Effect of exergame training with motor imagery on balance, cognitive functions and motor learning in healthy adults: Preliminary study

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Background: Previous studies reported that exergames could improve balance and cognitive function. Also, motor imagery (MI) applied with actual movements could increase balance control. If both are combined, balance and cognitive function may increase more.

Objective: To investigate the effect of exergame training with MI on balance, cognitive function and motor learning in healthy adults.

Methods: Twelve subjects were divided into 2 groups, the exergame training (ET, n = 6) and the exergame with MI training (ET + MI, n = 6). Both groups practiced exergame for 20 minutes. Then, the ET + MI group imagined exergame for 10 minutes. Subjects were trained 3 days per week for a period of 4 weeks. Balance and cognitive function were assessed before training, after 4 weeks of training, and in the follow-up period.

Results: The results showed a significant increase in the single-leg stance test and trunk position sense found only in the ET + MI group, whereas % performance of static balance was significantly increased in both groups after 4 weeks of training and in the follow-up period (P < 0.05). Cognitive functions significantly improved in both groups in the follow-up period when compared with before training, except a corsi task in the ET group were greater in the follow-up period (P < 0.05).

Conclusion: The ET with MI could facilitate better balance abilities. Interestingly, motor learning could be observed in the retention period in both training programs.

Keywords: Balance, cognitive function, exergame training, motor imagery, motor learning.

Balance control refers to the ability to control trunk and head positions and the coordination of movement strategies to stabilize the center of mass without falls. (1) An abundance of studies confirm that exercise could increase balance ability. However, resistance training alone may be a time-efficient compromise for improving balance ability in persons who are unable to perform large volumes or different type of exercise. (2) Previous studies found that exercise can improve balance control, due to an increase in the synergy of sensory systems (3), and an increase in anticipatory balance control mechanisms. (4)

Balance control requires cognitive function for adjust balance to suit different activities. (1) Prior studies revealed that exercise, particularly motor...
trainings like exercise to increase balance control, could increase cognitive ability better than resistance exercise. That is because the increase in balance control relative to cognitive processes relates to an increase in the size of the brain around the hippocampus and gray matter volume.\(^{(5)}\)

Besides the aforementioned exercises, games are also combined to increase balance control and cognitive ability. One specific game is called “exergame-based balance training”, which has been widely used for competency rehabilitation.\(^{(6)}\) Using games with exercise is a feedback mechanism for movement adjustment. This is useful to facilitate neural organization, neural plasticity, and motor learning.\(^{(7)}\) Previous studies reported that exergames could improve balance and movement abilities.\(^{(8, 9)}\) Moreover, exergames could develop cognitive processes \(^{(10)}\) because they might activate motor and visual pathways, and the frontal cortex of the brain, which relates to cognitive functions.\(^{(11, 12)}\)

Another way to activate brain functions is using motor imagery (MI). MI has a similar function system to that of physical movement. The difference is in sensibility of external stimuli, whereas imagining occurs automatically under working memory (WM). A number of studies found that actual movements and MI had similar loci of cortical activation.\(^{(13)}\) Also, previous studies revealed that MI applied with actual movements increased better balance control.\(^{(14)}\)

As mentioned above, it can be seen that exergame-based balance training and MI can increase balance ability. If both are combined, balance ability should increase more when compared to the use of exergames exclusively. Therefore, the objective of this study was to examine the effects of exergames training compared with exergames training with MI on balance, cognitive function, and motor learning. In this study, exergame consisted of motor and cognitive tasks, it may challenge for improving balance and cognitive functions in young adults. The data from this study will be fundamental to the development of training programs to increase balance ability and cognitive function.

Materials and methods

This study has been approved by the Ethics Committee of Naresuan University (NU-IRB P10041/63 and P10045/63). The trial was registered prior to commencement with the Thai Clinical Trials Registry (TCTR20200708002 and TCTR20200709004).

Study design

This study was designed as a pilot study and double blind. Balance, cognitive function and motor learning were monitored before training, after 4 weeks of training and in 2 weeks of the follow-up period. The assessors did not know which training group subjects were assigned to. Trainer was prevented from seeing the subjects’ assessment.

Subjects

Twelve females aged between 20 and 30 years old, were recruited from community-dwelling adults. Based on a previous study \(^{(15)}\), a statistical power of 80.0% and a confidence level of 95.0% were used to determine the sample size. Dropout rate was calculated and an acceptable percentage was set at 50.0% to compensate for losses. Subjects had to be able to perform a single-leg stance with their dominant leg for at least 30 seconds, have no exergame-based balance experience, and have no significant medical history or current problems affecting balance. Subjects with a MI ability score below 20, a habitual physical activity score over 6, or a Mini-mental state examination score below the cut-off score, adjusted for education, were excluded. All subjects could complete exercises as per the scheduled programs.

Experimental procedures

The interventions comprised exergame training for 20 minutes and observed the picture or imagined exergame of 10 minutes. Subjects were randomly assigned to receive either the exergame training (ET, \(n = 6\)) or the exergame with MI training (ET + MI, \(n = 6\)) by blindly drawing a sealed piece of paper. The ET group received the exergame training and looked at pictures, while the ET + MI group was assigned the exergame training and imagined exergame. Subjects were trained 3 days per week for a period of 4 weeks. The schedule of the training program is presented in Table 1.

Exergame training belongs to the Sensamove program (The Netherlands). Nine game modes focused on balance training which required weight shifting left-right and front-back to complete the task. Only one game, known as remember all oysters, was dual task, which required cognitive-motor function to achieve the goal (Figure 1). The progression of each game mode depended on individual performance.
### Table 1. The schedule of exergame-based balance programs with and without motor imagery for each week.

<table>
<thead>
<tr>
<th>Exergame-based balance programs</th>
<th>Time for exergame training (min)</th>
<th>Time for motor imagery training (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Week 1</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multi directional weight shifting</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Curve turtle</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Swim or be eaten</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Catch me if you can</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td><strong>Week 2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multi directional weight shifting</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Money and sharks</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>There is always a bigger fish</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Inside the bubble</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td><strong>Week 3</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multi directional weight shifting with a cognitive component</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Get oysters fast</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Remember all oysters</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td><strong>Week 4</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multi directional weight shifting with a cognitive component</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Watch out for the bubbles</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Get oysters fast</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Remember all oysters</td>
<td>7</td>
<td>4</td>
</tr>
</tbody>
</table>

![Figure 1. Exergame training program.](image-url)
As for the MI training, the same game modes practiced during exergame training were used. Subjects were asked to sit on a chair and put on a blindfold with eyes closed. In the trials, the subjects were asked to imagine rehearsing the shift in their weight left-right and front-back to complete the tasks. They also put a V 800 polar heart rate monitor (Polar Electro Ltd., Finland) on their chest in order to monitor heart rate variability (HRV) throughout the imagined trial. HRV indicates autonomic function, especially sympathetic nervous system is stimulated during imagined movement. Moreover, the subjects were asked to provide a vividness judgment after each game mode in order to give an impression of the strength of their imagined movements. To do so, subjects indicated on a 7-point scale how vividly they felt they had been able to imagine the movement (7 = as vivid as the feel of actual movement and 1 = no image at all). The HRV and vividness were used for monitoring imagined performance.

Outcome measures

Balance ability test

Single-leg stance test (SLT): The subjects were asked to stand barefoot comfortably on their dominant leg, with the other knee was flexed at 90°. The subjects were instructed to cross their arms over their chest throughout the test. The average amount of time of three trials was recorded.

Functional reach test (FRT): The subjects were asked to stand comfortably and perpendicular to a wall. A yardstick, which was horizontally attached to the wall, was applied at the level of the subject’s acromion. The subjects extended their dominant arm along the yardstick. The position of the middle fingertip was recorded before and after a maximal forward reach. The mean score of three successful trials was calculated.

Sensamove balance test

Static balance test: The subjects stood on a balance board and looked at a red point on the monitor. They were asked to keep the red spot in the center of the monitor by standing steady for 120 seconds. Then, the subjects were instructed to remember this feeling in order to conduct the trunk position sense test. The subjects were asked again to stand on the balance board and use their memory of feeling to keep the red spot in the center without visual feedback for 120 seconds. The percentage performance for balancing the red spot in the center was reported.

Dynamic balance test: The Dynamic Balance Test was conducted, separated into two planes of left-right and front-back. The subjects stood on the balance board and were instructed to shift their weight left-right or front-back for 10 seconds each time. During weight shifting, the red spot on the monitor was also moved in the same direction. The subjects had to keep the red spot path in the designated frame. The percentage performance for keeping the red spot path in the frame was reported.

Cognitive function test

A trail making test (TMT) was utilized for evaluating information processing speed. It consisted of two parts, part A and B. In part A, there were 25 numbered circles. The subjects were asked to draw lines to connect the numbers in ascending order. In part B, the circles comprised 13 numbers and 7 letters (A - L). The subjects were asked to draw lines to connect the circles, alternating between the numbers and letters in ascending order. The score for both the TMT, parts A and B, were reported as the number of seconds required to complete the task.

A digit span backwards test (DSBT) was utilized for evaluating working memory. This task evaluated the subjects’ ability to accurately recall an array of digits in reverse order of how they were presented. The DSB task consisted of 7 blocks, with 2 strings of digits per block. For each string, 1 point was scored for a correct response. The total score was presented as the sum of the string scores.

A corsi task (CT) was used for a working memory task. It comprised nine blocks that were shown on screen (Psytoolkit). The subjects were asked to tap the blocks in the same order that the experimenter showed. The test was repeated multiple times which different lengths of blocks. The score was recorded as the sum of correct orders.

A tower of London test (TOLT) was employed to denote planning, utilizing assessments of cognitive flexibility, inhibitory control, and working memory. It consisted of two boards with pegs and several beads with different colors. The assessor used one tower and a set of beads to display the desired goal, and the subjects had to re-arrange a second set of beads on a second tower to match the assessor’s configuration. There were 10 configurations. The scores were presented as the total number of moves and total times.
Statistical analysis

Normal distribution data were presented as mean ± standard deviation. Unpaired student t-test was used for physical characteristics. A two-way mixed (2 × 3) analysis of variance (ANOVA) was used to investigate the differences between groups (ET and ET + MI) and within groups (the period of time testing) for cognitive function data. Post hoc means comparisons were performed using a Bonferroni. Abnormal distribution data were expressed as median and interquartile. Mann-Whitney U test was used for physical characteristics. Balance ability and cognitive function were analyzed using a Friedman test for intra-group effects. Post hoc means comparison was performed using a Wilcoxon signed ranks test. The Mann-Whitney U test was used to analyze the differences between groups. The level of significance was set at \( P < 0.05 \).

Results

Physical characteristics

There was no significant difference between groups in physical characteristics (\( P > 0.05 \)) (Table 2).

Balance ability

Single leg stance test (SLT) and functional reach test (FRT): only the time for the SLT in the ET + MI group significantly increased after training and in the follow-up period (\( P < 0.05 \)).

Static balance test: % performance whilst balancing the red spot significantly increased for both groups, while trunk position sense only in the ET + MI group significantly enhanced after training and in the follow-up period (\( P < 0.05 \)).

Dynamic balance test: the ET + MI group’s % performance of keeping the red spot path in the left-right direction significantly enhanced after training, whereas % performance in follow-up period reduced significantly (\( P < 0.05 \)) (Table 3).

Table 2. Physical characteristics.

<table>
<thead>
<tr>
<th>Physical characteristics</th>
<th>ET (n = 6)</th>
<th>ET + MI (n = 6)</th>
<th>( P )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (kg)</td>
<td>54.5 ± 10.0</td>
<td>51.9 ± 6.3</td>
<td>0.339</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>159.3 ± 8.1</td>
<td>158.1 ± 6.5</td>
<td>0.615</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>21.3 ± 2.1</td>
<td>20.7 ± 1.5</td>
<td>0.403</td>
</tr>
<tr>
<td>Habitual physical activity</td>
<td>7.8 ± 0.6</td>
<td>8.2 ± 1.2</td>
<td>0.073</td>
</tr>
<tr>
<td>MMSE-Thai version</td>
<td>30.0 (29.8, 30.0)</td>
<td>30.0 (29.5, 30.0)</td>
<td>0.902</td>
</tr>
<tr>
<td>MIQ-R-Thai version (Kinesthetic imagery)</td>
<td>23.0 (20.0, 28.0)</td>
<td>23.5 (21.8, 25.0)</td>
<td>0.870</td>
</tr>
<tr>
<td>MIQ-R-Thai version (Visual imagery)</td>
<td>26.5 (23.8, 28.0)</td>
<td>25.0 (20.8, 25.0)</td>
<td>0.080</td>
</tr>
<tr>
<td>Single leg test</td>
<td>30.0 (30.0, 30.0)</td>
<td>30.0 (30.0, 30.0)</td>
<td>1.000</td>
</tr>
<tr>
<td>HRV (LF: HF) during balance training</td>
<td>76.0 : 29.2</td>
<td>71.2 : 28.7</td>
<td>-</td>
</tr>
<tr>
<td>HRV (LF: HF) during looking at pictures</td>
<td>76.3 : 23.4</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>HRV (LF: HF) during imagery</td>
<td>-</td>
<td>60.8 : 39.1</td>
<td>-</td>
</tr>
<tr>
<td>Vividness (during 4 weeks training)</td>
<td>-</td>
<td>6.5 ± 0.4</td>
<td>-</td>
</tr>
</tbody>
</table>

ET, exergame training group; ET + MI, exergame with motor imagery training group;
BMI, body mass index; MMSE-Thai version, mini mental state examination-Thai version;
MIQ-R-Thai version, movement imagery questionnaire-revised-Thai version; HRV, heart rate variability;
LF, low frequency; HF, high frequency.
Cognitive function

**TMT:** the interaction effect did not differ in TMTa and TMTb (P > 0.05). The main effect of the training period on TMTa and TMTb were significantly decreased in both groups in the follow-up period (P < 0.05).

**DSBT:** there was no interaction effect or main effect of the groups for the DSWT (P > 0.05), whereas the main effect of training period was significantly increased in the follow-up period for both groups (P < 0.05).

**CT:** the scores for the CT in the ET group were greater in the follow-up period (P < 0.05) while the ET + MI group’s scores did not change (P > 0.05).

**TOLT:** there was no interaction effect and the main effect of the groups for the TOLT A and B (P > 0.05). The main effect of training period on the TOLT A significantly decreased in the follow-up period (P < 0.05), whereas the TOLT B significantly decreased after training and in the follow-up period for both groups (P < 0.05) (Table 4).

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**Table 3.** Comparison of balance ability between the two groups at before, after 4 weeks of training and 2 weeks of follow-up period.

<table>
<thead>
<tr>
<th>Balance ability test</th>
<th>ET (n = 6)</th>
<th>ET + MI (n = 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>SLT (sec)</td>
<td>74.5</td>
<td>97.3</td>
</tr>
<tr>
<td>(48.1, 103.0)</td>
<td>(60.9, 108.6)</td>
<td>(62.5, 115.7)</td>
</tr>
<tr>
<td>FRT (cm)</td>
<td>34.8</td>
<td>35.9</td>
</tr>
<tr>
<td>(32.8, 36.1)</td>
<td>(33.9, 38.5)</td>
<td>(33.8, 37.6)</td>
</tr>
</tbody>
</table>

**Sensamove balance test**

- **Static balance (% Performance):** ET (90.5, 93.5), ET + MI (92.5, 94.0) (P < 0.05).
- **Trunk position sense (% Performance):** ET (85.0, 90.5), ET + MI (91.0, 94.5) (P < 0.05).
- **Left-Right (% Performance):** ET (100.0, 99.5), ET + MI (94.5, 99.0) (P < 0.05).
- **Front-Back (% Performance):** ET (98.0, 98.1), ET + MI (99.0, 99.0) (P < 0.05).

<sup>a</sup>significant difference when compared with before training period (P < 0.05).
<sup>b</sup>significant difference when compared with after training period (P < 0.05).

SLT, single leg stance test; FRT, functional reach test; ET, exergame training group; ET + MI, exergame with motor imagery training group.

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**Table 4.** Comparison of cognitive function between the two groups before training, after 4 weeks of training and 2 weeks into the follow-up period.

<table>
<thead>
<tr>
<th>Cognitive function</th>
<th>ET (n = 6)</th>
<th>ET + MI (n = 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>Information processing speed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TMTa</td>
<td>33.9 ± 7.8</td>
<td>30.0 ± 7.1</td>
</tr>
<tr>
<td>TMTb</td>
<td>80.4 ± 13.3</td>
<td>69.7 ± 17.7</td>
</tr>
</tbody>
</table>

**Working memory**

- **DSWT:** there was no interaction effect for the DSWT (P > 0.05), whereas the main effect of training period was significantly increased in the follow-up period for both groups (P < 0.05).

**CT:** the scores for the CT in the ET group were greater in the follow-up period (P < 0.05) while the ET + MI group’s scores did not change (P > 0.05).

**TOLT:** there was no interaction effect and the main effect of the groups for the TOLT A and B (P > 0.05). The main effect of training period on the TOLT A significantly decreased in the follow-up period (P < 0.05), whereas the TOLT B significantly decreased after training and in the follow-up period for both groups (P < 0.05) (Table 4).

<sup>a</sup>significant difference when compared with before training period (P < 0.05).
<sup>b</sup>significant difference when compared with after training period (P < 0.05).

TMTa, trail making test part A; TMTb, trail making test part B; DSWT, digit span backward test; CT, corsi task; TOLT A, tower of London part A; TOLT B, tower of London part B; ET, exergame training group; ET + MI, exergame with motor imagery training group.
Discussion

The exergames training and exergames with MI training could increase static balance ability, but the latter program could also increase dynamic balance and trunk position sense. No change of cognitive ability was found from both forms of training. An interesting point found in this study was the emergence of motor learning that occurred in both groups of healthy adults.

Balance ability

Both training program could increase static balance ability. However, the exergames training with MI group could improve in the SLT and trunk position sense after training and stopping training for 2 weeks. They could also increase balance during weight transfer left-right after training.

There are two reasons for improved static balance from exergame training. Firstly, exergames gave internal feedback from proprioception, vestibular, and visual systems. Also, augmented feedback was given by noticing the movements of characters in the games, and examining whether or not subjects moved correctly in order to control positions and control the orientation of the body’s position. Moreover, repetitive muscle contraction and joint movement also increase proprioception and spatial perception, probably leading to improve balance ability. Secondly, this program encouraged the enhancement of motor learning. The effects of training might have changed neural organization, leading to the increase of static balance ability. (21, 22)

Exergames with MI could increase static and dynamic balance, possibly due to MI containing planning processes and movement commands similar to actual movement processes. Previous study supported that MI training could increase the efficiency of movement planning and movement competency. (23) As a result, adding MI training into programs should improve better balance ability. (14, 15) In this study, the utilization of exergames with MI increased static and dynamic balance control. In contrast, only exergames could increase static balance. This might be because exergames with MI could transfer the experience in training from the virtual world to the real world, particularly standing on a narrow balance board. (24)

Other interesting points were: 1) exergames with MI could increase trunk position sense; and 2) the enhancement of motor learning. It is possible that the first point occurred because MI was trained without sensing the external environment, and by using automatic sensing under WM. The central nervous system and specific motor nervous system were motivated for movements from particular MI. (25)

In this study, the subjects were instructed to imagine and feel the positions of their joints and movements during exergames. This might have reduced their dependence on the visual system, activating proprioception functions instead to help balance control, and consequently leading to improved trunk position sense. (14, 15)

The second point of an enhancement in motor learning arose from training in both programs, but exergames with MI generated better motor learning than only exergames. This can be seen from the balance ability after stopping training for 2 weeks, whereby such ability still increased when compared with the pre-training phase. This phenomenon was called a retention effect, implying motor learning might occur from repetition of training, and thus motivated brain organization and plasticity. (26) It was proved that MI training could also increase efficiency of movement planning and generate brain plasticity like physical training. (27) Therefore, physical training with MI could promote better motor learning than physical training alone.

Cognitive ability

Although the results found that both training program did not affect cognitive functions differently after training, a retention effect was found from both training forms after stopping training for 2 weeks.

Prior studies supported that balance training could increase cognitive functions. (28) This might be because the vestibular system, part of sensory system for balance control, connected to different parts of brain (e.g., cerebellum, hippocampus, prefrontal and parietal cortices, is where cognitive processes are functioning) (29) Furthermore, research supporting that balance training affected an increase in volumes of the hippocampus. (5) However, this finding could not increase cognitive functions after 4-weeks, despite dual tasks between cognitive-motor task being added. This might be due to differences in age, training programs, and training duration. This study included healthy young adults, and cognitive tasks used might have been very simple for the subjects in this age range, or the training duration might have been very little resulting in simple training programs. Therefore, future studies should increase the difficulty of cognitive tasks and training duration should also be increased.
A previous study by Moriya M, Sakatani K. who explored the immediate effects of imagined time up and go (TUG) on cognitive function. The results found a significant increase in WM after imagined TUG. In contrast, this study found that exergames with MI did not affect cognitive change after training. The different results might again be due to training programs that were very simple for the studied age range. Also, MI training duration might have been limited. The systematic literature review revealed that 15 minutes was a suitable MI duration, but this study chose to adopt 10 minutes for MI training. Therefore, future studies should increase MI duration, along with measurement of anatomical brain changes.

Although there was no change of cognitive ability after training, after stopping training for 2 weeks from exergames, and exergames with MI, a retention effect showed in all aspects. This implied better planning and problem-solving ability, possibly because of increasing the data storage ability of the memory system. This study designed memory training into the exergames program, which probably affected the data storage system that could finally lead to an increase in cognitive functions. This study implied that despite early adulthood, if continuously trained with dual tasks, retention effect could occur and finally lead to motor learning. This was because continuous dual task training reduced attentional load, increased memory, and increased information processing speed.

The limitations of this research are as follows: 1) the number of subjects was relatively small despite significant differences. Therefore, it was challenging for generalization; 2) There was no control group; and 3) The subjects were in early adulthood, with good health and no balance problems. Therefore, the benefits of both programs in older adults or those with problems of movements are still unclear. Future studies should include more subjects, control group and more diverse groups of subjects. Furthermore, more challenging programs should be designed to suit samples, along with increasing duration of MI. Long-term effects of training and follow-up should be further studied.

Conclusion

The exergame training with MI could facilitate better balance abilities when compared with the exergame training. Although, the effect of short-term training from the both training programs on cognitive functions did not significantly change, continuous motor learning could be observed in the retention period of balance abilities and cognitive functions, which describe the effectiveness of the both training programs.

Acknowledgements

The authors would like to acknowledge all subjects who took part in this study. Also, we would like to thank the Allied Health Science Faculty, Naresuan University for supporting this research.

Conflicts of interest statement

The authors have each completed an ICMJE disclosure form. None of the authors declare any potential or actual relationship, activity, or interest related to the content of this article.

Data sharing statement

The present review is based on the references cited. Further details, opinions, and interpretation are available from the corresponding authors on reasonable request.

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