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Interval Walking Training for Middle-Aged and Older People: Methods and Evidence

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SUMMARY Faced with social problems such as rapidly aging society, the solutions have been expected in sports medicine. Humans became widely distributed on the earth from their birth by acquiring abilities to walk in an upright position and to adapt themselves to various natural environments. However, seeking a 'comfortable environment' in modern civilization has deteriorated these genetic characteristics of humans, and the consumption of resources and energy to acquire such a 'comfortable environment' has induced global warming-associated natural disasters and the destruction of social order. To halt this vicious cycle, we may reactivate the genetic characteristics in humans by doing exercise. To do this, we have developed a health promotion program for middle aged and older people, Jukunen Taiikudaigaku Program, in cooperation with the Japanese government, developed high-intensity interval walking training (IWT), and examined the physical and mental effects on 5,400 people for these 10 years. We found that IWT for 4 months increased physical fitness by 10–20%, decreased the indices of life-style related diseases by 10–20%. Since a prescription of IWT can be conducted by using an IT network system called e-Health Promotion System, the participants in the program were able to receive the prescription even if they lived remote from trainers, enabling them to perform IWT at their favored places and times, and also at low cost. Moreover, we found some single nucleotide polymorphisms closely related to inter-individual differences in the responses to IWT. Further, the system enables us to assess the inactivation/activation of genes for inflammatory responses which has been suggested to be involved in life-style related diseases. Also, the system enables us to search foods to promote health when they are consumed during exercise training. Thus, the system would have strong potential to promote health of middle-aged and older people in advanced aging society.

key words: *interval walking training, portable calorimeter, e-health promotion system, genomic variations, epigenetic effects, supplements*

1. Introduction

In Japan, the population over 65 years old is estimated to increase from 20.8% in 2006 to 30.5% in 2025 [1]. One of the serious problems in advanced aging society is high health care cost for older people. If the current medical system remains unchanged, it is estimated to increase from 17.1 trillion JPY (~171 billion USD) to 56 trillion JPY (~560 billion USD) in 2025 [2].

Figure 1 shows the relationship between age and functional capacity (physical fitness) [3]. As in the figure, the capacity marks the peak value in the twenties and thereafter it decreases by 5–10% every 10 decade and when it decreases below 25% of the peak value, we cannot live independently without helps by others. This decrease was mainly due to senile muscle atrophy, called as "sarcopenia", which is thought to be caused by the similar genetic mechanisms for aging phenomena; increases in gray hair and wrinkles on the skin with aging.

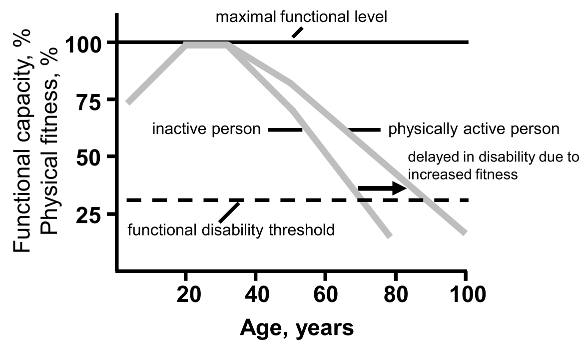

Fig. 1 The relationship between age and physical fitness. Physical activity delays functional disability with advanced aging [3].

It is interesting that health care cost increases with a decrease in physical fitness with aging. Pedersen [4] has suggested that a reduction in muscle metabolism with aging and/or low physical activity causes life-style related diseases by demonstrating that the reduction induces an increase in the visceral fat, invasion of macrophages to the fat, chronic inflammation in the whole body, resistance to insulin, atherosclerosis, deterioration of nervous system, and proliferation of cancer cells, which results in, at a glance, different diseases; diabetes, cardiovascular diseases, depression, dementia, and colonic and breast cancers; however, again, the fundamental cause for these diseases is low muscle metabolism and therefore, they call the diseases as the diseasome of physical inactivity. Moreover, since the syndrome is spread in a community where people share the similar life style, it may be regarded as a kind of infectious disease, and therefore, they recommended a community based exercise prescription system to prevent this.

2. Exercise Training Based on Individual Physical Fitness

Exercise training is the most effective strategy to prevent the deterioration of physical fitness with aging but it should be prescribed according to trainees' individual fitness levels [5]. For example, to increase muscle strength (resistance training), before training, trainees have to have their muscle strength of the target joints determined by trainers in a

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gym by measuring the maximal dumbbell weight which they can lift once, called one repetition maximum (1RM). Then, they are recommended to lift a dumbbell weight of 50–80% 1RM, at > 1 set of 3–15 times/day, 2–3 days/week. If they perform the training, thigh muscle strength for the target joint is expected to increase by 10–110% after the above stated regimens for resistance training for 3–6 months.

To increase aerobic capacity (aerobic training), before training, trainees have to have their peak capacity determine by trainers in a gym by measuring oxygen consumption rate during graded exercise on cycle ergometer or treadmill [5]. After the determination of $\dot{V}O_{2peak}$ whichever with machines or not, trainee may exercise at the intensity of 60–70% $\dot{V}O_{2peak}$, 30–60 min/day, 4–7 days/week. They may start exercise at 50% $\dot{V}O_{2peak}$ for the first month and then gradually increase the intensity to 60% for the 2nd month and end to 70% $\dot{V}O_{2peak}$ for the 3rd month but they may not beyond 85% $\dot{V}O_{2peak}$. If they perform the exercise at the intensity, 30–60 min/day, 4–7days/week, for 3–6 months, their $\dot{V}O_{2peak}$ are expected to increase by 10–20% [5].

However, it might be difficult for middle-aged and older people to visit a gym and to receive exercise prescription from trainers regularly due to time and money problems.

3. Interval Walking Training

The exercise regimens stated above have been thought to prevent age-associated diseases; hypertension, hyperglycemia, obesity, and dyslipidemia; however, it might be difficult for middle-aged and older people to perform such exercise training regimens at a given intensity regularly. We recently found in middle-aged and older people that 1) not only maximal aerobic capacity but also thigh muscle strength increased after aerobic exercise training for 5 months using cycle ergometer [6] and 2) that we were able to estimate maximal aerobic capacity by graded walking in the field without using machines; treadmill and cycle ergometer [7]. Accordingly, we have applied these findings to exercise prescription with "interval walking training (IWT)" on middle-aged and older people in the field, named as Jukunen Taiikudaigaku Project, starting in 1997 and since then, we have accumulated the database (DB) regarding the effects of IWT on physical fitness and the indices of life style related diseases. This project has been organized by Non-Profit Organization of Jukunen Taiikudaigaku Research Center (JTRC) since 2005, and the detailed information on the project is given by their web site [7]. As in Fig. 2, the project has four features as follows:

3.1 Interval Walking Training (IWT)

Before starting training, peak aerobic capacity ($\dot{V}O_{2peak}$) for walking was determined in individual participants. To do this, they walked at subjectively slow, middle, and fast speeds for 3 min each during which time energy expenditure and heart rate were measured every 5 sec by tri-axial

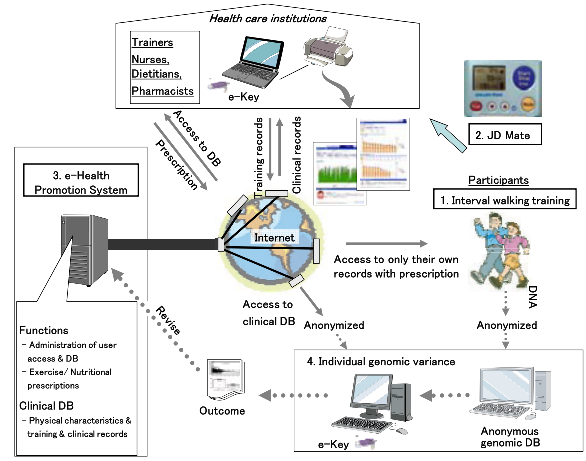

Fig. 2 Interval walking training and e-Health Promotion System. Participants in the training visit a health care institution, a drug store, or a local community office, every 2 weeks to transfer their walking records from the tracking device, JD Mate, to a central server computer through the Internet. Then, the server computer gives them back a trend graph of the records with advice automatically generated by the server. Based on them, the staff; nurses, dietitians, or trainer give them their advices. If participants have the facilities at their homes, they can receive the similar service from the staff through the Internet. By anonymizing and combining the DNA data stored in a separate offline computer and the clinical data stored in the central server computer, we have started to search the genomic variation explaining inter-individual variation in response to the training. The outcome from the research may be used to revise the e-Health Promotion System to develop the algorithm to predict the effects of interval walking training on physical fitness and the indices of life-style related diseases in individuals with different physical and genetic characteristics. e-Key is used to limit a person to access the data base (DB). The squares on the circle of Internet indicate the fire-wall function. The sloid arrows indicate online communications between users and the sever through internet and the dotted arrows indicate offline communications [11].

accelerometry and by near infrared ear pick up method (JD Mate, Kissei Comtec, Matsumoto), respectively, and the values for the last 30 sec of fast walking are averaged and adopted as $\dot{V}O_{2peak}$ and peak heart rate (HR_{peak}) for walking.

After the determination, participants were instructed to repeat IWT at their favorite time and places at low and high intensity of walking alternately at the targets of ~40% and ≥70% $\dot{V}O_{2peak}$, respectively, for 3 min each, ≥4 days/week, for 12 weeks. During IWT, energy expenditure was monitored with a tri-axial accelerometer (JD Mate) carried on the mid-clavicular line of the right or left waist. A beeping signal from the device alerted participants when a change of intensity was scheduled and another melody let them know the time when the intensity of fast walking reached the target level. Participants visited a local community office every 2 week, and data from the tracking devices were transferred to a central sever computer, the results were sent back to participants and they received instructions from trainers.

As a result, we found that $\dot{V}O_{2peak}$ increased by ~10% and knee extension and flexion forces increased by 17% and 13%, respectively, while systolic and diastolic pressures decreased by ~10 mmHg and ~5 mmHg, respectively, after 5-month training. On the other hand, their changes were all minimal after the standard walking training; moderate intensity continuous walking at 40% $\dot{V}O_{2peak}$ for 60 min/day, 4 days/week, for 5 months, which was similar to those after the sedentary life for the same period [8]. Moreover, we found in the study that $\dot{V}O_{2peak}$ was significantly correlated with isometric knee extension force ($R^2 = 0.49$, $P<0.0001$), suggesting that thigh muscle strength is a key determinant for $\dot{V}O_{2peak}$ in subjects of this age, where R indicates a correlation coefficient between the variables and P indicates possibility. When P is less than 0.05, it indicates the relation was statistically significant. Further, these results indicate that increased $\dot{V}O_{2peak}$ induced a marked reduction in blood pressures.

Recently, by using the techniques, we examined the effects of IWT on physical fitness and the indices of lifestyle related diseases (LSD) on 198 men and 468 women aged ~65 years old [9]. They performed IWT, ~60 min/day, ~4 days/week, for 4 months on average. We counted the scores of LSD before and after IWT according to the criteria in the health care guideline for Japanese by the government (Health Insurance Bureau, Ministry of Health, Labor, and Welfare, Japan 2007); 1) systolic blood pressure > 130 mmHg or diastolic blood pressure > 85 mmHg, 2) triglyceride > 150 mg/dl or blood high density lipoprotein cholesterol < 40 mg/dl, 3) blood glucose > 100 mg/dl, 4) BMI > 25 kg/m^2. Therefore, the full score was 4 points when met with all criteria.

To analyze the results, we divided the subjects into 3 groups according to $\dot{V}O_{2peak}$ in females (Fig. 3(A)) and males (Fig. 3(B)). The LSD scores decreased as $\dot{V}O_{2peak}$ increased and, moreover, when $\dot{V}O_{2peak}$ increased after training, the LSD score decreased in both genders. Further, when look at the LSD score in each criterion in females (Fig. 4(A)) and males (Fig. 4(B)), the hypertension score was 0.7–0.8, suggesting that 70–80% of subjects met the criterion in both genders. Similarly, 40–60% and 20–50% of subjects were in hyperglycemia and high BMI, respectively, in both genders. After training, subjects met each criterion decreased by 5–30% in hypertension, 10–40% in hyperglycemia, and 10–30% in high BMI but with no significant reduction in blood lipids. These results suggest that increased $\dot{V}O_{2peak}$ decreased blood pressures, blood glucose, and BMI in that order while the effects on blood lipids were modest.

3.2 Three Dimensional Accelerometry

We have developed a new portable calorie meter with which energy expenditure can be precisely measured even when they walk on inclines [10]. First, we measured VO_2 by respiratory gas analysis and vector magnitude (VM, G) from triaxial accelerations in middle-aged and older males and females aged ~63 years old during graded walking on a treadmill while the incline was varied from −15% to +15%. They walked at subjectively slow, moderate and fast speeds on level and uphill inclines and in addition to these, at their fastest speed at 0% incline. Similarly, they then walked on downhill inclines for 3 min each. We determined a regres-

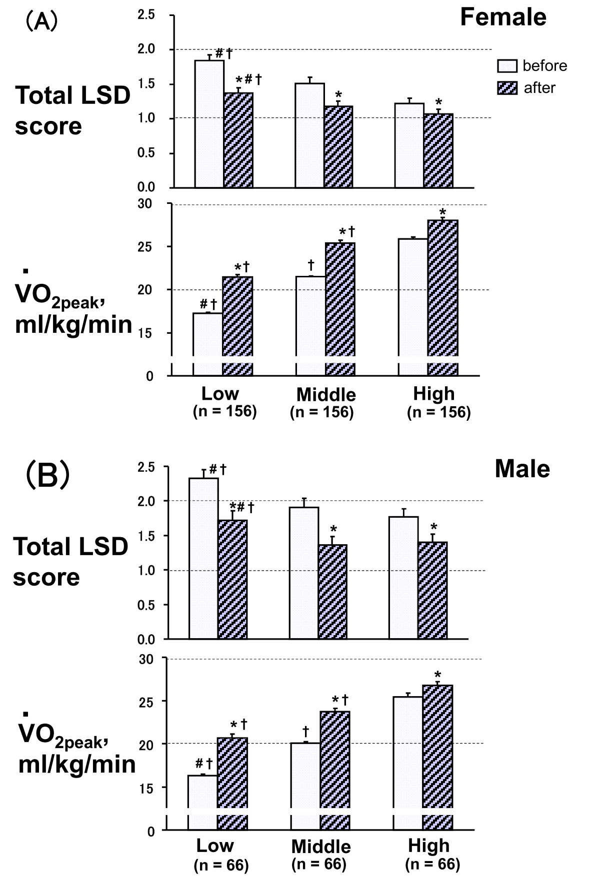

Fig. 3 Total lifestyle related disease (LSD) score and peak aerobic capacity for walking ($\dot{V}O_{2peak}$) before and after interval walking training in males (**A**) and females (**B**). When the subjects were divided equally into 3 groups according to $\dot{V}O_{2peak}$, the score was lower in higher $\dot{V}O_{2peak}$ groups. After interval walking training for 4 months, the score decreased as $\dot{V}O_{2peak}$ increased in every group [9].

sion equation to estimate VO_2 from VM and theoretical vertical upward speed (Hu, m/min) and downward speed (Hd, m/min) for the last 1 min of each trail as $VO_2 = 0.0044\,VM + 1.365Hu + 0.553Hd$.

Second, to validate the precision of the equation, we measured VM and altitude changes with a portable device (JD Mate) equipped with a triaxial accelerometer and a barometer in middle-aged and older subjects walking on an outdoor hill, and compared the estimated VO_2 by the equation stated above with the value simultaneously measured by respiratory gas analysis. As in Fig. 5, we found that the estimated VO_2 (y) from the equation was quite identical to the measured VO_2 by respiratory gas analysis during walking on an outdoor hill with −0.20 ml/kg/min of the mean difference and +/−6.95 ml/kg/min of 95% prediction limit over the range of 2.0–33.0 ml/kg/min in the Bland-Altman analysis. Thus, we have developed the device to estimate VO_2 precisely during walking regardless of geography where subjects walk. Moreover, subjects can perform high-intensity exercise training > 70% $\dot{V}O_{2peak}$ not only by fast walking on a flat place but also by slow or moderate speed of walking on inclines or stairs.

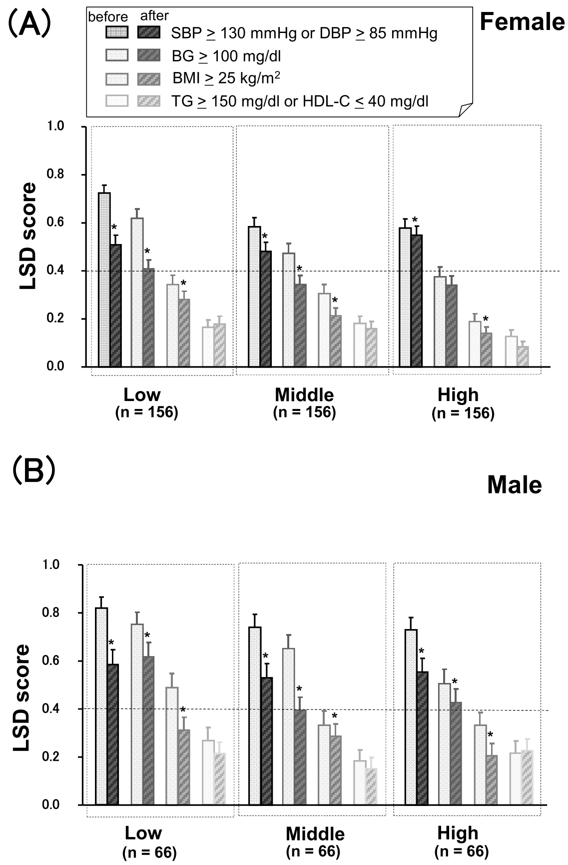

Fig. 4 Lifestyle related disease (LSD) score for each criterion; hypertension, hyperglycemia, high BMI, and dyslipidemia, in males (**A**) and females (**B**). When the subjects were divided equally into 3 groups according to $\dot{V}O_{2peak}$ before training, the score was higher in the order of hypetension, hyperglycemia, high BMI, and dyslipidemia in every group. After training, all scores except for dyslipidemia decreased by 10–40% [9].

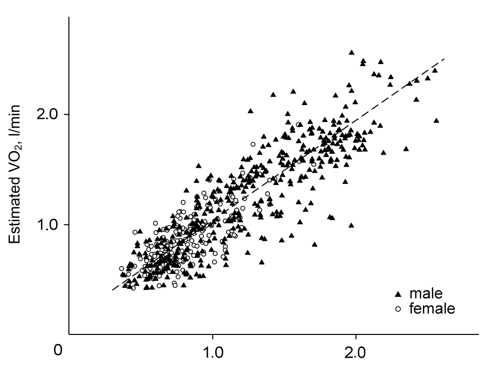

Fig. 5 Relationship between measured oxygen consumption rate (VO_2) by respiratory gas analysis and estimated VO_2 from the equation (see text) during walking in the field. The solid line indicates a regression line for all values [10].

3.3 e-Health Promotion System

Another reason for hindering us from extending exercise prescription for individuals to nationwide is the personnel cost for trainers who have the ability. To solve the problems, we have been developing the e-Health Promotion System as in Fig. 2 [11]. The participants in the program visit local health care institutes near their homes; a local community office and a drug store, every 2 weeks, transfer their walking records from the JD Mate to a central sever computer, and receive a trend graph of their achievements. According to the records, the staff; nurses, dietitians, pharmacists or trainers, give them exercise and nutritional prescriptions while referring to the DB in the server computer about the effects of IWT for 5 months on physical fitness and the indices of LSD in 4,000 subjects and that for more than 5 month in 1,000 subjects. If participants have the facilities at their own homes, they can receive the same service through the Internet without going out.

4. Individual Genomic Variance

Recently, we have started to analyze individual genomic variance in relation with inter-individual variation in response to IWT [12], [13]. Masuki et al. [13] assessed whether single nucleotide polymorphism rs1042615 of the vasopressin V1a receptor altered the indices of LSD in the subjects and, if so, whether it also altered the effects of IWT. CC, CT, and TT carriers of rs1042615 (42, 118, and 64 men; 113, 263, and 154 women, respectively) performed IWT, > 4 days/wk, for 5 months, where CC, CT and TT indicate base pairs (C, cytosine; T, thymine) on DNA (deoxyribonucleic acid) chains. Before IWT, BMI and diastolic blood pressure for men were both higher in TT than in CC; however the differences disappeared after IWT despite similar training achievement between groups. Moreover, after IWT, BMI and diastolic blood pressure (DBP) decreased more in TT than in CC with a greater decrease in low-density lipoprotein (LDL) cholesterol in TT than CC. The decreases in DBP and LDL cholesterol were still greater in TT even after adjustment for their pretraining values. On the other hand, for women, these parameters before IWT and their changes after IWT were similar between CC, CT, and TT. Thus, polymorphism rs1042615 of the V1a receptor altered BMI and DBP in middle-aged and older men, and the training-induced responses of DBP and LDL cholesterol, whereas women did not show any of these responses. These results suggest that single nucleotide polymorphism rs1042615 of the vasopressin V1a receptor was involved in inter-individual variance in responses to IWT in middle-aged and older men.

According to the outcome of these studies, we are developing a computer program to predict the effects of IWT on the physical fitness and the indices of LSD according to not only physical but also genetic characteristics of participants before training. If the program becomes available by the staff in the field, they would be able to give participants exercise prescriptions more fitted for individuals even though they are not specialized in the subjects very much. This would increase the number of participants in IWT.

5. Methylation of Genes Related to Inflammation

Increased aerobic capacity by endurance exercise training has been reported to reduce chronic inflammation in the whole body [14]. It has been suggested that ASC (apotosis-associated speck-like protein containing a caspase recruitment domain) gene is involved in inflammatory responses and that if it is too inactivated by methylation, it causes chronic inflammation and/or allergy while if the gene is too activated by de-methylation, it causes infectious diseases and/or cancers. Therefore, an appropriate methylation state is necessary to keep the body healthy. We compared the methylation of the gene between young (∼19 yr) and older (∼65 yr) subjects and also examined the effects of IWT on the methylation in middle-aged older older subjects. We found that the methylation decreased by ∼30% in older subjects compared with that in young subjects and that 5- mo IWT increased the methylation by ∼20%. Thus, the methylation of ASC gene was rejuvenated by IWT, supporting the idea that increased LSD scores with aging is closely related to the inflammatory responses. Moreover, it should be noted that these findings would not have been obtained without the system to enable a large number of middle-aged and older subjects to perform uniform and long-term exercise training.

6. Combined Effects of Exercise and Nutritional Treatments

Also, this system enables us to assess the combined effects of long-term exercise and nutritional treatments on muscle strength in middle-aged and older subjects. We examined whether post-exercise macronutrient supplementation during a 5-month IWT accelerated exercise-induced increases in skeletal muscle mass and strength in healthy middle-aged and older women [15]. We adopted the subjects having performed IWT for more than 6 months before participating in the study because muscle strength increased markedly for the first 5 months of IWT and reached the steady sate thereafter. Thereby, we examined the mere effects of supplementation on muscle strength by excluding possible effects of IWT alone. We divided subjects into two groups: IWT alone or IWT plus post exercise macro-nutrient (7.6 g protein, 32.5 g carbohydrate, and 4.4 g fat) supplementation. We found that hamstring muscle tissue, measured by computer tomography, increased ∼3% and isometric knee flexion force increased by ∼16% in the supplementation group while they remained unchanged in the control group. We confirmed that training achievement and food intake were not significantly different between groups. These results suggest that post-exercise supplementation of macronutrient during IWT enhanced an increase in muscle mass and strength in middle-aged older people. Again, the study would not have been accomplished without the system to track energy expenditure and food intake during a long-term intervention by exercise in a large population of subjects.

In conclusion, the IWT may significantly contribute the exercise prescription fitted for individual physical fitness broadly available in middle-aged and older people by using the JD Mate and the e-Health Promotion System. Moreover, IWT is such a simple intervention by exercise that it would enable us to develop exercise prescriptions more fitted for individuals including genetic characteristics. Finally, this system would also enable us to search foods to promote health in middle-aged and older people when they are consumed during exercise training.

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