Journal of Aging Research & Clinical Practice©
*Volume 5, Number 2, 2016*

J Aging Res Clin Practice 2016;5(2):98-101
Published online May 26, 2016, http://dx.doi.org/10.14283/jarcp.2016.98

*ORIGINAL RESEARCH*

# DIETARY MILK FAT GLOBULE MEMBRANE WITH SEMIWEEKLY LIGHT EXERCISE IMPROVES CHOICE STEPPING REACTION TIME IN HEALTHY JAPANESE ELDERLY SUBJECTS: A RANDOMIZED DOUBLE BLIND, PLACEBO-CONTROLLED TRIAL

*N. Ota[1], S. Soga[1], A. Shimotoyodome[1]*

**Abstract:** This study aimed to demonstrate the beneficial effects of nutritional supplementation with milk fat globule membrane combined with light exercise on agility, which predicts falls in the elderly. Twenty-five healthy volunteers (aged 60-74 years old; male/female = 11/14) were enrolled in a randomized, double-blind, placebo-controlled intervention study. The subjects ingested placebo or milk fat globule membrane (1 g/day) tablets daily for 5 weeks and engaged in a 30-min light exercise program semiweekly. After 5 weeks, agility was evaluated using the choice stepping reaction time. The milk fat globule membrane group had significantly shorter motion start and reaction times compared to the placebo group. The reduction in motion start and reaction times was significantly greater in the milk fat globule membrane compared to the placebo group. In conclusion, this study provides evidence that dietary milk fat globule membrane supplementation improves choice stepping reaction time and agility in the healthy elderly population.

**Key words:** Agility, choice stepping reaction time, elderly, milk fat globule membrane.

## Introduction

Aging is associated with an increased risk of falling. Fall-related injuries and deaths in the elderly are a major and increasingly common healthcare problem worldwide (1). Accordingly, preventing falls is a major healthcare priority in aging societies.

The risk of falling is increased by physiological impairments in agility, muscle strength, and balance (2). Exercise can reduce the fall risk by ameliorating these physiological impairments (3). However, further research is needed in order to clarify the optimal exercise program for reducing fall risk and occurrence. Since high-intensity, long-term exercise training is impractical for the elderly, more efficient strategies that boost the beneficial effects of exercise, are required to efficiently reduce the fall risk. Nutritional supplementation may facilitate physical improvement for untrained people more efficiently, even in combination with low-intensity, low-frequency exercises. Recent studies have demonstrated that dietary supplementation with amino acids (4) or tea catechins (5) plus regular low-intensity exercise improved muscle mass and strength in the elderly.

Our recent studies illustrated that dietary supplementation with milk fat globule membrane (MFGM) plus voluntary habitual exercise improves muscle mass and strength (6) and physical endurance capacity (7) in mice. MFGM is a structural membrane covering a triglyceride globule dispersed as emulsified bodies in milk (8). Our previous study revealed that the beneficial effects of dietary MFGM on skeletal muscles were associated with the stimulation of neuromuscular junction development (6), a critical structure of the motor unit (single motor neuron and all of the muscle fibers that it innervates). Because the motor unit is the critical functional unit for voluntary muscle contraction and physical movement, increases in the number of active motor units may improve agility, muscle strength, and balance. Our recent study demonstrated that MFGM intake plus regular exercise enhanced physical agility by improving fast-type motor unit maintenance in middle-aged adults (9). However, whether nutritional supplementation with MFGM plus low-intensity, low-frequency exercise can improve agility in the elderly and reduce fall risk, remains unclear.

This study sought to demonstrate the beneficial effects of dietary MFGM supplementation plus semiweekly

1. Biological Science Laboratories, Kao Corporation, Tochigi, Japan.

*Corresponding Author:* Akira Shimotoyodome, Biological Science Laboratories, Kao Corporation, 2606 Akabane, Ichikai-machi, Haga-gun, Tochigi 321-3497, Japan, Tel: (81)285-68-7589, Fax: (81)285-68-7495, E-mail: shimotoyodome.akira@kao.co.jp

*Received July 21, 2015*
*Accepted for publication August 25, 2015*

light exercise on choice stepping reaction time (CSRT), an indicator of agility (10) and significant predictor of falls (11) in the elderly.

## Methods

### *Subjects and test design*

In this study, 11 male (62–73 years old) and 14 female (60–74 years old) healthy volunteers were enrolled in Tochigi (Japan). Written informed consent was obtained after the subjects were fully informed about the study details and methods. The study was performed under the supervision of an occupational health physician, in accordance with the regulations of the Kao Corporation Ethics Committee for Internal Clinical Studies and in conformity with the Declaration of Helsinki.

In this double-blind randomized placebo-controlled trial, a person without study involvement conducted the computer-generated randomization, and the subjects and test staff remained unaware of the assignments. The subjects consumed either placebo (placebo group, n = 12 [male, n = 5; female, n = 7]) or MFGM tablets (MFGM group, n = 13 [male, n = 6; female, n = 7]). The average daily steps and intake of milk products such as yogurt, cheese, butter, and milk beverages in the placebo and MFGM groups were 6875 ± 845 and 7212 ± 842 steps, and 90 ± 21 and 127 ± 26 g/day, respectively.

### *Intervention*

The subjects ingested six tablets containing 1 g of either MFGM (containing 3.5% sphingomyelin) (9) or maltitol (placebo) daily during the 5-week study and completed the exercise program twice weekly on nonconsecutive days, under a single physician's supervision. The program consisted of 30-min low-intensity (50% of maximum heart rate) sessions involving walking and cycle exercises. On the exercise days, the subjects consumed the tablets within 1 h before training. On the other days, the subjects ingested the tablets at their favorite time during daily physical activity. The subjects were instructed not to change their daily physical activity or dietary habits during the study. In order to monitor their daily activities and intake of test tablets and milk products, the subjects used an electronic pedometer (FB-732, Tanita, Co., Tokyo, Japan) and record sheets, respectively.

### *Physical function test*

The primary outcome of this study was the CSRT, which is recognized as an indicator of agility (10), includes central processing speed and movement velocity (12), and is an independent and significant predictor of falls in the elderly (11). The tests were conducted before (baseline) and after the 5-week intervention.

The four-way CSRT was measured using a computerized force platform (TKK-1264, Takei Instruments, Niigata, Japan) (13). While standing on the center panel, the participants were instructed to quickly move forward, backward, left, or right, according to visual cues randomly presented on a screen. Eight trials were conducted for each of the stepping responses. The motion start time (MST) was defined as the interval between a visual signal and the removal of either foot from the center panel. The reaction time (RT) was defined as the time between a visual signal and removal of the other foot from the center panel. MST and RT were measured in milliseconds and recorded automatically. Body weight, muscle mass, and the body fat ratio were measured using a bioimpedance body fat analyzer (BC-621, Tanita Co., Tokyo, Japan).

### *Statistical analysis*

Data are presented as the mean ± SEM. Two-way analysis of variance was performed using the time point as the repeated measure and the group as the non-repeated measure. When a significant group-by-time interaction was observed, an unpaired t-test was used for intergroup comparisons at each time point, while a paired t-test was used for intragroup comparisons, respectively. In a separate analysis, percent changes in values from baseline to the end of the intervention were evaluated using an unpaired t-test for intergroup comparisons. For the statistical analysis, STATVIEW for WINDOWS (SAS Institute Inc., Cary, NC, USA) was used. All P-values were two-tailed, and a P value of $< 0.05$ denoted statistical significance.

## Results

Ingestion of the test tablets caused no adverse effects. Two subjects (one in each group) did not complete the study after randomization because of a lack of motivation for the intervention. No significant inter- or intragroup differences were noted in daily activities and milk intake (data not shown).

No significant changes in body weight, muscle mass, and the body fat ratio were observed during the intervention (Table 1). After 5 weeks, the MFGM group had a significantly shorter MST and RT (0.423 ± 0.014 and 0.939 ± 0.020 s, respectively) compared to the placebo group (0.480 ± 0.019 and 1.020 ± 0.029 s, respectively) (Table 2). Following the intervention, both the MST and RT declined in the MFGM group (−3.13 ± 2.71 and −3.39 ± 1.67%, respectively) and increased in the placebo group (+5.05 ± 2.53 and +2.55 ± 1.70%, respectively).

**Table 1**
Anthropometric variables at baseline and after the 5-week intervention

| | Baseline | After 5 weeks | Change (%) [a] |
|---|---|---|---|
| Body weight (kg) | | | |
| Placebo | 59.4 ± 2.9 | 59.0 ± 2.7 | −0.61 ± 0.45 |
| MFGM | 57.6 ± 2.3 | 57.8 ± 2.2 | 0.27 ± 0.33 |
| Muscle mass (kg) | | | |
| Placebo | 40.0 ± 2.7 | 40.0 ± 2.7 | 0.06 ± 0.38 |
| MFGM | 40.3 ± 2.1 | 40.4 ± 2.1 | 0.22 ± 0.39 |
| Body fat ratio (%) | | | |
| Placebo | 29.0 ± 2.6 | 28.6 ± 2.6 | −1.4 ± 1.2 |
| MFGM | 26.2 ± 2.1 | 26.2 ± 2.3 | −0.6 ± 1.3 |

MFGM, milk fat globule membrane; The values are expressed as the mean ± SEM of 11 (placebo group [men, n = 4; women, n = 7]) or 12 (MFGM group [men, n = 6; women, n = 6]) subjects; a. The value is the change (%) from baseline to the end of the 5-week intervention period.

**Table 2**
Choice stepping reaction time at baseline and after the 5-week intervention

| | Baseline | After 5 weeks | Change (%) [a] |
|---|---|---|---|
| Motion start time (sec) [b, c] | | | |
| Placebo | 0.458 ± 0.019 | 0.480 ± 0.019 | 5.05 ± 2.53 |
| MFGM | 0.439 ± 0.018 | 0.423 ± 0.014 [d] | -3.13 ± 2.71 [d] |
| Reaction time (sec) [b] | | | |
| Placebo | 0.998 ± 0.032 | 1.020 ± 0.029 | 2.55 ± 1.70 |
| MFGM | 0.974 ± 0.024 | 0.939 ± 0.020 [d] | −3.39 ± 1.67 [d] |

MFGM, milk fat globule membrane; ANOVA, analysis of variance; The values are expressed as the mean ± SEM of 11 (placebo group [men, n = 4; women, n = 7]) or 12 (MFGM group [men, n = 6; women, n = 6]) subjects; a. The value is the change (%) from baseline to the end of the 5-week intervention period; b. There was a significant group-by-time interaction ($P < 0.05$) in the repeated-measures ANOVA during the intervention period; c. There was a significant group effect ($P < 0.05$) in the non-repeated–measures ANOVA during the intervention period; d. There was a significant difference between the two groups in the results of the unpaired t-test ($P < 0.05$).

## Discussion

This study is the first to demonstrate significantly improved CSRT in healthy Japanese elderly subjects after dietary supplementation with MFGM (1 g/day) plus semiweekly light exercise for 5 weeks. In a CSRT test, both RT and MST involve central processing and neuromuscular transmission. Our previous studies demonstrated that MFGM plus voluntary exercise improved muscle strength in senescence-accelerated mice by stimulating "nervous system development" in the skeletal muscle (6). Our recent human study revealed that MFGM enhanced agility in middle-aged adults by improving fast-type motor unit maintenance (9). The seminal study of Lord and Fitzpatrick illustrated that CSRT was an independent and significant predictor of falls in older people, and elucidated the roles of neuropsychological, sensorimotor, speed, and balance factors in agility. It also demonstrated the mean CSRT in the younger (0.744 s) and older (1.264 s) populations, respectively (11). In our present study, MFGM ingestion plus exercise shortened the RT to 0.035 s, which is equivalent to having regained agility that was lost in the past three years. Taken together, the CSRT decreases after MFGM ingestion are consistent with our previous findings. This suggests that dietary MFGM plus low-intensity, low-frequency exercise increases motor unit activity by enhancing neuromuscular transmission, resulting in improved agility and fall prevention in the elderly.

The potential limitations of the present study include our small study population and the unclear underlying mechanism for CSRT improvement. Further studies with larger populations are required in order to clarify these issues.

In conclusion, this study suggests that dietary MFGM supplementation (1 g/day) combined with semiweekly light exercise improves CSRT, an agility marker (10) and fall predictor (11) in healthy Japanese elderly subjects. Daily intake of adequate amounts of MFGM from milk or dairy products is impractical because the amount (1 g) of MFGM used in the study corresponds to 600 mL of whole milk. Therefore, daily MFGM supplementation, together with low-intensity, low-frequency exercise, may improve agility and reduce fall risk in the elderly.

*Acknowledgements:* We are grateful to Akemi Kobayashi, Atsuko Otsuka, Hidefumi Kitazawa, Satoshi Sugita, Shingo Kakuo, and Yukari Yamashiro for their technical contributions. We also thank the staff of medical fitness at the Hokutokai Clinic for their excellent guidance in exercise training.

*Funding:*This study was supported by the Kao Corporation, and was conducted without additional funding or support.

*Conflict of interest disclosure:* All of the authors are employees of the Kao corporation

*Ethics standards:* The suty was reviewed and approved by the Kao Corporation Ethics Committee for Internal Clinical Studies and in conformity with the Helsinki Declaration.

## References

1. Tinetti ME. Clinical practice. Preventing falls in elderly persons. N Engl J Med 2003; 348:42-49.
2. Carter ND, Kannus P, Khan KM. Exercise in the prevention of falls in older people: a systematic literature review examining the rationale and the evidence. Sports Med 2001;31:427-438.
3. Liu-Ambrose T, Khan KM, Eng JJ, et al. Resistance and agility training reduce fall risk in women aged 75 to 85 with low bone mass: a 6-month randomized, controlled trial. J Am Geriatr Soc 2004;52:657-665.
4. Kim HK, Suzuki T, Saito K, et al. Effects of exercise and amino acid supplementation on body composition and physical function in community-dwelling elderly Japanese sarcopenic women: a randomized controlled trial. J Am Geriatr Soc 2012;60:16-23.
5. Kim H, Suzuki T, Saito K, et al. Effects of exercise and tea catechins on muscle mass, strength and walking ability in community-dwelling elderly Japanese sarcopenic women: a randomized controlled trial. Geriatr Gerontol Int 2013;13:458-465.
6. Haramizu S, Mori T, Yano M, et al. Habitual exercise plus dietary supplementation with milk fat globule membrane improves muscle function deficits via neuromuscular development in senescence-accelerated mice. Springerplus 2014;3:339.

7. Haramizu S, Ota N, Otsuka A, et al. Dietary milk fat globule membrane improves endurance capacity in mice. Am J Physiol Regul Integr Comp Physiol 2014;307:R1009-1017.
8. Cavaletto M, Giuffrida MG, Conti A. Milk fat globule membrane components-a proteomic approach. Adv Exp Med Biol 2008;606:129-141.
9. Ota N, Soga S, Hase T, Shimotoyodome A. Daily consumption of milk fat globule membrane plus habitual exercise improves physical performance in healthy middle-aged adults. Springerplus 2015;4:120.
10. Zemková E, Hamar D. Age-related changes in agility time in children and adolescents. Int J Sci Res 2014;3:280-285.
11. Lord SR, Fitzpatrick RC. Choice stepping reaction time: a composite measure of falls risk in older people. J Gerontol A Biol Sci Med Sci 2001;56:M627-632.
12. Khode V, Rajoor U, Ramdurg S, Ruikar K, Nallulwar S. Can chronoscopic reading in whole body reaction time be a tool in detecting cognitive dysfunction in hypertensives? findings from a case control study. Ann Med Health Sci Res 2013;3:233-237.
13. Kim HS, Tanaka K. The assessment of functional age using "activities of daily living" performance tests: a study of Korean women. J Aging Phys Activ 1995;3:39-53.