be a good and effective complementary and alternative intervention in the treatment of dementia patients.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

MT, TK, and TT discussed the importance of laughter and humor to dementia patients and drafted the manuscript. MO, ST, and TM searched for the data on the topics in the literatures. MT, RH, and GS devised the table. All authors have read and approved the final manuscript.

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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

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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 ($P < 0.05$).

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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,[24] 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.

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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

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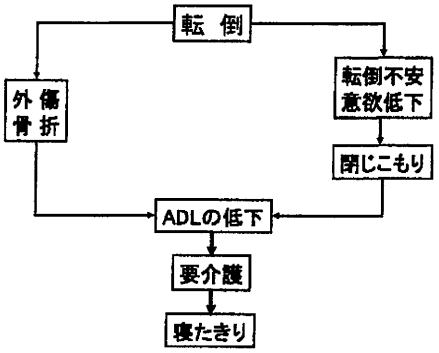

図1　転倒のもたらす影響
鈴木隆雄　老年医学 Update（文献2）より改変

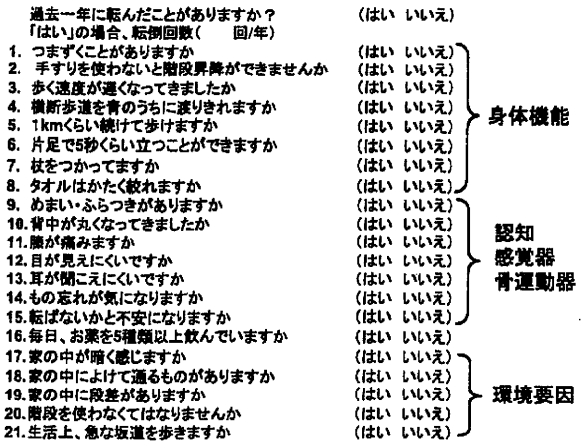

図2　転倒スコア
文献3より

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．

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Fall prevention in the elderly

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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)

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